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Plenary Sessions

Saturday, July 01 2023
Congress Opening Session

PLEN01_1

Opening Lecture: Towards a cell biology of Alzheimer's disease

T. Südhof
Department of Molecular & Cellular Physiology, Stanford University School of Medicine, Standford, USA

Sunday, July 02 2023
Presidential Symposium

PLEN02_1

Moritz Romberg Lecture: The continuous circle of translation

M.M. Reilly
Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, London, UK

There has been a revolution in the understanding of the causes and more recently in the development of treatments for inherited neurological diseases like the inherited neuropathies over the last few decades. The circle of translation starts and ends with the patient and involves in depth phenotyping of patients, gene identification, elucidation of the underlying pathogenetic mechanism, candidate therapy development, clinical trials and finally delivery of an efficacious therapy to the patient. For some forms of inherited neuropathy such as TTR amyloidosis there has been progress in each step but for many forms including Charcot Marie Tooth disease the circle is incomplete with many causative genes having been identified, multiple pre-clinical and a few clinical trials ongoing but no therapies yet available for patients. Each step of the translation cycle including when efficacious therapies are in clinical use raises further questions, opportunities, and challenges. Humans are complex and disease phenotypes are varied. The circle of translation not only delivers therapies but offers a continuous opportunity to further understand this group of diseases enabling better more personalised therapy development for patients.

Disclosure: M M Reilly has served on a steering committee for Eidos Therapeutics, and consulted for Akcea, Alnylam, Applied Therapeutics, Augustine Therapeutics and Inflectis.

PLEN02_2

Charles Edouard Brown-Sequard lecture: Experimental medicine and functional neurological disorders

M. Hallett
National Institute of Neurological Disorders and Stroke, NIH, Bethesda, USA

Functional Neurological Disorders are defined as being involuntary in nature. This is often disputed amidst confusion with malingering and factitious disorders. However, it has been difficult to prove that they are involuntary. Studies of human physiology have revealed underlying brain mechanisms related to the sense of self-agency, that is, the sense that a person is the agent of the movement that they made. Information from this physiology can be applied to understand the pathological condition. In this way, we follow in the footsteps of Brown-Séquard who was an advocate for Experimental Medicine, the study of Physiology and its translation to Pathology. The physiology of agency can be studied with functional magnetic resonance imaging (fMRI). In one such experiment, subjects made movements that were manipulated to vary the sense of agency. The subjective sense of agency was correlated with the fMRI signal, revealing a brain network with a major role of the right temporoparietal junction. We identified a cohort of patients with functional tremor who could voluntarily mimic their tremor. The tremors in the two situations looked the same, but the sense of voluntariness was different. With fMRI the major difference between the two was activation of the right temporoparietal junction. In the light of the physiology, there is an abnormality in the sense of self-agency that would lead to movements to be interpreted as involuntary. Thus, FND differs from malingering and factitious disorders.

Disclosure: Nothing to disclose.

PLEN02_3

Camillo Golgi Lecture: Autoimmune synaptic diseases: The basics and the latest

J. Dalmau
ICREA, IDIBAPS-Hospital Clinic, University of Barcelona, Barcelona, Spain; University of Pennsylvania, Philadelphia, USA

For many years investigators wondered why there were almost no disorders of the central nervous system mediated by autoantibodies, equivalent to the paradigm of myasthenia gravis. This concept changed about 20 years ago with three studies demonstrating antibodies against: VGKC in patients with Morvan syndrome or limbic encephalitis; AQP4 in patients with neuromyelitis optica, and the NMDA-receptor in patients with a novel neuropsychiatric disease. Some of these findings were initially met with hesitation but the number of published cases grew and further investigations led to the identification of close to 20 autoimmune encephalitides (AE) associated to antibodies against neuronal or glial surface receptors, ion channels, or other proteins. Admittedly, this category of diseases has changed the landscape of neurology and psychiatry showing that syndromes manifesting with memory impairment, psychosis, seizures, movement disorders or sleep dysfunction, often previously considered idiopathic, are immune-mediated. We have learned about predisposing factors (tumors, viruses, HLA) and that while some AE have an age preference, people of all ages can be affected. In all these diseases the antibodies alter the function of the antigens causing impairment of neurotransmission, synaptic plasticity, or imbalance of neuronal networks. There are now in vitro and animal models of passive transfer of patients' IgG, CSF, or monoclonal antibodies, and models of active immunization that provide new insights into the immunopathogenesis. Even though most AE respond to treatment, improvement is usually slow or incomplete, and current efforts are aimed to improve our understanding of the recovery process and develop better therapies.

Disclosure: Dra Dalmau receives royalties from Athena Diagnostics and Euroimmun for the use of several autoantigens as diagnostic tests. He has received research grants from SAGE Therapeutics and Euroimmun.

PLEN02_4

Brain Prize Lecture: Circuits for body movements

S. Arber
Biozentrum and Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

Abstract Movement is the behavioral output of the nervous system. This lecture will focus on recent work elucidating the organization and function of neuronal circuits central to the regulation of distinct forms of body movements, including locomotion and skilled forelimb movements. It will show that dedicated circuit modules in different regions of the brainstem and their interactions within the motor system play key roles in the generation of diverse actions.

Disclosure: This project is supported by ERC Advanced Grants, the Swiss National Science Foundation, the Kanton Basel-Stadt, the Novartis Research Foundation and the Louis Jeantet Prize for Medicine.

Saturday, July 03 2023
Using data science to transition to an era of precision health

PLEN03_1
What is the difference between personalized medicine and precision medicine?

N.W. Wood
Department of Molecular Neuroscience, National Hospital for Neurology and Neurosurgery, Queen Square, UK

PLEN03_2
Data driven care for patients with neurodegenerative disorders

G. Waldemar
Department of Neurology, Copenhagen University Hospital - Rigshospotalet, Copenhagen, Denmark

PLEN03_3
Multi-modal data approaches to predict clinical outcomes after stroke

C. Cordonnier
Department of Neurology, Hôpital Roger Salengro CHU, Lille, France

PLEN03_4
Developing and implementing decision support systems for the diagnosis and treatment of rare neurological disorders?

M.J. Molnar
Semmelweis University Institute of Genomic Medicine and Rare Disorders, Budapest, Hungary

Technological advances in digitalisation open the door to data driven precision medicine. We can witness, how artificial intelligence (AI) based tools are transforming healthcare. Early predictions, faster and more accurate diagnosis, personalized treatment plans, new AI based therapeutic, effective monitoring through digital biomarkers can offer a higher quality patient care. Good quality, accurate, complete and unbiased data seems to be one of the most important demand which can be collected by both physicians and AI itself. The black box of AI-boosted medicine is expected to be transparent with privacy-preserving guarantees and explainability to achieve trust in case of any kind of real-life application. However, there are some concerns about the lack of transparency and interpretability¸ the potential for bias in AI algorithms; and ethical considerations about data privacy/security, and disruption the doctor-patient relationship. Despite these challenges, the evolving relationship between humans and AI is promising in rare disease management. However, it is important to note that AI tools are currently considered as aids to clinical decision-making rather than replacements for human healthcare providers. They should be used in conjunction with a healthcare professional's expertise and judgment.

Disclosure: Nothing to disclose.

Tuesday, July 04 2023
Highlights and breaking news

PLEN04_6

Skin amyloid deposits and nerve fiber loss as markers of neuropathy onset and progression in hereditary transthyretin amyloidosis

L. Leonardi
Department of Neuroscience, Mental Health and Sensory Organs, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy

Background and purpose: This study was undertaken to assess skin biopsy as a marker of disease onset and severity in hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN), a treatable disease.
Methods: In this single center retrospective study, skin Congo red staining and intraepidermal nerve fiber density (IENFD) were evaluated in symptomatic ATTRv-PN patients and asymptomatic TTR gene mutation carriers between 2012 and 2019. Non-ATTRv subjects with suspected small fiber neuropathy who underwent skin biopsy during the same timespan were used as controls.
Results: One hundred eighty-three symptomatic ATTRv-PN patients, 36 asymptomatic carriers, and 537 non-ATTRv patients were included. Skin biopsy demonstrated amyloid depositions in 80% of the 183 symptomatic cases. Skin amyloid deposits were found in 75% of early stage ATTRv-PN patients, and in 14% of asymptomatic carriers. All 183 symptomatic and 34 of 36 asymptomatic patients displayed decreased ankle IENFD with a proximal-distal gradient distribution, and reduced IEFND correlated with disease severity and duration.
Conclusions: Our study demonstrates skin amyloid deposits are a marker of ATTRv-PN disease onset, and decreased IENFD a marker of disease progression. These results are of major importance for the early identification of ATTRv-PN patients in need of disease-modifying treatments.
Disclosure: Dr. Luca Leonardi received travel and speech grant for several national and international meetings from Alnylam Pharmaceuticals and SOBI.

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Symposia

Saturday, 01 July 2023

EAN/MDS-ES: New technologies & movement disorders: Towards a novel care paradigm

SYMP01_1

Wearable sensors in movement disorders

A. Sanchez Ferro
Department of Neurology, Hospital Universitario 12 de Octubre, Madrid, Spain

Wearable sensors are disrupting the way we understand medicine, neurology and movement disorders. Progressively, these tools are leveraging their potential to extract important features of movement disorders and aid in the management of different conditions, especially Parkinson's disease. This disruption will have a dramatic impact on the evaluation of our patients transitioning from a hospital-centric management to an almost 24/7 monitoring in an everyday life setting. We will review in this talk the main concepts related to this thrilling field as well as the main applications in current care as of to date with some practical examples.
Disclosure: Nothing to disclose.

SYMP01_2

Machine learning and artificial intelligence techniques in movement disorders

U. Gschwandtner
Department of Psychiatry, Universitätsklinik Basel, Basel, Switzerland

SYMP01_3

New neurophysiological biomarkers in dystonia and Parkinson's disease

R. Lofredi
Klinik für Neurologie und Experimentelle Neurologie, Charité Universitätsmedizin Berlin, Berlin, Germany

Deep brain stimulation (DBS) is an effective treatment option for movement disorders such as Parkinson's disease, dystonia and essential tremor syndromes. Recordings via DBS-electrodes have provided the unique opportunity to record brain activity from DBS-target nuclei within the basal ganglia that are otherwise not accessible due to their small size and location deep in the brain. Thereby, symptom-specific patterns in oscillatory brain activity of basal ganglia nuclei could be identified that is modulated by medication and DBS along with symptom alleviation. These patterns have been categorized as "neurophysiological biomarkers" and are currently tested as real-time feedback signal for demand-adapted DBS-paradigms by novel, sensing-enabled DBS-devices in international, clinical trials. In this talk, I will present the variety of neurophysiological biomarkers for symptom severity in movement disorders, current findings on their potential as feedback signal for DBS as well as an outlook for future technological development that will further help improving DBS-treatment for patients with movement disorders.
Disclosure: Nothing to disclose.

SYMP01_4

EAN/MDS-ES: New technologies in neuromodulation

A. Priori
Polo Universitario Ospedale San Paolo, Department of Health Sciences, University of Milan, Milan, Italy

EAN/EPNS: Neurology beyond big data – from multi-“omics” to bedside

SYMP02_1

Primer on proteomics

B. Tijms
Alzheimer Center Amsterdam, Neurology, Vrije Universiteit Amsterdam, Amsterdam UMC location VUmc, Amsterdam, the Netherlands

Alzheimer’s disease is the most common cause of dementia, and there are no cures available yet. One reason for this is that the brain is notoriously hard to access in patients. This makes it difficult to determine the precise underlying causes that are needed for an accurate diagnosis. Technical advances now make it possible to gain access to the brain through highly detailed proteomic techniques. These proteomic techniques hold great promise to discover novel mechanisms causing Alzheimer’s disease, or other disorders. Such information is key to refine diagnoses, which is ultimately necessary for personalised treatments. In this primer, I will show how proteomics in cerebrospinal fluid can be used to understand differences between patients in their underlying pathophysiological mechanisms, taking Alzheimer’s disease as an example. I will demonstrate how such insights can be used to develop new diagnostics and inform development of personalised treatments. In this primer, I will demonstrate how proteomics in cerebrospinal fluid can be used to understand differences between patients in their underlying pathophysiological mechanisms, taking Alzheimer’s disease as an example. I will explain how such insights can be used to improve diagnostics and inform development of personalised treatments.

Disclosure: Dr. Tijms is co-inventor on a patent on biological subtypes in Alzheimer’s disease (EU#20175497.2; US#17599316; owner Stichting VUmc).

SYMP02_2

Microbiota – linking the gut and the brain

C. Pot
Department of Neurology, Centre Hospitalier Universitaire Vaudoise, Lausanne, Switzerland

SYMP02_3

Studying large scale networks of the brain: Lessons from 10 years ENIGMA

P. Thompson
Keck School of Medicine - USC, Los Angeles, USA

SYMP02_4

“Omics” informed therapeutic strategies in neuro-muscular disorders

A. Roos
Department of Pediatric Neurology, University Medicine Essen, Essen, Germany

Clearing the brain at night: Glymphatics, sleep and neurodegeneration

SYMP03_1

Introduction to the human glymphatic system

N. Beschorner
Center for Translational Neuromedicine, University of Copenhagen, Copenhagen, Denmark

Traditionally, the role of cerebrospinal fluid has been perceived as suspending and cushioning the brain. With the description of the glymphatic system in 2012, a new concept of fluid exchange and solute clearance in the brain emerged, which offers new explanatory approaches with regard to neurological diseases. The glymphatic system is a brain-wide influx and efflux system formed by perivascular spaces around arteries and veins that are continuous with the subarachnoid space and act as pathways for CSF flow deep into the brain parenchyma. Astrocytes tightly enclose the PVS and create a barrier that allows CSF influx facilitated by aquaporin 4 water channels. Once in the extracellular space, the constant convective flow enables an interchange between CSF and interstitial fluid that contains potentially harmful waste products. These solutes are ultimately removed from the brain parenchyma via perivenous spaces. The discovery of the glymphatic system gave rise to a plethora of innovative in vivo experimental approaches to study fluid flow within the brain. Current knowledge comes primarily from studies with rodents and although recent advances in MR imaging have provided support for the existence of the glymphatic system in humans, translation is limited by the invasiveness of the methods available to study glymphatic flow. This presentation will focus on the transfer of experimental results in rodents to pigs, an intermediate species with a brain architecture more closely related to humans. Ultimately, we will draw conclusions about the extent to which experimental approaches from mice and pigs can be transferred to humans.

Disclosure: The author(s) declared no potential conflicts of interest.

SYMP03_2

Experimental imaging techniques to visualize the glymphatic system

L. Hirschler
Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands

The increasing interest in brain waste clearance has led to great insights into the way cerebrospinal fluid (CSF) acts as a lymphatic-like system. Current knowledge on CSF-mediated brain clearance mechanisms (glymphatics) is mostly based on invasive experimental studies performed in rodents using microscopy, which is a technique that cannot be applied in humans. MRI, however, is an excellent candidate to provide information on brain clearance dynamics in humans as CSF, the waste carrier, has different magnetic properties compared to blood and tissue. This talk will give an overview of different techniques to assess the human glymphatic system using MRI, from established invasive methods to new, fully non-invasive strategies. The current golden standard technique to assess CSF-mediated brain clearance in humans relies on the intrathecal injection of a contrast agent. It is widely considered as a break-through technology that provided the first insight into the human brain clearance system. A less invasive technique was proposed using intravenous contrast agent injections combined with delayed heavily T2-weighted imaging. In that way, clearance can be assessed more patient-friendly, albeit also in a less sensitive and standardized manner. In order to probe CSF-mediated brain clearance mechanisms in healthy subjects, in larger patient cohorts or in longitudinal follow-up studies, non-invasive strategies are emerging. These techniques probe various viewpoints and driving forces of the brain clearance system: from the entry/exit points of CSF, down to CSF motion in the subarachnoid and perivascular spaces. Applications of these approaches in healthy subjects, sleep and patients will be shown.

Disclosure: Nothing to disclose.

SYMP03_3

Improving brain clearance in neurological disorders

D. Arnaldi
DINOGMI, University of Genoa; IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Glymphatic system dysfunctions have been shown in animal models of neurological disorders, including Alzheimer's disease (AD), stroke, and traumatic brain injury. Recently, growing literature data are showing direct and indirect evidence that the glymphatic system may be impaired in humans affected by such neurological disorders. For example, clinical studies have shown that cerebrospinal fluid clearance is reduced in patients suffering from AD or idiopathic normal pressure hydrocephalus. Brain imaging techniques allow in vivo evaluation of the glymphatic system in humans, but they are minimally invasive, requiring intrathecal administration of contrast agents. Thus, few studies have been done and only in patients with clinical indication for the procedure. However, there are indirect evidence suggesting a role of the glymphatic system in the pathogenesis on several neurological disorders. For example, both beta-Amyloid and Tau levels are modulated by sleep deprivation in humans, indirectly suggesting a relationship between the clearance of such peptides, through the glymphatic system, and sleep alterations. In summary, several animal studies have demonstrated a crucial role of the glymphatic system for the brain homeostasis. Growing literature data are confirming these results also in humans, giving rise to new diagnostic, prognostic, and even therapeutic opportunities.
Disclosure: Nothing to disclose.

SYMP03_4

Sleep and brain clearance

R. Fronczek
Leiden University Medical Centre, Department of Neurology, The Netherlands

Unlike other organs and despite its high metabolic rate, the brain does not have a classic lymphatic system. The knowledge on how the brain cleans itself is scarce. During the last years, the glymphatic pathway has revealed itself to do this using cerebrospinal fluid (CSF) as the main carrier of waste products along perivascular pathways outside the blood-brain-barrier. Interestingly, it was discovered through animal and a few small human studies that this clearance system is mainly active during sleep. A breakdown of brain clearance is a potential root cause of protein accumulation in neurodegenerative disorders such as Alzheimer's Disease. Understanding how sleep affects the CSF-flow in brain clearance would thus provide crucial new avenues not only to elucidate brain clearance in general and the pathophysiology of protein accumulation diseases, but also hopefully result in sleep-modulating therapies that can slow down or perhaps even stop disease progression in the future. Dr. Fronczek will highlight the role of sleep in glymphatic functioning. He will also dive deeper in the tantalizing question how modifying sleep could improve brain clearance.
Disclosure: Nothing to disclose.

Emerging and re-emerging neuro-infections – old and new „friends“, even for the neurologist

SYMP04_1

Acute bacterial meningitis in Europe, the challenge by drug-resistance and vaccine evading serotypes

E. Schmutzhard
Department of Neurology, Medizinische Universität Innsbruck, Universitätsklinik für Neurologie, Innsbruck, Austria

SYMP04_2

Resistant mycobacteria may also cause Neuro-Tuberculosis

M. Klein
Department of Neurology, LMU Klinikum, Munich, Germany

SYMP04_3

Emerging and re-emerging vaccine-preventable neuro-infections

L. Papetti
Neurodevelopmental Unit, Bambino Gesù Children Hospital, IRCCS, Rome, Italy

Vaccine-preventable neuroinfections include a spectrum of conditions that in addition to being associated with high mortality and comorbidity in the acute phase are also associated with a high risk of short- and long-term neurological disorders. Although these diseases have a vaccine available that can prevent them, epidemics are being observed in several European countries which represent alarm bells for gaps in vaccination programmes. Measle is one of the most contagious diseases and requires maintaining high immunity of the population to prevent epidemics. It can cause encephalitis both in the acute phase of the disease and many years after the primary infection as seen in subacute sclerosing panencephalitis (SSPE). Vaccine hesitancy not only puts the individual at risk but impacts the community. Just think of congenital rubella syndrome (CRS), which has long-term health consequences, and it continues to be reported. We also have successful examples of how vaccine coverage has managed to control many neuroinfections such as neonatal tetanus or polio in much of Europe. The neurological complications of the aforementioned infections often present neurologists and pediatricians with diagnostic and therapeutic challenges. There are supportive therapies for these conditions that often have the effect of slowing down the progression of the disease, for example in SSPE, but to date the only effective treatment strategy is prevention with vaccines. Pediatricians and neurologists are called to know how to recognize these conditions in order to be able to adopt possible therapeutic strategies early.
Disclosure: Nothing to disclose.

SYMP04_4

Climate change and cascading risks from infectious disease(s), projection and adaptation

J. Semenza
European Center for Disease Prevention and Control, Stockholm, Sweden

Diagnosis and treatment of rare causes of cerebrovascular disorders: Practical guidance

SYMP05_1

Heritable small vessel diseases: European registries and data sharing

A. Bersano
Cerebrovascular Unit Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

SYMP05_2

Genetics of stroke: Big data

S. Debette
Population Health Research Center, University Hospital of Bordeaux, Bordeaux, France

SYMP05_3

Diagnosis and treatment of rare causes of cerebrovascular disorders: practical guidance

L. Caputi
Neurology and Stroke Unit, Department of Cardiocerebrovascular diseases, Maggiore Hospital, ASST Crema, Cremona, Italy

Primary Angiitis of the Central Nervous System (PACNS) is a rare form of idiopathic CNS vasculitis with an estimated incidence of 2.4 cases per 1,000,000 person/year. Few data are available regarding the pathogenesis since the immunological mechanisms are not definite and the potential triggers of the inflammatory process remain unknown. A definite diagnosis is obtained by the analysis of a tissue biopsy specimen whose specific requirement is the presence of a vasculocentric transmural inflammation with damage to the vascular wall. Granulomatous, lymphocytic and necrotizing histopathological patterns of PACNS are described. A probable diagnosis implies the finding of a profile consistent with PACNS, based mostly on abnormalities on angiogram, MRI and CSF, in the absence of tissue confirmation. CSF abnormalities are present in approximately 80–90% of cases. Neuroimaging is often abnormal, including cortical and sub-cortical infarctions, intracranial hemorrhages, leptomeningeal and parenchymal enhancement, tumor-like lesions, and very rarely, a diffuse leukoencephalopathy. Alternating areas of stenosis, ectasia, or both in more than one vascular bed are observed in case of intracranial arterial involvement. The diagnosis of PACNS is unlikely if MRI is normal. Clinical manifestations are non-specific and serological markers of inflammation are usually normal. Acute ischemic stroke and transient ischemic attack occur in >50% of patients, whereas brain hemorrhage in about 10-20%. Spinal cord involvement is in about 5% of patients, rarely in the absence of brain abnormalities. Promising non-invasive diagnostic techniques include the Vessel wall MRI imaging (VWI) whose most commonly described hallmark is a concentric vessel wall enhancement (VWE) located at the intracranial stenosis. Although VWE is not specific for PACNS, the addition of VWI seems to increase the accuracy of MR-angiography beyond 90%. Nowadays, treatment for PACNS is derived from therapeutic strategies used in other vasculitides and from the largest retrospective American and French studies on PACNS itself. No specific guidelines are available at the moment. Induction therapy rules in oral and/or ev steroids, followed, mostly, by oral and /or ev cyclophosphamide for 6 months. Maintenance therapy is based on low-dose steroids with mycophenolate mofetil (MMF) or azathioprine (AZA) whose duration differ from centers. Interestingly, rituximab therapy may be an effective and safe option in patients with PACNS refractory to conventional immunodepressants. Its role as a first line therapy is debated. Moreover, low-risk immunosuppressant such as AZA or MMF might be considered from the beginning in those PACNS patients with a potential good neurological outcome. Induction and maintenance therapy with an immunosuppressant would allow a long-term remission in 80-95% of patients without significant disability in three-fourths of them. Since the clinical and neuroradiological relapses were observed in 30-50% of subjects with an increasing risk of progressive neurological deterioration with severe disability, it is absolute necessary to be strictly adherent to the diagnostic process and to the therapeutic options. Artificial intelligence (AI) has been a key area of technologic innovation over the past decade and has the aim “to let the computer do those things human minds do”. Key application for AI in neurology imply its use in diagnosis, prognosis and treatment. The medical community refers to those advanced techniques related to AI as machine learning and natural language processing. Machine learning can be thought of as pattern recognition and works with algorithms that allow computers to learn from examples without being explicitly programmed. Natural language processing involves the comprehension and production of language. Within machine learning, “deep learning”, biologically inspired to neural networks not requiring predetermined inputs, involves artificial neural networks and appears to be the most productive. Recently, “deep learning approach” for an automated classification of multiple sclerosis and its mimics, including primary and secondary CNS vasculitis, was used, and compared to that of expert neuroradiologists. The overall performance of the automated method reached the highest accuracy in multiple sclerosis whereas intermediate-lower values in vasculitis, migraine and neuromyelitis optica spectrum disorders. These data, together with the increasing reports on AI and neurological disorders, would confirm the potential help of AI in a neurological work-up, mostly in those conditions, as PACNS, where the diagnosis might be extremely difficult, time-consuming and delaying the treatments thus pointing at risk the patients.

Disclosure: Nothing to disclose.

SYMP05_4

Diagnosis and management of not heritable rare cerebrovascular disorders

A. Arsovska
University Clinic of Neurology, University "Ss. Cyril and Methodius"-Medical Faculty, Skopje, Republic of North Macedonia

Cerebrovascular disorders remain major cause of death and disability worldwide. Most of them are caused by conventional vascular risk factors, such as hypertension, diabetes, atrial fibrillation, hyperlipidemia and smoking. In up to 30% of the cases, despite intensive investigations, the etiology of cerebrovascular disorders remains undetermined. Non-heritable rare cerebrovascular disorders are primary angiitis of the central nervous system (PACNS), Sneddon's syndrome and Divry–van Bogaert syndrome, Reversible cerebral vasoconstriction syndrome (RCVS), Susac syndrome, Takotsubo syndrome (TTS) and Moyamoya angiopathy (MA). The diagnosis and management of rare cerebrovascular disorders is a challenging process.

Disclosure: Nothing to disclose.

Tuesday, July 04 2023

EAN/ERN-EpiCARE: Personalized medicine for the diagnosis and care of patients with complex epilepsy syndromes

SYMP06_1

Personalized medicine in rare epilepsies: Pitfalls and successes

K. Klotz
Department of Neuropediatrics and Muscle Disorders, Center for Pediatrics, Medical Center- University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg,Germany

Personalized medicine is an emerging approach to healthcare that aims to tailor medical treatments to individual patients based on their unique genetic, environmental and clinical characteristics. Targeted therapy as a specific form of personalized treatment is an approach to develop therapies tailored to the specific molecular and cellular mechanism involved in the pathophysiology of diseases. This approach has shown great promise in the treatment of rare epilepsies, which are often caused by genetic mutations and are difficult to manage with conventional therapies. However, the implementation of personalized medicine and targeted therapies in rare epilepsies also poses significant challenges and potential pitfalls. Looking and some examples of personalized therapy approaches that have been explored for the treatment of rare epilepsies, we will discuss the difficulties and pitfalls along the way of treatment development: from gaining knowledge about molecular mechanisms, translating this knowledge into effective therapies, to high costs and limited availability. We will also discuss example of well-implemented precision therapy in rare epilepsies and what is needed in future to further develop precision therapy for rare epilepsies

Disclosure: I have received honoraria for lectures and travel expenses from Jazz, EISAI, Desitin and Zogenix. There are no conflicts of interest related to this talk.

SYMP06_2

Clinical trials in rare epilepsies: How to tackle the challenges?

K. Braun
Department of Neurology & Neurosurgery, University Medical Center Utrecht, Utrecht, the Netherlands

SYMP06_3

Multidisciplinary approaches for the management and personalized care of rare epilepsies

S. Balestrini
Department of Neuroscience, Meyer Children's Hospital, Firenze, Italy

SYMP06_4

Personalized treatment in rare epilepsies: What do we have and what is on the horizon?

G. Rubboli
Department of Neurology, Epilepsy Hospital Filadelfia, Dianalund, Denmark

EAN/ISNI: Immunosenescence and multiple sclerosis – relevance to immunopathogenesis and treatment

SYMP07_1

Immunosenescence and neuroimmunology

T. Berger
Department of Neurology, Medical University Vienna, Vienna, Austria

SYMP07_2

Immunosenescence and multiple sclerosis treatment

M. Adamczyk-Sowa
Department of Neurology, Independent Public Clinical Hospital Zabrze, Zabrze, Poland

SYMP07_4

Immunosenescence and comorbidity in multiple sclerosis patients

M. Nowak-Kiczmer
Department of Neurology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Poland

Immunosenescence and comorbidity in multiple sclerosis patients Immunosenescence is a phenomenon of changes in the immune system associated with ageing. To the characteristic features of this process belong: decline in immune response, chronic inflammation and an increased risk of autoimmune diseases. Increased risk for morbidity and mortality related to age is caused by chronic inflammatory process with persistent production of proinflammatory mediators, which is called ‘inflamm-ageing’. Although multiple sclerosis has typically onset in young adults, immunosenescence has influence on its course. The patients with multiple sclerosis are found to present with some features of immunosenescence at younger age than healthy controls. What’s more, comorbidities are found in these patients more common than expected. Immunosenescence has also impact on the safety and effectiveness of disease modyfing therapies. The role of immunosenescence in multiple sclerosis is complex and requires further investigation.
Disclosure: Nothing to disclose.

Neurodiversity in brain organization: Theoretical and clinical implications

SYMP08_1

Individual variability in functional brain organization

E. Karlsson
Department of Experimental Psychology, Ghent University, Ghent, Belgium

SYMP08_2

Natural variability in asymmetrical brain organization: clinical considerations

R. Gerrits
Department of Experimental Psychology, Ghent University, Gent, Belgium

The functional division between the hemispheres is a key organizational principle of the human brain. Although commonly assumed to follow a stereotypical pattern, in which the left hemisphere is dominant for speech and praxis, and the right hemisphere is dominant for spatial attention and recognizing faces, it has become increasingly apparent there is in fact much individual variability in hemispheric segregation. This natural variability poses some important considerations for clinical practice, which is the topic of my talk. One example is the therapeutic use of transcranial magnetic stimulation (TMS), which is well established for treating psychiatric conditions and is increasingly applied to treat neurological disorders. Many TMS treatment protocols are lateralized, in the sense that they target a region in a specific hemisphere or aim to upregulate one hemisphere, while suppressing the other side. These protocols should in principle take into account the patients' individual brain asymmetry for the underlying function that is targeted.
Disclosure: Nothing to disclose.

SYMP08_3

The role of laterality in neurological diseases: Recent advances and implications for clinical practice

A. Mundorf
Institute for Systems Medicine and Department of Human Medicine, MSH Medical School Hamburg, Hamburg, Germany

Hemispheric asymmetries in brain structure are found in over 90% of cortical and subcortical regions, and functional lateralization is known on many levels. These asymmetries are necessary for improved multi-tasking capabilities and action control. Atypical hemispheric asymmetries and resulting atypical behavioral asymmetries are also present in patients suffering from neurological diseases, such as Parkinson's disease, Alzheimer's disease, or multiple sclerosis. For example, in Parkinson's disease, lateralization of lesion onset is a known clinical feature with patients showing asymmetrical motor symptoms and unilateral symptom onset. This lesion laterality associated with symptoms is also reflected in the brain. Similarly, amyotrophic lateral sclerosis and multiple sclerosis often include the onset of limb weakness or numbness on only one side of the body. For Alzheimer's disease, asymmetric neurodegeneration and possible vulnerability of the left hemisphere are found. It is hypothesized that specific inherent differences may set up one hemisphere to be vulnerable to disease pathogenesis. In this talk, I will provide an overview of the current knowledge from clinical studies and animal models including an outlook for potentially underlying mechanisms. The study of hemispheric asymmetries allows us to further unravel disorder-specific neuronal implications and may unlock new therapeutic options.
Disclosure: Nothing to disclose.

SYMP08_4

Amygdala asymmetries in clinical and non-clinical populations: From structure to function

S. Ocklenburg
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The amygdala is a core structure in the neuronal network underlying emotion processing and is frequently investigated in patient cohorts. Across different clinical and nonclinical studies regarding the amygdala, one often-encountered finding is that the left and the right amygdala are not equivalent in terms of function and structure. Importantly, alterations in these asymmetries between the right and left amygdala are found in several neurodevelopmental, psychiatric, and neurological disorders. While the data is sometimes heterogenous, an important factor is to also assess hemispheric asymmetries in specific amygdala subnuclei. Knowing these specific hemispheric differences enables researchers to improve their study design and to clearly disentangle alterations found in patients. Thus, the study of hemispheric asymmetries in the amygdala allows to further unravel disorder-specific neuronal implications and can help advance treatment options. In the talk, I will provide an integrated overview of existing basic and clinical findings regarding amygdala asymmetries in structure, connections, and functions.

Disclosure: Nothing to disclose.

Focused Workshops

Saturday, July 01 2023
Dementia prevention and brain health

FW01_1
Dementia risk profiling and communication in persons with no cognitive impairment

G.B. Frisoni
Department of Psychiatry, Geneva University Hospitals, Geneva, Switzerland

FW01_2
Personalised dementia risk reduction

N. Villain
Department of Neurology, Pitié-Salpêtrière Hospital, Paris, France

FW01_3
Interventions for cognitive enhancement

M. Kivipelto
Clinical Geriatrics, Karolinska Institute, Solna, Sweden

Optimising the use of digital health technologies and telemedicine

FW02_01

Optimising the use of digital health technologies, telemedicine and wearables in clinical practice and disease monitoring

S, Sacconi
CHU de Nice - Hôpital Pasteur Centre de Référence des Maladies Neuro-Musculaire, SLA Nice France Service de Neurologie, Hopital Pasteur, Nice, France

FW02_2

Using digital solutions to transform the delivery of clinical trials and research

S. Beniczky
Aarhus University Hospital and Danish Epilepsy Centre, Aarhus, Denmark

Digital technology, wearable devices and use of artificial intelligence has revolutionized our way of life. Their application in medicine is increasing and potentially can change radically our practice. This lecture will highlight the implications of these technologies on clinical trials and clinical research, with special emphasis and with examples from monitoring seizures, choosing optimal antiseizure medication and analyzing electroencephalography.
Disclosure: Nothing to disclose.

FW02_03

Implementing digital technologies: how do we avoid widening health inequalities

E. Moro
Division of Neurology, Deparment of Psychiatry and Neurological Rehabilitation, CHU Grenoble, Grenoble, France

Diagnosis and management of patients after the first seizure

FW03_1

Clinical management of patients with a first seizure – seizures, mimics, chameleon

M. Seeck
Department of Neurology, Hopitaux Universitaires de Genève-HUG, Geneva, Switzerland

FW03_2

Imaging after a first seizure – structural lesions and beyond

F. Pizzini
Dept. of Department of Engineering for Innovation Medicine, Verona University, Verona, Italy

The clinical use of MRI in patients with epilepsy is very heterogeneous in Europe and worldwide. Therefore, recommendations have been discussed that address these main questions: when MRI should be performed (1), what is the optimal protocol to be applied (2), and how to evaluate the images (3)? Based on these considerations and the classification of seizures and epilepsy syndromes, the following answers can be proposed: (1) a. Every focal seizure -with or without consciousness-, with or without bilateral tonic-clonic evolution, needs radiological investigation, except for some self-limiting childhood seizures. b. Generalized seizure: Imaging can be indicated depending on the clinical taxonomy and on seizure onset and clinical phenotype c. Seizures with Unknown Onset requires Imaging. (2) Neuroimaging Task Force identified a minimum requirements for an MRI epilepsy protocol (HARDNESS). These indications are increasingly used in clinical routine, but, in highly specialized centers and research, the goal should also be to identify possible causes of epilepsies yet unknown to imaging, applying advanced functional and structural acquisition and multimodal analysis. (3) Image interpretation depends on the radiologist's expertise and access to electroclinical information through close collaboration with the requesting physician. Thus, radiological evaluation consists of visual recognition of structural brain abnormalities. But in 30%-50% of histology-positive cases visual inspection does not lead to a diagnosis with a sufficient degree of confidence or is not relevant. Therefore, increasing use of quantitative morphometric analysis software to support visual assessment should be encouraged to improve lesion identification. Acknowledgments. L.G. Bongiovanni and F. Darra.
Disclosure: Nothing to disclose.

FW03_3

EEG and MEG after a first seizure

S. Rampp
Department of Neurosurgery, University Hospital Erlangen, Erlangen, Germany

After a first unprovoked seizure, electroencephalography (EEG) contributes to differential diagnosis. Furthermore, it supports estimation of the recurrence risk, impacting the decision on anti-seizure medication (ASM) as well as on further diagnosis and treatment. With magnetoencephalography (MEG) and high-density EEG (HD-EEG), highly sensitive techniques are available. Combined with sophisticated signal analysis methods, such as source imaging and network analysis, they may offer novel tools for early diagnosis of epilepsy. The presentation will summarize current evidence on the use of EEG after a first seizure and explore the potential benefits of MEG/HD-EEG and novel analysis approaches in this setting.
Disclosure: Nothing to disclose.

The present and future value of body and brain autopsy in central nervous system diseases of the XXI Century

FW04_1

New findings provided by body and brain autopsy of 700 stroke patients with and without thrombolysis

L. Csiba
Department of Neurology, Debrecen University, Debrecen, Hungary

FW04_2

Contribution of full body autopsy to the understanding of neurodegenerative diseases

I. Alafuzoff
Institution of Immunology, Genetics and Pathology, Uppsala University Hospital, Uppsala, Sweden

Population based studies have indicated that cardiovascular disease (CVD), diabetes mellitus (DM), metabolic syndrome are associated with increased incidence of cognitive impairment and with Alzheimer's disease (AD). It has also been reported that hypertension, heart disease, dyslipedimia and DM are associated with vascular dementia/vascular cognitive impairment but not with AD. One caveat regarding these statements is that all alterations listed above are aging related. Neuropathologically AD is defined as a disease with ADNC, i.e., β-amyloid (Aβ) and hyperphosphorylated tau (HP-T) in the brain. Many subjects with a clinical phenotype of AD display at a neuropathological assessment not only ADNC but as well concomitant phosphorylated transactive DNA binding protein 43 (TDP43), phosphorylated α-synuclein (αS) or cerebrovascular lesions. Based on the complexity of brain alterations it is difficult, if not impossible to reliably assess the impact of various systemic diseases on the brain pathology. One approach to assess an association between systemic diseases and brain pathology is to investigate all organs of interest at the end stage. Postmortem assessment of the brain pathology can reliably be carried out due to standardized techniques and assessment strategies (extent of ADNC, αS and pTDP43) and combine this with a standardized assessment of pathology seen in vessels, heart, kidneys, pancreas and liver. This strategy is however negatively influenced by the low number of autopsies (2 - 20% in Europe) and even lower number of neuropathological assessments (0.3% in Sweden). In this presentation some data following the latter strategy are presented.
Disclosure: Nothing to disclose.

FW04_3

Contribution of digital neuropathology to study archival brain tissue on neurological conditions

G. Kovacs
University of Toronto and University Health Network, Toronto, Canada

Digital neuropathology includes computer-based morphometric evaluation of different markers in brain tissue. Archival brain collections mostly include formalin fixed paraffin embedded tissue blocks also samples still in formalin fixatives. Archival tissue sample collections include disease that are not collected in the recent years, such as untreated cerebrovascular or neurodegenerative diseases, neuroinfections, or rare neurometabolic conditions. Deep frozen tissue samples can be used for various biochemical, transcriptomic, and genomic studies, however, the storage conditions should be kept in mind because these can alter the quality of the evaluations. The following methods can be used in archival tissue samples: i) immunohistochemistry with morphometric, eventually artificial intelligence-based, evaluation of pathological disease associated proteins including a three-dimensional approach to understand spatial distribution of markers that are the target of research interest; ii) RNAscope and similar methods can be used to detect RNA molecules on a tissue and cell-based fashion; and iii) spatial transcriptomics/proteomics. All these methods require preserved quality of RNA and DNA; however, fortunately, paraffin embedded tissue blocks can preserve these for an extended time in contrast to tissue samples stored in formalin for many years. Samples that are in formalin can be used for postmortem neuroimaging and basic histochemical and immunohistochemical methods to compare tissue alterations. Finally, recent developments show that misfolded protein seeding assays used to detect disease-associated conformers of neurodegenerative disease related proteins can be applied in paraffin embedded tissue blocks. In summary, archival tissue is a valuable source for research but expertise is needed to coordinate these examinations.
Disclosure: Nothing to disclose.

EAN/WMS: Current treatment of immune-mediated neuromuscular disorders

FW05_1

Therapeutic approaches in inflammatory myopathies

M. De Visser
Department of Neurology, Academic Medical Centre Amsterdam, Amsterdam, the Netherlands

FW05_2

Cancer related immune-mediated neuromuscular disorders

C. Paradas
Neuromuscular Disorders Unit, Hospital Universitario Virgen del Rocío/Biomedicine Institute of Sevilla, Sevilla, Spain

Immune-related neuromuscular events (irNEs) may occur in cancer patients as per se, as paraneoplastic syndrome, or as adverse effect associated with immune checkpoint inhibitors (ICI), even ICI may trigger or exacerbate an auto-immune paraneoplastic syndrome. irNEs associated to ICI tend to present early after treatment onset and include peripheral nerve, neuromuscular junction and muscular involvement, as paraneoplastic syndromes. Many cases present mixed syndromes, sometimes coexisting central and peripheral nervous system involvement. In this scenario, the differential diagnosis is crucial to treat and manage both the neuromuscular disorder and the cancer. Neuromuscular autoantibody profiles may serve as a marker to diagnose and predict life-threatening ICI-induced irNEs. Transcriptomic profiling may help offering essential clues to improve the treatment of these patients, as the activation of type 1 and 2 interferon pathway found in ICI induced-myositis depending on specific pathology features. The recent generation of genetic mouse model that recapitulates the clinical pathology of these entities also supports mechanism-based therapeutic interventions. Taking altogether, the multidisciplinary management of these patients, including neurologist in the care teams, is clearly recommended.

Disclosure: Nothing to disclose.

FW05_3

Novel treatments in myasthenia gravis

K. Claeys
Department of Neurology, University Hospitals Leuven, Leuven, Belgium

EAN/EFAS: Neurogenic autonomic dysfunction: A red flag, life threatening, or the missing link?

FW06_1

Orthostatic hypotension in polyneuropathy: The missing link to an alpha-synucleinopathy?

A. Terkelsen
Department of Neurology, Aarhus University, Aarhus, Denmark

Readily available screening tests as well as specialized neurophysiological tests and nuclear imaging suited to specify neurogenic autonomic dysfunction and small fiber polyneuropathy shall be presented. Cardiac [123I] metaiodo-benzyl-guanidine (MIBG) scintigraphy image the sympathetic innervation of the heart and detects autonomic denervation in both diabetes and prodromal alfa-synucleinopathies. The workshop will show that patients with peripheral neuropathy and orthostatic hypotension or reversed blood pressure dipping pattern commonly have widespread autonomic dysfunction and abnormal cardiac MIBG scintigraphy and with this a possible undetected alfa-synucleinopathy.

Disclosure: Astrid Juhl Terkelsen participated in a clinical study supported by Sanofi-Genzyme and Alnylam Pharmaceuticals. Consultation for: Alnylam Pharmaceuticals, Akcea Therapeutics, Pfizer.

FW06_2

Life threatening, though different autonomic dysfunction in diabetes and Guillan-Barrè Syndrome (GBS)

M. Hilz
Depts. of Neurology, University of Erlangen-Nuremberg, Erlangen, Germany & Icahn School of Medicine at Mount Sinai, New York, USA

Autonomic dysfunction (AD) is common among patients with Guillain-Barré-Syndrome (GBS) or diabetic patients. Particularly cardiovascular AD contributes to poor prognosis and increased risk of mortality. In GBS, AD is common among patients needing mechanical ventilation. However, there is no clear association between AD and muscle weakness; AD can manifest during GBS-onset or -recovery. AD is life-threatening due to unpredictable shifts between sympathetic and parasympathetic hypo- and hyperactivity triggering bouts of tachyarrhythmias and bradyarrhythmia, arterial hypertension, and hypotension. Asystole may be induced by interventions such as tracheal suction. Baroreflex dysfunction may cause persistent arterial hypertension and hypotension, rapid blood pressure changes, and orthostatic hypotension (OH). Sudomotor dysfunction is often patchy with hyperhidrotic and anhidrotic skin areas. Bladder and gastrointestinal dysfunction may cause urine retention, diarrhea, constipation, or paralytic ileus. GBS patients routinely need autonomic testing and may require cardiac pacing. Long half-life cardiovascular drugs should be avoided. In diabetes, autonomic dysfunction afflicts all organs causing myriad symptoms. Erectile dysfunction is common and a premonitory sign of cardiovascular AD. Cardiovascular AD portends high mortality rates. Initial tachycardia due to cardiovagal impairment, later orthostatic hypotension, gastrointestinal, genitourinary dysfunction, stocking-like hypo- and anhidrosis, trophic skin changes, pupillomotor dysfunction with early miosis, chronic foot ulcers, osteomyelitis, painless myocardial infarctions, chemoreceptor dysfunction and sleep apnea, hypoglycemia unawareness are only some of many disease manifestations. Of note, rapid glycemic overcorrection often causes iatrogenic painful small fiber neuropathy and prominent autonomic dysfunction. Early treatment with glycemic control and lifestyle changes is essential to halt or slow disease progression.

Disclosure: I received lecturing honoraria and travel support from Sanofi and Amicus Therapeutics, and consultancy fees from Sanofi and Pfizer. I have not received any support related to my presentation at EAN 2023.

FW06_3

Autonomic dysfunction as a red flag for underlying autoimmune or paraneoplastic conditions

A. Fanciulli
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Artificial intelligence: Advances and applications in neuro-oncology

FW07_1

PET/MRI radiomics in neuro-oncology

N. Galldiks
Deptartment of Neurology, University Hospital Cologne, Cologne, Germany

Since neuroimaging is integral and decisive for the management of patients with gliomas and brain metastases, the main part of this presentation is focused on novel developments in this field. In particular, recent imaging developments suggest that artificial intelligence (AI) / radiomics has a great potential to provide novel imaging biomarkers that could be helpful in the field of Neuro-Oncology. With high-throughput computing, it is now possible to rapidly extract innumerable quantitative features from standard-of-care tomographic images (usually MRI as well as PET). The conversion of digital medical images into diverse data, a process that is known as radiomics, is motivated by the concept that biomedical images contain information that can be applied within the clinical decision process in order to improve diagnostic, prognostic, and predictive accuracy.

Disclosure: Norbert Galldiks received honoraria for lectures from Blue Earth Diagnostics and for advisory board participation from Telix Pharmaceuticals.

FW07_2

Issues in connectomics: impact of low grade gliomas in normal brain functions

H. Duffau
Department of Neurosurgery, University Medical Center, Montpellier, France

Body: In the traditional literature, brain processing was thought in a localisationist framework, in which one given function was sustained by a discrete cortical area, with a similar organization across individuals. However, this static view of cerebral functioning does not explain postlesional recovery. Here, the goal is to revisit this classical modular and inflexible model by evolving towards a dynamic organization of neural circuits, which enables adaptive phenomena. In addition to anatomic dissection in specimen, serial mappings performed in patients who underwent awake surgery for low-grade glioma provided new insights into the brain anatomo-functional architecture. They evidenced a network distribution and resulted in the reappraisal of neural foundations underpinning movement, language, executive and emotional functions. Moreover, combination of neuropsychological assessments and functional neuroimaging before and after operation(s) demonstrated that massive resections of “critical” regions were feasible without eliciting permanent neurological deficits, thanks to neural reconfiguration mechanisms. These findings on brain connectome challenge the outdated localisationist view and lead to an alternative meta-networking theory, in which complex behaviors arise from the spatiotemporal integration of distributed cortico-subcortical networks subserving conation and cognition. Constant circuit interactions result in a perpetual succession of new neural equilibrium states, explaining interindividual behavioral variability and neuroplastic phenomena. A meta-networking organization underlies the uniquely human propensity to learn news abilities and enables functional compensation in brain-damaged patients. The implications of this original neuroanatomical model are discussed in fundamental neurosciences and in clinical neuro-oncology, especially in surgery for low-grade glioma, with an optimization of survival and quality of life.

Disclosure: Nothing to disclose.

FW07_3

Relevance of artificial intelligence to brain tumour management

R. Soffietti
Div. Neuro-Oncolgy, Department of Neuroscience, University of Turin, Turin, Italy

Purpose of review is to discuss recent applications of artificial intelligence within the field of neuro-oncology and highlight emerging challenges in integrating artificial intelligence within clinical practice. In the field of image analysis, artificial intelligence has shown promise in aiding clinicians with incorporating an increasing amount of data in genomics, detection, diagnosis, classification, risk stratification, prognosis, and treatment response. Artificial intelligence has also been applied in epigenetics, pathology, and natural language processing. Although nascent, applications of artificial intelligence within neuro-oncology show significant promise. Artificial intelligence algorithms will likely improve our understanding of brain tumors and help drive future innovations in neuro-oncology.
Disclosure: Nothing to disclose.

Sunday, July 02 2023

EAN/MDS-ES: Early/prodromal detection and risk stratification in Parkinson‘s disease and dementia with Lewy bodies

FW08_1

Insight from genetics

C. Klein
Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

FW08_2

Insight from imaging

I. Rektorova
Department of Neurology, Mararyk University, Brno Teaching Hospital Svata Anna, Brno, Czech Republic

FW08_3

Insight from fluid biomarkers

W. Meissner
Service de neurologie - maladies neurodégénératives, Hôpital Pellegrin, CHU de Bordeaux, Bordeaux, France

Management of epilepsy before, during and after pregnancy: An evidence-based update

FW09_1

Women with epilepsy: What to do about contraception and folic acid supplements?

M. Bjork
Department of Neurology, Haukeland University Hospital, Bergen, Norway

FW09_2

New antiseizure medications and pregnancy: Which drug to choose and dose titration during and after pregnancy?

T. Tomson
Department of Clinical Neuroscience, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden

The challenge in treatment of epilepsy during pregnancy is to balance the teratogenic risks with antiseizure medications (ASMs) against maternal and fetal risks associated with maternal seizures. The aim is to maintain seizure freedom with minimized exposure to potentially teratogenic drugs. Exposure to some first generation ASMs, in particular valproate, is associated with increased risks of malformations as well as adverse developmental outcomes to the extent that valproate is contraindicated in pregnancy. Among second generation ASMs, lamotrigine and levetiracetam appear to be comparatively safe with regard to teratogenic effects, whereas topiramate seems to have teratogenic risks similar to valproate. Data on other second or third generation ASMs are too limited to draw any firm conclusions regarding safety of use during pregnancy. The selection of ASMs for women that may become pregnant and the use of these ASMs during pregnancy is further complicated by the fact that pregnancy can affect maternal serum concentrations of ASMs thereby reducing their effectiveness. These pharmacokinetic (PK) effects of pregnancy vary between ASMs, and have been shown to be pronounced for many second generation drugs including lamotrigine, levetiracetam, zonisamide, topiramate, and lacosamide, more so than with some older ASMs such as carbamazepine. Being unpredictable, the PK changes complicate the treatment during pregnancy. Drug level monitoring can be used as a tool to facilitate dose adjustments. We will discuss how the current knowledge and lack of knowledge regarding teratogenic risks with newer ASMs as well as PK changes can affect ASM selection and the practical management.
Disclosure: Nothing to disclose.

FW09_3

Lactation and Antiseizure medications: Yes or no?

B. Nucera
Department of Neurology, Franz Tappeiner Hospital Merano, Merano, Italy

The benefits of breastfeeding are widely documented and acknowledged. Although recent position papers and guidelines recommend women with epilepsy (WWE) to breastfeed and highlight the benefits of breastfeeding, only 42% of WWE breastfeed at 3 months. Several factors contribute to the discontinuation of breastfeeding, but the most important is the mistaken belief that antiseizure medications (ASMs) taken by the mother are transferred to the baby through breastmilk and can cause adverse effects. ASMs can be detected at various concentrations in plasma or serum samples of infants who were exposed via breastmilk. Several methods are described in the literature for calculating the infant's exposure to maternal drugs taken during breastfeeding and among these, the milk/plasma ratio (M/P ratio) is certainly the best known. However, in clinical practice, these methods may not be readily available and, in general, there are limited data on the safety of breastfeeding, based on clinical experience, case reports and series or observational studies. Most of them evaluated concentrations of lamotrigine in breastmilk and in serum of both mothers and their infants in the first month after delivery, other studies were conducted to quantify concentrations of levetiracetam and topiramate in biological fluids of breastfeeding WWE and their infants. Unfortunately, data on excretion in human breast milk and the effects of infant exposure to breastfeeding are, however, very limited. In addition, there are also very few data on the possible effect that drugs taken during breastfeeding may have on the child's neuro-cognitive development.
Disclosure: Nothing to disclose.

EAN/ECTRIMS: Silent disease activity in MS: How to measure, which relevance

FW10_1

The clinical perspective

L. Kappos
Research Center Clinical Neuroimmunology and Neuroscience Basel, University Hospital and University of Basel, Basel, Switzerland

The current classification of disease courses relies on the premise that relapsing disease is characterized by periods between relapses that are free of worsening whilst progressive disease presents with a more or less steep continuous decline of neurological functions. In the last years evidence from different fields (neuropathology, neuroimaging, biomarker measurements in blood) and more and more clinical observations suggests that progression independent of relapse activity (PIRA, also called "silent progression") occurs across the full spectrum of MS phenotypes and is the main driver of disability accrual, even in early RR MS and CIS. The advancement in our ability to detect PIRA was possible by the availability of comprehensive and standardized longitudinal clinical observations in large groups of pwMS and treatments that effectively suppress or even completely abrogate relapse activity – thus reducing the relapse "noise" that may interfere with the detection of subtle signs of steady progression. Accurate and sensitive detection of the features of progression across the full spectrum of MS will be central for further advance in daily management and the development of new treatment options to better control disability progression. We need to agree on unified definitions of PIRA that should be based on the use of standardized quantitative physician based assessments (e.g. Neurostatus-eEDSS and Composite Measures like 9-HPT, 25fWT, SDMT) and – increasingly - patient administered comprehensive digital biomarkers including active tasks, passive monitoring and patient reported outcomes (PROs).
Disclosure: Nothing to disclose.

FW10_2

The imaging perspective

M. Rocca
Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy

During the past few years, the notion that in patients with multiple sclerosis (MS) there is a continuous and insidious progression of clinical disability independent from acute overt neurological attacks and the formation of active lesions at MRI has significantly changed the approach to these patients. There is the need to identify new measures able to capture this silent activity to be applied not only in the context of clinical trials, but also during daily life clinical activity. This is fundamental not only to get closer to the pathophysiological processes of MS, but also to be able to define response to the many available disease-modifying treatments. Due to its specificity towards the heterogeneous pathological substrates of the disease and its repeatidibility, MRI is a candidate tool to identify and monitor these processes. During this workshop, the main putative MRI biomarkers of silent disease activity will be presented. These will include not only novel lesional markers (i.e., slowly expanding lesions, paramagnetic rim lesions), but also measures classically associated with longlasting MS and neurodegeneration (atrophy of the deep gray matter, cortical gray matter and spinal cord), which offer the unique capability to identify patients with a steeper evolution towards a more severe form of the disease. Adavantages and disadvantages of available measures will be presented and the feasibility of their use in a clinical scenario will be discussed. The ultimate goal will be to make clinicians more confident with the interpreation of these measures to guide their future implamentation in the clinic.
Disclosure: M.A. Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva. She receives research support from the MS Society of Canada, the Italian Ministry of Health, and Fondazione Italiana Sclerosi Multipla. She is Associate Editor for Multiple Sclerosis and Related Disorders.

FW10_3

Moving from clinical trials to real-life

J. Sastre-Garriga
MS Center of Catalonia, Hospital General de la Vall d'Hebron, Barcelona, Spain

Recent developments in acute reperfusion therapies

FW11_1

Recent developments of intravenous thrombolysis

D. Aguiar de Sousa
Lisbon Central University Hospital, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

Intravenous thrombolysis (IVT) is a critical treatment for acute ischemic stroke. IVT with alteplase has been the standard treatment for acute ischemic stroke for over two decades but its use is limited by a narrow therapeutic window and concerns about hemorrhagic transformation. Over the past years, several new developments in IVT have emerged that may improve patient outcomes. Advanced imaging techniques, such as CT perfusion and MRI, can identify patients who are likely to benefit from IVT beyond the standard time window. Tenecteplase, a genetically modified version of alteplase with higher fibrin specificity and longer half-life, is a promising development that has shown non-inferiority to alteplase in terms of safety and efficacy. Additionally, efforts are being made to improve access to IVT, particularly in rural and underserved areas, through telestroke and mobile stroke units. This lecture aims to provide attendees with an understanding of the latest advances in thrombolysis treatment and how they can be applied to improve patient care. By utilizing these new developments in IVT, such as tenecteplase, advanced imaging techniques, and innovative approaches to care delivery, we can potentially improve outcomes for patients with acute ischemic stroke.

Disclosure: Nothing to disclose.

FW11_2

Recent developments of mechanical thrombectomy

U. Fischer
Department of Neurology, University of Basel, Inselspital, Basel, Switzerland

FW11_3

Bridging therapy vs direct mechanical thrombectomy

G. Turc
Department of Neurology, GHU Paris Psychiatrie et Neurosciences, Paris, France

Artificial intelligence: Advances and applications in neurology

FW12_1

Brain network's structure and function: A paradigm shift?

R. Wiest
Institute of Diagnostic and Interventional Neuroradiology, Neurocenter Inselspital, University of Bern, Bern, Switzerland

An important objective of neuroimaging research is to identify biomarkers that assist the diagnosis of brain disorders and monitor disease progression. The presentation will provide an overview of recent advances of AI applications in neuroimaging, encompassing five distinct topics: (i) implementation of fast and reliable brain morphometry in clinical routine, (ii) implementation of decision support systems to identify deviations from normative data, (iii) network based image analysis of cerebral blood flow and volume, (iv) analysis of structural covariance networks and v) applications of AI-guided functional imaging.

Brain morphometry quantifies the shape of the brain and its substructures and enables quantitative analysis of patient data and controls, enriching the variety of accessible image based information. Recent advances in algorithm development enable acceleration of data processing. Synthetic data analysis demonstrated advantages of deep learning based approaches in high-throughput analysis of large-scale structural brain networks.

Deep learning based segmentation and radiomic shape analysis enables user-independent lesion classification by neurologists and demonstrates gains in accuracy and inter-rater agreement in clinical research and routine. Structural covariance network analysis enables the detection of distinct patterns of cortical thinning and identification of global network properties at a group-level. In functional imaging, applications for perfusion imaging and BOLD fMRI enable standardized analysis of regional and global hemodynamic dysfunction. The presentation will discuss potential clinical applications in epilepsy, neurodegenerative disorders and stroke recovery. It will further address the susceptibility of AI to biases in data quality and variation.

Disclosure: Nothing to disclose.

FW12_2

AI and protein structure and function in neurological disease: Relevance to disease management

T.F. Outeiro
Department of Experimental Neurodegeneration, University Medical Center Göttingen, Göttingen, Germany

FW12_3

AI and neuro-stimulation devices and protocols: What have we learned?

P. Limousin
Department of Neurology, National Hospital for Neurology and Neurosurgery, London, UK

Monday, July 03 2023
EAN/MDS-ES: Pediatric syndromes with movement disorders and epilepsy

FW13_1

Clinical approach of movement disorders and epilepsy in children

G. Zorzi
Neuropsichiatria Infantile - Disordini del Movimento. Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Movement disorders (MDs) and epilepsy comprise a large number of conditions with onset in childhood, characterised by the co-occurrence of MDs and epilepsy as a core feature. These conditions range from isolated epilepsy and movement to complex phenotypes in which epilepsy, movement disorder and other neurological and non-neurological features are associated. In recent years, next-generation sequencing technologies have contributed to the discovery of new causative genes, but have also shown that similar phenotypes can be associated with different causative genes and that the same gene alteration can cause different phenotypes. In addition, a significant proportion of patients remain without a genetic diagnosis. In patients with movement disorders and epilepsy, the phenomenology of the MD may be hyperkinetic or hypokinetic with a chronic or paroxysmal occurrence , or both. Epilepsy may be generalised or focal and may range from isolated seizures to developmental/epileptic encephalopathies. However, there are some syndromic associations that are seen more frequently and that are important to recognise because may be of diagnostic value or treatable We will discuss the clinical approach to patients with movement disorders and epilepsy, proposing a clinical reasoning scheme that will help in orienting the diagnosis.
Disclosure: Nothing to disclose.

FW13_2

Diagnostic workup and differential diagnosis of disorders presenting with movement disorders/Epilepsy in childhood

M. Kurian
Developmental Neurosciences Department, UCL GOSInstitute of Child Health, UCL, London, UK

FW13_3

Medical and surgical treatment

M. Carecchio
Department of Neuroscience, University of Padua, Padua, Italy

EAN/ESO: Is it just a mini-stroke?

FW14_1

TIA symptoms and risk of stroke

P. Rothwell
Department of Neurosciences, John Radcliffe Hospital Oxford, Oxford, UK

FW14_2

Is it just a mini-stroke?

H. Christensen
Bispebjerg Hospital & University of Copenhagen, Copenhagen, Denmark

25 years ago, TIA symptoms were considered innocent and did not lead to vascular work up or secondary prevention in clinical practice. Presently, the urgency of TIA is well recognized by all professionals working in neurology. Diagnosis of TIA, however, remains based on patient history including duration of symptoms below 24 hours, some use support from instruments like the ABCD2 score, which predicts risk of a recurrent event. The uncertainty of a clinical TIA diagnosis is high also amongst experienced neurologist as this is depending solely on the patients report and sometimes quite elusive symptoms. MRI (DWI) allows for identifying the acute ischemic lesion in TIA with a high diagnostic certainty and the increasing access to MRI now allows for using this modality in TIA work up in many European many countries. Existing recommendations on management of TIA are however based on a clinically identified TIA-population. This talk will discuss cons, pros, and caveats of a tissue-based diagnosis of TIA.
Disclosure: Nothing to disclose.

FW14_3

Cognitive deficits after TIA or minor stroke

T. Quinn
School of Cardiovascular & Metabolic Health, University of Glasgow, Glasgow, UK

The syndrome of transient ischaemic attack (TIA), by definition, should not be associated with longer term effects. However, an increasing body of research suggests that TIA is not as benign a diagnosis as previously suggested. This may be especially true for neurocognitive issues, the so called ‘hidden deficits’ of cerebrovascular disease. In this session, we will assess the epidemiology of neurocognitive deficits following TIA. Underlying mechanisms will be explored, including the importance of shared risk factors and appreciating the bi-directional relationship between neurocognitive disorders and cerebrovascular disease. Finally, the implications for clinical pathways will be discussed making reference to novel services for follow-up of TIA and minor stroke.
Disclosure: Nothing to disclose.

EAN/EFIC: Difficult-to-treat neuropathic pain patients. How to use third-line drugs and cannabinoids

FW15_1

Opioids in patients with neuropathic pain

W. Häuser
Department of Internal Medicine, Klinikum Saarbrücken, Saarbrücken, Germany

Background: Systematic reviews have come to different conclusions on the efficacy and safety of on opioids for chronic neuropathic pain. Evidence-based guidelines on the management of neuropathic pain have come to different recommendations for opioids ranging from third line treatment options to negative recommendations.
Methods: In my lecture, I will explore potential reasons for these discrepancies such as the definition of opioids, the types of studies analysed and the methods to balance risks and harms.
Results: I will discuss systematic reviews of my working group in detail. The systematic review with placebo-controlled studies included 16 trials with 2,199 participants. Study duration ranged between 4 and 12 weeks. Some opioids (buprenorphine, morphine, oxycodone, tramadol, tapentadol) provided substantial pain relief compared to placebo in postherpetic neuralgia and peripheral neuropathies of different aetiologies for 4–12 weeks. There are two head-to- head comparisons of opioids versus first-line medications for neuropathic pain available. Morphine was compared antidepressants (nortriptyline or desipramine) in lumbar root and postherpetic neuralgia pain (one study each) and to the anticonvulsant gabapentin in post-zoster neuralgia and diabetic neuropathy pain (one study each) (total 563 participants). There were no statistically significant differences between opioids compared to antidepressants and anticonvulsants in reduction of pain and disability and drop out rate due to adverse events.
Conclusions: It is not justified from a statistical point of view to prefer antidepressants or anticonvulsants over opioids in the management of chronic neuropathic pain.
Disclosure: I have no financial conflicts of interest to declare. I was the author of systematic reviews on opioids for chronic non-cancer pain conditions and was head of the position paper of the European Pain Federation on opioids for the management of chronic non-cancer pain

FW15_2

Cannabis-based medicine. Current evidence and clinician-based indications in patients with neuropathic pain

E. Eisenberg
Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel

FW15_3

Botulinum Toxin in patients with neuropathic pain

N. Attal
Department of Pain Treatment, Hôpital Ambroise Paré, Boulogne-Billancourt, France

The beneficial effect of BTX-A in muscle disorders results from the blockade of presynaptic nerve terminals releasing acetylcholine. However, early in the use of BTX-A for dystonia, authors had noticed that pain relief preceded muscle decontraction and exceeded what would be expected solely as a consequence of muscle relaxation. These findings suggested that BTX-A might have analgesic properties independently of its myorelaxant action. The sustained effects for up to 3 months of one or 2 repeated administrations of botulinum toxin A (100 to 300 U) injected ID or SC into the painful area were further reported in neuropathic pain by several independent teams (1), although 2 upublished trials were negative. The efficacy of BTX-A may be related to central mechanisms through retrograde axonal transport. BTX-A is now recommended generally as second or third line for peripheral neuropathic pain (2), but has no approval for use. This presentation will provide with an overview of the use, clinical studies and recent meta-analyses regarding BTX-A in neuropathic pain including trigeminal neuralgia, and show how to predict its efficacy by the use of specific questionnaires (3) (1) Attal N, de Andrade DC, Adam F et al. Lancet Neurol. 2016 ;15 :555-65. (2) Moisset X, Bouhassira D, Avez Couturier J et al. Rev Neurol (Paris). 2020;176 :325-352 (3) Bouhassira D, Branders S, Attal N, et al. Pain. 2021 ;162 :1038-1046.
Disclosure: The author has received honoraria from Merz regarding potential development of BTX-A in neuropathic pain, and from Pfizer, Grunenthal, Novartis, Upsa, Biogen over the past 36 months outside the submitted work.

Artificial Intelligence: Real world applications in neurology – from knowledge-based systems to deep learning

FW16_1

Generating trust in AI: Prerequisites for clinical use

R. McKinley
Department of Neuroradiology, Inselspital, Bern, Switzerland

FW16_2

Decision support with AI: Real world applications in acute neurology

S. Wegener
Department of Neurology, University Hospital Zurich, Zurich, Switzerland

FW16_3

Disease monitoring with AI: What, when and how?

S. Auger
Department of Neurology, Imperial College London, London, UK

There is certainly an opportunity for recent advancements in machine learning and other technologies to transform certain areas of clinical practice in neurology. Clinicians could learn important insights into the needs of their patients, with objective and pragmatic measures supporting them to provide more responsive treatment decisions. Fine-grained monitoring has also revealed valuable, novel insights into our understanding of neurological disease. The full potential of these technological advances is far from being realised though. I will provide some examples where AI systems could offer meaningful impact for patients and those caring for them; as well as outlining some of the current limitations of AI systems and barriers which need to be overcome for their successful implementation in routine clinical practice.

Disclosure: Salary/grant support from a National Institute for Health and Care Research Academic Clinical Fellowship.

A new era of migraine treatment: What is right for our patients?

FW17_1

Place of CGRP targeting treatments in migraine prevention

S. Sacco
Clinical Neurology Research Unit, University of L'Aquila, L'Aquila, Italy

FW17_2

Place of non-invasive neuro-stimulation in migraine treatment

G. Lambru
Guy's and St Thomas' Hospital NHS Foundation Trust, London, UK

FW17_3

Spotlight on treating rare migraine syndromes

I. De Boer
Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands

Migraine has a strong genetic component and often has a polygenic complex inheritance pattern. In the minority of patients their migraine attacks are caused by a single DNA mutation. It is important that neurologists recognize and address rare migraine disorders, as often a different approach is needed for diagnosing, treating and counseling these patients compared with common migraine patients. In autosomal dominant familial or sporadic hemiplegic migraine a pathogenic mutation in CACNA1A, ATP1A2 or SCN1A can cause the disease. In these patients, the auras include motor weakness in addition to other symptoms of migraine with aura. In patients with monogenic cerebral small vessel diseases, including cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations (RVCL-S), and Dutch-type cerebral amyloid angiopathy (D-CAA), a high prevalence of migraine is also observed. Due to the rarity of these conditions, no clinical treatment trials are available. Thus, treatment is often based on empirical data and personal experience of the treating neurologist. Treatment choices need to take into account specific risks and comorbidities associated with monogenic migraine syndromes. Examples of this include risk of ischemic events and psychiatric illnesses. While historically some (acute) treatments might not be prescribed due to fear of adverse events, extensive clinical experience has shown that some of these treatments can be given safely. Nonetheless, some compounds should be treated with caution. By combining available evidence with expert opinions, neurologist can be assisted in recognizing and treating patients with monogenic migraine disorders.

Disclosure: Author has received grant support by the Dutch Heart Foundation and the International Retinal Research Foundation.

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Special Sessions

Saturday, July 01 2023
MDS-ES Basal Ganglia Club

SPS01_1

MDS-ES C. David Marsden Award Lecture

C. Trenkwalder
Department of Neurology, Paracelsus Elena Klinik, Kassel, Germany

Isolated REM sleep behavior disorder (iRBD) is currently the most specific prodromal feature of α-synuclein pathology, which may manifest even a decade before motor symptoms of Parkinson Disease (PD), Dementia with Lewy Bodies (DLB) or Multiple System Atrophy (MSA) start. Clinical RBD is characterized by dream enactement with vocalizations, small jerky movements of the extremities up to complex movements of the whole body with a risk of injury. Assessment and diagnosing of iRBD with screening questionnaires or history fail as affected people rarely remember the nocturnal events and bedpartners' descriptions are crucial. The detailed scoring of a video-synchronized polysomnography should include the detection of an increased muscle tone of the chin (REM without atonia, RWA) recorded during REM sleep according to standardized criteria (Frauscher et al Sleep 2012).

Since the early 2000 years, cohorts with iRBD subjects were followed showing a phenoconversion to any α-synucleinopathy of up to 80% within 18 years in a single cohort (Schenck et al, 2013) and 73.5% within 12-year follow-up in a multi-center approach (Postuma et al 2020). Adding further non-motor features such as hyposmia, autonomic symptoms, cognitive decline or biomarkers such as DAT-scan or α-synuclein aggregation measures in CSF or nasal mucosa increases the likelihood of detecting the phenoconversion date, necessary to include people in future clinical trials of neuroprotective therapies. In a recent multi-center study it could be demonstrated, that phenoconverters showed overall greater progression in motor, olfactory, cognitive, and certain autonomic markers, compared to the non-converters. (Joza et al 2023).

The prevalence of RBD in newly diagnosed PD patients is about 25% (Mollenhauer et al 2013) with an increasing percentage during the course of the disease, both for RWA (Zimansyk et al 2021) and clinical RBD. Small motor events in REM sleep (REM events, Sixel-Doering et al 2014) may introduce the very beginning of an α-synuclein finally leading to a fully developed iRBD. During the course of Parkinson disease further sleep features occur, with sleep fragmentation, frequent periodic limb movements, and in advanced stages the lack of sleep cycles with increased wakefulness at night and daytime sleepiness, finally the progression of the disease reveals the picture of a severely disturbed brain health reflected in sleep both polysomnographically and clinically.

Disclosure: Nothing to disclose.

SPS01_2

Dystonia Europe David Marsden Award Lecture

Sunday, July 02 2023

Save the date: Meet the new EAN guidelines

SPS02_1

Guideline Production Group: Building a better path for EAN guidelines

J. Costa
Department of Clinical Pharmacology, Faculdade de Medicina Universidade de Lisboa, Lisbon, Portugal

SPS02_2

EAN guidelines for a precise diagnosis of HyperCKemia

T. Kyriakides
Department of Basic and Clinical sciences, University Nicosia, Nicosia, Cyprus

SPS02_3

EAN guideline on the management of amyotrophic lateral sclerosis in collaboration with ERN Euro-NMD

P. Van Damme
Department of Neurology, University Hospital Gasthuisberg, Leuven, Belgium

SPS02_4

EAN-EFAS-INUS: Management of neurogenic lower urinary tract and sexual dysfunction for the practicing neurologist

J. Panicker
Department of Uroneurology, The National Hosptial for Neurology and Neurosurgery, London, UK

Clinical Grand Round: Neurological diseases do not learn neurology!

SPS03_1

Differential diagnosis of ataxia in a young male patient: a long bumpy road

A. Papp, A. Kamondi
Department of Neurology, National Institute of Mental Health, Neurology and Neurosurgery, Budapest, Hungary

A young waiter first complained about clumsiness when serving his guests in his restaurant, and later he developed severe gait ataxia. The road to the final diagnosis proved to be longer and bumpier than it was expected at first.
Disclosure: Nothing to disclose.

SPS03_2

Acute onset of coma and nuchal rigidity in a young male

I. Vastagh, J. Nadas, P. Golopencza
Department of Anesthesiology and Intensive Care, Bajcsy-Zsilinszky Hospital Budapest, Budapest, Hungary

A 27-years-old male admitted (with history of Hashimoto-thyroiditis) to the emergency department with fever, altered mental state (GCS: 1-1-2), hypoglycemia and nuchal rigidity. His SARS-COV-2 antigen test was positive. Obvious clinical setting for a severe bacterial meningitis. Beside the immediate starting of the empirical therapy, some unexpected diagnostic results occurred. The final diagnosis could be presented with a multidisciplinary brainstorming.
Disclosure: We are inviting the dear collegues to think over the presented case and step by step find out what the possible cause could be.

SPS03_3

Extreme fatigue, coughing, unusual headache but without fever

M. Kozak
Department of Neurology, Debrecen University, Debrecen, Hungary

A 61-year old female patient complains about an acute onset of coughing, dyspnoe, chest pain and fatigue. Pneumonia, pulmonary embolism, myocardial infarct? The difficult road to the final diagnosis and good outcome will be presented.
Disclosure: Nothing to disclose.

SPS03_4

Subacute onset of dysphagia and diplopia

L. Olah, L. Csiba
Department of Neurology, University of Debrecen, Debrecen, Hungary

A 70-year-old patient complained of dysphagia and dysarthria, which developed over 3-4 days. On his first examination, he had mild dysarthria and moderate dysphagia, which was later accompanied by mild, fluctuating diplopia. His consciousness was intact, he had no fever, no paresis, and no complaints of headache. The progression of symptoms and the examinations shed light on a rare cause.
Disclosure: Nothing to disclose.

Monday, July 03 2023
EAN/ESC: Brain & Heart interactions

SPS04_1
Cardiac interventions to protect brain health

J. Kovac
Department of Cardiology, Glenfield Hospital, Leicester, UK

SPS04_2
The stroke-heart-syndrome

M. Endres
Klinik und Hochschulambulanz für Neurologie mit Experimentelle Neurologie, Charité-Universitätsmedizin Berlin, Berlin, Germany

After ischemic stroke, there is a significant burden of cardiovascular complications, both in the acute and chronic phase. Severe adverse cardiac events occur in 10% to 20% of patients within the first few days after stroke and comprise a continuum of cardiac changes ranging from acute myocardial injury and coronary syndromes to heart failure or arrhythmia. Recently, the term stroke-heart syndrome was introduced to provide an integrated conceptual framework that summarizes neurocardiogenic mechanisms that lead to these cardiac events after stroke. New findings from experimental and clinical studies have further refined our understanding of the clinical manifestations, pathophysiology, and potential long-term consequences of the stroke-heart syndrome. Local cerebral and systemic mediators, which mainly involve autonomic dysfunction and increased inflammation, may lead to altered cardiomyocyte metabolism, dysregulation of (tissue-resident) leukocyte populations, and (micro-) vascular changes. However, at the individual patient level, it remains challenging to differentiate between comorbid cardiovascular conditions and stroke-induced heart injury. Therefore, further research activities led by joint teams of basic and clinical researchers with backgrounds in both cardiology and neurology are needed to identify the most relevant therapeutic targets that can be tested in clinical trials. (see Scheitz et al JAHA, 2022 and Scheitz et al. Lancet Neurology. 2018)

Disclosure: Acknowledgements
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Conflicts of interest
ME reports grants from Bayer and fees paid to the Charité from Abbot, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Daiichi Sankyo, Sanofi, Novartis, Pfizer, all outside the submitted work.

SPS04_3
Takotsubo syndrome – neuronal mechanisms

C. Cordonnier
Department of Neurology, Hôpital Roger Salengro CHU, Lille, France

SPS04_4
Dementia prevention and Carotid endarterectomy – 20 years of experience

A. Halliday
Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK

EJON: Cognitive impairment beyond neurodegenerative and vascular dementias

SPS05_1

Cognition and Epilepsy

M. Miatton
Department of Neurology, University Hospital Ghent, Ghent, Belgium

Cognition and Epilepsy – Marijke Miatton It is estimated that worldwide 70 million people suffer from chronic epilepsy. Cognitive deficits in patients with epilepsy are common and may have a considerable impact on daily life functioning, professional activities and quality of life. Although for a long time the presence of cognitive deficits has been attributed to an accumulation of cerebral damage due to uncontrolled epilepsy, we now know that also patients with new onset epilepsy can display cognitive shortcomings. Both patients with new onset epilepsy and patients with refractory epilepsy can display deficits in attention/executive functioning, memory, psychomotor speed, language, visuospatial abilities and social cognition. The etiology, the type of epilepsy, seizure frequency and severity, treatment and psychiatric comorbidities are related to these cognitive deficits. In this talk, I will discuss the cognitive profile of adult patients with epilepsy as well as the effects of treatment (AED, surgery, brain stimulation) on cognition.
Disclosure: Nothing to disclose.

SPS05_2

Cognition and Multiple Sclerosis

I.K. Penner
Department of Neurology, Inselspital Bern University Hospital, Bern, Switzerland

SPS05_3

Cognition and COVID-19

F. Chollet
Department of Neurology, CHU Toulouse Purpan - Hôpital Pierre Paul Riquet, Toulouse, France

SPS05_4

Cognition and Migraine

I. Martins
Department clinical neurociences, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Migraine is an old disorder that became an exciting field of research in recent years, with new evidence on pathogenesis and treatment. Is typically characterized by episodes of headache, its spectrum of symptoms extends far beyond pain and include cognitive complaints and atypical sensory processing. During migraine attacks patients often experience difficulties in word retrieval, working memory and a slowing of processing speed, resulting in an increased mental effort to accomplish daily tasks. These symptoms, that contribute to disability, cannot be entirely attributed to headache because they are present in the prodromal and post ictal phases and persist after the relief of pain. This reversible cognitive decline has been documented in evaluations performed during migraine attacks and may be attributed to changes in brain networks that fluctuate along the migraine cycle. Moreover, outside the attacks, migraine patients report cognitive complaints more frequently than subjects without headache. According to some studies and a metanalysis they may have a worse cognitive performance than controls, particularly those with frequent or chronic forms of migraine. Several factors may account for these findings, namely migraine comorbidities (sleep disorders, anxiety and depression), the effects of preventive medication and subclinical white matter changes, that are more common in this population. These observations raise the question of the relative risk of age-related cognitive decline associated with migraine. This is relevant given the high prevalence of migraine in the population, but the evidence is controversial and it remains an ongoing topic of research.
Disclosure: Nothing to disclose.

EAN/EPA: COVID-19 at the crossroads of Neurology & Psychiatry

SPS06_1

The triple threat of COVID-19 to mental health

L. De Picker
University Psychiatric Hospital Duffel and University of Antwerp, Antwerp, Belgium

For over three years, the COVID-19 pandemic has continued to challenge us with new variants and complications. It has long been known that acute infections– such as influenza, rubella, and more recently MERS, SARS and Covid-19 – can trigger acute and late-onset psychiatric presentations, and neuroscience researchers and clinicians have thus been warning that we could see new-onset mental health problems as a late consequence of the pandemic. Research findings from around the world are now confirming this "triple threat" of COVID-19 on our global mental health: [1] Increased levels of subclinical and clinical mental health problems are observed in the population in general, and among women, young people, and healthcare workers in particular; [2] Acute and chronic neuropsychiatric complications in 20-50% of COVID-19 survivors; and [3] Morbidity, mortality and vaccination gaps among people with pre-existent mental disorders. In the next decade, mental health workers and services will need adequate guidance and resources to deal with the mental health fallout of the pandemic. Dr. De Picker will discuss the probable impact on services and actions which need to be taken to prepare for this challenge.
Disclosure: Nothing to disclose.

SPS06_2

Psychiatric post-COVID-19 conditions

K. Adorjan
Department of Psychiatry and Psychotherapy, LMU University Hospital, Munich, Germany

SPS06_3

The clinical spectrum and pathogenesis of neurological COVID-19 manifestations

F. Cavallieri
Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS of Reggio Emilia, Reggio Emilia, Italy

Coronavirus disease 2019 (COVID-19) presents with complex clinical features and frequently involves the peripheral and central nervous systems. The most common acute and subacute symptoms of the disease include fatigue, myalgia, anosmia, ageusia, headache, and sleep disturbances. Encephalopathy, ischemic stroke, seizures, and autoimmune peripheral neuropathies represent the most common clinical syndromes associated with COVID-19. Depending on the specific manifestation, neurologic manifestations can rely on different pathogenetic mechanisms, including viral neurotropism, systemic inflammatory response (with the so-called cytokine storm), endothelitis with vascular damage and ischemia, hypercoagulation state with thrombosis and hemorrhages, and autoimmune reactions. In the first year of the outbreak, the information available about neurological manifestations of COVID-19 was based on case reports and retrospective clinical series, sources which are open to selection bias. Subsequently, several prospective cohort studies and registries have assessed in detail the clinical course of patients with neurological manifestations of COVID-19 and the impact of pre-existing neurological diseases on infection (like the EAN Euro-covid ReGistrY Consortium, ENERGY). However, little is known about the long-term consequences of the infection, the so-called long-COVID syndrome, which may be characterized by several neurological manifestations. In this setting neurologists are likely to require an understanding of relevant symptoms to develop optimal management strategies and services. Furthermore, the possible role of SARS-CoV-2 as a trigger for the development of neurodegenerative diseases has yet to be fully elucidated, highlighting the need for a longitudinal accurate follow-up of patients affected by COVID-19.
Disclosure: Nothing to disclose.

SPS06_4

Post-COVID-19: What is the role of neurorehabilitation?

S. Filipovic
Department of Neurology, Human Neuroscience Group, Institute for Medical Research, University of Belgrade, Serbia

Following recovery from COVID-19, a considerable proportion of people develop various psychiatric and neurologic symptoms. COVID-19 is associated with high levels of emotional distress, including anxiety and depression, leaving some people with post-traumatic stress symptoms and post-traumatic stress disorder. Neurologic symptoms may develop in 30 - 45% of people following recovery from COVID-19. They range from general symptoms (such as headache, dizziness, fatigue, muscle aches, and problems with memory and attention/ concentration), to more specific ones (such as orthostatic intolerance, tinnitus, loss of taste, loss of smell, and neuralgias and other sensory symptoms). Some of these symptoms are amenable to pharmacological therapies used for similar symptoms in other conditions, but in a considerable proportion of patients, this is not enough good. Although high-quality evidence is still lacking, from sporadic studies, case reports, and everyday experience, it can be concluded that a complex multidisciplinary approach is needed in the rehabilitation of the people affected by these post-COVID-19 symptoms. This should involve careful assessment for the presence of psychiatric and neurologic symptoms, not only during COVID-19 but also several months after the illness. Although most people will recover with reassurance and compassionate support from the treating practitioners, a non-negligible proportion of people would require complex professional management. This should consist of psychological, physiotherapy, and occupational therapy interventions tailored towards specific needs, with social services support when required. For people with severe symptoms, this type of care could be provided best in specialised neurorehabilitation facilities. However, given the scale of the pandemic, to cope with the number of people that (would) need help eventually, it will be necessary to develop appropriate capacities and expertise within community services.

Disclosure: Nothing to disclose.

Oral Presentations

Saturday, July 01 2023
Cerebrovascular diseases 1

OPR-001

Thrombus detection in the left atrial appendage during acute stroke imaging using extended CT angiography

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Background and aims: Current guidelines recommend transthoracic echocardiography (TTE) for routine screening of cardiac emboli, however the visualisation of the LAA where the thrombi are commonly found is poor. Transesophageal echocardiography (TEE) would provide better detectability of LAA thrombus, but it is time-consuming and semi-invasive method. Extending non-gated carotid CTA examination to the LAA could reliably detect thrombi, and could also aid treatment and secondary prevention of stroke.
Methods: We extended the CTA scan range of acute stroke patients 4cm below the carina to include the left atrium and appendage. During the review we evaluated LAA thrombi based on contrast relations. We then used partial least squares (PLS) to identify the most important predictors of LAA thrombi from a variety of different clinical parameters.
Results: We examined 214 acute stroke patients' extended CTA scans. We detected LAA thrombi in six cases (2.8%), four of them had atrial fibrillation. 22.43% of all patients (48 cases) had recently discovered or previously known atrial fibrillation. Windsack and cauliflower morphologies were the most common LAA morphologies associated with filling defect. According to the PLS analysis, tricuspidal insufficiency, atrial fibrillation, smoking, congestive heart failure, diabetes and age showed the most predictive value for thrombi.
Conclusion: Our extended CTA scans reliably detected LAA thrombi even in cases where TTE did not, and showed that two patients' LAA thrombus would have been untreated based on ECG monitoring and TTE. We also showed that the benefits of CTA outweigh the disadvantages arising from the slight amount of excess radiation.
Disclosure: The study was supported by a GINOP-2.3.2-15-2016-00034 grant, an EFOP-3.6.1-16-2016-00008 grant, by a Horizon 2020 grant (H2020-MSCA-RISE-2016 734718), NAP 2.0 (2017-1.2.1-NKP-2017-00002) and the National Brain Research Program (KTIA_13_NAP-A-II/20).

OPR-002

Susceptibility vessel sign, a predictor of long-term outcome in stroke patients treated with mechanical thrombectomy.

M. Beyeler[1], L. Weber[1], N. Belachew[3], E. Aleman[3], M. Kielkopf[1], C. Kurmann[2], L. Grunder[2], E. Piechowiak[2], T. Meinel[1], M. Heldner[1], D. Seiffge[1], S. Pilgram-Pastor[2], T. Dobrocky[2], T. Pabst[4], M. Berger[4], S. Jung[1], M. Arnold[1], J. Gralla[2], U. Fischer[5], A. Mujanovic[2], J. Kaesmacher[2]
[1]Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland, [2]Institute for Diagnostic and Interventional Neuroradiology, Inselspital, Bern University Hospital, and University of Bern, Switzerland, [3]Department of Neuroradiology, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Germany, [4]Department of Medical Oncology, Inselspital, Bern University Hospital, and University of Bern, Switzerland, [5]Neurology Department, University Hospital of Basel, University of Basel, Basel, Switzerland

Background and aims: The absence of susceptibility vessel sign (SVS) in patients treated with mechanical thrombectomy (MT) is associated with poor radiological and clinical outcomes after three months. Underlying conditions, such as cancer, are assumed to influence the SVS status and could potentially impact the long-term outcome. We aimed to assess the SVS status as an independent predictor of long-term outcomes in MT-patients.
Methods: SVS status was retrospectively determined in consecutive MT-patients at a comprehensive stroke center between 2010 and 2018. Predictors of long-term mortality and poor functional outcome (modified Rankin Scale [mRS] $\geq$ 3) were identified using multivariable cox and logistic regression, respectively.
Results: Out of the 558 patients included, SVS was absent in 13% (n=71) and present in 87% (n=487) on baseline imaging. Patients with absent SVS were more likely to have active cancer (P=0.003) and diabetes mellitus (P<0.001) at the time of stroke. The median long-term follow-up time was 1058 days (interquartile range 533-1671 days). The absence of SVS was associated with long-term mortality (adjusted hazard ratio [aHR] 2.11, 95% CI 1.35-3.29, Figure 1) and poor functional outcome (adjusted odds ratio [aOR] 2.90, 95% CI 1.29-6.55, Figure 2). This was also the case for active cancer (aHR 3.08, 95% CI 1.93-4.91, and aOR 3.97, 95% CI 1.53-10.28) and diabetes mellitus (aHR 1.78, 95% CI 1.19-2.64, aOR 2.85, 95% CI 1.39-5.85).

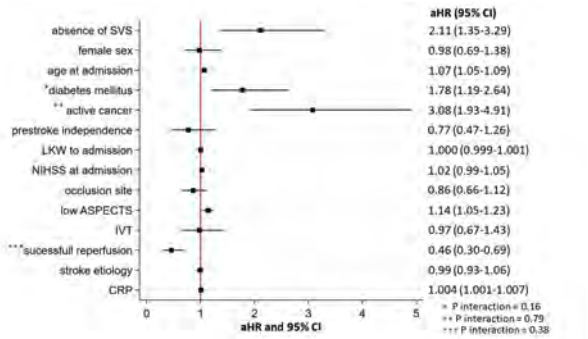

Figure 1. Association between long-term mortality and demographics, relevant risk factors, and stroke parameters.

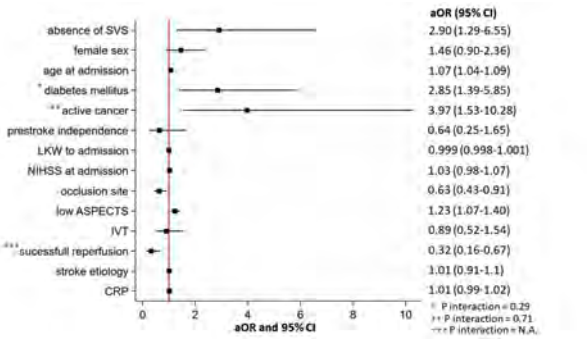

Figure 2. Association between long-term mortality and demographics, relevant risk factors, and stroke parameters.

Conclusion: Patients with absence of SVS have a poorer long-term functional outcome. This could results from an underlying cancer, diabetes mellitus or other underlying conditions not identified yet.

Disclosure: Dr. Kaesmacher reports grants from the Swiss Academy of Medical Sciences/Bangerter Foundation, Swiss Stroke Society, and Clinical Trials Unit Bern during the conduct of the study. Dr. Fischer reports grants during the conduct of the study from Medtronic, Stryker, and CSL Behring, unrelated to the submitted work. Dr. Gralla is a global principal investigator of STAR (Solitaire FR Thrombectomy for Acute Revascularisation), Clinical Event Committee member of the PROMISE study (Prospective, Multicenter, Observational, Single-Arm European Registry on the ACE Reperfusion Catheters and the Penumbra System in the Treatment of Acute Ischemic Stroke; Penumbra), and a principal investigator and consultant for the SWIFT DIRECT study (Solitaire With the Intention for Thrombectomy Plus Intravenous tPA Versus DIRECT Solitaire Stent-Retriever Thrombectomy in Acute Anterior Circulation Stroke; Medtronic) and receives Swiss National Science Foundation grants for magnetic resonance imaging in stroke. Dr. Arnold reports personal fees from Bayer, Bristol-Myers Squibb, Medtronic, Amgen, Daiichi Sankyo, Nestlé Health Sciences, Boehringer Ingelheim, and Covidien during the conduct of the study. Dr. Meinel reports research support from the Bangerter Rhyner Foundation, Swiss National Foundation, and the Swiss Heart Foundation.

OPR-003

Early neurological deterioration in minor stroke with isolated M2 occlusion: a retrospective multicenter study

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Background and aims: Patients with minor stroke and isolated M2 occlusion undergoing best medical management (BMM) may face early neurological deterioration (END) that can lead to poor long-term outcome. The purpose of this study was to define risk factors for unfavorable outcome in these patients and to identify possible predictors of END.

Methods: The databases of 16 high-volume stroke centers were retrospectively screened for consecutive patients with isolated M2 occlusion and a baseline National Institute of Health Stroke Scale (NIHSS) score ≤ 5 that received BMM (including intravenous thrombolysis when applicable) with the possibility of rescue mechanical thrombectomy (rMT) on END. Primary clinical outcome measure was a 90-day modified Rankin Scale score of 0-1.

Results: Among 208 patients available for analysis, END was reported in 87 patients that were therefore subjected to rMT. In a logistic regression model, END [OR, 3.386; 95% CI 1.428-8.032; p = 0.006], baseline NIHSS score [OR, 1.362; 95% CI 1.004-1.848; p = 0.047] and a pre-event mRS score = 1 [OR, 3.226; 95% CI 1.229-8.465; p=0.017] were associated with unfavorable outcome. In patients with END, rMT was associated with higher odds of favorable

outcome. Among baseline clinical and neuroradiological features, presence of atrial fibrillation was the only predictor of END [OR, 3.547; 95% CI 1.014-12.406; p=0.048].
Conclusion: Our study suggests that patients with minor stroke due to isolated M2 occlusion and concomitant atrial fibrillation, that are initially intended for BMM, should be closely monitored for possible worsening and, if END occurs, promptly considered for rMT.
Disclosure: Nothing to disclose.

OPR-004

Is occult cardioembolism a possible cause of multiple acute lesions in patients with minor ischemic stroke?

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Background and aims: Short-term dual antiplatelet treatment (DAPT) is recommended for secondary prevention of non-cardioembolic minor ischemic stroke or high-risk TIA. Despite optimal treatment, some patients have recurrent ischemic events possibly due to an occult cardioembolism. We aim to evaluate frequency of multiple acute ischemic lesions – radiological hallmark of cardio-embolism – in patients receiving DAPT in clinical practice.
Methods: The Real-life study on short-term dual antiplatelet treatment in patients with ischemic stroke or transient ischemic attack (READAPT) is a prospective, nationwide, multicentre, observational study, which has included patients with non-cardioembolic minor ischemic stroke or high-risk TIA receiving short-term DAPT in clinical practice since February 2021. The recruitment and 90-day follow-up are still ongoing.
Results: As of 8th January 2023, out of 1578 patients included from 62 centres, 1553 (98.4%) had a CT scan and 1153 (73.1%) an MRI scan. Among patients with a MRI scan, 251 (21.8%) had no acute lesions, 558 (48.4%) single and 344 (29.8%) multiple acute lesions. In this latter group, the event was mostly undetermined or due to large vessel occlusion (203, 59% and 106, 30.8% respectively), and more rarely (35, 10.2%) due to other defined cause; 272 (79%) had >24 hours cardiac monitoring in the acute phase. Seventy (20.3%) cases had multiple acute lesions in different vascular territories, of which 46 (65.7%) were of undetermined cause.
Conclusion: We found that around one third of patients receiving DAPT for minor stroke and TIA have multiple lesions, which were mostly due to arterial stenosis or undetermined cause.
Disclosure: No conflict of interests to disclose.

OPR-005

Thalamic strokes: contributions to sleep stability, topography and cognition in humans and mice.

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Background and aims: Thalamic vascular syndromes result in various clinical outcomes that may depend on the thalamic territory affected by the lesions. Here we sought to investigate the relationship between the thalamic topography of the lesion, sleep-wake regulation, and oscillatory activity in a novel stroke mouse model and stroke patients.
Methods: Fifteen thalamic stroke patients with age/gender-matched controls and optical mini-stroke (OPTO-Stroke) with SHAM control mice were included in the study. Diffusion-weighted images were used for the categorization of thalamic lesions. High-density and frontal-parietal EEG recordings were used in humans and mice to characterize sleep-wake architecture and oscillations. In mice, acoustic SW induction was used to recover stroke deficits.
Results: Patients with stroke lesions in the intralaminar (IL) or mediodorsal (MD) nuclei but not in the lateral-thalamus showed increased sleepiness ($p<0.001$), NREM1 percentage, and NREM2-NREM1 or NREM1-wake transitions ($p<0.01$) compared to controls. Remarkably, frontal EEG derivations decreased spindle power in humans and mice ($p<0.001$). Interestingly, medial thalamic strokes in mice showed decreased IL-prefrontal cortex connectivity that correlated with deficits in sleep, spindling, working memory, and pain that were generally recovered after acoustic SW therapy.
Conclusion: Our work confirms previous reports on the role of thalamic regulation of sleep and spindle dynamic and provides with novel insights into specific thalamic sub-networks linked to sleep, sensory processing, and cognition. Moreover, based on the mouse model data, typical working memory and pain deficits may be due to changes in frontal thalamocortical connectivity. Importantly, it identifies potential targets for sleep-related therapies.
Disclosure: Authors have nothing to disclose.

MS and related disorders 1

OPR-006

Optimal responders to platform disease modifying therapies in the Italian MS Registry

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Background and aims: The superiority of early introduction of high-efficacy disease modifying therapies (heDMT) in relapsing Multiple Sclerosis (MS) is being increasingly recognized. The objective of this study is to identify the proportion and characteristics of patients who can obtain greater benefits from platform DMT (pDMT).

Methods: Relapsing MS patients starting a pDMT (interferons, glatiramer acetate, teriflunomide, dymethilfumarate, azathioprine), with follow-up ≥10 years (n=7852) were extracted from the Italian MS Registry. Six-month confirmed disability accrual (CDA) was defined as an increase in Expanded Disability Status Scale (EDSS) score. Optimal responders to pDMT (patients remaining on pDMT and without any CDA) were compared with patients remaining on pDMT experiencing a CDA and patients switching to heDMT using multinomial regression models.

Results: Over a follow-up of 14.7+/-3.8 years, 2112 (26.9%) patients were optimal responders to pDMT, while 2238 (28.5%) experienced a CDA and 3502 (44.6%) switched to a heDMT. As compared with patients still on pDMT and those experiencing a CDA, optimal responders had younger age (OR=0.96, 95%CI 0.95-0.97, p<0.001) and shorter disease duration at baseline (OR=0.97, 95%CI 0.96-0.98, p<0.001). As compared with switchers, optimal responders had older age (OR=1.03, 95%CI 1.02-1.04, p<0.001), shorter disease duration (OR=0.98, 95%CI 0.97-0.99, p<0.001), lower EDSS at baseline (OR=0.76, 95%CI 0.72-0.80, p<0.001) and monofocal onset (OR=1.26, 95%CI 1.05-1.51, p=0.011).

Conclusion: In this real-world population, the majority of patients initially treated with pDMT had poor outcomes or switched to heDMT in the long term. PDMT might be considered in young adults with monofocal onset, short disease duration and low disability levels. The analysis on magnetic resonance imaging and cerebrospinal fluid parameters is ongoing.

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OPR-007

Abstract withdrawn

OPR-008

Retinal layer thickness predicts disability accumulation in early relapsing multiple sclerosis

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Background and aims: Thickness of peripapillary retinal nerve fiber layer (pRNFL) and macular ganglion-cell-and-inner-plexiform layer (GCIPL) measured by optical coherence tomography (OCT) have not been studied as predictors of disability accumulation in the context of first clinical manifestation of relapsing multiple sclerosis (RMS).

Methods: From a prospective observational study, we included patients with newly diagnosed RMS and obtained spectral-domain OCT scan within 90 days after RMS diagnosis. Impact of pRNFL and GCIPL thickness for prediction of disability accumulation (confirmed Expanded Disability Status Scale score ≥3.0) was tested by multivariate (adjusted hazard ratio [HR] with 95% confidence intervals [CI]) Cox regression models.

Results: We analyzed 231 MS patients (mean age 30.3 years [SD 8.1], 74% female) during a median observation period of 61 months (range: 12 - 93). EDSS ≥3 was reached 28 patients (12.1%) after a median 49 months (9 – 92). EDSS ≥3 was predicted with GCIPL <77µm (HR 2.7, CI: 1.6 – 4.2, p<0.001) and pRNFL thickness ≤88µm (HR 2.0, CI: 1.4 – 3.3, p<0.001). Higher age (HR 1.4 per 10 years, p<0.001), incomplete remission of first clinical attack (HR 2.2, p<0.001), ≥10 MRI lesions (HR 2.0, p<0.001) and infratentorial MRI lesions (HR 1.9, p<0.001) were associated with increased risk of disability accumulation, while highly effective DMT was protective (HR 0.6, p <0.001). Type of first clinical attack and presence of oligoclonal bands were not significantly associated.

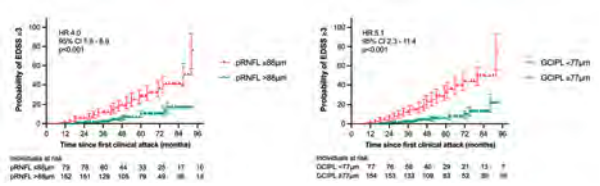

Figure 1. Risk of EDSS ≥3 depends on retinal layer thickness. Cumulative fraction (percentage) of patients reaching EDSS ≥3 according to (A) peripapillary retinal layer thickness (pRNFL) ≤/>88µm and (B) ganglion cell and inner plexiform layer (GCIPL)

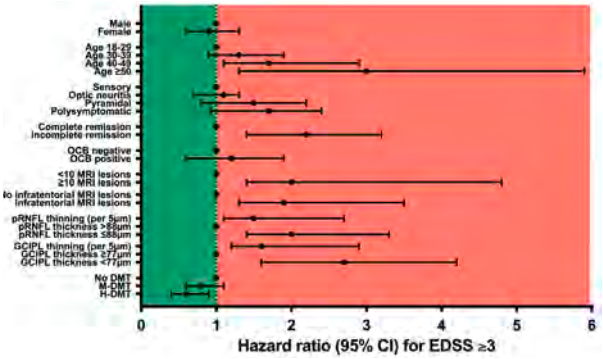

Figure 2. Effect of baseline clinical, CSF, MRI and OCT factors on risk for EDSS ≥3. Hazard ratios (HR) and 95% confidence intervals (CI) for reaching EDSS ≥3 calculated by multivariate Cox proportional hazard regression models.

Conclusion: Retinal layer thickness (GCIPL more than pRNFL) is a useful predictor of future disability accumulation in RMS, independently adding to established markers.

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OPR-009

Kappa Free Light Chain and Neurofilament Light independently predict early Multiple Sclerosis Disease Activity

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Background and aims: Inter-individual courses of multiple sclerosis (MS) are extremely variable. The objective of this study was to investigate whether κ-free light chain (κ-FLC) index and serum neurofilament light (sNfL) have an additive predictive value for MS disease activity.

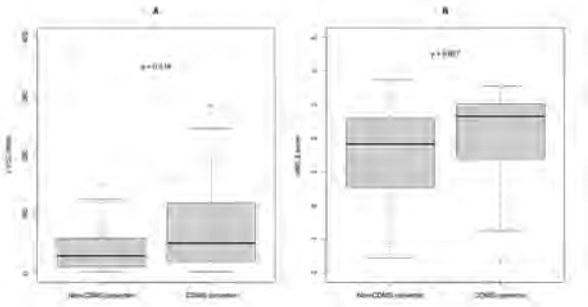
Methods: Patients with early MS and cerebrospinal fluid (CSF)/ serum sampling at disease onset were followed for four years. At baseline, age, sex, disease duration, number of T2-hyperintense (T2L), and contrast-enhancing T1 lesions (CEL) on MRI were determined. During follow-up, occurrence of relapse and start of disease-modifying treatment (DMT) were registered. κ-FLC index was calculated as [CSF κ-FLC/serum κ-FLC]/albumin quotient. For sNfL, age- and body-mass-index adjusted Z scores were calculated.

Results: Of 86 patients (mean age 33±10 years, 67% females), 36 (42%) experienced relapse during follow-up. Cox regression analysis adjusted for age, sex, T2L, CEL, disease and follow-up duration, and DMT use during follow-up revealed that both κ-FLC index and sNfL Z score independently predict time to relapse. The chance for freedom of relapse within 12 months was 2% in patients with high levels of κ-FLC index (>100) and high sNfL Z score (>3), 30% in patients with high κ-FLC index (>100) and lower sNfL Z score (≤3), 70% in patients with lower κ-FLC index (≤100) but high sNfL Z score (>3), 90% in patients with lower levels of κ-FLC index (≤100) and sNfL Z score (≤3).

Conclusion: κ-FLC index and sNfL Z score are predictive for early MS disease activity not only additive to known (para)clinical predictors but also independent of each other.

Disclosure: This study was funded by a grant of the Austrian Multiple Sclerosis Society (charitable foundation).

Figure 1: Increased κ-FLC index and sNfL Z score in patients who convert to CDMS



Legend:

(A) κ-FLC index at baseline is significantly higher in patients who convert to CDMS during 4-year follow-up compared to patients who remain relapse-free.

(B) sNfL Z score at baseline is significantly higher in patients who convert to

Figure 2: Relapse free probability at 12 months depending on κ-FLC index and sNfL Z score

		sNfL Z score		
		≤1.5	>1.5 – 3	>3
κ-FLC index	≤6.1	98%	91%	81%
	>6.1 – 100	97%	84%	68%
	>100	71%	17%	2%

Legend:

The probability of staying relapse-free within 12 months after disease onset is given for each of the possible combinations of negative, elevated and highly elevated κ-FLC index and sNfL Z score.

Abbreviations: κ-FLC, κ free light chain; sNfL, serum neurofilament light

OPR-010

Age-related disability accrual in Multiple Sclerosis: when it starts and how progresses over time

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Background and aims: The objectives of this study were to assess the age-related incidence and predictive factors of the first 48-week confirmed progression independent of relapse activity (PIRA) events and to compare disability trajectories between three subgroups with pediatric (POMS), adult (AOMS) and late (LOMS) multiple sclerosis onset.

Methods: MS patients with ≥5-year follow-up and ≥1 visit every 6 months were selected from the Italian MS Registry. Age-related cumulative incidence, risk of reaching the first PIRA events and disability trajectories were assessed by Kaplan–Meier curves, multivariable Cox models and longitudinal models for repeated measures, respectively.

Results: 3777 RMS patients (268 POMS, 3282 AOMS and 227 LOMS) were included. The first 48-week-confirmed PIRA occurred in 844 (22.3%). The cumulative incidence of the first PIRA (from 0% to 1.3% between 10-20 years; 1.3%-9.0% between 20-30 years; 9%-21.6% between 30-40 years; 21.6 %- 39.1% between 40-50 years; 39.1%-60.8%, between 50-60 years; 60.8%-78.7% between 60-70 years) and the relative contribution of PIRA to overall CDA increased with age. Age and relapses significantly predicted the risk of PIRA (p=0.03). The slope of disability trajectories over 5 years was significantly lower in POMS than in AOMS and LOMS (p<0.004).

Conclusion: PIRA events are rare in childhood. The cumulative incidence increases with increasing age. Age and relapses are the most significant drivers of PIRA. POMS show a less steep increase in EDSS scores over time than older patients. These findings indicate that age remains highly relevant in determining the onset and the rate of disability progression in MS.

Disclosure: The authors report no conflicts of interest with respect to the contents of the current study, but note that the patients in the study were treated with a number of disease-modifying drugs and that authors have received advisory board, membership, speakers honoraria, travel support, research grants, consulting fees or clinical trial support from the manufacturers of those drugs, including Actelion, Allergan, Almirall, Bayer Schering, Biogen, Celgene, Excemed, Genzyme, Forward Pharma, Ipsen, Medday, Merck, Merz, Mylan, Novartis, Sanofi, Roche, Teva and their local affiliates.

Muscle and neuromuscular junction disorder; Motor neurone diseases

OPR-011

3D in vitro models to identify early neuronal vulnerability and test therapies in C9ORF72-Amyotrophic Lateral Sclerosis

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Background and aims: Amyotrophic lateral sclerosis (ALS) is an untreatable neurodegenerative disorder whose pathogenic mechanisms are still incompletely understood. C9ORF72, whose hexanucleotide repeat expansion (HRE) represents the main genetic cause of ALS, has been postulated to play a role in neurodevelopment. To investigate whether early developmental vulnerability in ALS could result in late onset neurodegeneration, we will exploit 3D patient-specific in vitro models of central nervous system (CNS).
Methods: We generated induced Pluripotent Stem Cell (iPSC)-derived brain (BrOs) and spinal cord (ScOs) organoids of C9ORF72-ALS patients and isogenic controls, using a free-floating, 3D-culture method, based on EBs aggregation, matrigel embedment and agitation in spinning bioreactor. Structural and functional characterization was performed. Organoids were treated with an antisense oligonucleotide (ASO) targeting C9ORF72-HRE.
Results: BrOs and ScOs expressed pluripotency markers and mature neuronal markers in early and late stages, respectively. C9ORF72-ALS organoids presented higher rate of cell death and a lower degree of maturity compared to isogenic controls. C9ORF72-ALS organoids recapitulated disease hallmarks and displayed disrupted key cellular processes, like DNA and axonal damage. BrOs and ScOs are functionally active at calcium imaging recording but behave differently after glutamate stimulation, suggesting a different neuronal excitability in ALS. Treatment with C9ORF72-directed ASO was effective in ameliorating disease phenotype.
Conclusion: Patient-specific iPSC-derived 3D-CNS models reproduce at different time points the maturation of neural and glial cells, resembling physiologic human neurodevelopment. BrOs and ScOs are valuable tools for disease modeling since they improve the characterization of C9ORF72-ALS pathology, dissecting specific disease hallmarks, and provide the opportunity to test therapeutic strategies.
Disclosure: Nothing to disclose.

OPR-012

Discovering disease specific metabolites in Amyotrophic Lateral Sclerosis (ALS): new direction to personalised medicine?

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Background and aims: We employed a new methodology for applying Mendelian randomization (MR) across hundreds of exposures simultaneously and identified metabolites toxic or protective for Amyotrophic Lateral Sclerosis (ALS).
Methods: An unbiased screen of 974 serum metabolites was conducted using MR to identify metabolites that may modify the risk of ALS. We identified three metabolites of interest for ALS. We also analysed shotgun metagenomic sequencing data from the faecal samples from ALS patients (n=37) and controls (n=29) to identify bacterial diversity and metabolic pathways in ALS and controls.
Results: We identified a protective role for serum estrone-3 sulfate and bradykinin and a harmful role for serum isoleucine. Isoleucine metabolism consumes vitamin B12. MR for vitamin B12 revealed a protective effect on ALS (Fig:1B,1C); in fact, the effect of isoleucine was conditioned on vitamin B12 as measured by multivariable MR. Probing the bacterial pathways for isoleucine biosynthesis revealed 407 bacteria involved in five different isoleucine synthesis pathways. Interestingly, the most upregulated bacteria found in ALS, Catenibacterium mitsuokai is involved in isoleucine biosynthesis (Fig:2B).

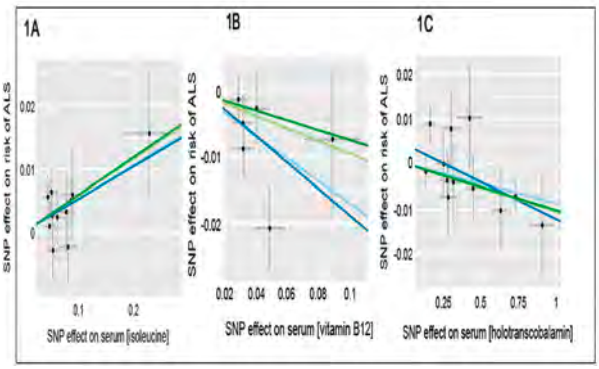

Figure 1: Scatter plots demonstrating positive correlation of serum A) Isoleucine and negative correlation of B) Vitamin B12 and C) Holotranscobalamin concentrations with SNP effect on ALS risk.

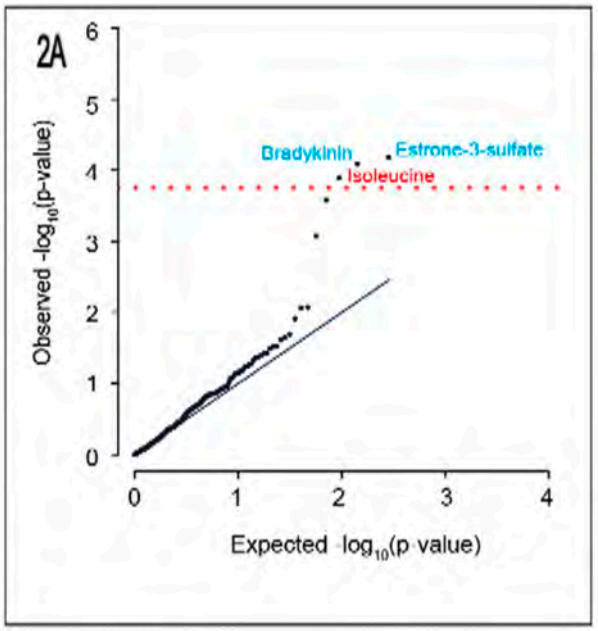

Figure 2: A) QQ-plot demonstrates three metabolites including isoleucine were significant after Bonferroni multiple testing correction (red line). Blue text denotes a protective association whereas red text denotes a harmful association.

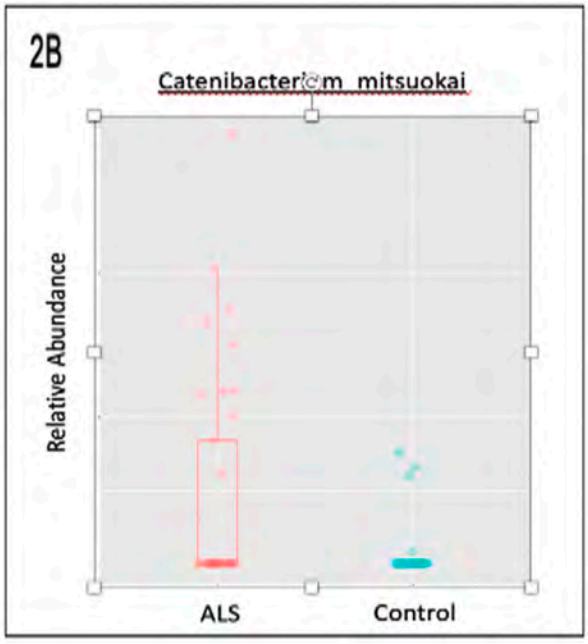

Figure 2: B) Of the 407 bacteria considered, most up regulated in ALS is Catenibacterium mitsuokai which is implicated in Isoleucine biosynthesis.

Conclusion: Our analysis shows that higher serum isoleucine increases the risk of ALS via the depletion of vitamin B12. A bacterium involved in Isoleucine synthesis was found to be in higher abundance in ALS patients' guts. Further large-scale population-based microbiome-metabolome study is required to consolidate the impact of this discovery and in the future, it has the potential to develop as a personalized treatment strategy for ALS e.g. antibiotic, probiotic or faecal transplants.
Disclosure: Nothing to disclose.

OPR-013

Characteristics of patients with Late Onset Pompe Disease in France: insights from the French Pompe registry in 2022

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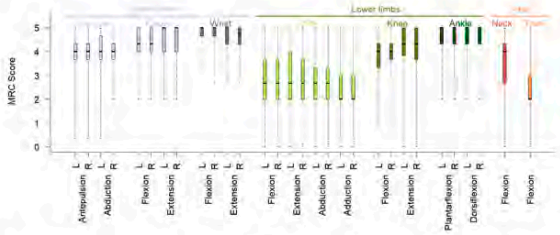
Background and aims: The French Pompe disease registry was created in 2004, for studies of the natural course of the disease in patients. It rapidly became a major tool for assessing the long-term efficacy of enzyme replacement therapy (ERT) following the market release of alglucosidase-alfa.

Methods: Almost 10 years after publication of the baseline characteristics of the 126 patients of the registry, we provide here an update of the clinical and biological features of patients included.

Results: We describe 210 patients followed at 31 hospitals-based French neuromuscular centers. The first symptom was progressive lower limb muscle weakness; either isolated (50%) or associated with respiratory symptoms (18%), at a median age of 38 ± 14.9 years. Positive associations were found between Motor Function Measure, Manual Motor Testing, and 6-Minutes-Walking-Test (6MWT), and these parameters were inversely associated with the time taken to sit up from a lying position at inclusion time. Comparison of two matched group of 24 untreated and 158 treated Pompe disease patients showed significant difference between evolution over time on 6MWT ($p<0.001$) and on sitting forced vital capacity (FCV) ($p=0.002$).

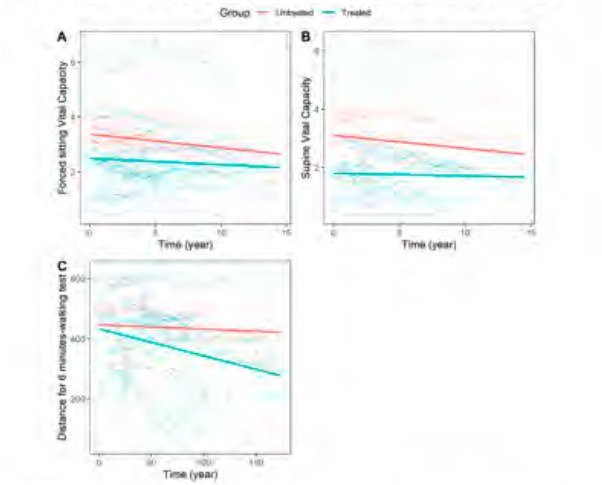
Figure 1: Clinical topography of muscle weakness



Box plots are drawn for sub scores of the MRC scale. The median is indicated by the line bisecting the box. The box represents the middle 50% of scores: the interquartile range. The upper and lower whiskers represent the minimum and maximum scores.
L: Left, R: Right.

- The more severe weakness predominates for hip muscles. Median score is under 3/5 for flexion, extension, abduction and adduction of the hips, corresponding to inabilities for an active movement against gravity.
- Axial weakness predominates for trunk muscles with a median score of 2/5, corresponding to an active movement with gravity eliminated.
- Distal motor function is more preserved with median score of 4/5 or more: wrist, ankle, and also elbow and knee.

Figure 3: Disease course of untreated patients vs patients treated by ERT: walk and respiration



A. *6-MWT*:
- At inclusion, no significant difference between both groups: 444.6 ± 36.7 meters for untreated, 13.5±46.6 meters lower, that is and 431.1 meters ($p=0.77$).
- Over time, untreated patients evolution is stable with a coefficient of -0.15 ± 0.2, evolution slope of treated patients is accentuated of 0.85 ± 0.2, that is a mean evolution of -1.00 ($p<0.001$).

B. *Sitting FVC*
- At inclusion, mean untreated value is 3.36 ± 0.3L, mean treated value is 0.75 ± 0.4 L lower, that is 2.61 ($p=0.056$).
- Over time, mean evolution of untreated patients is -0.07 ± 0.009 ($p<0.001$), and lesser of 0.02 ± 0.01 L for treated patients, that is -0.05 ($p=0.002$).

C. Supine FVC
- At inclusion, no significant difference between both groups: mean untreated value is 2.95 ±0.3 L, 0.82 ±0.5 L lower for treated patients, that is 2.13 ($p=0.08$).
- Over time, no significant difference between both groups: mean evolution for untreated patients is -0.07 ± 0.01 ($p<0.001$), and lesser for treated patients of 0.01 ± 0.01 L, that is -0.06 L ($p=0.40$).

Disease course of untreated patients vs patients treated by ERT: walk and respiration

Conclusion: The French Pompe disease registry provides an exhaustive, nationwide overview of Pompe disease, and allows the assessment of individual and global responses to future treatments. 6MWT remains an important method for assessing motor performance and walking ability. Untreated patient present a global stability for 6MWT and a lesser aggravation for sitting FCV compared to treated patients, suggesting several evolutionary patient's profiles.

Disclosure: Claire Lefeuvre receive fees for consulting and sponsoring for scientific congress by Sanofi-Genzyme. Françoise Bouhour and Emmanuelle Salort-Campana receive fees for participation to scientific boards and sponsoring for scientific congress by Sanofi-Genzyme and Amicus Therapeutics. Anthony Béhin, Shahram Attarian receive fees for participation to scientific boards and sponsoring for scientific congress by Sanofi-Genzyme. Aleksandra Nadaj Pakleza receive fees for participation to scientific boards by Sanofi-Genzyme and Amicus Therapeutics. Marco Spinazzi receive fees for participation to scientific boards by Sanofi-Genzyme. Celine Tard, Maud Michaud Anne-Laure Bedat-Millet receive sponsoring for scientific congress by Sanofi-Genzyme. JeanBaptiste Noury receive fees for participation to scientific boards by Amicus Therapeutics and sponsoring for scientific congress by Sanofi-Genzyme. Pascal Laforêt receive fees for participation to scientific boards by AMICUS Therapeutics, Sanofi Genzyme, Spark Therapeutics, consulting fees by Sanofi Genzyme, BioMarin, Sanofi Genzyme, Spark

Therapeutics and sponsoring for scientific congress by Sanofi Genzyme, Amicus Therapeutics, Spark Therapeutics. Marie De Antonio, Emmeline Lagrange, Sabrina Sacconi, Dalil Hamroun, Pascal Cintas, Guilhem Solé, Armelle Magot, Arnaud Lacour, Stéphane Beltran, Dimitri Renard, Anne-Laure Bedat-Millet, Hélene Prigent, Nadjib Taouagh, Azzeddine Arrassi have no conflict to declare.

OPR-014

CCDC78: unveiling the function of a novel gene associated to hereditary myopathy

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Background and aims: Congenital myopathies are a group of inherited disease caused by genetically determined muscle protein defects. The coiled-coil domain-containing protein 78 (CCDC78) gene has been suggested in 2012 by Majczenko et al. as novel candidate gene for the autosomal dominant centronuclear myopathy-4 (CNM4). However, to date, only one family has been described and CCDC78 role in muscle function remains unclear.

Methods: We deeply analyzed for the first time a family harbouring a CCDC78 nonsense mutation. We performed optic, electron microscopy study and multiple immunofluorescent assays on muscle biopsy. We analyzed CCDC78 transcripts and protein in different tissues from healthy and mutated subjects, and we performed transcriptome profiling by RNA-seq and RT-qPCR from muscle tissues. Coimmunoprecipitation assay and mass spectroscopy studies were carried on extracted muscle proteins from healthy and mutated subjects.

Results: Histopathological features encompassed, as novel disease hallmark, a peculiar dilated terminal sarcoplasmic reticulum with whirls of redundant membranes. We provided evidence of nonsense mediated decay, suggesting an haploinsufficiency mechanism, and we found novel CCDC78 transcripts selectively expressed in muscle. By RNA-seq, 1035 muscular differentially expressed genes (DEGs) were detected: they clusterized in specific pathways showing a statistically significant enrichment for functionally interesting biological processes including muscle contraction and development. Lastly, among the most significant DEGs, we identified the principal CCDC78 interactors in muscle.

Conclusion: Our findings clarify for the first time the specific CCDC78 muscle function and its pathomechanism. Our date expands the phenotype previously associated with CCDC78 gene mutation and allows us to definitely associate this candidate gene to CNM4.

Disclosure: The authors have no conflicts of interest to disclose.

OPR-015

Smoking and alcohol associated to the risk of developing Myasthenia gravis in a Swedish nationwide prevalent cohort

M. Petersson[1], D. Jons[2], A. Feresiadou[3], A. Ilinca[4], F. Lundin[5], R. Johansson[6], A. Budzianowska[7], A. Roos[8], V. Kågström[9], M. Gunnarsson[10], P. Sundström[11], L. Klareskog[1], T. Olsson[1], I. Kockum[1], F. Piehl[12], L. Alfredsson[1], S. Brauner[12]

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Background and aims: Myasthenia gravis (MG) is a complex disease, where lifestyle and environment are believed to contribute to the majority of the risk. Here, we examine the influence of smoking and alcohol on MG disease development.

Methods: In a cross-sectional prevalent cohort study, the Genes and Environment in Myasthenia Gravis study (GEMG), performed November 2018 - August 2019, Swedish MG patients were invited to submit an extensive questionnaire. Cases were matched to up to 15 randomly selected controls, based on year of birth, age at disease onset and sex. Smoking and alcohol habits were investigated in relation to disease onset using conditional logistic regression.

Results: The response rate was 74% covering 42% of the MG population in Sweden. We matched 796 patients to a total of 7380 controls. Alcohol use exhibited a dose-dependent protective association. Compared to no consumption, the OR for low, moderate and high alcohol consumption were 0.48 (0.39-0.59), 0.37 (0.28-0.49) and 0.30 (0.20-0.44) respectively, all P<0.001. Smoking at onset was associated to an increased risk of being a MG case (OR 1.63, 1.24-2.14, P<0.001) and when adjusting for alcohol

consumption the estimate increased (Figure 1). The risk of MG was however not associated to ever having smoked.

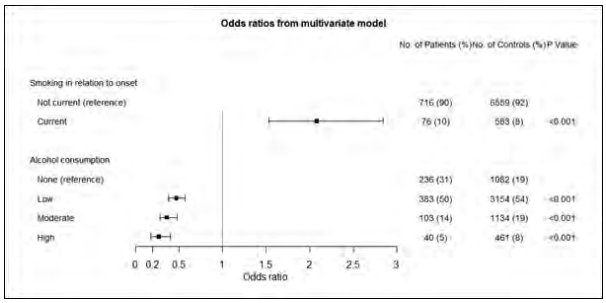

Figure 1. Odds ratios from multivariate model

Conclusion: Alcohol use is associated with a protective effect of developing MG. Alcohol use might be a negative confounder for smoking. Current smoking is associated with an increased risk of MG, and the association is stronger when controlling for alcohol consumption.

Disclosure: Malin Petersson has nothing to declare. Daniel Jons has nothing to declare. Amalia Feresiadou has nothing to declare. Andreea Ilinca has nothing to declare. Fredrik Lundin has nothing to declare. Rune Johansson has nothing to declare. Anna Budzianowska has nothing to declare. Anna-Karin Roos has nothing to declare. Viktor Kågström has nothing to declare. Martin Gunnarsson has nothing to declare. Peter Sundström has nothing to declare. Lars Klareskog has nothing to declare. Tomas Olsson has nothing to declare. Ingrid Kockum has nothing to declare. Fredrik Piehl has, unrelated to the current study, received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis. Lars Alfredsson has nothing to declare. Susanna Brauner has received grants from UCB Pharma unrelated to the current study.

MS and related disorders 2

OPR-016

Pregnancy Outcomes After Exposure to Dimethyl Fumarate in an Italian multicentric cohort of women with MS

D. Landi[1], S. Bartolomeo[1], F. Bovis[2], G. Borriello[3], M. Buccafusca[4], M. Cellerino[5], A. Conte[6], R. Docimo[7], R. Fantozzi[8], E. Ferraro[9], M. Foschi[10], A. Gallo[11], F. Granella[12], L. Lorefice[13], M. Lucchini[14], G. Mataluni[1], L. Moiola[15], C. Nicoletti[1], F. Patti[16], P. Ragonese[17], E. Signoriello[18], D. Vecchio[19], G. Marfia[1], O. DMF pregnancy Study Group[1]

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Background and aims: Dimethyl fumarate (DMF) is a widely used treatment for relapsing-remitting multiple sclerosis (RRMS), but evidence on its impact during pregnancy is limited. This retrospective, multicenter study aimed to assess maternal and fetal safety of DMF exposure during pregnancy.

Methods: Women with RRMS treated with DMF before conception and accidentally exposed to DMF during early pregnancy were identified from 29 Italian MS Centers. Clinical outcomes were collected from mothers and their newborns.

Results: We identified 147 pregnancies among 146 women interrupting DMF after conception, 124 were eligible for analysis. Median treatment duration was 19.13 months (3.00-72.89); 90 women restarted DMF after delivery (median interval 1.38 months (0.03-11.01)). DMF interruption at early pregnancy was not associated with increased relapse rate. ARR in the previous year 0.21 (95%CI:0.14-0.30), ARR during pregnancy 0.07 (95%CI:0.03-0.14), p=0.003). Multivariable analysis showed that higher age at conception (RR 0.87(95%CI:0.76-0.99) p=0.035), early therapy restart postpartum (<1 month) (RR 0.16 (95%CI:0.03-0.57) p=0.012) and breastfeeding (RR 0.22 (95%CI:0.03-0.89) p=0.069) were associated with lower relapse risk in the year after delivery. Recorded abortions/stillbirths were 12 and 1, respectively. 134 live births were analyzed. Mean fetal DMF exposure was 1.12 months (0.00-7.07), birth weight 3132.14 g (±433.29), length 49.71cm (±2.52). Minor congenital anomalies were reported in 5/134 newborns and hyperbilirubinemia in 1/134.

Conclusion: DMF interruption at early pregnancy is not associated with MS reactivation and prompt DMF restart after delivery is protective against postpartum relapses. Although further studies are needed, short fetal DMF exposure seems to not increase the risk of fetal complications.

Disclosure: "Doriana Landi received travel funding from Biogen, Merck Serono, Sanofi-Genzyme, Teva, Bristol Myers Squibb, Mylan, speaking or consultation fees from Sanofi-Genzyme, Merck Serono, Teva, Biogen, Roche, Novartis, Bristol Myers Squibb, Bayer-Schering. " DMF pregnancy study group includes: Bonavita S., Cavalla P., D'Amico E., Di Filippo M., Lanzillo R., Napoli F., Portaccio E., Realmuto S., Sinisi L., Stromillo ML, Tomassini V., Ziccone V.

OPR-017

Autologous hematopoietic stem cell transplantation may halt PIRA in early relapsing-remitting multiple sclerosis

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Background and aims: Progression independent of relapse activity (PIRA) seems the main driver of disability progression since early relapsing-remitting multiple sclerosis (RR-MS), with little effect of disease-modifying treatments (DMTs). The hypothesis that autologous haematopoietic stem-cell transplantation (AHSCT) could halt PIRA in RR-MS was explored by comparing AHSCT- vs natalizumab (NTZ)-treated patients.

Methods: Retrospective monocentric matched study on RR-MS patients treated with BEAM-AHSCT (cases) or NTZ (controls) at a single centre in Florence between 2007 and 2018. The cumulative proportion of patients with relapse, EDSS worsening, relapse-associated worsening (RAW), and PIRA was estimated using Kaplan-Meier analyses during treatment-epoch (censoring controls at NTZ discontinuation) and whole follow-up (including switch from NTZ to alternative DMTs).

Results: Thirty RR-MS were included in each group (Table 1). During treatment epoch, AHSCT was superior to NTZ on relapse suppression (p<0.001), but not on disability outcomes (Figure 1). Twenty-nine/30 patients discontinued NTZ after median 24 doses (range 9–59), mostly for JCV positivity (77%), and started alternative DMTs. During the overall follow-up (median 84.5 months), AHSCT was superior to NTZ+DMTs on all the outcomes except for PIRA, where the difference, although remarkable (11% vs 42% at year 8), was close to significance (p=0.068). Age and EDSS at baseline of treatments independently predicted PIRA (HR 1.12 and 1.59, respectively).

	AHSCT, n = 30		Natalizumab, n = 30		p value
	median	(range)	median	(range)	
Age at treatment, years	35	(20 – 53)	37.5	(18 – 63)	0.277
Disease duration at treatment, years	9.5	(1 – 22)	10.5	(0 – 26)	0.657
Previous treatment duration, years	6	(0 – 21)	6.5	(0 – 15)	0.463
Number of previous treatments	3	(0 – 7)	2	(0 – 5)	0.001
ARR in the previous 2 years *	1.30	(0.96 – 1.64)	1.21	(0.95 – 1.45)	0.592
EDSS at baseline	2.75	(1 – 7)	2.75	(0 – 6.5)	0.982
Delta-EDSS in the year prior to treatment	0.5	(-1.5 - 1.5)	0	(-1.5 – 2)	0.439
	n	(proportion)	n	(proportion)	p value
Gender, female	22	(73%)	23	(77%)	0.500
Naive to treatment at baseline	1	(3%)	2	(7%)	1.000

*reported as mean (95% confidence interval, CI)

Table 1: Baseline clinical-demographic characteristics of the AHSCT and NTZ patients included after propensity-score matching.

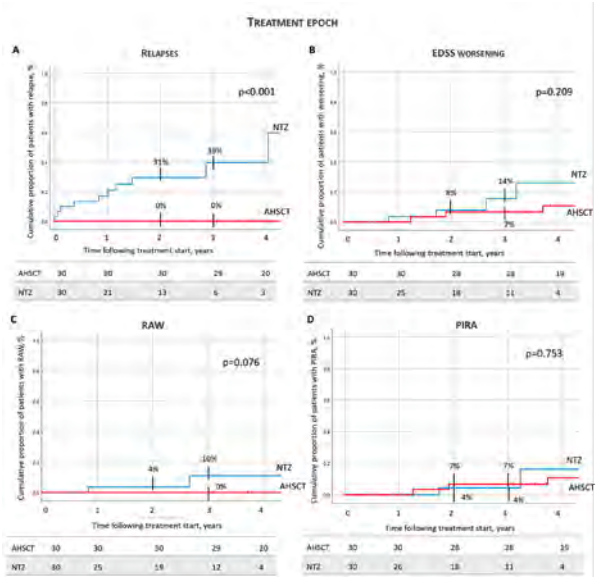

Figure 1: Outcomes during treatment epoch (i.e. NTZ patients censored at NTZ discontinuation). The proportion of cases with relapses was lower in AHSCT-treated than in NTZ-treated patients (A), without differences in disability outcomes (B, C, D).

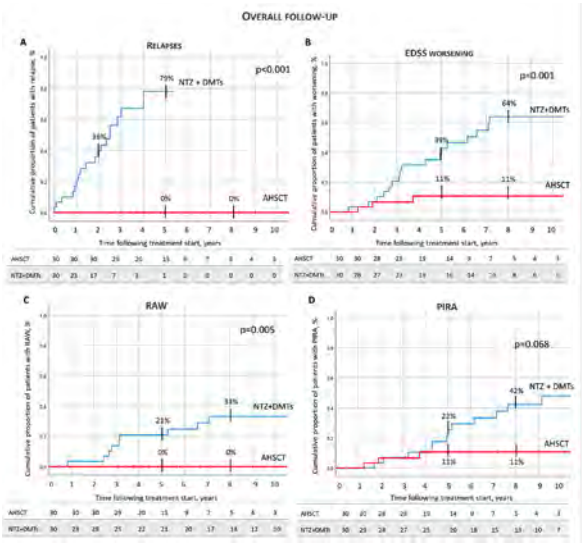

Figure 2: Outcomes over the whole follow-up (i.e including the period after NTZ discontinuation - NTZ+DTMs). AHSCT was superior to NTZ+DMTs in all the outcomes, except for PIRA, where a remarkable (close to significance) effect was also observed.

Conclusion: AHSCT was superior to NTZ in suppressing relapse-activity and to NTZ+DMTs on relapses, EDSS worsening and RAW, with a trend for possible superior effectiveness also on PIRA. Early treatment with highly effective DMTs active on compartmentalized inflammation might prevent PIRA in RR-MS.

Disclosure: Nothing to disclose.

OPR-018

Relevance of spatial correspondence between regional gene expression and gray matter atrophy in multiple sclerosis

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Background and aims: Specific regional gene expressions may contribute to a non-random gray matter (GM) atrophy in multiple sclerosis (MS). Here, we investigated the spatial associations between regional GM atrophy and gene expression in a large MS patients' cohort.
Methods: Brain 3T MRI, neurological and neuropsychological assessment were obtained from 286 MS patients and 172 healthy controls (HC). The spatial cross-correlations between regional GM atrophy patterns derived from voxel-based morphometry (VBM) and expressions of 2710 genes associated with MS provided by Allen Human Brain Atlas were explored using the MENGA platform. Using ToppGene Suite, enrichment analyses were performed to explore over-represented molecular functions and cellular components involving gene expressions significantly associated with VBM-derived GM maps ($p<0.05$, Bonferroni-corrected).
Results: Compared to HC, MS patients showed widespread GM atrophy being significantly associated with the regional expression of 74 genes, involved in synaptic GABA receptor functions and mitochondrial oxidoreductase activities. Lower volume in deep GM, cerebellum and left insula was significantly associated with a higher clinical disability and with the expression of 44 genes being enriched in the mitochondrial and cellular nucleoids. Cognitively-impaired (n=113) vs cognitively-preserved (n=173) MS patients had distributed GM atrophy being significantly associated with the expression of 64 genes involved in protein heterodimerization and oxidoreductase activities of mitochondrial and organelle membranes/envelopes.
Conclusion: Different regional expressions of genes involved in synaptic GABA receptor and mitochondrial oxidoreductase functions are associated with a clinically-relevant regional GM atrophy in MS. Such differences may influence regional susceptibility to MS-related excitatory/inhibitory imbalance, oxidative stress, and GM atrophy development.
Disclosure: The authors have nothing to disclose.

OPR-019

Functional correlates of intelligence quotient and cognitive abilities vary according to maturation in pediatric MS

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Background and aims: Clinical and cognitive features of pediatric multiple sclerosis (MS) differ from adult-onset patients. Here, we tested maturation effects on neuropsychological profiles and resting-state (RS) fnctional connectivity (FC) of pediatric MS.
Methods: Seventy-six pediatric MS underwent neuropsychological assessment of Wechsler-Intelligence-Scales for Intelligent Quotient (IQ), Semantic/Phonemic Verbal Fluency Test (SVFT/PVFT), Symbol Digit Modalities Test (SDMT), Coding (CD) and Block Design (BD), Trial Making Test (TMT-A/B). In 58 right-handed MS patients and 22 matched healthy controls, RS FC within executive, language, motor, default-mode and basal ganglia networks was estimated. Maturation effects were assessed by splitting pediatric MS in those <16 years (B16) (n=46) and those >16 years (A16) (n=30).
Results: Most patients (81.6%) achieved IQ scores at or above average values (median IQ=97.5). The most frequently failed test were the CD (21.1%), TMT-B (15.8%), TMT-A (10.5%), and SDMT (9.2%). In B16 patients, reduced RS FC in the basal ganglia, language, and sensorimotor networks was detected, which was associated ($p<0.05$) with poorer cognitive performance (r range=0.39/0.56). A16 patients showed reduced RS FC in basal ganglia, sensorimotor and language networks as well, but they also showed increased RS FC in the basal ganglia, default-mode, sensorimotor, executive, and language networks, which was associated ($p<0.05$) with a poorer performance in executive speed and language abilities (r range=-0.40/-0.59). In both groups, lower RS FC of the

caudate nucleus within sensorimotor, language and executive networks was associated with poorer IQ and cognitive performance.
Conclusion: Maturation significantly impacts on RS FC abnormalities and on their association with cognitive performances.
Disclosure: The authors have nothing to disclose.

OPR-020

Cerebrospinal fluid B cell and neuroaxonal damage biomarkers: correlation with relapses and long-term disability in MS

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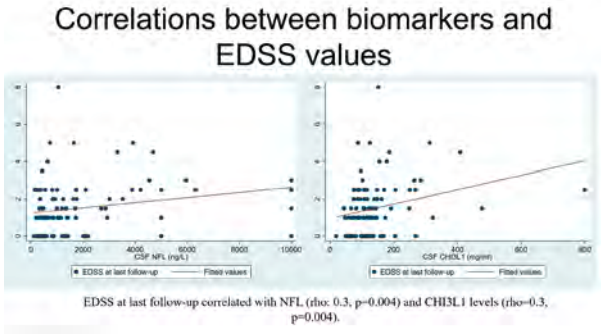
Background and aims: Aim of the study was to assess the long-term prognostic role of multiple CSF biomarkers at onset in a longitudinal cohort of MS patients.
Methods: We measured CSF Neurofilament light chain (NFL), tau protein, chitinase-3-like 1 protein (CHI3L1), CXCL13, IgG and IgM oligoclonal bands and kappa index (CSF/serum kappa free light chains divided by CSF/serum albumin) and correlated them with the risk of reaching an EDSS of 2/3/4/6, a secondary progressive course, with the time to a relapse, the number of total relapses and with the use of a second-line treatment.
Results: Ninety-six patients (61F, 35M, mean age: 34 ± 11 years) were followed up for a median of 135 months (IQR: 100-162). EDSS at last follow-up correlated with NFL (rho: 0.3, p=0.004) and CHI3L1 levels (rho=0.3, p=0.004). Only NFL increased the risk of reaching an EDSS of at least 3 (p=0.037). CXCL13 and CHI3L1 (rho: 0.3, p<001 and 0.005, respectively) correlated with the number of relapses during follow-up and the time to a first relapse was influenced by high values (> median value) of CXCL13 (>14pg/ml) (p=0.043). NFL levels greater than 1000ng/L influenced the risk of initiating second-line treatment (OR 3.9, 95%CI: 1.5-10.7, p=0.007) and the time to its initiation (p=0.003).



Correlation between CSF NFL and CHI3L1 levels and EDSS at last follow up.

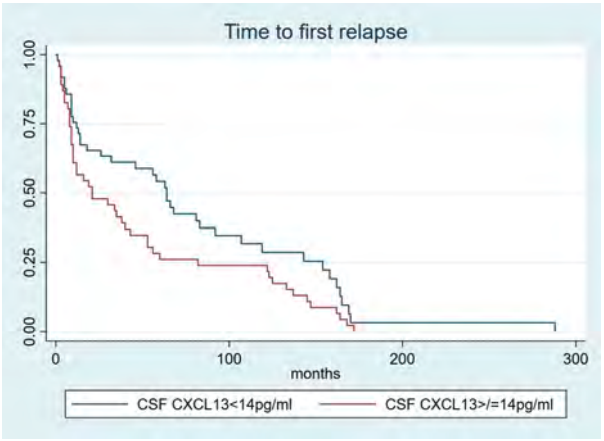


Figure 1. Survival analysis showing how CXCL13 levels influence time to first relapse.

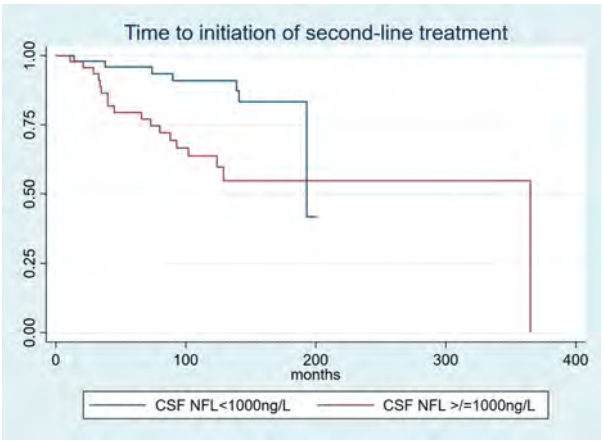


Figure 2. Survival analysis showing how CSF NFL levels influence time to initiation of a second line treatment.

Conclusion: CXCL13 was associated with an early occurrence of relapses and with the total number of relapses, while NFL was associated with long-term disability and predicted the use of second-line treatment during the disease course.
Disclosure: Krzysztof Smolik: nothing to disclose, Roberta Bedin: nothing to disclose, Federica Casari: nothing to disclose, Martina Cardi: nothing to disclose, Francesca Vitetta has received travel grants and/or speaker/advisory board honoraria from Merck, Novartis, Sanofi, Biogen and Roche, Patrizia Sola: nothing to disclose, Diana Ferraro has received travel grants and/or speaker/advisory board honoraria from Biogen, Merck, Sanofi, Novartis and Roche.

OPR-021

Myelin oligodendrocyte glycoprotein (MOG) antibodies in adults with a first demyelinating syndrome.

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Background and aims: MOG antibodies (MOG-Ab) appear to distinguish multiple sclerosis (MS) from MOG-associated disease (MOGAD) in most cases. However, studies analyzing MOG-Ab at time of a first demyelinating syndrome in adults are scarce. We aimed to 1) evaluate the prevalence of MOG-Ab in a first demyelinating syndrome cohort, and 2) compare baseline clinical features and disease course between seropositive (MOG-Ab+) and seronegative (MOG-Ab-) patients.

Methods: From a cohort of 1263 patients prospectively enrolled between 1995 and 2020, we included 641 with available serum samples obtained within 6 months from the event. MOG-Ab were analyzed using a live cell-based assay. Parametric and non-parametric tests as well as logistic regression and survival models were used.

Results: MOG-Ab were positive in 17/641 (2.7%). 14/17 (82.4%) MOG-Ab+ patients presented with optic neuritis (ON) compared to 231/624 (37.0%) MOG-Ab-, p=0.003. Oligoclonal bands (OBs) were found in 2/16 (12.5%) MOG-Ab+ in contrast to 338/546 (61.9%) MOG-Ab-, p<0.001. Baseline brain magnetic resonance imaging was normal in 10/16 (62.5%) MOG-Ab+ vs. 155/596 (26.0%) MOG-Ab- patients, p=0.016. Clinical characteristics are summarized in table 1. Absence of OBs and ON at onset were independently associated with testing positive for MOG-Ab (table 2): Odds-Ratio (OR) 8.1; 95%Confidence Interval (95%CI) 1.8-37.0, p=0.007, and OR 7.1; 95%CI 1.4-33.3, p=0.018, respectively. MOG-Ab+ patients were at lower risk of reaching McDonald 2017 criteria (log-rank p=0.003) (figure 1).

Conclusion: MOG-Ab are infrequent in adults with a first demyelinating syndrome suggestive of MS, and should be tested in patients presenting with ON and absence of OBs.

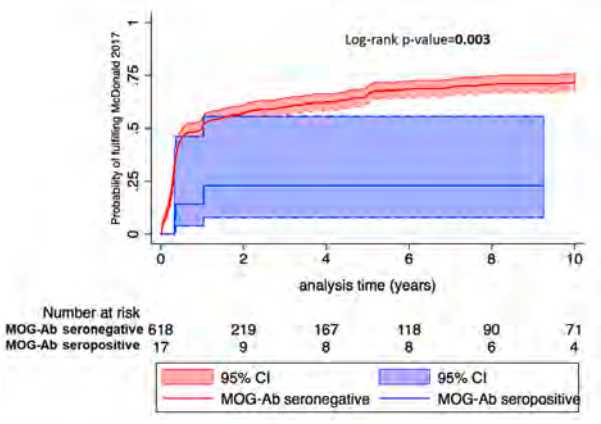
Disclosure: J. Villacieros-Álvarez has received grant from Instituto de Salud Carlos III, Spain; FI21/00282 A. Cobo-Calvo has received grant from Instituto de Salud Carlos III, Spain; JR19/00007.

	CIS-MOG- (n=624)	CIS-MOG+ (n=17)	P-value
Female; n (%)	428 (68.59)	11 (64.71)	0.793
Age at onset (years); median (IQR)	32.82 (26.58-39.56)	32.51 (23.61-34.02)	0.251
CIS topography; n (%) Optic nerve Spinal cord Brainstem Multifocal	 231 (37.02) 167 (26.76) 149 (23.88) 77 (12.34)	 14 (82.35) 1 (5.88) 1 (5.88) 1 (5.88)	0.003
EDSS at onset; median (IQR)	2.00 (1.00-2.50)	2.00 (1.00-3.00)	0.403
EDSS at last follow-up; median (IQR)	1.50 (1.00-2.00)	1.00 (0-2.00)	0.133
ARR at last follow-up; median (IQR)	0.22 (0.12-0.41)	0.16 (0.11-0.54)	0.531
Fulfilment of McDonald 2017 criteria during the first year of the disease; n (%)	324/467 (69.38)	3/17 (17.65)	<0.001
Disease-modifying treatment at any time; n (%)	332 (53.21)	4 (23.53)	0.020
Follow-up in years; median (IQR)	9.17 (4.30-16.03)	6.67 (0.99-10.63)	0.050
Presence of OBs; n (%)	338/546 (61.90)	2/16 (12.50)	<0.001
Normal brain MRI; n (%)	155/596 (26.01)	10/16 (62.50)	0.016
Normal spinal cord MRI; n (%)	243/373 (60.15)	8/10 (80.00)	0.755
Gd-enhanced lesions; n (%)	145/437 (34.80)	3/11 (27.30)	0.800
New T2 lesions on brain MRI at last follow-up; n (%)	314/558 (56.27)	3/13 (23.08)	0.023

Table 1. Demographic and clinical characteristics between seronegative (MOG-Ab-) and seropositive (MOG-Ab+) patients.

	Univariable analysis		Multivariable analysis	
Baseline variables	Odds-Ratio (95% CI)	p-value	Odds-Ratio (95% CI)	p-value
Age at onset	0.97 (0.91-1.03)	0.254		
Sex	0.84 (0.31-2.30)	0.736		
EDSS at onset	1.21 (0.84-1.76)	0.322		
Optic neuritis	7.94 (2.26-27.92)	<0.001	8.12 (1.78-37.02)	0.007
Absence of OBs	11.23 (2.53-49.85)	<0.001	7.14 (1.39-33.33)	0.018
Normal brain MRI	4.74 (1.70-13.26)	<0.001	1.34 (0.42-4.29)	0.617
Presence of Gd-enhanced lesions	0.70 (0.18-2.69)	0.598		

Table 2. Logistic regression model for the presence of MOG-Ab according to baseline variables.



Kaplan-Meier survival analysis for the time to reach the McDonald 2017 criteria according to serostatus.

Sunday, July 02 2023
Neurogenetics

OPR-022

Novel pathogenic repeat configurations in RFC1 causing CANVAS and disease spectrum

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Background and aims: Cerebellar Ataxia, Neuropathy and Vestibular Areflexia Syndrome (CANVAS) is an autosomal recessive ataxia, usually caused by biallelic (AAGGG)n repeat expansions in RFC1. However, a minority of CANVAS patients do not carry AAGGG repeat expansions. We identified three novel repeat motifs associated with CANVAS and we demonstrated a pathogenic role for large AAAGG repeat expansions.
Methods: We analysed 893 short-read-WGS from adult patients with ataxia diagnosis and 8107 controls from the 100000GenomeProjects, and detected repeat expansions at the RFC1 locus using ExpansionHunterDeNovov0.9.0. Repeat motifs in homozygosis or compound heterozygosis with AAGGG in patients and absent in controls were further investigated by long read sequencing. Compound heterozygous AAAGG/AAGGG carriers were also further studied, given their higher frequency in ataxia cases.
Results: We identified six CANVAS patients carrying novel repeat expansions in RFC1, namely (AGGGC)n (n=3), (AAGGC)n (n=2), (AGAGG)n (n=1), which were absent in controls. Repeat size was >500 repeat units in all cases and up to 3400 in AGGGC repeat expansion carriers. Long-read-sequencing revealed a pure AGGGC expansion in three patients, whereas the other patients presented complex motifs with AAGGG or AAAGG interruptions. These configurations seem to have arisen from a common haplotype. Clinical features of patients with novel repeat configurations were mostly indistinguishable from biallelic AAGGG repeat expansions carriers.
Conclusion: The identification of novel pathogenic configurations and the demonstration of a pathogenic role for the AAAGG repeat expands the genetic heterogeneity of RFC1 disease. The assessment of these novel configurations is warranted in CANVAS patients with inconclusive genetic testing.
Disclosure: Elena Abati received a scholarship from the Rotary Club Milano Ovest.

OPR-023

ALEXANDER DISEASE IN A LARGE ITALIAN COHORT OF ADULT PATIENTS

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Background and aims: Alexander disease (ALXDRD, OMIM #203450) is a rare astrocytic leukodystrophy caused by autosomal dominant, mostly de novo, gain-of-function GFAP pathogenic variants. Our work is aimed at describing an Italian cohort of adult ALXDRD patients to expand the disease knowledge.
Methods: We recruited the patients from the Carlo Besta Adult Leukodystrophy Database from January 2004 to December 2022.
Results: We identified 41 adult patients (27 males; 28 sporadic; median follow-up: 6 years) with 24 different GFAP pathogenic variants. MRI constantly showed bulbar and cervical spinal cord atrophy with signal abnormalities. 34 patients were symptomatic (age-of-onset: >12 years in 30 patients; first typical manifestation: ataxic-spastic gait), and their disease course was unevenly progressive, with varying degree of dysarthria, dysphagia, and urge-incontinence. Seven patients remained asymptomatic, with one subject diagnosed at age of 50 because of a symptomatic relative, and six subjects diagnosed incidentally between the age of 32 and 68. Notably, all these incidentally-diagnosed subjects had the same c.1127C>T (p.Arg376Leu) pathogenic variant. In vitro studies on this variant showed mild GFAP assembly pattern change with marked decrease of GFAP protein production caused by interference with intron-exon splicing.
Conclusion: In adults, MRI bulbospinal abnormalities are the ALXDRD hallmark. The variability in disease progression of late-onset forms should promote the development of specific clinical assessment tools, also for forthcoming studies with disease-modifying drugs. Mutations causing low/null expression of abnormal GFAP

protein lead to lack of symptoms, thus supporting the rationality of a therapeutic approach based on gene silencing.

Disclosure: Nothing to disclose.

OPR-024

Biallelic MED27 variants lead to variable ponto-cerebello-lental degeneration with movement disorders

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[1]Department of Neuromuscular Diseases, UCL Institute of Neurology, University College London, UK, [2]Department of Biology, Faculty of Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran, [3]University of Oxford, Wellcome Centre for Human Genetics, Oxford, UK, [4]Istituto Giannina Gaslini, Neuroradiology, Genoa, Italy, [5]Columbia University Medical Center, New York City, NY, USA, [6]Human Molecular Genetics Laboratory, Health Biotechnology Division, National Institute for Biotechnologyvg (NIBGE), PIEAS, Faisalabad, Pakistan

Background and aims: MED27 is a subunit of the Mediator multiprotein complex, which is involved in transcriptional regulation. Biallelic MED27 variants have recently been suggested to be responsible for an autosomal recessive neurodevelopmental disorder with spasticity, cataracts, and cerebellar hypoplasia. We further delineate the clinical phenotype of MED27-related disorder by characterizing the clinical and radiological features of 55 affected individuals from 28 unrelated families with biallelic MED27 variants.

Methods: Utilizing exome sequencing and extensive international genetic data sharing, 37 unpublished affected individuals from 16 independent families with biallelic missense variants in MED27 have been identified (29 females, mean age at last follow-up 17±12.4 years, range 0.1-45). Follow-up and hitherto unreported clinical features were obtained from the published 12 families. Brain MRI scans from 34 cases were reviewed.

Results: The condition is characterised by global developmental delay/intellectual disability, ranging from mild to profound (100%), bilateral cataracts (88%), infantile hypotonia (73%), microcephaly (62%), gait ataxia (63%), dystonia (58%), variably combined with epilepsy (52%), limb spasticity (53%), facial dysmorphism (36%), and premature mortality (17%). Brain MRI revealed cerebellar atrophy (100%), white matter volume loss (76.4%), pontine hypoplasia (47%) and basal ganglia atrophy with signal alterations (44.1%). Previously unreported 37 affected individuals had six homozygous pathogenic missense MED27 variants, five of which were recurrent. An emerging genotype-phenotype correlation was observed.

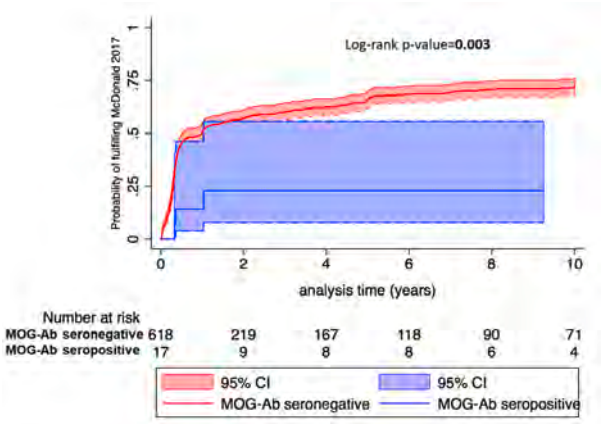

Figure 1. Pedigrees of affected families. a) new families, b) reported families. Solid black: affected. Genotype, where indicated, represent results of evaluation of the variants by Sanger sequencing.

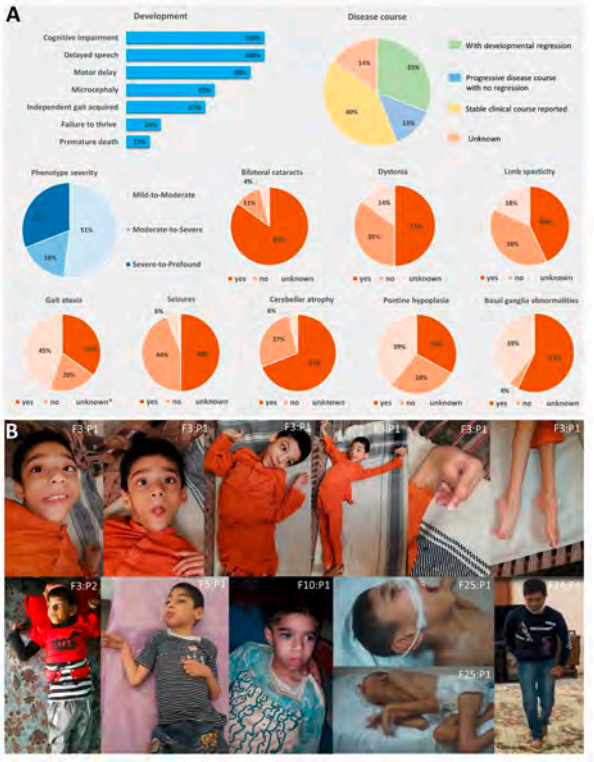

Figure 2. Clinical features of MED27-related disorder

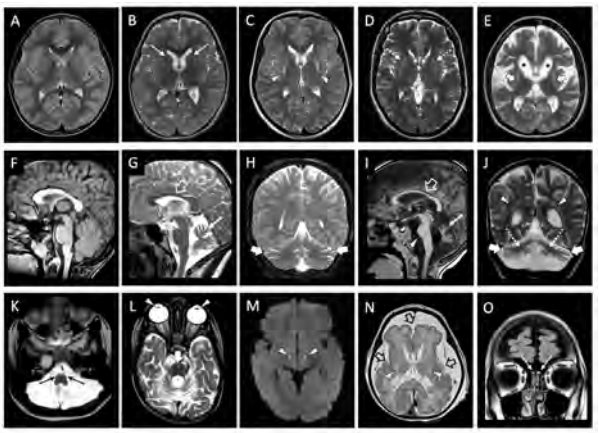

Figure 3. Neuroradiological features of MED27-related disorder. ological features of MED27-related disorder.

Conclusion: This study provides a comprehensive clinical-radiological description of MED27-related disease, establishes genotype-phenotype and clinical-radiological correlations, and suggests a differential diagnosis with syndromes of cerebello-lental neurodegeneration and other subtypes of "neuro-MEDopathies".
Disclosure: No financial disclosures.

OPR-025

Altered Nt-acetylation processes, a new disease-mechanism for Autosomal Recessive Primary Familial Brain Calcifications

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Background and aims: Primary familial brain calcification (PFBC) is characterized by calcium deposition in the brain, causing progressive movement disorders, psychiatric symptoms, and cognitive decline. PFBC is a heterogeneous disorder currently linked to variants in six different genes, but most patients remain genetically undiagnosed.
Methods: We performed genome-wide sequencing, homozygosity mapping, segregation analysis and in-depth clinical and neuroimaging phenotyping for novel disease-causing gene discovery. We used immunofluorescence and fluorescence microscopy to assess subcellular distribution and characterization of disease variants as well as an in vitro carbon [14-C]-Nt-acetylation assay on immunoprecipitated variants to investigate their enzymatic activity. We used a zebra fish to model the disease and assess the phenotype. Pathogenicity was further confirmed by surface biotinylation assays and extracellular free phosphate quantification on patient-derived fibroblasts.
Results: Here, we identify biallelic NAA60 variants in seven individuals from four families with autosomal recessive PFBC. The NAA60 variants lead to loss-of-function with lack of protein N-terminal (Nt)-acetylation activity. We show that the phosphate importer SLC20A2 is a substrate of NAA60 in vitro. In cells, loss of NAA60 caused reduced surface levels of SLC20A2 and a reduction in extracellular phosphate uptake. A zebrafish disease model

of NAA60 deficiency displayed a motor deficit with altered phosphate homeostasis.
Conclusion: This study establishes NAA60 as a causal gene for PFBC, provides a biochemical explanation of its disease-causing mechanisms and underscores NAA60-mediated Nt-acetylation of transmembrane proteins as a fundamental process for healthy neurobiological functioning.
Disclosure: Nothing to disclose.

OPR-026

Genotype Phenotype correlation in PRKN-associated Parkinson's disease

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Background and aims: Mutations in PRKN are the most common cause of early-onset autosomal recessive inherited PD, with over 140 different mutations spanning the entire gene described as being pathogenic.
Methods: PD patients with bi-allelic pathogenic mutations in PRKN and with no pathogenic mutations in other genes known to result in monogenic PD were included. The type of mutation in PRKN was analysed for an association with the age at onset and motor severity, considering disease duration as a covariant.
Results: 644 patients were included for analysis [age at onset (31.4±11.38 years), disease duration (18±12.5 years)]. Mean UPDRS part III (on) score at the time of disease onset was 12.6±1.4 and increased by 3.85±0.6 points every 10 years (n=310, p=3.6e-09).The average initial LEDD amongst those who never had deep brain stimulation was 320±71 mg, and this increased by 118±30 mg every 10 years (n=94, p=0.0013). Patients with 2 missense variants had a later age of onset (36.4±12.3 years), compared to those with 2 structural variants (31.2±10.8 years) (p=0.004). Variants located at the N-terminus of the protein (exon 1–3), were associated with an earlier age at onset of PD, 30.9±10.3 years, compared to variants located at the C-terminus (exons 7-12), 34.9±12.5 (p=0.05)
Conclusion: We demonstrate that missense variants and variants located in the N-Ter of the protein are associated with a more benign progression of the disease, a finding which has never before been demonstrated in bi-allelic PRKN-PD.
Disclosure: Poornima Jayadev Menon is funded by the Edmond J Safra fellowship in movement disorders.

Diagnostics in Neurology

OPR-027

Physical-adjusted normal values for total, central and peripheral latency of motor evoked potentials from a large cohort

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Background and aims: Differentiating physiologic from altered motor evoked potentials (MEPs) due to central or peripheral nervous system disease is crucial. However, some physical features may introduce variability unrelated to neural dysfunction. We provide age- and height-adjusted normal values for MEP cortical latency (MCL), central motor conduction time (CMCT), and peripheral motor conduction time (PMCT) in a large cohort.
Methods: 587 healthy subjects were included. MCL was determined, bilaterally, from the First Dorsal Interosseous and Tibialis Anterior muscles during mild tonic contraction. CMCT was estimated as the difference between MEP cortical latency and PMCT by cervical or lumbar magnetic stimulation. Right-to-left differences were also calculated. For each parameter, multiple linear regression models of increasing complexity were fitted using height and age as regressors.
Results: MCL, PMCT, and CMCT were age- and height-dependent, although age had only a small effect on CMCT. MCL and PMCT were explained best by linear models, indicating a positive correlation with both height and age. For CMCT height-only models, indicating a positive correlation, were selected in the majority of cases. Right-to-left-differences were explained by neither height nor age. Then, sex-specific reference values were obtained for all latencies and inter-side differences, with adjustments for height and age where warranted.
Conclusion: A significant relationship was found between height and age and all MEP latencies at four limbs, thus facilitating the evaluation of MEP in clinical and research settings. Unlike previous reports, we also highlighted the contribution of sex, which might influence both MEP responses and the effects of neuromodulatory techniques.
Disclosure: Nothing to disclose.

OPR-028

Automated pupillometry to detect cognitive motor dissociation in ICU patients with acute brain injury

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Background and aims: Cognitive motor dissociation (CMD) defines a subset of clinically unresponsive patients who can engage in active mental paradigms, suggesting covert consciousness. CMD is prevalent in 15-20% of unresponsive patients with acute brain injuries. As cognitive and emotional processes can be reflected by pupil dilations, which are easily detectable using automated pupillometry, we hypothesized that automated pupillometry can identify CMD.
Methods: We serially evaluated patients in the intensive care unit (ICU) with an automated pupillometry paradigm focusing on inducing cognitive load. The active paradigm consisted of two sets of five mental arithmetic tasks with increasing complexity. Responding with a pupil dilation to at least three of the tasks in one set was considered command-following behavior.
Results: Utilizing automated pupillometry, we assessed 91 ICU-patients (male 69%; mean age 60 years (SD±13.8)) with acute traumatic and non-traumatic brain injury (56≤UWS/VS; 35≥MCS) and 26 age- and sex-matched healthy controls. Sixty% of clinically responsive patients (MCS or better) were able to generate ≥3 pupil dilations when performing mental tasks versus 23% of clinically unresponsive patients (X2, odds ratio 4.96 [95%CI:1.98-12.42]). In comparison, 77% of healthy controls could generate ≥3 pupil dilations. Of patients with unresponsive wakefulness syndrome (n=20), automated pupillometry detected pupillary responses to mental tasks in 15%.
Conclusion: Automated pupillometry combined with mental tasks could detect command-following behavior at the bedside in 15% of clinically unresponsive patients, which is the same amount of CMD patients as typically found with fMRI and EEG paradigms, indicating that automated pupillometry can identify CMD in the early stages of ICU-admission.
Disclosure: No relevant or material financial interests that relate to the research described in this paper.

OPR-029

Plasma cfDNA liquid biopsy in the follow-up of high-grade gliomas

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Background and aims: In high-grade gliomas, tissue biopsy cannot be repeated over-time to monitor treatment-response. Thus, we investigated the potential value of plasmatic cell-free DNA(PcfDNA) as a non-invasive 'liquid biopsy' marker of disease evolution.
Methods: Patients' blood was collected at 4 time points(TP), in parallel to clinical follow-up. Concentration and molecular status of PcfDNA were analyzed. MRI volumes were segmented in T1+contrast and T2-FLAIR sequences.
Results: Fifty-four high-grade glioma patients and 14 healthy controls were enrolled. Blood samples were collected from all 54 patients at radiological diagnosis before surgery(TP0), from 33 patients after surgery(TP1), from 21 patients after radio-chemotherapy(TP2), from 10 patients at the first radiological progression (TP3)(Figure1). At T0, a significantly higher concentration of PcfDNA was detected in patients than in controls(Figure2A). IDH-wild-type gliomas showed a trend toward higher PcfDNA when compared with IDH-mutant gliomas. Digital-droplet PCR, performed at T0 on PcfDNA of 4 patients with IDH-mutations in tumor tissues, identified the same IDH1-R132H mutation in all cases. When PcfDNA at TP0 was compared to that at TP1 of the same patient (n=33), there was a significant reduction of plasmatic cfDNA after surgery, mirroring the extensive tumor-resection shown by MRI(Figure2B). Finally, PcfDNA was evaluated in 10 patients until their radiological progression. Interestingly, PcfDNA levels not only followed the same trend of the volumes of T2-FLAIR hyperintensities and T1 contrast-enhancements, but were also mirrored by the evolution of KPS and NANO scores(Figure3).

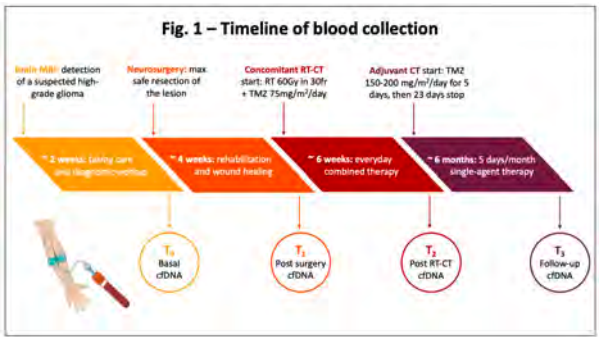

Fig. 1 – Timeline of blood collection: Blood withdrawals have been performed at four consecutive timepoints during patient's clinical history and follow-up, always in parallel to MR imaging and clinical evaluation.

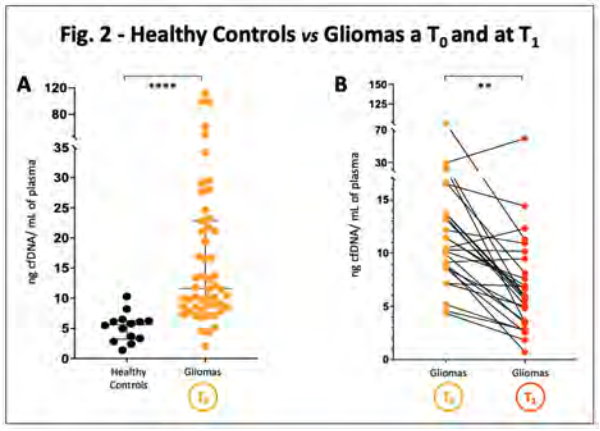

Fig. 2 - Healthy Controls vs Gliomas a T0 and at T1: A) PcfDNA values of patients at T0 are higher than in controls (Mann Whitney test, $p<0.0001$). B) PcfDNA values of patients at T0 are higher than at T1 (Wilcoxon matched pairs, $p<0.0035$)

Conclusion: Preliminary results suggest that PcfDNA content may be an informative tool to complement MRI during the follow-up of high-grade gliomas.
Disclosure: Nothing to disclose.

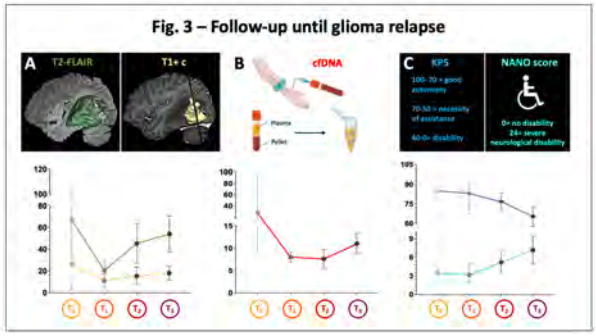

Fig. 3 – Follow-up until glioma relapse. Values of ten patients are shown, from glioma diagnosis to relapse A) Tumor volumes in T2-FLAIR (green) and T1+c (yellow). B) Quantity of PcfDNA (red). C) Assessments of KPS (blue) and NANO score(light blue)

OPR-030

BCI-STAR Project: Associative brain computer interface for upper limb rehabilitation following stroke

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Background and aims: Associative Brain Computer Interface (BCI)-aided rehabilitation of the upper extremity has been shown to improve post stroke upper limb recovery. In the associative BCI, electrical stimulation of a peripheral nerve is triggered such that the resulting sensory volley arrives precisely during the most active phase of the motor cortex during movement of the paretic limb. The aim of this current study is to investigate the functional outcomes of stroke patients with upper limb weakness following associative BCI training.
Methods: In this ongoing study, 60 hospitalized subacute stroke patients are offered 12 BCI training sessions over 4-5 weeks. Participants are randomly assigned to receive either functional electrical stimulation (intervention) or sub-sensory "sham" stimulation (control). Corticospinal excitability is evaluated by measuring motor evoked potentials (MEPs) in response to transcranial magnetic stimulation (TMS), and recovery is assessed using Fugl-Meyer upper extremity (FM-UE) and Action Research Arm Test (ARAT) scales.
Results: Preliminary results show significantly improved corticospinal excitability in the intervention group, immediately and 30 minutes after the training. This has not been found in the control group. Both groups experience functional improvements, but we have not found differences between the two groups, likely due to low sample size.
Conclusion: Associative BCI training increases the corticospinal excitability in subacute stroke patients with upper limb weakness, and provides a novel tool to neurotechnology-aided rehabilitation. We expect to see significantly increased recovery in the intervention group compared to the control group as sample size increases, mirroring the results seen in earlier studies.
Disclosure: The authors declare no conflicts of interest.

OPR-031

Exploring a novel bedside-approach to communication in brain injury: Tongue-based motor imagery documented by fNIRS

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Background and aims: Patients suffering from severe brain injuries have difficulties with verbal and motor communication, posing challenges in cognitive assessment. Functional near-infrared spectroscopy (fNIRS) provides a non-invasive alternative for evaluating motor cortex activation in the absence of physical movement, by detecting changes in cortical blood oxygenation levels. This proof-of-concept study investigates the potential of using tongue-based commands as a novel motor imagery communication method via fNIRS.
Methods: Twenty healthy staff at the Copenhagen University Hospital volunteered to undergo fNIRS measurements from the fronto-parietal and primary motor cortices while performing tongue motor and tongue motor imagery tasks. We used a support vector machine classifier to classify the brain activation patterns to distinguish between tongue motor imagery and a relaxed state.
Results: Our results showed that all participants were able to elicit activation in the tongue motor homunculus through tongue motor imagery, comparable to activation responses observed during physical tongue movement. The activation was localized to the left hemisphere with both tongue motor and tongue motor imagery tasks. Additionally, tongue imagery activated the fronto-parietal regions associated with cognitive processing. The classifier successfully distinguished motor imagery from the relaxed state with a 92% accuracy.
Conclusion: Our study provides proof-of-concept for the use of a novel tongue motor imagery paradigm in healthy individuals, highlighting the potential for fNIRS to facilitate cognitive assessments and meaningful interactions in patients with severe brain injury.
Disclosure: The authors have no conflicts of interest to declare.

Cerebrovascular diseases 2

OPR-032

Intensive Blood Pressure Reduction Attenuates Hematoma Growth in Fast Bleeding Intracerebral Hemorrhage Patients

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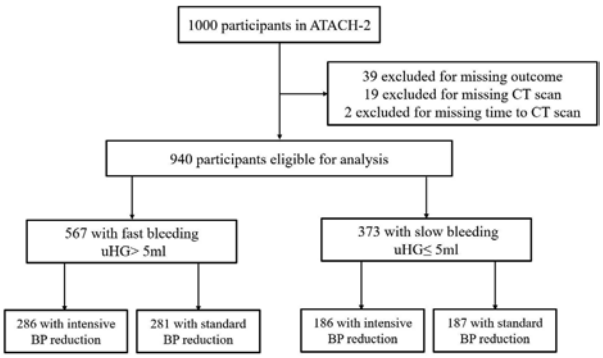
Background and aims: Spontaneous intracerebral hemorrhage (ICH) patients at highest risk of hematoma growth are those with the most potential to benefit from anti-expansion treatment. We aim to determine whether intensive blood pressure reduction could benefit patients with fast bleeding ICH.
Methods: An exploratory analysis of data from the Antihypertensive Treatment of Acute Cerebral Hemorrhage II (ATACH-II) randomized controlled trial was performed. Fast bleeding ICH was defined as an ICH volume/onset-to-CT time >5ml/h. Multivariable logistic regression analysis was used to identify predictors of hematoma expansion and explore whether fast bleeding ICH patients specifically benefit from intensive BP reduction.
Results: A total of 940 patients were included (mean age 62.1 years, 61.5% male), of whom 214 (22.8%) experienced hematoma expansion. Of these, 567(58.9%) met the definition of "fast bleeding" with baseline ICH volume/time to presentation of at least 5ml/h. Intensive blood pressure reduction was associated with a significantly lower rate of hematoma growth in fast bleeding patients (20.6% vs 31.0%, p =0.005). Intensive blood pressure reduction was associated with reduced rate of hematoma growth in fast bleeding patients in the multivariable regression analysis (OR 0.58, 95%CI:0.39-0.85, p=0.006), but not in slow bleeding patients (OR 1.01, 95% CI 0.59-1.72, p = 0.981). In a subgroup of 266 (46.9%) fast-bleeding patients who received treatment within 2 hours after symptom onset, intensive BP lowering was associated with improved functional independence (OR 1.98, 95%CI:1.06-3.69, p=0.031).



Flowchart of Patient Selection

Conclusion: Our results suggest that early use of intensive BP reduction may reduce hematoma growth and improve outcome in fast bleeding patients.
Disclosure: Nothing to disclose.

OPR-033

European society of neurosonology and cerebral haemodynamic stroke focus cardiac ultrasound (s-focus)

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Background and aims: In the last decade a new ultrasound approach using point-of-care ultrasound concept has been expanding in many fields of medicine including neurology. Standard echocardiogram is used by specialists to detect stroke relevant pathologies. Focus cardiac ultrasound, in view of its limitations, can be used by echocardiography

non-specialists as an efficient bedside tool to detect specific cardiac conditions.
Methods: ESNCH Focused echocardiography working group included members from different countries that have various pathways, protocols, levels of experience and training and educational programmes, developed a new stroke relevant focused cardiac ultrasound (S-FoCUS) programme in 2022. We developed a protocol, educational and training programme and initiated a process of implementation of S-FoCUS, including development of clinical pathways. During the development process we took into consideration the European Association of Cardiovascular Imaging recommendations for focus cardiac ultrasound to develop a highly compatible S-FoCUS programme.
Results: The S-FoCUS protocol, educational and training programme was developed by working group members specialised in neurology, stroke medicine, cardiology and internal medicine. We developed a protocol and reporting form comprising of eleven questions with binary answers focusing on specific target structures and function: left ventricle, left atrium, right ventricle, gross valvular abnormalities, large intracardiac masses, aortic plaque, pericardium, hypovolaemia with six standardized echocardiographic views. We developed ESNCH S-FoCUS educational and training programme with structured curriculum and syllabus focused on generic and specific knowledge with training and certification pathway.
Conclusion: ESNCH Focused echocardiography working group developed and started the implementation and evaluation process of the ESNCH stroke relevant focus cardiac ultrasound (S-FoCUS).
Disclosure: Nothing to disclose.

OPR-034

The effect of cardiovascular risk factors and NOTCH3 variant position on the CADASIL phenotype: a retrospective study

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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare heritable small vessel disease caused by a cysteine-altering mutation in one of the thirty-four epidermal growth factor-like repeat (EGFR)-domains of the NOTCH3 gene. CADASIL has a variable phenotypic presentation. Although a genotype-phenotype relationship has never been found in past years, mutations in EGFRs 1-6 have recently been described to correlate with greater disease severity. However, the contribution of the location of the variants and the presence of cerebrovascular risk factors in CADASIL phenotype is still unclear. Herein, we investigated the influence of mutation site and cerebrovascular risk factors on the clinical presentation of the disease.
Methods: Between 2008 and 2022, we retrospectively recruited 153 individuals carrying a NOTCH3 pathogenic variant. For each patient, demographic and clinical data were collected, including CHA2DS2-VASc and modified-Rankin scale(mRS).
Results: 103 symptomatic and 50 asymptomatic cases were included(Figure-1A). Mutations clustered on the first 6 exons were associated with an increased risk of stroke (odds ratio [OR]:3.01;95%CI:6.81-1.33) and migraine (OR:1.09;95%CI:3.49-0.71) (Figure-1B). On Kaplan-Meier analysis, these patients had also a shorter stroke-free survival compared with cases with a mutation on the 7-25 exon(Figure-2A). However, cardiovascular risk factors were found to be associated with penetrance of these variants as assessed by mRS (p-value:0.0002,Figure-2B) and were significantly more common among symptomatic patients(Figure-3).

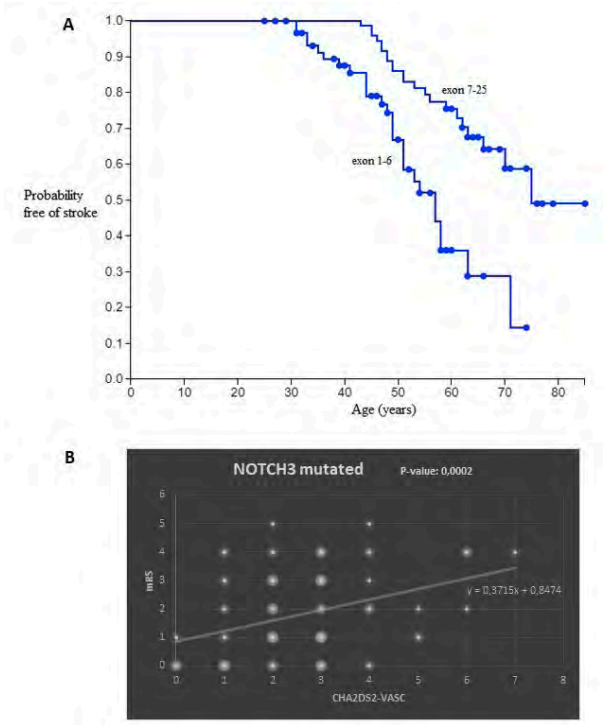
A

	Symptomatic (n=103)	Asymptomatic (n=50)
Age at last visit, mean (SD)	57,6 (11,7)	43,9 (14,4)
Age at onset, mean (SD)	45,5 (14,3)	
Men, n (%)	45 (43,7)	20 (40)
CHA2DS-VASC, mean (SD)	2,6 (1,4)	1,0 (1,1)
mRS, mean (SD)	1,8 (1,5)	0,2 (0,6)
Clinical symptoms		
Stroke, n (%)	45 (43,7)	
TIA, n (%)	31 (30,1)	
Migraine with aura, n (%)	28 (27,2)	
Migraine without aura, n (%)	19 (18,4)	
Depression, n (%)	43 (41,7)	
Mild cognitive impairment, n (%)	26 (25,2)	
Dementia, n (%)	12 (11,6)	
Cardiovascular risk factors		
Hypertension, n (%)	37 (35,9)	5 (10)
Dyslipidemia, n (%)	43 (41,7)	7 (14)
Diabetes, n (%)	7 (6,8)	1 (2)
Past or current smoker, n (%)	45 (43,7)	10 (20)
Coronary artery disease, n (%)	2 (1,9)	0 (0)
Family history		
Stroke, n (%)	74 (71,8)	37 (74)
Dementia, n (%)	51 (71,8)	30 (60)

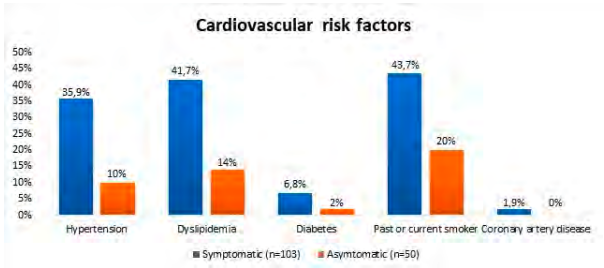
B

NOTCH3 variant	Age onset >65 OR (95% CI)	Migraine OR (95% CI)	Stroke OR (95% CI)	Depression OR (95% CI)	Dementia OR (95% CI)
Exon 1-6 (n=42)	0,12 (0,01-1,01)	1,58 (3,49-0,71)	3,01 (6,81-1,33)	0,91 (2,03-0,41)	0,55 (1,33-0,22)
Exon 7-25 (n=61)	1,71 (5,71-0,51)	0,63 (1,39-0,28)	0,33 (0,74-0,14)	1,09 (2,42-0,49)	1,80 (4,35-0,74)

1A. Clinical features, cardiovascular risk factors, and family history of symptomatic and asymptomatic cases with a NOTCH3 variant - 1B. Differences in clinical manifestations and age onset stratified according to variant position (exon 1–6 vs exon 7–25)



2A. Kaplan-Meier plot showing the difference in age at onset of the first stroke for patients with exon 1–6 variants and those with exon 7–25 variants - 2B. Association of CHA2DS2-Vasc with modified Rankin Scale among patients with NOTCH3 variants



3. Comparison of the frequency of cardiovascular risk factors between symptomatic and asymptomatic cases with a NOTCH3 variant

Conclusion: The presence of NOTCH3 variants is not an independent prognostic variable of CADASIL and their location may modulate the clinical expression. Cardiovascular risk factors may influence the clinical presentation and, therefore, should be treated aggressively.
Disclosure: Nothing to disclose.

OPR-035

Emergent carotid stenting versus no stenting for acute ischemic stroke due to tandem occlusion: a meta-analysis

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Background and aims: Emergent carotid artery stenting (eCAS) is often performed in the context of mechanical thrombectomy for acute ischemic stroke with tandem occlusion. However, the optional management strategy in this setting is still unclear. Here we provide a systematic review and meta-analysis to investigate safety and efficacy of such procedure in patients with extra-cranial internal carotid artery stenosis and acute large vessel occlusion.
Methods: The systematic review followed a PROSPERO registered protocol (CRD42021279218). MEDLINE, EMBASE and Scopus were searched from 1/1/04 to 1/10/21 for studies comparing eCAS vs no-stenting approach in cases of stroke due to tandem occlusion. Primary endpoint was good functional outcome (90 days mRS 0-2); secondary outcomes were (i) sICH, (ii) recurrent stroke, (iii) successful recanalization (TICI 2B-3), (iv) embolization in new territories, (v) procedural complications and (v) re-stenosis during follow-up. Meta-analysis was performed using the Mantel-Haenszel method and random-effect modeling.
Results: Overall, 38 studies reached qualitative synthesis. eCAS was associated with higher chance of achieving good functional status at follow-up compared to no-stenting approach (OR=1.14, 95%CI 1.14-1.91). ECAS carried a marginal increase in sICH risk (OR=2.14, 95%CI 0.93-4.89), and a higher chance of successful recanalization (OR=2.38, 95%CI 1.55-3.67). Restenosis rate was lower in eCAS group vs no-stenting group (2% vs 9%, p=0.001).
Conclusion: eCAS seems to be associated with a higher good functional outcome than mechanical thrombectomy with no-stenting in patients with acute ischemic stroke due to tandem occlusion.
Disclosure: Nothing to disclose.

OPR-036

Increased platelet-leukocyte aggregates in pial blood samples before thrombectomy in human stroke

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Background and aims: Studies in rodent stroke demonstrated that platelets and leukocytes interact and contribute to infarct progression by a process termed thrombo-inflammation (Stoll & Nieswandt, Nat Rev Neurol 2019). The aspiration of minute samples of ischaemic arterial blood directly from the pial cerebral collateral circulation before thrombectomy enables confirmatory studies in human ischaemic stroke. We here assessed platelet-leukocyte aggregates (PLAs) as biomarkers of inflammatory platelet activation.

Methods: Upon informed consent we collected arterial blood samples from 15 patients with middle cerebral artery occlusion, one distal to the occlusion site immediately before thrombectomy, the second at the level of the carotid artery which served as intraindividual control. Circulating PLAs were quantified by flow cytometric analysis and representative blood smears stained by immunocytochemistry by an anti-neutrophil elastase antibody and anti-CD42b for platelets.

Results: Platelets formed significantly more aggregates with granulocytes and monocytes within the ischaemic vasculature compared to systemically aspirated blood, whereas the extent of lymphocyte binding was unaltered (platelet-granulocyte aggregates systemic 16.91 ± 12.08% vs ischaemic 22.97 ± 14.52%, $p<0.05$; platelet-monocyte aggregates systemic 45.69 ± 18.80% vs ischaemic 64.06 ± 17.02%, $p<0.001$; platelet-leukocyte aggregates systemic 10.81 ± 6.93% vs ischaemic 11.93 ± 6.45%). PLA formation could be confirmed by immunohistochemistry of blood smears.

Conclusion: The finding of increased PLA formation within the compromised ischaemic brain circulation under occlusion provisionally nourished by collateral flow supports the concept of detrimental platelet-leukocyte interactions in human stroke and clinical approaches to block platelet glycoprotein (GP)Ib and/or GPVI as key mediators of PLA formation.

Disclosure: The authors have nothing to disclose related to the content of this abstract.

OPR-037

Biomarkers Predictive of Atrial Fibrillation in Patients with Cryptogenic Stroke. Insights from The NOR-FIB Study

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Background and aims: There are currently no biomarkers used to select cryptogenic stroke (CS) patients for monitoring with insertable cardiac monitors (ICMs), the most effective tool for diagnosing atrial fibrillation (AF) in CS. The purpose of this study was to assess clinically available biomarkers as predictors of AF.

Methods: Eligible CS and cryptogenic transient ischemic attack (TIA) patients underwent 12-month monitoring with ICMs, clinical follow-up, and biomarker sampling. Levels of cardiac and thromboembolic biomarkers, taken within 14 days from symptom onset, were compared between patients diagnosed with AF (n=74) during monitoring and those without AF (n=185). Receiver operating characteristic (ROC) curves were created. Biomarkers reaching area under ROC curve (AUC) ≥ 0.7 were dichotomized by

finding optimal cut-off values and used in logistic regression establishing their predictive value for increased risk of AF in unadjusted and adjusted models.
Results: B-type natriuretic peptide (BNP), N-terminal pro-brain natriuretic peptide (NT-proBNP), creatine kinase, D-dimer, high-sensitivity cardiac Troponin I and T were significantly higher in the AF than non-AF group. BNP and NT-proBNP reached predefined AUC level, 0.755 and 0.725 respectively. Optimal cut-off values were 33.5 ng/L for BNP, and 87 ng/L for NT-proBNP. Regression analysis showed that NT-proBNP was a predictor of AF in both unadjusted, odds ratio (OR) 7.72 (95% confidence interval [CI] 3.16–18.87), and age and sex adjusted models, OR 4.82 (95% CI 1.79–12.96).
Conclusion: Several clinically established biomarkers were associated with AF. NT-proBNP performed best as AF predictor and could be used for selecting patients for long-term monitoring with ICMs.
Disclosure: DA has received honoraria and consultation fees from Actelion, Amgen, AstraZeneca, BMS/Pfizer, Bayer, Boehringer-Ingelheim, MSD, Novartis, Pharmacosmos, Roche Diagnostics, Sanofi, Takeda, and Vifor Pharma, and research funding (to the institution) from BMS/Pfizer, Bayer, Roche Diagnostics and Medtronic. AHA has received travel support, and honoraria for advice or lecturing from Bayer, Boehringer Ingelheim, BMS, Abbvie, Novartis, Roche, Pfizer, and Teva, research grant from Boehringer Ingelheim, and partial financial support from Medtronic and BMS for operating costs in ongoing clinical studies. ATL and BRT have received travel funding from Medtronic and are funded by a PhD fellowship from Helse Sør-Øst (South-Eastern Norway Regional Health Authority). Funding: NOR-FIB is an investigator driven academic study, supported by Oslo University Hospital, Norwegian Health Association, South-Eastern Norway Regional Health Authority, Østfold Hospital Trust and the European Cerebrovascular Research Infrastructure (ECRI). Devices were partly provided by Medtronic.

Monday, July 03 2023
COVID-19; Infectious diseases

OPR-038

Risk of disease relapse and safety of SARS-CoV-2 vaccination in patients with chronic inflammatory neuropathies

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Background and aims: To evaluate the risk of relapse after SARS-CoV-2 vaccination, and its safety and tolerability, in chronic inflammatory neuropathies patients.
Methods: In this multicenter, cohort, and case-crossover study, the risk of relapse associated with SARS-CoV-2 vaccination was assessed by comparing frequency of relapse in CIDP and MMN patients who underwent or did not undergo vaccination. Frequency of relapse in the three months prior and after vaccination, and safety and tolerability of SARS-CoV-2 vaccination were also assessed.
Results: 336 patients were included (278 CIDP; 58 MMN). 307 (91%) patients underwent SARS-CoV-2 vaccination, including 269 (88%) with BNT-162b2 (Pfizer/BioNTech), 28 (9%) with mRNA-1273 (Moderna), and 10 (3%) with ChAdOx1 (AstraZeneca). Twenty-nine patients (9%) did not undergo vaccination. Clinical relapse was observed in 16 (5%) patients (13 CIDP; 3 MMN) after SARS-CoV-2 vaccination and in none of the patients who did not undergo vaccination (RR= 3.21, 95% CI, 0.19-52.25). There was no increase in the specific risk of relapse associated with type of vaccine or diagnosis. Comparison with the 3-month control period preceding vaccination revealed an increased risk of relapse after vaccination (RR= 4.00; 95% CI, 1.35-11.82), which was restricted to CIDP patients (RR= 3.25, 95% CI, 1.07-9.84). The safety profile of SARS-CoV-2 vaccination was characterized by short-term, mild-to-moderate local and systemic adverse events.

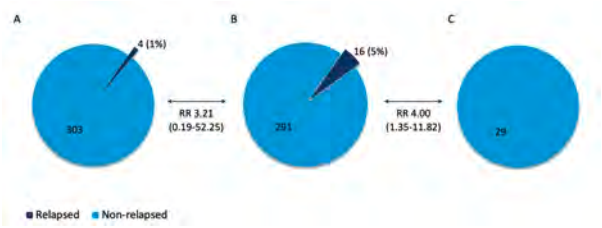

Fig. 1

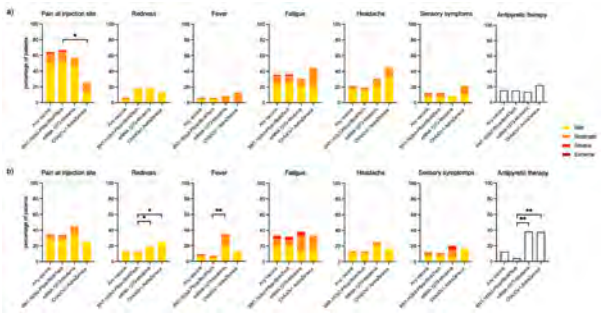

Fig. 2

Conclusion: SARS-CoV-2 vaccination in CIDP patients seems to be associated with a small increased risk of relapse and with an acceptable short-term safety profile. The benefits of SARS-CoV-2 vaccination in CIDP and MMN patients outweigh the risk of disease relapse.
Disclosure: The other authors declare no conflict of interest.

OPR-039

Clinical characteristics of Small Fiber Neuropathy following SARS-CoV2 infection or vaccination

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Background and aims: Small fiber neuropathy (SFN) is a peripheral nervous system disorder which can be caused by infection from particular pathogens (e.g., HIV) and by the immune response against them. This study aims to characterize patients reporting with symptoms compatible with SFN temporally related to either SARS-CoV2 infection or vaccination, as already suggested by several reports.
Methods: Skin biopsy was performed in patients presenting with symptoms compatible with SFN in close temporal connection (≤ 2 months) to either SARS-CoV2 infection or

vaccination. Large fiber neuropathy was excluded by neurological examination and nerve conduction studies. Clinical data, comprising time from infection or vaccination to symptoms, pain characteristics and localization, type of vaccination and response to therapy were collected. Additionally, the Douleur Neuropathique-4 Questionnaire was administered to characterize pain, as well as the Composite Autonomic Symptom Score in order to assess autonomic fiber involvement and Short Form Health Survey-36 for assessment of quality of life.

Results: 33 patients were studied (13 male, 20 female), of which 6 after infection and 27 after vaccination. Onset from event to clinical presentation was on average 20.5 days (range 7-76 days) for infection and 7.2 days for vaccination (range 1-42 days). Skin biopsy revealed reduced intraepidermal nerve fiber density compatible with SFN in 90% of infected patients and 70% of vaccinated ones.

Conclusion: In line with other studies, these results suggest a link between SFN and SARS-CoV2 infection or vaccination. A possible explanation could be the immune response against the Spike glycoprotein of SARS-CoV2 causing small fiber damage.

Disclosure: The authors have no conflicts of interest to disclose.

OPR-040

Distinctive Functional Antibody Signatures To Mycobacterium Tuberculosis In Pulmonary And Nervous System Infection

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Background and aims: Mycobacterium tuberculosis (Mtb) is primarily a respiratory pathogen; nevertheless, it can spread to the central nervous system (CNS) and cause TB meningitis. Despite being the most severe extrapulmonary form of Mtb infection, the pathogenesis of TB meningitis is poorly understood. Immune mechanisms, including Mtb-specific antibodies, are thought to be key in the control of Mtb infection in the lungs; however, their role in the development of TB meningitis remains unexplored.

Methods: Using systems serology, we deeply profiled the antibody responses against 10 different Mtb antigens in individuals with pulmonary (n=10) vs CNS (n=60) Mtb infection. In the latter, we compared the responses between serum and cerebrospinal fluid (CSF) and identified prognostic factors associated with disease severity (calculated using the modified British Medical Research Council (BMRC) grading system).

Results: Compared to pulmonary TB, Mtb-antibodies in the serum from meningitis were characterized by increased capacity to activate monocyte phagocytosis (ADCP), despite lower IgG titers (but similar IgM) and Fcg receptors (FcgR)-binding capacity (Fig 1). In individuals with TB meningitis, moreover, we identified CSF-specific antibody profiles that marked a unique and compartmentalized humoral response against Mtb, characterized by highly functional antibodies mediating complement (ADCD) and C1q binding (Fig 2). Importantly, CSF-enrichment of phagocytosis-mediating (ADCP, ADNP) antibodies was associated with milder meningitis severity (Fig 3).

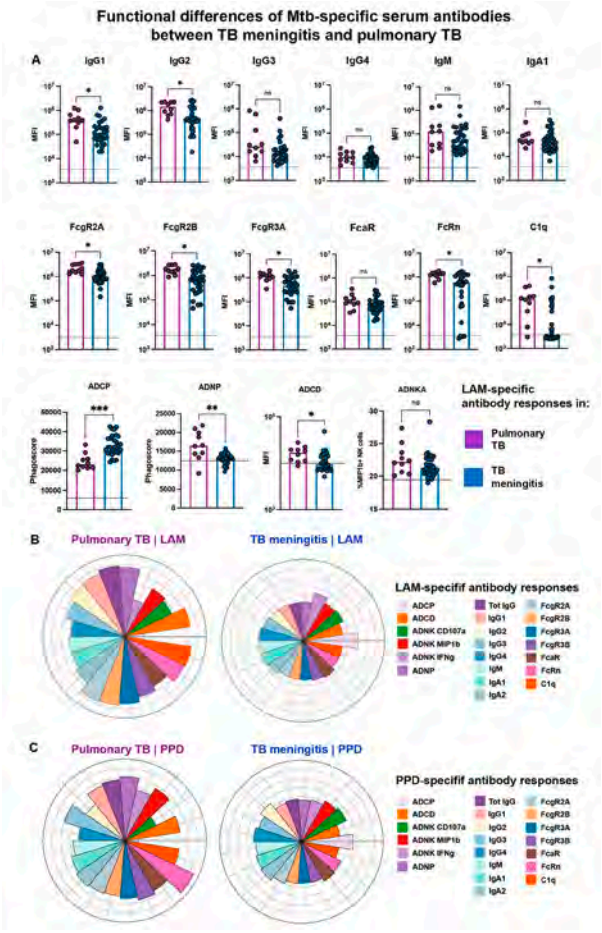

Fig 1. Functional differences of LAM-specific serum antibodies between TB meningitis and pulmonary TB

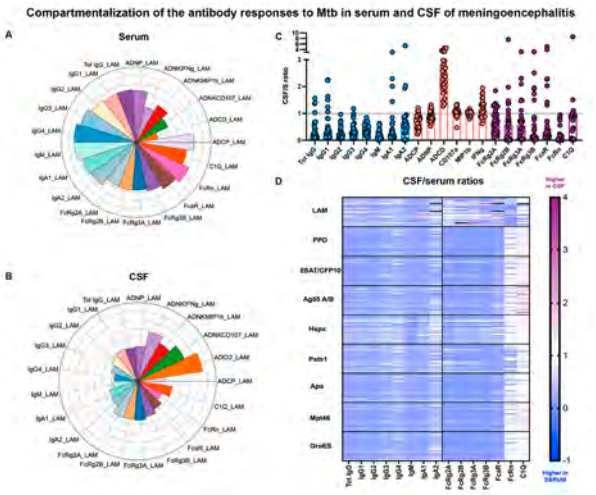

Fig 2. Compartmentalization and coordination of the humoral response to mycobacterium tuberculosis in the serum and CSF of TB meningitis

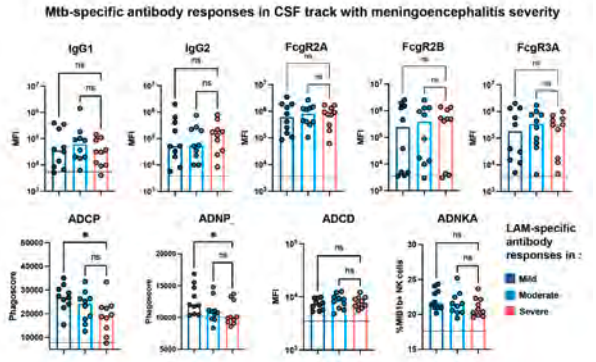

Fig 3. TB-specific antibody responses track with disease severity of TB meningitis

Conclusion: Antibody responses against Mtb are functionally different depending on the site of active infection, and are highly compartmentalized within the CSF. CSF-antibodies mediating monocyte phagocytosis might be involved in attenuated neuropathology and better outcome in TB meningitis.

Disclosure: Dr Spatola receives financial support for her research by the Swiss National Foundation for Science (FNS) and the la Caixa Foundation.

OPR-041

Diagnostic accuracy of granulocyte percentage in cerebrospinal fluid of adults with suspected CNS infection

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Background and aims: We aimed to assess the diagnostic accuracy of granulocyte percentage in cerebrospinal fluid (CSF) leukocytes for the diagnosis of central nervous system (CNS) infections.

Methods: In two prospective cohort studies we included patients ≥16 years suspected of having a CNS infection who underwent a diagnostic lumbar puncture. All patients with an elevated leukocyte count (i.e. >4) in the CSF were included in this analysis. Patients were categorized as having bacterial meningitis, viral meningitis or encephalitis, other CNS infection, CNS inflammatory (auto-immune) disease or other (neurological) disease.

Results: Between 2012-2015 and 2017-2022 1210 episodes from 12 hospitals in the Netherlands were included of which 594 (49%) had an elevated CSF leukocyte count. In total 138 of 594 (23%) were diagnosed with bacterial meningitis, 155 (26%) with viral meningitis or encephalitis, 53 (9%) with other CNS infections, 84 (14%) with CNS inflammatory diseases and 164 (28%) with other (neurological) diseases. The median granulocyte percentage was 87% (IQR 76-95) for bacterial meningitis, 5% (IQR 1-28) for viral meningitis or encephalitis, 7% (IQR 0-50) for other CNS infections, 6% (IQR 0-27) for CNS inflammatory diseases and 18% (IQR 0-56) for other (neurological) diseases (Fig 1). The area under the curve to differentiate bacterial meningitis from other causes was 0.92 [95% CI 0.89-0.95].

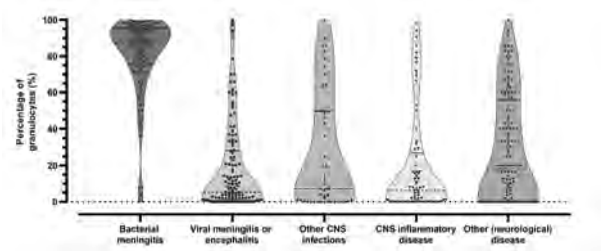

Figure 1. Violin plot showing the percentage of granulocytes in CSF per individual, divided by category. The dotted and solid line respectively shows the median and IQR per category.

Conclusion: The percentage of granulocytes in CSF is highest in patients with bacterial meningitis, however a high granulocyte percentage also occurs in other infections or inflammatory diseases of the CNS, limiting its diagnostic accuracy in clinical practice.

Disclosure: Nothing to disclose.

OPR-042

COVID-19 vaccination and relapse activity: A nationwide cohort study of patients with MS in Denmark

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Background and aims: Vaccination remains a key strategy to reduce spread and severity of COVID-19, but few, small sample size studies have investigated its effect on relapse occurrence in patients with multiple sclerosis (MS). Here, we evaluated whether there was a difference in pre- and post-COVID-19 vaccination relapse occurrence in a large cohort of Danish patients with relapsing MS.
Methods: We conducted an observational, prospective, nationwide cohort study using data from different national Danish registries, with a cut-off date at October 1st, 2022. We used McNemar tests to assess changes in the proportion of patients experiencing relapses within i) 90 days and ii) 180 days pre- and post- first vaccination dose, and a negative binomial regression model to compare the 90 and 180 days post-vaccination annualized relapse rate (ARR) to the 360 days pre-vaccination ARR.
Results: We identified 8,172 vaccinated (87.3% Comirnaty) patients with relapsing MS (2.1% clinically isolated syndrome; 97.9% relapsing-remitting MS; mean age 48.5 years) without a history of COVID 19. We did not find statistically significant changes in the proportion of patients with relapses in the 90 days (1.3% vs 1.4% of patients, p=0.53) and 180 days (2.7% vs 2.6% of patients, p=0.88) pre- and post- vaccination. Also, a comparison of the ARR 360 days before with the ARR 90 and 180 days after vaccination did not show statistically significant differences.
Conclusion: In a nationwide population of patients with relapsing MS, we did not find evidence of a higher relapse activity after compared to before COVID-19 vaccination.
Disclosure: This work was supported by the Czech Ministry of Health grant [grant number AZV NU22-A-150].

OPR-043

Global uncertainty in the diagnosis of neurological complications of COVID-19: An international inter-observer study

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Background and aims: Uniform case definitions are required to ensure harmonised reporting of neurological syndromes associated with SARS-CoV-2. Moreover, it is unclear how clinicians perceive the relative importance of SARS-CoV-2 in neurological syndromes, which risks under- or over-reporting.
Methods: We invited clinicians worldwide to assess ten anonymised vignettes of SARS-CoV-2 neurological syndromes. Using Case Definitions, clinicians assigned a diagnosis and ranked association with SARS-CoV-2. We compared diagnostic accuracy and assigned association ranks between different settings and specialties and calculated inter-rater agreement for Clinical Definitions as "poor" ($\kappa \leq 0.4$), "moderate" or "good" ($\kappa > 0.6$).
Results: 1,265 diagnoses were assigned by 146 participants representing 45 countries on six continents. The highest proportion of correct responses was recorded for cerebral venous sinus thrombosis (CVST; 95.8%), Guillain-Barré syndrome (GBS; 92.4%) and headache (91.6%) and the lowest for encephalitis (72.8%), psychosis (53.8%) and encephalopathy (43.2%). Diagnostic accuracy was similar between neurologists and non-neurologists (median 8 vs. 7/10 correct responses, p=0.09). Good agreement was observed for five diagnoses: cranial neuropathy, headache, myelitis, CVST and GBS and poor agreement for encephalopathy. In >10% of vignettes, clinicians incorrectly assigned lowest association ranks, regardless of setting and specialty.

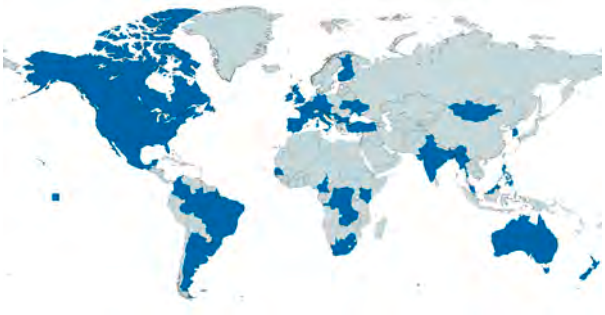

Figure 1. Countries of origin (in blue) of the 146 survey respondents.

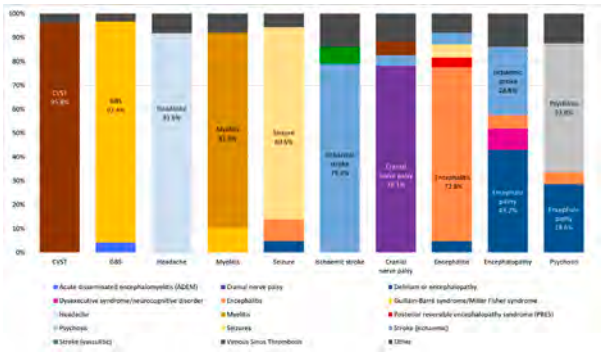

Figure 2. Diagnostic labels assigned to each clinical scenario. Each bar represents one of the ten clinical scenarios. The correct diagnosis is given at the bottom of each bar (x axis). The y axis shows the proportion of responses for each scenario.

Figure 3. Distribution of association ranks assigned by survey respondents, compared to the distribution expected if all association ranks were assigned according to the provided definitions (i.e. 100% correct responses).

Conclusion: Case Definitions can help with reporting of neurological complications of SARS-CoV-2, also in settings with few neurologists. However, diagnosis of encephalopathy, encephalitis, and psychosis remains challenging, and some clinicians may underestimate the association with SARS-CoV-2. Future work should refine Cases Definitions and provide training if global reporting of neurological syndromes associated with SARS-CoV-2 is to be robust.

Disclosure: Nothing to disclose.

Movement disorders 1

OPR-044

Predicting motor outcomes of patients with advanced Parkinson's disease under LCIG using machine learning modeling

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Background and aims: Despite the careful selection of candidate patients, the Levodopa-carbidopa intestinal gel (LCIG) treatment of advanced Parkinson's Disease (PD) remains challenging due to a complex interplay between motor and non-motor symptoms. We aimed to develop a novelmachine learning model (ML) to determine the motor outcomes of patients with advanced PD at 2 years under the LCIG therapy based onboth motor and non-motor longitudinal data.
Methods: This was a longitudinal 24-month, observational study of 59 patients with advanced PD of a Greek multicenter registry under LCIG treatment from September 2019 to September 2021. Motor status was assessed with the Unified Parkinson's Disease Rating Scale (UPDRS) part III and IV. Non-motor symptoms (NMS) were assessed by the Non-Motor Symptoms Questionnaire (NMSQ) and the Geriatric Depression Scale (GDS), and quality of life by PDQ-39. Multivariate linear regression models were firstly used. ARIMA model was derived for the time series, a deep learning method was presented and LSTM-RNN model was used.
Results: Data analysis shows that among the seven studied characteristics related to PD patients, dyskinesia duration and UPDRS-IIIweresignificantly improved after LCIG treatment(30% greater improvement in men compared to women). Multivariate linear regression models showed that PDQ-39 was associated with Hoehn&Yahr, while NMS were associated with UPDRS-IV and Hoehn&Yahr. Among all the time series models (SARIMA, ARIMA), the LSTMRNN model predicts these features with highest accuracy MSE=0.0069. .
Conclusion: The LSTM-RNN model predicts with highest accuracy the motor outcomes of patients with advanced PD after two years of LCIG therapy.
Disclosure: Nothing to disclose.

OPR-045

Pain and sensory profile in Parkinson's Disease and Parkinsonisms

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Background and aims: In Parkinson's disease (PD) and Multiple System Atrophy (MSA), pain is frequently reported as non-motor symptom of the disease. Conversely, in other neurodegenerative disorders including Progressive Supranuclear Paralysis (PSP) and Corticobasal degeneration (CBD), painful symptoms are rare and pain perception is impaired. We aimed to evaluate pain thresholds and pain tolerance in PD, MSA, PSP, and CBD patients.
Methods: We enrolled consecutive patients with a probable diagnosis of MSA, PD, PSP, and CBD. Patients with cognitive impairment, other painful conditions, or significant comorbidities were excluded. All performed extensive clinical, neuroalgological examinations, including clinical scales, neuropsychological examination, and psychological scales. Quantitative sensory testing (QST) battery including 12 somatosensory parameters, was performed in all patients, bilaterally, in upper and lower limbs, in L-Dopa ON and OFF conditions. We tested for differences in pain profile between groups, and association with neuropsychological tests.
Results: We included 18 MSA, 20 PD, 18 PSP, 11 CBD, and 55 healthy subjects (HS), sex, and age-matched. Ongoing or evoked painful symptoms were reported in 11 patients with MSA, 12 patients with PD, and in 5 patients with CBD, none in the PSP group. Warm thresholds were higher in MSA and PSP compared with PD and HS, and heat pain thresholds were higher in PSP, and lower in MSA. PSP and CBD reported errata perception of different sensory modalities. Central sensitization phenomena were also prevalent in PD and MSA, compared with other groups.
Conclusion: Sensory and painful processing showed different abnormalities between PSP, MSA, and PD groups, related to different underlying mechanisms.
Disclosure: Nothing to disclose.

OPR-046

Quality of life and non motor symptoms in PRRT2-related paroxysmal kinesigenic dyskinesia patients

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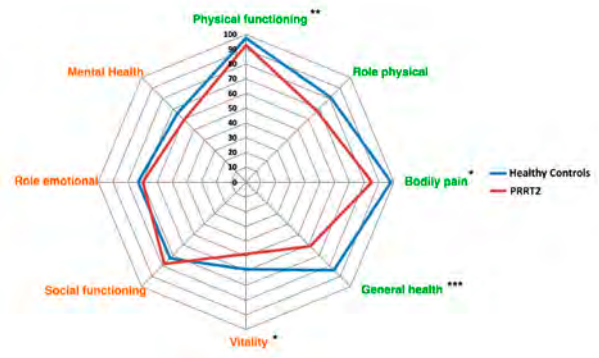
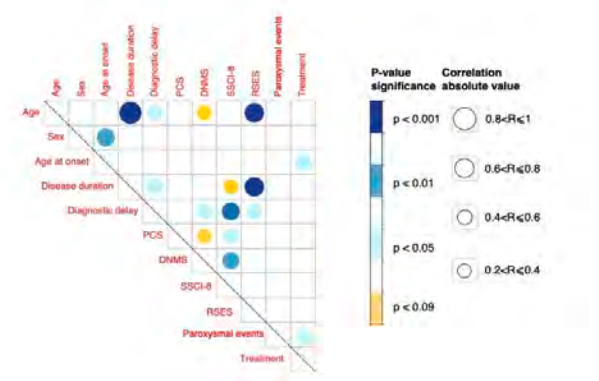
Background and aims: Monoallelic pathogenic variants of PRRT2 often result in paroxysmal kinesigenic dyskinesia (PKD). Little is known about health-related quality of life, non-motor manifestations, self-esteem and stigma in patients with PKD.
Objectives: We investigated non-motor symptoms and how they relate to quality of life in a genetically homogeneous group of PRRT2-PKD patients and their age and sex-matched controls. We paid special attention to perceived stigmatization and self-esteem.
Methods: We prospectively enrolled 21 consecutive PKD patients with a pathogenic variant of PRRT2, and 21 healthy

controls matched for age and sex. They were evaluated with dedicated standardized tests for non-motor symptoms, quality of life, anxiety, depression, stigma, self-esteem, sleep, fatigue, pain and psychological well-being.
Results: Patients reported an alteration of the physical aspects of health-related quality of life (HrQoL), regardless of the presence of residual paroxysmal episodes. Non-motor manifestations were frequent, and are an important determinant of the alteration of HrQoL. In addition, patients perceived a high level of stigmatization positively correlated with delay in diagnosis (ρ=0.615, p=0.003) and fear of being judged (ρ=0.452, p=0.04), but not with the presence of paroxysmal episodes (ρ=0.203, p=0.379).



Quality of life



Correlations

Conclusion: Our findings have important implications for management of these patients and medical education on paroxysmal dyskinesia. PRRT2-PKD patients should be screened for non-motor disorders in routine care. Since a long history of wavering diagnosis may play a role in the high level of perceived stigmatization, there is a need to increase the knowledge on the diagnosis clues to PKD.
Disclosure: Nothing to disclose.

OPR-047

Covariant Patterns of cholinergic transmission correlates with severity of Freezing of Gait in PD: A PET study

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Background and aims: Freezing of Gait (FoG) is common in Parkinson's Disease (PD). As disease progresses, patients develop symptoms such as postural instability, stooped posture and FoG, predisposing to falls. Our observational study used FEOBV and FDG PET, analyzed by principal component analysis (PCA) to identify covariance patterns of cholinergic and metabolic markers and to evaluate the relationship of these with FoG in PD.
Methods: Fourteen patients with PD and FoG underwent PET/MR, using FDG and the vesicular acetylcholine transporter ligand FEOBV. To derive functional networks, voxel-wise standardized uptake was reduced by PCA. Images obtained from FDG were normalized to the global mean uptake. For FEOBV, images were masked, thresholded and scaled using centrum semiovale as reference tissue. The individual expression of linear combinations of sequential PCs were correlated with FoG severity.
Results: For FEOBV, three PCs were combined. For FDG, two PCs were combined. The R2 between subject scaled expression of combined PCs and severity of FoG was moderate for both covariance patterns. Correlations were statistically significant (p=0.0110, p=0.0390). The pattern observed for FEOBV is consistent with decreased mesencephalic cholinergic transmission, projecting to the frontal and occipital cortices. The FoG-related pattern of FDG uptake is less clearly defined.
Conclusion: Our results support a relationship between decreased cholinergic transmission from the mesencephalic locomotor region and FoG severity. Further investigation is required to interrogate causative relationships and whether the identified pattern can be used to monitoring of treatment effect. For FDG, the time-course of development of the pattern observed warrants investigation.
Disclosure: Nothing to disclose.

OPR-048

Predicting phenoconversion of REM sleep behaviour disorder due to synucleinopathy using dopaminergic imaging

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Background and aims: REM sleep behaviour disorder (RBD) is a REM sleep parasomnia that in the majority of cases precedes the development of overt alpha-synucleinopathies. Aim of this study was to apply a machine learning analysis to clinical and presynaptic dopaminergic imaging data of iRBD patients to investigate whether it is possible to identify those patients eventually developing Parkinson's disease (PD) compared with those developing dementia with Lewy bodies (DLB).

Methods: This is a retrospective international multicentre study of the International RBD Study Group. Patients with polysomnography-confirmed RBD who phenoconverted to overt alpha-synucleinopathy were enrolled and underwent baseline clinical and presynaptic dopaminergic imaging assessment. Motor, cognitive, olfaction and constipation data were collected.

Results: 173 patients with RBD due to synucleinopathy (mean age 70.3±6.3 years, 70.5% males) were enrolled. After a mean follow-up of 41.1±30.0 months, 94 (54.3%) patients developed PD, 74 (42.8%) DLB and 5 (2.9%) multiple system atrophy. The machine learning analysis showed that clinical data alone poorly predicted phenoconversion. Presynaptic dopaminergic imaging significantly improved the prediction, especially in combination with clinical data (89% sensitivity, 89% specificity). Compared with patients developing DLB, those developing PD were younger and showed more severe baseline presynaptic dopaminergic imaging deficit.

Conclusion: Routine clinical data alone are not able to predict the phenoconversion diagnosis in patients with RBD due to synucleinopathy. Conversely, presynaptic dopaminergic imaging may help in achieving a good prediction of forthcoming phenoconversion diagnosis. This finding may be used in designing future disease-modifying trials.

Disclosure: Nothing to disclose.

Ageing and dementia 1

OPR-049

Spatial navigation deficits are associated with a specific pattern of brain atrophy in normal and pathological ageing

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Background and aims: Spatial navigation (SN) impairment is a marker of Alzheimer's disease (AD) associated with specific brain changes. We examined associations between SN and atrophy of the medial temporal lobe (MTL) and parietal regions, and assessed SN differences between AD biomarker positive (AD aMCI) and negative (non-AD aMCI) older adults with amnestic mild cognitive impairment (aMCI), individuals with mild AD dementia, and cognitively normal (CN) older adults.
Methods: Participants with AD aMCI (n=26), non-AD aMCI (n=23), mild AD dementia (n=22) and CN participants (n=29) underwent brain MRI and three virtual SN tasks focused on route learning, wayfinding and perspective taking/wayfinding. Left and right hippocampal head (HH), body (HB) and tail (HT), anterolateral (alEC) and posteromedial (pmEC) entorhinal cortex, precuneus (PC), isthmus cingulate (IC) and posterior parietal cortex (PPC) volumes were measured.
Results: Route learning deficits were associated with bilateral PC and PPC atrophy (ß>=0.28, p<0.01), wayfinding deficits were associated with right HB and bilateral pmEC atrophy (ß>=0.24, p<0.05), and perspective taking/wayfinding deficits were associated with left HB, right HT and IC, and bilateral pmEC, PC and PPC atrophy (ß>=0.26, p<0.05). In route learning, AD aMCI performed worse than non-AD aMCI (p<0.001), who were similar to CN. In wayfinding, aMCI participants performed worse than CN (p<=0.009) and AD aMCI performed worse than non-AD aMCI in the second task session (p=0.032). In perspective taking/wayfinding, aMCI participants performed worse than CN (p<=0.001).
Conclusion: SN deficits were associated with posterior MTL and parietal atrophy and had different profiles in AD biomarker positive and negative older adults with aMCI.
Disclosure: This study was supported by the National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107) – Funded by the European Union – Next Generation EU, the Institutional Support of Excellence 2 2. LF UK (Grant No. 6980382), the Czech Science Foundation (GACR) (Grant No. 22-33968S), the EEA/ Norway Grants 2014–2021 and the Technology Agency of the Czech Republic (Grant No. TO01000215), and the Grant Agency of Charles University (Grant No. 327821).

OPR-050

European consensus for the biomarker-based diagnosis of neurocognitive disorders

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Background and aims: In vivo biomarkers enable early etiological diagnosis of neurocognitive disorders. While they have good analytical validity, their clinical validity and utility are uncertain. A European multidisciplinary task force set out to define a patient-centred diagnostic workflow for the rational and cost-effective use of biomarkers in memory clinics.
Methods: Twenty-two experts from eleven European scientific societies and the Alzheimer Europedirector participated in six rounds of a Delphi consensus and voted on questions drafted by an impartial executive board, based on systematic reviews and their own expert opinion.
Results: The workflow features three waves of assessment (W): W1 defines eleven clinical profiles based on the results of clinical and neuropsychological assessments, blood exams, brain imaging, and, in specific cases (e.g., late-onset or autoimmune epilepsy, CJD), EEG; W2 defines the first-line biomarker based on the W1 clinical profiles; and W3 defines the second-line biomarker based on W2 biomarker results. When the clinical profile suggests Alzheimer's disease and in undefined cases, cerebrospinal fluid (CSF) biomarkers are first-line; FDG-PET is second line when CSF is inconclusive. When the clinical profile suggests frontotemporal lobar degeneration or motor tauopathies, FDG-PET is first-line and CSF biomarkers second-line in atypical metabolic pattern cases. When the clinical profile suggests Lewy body disease, dopamine transporter SPECT is first-line and cardiac 123I-metaiodobenzylguanidine scintigraphy second-line. Biomarker use is recommended below age 70, discouraged above age 85, and to be discussed case-by-case in-between.

Conclusion: This diagnostic workflow will promote consistency of the diagnosis of neurocognitive disorders across European countries, and a rational use of resources.
Disclosure: Unrestricted grants from F. Hoffmann-La Roche Ltd., Biogen International GmbH, Eisai Europe Limited, Life Molecular Imaging GmbH, OM Pharma Suisse SA. The Task force of the European Inter-Societal Consensus on the Biomarker-Based Diagnosis of Dementia: Aarsland D, Agosta F, Babiloni C, Boada-Rovira M, Borroni B, Cappa S, Dubois B, Frederiksen KS, Froelich L, Garibotto V, Georges J, Haliassos A, Hansson O, Jessen F, Kamondi A, Kessels RPC, Morbelli S, O'Brien J, Otto M, Perret-Liaudet A, Pizzini FB, Ritchie CW, Scheltens P, Van der Flier W, Vandenbulcke M, Vanninen R, Verhey F, Vernooij MW, Yousry T.

OPR-051

Alterations of spontaneous speech in primary progressive aphasia variants: a neuropsychological and brain MRI study

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Background and aims: To identify which features of spontaneous speech most effectively distinguish PPA variants (non-fluent/agrammatical [nfvPPA], semantic [svPPA], and logopenic [lvPPA]) from healthy controls (HC) and each other; and to determine whether the speech measures associated to each variant are related to gray matter (GM) density of specific language brain circuits.
Methods: 95 PPA patients (40 nfvPPA, 35 svPPA, and 20 lvPPA) and 25 HC underwent the audio-recorded 'Picnic Scene' test from the Western Aphasia Battery and a brain MRI. Stepwise regression models detected the best speech parameters able to distinguish the groups, and multiple regressions were performed between the detected speech parameters and GM volumes.
Results: The best model differentiating PPA patients and HC included: false starts and mean production rate for lvPPA; production rate and self-corrected sequences for nfvPPA; mean frequency of produced nouns for svPPA. In lvPPA, nfvPPA and svPPA, z-scores of each 'best-model' variables were positively associated with the GM density of left postcentral, inferior frontal, and inferior temporal gyri, respectively. The best model to distinguish: lvPPA from nfvPPA cases included incomplete and subordinate sentences; lvPPA from svPPA included proportion of sentences and verbs; nfvPPA from svPPA included number of produced verbs and sentences, and production rate.
Conclusion: The speech variables that we identified and that were related to specific GM circuits, may be used in the clinical practice for patients' differential diagnosis, prognosis, and planning pharmacological and non-pharmacological interventions.
Disclosure: Supported by: Italian Ministry of Health (RF-2010-2313220; RF-2011-02351193; GR-2013-02357415); European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease.

OPR-052

Egocentric and Allocentric Spatial Navigation Deficits in Early Alzheimer´s Disease

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Background and aims: Spatial navigation deficits are typical for early Alzheimer´s disease (AD). We evaluated a potential of a realistic looking spatial navigation task to detect AD-related spatial navigation impairment in AD biomarker positive participants.
Methods: Participants with AD mild cognitive impairment (AD MCI, n=30), mild AD dementia (n=12) and cognitively normal (CN) older adults (n=34) underwent spatial navigation assessment in the virtual Supermarket task. Participants passively travelled through the supermarket and followed different routes to reach specific locations. In the final location, the participants had to indicate their starting location (egocentric navigation), and their current location and final heading orientation on an aerial spatial map of the supermarket (both measures of allocentric navigation).
Results: In the egocentric task, both the AD MCI and mild AD dementia groups indicated their original starting location less accurately than the CN group ($p<0.001$). Similar differences were found in both allocentric tasks, first, the AD MCI and mild AD dementia groups indicated their positions on a paper aerial map of the supermarket with greater distance errors than the CN group ($p<0.001$), and secondly, both the AD MCI and mild AD dementia groups made more errors indicating final heading orientation

(p<0.001). The mild AD dementia group had worse performance in both allocentric tasks compared to the AD MCI (p≤0.048), and similar performance in the egocentric task (p=0.853).

Conclusion: Both, egocentric and allocentric spatial navigation tasks detect spatial navigation impairment typical for AD. The virtual Supermarket task has a potential to become a screening tool for early AD-related spatial navigation deficits.

Disclosure: National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107) – Funded by the European Union – Next Generation EU, the Institutional Support of Excellence 2 2.LF UK (Grant No. 6980382), and the Grant Agency of Charles University grant no. 327821.

OPR-053

Machine learning model to predict progression from subjective to objective cognitive decline: a 12-year follow-up study

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Background and aims: Subjective cognitive decline (SCD) represents a target population to be screened for dementia. Previous studies identified demographic, cognitive and generic features associated with higher risk of progression to mild cognitive impairment (MCI) and Alzheimer's disease (AD). We aim to test the accuracy of a machine learning model, trained on features derived from non-invasive and easily accessible techniques, in predicting conversion from SCD to MCI and AD.

Methods: We included 150 SCD patients who underwent neuropsychological examination, assessment of cognitive complaint, mood disorders and cognitive reserve, APOE genotyping at baseline. All patients underwent clinical-neuropsychological follow-up every 12-24 months for a mean time of 12 years.

Results: During the follow-up, 63 patients were classified as progressive SCD (p-SCD, 42.0%[95% C.I.=34.1:49.9], including 41 MCI (27.3% [95%C.I.=20.2:34.5]) and 22 AD (14.7% [95%C.I.=9.0:20.3]). 87 patients were classified as non-progressive SCD (np-SCD, 58.0% [95%C.I.=50.1:65.9]). We split the whole sample into a training (80%) and a test group (20%). A gradient boosted trees algorithm was trained on 15 selected features including: age, APOE, education, test assessing for global cognition, immediate and delayed verbal, ecological memory and working memory, language, visuospatial abilities, phonemic fluency and cognitive reserve (Fig.1). This model showed a good accuracy (0.83, AUC=0.78) in distinguishing p-SCD and np-SCD in the test group (Fig.2 and Fig.3).

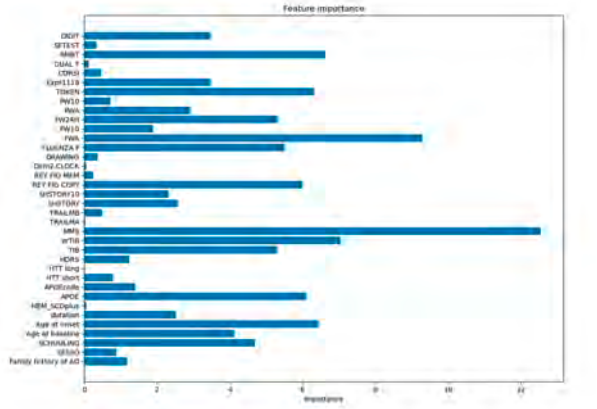

Figure 1. Bar chart showing the importance of each feature considered to train the gradient boosted trees algorithm

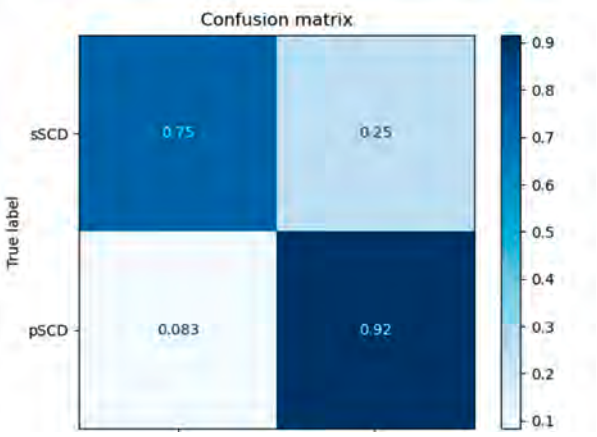

Figure 2. Confusion matrix of the machine learning model

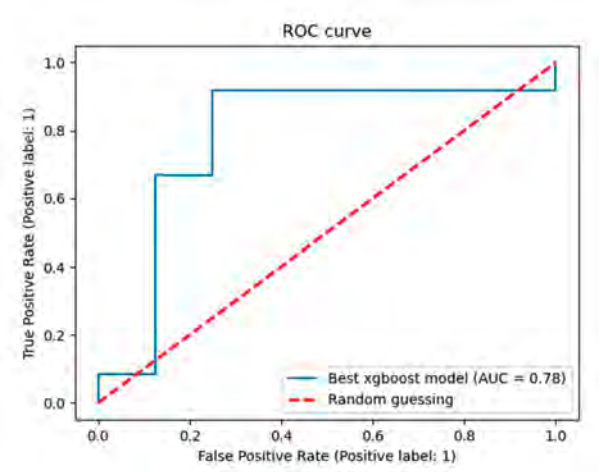

Figure 3. ROC curve showing the accuracy of machine learning model in distinguishing p-SCD and np-SCD patients within the test group.

Conclusion: Our machine learning models might represent a reliable, cost-effective and globally scalable tool for a first step screening of SCD patients before confirmation of AD pathology via more invasive and expensive tests.
Disclosure: The authors declare no commercial or financial relationships that could be construed as a potential conflict of interest.

Headache and Pain

OPR-054

Neurological complications of excessive recreational nitrous oxide use: a case series

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Background and aims: The recreational use of nitrous oxide (N2O) has gained popularity over recent years. We present a case series of excessive N_2O-users with neurological complications.

Methods: In this retrospective three-center study, we searched for patients who used N_2O recreationally and visited a neurologist. We collected data on the quantity and duration of N_2O-use, symptoms and signs, laboratory findings, imaging results, neurophysiological studies, treatment, admissions, and recovery.

Results: Over a six-year period, we identified 251 patients: 63% male, median age 22 years. The median duration of N2O-use was 11 months, median amount used per day 1.6kg, 29% were daily users. Clinically, polyneuropathy (78%), myelopathy (41%), and encephalopathy (14%) were the most common diagnoses. An absolute vitamin B12 deficiency of <150 pmol/L was found in 40%. In 90%, either vitamin B12, homocysteine, or methylmalonic acid was abnormal. MRI showed signs of myelopathy in 30/55 cases. In 28/44 cases, evidence of axonal polyneuropathy was found with electromyography, only one patient had demyelinating characteristics. Most (83%) were treated with vitamin B12 suppletion and 79% showed partial or complete recovery. As compared with literature, our patients were severely disabled and cognitive problems (14%), headache (13%), and seizures (5%) were commonly observed.

Conclusion: In our large case series of excessive recreational N_2O-use, we describe a high prevalence of polyneuropathy, myelopathy, and encephalopathy The frequently observed axonal neuropathy, cognitive decline, headache, and seizures, probably reflect direct N2O toxicity and chronic mild hypoxemia. Effective treatment should incorporate supplementation of vitamin B12 and strategies to prevent relapses in N_2O use.

Disclosure: Nothing to disclose.

OPR-055

Neuroimaging, Neurophysiological and Psychophysiological Analysis of Concomitant Continuous Pain in Trigeminal Neuralgia

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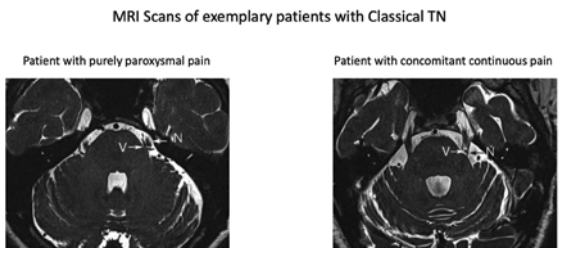
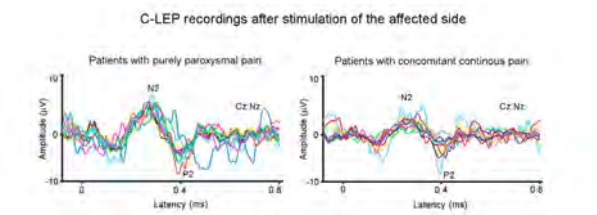
Background and aims: A distinctive phenotype of Trigeminal Neuralgia (TN) is characterized by the presence of an additional type of pain, continuous and burning, besides the characteristic electric shock-like paroxysmal pain. Since this continuous pain tends to respond less to available treatments, it may be due to a different pathogenetic mechanism.

Methods: Patients with a definite diagnosis of Primary Trigeminal Neuralgia were subclassified according to the presence of concomitant continuous pain. Both groups underwent high-resolution 3T MRI with a volumetric study of the trigeminal nerve, laser-evoked potentials (LEP), and quantitative sensory testing (QST) according to the DFNS protocol.

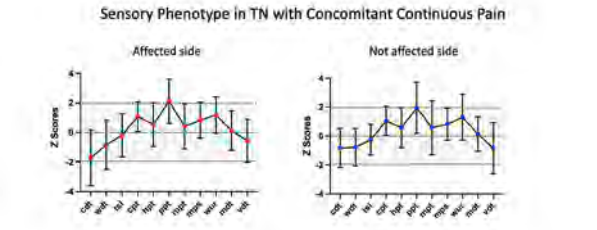
Results: A total of 73 TN patients were enrolled, of which 28 reported concomitant continuous pain (38%). Patients with concomitant continuous pain showed a more severe trigeminal root atrophy ($p<0.001$), an attenuation of the LEP elicited by stimulation of C fibres ($p<0.005$) and of the Cold Detection Threshold as assessed by QST ($p<0.05$). The volume of the affected nerve showed a correlation with Wind-Up Ratio ($p<0.05$).



MRI Scans of exemplary patients with Classical TN. Left: patient with purely paroxysmal pain which affected nerve (N) does not show atrophy. Right: patient with concomitant continuous pain, which affected nerve (N) shows atrophy



C-LEP recordings in TN patients after stimulation of the affected side. Left: Patients with purely paroxysmal pain. Right: Patients with concomitant continuous pain. An attenuation of amplitude of the N2 response can be clearly distinguished.



Sensory phenotype in patients with TN with concomitant continuous pain. Left: Affected side. Right: Not affected side. A difference in Cold Detection Threshold (CDT), lower on the affected side, can be clearly distinguished.

Conclusion: Our multimodal findings converged in showing that concomitant continuous pain is characterized by axonal loss and impairment of the small trigeminal fibres. The correlation of the volume of affected nerve with Wind-Up Ratio suggests that the axonal loss may trigger hyperexcitability in the second order neuron. This abnormal activity could underlie the development of concomitant continuous pain.

Disclosure: Part of this work has been founded by the European Academy of Neurology through Research Fellowship 2021.

OPR-056

Multicenter real-world case-control study of effectiveness,tolerability and anti-CGRP response predictors in the elderly

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Background and aims: To evaluate clinical characteristics, effectiveness, and tolerability of preventive anti-CGRP therapies in the elderly, a group in which information is scarce.

Methods: We performed a multicenter study nested in a prospectively collected cohort of cases(patients over 65 years old) and controls (sex-matched patients under 55 years old) with migraine receiving anti-CGRP therapies. Demographic characteristics, effectiveness-reduction in the number of monthly headache days (MHD) and monthly migraine days (MMD), 30%, 50% and 75% responder rates and adverse events were collected; the primary endpoint was the 50% response rate regarding MHD at weeks 20-24; exploratory 50% response predictors in the elderly were evaluated.

Results: 228 patients were included-114 cases and 114 controls-. Among cases 84.2%(96/114) were women, 79.8%(91/114)chronic migraine; mean age of cases 70.1 years old(range:66-86);mean age of controls was 42.9 years old(range:38-49). Cases had a higher percentage of vascular risk factors, older age of onset and more reported prior prophylactics. Regarding effectiveness, in cases, 50% response rate was achieved by 59%(90/152) at 20-24 weeks, with a lower reduction in the MHD at 8-12 weeks(p=0.001) and a higher reduction in MMD at 20-24 weeks(p=0.04) compared to the controls. The percentage of adverse events was similar in the two groups. Diagnosis of episodic migraine(p=0.003) and a lower number of MHD at baseline(p<0.001) were associated with a 50% response in the elderly in univariate analysis.

Conclusion: Our study provides class-III real-world evidence of effectiveness and safety of anti-CGRP therapies for migraine in patients without upper age-limit. Additionally, migraine type and frequency might predict anti-CGRP response in the elderly.

Disclosure: Alicia Gonzalez-Martinez:speaker honoraria from TEVA. Jaime Samuel Rodríguez-Vico:Abbvie, Novartis, Lilly, TEVA and UCB, Lilly, Novartis and Abbvie. Javier Díaz de Terán: speaker honoraria from Novartis, Lilly and TEVA. Nuria González García: Lilly, Abbie, Novartis, Teva, Chiesi, Exeltis. Jesús Porta-Etessam:Allergan, Chiesi, Eli Lilly, Novartis and Teva. Sonia Quintas:Lilly and Novartis. Javier Casas Limón:Novartis, Eli Lilly and Teva. Germán Latorre:Lilly, Novartis, Teva, Chiesi and Allergan. David García-Azorín:Teva, Lilly, Allergan-Abbvie, Novartis and

Lundbeck, and has served on an advisory board for Allergan-Abbvie. Ángel Luis Guerrero-Peral:Lilly, TEVA, Novartis, Allergan-Abbvie and Exeltis, and research support from Allegan-Abbvie and TEVA. Cristina Trevino-Peinado:TEVA. Ana Beatriz Gago-Veiga: Lilly, Novartis, TEVA, Abbvie-Allergan, Exeltis and Chiesi. Alex Jaimes, Álvaro Sierra, Ancor Sanz-Garcia, Andrea Gómez García, Javier Membrilla, María Sastre, Carlos Calle de Miguel, Patricia Heredia, Sendoa Gil Luque, Ana Echavarría, reports no disclosures relevant to the abstract.relevant to the manuscript. The authors do not have any conflict of interest regarding this abstract.

OPR-057

The Effect of Cannabis-Based Medicine on Central Neuropathic Pain – Results from a Randomized, Placebo-controlled Trial

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Background and aims: CBM has been suggested as a treatment for a wide range of diseases and symptoms including central neuropathic pain (CP). Patients with multiple sclerosis (MS) or spinal cord injury (SCI) frequently suffer from CP. Unfortunately, CP is often difficult to treat due to limited effects or unacceptable side effects. Animal studies have shown promising results for the use of CBM. However, the evidence for the use of CBM for CP in humans is limited.

Methods: In a Danish multi-center study the efficacy of CBM on CP and spasticity was investigated in a population of patients with MS or SCI. Here we report the results on CP. The two cannabinoids cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC) were investigated alone or in combination (THC&CBD) against a placebo, in a 7-week placebo-controlled, double-blinded parallel design. Pain intensity was registered daily at a 7-days baseline, during 7 weeks of treatment, and at follow-up on a Numeric Rating Scale (NRS 0-10)

Results: 114 patients with CP due to MS or SCI were included (n= patients in each group with CP>3 at baseline). The mean difference (mean, 95%CI) in pain intensity from baseline to last week of treatment was; Placebo (n= 35) 1.8 (1.17-2.43), THC (n= 24) 1.4 (0.53-2.24), CBD (n= 27) 1.4 (0.72-1.98), and THC&CBD (n= 28) 1.6 (0.94-2.34), respectively. No significant difference in pain reduction was observed between the groups (p=0.74, one-way ANOVA).

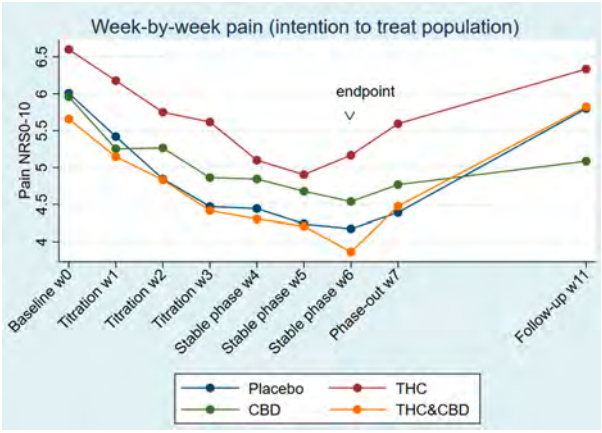

Figure 1: Mean NRS week-by-week for each treatment group in the intention to treat population. For simplicity, the 95%CI has been omitted. The baseline was before treatment started, weeks 1-3 was titration, weeks 3-6 was a stable phase, the end of week 6

Conclusion: CBM did not prove more effective than a placebo in the treatment of CP in a 7-weeks treatment period.

Disclosure: The Danish Ministry of Health, The Danish Multiple Sclerosis Society, Bdr. Hartmann Foundation, Karen A Tolstrup Foundation, "Direktør Ejnar Jonasson kaldet Johnsen og Hustru's Mindelegat" JSH Travel grants: Almirall and Roche HK Scientific advisory boards: Lundbeck A/S and Novartis, travel grants: IPSEN, Merck PVR Speaker honoraria: Biogen, Roche, Merck, Alexion, Novartis; congress participation: Merck, Roche, Sanofi; advisory boards: Bristol-Myers-Squibb, Merck, Roche, Novartis, Biogen, Sanofi, Alexion RMH Congress participation: Merck, Ipsen; speaker honoraria: AbbVie TP Research support: Merck, Alexion, Roche, Biogen, Novartis, Sanofi. FS Scientific advisory boards, consultant, congress participation, research support, and speaker honoraria: Alexion, Biogen, Bristol Myers Squibb, H. Lundbeck A/S, Merck, Novartis, Roche, Sanofi Genzyme. ABO Scientific advisory boards: Biogen Idec; research support: Novartis, Biogen Idec; speaker honoraria: Biogen Idec, Novartis, TEVA; congress participation: Merck, TEVA, Biogen, Roche, Novartis, Sanofi Genzyme. SG congress participation: Merck NBF Consultancy fees from Almirall, NeuroPN, Vertex, Nanobiotix, Novartis Pharma, consultancy work for Aarhus University with remunerated work for Biogen, Merz, Confo Therapeutics; grants: IMI2PainCare, an EU IMI 2 (Innovative Medicines Initiative) public-private consortium, and the companies involved are Grunenthal, Bayer, Eli Lilly, Esteve, Teva KBS travel grants:TEVA, Biogen, Merck, Novartis

OPR-058

Alterations of the EEG alpha-rhythm as potential biomarker of visual snow syndrome

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Background and aims: Patients with visual snow syndrome (VSS) suffer from "visual snow" and additional visual symptoms. Migraine is a comorbidity in about 60% of patients. The underlying pathophysiology might involve a disturbance in neuronal networks implicated in the processing of visual stimuli. On the level of neuronal oscillations the EEG, alpha-rhythm modulates visual perceptual thresholds. This study evaluates if there are changes in the resting-state alpha-rhythm that are characteristic for VSS.
Methods: Routine EEGs of 21 VSS patients were compared to 21 age-, gender- and migraine-matched controls. EEG data was preprocessed with EEGlab and included filtering, independent component analysis and re-referencing to common average. Fast Fourier transformation was done to identify the individual alpha peak frequencies. The mean power spectral density was calculated around the alpha peak (+1/-1 Hz) on the electrodes O1 and O2. Group comparisons were done with the Wilcoxon rank sum test.
Results: There were no statistically significant difference in the alpha power spectral density over the occipital electrodes between the groups (trend towards decreased power spectral density in the VSS group (O1: p= 0.1020; O2: p= 0.0627). The difference in the individual alpha frequencies only showed a trend to higher frequencies in the VSS groups (O1: p= 0.1627; O2: p= 0.4355). In an exploratory subgroup analysis investigating only subjects without migraine, the VSS group had higher alpha frequencies compared to control subjects (N=7 per group; p=0.01).
Conclusion: This study provides preliminary evidence of a difference in the individual alpha frequencies in persons with VSS and without migraine.
Disclosure: None relevant for this work. Outside this work: CJS: Consulting, advisory boards, speaker, travel support from/for Novartis, Eli Lilly, Teva Pharmaceuticals, Allergan, Abbvie, Amgen, Almirall, Lundbeck, MindMed, Pfizer, Grünenthal. Part-time employee at Zynnon.

OPR-059

Treatment with GLP-1 agonists in patients with idiopathic intracranial hypertension: a pilot case-control study

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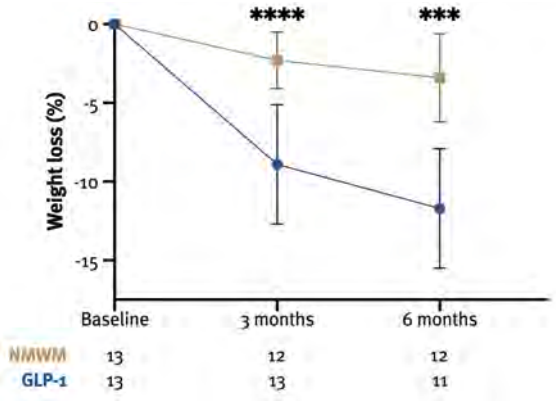
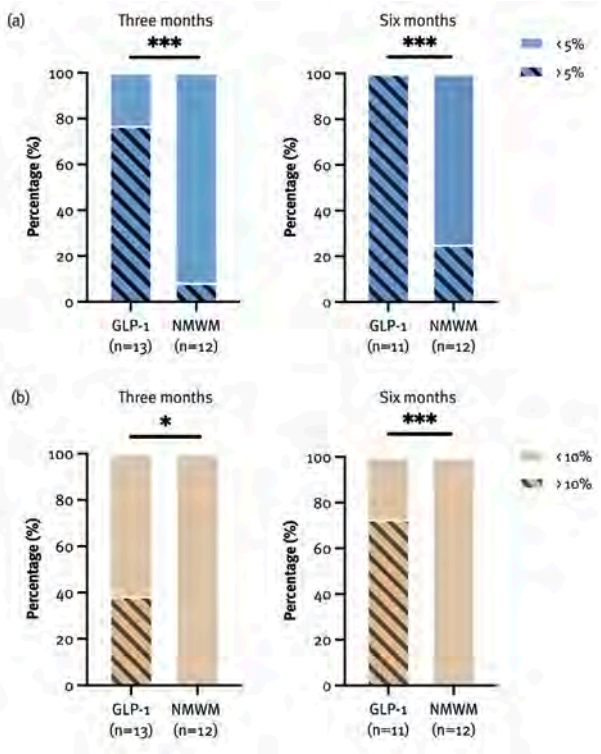
Background and aims: Idiopathic intracranial hypertension (IIH) is a disease mostly occurring in young obese women. Glucagon-like peptide-1 agonists (GLP-1Ag) present an attractive treatment option for sustained weight loss.
Methods: In this pilot single-centre case-control study, pwIIH (BMI ≥30) were offered to receive GLP-1Ag (liraglutide, semaglutide) besides non-medical weight management (NMWM). Age-, sex- and BMI-matched pwIIH electing for NMWH served as controls. The primary endpoint was percentage weight loss at three (M3) and six months (M6). Secondary endpoints were defined as follows: (1) ≥5% and/or ≥10% weight loss, (2) improvement of headache days (≥50%) and headache freedom, (3) visual worsening (deterioration of visual acuity by ≥0.2 logMAR and/or by ≥2.0 dB in static threshold perimetry), (4) adverse events (AE).
Results: Twenty-six pwIIH (mean age 33.5 years [SD 7.8], 92.4% female, median BMI 36.1 [IQR 32.2–40.8]) were included (13 pwIIH receiving GLP-1Ag). Mean weight loss was higher in the GLP-1Ag group at M3 (–8.9% [3.8] vs. –2.3% [1.8]; p<0.001) and M6 (–11.7% [3.8] vs. –3.4 [2.8]; p<0.001). Higher proportion of pwIIH receiving GLP-1Ag lost ≥5% weight at M3 (76.9% vs. 8.3%; p=0.001) and M6 (100.0% vs. 25.0%; p<0.001). Only pwIIH receiving GLP-1Ag lost ≥10% weight (M3: 38.5%; M6: 72.7%). Most common AEs were nausea (69.2%), inappetence (15.4%) and abdominal pain (7.7%), with no serious AE. No elevation of liver/pancreatic enzymes was seen. There was no discontinuation of treatment.



Patients treated with GLP-1 agonists lost significantly more weight at M3 and M6.



Higher proportion of patients treated with GLP-1 agonists reached ≥5% (a) and ≥10% weight loss (b) at M3 and M6. At M6, all patients treated with GLP-1 agonists reached ≥5% weight loss, and 72.7% of treated patients also reached ≥10% weight loss.

Conclusion: GLP-1Ag present a safe, efficient and well-tolerated treatment option for achieving significant weight loss in pwIIH with yet unknown effect on headache and visual outcomes.

Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

Sleep-wake disorders

OPR-060

Abstract withdrawn

OPR-061

SLEEP FEATURES AND LONG-TERM INCIDENT NEURODEGENERATIVE DISEASES: A POLYSOMNOGRAPHIC STUDY

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Background and aims: Sleep is altered early in neurodegenerative diseases (NDDs) and may contribute to neurodegeneration. Long-term, large sample size studies assessing this association with objective sleep measures are scant. We aimed to investigate whether polysomnography-based sleep features are associated with long-term NDDs incidence.
Methods: Retrospective cohort-study of patients referred 2004-2007 to the Sleep Disorders Unit, Neurology, Medical University Innsbruck, Austria. All patients ≥18 years undergoing PSG and without NDDs at baseline or within five years were included. Main outcome was NDDs diagnosis ≥five years after PSG (until December 2021).
Results: 999/1454 assessed patients (68.7%) met inclusion criteria (68.3% men; median age 54.9 (IQR 33.9-62.7) years). Seventy-five patients(7.5%) developed NDDs and 924(92.5%) remained disease-free after a median of 12.8(IQR 9.9-14.6) years. After adjusting for demographic, sleep, and clinical covariates, one-percentage decrease in sleep efficiency, N3-, or REM-sleep was associated with 1.9%, 6.5%, or 5.2% increased risk of incident neurodegeneration, respectively (HR 1.019, 1.065, 1.052, respectively). One-percentage decrease in wake within sleep period time (SPT) represented a 2.2% reduced risk of incident NDDs(HR 0.978). Patients in the highest wake-in-SPT quartile(>18.6%) or the lowest REM-(<13.0%) or N3-sleep(0%) quartile had the shortest overall mean disease-free survival time (14.9, CI 14.6-15.3 years).
Conclusion: In this cohort, altered sleep architecture at baseline with reduced sleep efficiency, REM- or N3-sleep, or increased wake-in-SPT, was associated with incident neurodegeneration after ≥five years. These findings support the hypothesis that sleep changes may contribute to NDDs pathogenesis, and point to sleep as early neurodegeneration marker and potential target of neuroprotective strategies.
Disclosure: Financial disclosure: None. Non-financial disclosure: Nothing to disclose.

OPR-062

Distressing dreams in childhood and risk of cognitive impairment or Parkinson's disease in adulthood

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Background and aims: Distressing dreams in middle-aged and older adults have been associated with an increased risk of developing cognitive impairment (including dementia) and Parkinson's disease (PD). Whether distressing dreams in younger people might be associated with an increased risk of developing these conditions is unknown. This study investigated the association between distressing dreams in childhood and the risk of developing cognitive impairment or PD in adulthood.
Methods: Data were obtained from the 1958 British Birth Cohort Study. Information on distressing dreams were obtained prospectively from the children's mothers at ages 7 (1965) and 11 (1969). Cognitive impairment and PD at age 50 (2008) were determined by cognitive assessment and doctor-diagnosis respectively. The association between distressing dreams at ages 7 and 11 (no time-point, 1 time-point, 2 time-points) and cognitive impairment or PD at age 50, was evaluated using multivariable logistic regression.
Results: Among 6,991 children with follow-up at age 50, 267 developed cognitive impairment or PD. After adjustment for all covariates, having more regular distressing dreams during childhood was linearly and statistically significantly associated with higher risk of developing cognitive impairment/PD (P for trend = 0.044). Compared with children who never had distressing dreams (no time point), children who had persistent distressing dreams (2 time points) had an 82% increased risk of developing cognitive impairment or PD by age 50 (OR = 1·82; 95% CI: 1·07, 3·07).
Conclusion: In this prospective birth cohort, having persistent distressing dreams during childhood was associated with an increased risk of developing cognitive impairment or PD during adulthood.
Disclosure: Nothing to disclose.

OPR-063

Sleepiness, fatigue, and obstructive sleep apnea in stroke

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Background and aims: Obstructive sleep apnea (OSA) is highly prevalent among stroke patients with a prevalence of about 70%. A common symptom in post stroke patients is fatigue and subjective sleepiness. Continuous positive

airway pressure (CPAP) treatment for OSA decrease sleepiness. However, it is still not known whether CPAP decreases sleepiness and fatigue in stroke patients with OSA.
Methods: We screened 1570 stroke patients for sleep apnea with cardiorespiratory monitoring (CRM) and offered CPAP to patients with an AHI >15. Additionally, patients were at inclusion screened with Epworth Sleepiness Scale (ESS) and visual analog scale (VAS) - fatigue. Follow-ups were done between 1-3 months and 6-12 months after the stroke where AHI, CPAP compliance, ESS and VAS-fatigue were recorded. Patients were classified according to their compliance levels.
Results: Fatigue and sleepiness decreased with treatment from baseline to the first follow-up in the high compliance group (p-valueVAS-fatigue =0.004 and p-valueESS=1.9*10-9 and). However, patients with low CPAP treatment compliance only gave a slight decrease in sleepiness and there was no significant decrease in fatigue.
Conclusion: Our findings are the first to suggest that post-stroke fatigue may decline in stroke patients with OSA treated with CPAP. However, the effect of CPAP depends on patient adherence.
Disclosure: Nothing to disclose.

OPR-064

A novel equilibrative nucleoside transporter 1 (ENT1) inhibitor as a hypnotic for insomnia treatment

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Background and aims: Current hypnotics are relatively safe but adverse effects have been noticed. Adenosine is an endogenous somnogenic factor. This study investigated whether a novel equilibrative nucleoside transporter (ENT) 1 inhibitor regulates adenosine homeostasis and exhibits efficacy on insomnia treatment, and further revealed its underlying mechanisms.
Methods: The ENT1 inhibitor was orally administered to evaluate its efficacy on physiological sleep-wake activity and caffeine-induced or stress-induced insomnia in mice. Antagonists of adenosine receptor type 1 (A1R; DPCPX) and type 2A (A2AR; SCH58261) were intracerebroventricularly administered to elucidate the involvements of adenosine receptors. Administration of caffeine and change of cage bedding were used to induce acute insomnia. The c-fos expression within GABAergic neurons of ventrolateral preoptic area (VLPO), the major sleep regulation area, was determined by using GAD67-GFP mice. A 24h sleep-wake activity was acquired and analyzed.
Results: ENT1 inhibitor dose-dependently increased non-rapid eye movement (NREM) sleep, while REM sleep was not altered. Applications of A1R antagonist DPCPX or A2AR antagonist SCH 58261 blocked ENT1 inhibitor-induced NREM sleep enhancement. ENT1 inhibitor increased c-fos expression within GABAergic neurons of VLPO. Furthermore, this ENT1 inhibitor also blocked caffeine-induced sleep suppression and change of cage bedding-induced acute insomnia in mice.
Conclusion: Our result indicated that this novel ENT1 inhibitor elicited somnogenic effect and effectively ameliorated the caffeine- and stress-induced insomnia. Both adenosine A1R and A2AR were involved in the mechanism, and activation of GABAergic neurons within VLPO play an important role. This result suggests that this novel ENT1 inhibitor could be a potential hypnotic to treat insomnia.
Disclosure: The authors have nothing to disclose.

Neuroimmunology

OPR-065

Anti-Iglon5 Disease: A French Cohort Study

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Background and aims: IgLON5 antibodies (IgLON5-Abs) are biomarkers of a clinically heterogeneous and probably underdiagnosed neurological disease. We analysed a French retrospective cohort of patients with IgLON5-Ab disease.
Methods: All patients tested positive for IgLON5-Ab in a French referral centre (2016-2022) were included.
Results: The number of patients with IgLON5-Abs (n=43) increased year by year (Figure 1). Clinical data were available for 37 patients (68% male, median age at diagnosis 72 years, range 49-82). Median diagnostic delay was 23 months (range 0-16) and decreased year by year ($p<0.01$). At onset (acute/subacute in 19%), patients had sleep disorders (54%), bulbar symptoms (41%), movement disorders (22%), cognitive impairment (14%), gait instability (11%), depression (11%), hallucinations (8%), seizures (5%), diplopia (5%), dysautonomia (3%); either alone (57%) or in combination (43%). All patients evolved to a multi-system disorder dominated by bulbar symptoms (86%), gait instability (82%), and/or sleep disorders (76%). Median modified Rankin score (mRS) at diagnosis was 3 (range 0-6). Immunotherapy was administered in 70% patients (corticosteroids, 35%; immunoglobulins, 35%; rituximab, 35%; cyclophosphamide, 30%; plasma exchange, 11%), with response (improvement or stabilization) rates ranging from 50% to 77%. Median mRS at last visit (median 31 months after onset, range 1-149) was 3 (range 0-6), and 6 patients (16%) died due to anti-IgLON5 disease.

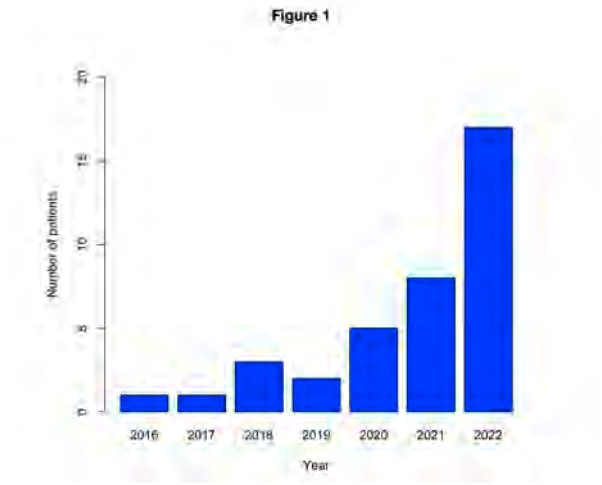

Figure 1. Annual number of patients with IgLON5-Abs disease diagnosed in the study centre.

Conclusion: The growing number of diagnoses and the progressive reduction of diagnostic delay suggest increased awareness of IgLON5-Ab disease in France. Sleep disorders and bulbar symptoms prevail at onset and, along with gait instability, at full-blown syndrome. Immunotherapy may stabilize the disease.
Disclosure: Antonio Farina received a research fellowship grant from the European Academy of Neurology. Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero.

OPR-066

Choroid plexus volume correlates with auto-antibodies and neuropsychiatric involvement in systemic lupus erythematosus

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Background and aims: Choroid plexus (CP) enlargement has been suggested as a marker of neuroinflammation in multiple sclerosis, being associated with disease activity and disability. CP involvement has been hypothesized also in systemic lupus erythematosus (SLE) immunopathology. We evaluated whether CP enlargement occurs in SLE patients compared to healthy controls (HC) and explored its association with auto-antibody status, neuropsychiatric (NP) involvement and structural brain damage.

Methods: Brain dual-echo and T1-weighted sequences were acquired from 32 SLE patients and 32 age- and sex-matched HC. Normalized CP volumes (Fig. 1) were compared between HC and SLE patients stratified according to auto-antibody status (antiphospholipid [APA] and anti-double-stranded DNA [ADNA] antibodies) and NP involvement using linear models. Associations between CP volume and clinical and structural MRI variables were explored using linear regression analyses.

Results: The demographic characteristics of the study population are reported in Table 1, whereas Table 2 shows the main results. Considering auto-antibody status, compared to HC, SLE patients with APA (n=18) or ADNA antibodies (n=24) showed higher T2 lesion volume (T2LV) (p=0.020 and 0.033). Only SLE patients with APA had a significant CP enlargement (p=0.013). According to NP involvement, compared to HC, both SLE patients without NP involvement (non-NP-SLE, n=20) and SLE patients with NP involvement (NP-SLE, n=12) showed higher CP volume (p=0.002 and p<0.001). Compared to non-NP-SLE, NP-SLE patients had significantly higher CP volume (p=0.024) and T2LV (p=0.015).

Table 1. Main characteristics of the subjects of the study (32 patients and 32 HC)

	HC (n = 32)	SLE (n = 32)	SLE vs HC p-value	Non-NP-SLE (n = 20)	NP-SLE (n = 12)	NP-SLE vs non-NP-SLE P-value
Male/Female	6/26	6/26	n.s.	5/15	1/11	n.s.
Age (years)	40.4 ± 12.6	39.9 ± 12.4	n.s.	39.0 ± 13.0	41.4 ± 11.8	n.s.
Disease duration (years)	-	16.3 ± 7.8	-	13.7 ± 7.4	18.8 ± 8.0	n.s.
APA + / APA – (%/%)	-	18/14	-	8/12 (40/60)	10/2 (83.3/16.6)	**0.028**
ADNA + / ADNA – (%/%)	-	20/12	-	15/5 (75/25)	9/3 (75/25)	n.s.
SLEDAI-2K score	-	2.0 (1.0-3.0)	-	2.0 (1.5-3.0)	2.0 (1.0-4.0)	n.s.
ECLAM index score	-	1.5 (0.5-2.0)	-	1.5 (0.5-2.5)	1.5 (1.0-2.0)	n.s.
SLICC / ACR damage index score	-	0.0 (0.0-1.0)	-	0.0 (0.0-1.0)	0.0 (0.0-1.0)	n.s.
Total BILAG index score	-	1.0 (1.0-3.0)	-	1.0 (1.0-2.0)	1.0 (1.0-8.0)	n.s.
Treatment (none / PDN / IMM / PDN+IMM)	-	2/0/10/20	-	1/0/5/14	1/0/5/6	n.s.
T2 LV (mL)	0.0 (0.0-0.0)	0.3 (0.1-0.7)	**<0.0001**	0.1 (0.0-0.3)	0.7 (0.2-1.2)	**0.004**
T1 LV (mL)	0.0 (0.0-0.0)	0.1 (0.1-0.4)	**<0.0001**	0.1 (0.0-0.2)	0.4 (0.0-0.7)	**0.005**

Table 1. Main characteristics of the subjects of the study (32 patients and 32 HC)

Table 2. T2 LV and CP volume in HC and SLE patients stratified according to APA and ADNA status and NP involvement

	HC	APA negative SLE	APA positive SLE	APA - SLE vs HC	APA + SLE vs HC	APA - vs APA + SLE
T2 LV (SD) [mcL]	9.50 (290.57)	525.04 (399.17)	959.46 (375.14)	0.242	**0.020**	0.398
CP Volume (SD) [mcL]	2719.77 (108.17)	2882.96 (151.04)	3111.26 (138.83)	0.354	**0.013**	0.231
	HC	**ADNA negative SLE**	**ADNA positive SLE**	**ADNA - SLE vs HC**	**ADNA + SLE vs HC**	**ADNA - vs ADNA + SLE**
T2 LV (SD) [mcL]	19.59 (291.83)	643.94 (514.39)	799.40 (329.99)	0.238	**0.033**	0.789
CP Volume (SD) [mcL]	2707.31 (107.95)	3193.94 (189.23)	2936.31 (124.40)	**0.019**	0.120	0.239
	HC	**Non-NP-SLE**	**NP-SLE**	**Non-NP-SLE vs HC**	**NP-SLE vs HC**	**Non-NP-SLE vs NP-SLE**
T2 LV (SD) [mL]	38.34 (280.30)	357.21 (323.34)	1582.18 (438.96)	0.412	**0.001**	**0.015**
CP Volume (SD) [mcL]	2520.88 (120.81)	3171.86 (128.88)	3628.99 (188.46)	**0.002**	**<0.001**	**0.024**

Table 2. T2 LV and CP volume in HC and SLE patients stratified according to APA and ADNA status and NP involvement

Conclusion: CP enlargement occurs in SLE patients, especially in those with APA and NP involvement, suggesting its potential role in the pathophysiology of SLE-related brain involvement.

Disclosure: This study received no funding.

OPR-067

Paraneoplastic neurological syndromes and autoimmune encephalitis in the Netherlands: epidemiology and antibody testing

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Background and aims: Epidemiologic studies in paraneoplastic neurological syndromes (PNS) and autoimmune encephalitis (AIE) are scarce. Furthermore, results from neuronal antibody tests are often misinterpreted.
Methods: We searched all serum and cerebrospinal fluid (CSF) samples tested for antibodies against cell-surface neuronal antigens or intracellular antigens at the Dutch national referral center between 2016 and 2021, ascertaining nationwide coverage. Positive results were evaluated by additional techniques depending on antibody type. Clinical information was collected through chart review and/or contact with referring physicians. Definite or probable AIE/PNS was diagnosed according to published consensus criteria.
Results: We identified 27081 samples from 18891 patients, of which 3915 samples from 2162 patients tested positive for one or more antibodies. A total of 2073 samples from 691 patients with probable or definite AIE/PNS remained, after excluding unconfirmed samples (n=476), atypical clinical syndromes (n=1021) and samples with missing information (n=344). Crude incidence rate for AIE/PNS was 6.7 (95% confidence interval 6.2-7.1) per million person-years. Most common antibodies in AIE/PNS were: anti-NMDAR, anti-Hu and anti-LGI1. Most common unconfirmed or false-positives were: (low-titer) anti-GAD65, anti-NMDAR (serum-only), anti-Yo and anti-CV2. In 180 patients with discordant antibody status (i.e. antibodies only present in serum or CSF), 29/32 (91%) of CSF-only positives had probable or definite AIE/PNS, compared to only 46/148 (31%) of serum-only positives.
Conclusion: Incidence rates of AIE/PNS are still increasing over the years. However, interpretation of results in the context of clinical information, confirmation by second technique, and, whenever possible, testing both serum and CSF (especially for AIE) are essential to avoid misinterpretation.
Disclosure: The authors have nothing to disclose.

OPR-068

Autonomic and cutaneous biomarkers differentiate seropositive and seronegative autoimmune autonomic ganglionopathy

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Background and aims: Autoimmune autonomic ganglionopathy (AAG) is a rare treatable disease presenting with subacute pandysautonomia. 50% have antibodies against the ganglionic acetylcholine receptor (gAChR-Ab). We hypothesised that detailed phenotyping with multimodal autonomic and cutaneous biomarkers could differentiate between gAChR-Ab-positive and gAChR-Ab-negative AAG.
Methods: 27 patients with AAG (14 seropositive, 13 seronegative) underwent cardiovascular testing, pupillometry, post-void bladder ultrasound, dynamic sweat testing, and skin biopsies from the distal leg and anterior thigh to quantify intraepidermal and pilomotor innervation using pan-neuronal, cholinergic and adrenergic markers.
Results: More seropositive patients had combined parasympathetic/sympathetic pupillary deficits (93% vs 31% in seronegative group). All seropositive patients and none of the seronegative patients demonstrated pupil fatigue. Both groups had a high proportion with elevated post-void residual volume >100ml (>70%), with about half requiring catheters. Most patients had postganglionic sudomotor dysfunction, with a length dependent pattern in 55% of seronegative patients vs 21% of seropositive patients. Compared to healthy controls, both seropositive and seronegative patients demonstrated intra-epidermal and pilomotor denervation, but seronegative patients had greater adrenergic denervation at both proximal and distal sites ($P<0.05$). Improvements in somatic and autonomic innervation were seen in follow up biopsies following immunotherapy in both seropositive and seronegative patients.

Conclusion: Patients with seropositive AAG had widespread autonomic failure, pupil fatigue, non-length dependent postganglionic dysfunction, and cholinergic and adrenergic cutaneous denervation. The autonomic phenotype differed in seronegative AAG, where patients more commonly had length dependent postganglionic dysfunction and greater adrenergic denervation. There was encouraging evidence for improved cutaneous innervation after immunotherapy in both seropositive and seronegative patients.

Disclosure: Dr S Koay was supported by the Guarantors of Brain Entry Fellowship. Dr V Iodice Dr J Panicker, and Prof M Lunn are supported by NIHR UCLH Biomedical Research Centre.

OPR-069

Mimics of autoimmune encephalitis: pitfalls for misdiagnosis

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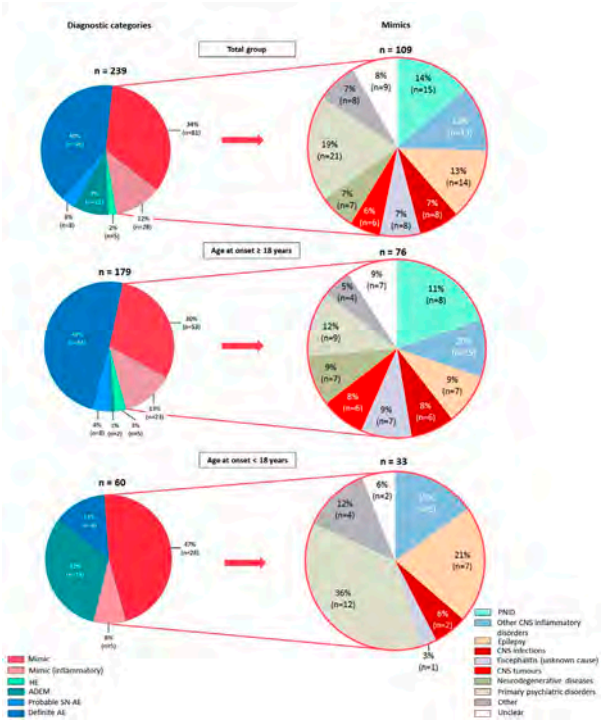
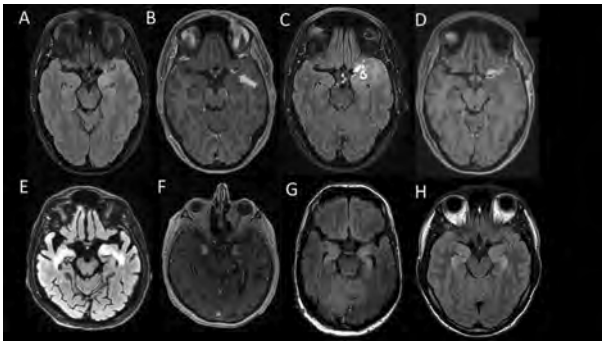
Background and aims: Clinical criteria for autoimmune encephalitis (AE) were proposed by Graus et al. in 2016. This accuracy is highly relevant, as various disorders can mimic AE. In this study, common AE mimics were described and 2016 AE criteria were validated.

Methods: From July 2016 to December 2019, consecutive patients with suspicion of AE were included. All patients were evaluated according to the 2016 AE criteria.

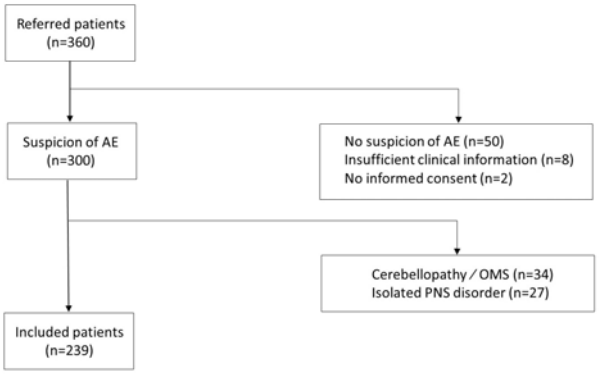
Results: 239 patients were included. AE was diagnosed in 104 patients (44%), while 109 patients (46%) were classified as AE mimic. The most common AE mimics were neuroinflammatory CNS disorders (26%), psychiatric disorders (19%), epilepsy (13%), CNS infectious disorders (13%), neurodegenerative diseases (7%) and CNS neoplasms (6%). Common pitfalls were mesiotemporal lesions on brain MRI (17%) and false-positive antibodies in serum (12%). The presence of ≥1 additional radiological features (enhancement, diffusion restriction) was more common in AE mimics (61% vs. 24%; p=0.005).



Overview of patient categories



Examples of AE mimics (brain MRI)



Overview of patient categories ham

Conclusion: AE mimics occur frequently and are diverse. Common pitfalls are mesiotemporal lesions on brain MRI and false-positive antibodies. The specificity of the criteria for possible AE is low and should therefore be regarded as an entry criteria requiring thorough work-up. Criteria for probable and definite AE are applicable for decisions on immunotherapy in early disease stage, as specificity is high.
Disclosure: - Peter A.E. Sillevis Smitt holds a patent for the detection of anti-DNER and received research support from Euroimmun. - Rinze F Neuteboom reports participates in pediatric MS studies with Novartis, Roche and Sanofi-Genzyme. He received consultancy fees from Novartis, Sanofi-Genzyme and Zogenix. His received research grants from the Dutch MS research foundation. DreaMS foundation, Postcode Loterij, Vrienden Loterij, Stichting Vrienden van het Sophia. - Maarten J. Titulaer has filed a patent, on behalf of the Erasmus MC, for methods for typing neurological disorders and cancer, and devices for use therein, and has received research funds for serving on a scientific advisory board of Horizon Therapeutics, for consultation at Guidepoint Global LLC, for consultation at UCB, for teaching colleagues at Novartis. MT has received an unrestricted research grant from Euroimmun AG, and from CSL Behring.

Neuropathies

OPR-070

Photobiomodulation in the management of chemotherapy-induced peripheral neuropathy: a randomized, controlled trial

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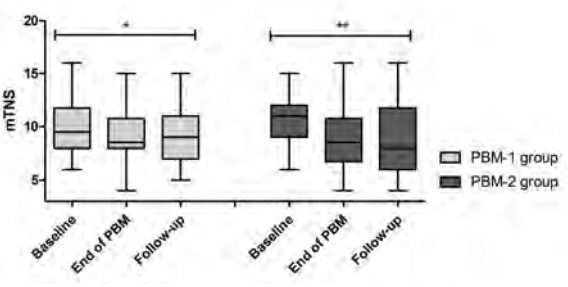
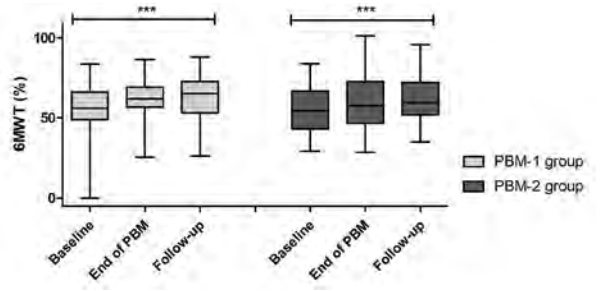
Background and aims: Cancer treatment is often accompanied by incapacitating side effects, such as chemotherapy-induced peripheral neuropathy (CIPN). CIPN limits the patients' quality of life and current therapeutic options lack effectiveness. Photobiomodulation (PBM) therapy uses (near)-infrared light to activate cell repair mechanisms and reduce pain and inflammation. Research has shown the efficiency of PBM in preventing CIPN. This trial aimed to evaluate the efficacy of PBM in treating CIPN while assessing the optimal PBM dosage.
Methods: A randomized controlled trial was conducted at the Jessa Hospital (Hasselt, Belgium). Sixty cancer patients, diagnosed with CIPN, were randomly allocated to the PBM-1 group (6 J/cm², n=28) or PBM-2 group (8 J/cm², n=32) and received PBM twice a week for three weeks. The severity of CIPN and the patients' mobility were assessed using the modified Total Neuropathy Score (mTNS) and the six-minute walk test (6MWT), respectively. Outcome measures were collected at baseline, the end of PBM, and three weeks post-PBM.
Results: The mTNS decreased significantly over time in both the PBM-1 and PBM-2 group (P=0.021 and P=0.007, respectively). Moreover, the mTNS remained constant between the end of PBM and the follow-up visit in both groups (Figure 1). Similarly, according to the 6MWT (Figure 2), the patients' mobility significantly improved over time in the PBM-1 and PBM-2 group (Ps≤0.001).



Comparison of modified Total Neuropathy Score (mTNS) over time when treated with photobiomodulation (PBM). A higher score indicates a more severe grade of peripheral neuropathy. Significance is shown as *P ≤ 0.05, ** P ≤ 0.01



Comparison of six-minute walk test (6MWT) distance over time. Percentages are calculated using reference standards based on the patients gender, age, and BMI, wherein a higher score indicates a better mobility. Significance is shown as *** P ≤ 0.001.

Conclusion: In conclusion, PBM reduces the symptoms associated with CIPN resulting in better mobility. No significant differences between groups could be detected based on the applied dosage. Further research is necessary to optimize the PBM treatment and irradiation parameters.

OPR-071

Unclassified clinical presentations of chronic inflammatory demyelinating polyradiculoneuropathy

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Background and aims: To assess the ability of the EAN/PNS clinical criteria for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) to include within their classification the whole spectrum of clinical heterogeneity of the disease and to define the clinical characteristics of the unclassifiable clinical forms.
Methods: The EAN/PNS clinical criteria for CIDP were applied to 329 patients fulfilling the electrodiagnostic and supportive criteria for the diagnosis of CIDP. Clinical characteristics were reviewed for each patient not strictly fulfilling the clinical criteria ('unclassifiable').
Results: At study inclusion, 124 (37.5%) patients had an unclassifiable clinical presentation, including 110 (89%) with a typical CIDP-like clinical phenotype in whom some segments of the four limbs were unaffected by weakness ('incomplete typical CIDP'), 10 (8%) with a mild distal, symmetric, sensory or sensorimotor polyneuropathy confined to the lower limbs with cranial nerve involvement ('cranial nerve predominant CIDP'), and 4 (1%) with a symmetric sensorimotor polyneuropathy limited to the proximal and distal areas of the lower limbs ('paraparetic CIDP'). Eighty-one (65%) patients maintained an unclassifiable presentation during the entire disease follow-up while 13 patients progressed to typical CIDP. Patients with the unclassifiable clinical forms compared to patients with typical CIDP had a milder form of CIDP, while there was no difference in the distribution patterns of demyelination.

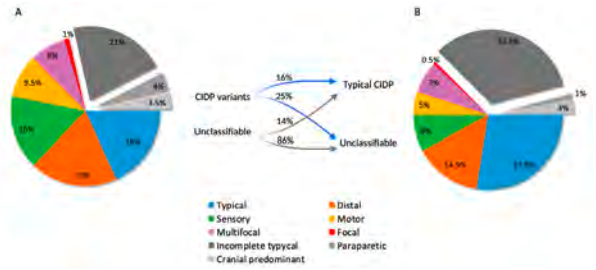

Fig.1

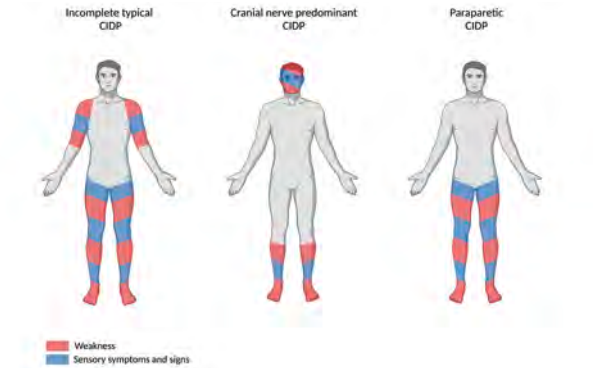

Fig. 2

Conclusion: A proportion of patients with CIDP do not strictly fulfill the EAN/PNS clinical criteria for diagnosis. These unclassifiable clinical phenotypes may pose diagnostic challenges and thus deserve more attention in clinical practice and research.
Disclosure: The authors declare no conflict of interest.

OPR-072

A Rare Disease Affecting the Central and Peripheric Nervous System: Giant Axonal Neuropathy

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Background and aims: Giant axonal neuropathy (GAN) is an autosomal recessive disease characterized by a mutation in the gigaxonine protein that affects both the peripheral and central nervous systems. Axon loss and giant axonal swellings seen in nerve biopsy are important findings. Classic phenotype is a severe axonal neuropathy with kinky hair and white matter involvement in neuroimagings. In this study, the clinical, electrophysiological, radiological and genetic features of seven patients diagnosed with GAN in three families will be discussed.
Methods: Seven patients from three families with a preliminary diagnosis of polyneuropathy were examined. After biochemical, metabolic and electrophysiological examinations, all patients were diagnosed with GAN as a result of the recessive mutation in the gigatoxin gene from the data whole exome analysis (p.R242X(c.724C>T)).
Results: Peripheral neuropathy and central nervous system involvement were found in all patients. Scoliosis was found five of the seven patients. Epileptic seizures started in two of the patients during the follow-up, and mental retardation was observed in two siblings in same family. Neuroimaging showed symmetrical involvement in the supra- and infratentorial white matter in all patients
Conclusion: Gigaxonin protein is encoded by GAN gene on the long arm of chromosome 16. This protein is in the ubiquitin-proteosome pathway and controls the processing of intermediate filament in nerve cells to maintain of cytoskeletal structure. Absence or loss of gigaxonin results in disorganization of intermediate filaments and swelling of axons. There is still no definitive cure for this fatal neurodegenerative disease. As the number of patients increase, the genotype-phenotype correlation will increase.
Disclosure: Authors have nothing to disclose.

OPR-073

Use of lenadogene nolparvovec gene therapy for Leber hereditary optic neuropathy in early access programs

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Background and aims: Lenadogene nolparvovec is an unapproved gene therapy for patients with Leber hereditary optic neuropathy (LHON) due to the m.11778G>A MT-ND4 mutation. Through early access programs (EAP), patients with MT-ND4-LHON can benefit from lenadogene nolparvovec before marketing authorization.
Methods: Lenadogene nolparvovec was provided based on unsolicited requests. Patients with confirmed MT-ND4-LHON received lenadogene nolparvovec as a unilateral or bilateral intravitreal injection (9x1010 viral genomes/eye). Baseline characteristics, efficacy, and safety data were collected.
Results: Between August 2018 and March 2022, 63 patients received lenadogene nolparvovec in EAP; 35 (55.6%) in France, 9 (14.3%) in Italy, 1 (1.6%) in the UK and 18 (28.6%) in the US. Most patients (66.7%) were administered bilaterally. At first injection, mean (SD) age was 34.5 (16.6) years (range=13.5-74.7) and vision loss in the first-affected eye had lasted a mean of 11.4 (9.7) months; idebenone therapy was ongoing in 72.6% of patients. A total of 47 patients reached the 1-year post treatment time point, but 1-year BCVA values are available for 38; mean (SD) change in BCVA from baseline was -0.29 (0.67) LogMAR (+14.5 EDTRS letters). An improvement in BCVA of -0.36 (0.73) LogMAR (+18 ETDRS) was seen in the 25 bilaterally treated patients. Safety was favorable with data comparable to clinical studies.
Conclusion: Patients receiving lenadogene nolparvovec in EAP were predominantly European and received therapy mostly in both eyes. Preliminary analyses show that lenadogene nolparvovec injection was associated with clinically meaningful improvement in visual acuity and favorable safety similar to that observed in the clinical studies.
Disclosure: Chiara La Morgia has no conflict of interest.

OPR-074

Clinical progression in Acquired Amyloidosis after domino liver transplantation: a case-control study

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Background and aims: Cases of acquired amyloidosis have been described after domino liver transplantation using a liver from a donor with hereditary transthyretin (ATTRv) amyloidosis. We aimed to compare the clinical progression of neuropathy in patients with acquired amyloidosis (AA) versus patients with untreated ATTRv amyloidosis with neuropathy (ATTRv-NP).
Methods: A historical cohort of patients with untreated AA and ATTRv-NP followed in Lisbon's Paramyloidosis Reference Center from 1994 to 2022 were included. Other causes of polyneuropathy were excluded. Neuropathy clinical progression was evaluated using the Neurological Impairment Score (NIS).
Results: Twenty-two patients with AA and forty-nine with ATTRv-NP with similar age at onset of symptoms and no gender difference were included. The time from transplant to clinical neuropathy onset in AA was 8±2.5 years. During follow-up, 8 deaths in the AA and 22 in ATTRv-NP group were registered. There was no difference in time from onset of symptoms to death between the two groups(5.6±3.2 years in the AA group versus 8.9±5.3 in the ATTRv-NP group; p=0.09). For assessment of neuropathy progression, 8 patients with AA and 19 with ATTRv-NP with at least 2 clinical evaluations were identified. Neuropathy showed a tendency towards a more rapid progression in the ATTRv-NP group, although no statistically significant difference between groups was detected (+4.9±5.2 NIS points/year in AA versus +11.7±15.6 NIS points/year ATTRv-NP; p=0.48).

Conclusion: Progression of neuropathy and mortality in AA patients appear to be less pronounced than ATTRv-NP natural history. Larger sample studies are needed to corroborate these findings.
Disclosure: Nothing to disclose.

OPR-075

Neuropathies related to Hepatitis E virus infection in Switzerland: A prospective, matched case-control study

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Background and aims: Acute hepatitis E virus (HEV) infection recently emerged as a potential trigger for acute immune neuropathies, but prospective controlled studies to investigate causality are lacking. We compared the frequency of acute HEV infection in patients with Guillain-Barré syndrome (GBS), neuralgic amyotrophy (NA), and facial nerve palsy with a control population.
Methods: Multicentre (11 Swiss centres), prospective, observational case-control study over 3 years (09.2019-10.2022). All patients were recruited within 3 months from disease onset. Controls were healthy blood donors matched for age, sex, geographical location, and time. Diagnostic criteria for acute hepatitis E were reactive serum anti-HEV IgM and anti-HEV IgG assays (ELISA test) and/or HEV RNA detection in serum by Real-time PCR. RT-PCR on sera (HEV RNA detection) was performed to confirm IgM+ results.
Results: We included 180 patients (59 GBS, 51 NA, and 70 facial palsy) and corresponding controls (for both groups: median age 51 years; male 48%). Six IgM+ cases were detected in the NA group, two in the GBS group, and none in the facial palsy group. No IgM+ was detected in the controls. Cases with acute HEV infection had significantly higher values of ALT and GGT at disease onset. The Fisher‘s exact test showed a moderate association ($p=0.027$; Cramér’s $V = -0.25$) only between acute HEV infection and NA.
Conclusion: Our study suggests a causal association between acute HEV infection and NA (10% of cases), but not with other autoimmune neuropathies such as GBS nor with facial nerve palsy.
Disclosure: Nothing to disclose.

Neuroimaging; Neurosonology

OPR-076

Investigating grey matter atrophy and its relationship with lesions in MS, MOGAD and AQP4+NMOSD

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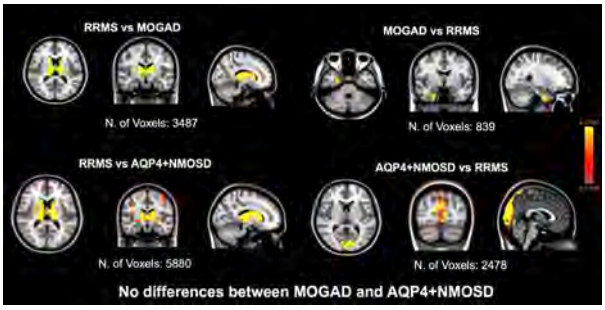
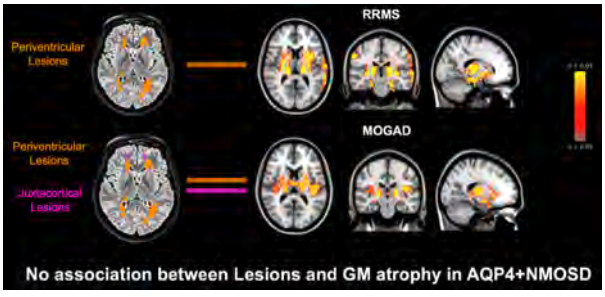
Background and aims: A relationship between GM atrophy and lesions has been reported in MS, but their interplay is unclear in MOGAD and AQP4+NMOSD. We aim to characterise GM atrophy in MOGAD and AQP4+NMOSD and its relationship with spatial patterns of WML.

Methods: We collected brain MRIs of non-acute RRMS/MOGAD/AQP4+NMOSD patients and healthy controls (HC) from 16 international centres. Lesions were classified as periventricular/juxtacortical/deepWM/deepGM/infratentorial. Voxel-wise analyses were performed using permutation testing. Differences in GM volumes were assessed using design matrices with disease as variable of interest and age, sex, centres as covariates, and number of lesions in each location as regressor. For significant results ($p<0.05$), the number of voxels (V) is reported.

Results: We studied 175 RRMS (132F, 40y±10), 135 MOGAD (83F, 41y±14), 135 AQP4+NMOSD (111F, 51y±14) patients, and 144 HC (87F, 37y±11). Compared to HC, lower GM volumes were found in RRMS diffusely (V:32576), in MOGAD in the temporal lobe and deep GM (V:9474), in AQP4+NMOSD in the occipital cortex (V:4104). Lower GM volume was found in the deep GM in RRMS vs MOGAD (V:3487) and vs AQP4+NMOSD (V:5880), in the temporal cortex in MOGAD vs RRMS (V:839), in the occipital cortex in AQP4+NMOSD vs RRMS (V:2478). In MOGAD a higher number of periventricular and juxtacortical lesions was associated with reduced volume in the temporal cortex, deep GM and insula (V:5021 and V:5666).



Differences in grey matter (GM) volumes between relapsing remitting MS (RRMS), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and aquaporin-4-antibody neuromyelitis optica spectrum disorder (AQP4+NMOSD)using a Voxel-wise analysis



Association between lesion distribution and grey matter (GM) volumes in RRMS, MOGAD and AQP4+NMOSD

Conclusion: Cortical GM atrophy seems to be prominent in MOGAD and AQP4+NMOSD. The relationship between atrophy and lesions in MOGAD suggests a disruption of the WM bundles projecting into the GM.

Disclosure: Nothing to disclose.

OPR-077

Reduction of Functional Connectivity Dynamism is Relevant for Clinical Worsening in Multiple Sclerosis: A 2.5-Year Study

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Background and aims: In multiple sclerosis (MS), time-varying functional connectivity (TVFC) analysis showed abnormalities of the main functional networks, correlated with more severe clinical and cognitive disability. MS-related cognitive decline was found to be associated with progressive TVFC destabilization. However, the clinical relevance of longitudinal TVFC changes has not been investigated yet.
Methods: 3T-MRI scans and clinical evaluations were obtained at baseline and at median follow-up of 2.5 years from 129 MS patients (103 relapsing-remitting [RR] and 26 progressive [P] MS) and 28 matched healthy controls (HC). At 2.5-year follow-up, patients were classified as clinically stable/worsened according to their disability change. TVFC was quantified at voxel-wise level as the coefficient of variation (CoV) across sliding-windows of degree centrality.
Results: At baseline, MS patients showed reduced TVFC vs HC in the bilateral orbitofrontal cortex ($p<0.05$, family-wise error corrected), left cerebellum, right precuneus and left thalamus. At 2.5-year, a widespread reduction of TVFC ($p<0.05$, family-wise error corrected) was found in cortical lobes and cerebellum. Such a pattern of TVFC reduction was also found when looking at clinically stable MS patients. Clinically worsened MS presented peculiar TVFC reductions in areas of the default-mode network and basal ganglia. Reduced TVFC in the left putamen in clinically worsened vs stable MS patients was significant at time x group interaction analysis.
Conclusion: At 2.5-year follow-up, MS patients showed widespread TVFC reductions in cortical lobes and cerebellum. The peculiar involvement of deep grey matter in clinically worsened MS patients may represent a biological substrate of disability worsening.
Disclosure: The study did not receive funding.

OPR-078

Diagnostic utility of transorbital sonography in idiopathic intracranial hypertension.

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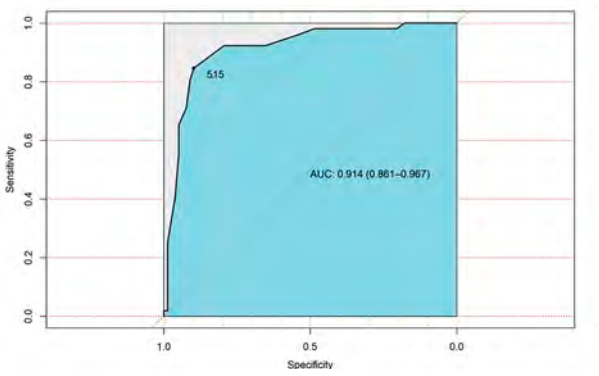
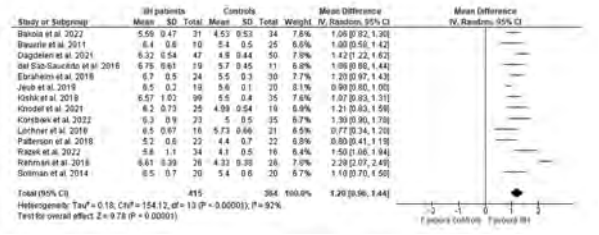
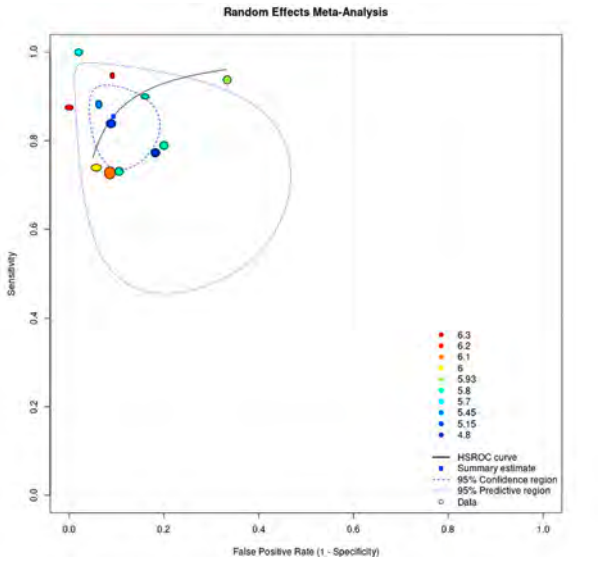
Background and aims: Transorbital sonography (TOS) provides a useful non-invasive tool to detect and further monitor intracranial pressure by assessing optic nerve sheath diameter (ONSD) and optic disc elevation (ODE). The utility of TOS in the diagnosis of idiopathic intracranial hypertension (IIH) has been increasingly recognized.
Methods: A single-center case-control study sought to compare TOS-acquired ONSD and ODE among IIH-cases versus patients with other neurological diseases (controls). Furthermore, a systematic review and meta-analysis was conducted to present pooled mean differences and diagnostic measures of ONSD and ODE between IIH-cases and controls.
Results: In the single-center study, consisting of 31 IIH-cases and 34 sex- and age-matched controls, ONSD values were higher among IIH-cases than controls ($p<0.001$), while ODE was more prevalent in cases (65% vs. 15%; $p<0.001$). The ROC-curve analysis revealed that the optimal cut-off value of ONSD for predicting IIH was 5.15 mm, with an area-under-the-curve (AUC) of 0.914 (95%CI:0.861–0.967; Figure-1) and sensitivity and specificity values of 85% and 90%, respectively. In a meta-analysis of 14 included studies with 415 IIH-cases, ONSD and ODE values were higher in IIH-cases than controls (mean difference in ONSD 1.20mm; 95%CI:0.96-1.44mm; Figure-2 and in ODE 0.3mm; 95%CI:0.33-0.67mm). With regard to ONSD, pooled sensitivity, specificity, and diagnostic odds ratio were calculated at 85.5% (95%CI:77.9-90.8%), 90.7% (95%CI:84.6-94.5%), and 57.394 (95%CI:24.597-133.924), respectively. The AUC in summary ROC-curve analysis was 0.878 (95%CI:0.858-0.899; Figure-3).



Receiver Operation Curve (ROC) for optic nerve sheath diameter (in mm) in idiopathic intracranial hypertension (IIH) diagnosis.



Forest plot presenting the mean difference (in mm) of optic nerve sheath diameter in patients with idiopathic intracranial hypertension versus controls.



Summary receiver operating curve (sROC) plot for the diagnostic performance of increased optic nerve sheath diameter in idiopathic intracranial hypertension (IIH) diagnosis. Cut-off points used in each study for optic nerve sheath diameter (in mm) are dep

Conclusion: TOS has a high diagnostic utility for the non-invasive diagnosis of IIH and may deserve wider implementation in everyday clinical practice.
Disclosure: Nothing to disclose.

OPR-079

Stepwise functional brain architecture from disease epicenter correlates with atrophy in progressive supranuclear palsy

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Background and aims: MRI connectomics tests the model of network-based spread of pathological aggregates in neurodegeneration. Stepwise functional connectivity (SFC) is a graph-theory-based neuroimaging method detecting functional couplings of a selected region, at increasing link-step topological distances. SFC was applied to test if topological stepwise architecture propagating from disease epicenter would shape patterns of grey matter (GM) atrophy in progressive supranuclear palsy (PSP).
Methods: Twenty-eight patients with PSP and 50 healthy controls underwent 3D-T1 and resting-state functional MRI sequences. GM was parcellated into 90 regions. Correlations between SFC architecture in controls and atrophy patterns in patients were tested. Disease epicenter was identified as the peak of atrophy in an independent cohort of 13 cases with post mortem PSP pathology, and used as seed region for SFC analysis.
Results: Left midbrain tegmentum was identified as disease epicenter. Compared with controls, PSP patients showed atrophy of subcortical GM (thalami and caudate nuclei), and frontal, parietal and cerebellar cortex. For each region, a strong correlation was found between average link-step distance from the left midbrain in controls and mean normalized GM volume in PSP patients ($r=0.37$, $p<0.001$).
Conclusion: The brain architectural topology, as described by SFC propagating from disease epicenter, shapes the pattern of atrophic changes in PSP. Stepwise analysis holds the promise to be used to model disease progression in future longitudinal studies.

Disclosure: Funding: European Research Council (StG-2016_714388_NeuroTRACK); US National Institute of Health (R01-DC010367, R01-DC12519, R01-DC14942, R01-NS89757, R21-NS94684); Foundation Research on Alzheimer Disease.

OPR-080

Comparing standard vs extended time window reperfusion treatments in an MRI based stroke care system

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Background and aims: Current ESO guidelines recommend extended time window reperfusion therapies based on advanced imaging, however, the workload and clinical benefit of extending time windows on a population basis are not known. Aim: To determine the caseload, treatment rates, and outcomes in the extended as compared to the standard time windows for reperfusion therapies in an MRI-based stroke care system.

Methods: All consecutive ischemic stroke patients within 24h from 1st March 2021 to 28th of February 2022 were included in a prospective single-centre study. Eligibility in the extended time windows or wake-up strokes recognized within 4h was based on MRI DWI/PWI or DWI-FLAIR mismatch using current ESO guideline criteria. MRI was only available during working hours (8-20 h). Clinical outcome in treated patients was assessed at 3 months.

Results: During this 12-month period 777 patients were admitted, 252 (32%) had MRI. 120/304 (39.4%) patients were thrombolysed in standard and 14/231 (6%) in the extended time window. Independent clinical outcome (mRS≤2) was seen in 57/116 (49.1%) early and 4/14 (28.6%) late-treated patients (P=0.25). 38/386 (9.84%) patients underwent thrombectomy in the standard and 16/391 (4%) in the extended time window. Independent clinical outcome (mRS≤2) was seen in 10/29 (34.5%) early and 4/13 (31%) late-treated patients (P=0.99).

Conclusion: Even with limited availability of advanced imaging extending time windows for reperfusion therapies resulted in a 11.6% increase in thrombolysis and a 42% increase in thrombectomy with similar clinical outcomes in early and late-treated patients at the price of increased burden of clinical and imaging screening.

Disclosure: Nothing to disclose.

Movement disorders 2

OPR-081

Impact of treatment on blood-brain barrier integrity in Wilson's disease

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Background and aims: In Wilson's disease (WD), free copper may impair the blood-brain barrier (BBB) function and contribute to central nervous system damage. The study assessed changes in serum concentrations of BBB integrity markers in untreated and treated WD patients and examined correlations between these changes and neurological impairment.
Methods: The study groups included 171 patients with WD (77 with hepatic and 94 with neurological manifestations), treated for up to 5 or 15 years, and 88 healthy controls. Serum concentrations of intercellular adhesion molecule 1 (ICAM1), P-selectin, matrix metallopeptidase 9 (MMP9), glial fibrillary acidic protein (GFAP) and S100 calcium-binding protein B (S100b) were measured before and during anti-copper treatment. The Unified Wilson's Disease Rating Scale (UWDRS) was used to assess neurological advancement.
Results: ICAM1 concentrations were elevated before and during anti-copper treatment compared with controls, but therapy led to a substantial decrease. P- selectin concentrations remained elevated before and during treatment. MMP9 concentrations before treatment were lower but reached control levels during treatment. GFAP concentrations were elevated in untreated neurological patients compared with controls and decreased during treatment. No changes were observed in S100b. Only ICAM1 concentrations positively correlated ($r = 0.27$, $p < 0.001$) with the UWDRS.
Conclusion: Elevated ICAM1 concentrations and their correlation with neurological advancement confirm BBB impairment in WD patients. Decreased MMP9 concentrations are probably the result of active liver fibrosis. Elevated P-selectin concentrations indicate an ongoing inflammatory process, while GFAP may serve as a biomarker for brain injury.
Disclosure: Nothing to disclose.

OPR-082

Motor reserve's networks in Parkinson's disease

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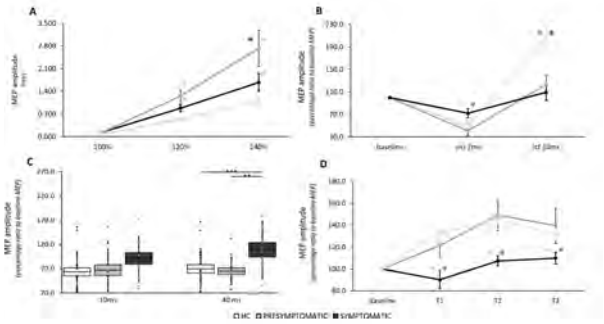
Background and aims: Motor reserve (MR) is defined as the resilience mechanisms of the brain coping with neurodegeneration in idiopathic Parkinson's Disease (PD). No investigation of MR focused on lateralized PD with bilateral binding reduction at dopamine transporter (DAT) imaging.
Methods: Sixteen PD and 28 controls were included. Patients underwent video-recorded clinical assessment (Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Hoehn & Yahr (H&Y) stage) and DATQUANT imaging. MR was quantified in each hemisphere with Motor Reserve Coefficient (MRC). Transcranial magnetic stimulation was performed on presympotmatic (PH) and symptomatic hemisphere (SH) primary motor cortices (M1).
Results: All patients had lateralized PD (H&Y<1.5, presymptomatic side MDS-UPDRS-III≤3) though bilateral biding reduction in putamen. TMS testing revealed increased corticospinal excitability and reduced intracortical-facilitation (ICF) on PH and a different pattern, including increased corticospinal excitability and reduced short-interval-intracortical-inhibition, ICF, paired-associative-plasticity (PAS), on SH. Moreover, we found reduced PH-to-SH interhemispheric-inhibition (IHI). Reduced putamen binding was predicted by enhanced PAS and reduced IHI in PH, and by reduced ICF in SH. Putamen/caudate ratio was directly predicted by corticospinal excitability in PH and inversely by PAS in SH. MRC distinguished PH from SH (AUC 0.9844), being predicted in PH by PAS increment, IHI and corticospinal excitability reduction.

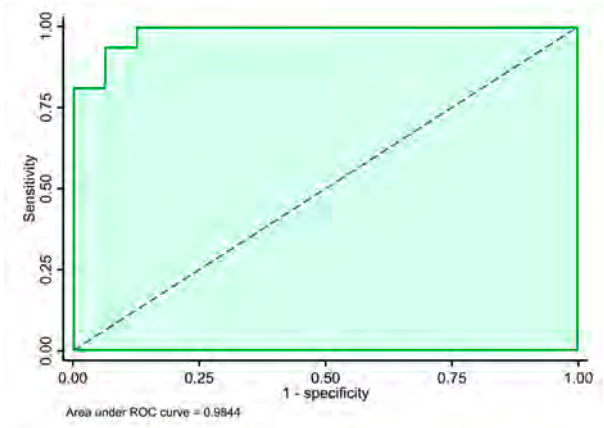
	Presymptomatic	Symptomatic	HC	P*	P **	P ***
Age, *years*	58.1 ± 8.8	=	63.9 ± 11.02	-	0.159	-
Sex, *F/M*	8F/8M	=	14F/14M	-	0.824	-
Disease Duration, *months*	38.2 ± 20.6	=	-	-	-	-
Side, *RS/LS*	8RS/8LS	8RS/8LS	28RS	-	-	-
MDS-UPDRSIII$_{side}$, rater I	0.6 ± 0.6	9.7 ± 2.4	-	**<0.001**	-	-
MDS-UPDRSIII-wr$_{side}$, rater I	0.6 ± 0.6	8.5 ± 2.9	-	**<0.001**	-	-
MDS-UPDRSIII-wr$_{side}$, rater II	0.9 ± 1.0	9.4 ± 3.2	-	**<0.001**	-	-
Inter-rater	0.324	0.458	-	-	-	-
MDS-UPDRSIII$_{TOT}$, rater I	16.8 ± 3.3	=	-	-	-	-
MDS-UPDRSIII-wr$_{TOT}$, rater I	15.1 ± 3.6	=	-	-	-	-
MDS-UPDRSIII-wr$_{TOT}$, rater II	17.2 ± 3.7	=	-	-	-	-
Inter-rater	0.165	=	-	-	-	-
MDS-UPDRS I	4.9 ± 2.7	=	-	-	-	-
MDS-UPDRS II	3.9 ± 2.3	=	-	-	-	-
MDS-UPDRS IV	0.0	=	-	-	-	-
MDS-UPDRS	25.6 ± 5.4	=	-	-	-	-
NMSS	14.1 ± 13.7	=	-	-	-	-
LEDD	260.6 ± 138.7	=	-	-	-	-
Striatus Z-score	-1.671 ± 0.711	-2.378 ± 0.794	-	**<0.001**	-	-
Putamen Z-score	-2.193 ± 0.655	-2.879 ± 0.713	-	**<0.001**	-	-
Caudate Z-score	-0.580 ± 0.896	-1.243 ± 1.046	-	**0.001**	-	-
Putamen / Caudate ratio	0.716 ± 0.066	0.664 ± 0.187	-	0.276	-	-
AMT, *%MSO*	33.0 ± 5.7	35.8 ± 7.4	36.8 ± 7.0	0.283	0.106	0.708
RMT, *%MSO*	46.8 ± 9.5	49.5 ± 11.7	51.4 ± 9.3	0.525	0.156	0.587
Imv, *%MSO*	55.8 ± 12.2	56.8 ± 11.3	58.3 ± 7.2	0.426	0.525	0.328
Test MEP, *mV*	1.061 ± 0.150	1.070 ± 0.093	0.940 ± 0.276	0.854	0.149	0.108

PD= idiopathic Parkinson's Disease, HC = healthy controls; F= female, M =male, RS= right side, LS = left side, MDS-UPDRS = Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; wr = without rigidity; NMSS = Non Motor Symptoms Scale; AMT = active motor threshold; PD = Parkinson's disease; RMT = resting motor threshold, MSO = maximum stimulator output, MEP= motor evoked potential.

Demographic, clinical, DAT data and motor thresholds in PD and HC are reported as mean values ± SD. *P-values: Presymptomatic vs Symptomatic. **P-values: Presymptomatic vs HC. ***P-values: Symptomatic vs HC.



A Input-output curve of motor evoked potentials (MEP) at baseline. B Curve of short-interval-intracortical-inhibition (SICI) and intracortical-facilitation (ICF). C Intehemispheric-inihibtion. D Curve of paired associative stimulation effect.



Area under ROC curve of Motor Reserve Coefficient. Considering as binary prediction (presymptomatic vs symptomatic). Sensitivity 93.75%, Specificity 93.75%, Positive predictive value 93.75%, Negative predictive value 93.75%, Accuracy 93.75%

Conclusion: In PD response to neurodegeneration involves a M1-putamen network, and cortico-M1 connections, responsible for excitability and plasticity changes, depending on caudate activity and becoming more effective with binding reduction in putamen. Further insight on PD MR networks is relevant for novel neuromodulation approaches, aimed at reducing motor burden in daily life.
Disclosure: The authors have nothing to disclose.

OPR-083

Neuroimaging correlates of postural instability in motor subtypes of Parkinson's disease

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Background and aims: Neuroimaging correlates of postural instability (PI) in Parkinson's disease (PD) are largely unknown. We aimed to identify the brain structures associated with PI in PD subtypes using different MRI approaches.
Methods: We consecutively enrolled 142 PD patients (postural-instability-and-gait-difficulty [PIGD], n=66; tremor-dominant [TD], n=76) and 45 control subjects. PI was assessed using MDS-UPDRS-III pull-test item (PT). A whole-brain multi-regression analysis identified brain areas where grey matter (GM) volume correlated with the PT score in PD. Voxel-based morphometry (VBM) and Tract-Based Spatial Statistics (TBSS) were used to compare unsteady (PT>=1) and steady (PT=0) PD patients. Associations between GM volume in regions of interest and several clinical features were then investigated using a multivariate regression analysis.
Results: PI was present in 65.1% of PIGD and 26.3% of TD patients. The whole-brain multi-regression analysis identified bilateral inferior frontal gyrus (IFG) and superior temporal gyrus (STG) as the only regions associated with the PT score. VBM showed reduced GM volume in fronto-temporal areas (superior, middle, medial and inferior frontal gyrus, and STG) in unsteady compared with steady PD patients, while TBSS did not show any difference between groups. GM volume in these fronto-temporal areas was significantly associated with the PT score, after correcting for confounding factors.

Conclusion: This study demonstrates a significant atrophy of the IFG and STG in unsteady PD patients, suggesting that these brain areas may play a role in the pathophysiological mechanisms underlying postural instability in PD. This result paves the way for further studies on postural instability in parkinsonism.
Disclosure: Nothing to disclose.

OPR-084

Transcranial sonography and differential diagnosis of synucleinopathies at early stages

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Background and aims: Diagnosis of synucleinopathies, such as Parkinson's disease (PD) and Dementia with Lewy bodies (DLB), is challenging. Objective: to assess the usefulness of transcranial B-mode sonography (TCS) in the differential diagnosis of synucleinopathies at their earlier stages.
Methods: We prospectively include PD and DLB patients with less than 3 years from onset, scoring 3-4 in Global Deterioration Scale. A group of recently diagnosed Alzheimer's disease (AD) patients and controls were included. TCS was performed to assess the echogenicity of substantia nigra (SN), width of third ventricle (IIIv), size of frontal horn of lateral ventricles (LV). The medical image viewer Horos was used to analyze the intensity of the echogenicity of these structures.
Results: Ninety-eight participants included (25PD,17DLB,25AD,31controls). Mean age was 74±3,44 years for DLB and 69±6,63 for PD patients. PD and DLB patients showed a higher percentage of hyperechogenicity of the SN (72.7%,76.5%) than AD and controls (10.5%,31%;p<0.001). The area of hyperechogenicity of the SN was higher in PD and DLB patients (Right0.205±0.085cm2,Left0.241±0.08cm^2; R0.213±0.097cm^2, L0.253±0.09cm^2), than AD and controls (R0.0134±0.054, L0.125±0.066; R0.104±0.038, L0.118±0.05; p<0.001). AD patients had the highest percentage of widened IIIv (AD23.8%,PD0%,DLB6.3%,controls7.1%; p=0.046). The size of LV was higher in AD and DLB patients (50%,42.9%) than PD and controls (10%,20.8%;p=0.034). No differences were found in the intensity of the echogenicity of the SN using the image viewer.
Conclusion: TCS is a valid tool for the differential diagnosis of the early stages of synucleinopathies. Application of an image viewer to quantify the intensity of the echogenicity of the SN does not seem to be useful.
Disclosure: Nothing to disclose.

OPR-085

Staging Parkinson´s Disease According to the MNCD Classification Correlates with Disease Severity and Quality of life

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Background and aims: Recently, a novel simple classification called MNCD, based on 4 axes (Motor; Non-motor; Cognition; Dependency) and 5 stages, has been proposed to classify Parkinson´s disease (PD). Our aim was to apply the MNCD classification in a cohort of PD patients for the first time and also to analyze the correlation with quality of life (QoL) and disease severity.
Methods: Data from the baseline visit of PD patients recruited from 35 centers in Spain from the COPPADIS cohort from January 2016 to November 2017 were used to apply the MNCD classification.

Results: Four hundred and thirty-nine PD patients (62.05 ± 7.84 years old; 59% males) were included. MNCD stage was: stage 1, 8.4% (N=37); stage 2, 62% (N=272); stage 3, 28.2% (N=124); stage 4-5, 1.4% (N=6). A more advanced MNCD stage was associated with a higher score on the PDQ39SI (p<0.0001) and a lower score on the PQ-10 (p<0.0001) and EUROHIS-QOL8 (p<0.0001) (Table 1 and 2 and Figure 1). In many other aspects of the disease, such as disease duration, levodopa equivalent daily dose, motor symptoms, non-motor symptoms, and autonomy for activities of daily living, an association between the stage and the level of affectation was observed, with data indicating a progressive worsening related to disease progression throughout the proposed stages.

Table 1. Disease related characteristics, motor and non-motor symptoms, autonomy for activities of daily living and quality of life in PD patients with different stage according to the MNCD classification (N=439).

	Stage 1 (N=37)	Stage 2 (N=272)	Stage 3 (N=124)	Stage 4-5 (N=6)	Total (N=439)	p
Age	61.84 ± 7.45	59.8 ± 9.61	67.01 ± 7.32	63.33 ± 7.47	62.05 ± 7.84	<0.0001
Males (%)	50.8	60.7	59.6	66.7	59	0.773
Weight (kgs)	77.51 ± 16.28	75.62 ± 13.91	76.74 ± 12.41	70.41 ± 10.08	76.02 ± 13.67	0.716
Disease duration (years)	4.06 ± 3.43	5.4 ± 3.81	8.73 ± 5.41	0.8 ± 5.4	5.73 ± 4.39	0.003
Antiparkinsonian drugs:						
- Levodopa	45.9	67.6	83.1	83.3	70.4	<0.0001
- Dopamine agonist	67.6	71.7	65.3	66.7	69.8	0.115
- MAO-B inhibitor	75.7	76.8	64.5	50	72.9	0.016
- COMT inhibitor	5.4	18.4	24.2	50	19.4	0.002
- Amantadine	5.4	6.8	11.3	16.7	9.3	0.088
L-dopa eq. daily dose (mg)	356.97 ± 276.78	540.01 ± 388.36	674.71 ± 441.8	1087.2 ± 782.12	569.48 ± 413.18	<0.0001
Number of non antip. drugs	1.89 ± 1.85	2.21 ± 2.22	3.66 ± 2.98	3.8 ± 2.88	2.61 ± 2.82	<0.0001
Motor phenotype (%)						0.282
- Tremoric dominant	48.9	44.9	38.7	0	42.6	
- PIGD	37.8	39.7	48.4	83.3	42.6	
- Indeterminate	18.2	15.4	12.9	16.7	14.8	
Hoehn & Yahr - OFF	2 [1.5; 2]	2 [1.5; 2]	2 [2; 2.5]	2 [2; 3]	2 [2; 2]	<0.0001
- Stage from 3 to 5 (%)	0	7.8	15.6	50	10	<0.0001
UPDRS-III - OFF	16.84 ± 8.67	21.55 ± 11.01	26.24 ± 11.99	39.17 ± 13.51	22.97 ± 11.49	<0.0001
UPDRS-IV	0.43 ± 0.6	1.91 ± 2.17	2.67 ± 2.78	6 ± 3.95	2.06 ± 2.41	<0.0001
- Motor fluctuations (%)	0	31.2	45.2	83.3	33.5	<0.0001
- Dyskinesia (%)	0	7.4	8.9	33.3	7.5	0.024
FOGQ	0.58 ± 1.29	3.2 ± 3.06	8.62 ± 5.15	16.83 ± 4.07	3.87 ± 4.85	<0.0001
- Patients with FOG (%)	0	4.4	8.1	66.7	5.9	<0.0001
- Patients with falls (%)	0	1.8	12.1	50	5	<0.0001
PD-CRS total score	99.62 ± 10.71	99.34 ± 11.72	73.66 ± 11.97	72.17 ± 11.91	91.67 ± 19.51	<0.0001
NMSS	12.54 ± 10.39	42.82 ± 32.94	90.77 ± 40.73	76.33 ± 43.98	45.79 ± 36.65	<0.0001
BDI-II	9.14 ± 2.93	9.32 ± 6.97	13.09 ± 8.49	16.5 ± 8.59	9.94 ± 7.77	<0.0001
- Major depression (%)	0	13.6	27.4	50	16.9	<0.0001
NPI	1.77 ± 2.94	5.48 ± 7.25	9.24 ± 9.99	7.17 ± 6.71	6.27 ± 8.16	<0.0001
QUIP-RS	1.24 ± 3.57	5.16 ± 9.31	4.25 ± 8.02	3.5 ± 6.57	4.55 ± 8.65	0.015
- ICD and/or CB (%)	0	20.2	18.5	16.7	18	0.028
PDSS	130.82 ± 9.52	112.28 ± 27.82	109.53 ± 24.68	82.33 ± 34.78	113.12 ± 27.28	<0.0001
VAS-PAIN	1.68 ± 2.24	2.61 ± 2.86	3.48 ± 3.34	5.16 ± 3.02	3.15 ± 2.83	<0.0001
VASF - physical	0.93 ± 1.7	3.02 ± 2.74	3.91 ± 2.64	5.66 ± 2.96	3.15 ± 2.83	<0.0001
VASF - mental	0.63 ± 1.13	2.21 ± 2.61	2.72 ± 2.86	3.66 ± 2.67	2.24 ± 2.65	<0.0001
ADLS	94.05 ± 4.97	90.73 ± 6.72	82.41 ± 12.77	41.66 ± 11.69	87.99 ± 11.1	<0.0001
PDQ-39SI	6.65 ± 4.27	15.5 ± 11.24	23.8 ± 16.14	46.36 ± 11.67	17.52 ± 13.76	<0.0001
EUROHIS-QOL8	4.19 ± 0.39	3.83 ± 0.52	3.54 ± 0.58	3.12 ± 0.5	3.76 ± 0.56	<0.0001
PQ-10	8.08 ± 1.38	7.41 ± 1.42	6.85 ± 1.8	5.17 ± 2.78	7.22 ± 1.63	<0.0001

The results represent percentages, mean ± SD or median (p25; p75). Chi-squared, ANOVA and/or Kruskal-Wallis test were applied. Data about H&Y and UPDRS-III are during the OFF state (first thing in the morning without taking medication in the previous 12 hours).

ADLS, Schwab and England Activities of daily living Scale; BDI-II, Beck Depression Inventory II; COMT, catechol O-methyltransferase; CB, compulsive behavior; EUROHIS-QOL8, EUROHIS-QOL 8-item index; FOGQ, Freezing of Gait Questionnaire; ICD, impulse control disorder; MAO-B, Monoamine oxidase-B; NMSS, Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD, Parkinson's disease; PD-CRS, Parkinson's Disease Cognitive Rating Scale; PDQ-39, 39-item Parkinson's disease Questionnaire; PDSS, Parkinson's Disease Sleep Scale; PIGD, Postural Instability Gait Difficulty; QUIP-RS, Questionnaire for Impulsive Compulsive Disorders in Parkinson's Disease Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAFS, Visual Analog Fatigue Scale; VAS-Pain, Visual Analog Scale-Pain

Table 1. Disease related characteristics, motor and non-motor symptoms, autonomy for activities of daily living and quality of life in PD patients with different stage according to the MNCD classification (N=439).

Table 2. Health-related and global quality of life in PD patients with different stage according to the MNCD classification (N=439).

	Stage 1 (N=37)	Stage 2 (N=272)	Stage 3 (N=124)	Stage 4-5 (N=6)	p_1	p_2	p_3	p_4
HEALTH-RELATED QOL								
PDQ-39SI	6.65 ± 4.27	15.5 ± 11.24	23.8 ± 16.14	46.36 ± 11.67	<0.0001	<0.0001	<0.0001	0.002
- Mobility	3.91 ± 6.39	12.97 ± 14.67	27.98 ± 24.32	70.83 ± 14.6	<0.0001	<0.0001	<0.0001	0.001
- Activities of daily living	5.77 ± 10.04	17.33 ± 18.25	32.79 ± 21.15	49.97 ± 29.11	<0.0001	0.006	0.018	0.016
- Emotional well-being	9.1 ± 10.13	20.99 ± 20.04	28.6 ± 29.94	38.15 ± 19.23	<0.0001	<0.0001	0.007	0.298
- Stigmatization	7.59 ± 12.67	12.42 ± 18.25	15.16 ± 22.36	29.8 ± 26.39	0.545	0.263	0.842	0.388
- Social support	2.47 ± 9.18	7.19 ± 15.24	11.29 ± 19.7	1.38 ± 3.4	0.014	0.027	0.861	0.252
- Cognition	7.52 ± 9.6	16.94 ± 16.18	27.85 ± 19.55	43.71 ± 14.26	<0.0001	0.001	<0.0001	0.033
- Communication	2.92 ± 6.85	8.26 ± 13.26	12.69 ± 17.52	38.86 ± 24.51	<0.0001	0.011	0.051	0.007
- Pain and discomfort	11.47 ± 13.2	26.93 ± 22.09	32.09 ± 25.68	63.86 ± 16.36	<0.0001	<0.0001	0.112	0.095
GLOBAL QOL								
PQ-10	8 ± 1.38	7.41 ± 1.42	6.85 ± 1.8	5.17 ± 2.78	<0.0001	0.015	<0.0001	0.161
EUROHIS-QOL8	4.19 ± 0.39	3.83 ± 0.52	3.54 ± 0.58	3.12 ± 0.5	<0.0001	<0.0001	<0.0001	0.068
- Quality of life	4.22 ± 0.68	3.87 ± 0.85	3.48 ± 0.78	3.17 ± 0.98	<0.0001	0.004	0.026	0.476
- Health status	3.46 ± 0.86	3.14 ± 0.89	2.91 ± 0.95	2.33 ± 0.81	0.001	0.022	<0.0001	0.148
- Energy	4.3 ± 0.7	3.81 ± 0.75	3.42 ± 0.88	2.83 ± 0.75	<0.0001	<0.0001	<0.0001	0.072
- Autonomy for ADL	4.22 ± 0.67	3.89 ± 0.83	3.23 ± 0.91	2.17 ± 0.41	<0.0001	<0.0001	<0.0001	0.004
- Self esteem	4.16 ± 0.64	3.87 ± 0.77	3.55 ± 0.91	3.33 ± 0.81	<0.0001	0.035	0.001	0.501
- Social relationships	4.32 ± 0.56	4.12 ± 0.67	3.92 ± 0.73	3.33 ± 0.81	0.001	0.092	0.013	0.064
- Economic capacity	4.2 ± 0.7	3.89 ± 0.77	3.62 ± 0.83	3.83 ± 0.75	<0.0001	0.001	0.002	0.642
- Habitat	4.08 ± 0.61	4.28 ± 0.71	4.23 ± 0.63	4 ± 0	0.149	0.137	0.256	0.246

The results represent mean ± SD. ANOVA and/or Kruskal-Wallis and Mann-Whitney-Wilcoxon test were applied: p_1, all groups; p_2, stage 1 vs stage 2; p_3, stage 2 vs stage 3; p_4, stage 3 vs stage 4.

ADL, Activities of daily living; QoL, quality of life.

Table 2. Health-related and global quality of life in PD patients with different stage according to the MNCD classification (N=439).

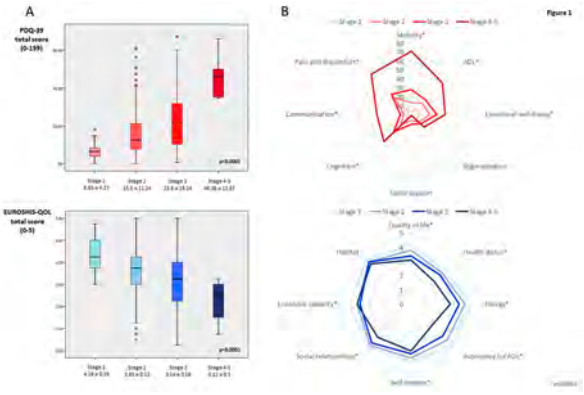

Figure 1. A. Health-related (PDQ-39SI) and global quality of life (PQ-10 and EUROHIS-QOL8) are represented in patients regarding to the MNCD stage, from stage 0 to stage 4-5. B. Comparison of the mean score on each domain of the PDQ-39SI and EUR

Conclusion: Staging PD according to the MNCD classification was significantly associated with QoL and disease severity. The MNCD could be a proper tool to monitor the progression of PD.

Disclosure: COPPADIS and the present study were developed with the help of Fundación Española de Ayuda a la Investigación en Enfermedades Neurodegenerativas y/o de Origen Genético (https://fundaciondegen.org/) and Alpha Bioresearch (www.alphabioresearch.com). Also, we received grants from the Spanish Ministry of Economy and Competitiveness [PI16/01575] co-founded by ISCIII (Concesión de subvenciones de Proyectos de Investigación en Salud de la convocatoria 2020 de la Acción Estratégica en Salud 2017-2020 por el Proyecto "PROGRESIÓN NO MOTORA E IMPACTO EN LA CALIDAD DE VIDA EN LA ENFERMEDAD DE PARKINSON") to develop a part of the COPPADIS project.

Ageing and dementia 2

OPR-086

The relation between circulating microRNAs and hippocampal structure in the general population

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Background and aims: MicroRNAs, small RNA molecules that post-transcriptionally downregulate gene expression, are regulators of brain physiology and putative biomarkers of neurodegeneration. Our study aims to determine the relation between circulating microRNAs and the structure of the hippocampus, a hub of cognition and neurodegeneration.
Methods: Our analysis was based on 2024 participants (57% women, mean age: 54.2 years, age range: 30 to 90 years) of the Rhineland Study, a population-based study in Bonn, Germany. Left and right hippocampal volume (HCV) were measured using Freesurfer on 3T T1 Magnetic Resonance (MR) images, and microRNA and gene expression were measured in blood samples. Using multiple multivariable linear regression models, we examined the association of microRNA expression (independent variable) with HCV, hippocampal asym.metry, and target gene expression (dependent variables), controlling for age and sex. Statistical significance was set at false discovery rate ≤ 0.05
Results: The expression of 4 microRNAs was significantly or borderline significantly associated with left HCV. This association was independent of and unmodified by age and sex. No microRNAs were significantly associated with right HCV or hippocampal asymmetry. Overexpression of the 4 microRNAs was associated with downregulation of target genes related to inflammation, vasculature development, and amyloid-beta. Target genes expressed in the hippocampus were additionally related to neuron death and oxidative stress.
Conclusion: Here, we identified 4 microRNAs related to hippocampal volume in the general population, and determined underlying mechanisms. Our findings emphasize the role of epigenetics in brain health and will aid neurodegenerative diseases research.
Disclosure: Nothing to disclose.

OPR-087

Different Temporal Dynamics of Monoaminergic Disfunctions across Neurodegenerative Conditions

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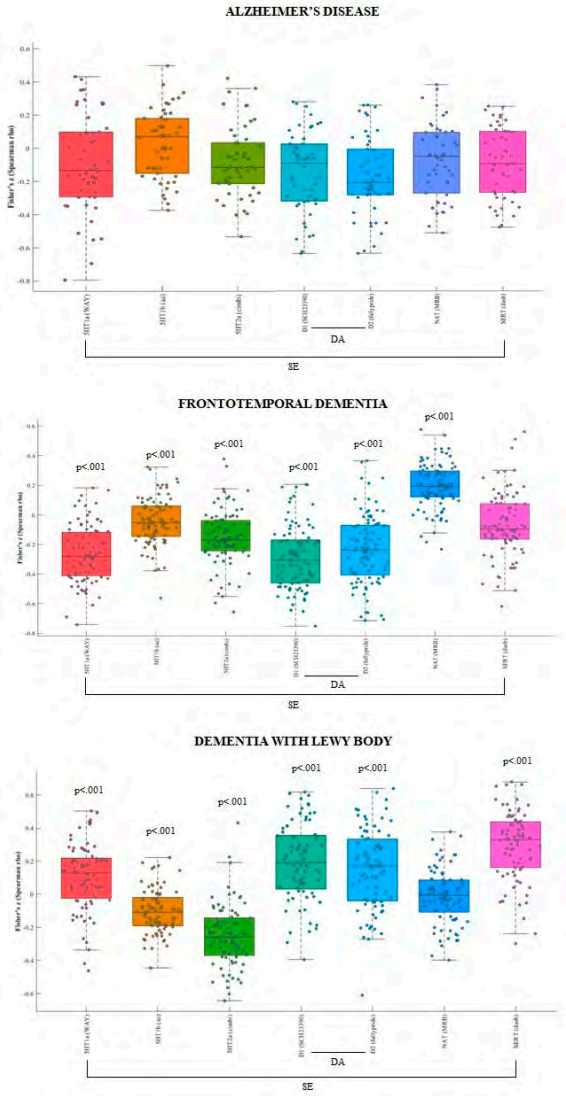
Background and aims: Monoaminergic systems are a target for symptomatic therapies and a window for the study of disease progression. We explore the progression and the distribution of monoaminergic deficits across three main dementing pathologies along with the spreading of cognitive impairment.
Methods: We included 50 Alzheimer's Disease (AD) patients, 93 Frontotemporal dementia (FTD), 81 Dementia with Lewy Body (DLB) and 42 healthy controls (HC). We acquired brain [18F]FDG-PET images and MMSE. Using JuSpace toolbox we explored correlation between [18F] FDG-PET images and PET maps of dopaminergic (DA), serotonergic (SE) and noradrenergic (NAT) systems. We performed an ANOVA between pathologies and neurotransmitters scores to explore differences across conditions. Subjects within each pathology were divided into 3 subgroups based on MMSE score, to explore the progression of neurotransmitters and cognitive impairment.
Results: Sample characteristics are provided in Table 1. Compared to HC, metabolic changes were significantly associated with spatial distribution of SE, DA and NAT in FTD, and DA and SE in DLB. Detailed results are shown in Figure 1. The ANOVA showed a significant difference across diseases for SE and NAT systems, at Tukey post-hoc test SE and NAT impairment were significantly different between AD and FTD, FTD and DLB, but not between AD and DLB. Results from voxel-based analysis and spatial distribution across groups of severity are shown in Figure 2.

	Alzheimer's Disease n = 80			Frontotemporal Dementia n = 93			Dementia with Lewy Bodies n = 81			Healthy Controls n = 42
	MMSE			MMSE			MMSE			
	<24 n = 36	24 - 27 n = 20	>27 n = 14	<24 n = 27	24 – 26 n = 36	>27 n = 30	<24 n = 30	23 – 26 n = 25	>27 n = 23	
Age	69.93 ± 10.36	74.85 ± 4.81	72.64 ± 8	74.81 ± 7.6	72 ± 7.92	74.26 ± 7.13	78.63 ± 5.16	77.17 ± 5.53	73.26 ±7.62	70 ± 8.53
Sex (%M)	31.25%	35%	35.14%	33.33%	41.66%	46.66%	46.66%	50%	69.56%	35.71%
Education	10.43 ± 4.17	10.25 ± 4.21	12 ± 4.43	8.33 ± 4.5	9.55 ± 4.62	11 ± 4.38	7.2 ± 3	8.78 ± 3.86	13.13 ± 4.23	11 ± 3.84
Serotonin	-0.11 ± 0.15	-0.08 ± 0.14	0.03 ± 0.08	-0.18 ± 0.07	-0.14 ± 0.1	-0.15 ± 0.08	-0.02 ± 0.1	0.01 ± 0.09	0.006 ± 0.14	
Dopamine	-0.06 ± 0.3	-0.09 ± 0.26	0.01 ± 0.17	-0.07 ± 0.18	-0.09 ± 0.14	-0.28 ± 0.19	0.01 ± 0.17	0.19 ± 0.23	0.18 ± 0.25	
Noradrenaline	0.04 ± 0.21	0.06 ± 0.24	0.02 ± 0.3	0.19 ± 0.16	0.18 ± 0.15	0.2 ± 0.14	0.01 ± 0.18	-0.04 ± 0.15	-0.01 ± 0.15	

Table 1: Demographics and clinical characteristics of the sample. Values are shown as mean ± sd. Abbreviations: M = Male; MMSE = Mini Mental State Examination; n = number.



Spatial distribution of Serotonergic (SE), Dopaminergic (DA) and Noradrenergic (NAT) systems in AD, FTD and DLB. (we z-scored 5HT1a-5HT1b-5HT2a and SERT, D1 and D2 receptor values so to have a single subject-score for SE and DA).

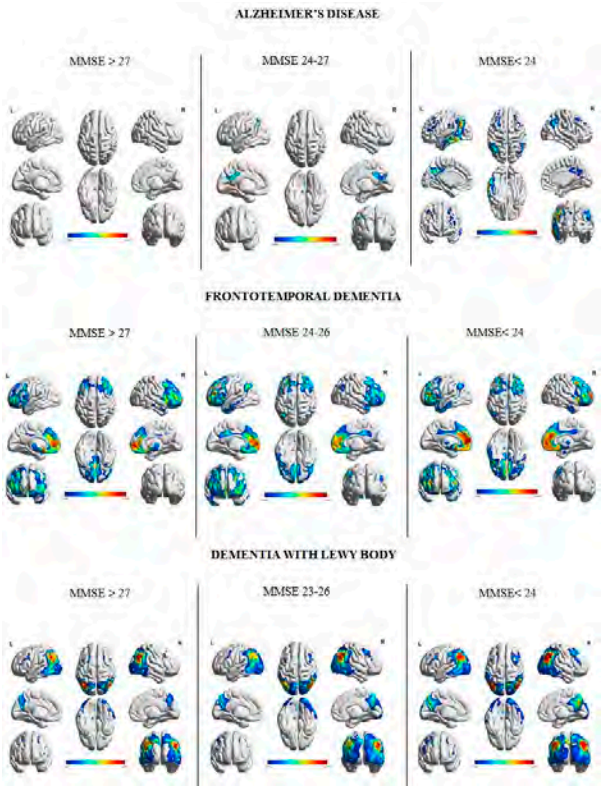


Figure 2: Results of voxel-based analysis and Spatial distribution of Serotonergic (SE), Dopaminergic (DA) and Noradrenergic (NAT) systems in subgroups of severity of AD, FTD and DLB.

Conclusion: In FTD and DLB monoaminergic disfunctions are evident already at the early stage of the disease, while in AD a SE impairment is observed at later stage.
Disclosure: Nothing to disclose.

OPR-088

Frequency and course of behavioural and neuropsychiatric symptoms in genetic frontotemporal dementia

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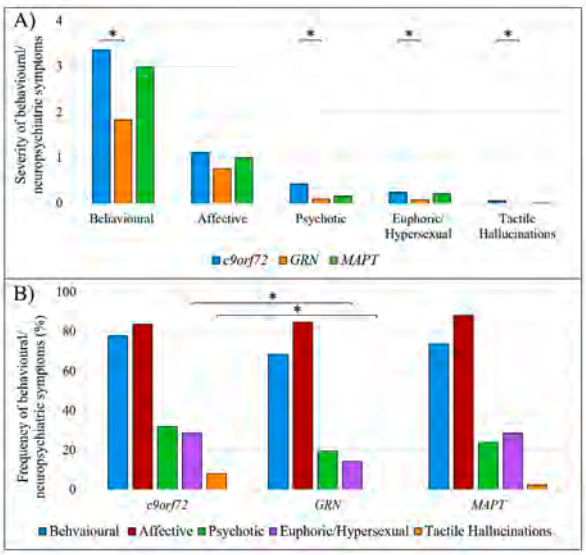
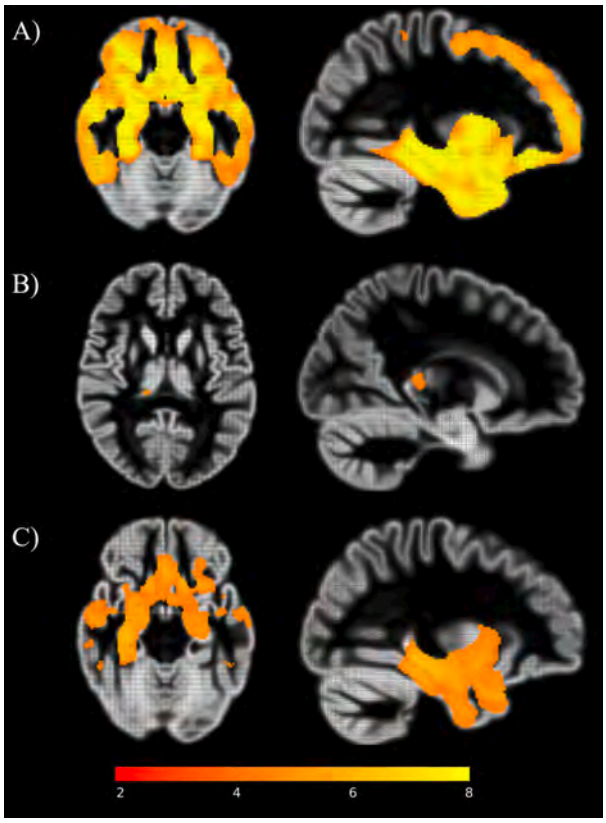
Background and aims: We aimed to describe behavioural and neuropsychiatric phenotypes in genetic FTD, quantify their temporal association and their regional association with brain atrophy.

Methods: We analyzed data of pathogenic variant carriers in the c9orf72, GRN or MAPT gene from the Genetic Frontotemporal dementia Initiative. Principal component analysis was performed to identify behavioural and neuropsychiatric clusters that were compared between groups. Associations with atrophy were determined using voxel-wise regression. We applied linear mixed effects models to describe the evolution of symptoms.

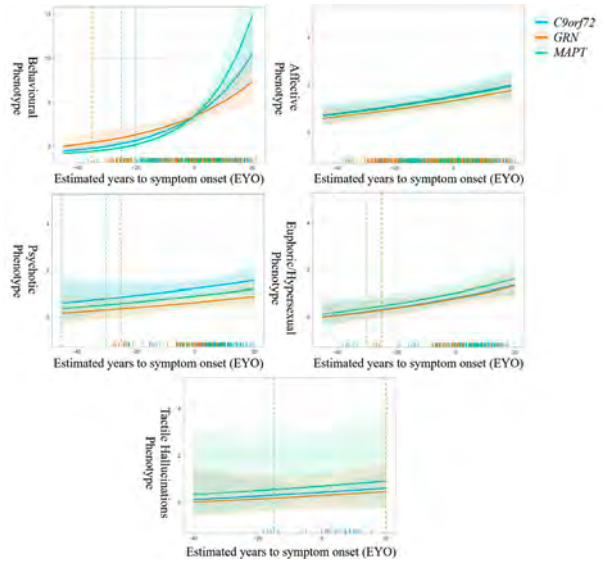
Results: 522 subjects were included in the analysis: 221 c9orf72, 213 GRN and 88 MAPT pathogenic variant carriers. Principal component analysis revealed five phenotype clusters: behavioural, affective, psychotic, euphoric/hypersexual and tactile hallucinations. Affective symptoms were most frequent, followed by behavioural symptoms. In c9orf72 and GRN pathogenic variant carriers psychotic symptoms were more frequent than euphoric/hypersexual symptoms, which was the opposite in MAPT pathogenic variant carriers. While behavioural symptoms were associated with frontotemporal atrophy, only a small atrophy cluster in the right posterior thalamus was associated with psychotic symptoms. Euphoric/hypersexual symptoms were associated with atrophy in both temporal lobes and the anterior cingulate cortex. Time to onset, genetic group, education and gender influenced behavioural and neuropsychiatric symptoms.



Severity and frequency of behavioural and neuropsychiatric symptoms



Correlation of Sum Scores of behavioural and neuropsychiatric phenotypes with cerebral atrophy using linear regression models



Sum scores vs. estimated years to symptom onset

Conclusion: These results indicate the presence of clusters of behavioural and neuropsychiatric symptoms in genetic FTD, correlated with specific atrophy patterns. Their severity depends on time, affected gene, gender and education. These clinico-genetic associations can guide diagnostic evaluations and the design of clinical trials.

Disclosure: This study was funded by the UK Medical Research Council, Deutsche Forschungsgemeinschaft, the Italian Ministry of Health, a Canadian Institutes of Health Research operating grant, the Bluefield Project, and a JPND grant.

OPR-089

Mild and complex multimorbidity and structural brain changes in older adults

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Background and aims: Diseases co-occur in the same person based on shared risk factors and individual predisposition and a high disease burden is responsible for accelerated cognitive aging. However, the impact of multimorbidity (co-occurrence of two or more diseases in the same person) on brain has been rarely investigated. We aimed to explore the impact of mild (i.e., involving one or two body systems) and complex (i.e., involving three or more systems) multimorbidity on brain volumes in a population-based study with six years repeated brain magnetic resonance imaging (MRI).

Methods: We used data from 450 participants of the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) who underwent brain MRI. Individuals were divided into three groups: no multimorbidity (reference), mild and complex multimorbidity. Linear mixed models were used to estimate the association between mild/complex multimorbidity and structural brain changes. All volumes were adjusted for total intracranial volume and the analyses were adjusted for age, sex, education, APOE and baseline Mini-Mental State Examination.

Results: During 6.2 (0.2) years of follow-up, participants with complex multimorbidity (n= 252) showed the greatest reduction in total brain (β:-8.1; 95%CI -12.0;-4.2) and hippocampal volumes (β:-0.12; 95%CI -0.18;-0.06). They also exhibited the greatest ventricular enlargement (β:1.3; 95%CI 0.4;2.2) and white matter hyperintensities accumulation (β:1.2; 95%CI 0.5;1.9). Intermediate trajectories of brain changes were observed in participants with mild multimorbidity, following a dose-response relationship.

	TBTV β (95% CI)	Hippocampal volume β (95% CI)	Ventricular volume β (95%CI)	WMH volume β (95%CI)
Multimorbidity (baseline)				
No multimorbidity	Ref.	Ref.	Ref.	Ref.
Mild multimorbidity	-21.8 (-37.3, -6.4)	-0.11 (-0.31, 0.09)	4.4 (0.0, 8.8)	0.2 (-2.3, 2.7)
Complex multimorbidity	-25.9 (-40.0, -11.8)	-0.13 (-0.31, 0.04)	7.1 (3.1, 11.1)	1.8 (-0.5, 4.1)
Multimorbidity (x time)				
No multimorbidity	Ref.	Ref.	Ref.	Ref.
Mild multimorbidity	-3.7 (-8.2, 0.8)	-0.05 (-0.12, 0.02)	0.5 (-0.5, 1.6)	0.6 (-0.3, 1.4)
Complex multimorbidity	-8.1 (-12.0, -4.2)	-0.12 (-0.18, -0.06)	1.3 (0.4, 2.2)	1.2 (0.5, 1.9)

Table 1. Association between multimorbidity patterns and brain magnetic resonance imaging changes. Coefficients are derived from linear mixed models and are adjusted for age, sex, education, APOE genotype and baseline Mini-Mental State Examination.

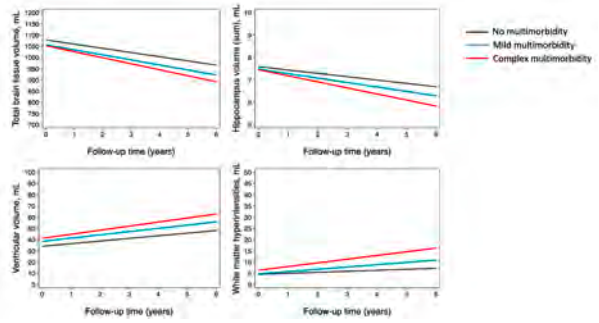

Figure 1. Trajectories of brain MRI changes over six years of follow-up by multimorbidity patterns. Linear mixed models adjusted for age, sex, education, APOE genotype and baseline MMSE.

Conclusion: Chronic diseases' burden, particularly when involving multiple systems, is associated with accelerated brain structural changes linked to both neurodegeneration and cerebrovascular damage.
Disclosure: Authors declare no conflict of interest.

OPR-090

Dizziness in Cognitive Impairment (DCI) – a novel clinical entity associated with a specific brain atrophy pattern

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Background and aims: Dizziness may be a symptom of impeding cognitive decline. In this prospective cohort study, elderly patients with the chief complaint dizziness were screened for cognitive and vestibular impairment and for specific patterns of brain atrophy.
Methods: One hundred forty-four consecutive patients >60 years of age, who seeked medical advice in a tertiary dizziness unit (DSGZ, LMU Munich) for the key symptom of dizziness, received comprehensive neuro-otological testing and neuro-psychological screening (by MoCA test). Routine brain MRIs were collected and transformed to a 1mm 3D-MP-RAGE image using a validated SynthSR-tool. VBM analysis was done with MoCA scores or caloric mean excitability as dependent variables, corrected for age.
Results: One third of patients had a MoCA score of <24, 22.2% of |24,25| and 44.4% of ≥26 points. Caloric vestibular excitability was comparable across these patient subgroups. Whole-brain VBM revealed a significant correlation of MoCA scores with brain atrophy in the right>left posterior insula, parietal lobule, superior temporal gyrus, anterior cingulate gyrus, bilateral parahippocampal gyrus, posterolateral/anteromedial thalamus, caudate nucleus and cerebellum. Caloric mean excitability did not correlate significantly with the above-mentioned brain regions.
Conclusion: Findings suggest that insular and temporo-parietal atrophy with a rightside predominance, including multisensory vestibular processing networks, but not peripheral vestibular pathology play a substantial role in the pathophysiological explanation of dizziness in patients with cognitive impairment. We suggest to newly introduce the term "Dizziness in Cognitive Impairment" (DCI) for this rather frequent syndrome and routinely include cognitive screening tests in the workup of elderly dizzy patients.
Disclosure: The authors have nothing to disclose.

Tuesday, July 04 2023
Epilepsy

OPR-091

The International Consortium for Health Outcomes Measurement recommendations for epilepsy practice outcome assessment

J. Mitchell[1], F. Sossi[2], I. Miller[2], A. Amos[3], J. Austin[4], S. Badzik[5], G. Baker[6], B. Ben Zeev[7], J. Bolton[8], S. Cassel[9], H. Cross[10], D. Chan Wei Shih[11], C. Gericke[12], L. Lally[3], S. Mbugua[13], T. Mesa[14], T. Von Oertzen[15], E. Perucca[16], A. Pullen[17], G. Ronen[18], M. Sajatovic[19], M. Singh[20], J. Wilmshurst[21], L. Wollscheid[22], A. Berg[23]
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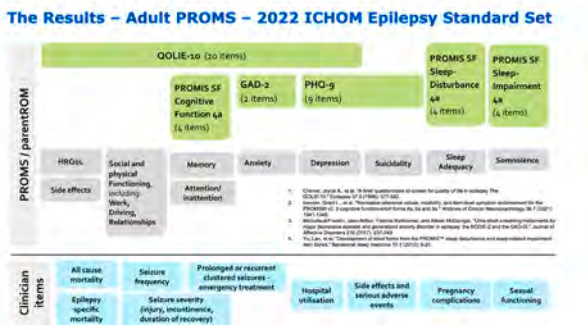
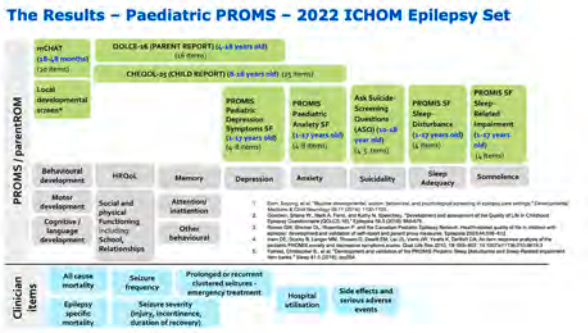
Background and aims: There is increasing recognition of the importance of delivering value-based health care, where value is assessed by measuring health outcomes against the cost of delivery. This approach leads to improved health outcomes with reduced healthcare utilisation by using well defined clinical and patient-reported outcome measures (PROMS).
Methods: The International Consortium for Health Outcomes Measurement convened an international working group of experts in epilepsy, people with epilepsy and their representatives. The group developed minimum sets of standardised outcomes and outcome measurement methods to support clinical decision making and quality improvement. The focus was to ensure international applicability, with a preference for measurement tools that have been validated in many settings, cultures, and languages. Measurement tools that capture all core outcomes were identified through Delphi based online consensus methods, with consecutive rounds of voting supplemented by open discussion and external validation surveys.
Results: 22 core outcomes were identified, of which many non-seizure outcomes were included: anxiety, depression, suicidality, memory and attention, sleep quality, somnolence, and neurodevelopmental status. Measurement tools including PROMS were recommended based on evidence of strong clinical measurement properties, feasibility of implementation, acceptability to people with epilepsy and cross-cultural applicability. Different age-appropriate outcome measurement instruments have been recommended for infants, children, adolescents and adults with epilepsy.



ICHOM Epilepsy Standard Set - Adult core outcomes and measurement instruments



ICHOM Epilepsy Standard Set - Paediatric core outcomes and measurement instruments

Conclusion: Implementing the proposed set of outcomes and measurement methods in daily practice should establish the use of patient-centred outcomes and ensure holistic care. Widespread adoption could reduce outcome measurement heterogeneity, accelerate big-data science and lead to improved care.
Disclosure: This work was supported by the sponsors: UCB, LivaNova, Nile and KK Women's and Children's Hospital.

OPR-092

The Top 10 Epilepsy Research Priorities: A UK Priority Setting Partnership

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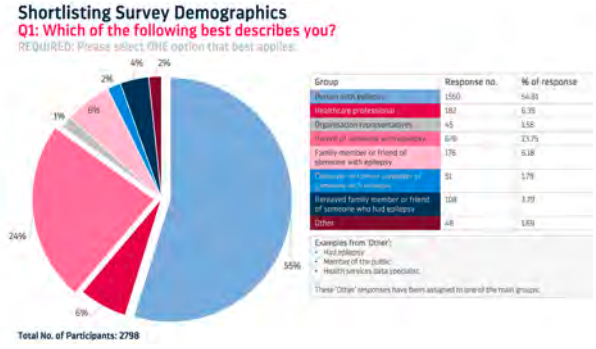
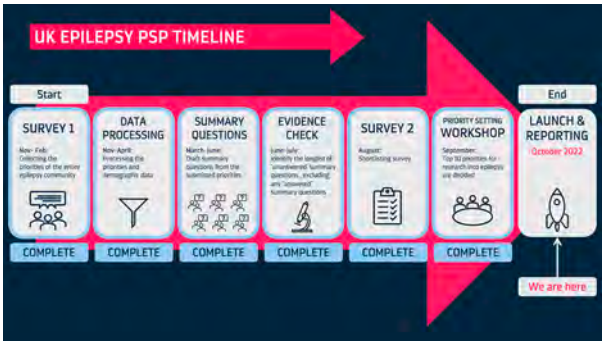
Background and aims: Despite being one of the most prevalent, serious neurological conditions, epilepsy received only 0.3% of the total £4.8 billion UK Government funding spent on health-related research in 2018. To evidence the need for greater investment, a James Lind Alliance (JLA) Priority Setting Partnership (PSP) was conducted to identify the Top Ten unanswered questions for epilepsy research.

Methods: Adopting JLA methodology, the UK Epilepsy PSP formed a steering group of 23 individuals affected by and working in epilepsy, from across the UK. They developed the survey that collected the community's research priorities, which were categorised and translated into distinct researchable questions. Questions previously answered by research were removed during the evidence-checking process, while unanswered questions formed the basis of a second shortlisting survey. Shortlisted questions were reviewed and discussed at the UK Epilepsy PSP Workshop, where the final Top Ten questions for epilepsy research were agreed.

Results: Collectively, the UK Epilepsy PSP received nearly 5,000 individual responses from across the UK. The highest proportion of responses were from people with epilepsy followed by parents of children with epilepsy and healthcare professionals, and antiseizure medication, SUDEP and epilepsy in women were among the most frequently reported research priorities. The final Top Ten research questions were published in October 2022.



Shortlisting Survey Demographics



UK Epilepsy Priority Setting Partnership (PSP) Timeline

UK Epilepsy Priority Setting Partnership (PSP) Top Ten

Conclusion: The UK Epilepsy PSP is a once-in-a-generation, national consensus that collated and ranked the research priorities of the epilepsy community, generating the evidence needed to influence funders to provide equitable investment for epilepsy research, which will focus on the priorities of those most affected.

Disclosure: Epilepsy Research UK funded, led and managed the programme.

OPR-093

Co-medication management: key to optimize the efficacy and tolerability of Cenobamate.

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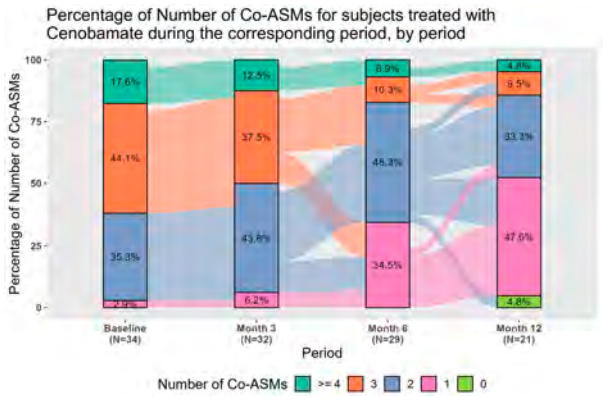
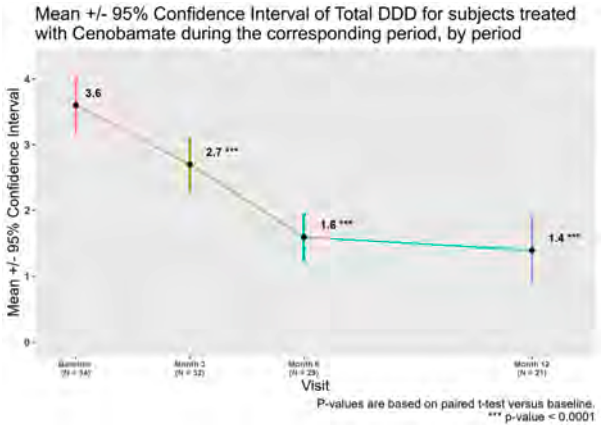
Advanced Neurology Center, Epilepsy Unit, Sevilla, Spain

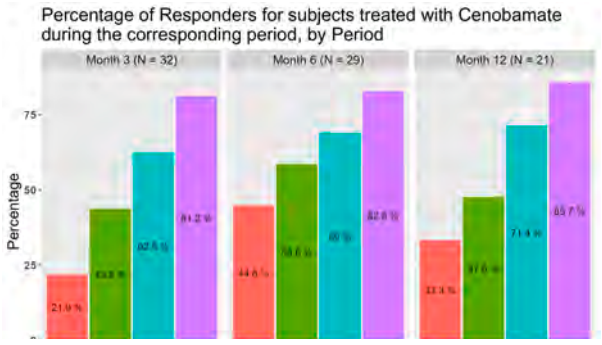
Background and aims: The high efficacy of cenobamate (CNB) has led this recently approved anti-seizure drug to the front line in the fight against drug-resistant epilepsy (DRE). In this study we provide our experience as an epilepsy unit in a real-world practice on optimizing CNB efficacy and minimizing adverse effects (AEs) by rapidly reducing co-medications.
Methods: We performed a prospective observational study of patients with focal DRE treated with CNB in our clinic.
Results: Thirty-four patients were included. Twenty-one patients had reached 12 months of follow-up by December 2022. Median seizure reduction was 93.3% at 6 months and 88.9% at 12 months of follow-up. Response rate (>50% seizure reduction) was 85.7% at 12 months. Responder rate >90% was achieved by 10 patients (47.6%) at 12 months. Seizure freedom was reached by 7 patients (33.3%) at 12 months. The total defined daily dose (DDD) of co-administered ASDs decreased significantly during follow-up (mean 3.6 DDD, SD 1.3 at baseline; mean 1.4 DDD, SD 1.2 at 12 months of follow-up; p<0001). AEs were frequent initially (35.3% ataxia, 52.9% dizziness and 64.7% drowsiness) but decreased significantly at 12 months (3.8% ataxia, no dizziness, 33.3% drowsiness at 12 months). No skin rash was detected.



Evolution of number of co-administered ASDs during CNB treatment



Mean defined daily dose (DDD) of co-administered ASDs during CNB treatment



Percentage of responders

Conclusion: We report an outstandingly high seizure frequency reduction and seizure freedom rates when using CNB in highly refractory patients while at the same time reducing co-medication more than half its initial dose. We suggest rapid co-medication reduction might be the approach needed to optimize efficacy and minimize AEs when using CNB.
Disclosure: Nothing to disclose.

OPR-094

Long-term outcome of alcohol withdrawal seizures

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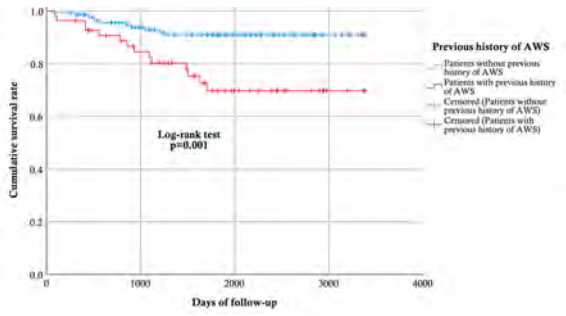
Background and aims: Alcohol withdrawal seizures (AWS) usually occur around 6-48 hours after major intake reduction. While they are often a single event, there is little knowledge on long-term evolution after AWS and risk factors for AWS relapse.
Methods: We reviewed our database between 01.01.2013-10.08.2021 and identified all patients admitted to the emergency department after AWS and for whom an EEG was requested. AWS relapses were researched until 29.04.2022. History, laboratory, possible antiepileptic drug treatment, EEG and CT findings were compared between patients with and without AWS relapse.
Results: 199 patients were enrolled (mean age 53.5±12.3 years, 78.9% male). Brain CTs (n=182) showed pathological findings in 35.7%: significant brain atrophy (25.8%), intracranial haemorrhages (10.4%), traumatic sequelae (3.3%) and skull fractures (2.2%). 11% suffered from AWS relapses, after a median of 470.5 days. Risk factors for relapses were history of AWS (p=0.013), epileptiform EEG abnormalities (p=0.042), skull fractures (p<0.001) and severe hyponatremia (p=0.034). Prior or current benzodiazepine or antiseizure treatments were not associated with relapses. Mortality rate was 2.6%/year of follow-up and risk factors for death were history of AWS (p<0.001) and encephalopathic EEG (p=0.041).



Survival rate comparison between patients with and without previous history of AWS (event=death). Blue curve: patients without previous history of AWS; red curve: patients with previous history of AWS. Chi-square =10.4, p=0.001.

Conclusion: AWS occur mostly in middle-aged males with a relapse rate of 11% and are associated with high mortality rate. Risk factors for relapse are previous history of AWS, epileptiform EEG abnormalities, skull fractures, which also predispose patients to epilepsy. Prior AWS are also a risk factor for death. Further studies are needed to confirm our findings and identify approaches to prevent AWS relapses and, consequently, fatal outcome.
Disclosure: Nothing to disclose.

OPR-095

10 years of findings evaluating response of People with Intellectual Disability to Anti-Seizure Medications & Treatments

A. Sellers[1] , J. Allard[1], W. Henley[2], B. McLean[1], R. Shankar[1]
[1]Cornwall Intellectual Disability (CIDER), Cornwall Partnership NHS Foundation Trust, UK, [2]University of Exeter, UK

Background and aims: Epilepsy is present in nearly 25% of People with Intellectual Disability (PwID) (general population – 1%) and associated with increased healthcare costs, morbidity and mortality, polypharmacy, treatment resistance and adverse effects. Prescribing practices remain primarily based on medication trials excluding PwID. Objectives of UK NHS Epilepsy and Intellectual Disability (EpID) Database Research Register: 1. Evaluate the efficacy for PwID and epilepsy of - a. New (post 2005) Anti-Seizure Medications (ASMs) b. Most common used ASM in UK – Levetiracetam (LEV) 2. Compare new ASMs to each other and LEV
Methods: This NHS ethically approved and NIHR adopted study applies a rigorous systematic methodology for collecting and analysing large datasets of retrospective observational patient data, detailing real world responses to ASMs and treatments for PwID to generate level 2 evidence. Patient data is collected on demographics, concomitant ASMs, dose, exposure length, adverse effects, retention rates, seizure type and frequency for first 12 months of treatment. PwID and general population epilepsy data is compared.
Results: Since 2014, 1180 research participants have been studied across five ASMs (Perampanel, Lacosamide, Eslicarbazepine, Brivaracetam and Levetiracetam). Similar ASM responses (group differences reported as odds ratios estimated from logistic regression models) are reported, with higher comorbidity, adverse effects and slower titration for PwID. The database register allows for comparison with European collaborators and more recent focus on new treatments, including Epidiolex.

Table 1: Recruitment to EpID Register 2014-2023 (n=1185)

	No ID	ID	Total
Perampanel	157	121	278
Eslicarbazepine	57	36	93
Lacosamide	156	76	232
Brivaracetam	106	33	139
Levetiracetam	230	200	430
Epidiolex (ongoing)	2	11	13

Table 1: Recruitment to EpID Register 2014-2023 (n=1185)

	All participants	No ID	ID
Perampanel[1]			
Missing	6 (4.2%)	1	5
Worsening	2 (1.4%)	1	1
No change / < 50% improvement	111 (77.1%)	58	49
> 50% improvement	25 (17.3%)	98	91
Eslicarbazepine[2]			
Missing	14 (15.1%)	11	3
Worsening	7 (7.5%)	5	2
No change / < 50% improvement	32 (34.4%)	21	11
> 50% improvement	40 (43%)	98	91
Lacosamide[3]			
Missing	61 (26.3%)	45	16
Worsening	27 (11.7%)	19	8
No change / < 50% improvement	72 (31%)	44	20
> 50% improvement	72 (31%)	48	15
Levetiracetam[4]			
Missing	99 (23%)	51	48
Worsening	35 (8%)	23	12
No change / < 50% improvement	107 (25%)	58	49
> 50% improvement	189 (44%)	98	91

[1]Perampanel (p=0.11 for association between ID group and efficacy). Additional Perampanel data for 134 participants currently in analysis.

[2]Eslicarbazepine (p=0.43 for association between ID group and efficacy).

[3]Lacosamide (p=0.93 for association between ID group and efficacy).

[4]Levetiracetam (p=0.10 for association between ID group and efficacy).

Table 2: Efficacy data for Perampanel, Eslicarbazepine, Lacosamide and Levetiracetam (Brivaracetam data currently in analysis, Epidiolex recruitment ongoing)

Conclusion: The EpID database register highlights an innovative research methodology. Findings have informed prescribing guidance for specific new ASMs, offering opportunities for comparison with established ASMs and new treatments.

Disclosure: Funding for the EpID database arms has been provided by Eisai, Bial UK, UCB S.A., Autistica, and GW Pharmaceuticals (Jazz Pharmaceuticals). Author affiliations: Adrian Sellers 1, Jon Allard 1,2, William Henley 3, Brendan McLean 1, Rohit Shankar 1,2. 1 Cornwall Intellectual Disability and Epilepsy Research Centre (CIDER) - Cornwall Partnership NHS Foundation Trust, UK, 2 University of Plymouth, UK. 3 University of Exeter, UK.

OPR-096

Guidelines on Status Epilepticus neglet the quality domain of applicability: a systematic review

L. Vignatelli[1], V. Tontini[2], S. Mazzoni[1], M. Camerlingo[3], F. Bisulli[1], G. Giovannini[4], S. Meletti,[4], E. Pasini[1], R. Michelucci[1], P. Tinuper[5], L. Di Vito[1]

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Background and aims: Status epilepticus (SE) is a neurological emergency characterized by high mortality that could be partly explained by general aging of population but also by the gap between management based on guidelines and clinical practice. Several studies have reported that recommendations for management of SE are often not followed by clinicians. The aim of this systematic review is to appraise quality of guidelines, assuming that applicability domain may be particularly overlooked, and make a comparison of topics covered.

Methods: Guidelines on management of SE in adults, published since 2010, were included. This systematic review followed the methodology by Johnston (2019) and was registered with PROSPERO database (CRD42022314153). We searched PubMed and EMBASE databases, guideline registries, websites of governmental organisations and neurologic societies. Quality of guidelines was assessed with the AGREE-II tool (Brouwers 2010).

Results: Fifteen guidelines were included. Regarding quality analysis, the AGREE-II domains "Scope and Purpose" and "Clarity of Presentation" were assigned the highest overall median scores (69% and 78%). "Applicability" was assigned the lowest median score of 10%. The domains "Stakeholder Involvement", "Rigor of Development" and "Editorial Independence" were underreported (median score range 44-61%). Pre-hospital management and treatment and EEG monitoring were the main topics reported (87%-80% of guidelines) while those less considered were diagnostic investigation (40%), refractory SE treatments (47%) and timing for EEG registration (47%). Only 33% exploited tools/algorithms to implement guidelines.

Developer	Reference
European Federation of Neurological Societies	Meierkord et al., 2010
Neurocritical Care Society	Brophy et al., 2012
European Society of Intensive Care Medicine	Claassen et al., 2013
Argentinian Society of Neurology	Bernater et al., 2013
American College of Emergency Physicians	Huff et al., 2014
American Clinical Neurophysiology Society	Herman et al., 2015
American Epilepsy Society	Glauser et al., 2016
Spanish Society of Neurology	Mercadé Cerdá et al., 2016
Emergency medical services / Medical Directors Association of California	Silverman et al., 2017
Scottish Intercollegiate Guidelines Network	SIGN, 2018
Colombian Neurology Association	Vergara et al., 2019
Italian Legue Against Epilepsy	Minicucci et al., 2020
French Resuscitation Society, French Society of Emergency Medicine	Outin et al., 2020
German Society of Neurology, Austrian Society of Neurology	Rosenow and Weber, 2021
National Institute for Health and Care Excellence	NICE, 2021

Figure 1. Clinical practice guidelines on Status Epilepticus included in the systematic review.

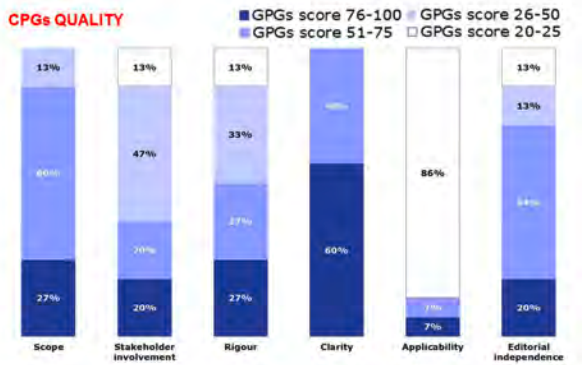

Figure 2. Quality of clinical practice guidelines on status epilepticus

TOPICS COVERED BY CPGs	GPGs covering the topic
Pre-hospital management indication	13 (87%)
Specific health professionals explicitly required	2 (13%)
EEG: Indication of Use	11 (73%)
EEG: Timing	7 (47%)
EEG: Type of monitoring	9 (60%)
TREATMENT OF SE: Topic covered	12 (80%)
TREATMENT OF SE: Based on SE classification (CSE/NCSE)	9 (60%)
TREATMENT OF SE: Based on previous medicaments failure	11 (73%)
TREATMENT OF SE: Based on timing Y/N	9 (60%)
RSE-SRSE: Other treatment proposed (other than ASM/anaesthetics)	7 (47%)
Advanced Diagnostic investigation proposed	6 (40%)
Tools or algorithms	5 (33%)

Figure 3. Topics coverd by the clinical practice guidelines

Conclusion: It seems that guidelines deal extensively with some issues, leaving out others fundamental in clinical practice. As hypothesized, applicability domain of guidelines is particularly neglected.
Disclosure: Nothing to disclose.

ePresentations

Saturday, July 01 2023
Ageing and dementia

EPR-001

Characterization of FTLD spectrum through advanced diffusion-weighted MRI metrics: a connectome approach

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Background and aims: To investigate structural alterations in brain network of FTLD spectrum using connectome analysis with advanced diffusion-weighted MRI metrics.
Methods: Thirty-four behavioral-variant frontotemporal dementia (bvFTD), 11 semantic variant primary progressive aphasia (svPPA), 11 nonfluent variant primary progressive aphasia (nfvPPA) and 18 motor neuron disease (MND) patients and 48 controls were underwent multi-shell diffusion MRI. Fractional anisotropy (FA) maps were computed. Intra-cellular Volume Fraction (ICVF) maps were estimated using NODDI model. Graph analysis and connectomics assessed global and local network properties and regional connectivity.
Results: Widespread structural changes were observed in bvFTD patients relative to controls, MND and svPPA patients. nfvPPA patients showed altered FA properties at global and lobar (frontal, basal-ganglia, parietal, and temporal areas) levels compared to controls and MND patients. svPPA patients showed altered ICVF measures in temporal lobe compared to controls and MND patients. Considering connectivity analysis, bvFTD patients showed widespread decreased FA compared to MND patients and controls. In addition, bvFTD patients showed decreased FA relative to svPPA patients in the right hemisphere, involving frontal, parietal and temporal areas. nfvPPA patients showed decreased FA in the left hemisphere relative to controls and MND patients, involving precentral gyrus, insula, putamen and temporal lobe. Considering ICVF, greater alterations were detected compared to FA maps, showing differences between svPPA and nfvPPA patients.
Conclusion: Connectome-analysis based on advanced diffusion-weighted models is useful to evaluate structural disruptions with greater differentiation among FTLD syndromes compared to diffusion-tensor derived measures.
Disclosure: Supported-by: European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease.

EPR-002

Modeling pathological spread through the structural connectome in the FTLD spectrum

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Background and aims: To explore the relationship between network vulnerability and longitudinal atrophy progression in FTLD spectrum, using Network Diffusion Model (NDM) of pathology spread.
Methods: Thirty-four behavioural-variant frontotemporal dementia (bvFTD), 11 semantic-variant primary progressive aphasia (svPPA) and 11 nonfluent/agrammatic-variant primary progressive aphasia (nfvPPA) patients underwent longitudinal T1-weighted MRI. Forty-eight young controls underwent multi-shell diffusion MRI scan. NDM was developed to assess the progression of FTLD pathology originating from a seed (right orbitofrontal cortex [bvFTD], left inferior temporal gyrus [svPPA], and left supplementary motor area [nfvPPA]) and proceeding through the healthy connectome. The connectivity measures were fractional anisotropy (FA) and intra-cellular volume fraction (ICVF). Correlations were tested between atrophy estimated by NDM and those empirically obtained in FTLD patients over a follow-up of 24 months.
Results: In bvFTD, NDM showed an early spread to frontal lobe and basal-ganglia and to right sensorimotor, parietal, temporal and occipital lobes, with a subsequent involvement of the left hemisphere. In svPPA, NDM suggested an early spread of pathology to the left occipital and frontal lobes, while parietal lobe was reached later. In nfvPPA, NDM-predicted spread through all brain regions, except for occipital lobe. NDM-predicted atrophy of each region was positively correlated to longitudinal atrophy empirically observed in all three FTLD variants. Overall, NDM with ICVF connectome provided higher correlation values relative to NDM with FA maps.
Conclusion: The NDM implementation to cross-sectional structural connectome is a valuable tool to predict atrophy patterns and pathology spreading in FTLD variants.
Disclosure: Supported by. European-Research-Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer's Disease.

EPR-003

Usefulness of visual rating scales of atrophy in Primary Progressive Aphasia

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Background and aims: Differential diagnosis among subjects with Primary Progressive Aphasia (PPA) can be challenging. Structural MRI can support the clinical profile, in particular Logopenic has a left temporo-parietal atrophy, Semantic bilateral temporal pole involvement, more pronounced on the left, while Agrammatic frontal opercular atrophy. Visual rating scales are a simple and reliable tool to assess brain atrophy in the clinical setting. The aim of the study is to identify brain regions, using visual rating scales, that differentiate among variants of PPA.
Methods: Patients with a diagnosis of PPA, according to current criteria, from 2 centers (Policlinico of Milan and Hospital Clìnic of Barcelona) were included. All subjects underwent general and neurological examination, neuropsychological testing and MRI. The MRI of the subjects were assessed using a protocol of 6 visual rating scales for atrophy and 2 of white matter hyperintensities by two expert raters.
Results: 150 Subjects were included, with 44 Logopenic, 19 Agrammatic, 31 Semantic, 11 Undetermined and 45 Controls. All the scales showed a good to excellent intra and inter-rater agreement. All left scales were able to differentiate between the various types of PPA and Controls except Anterior cingulate for the Logopenic. Scales of left anterior and medial temporal could differentiate between Semantic and all the others while left Parietal scale differentiate Logopenic from Semantic. No scale could differentiate between Logopenic and Agrammatic.
Conclusion: All left visual rating scales differentiate PPA from controls, while left anterior and medial temporal scales distinguishes Semantic from others variants of PPA.
Disclosure: Nothing to disclose.

EPR-004

Plasma p-tau181 as a promising non-invasive biomarker of Alzheimer's Disease pathology in Subjective Cognitive Decline

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Background and aims: Plasma phosphorylated tau (p-tau) 181 is becoming notable in prodromal stages of Alzheimer's Disease (AD), as a valuable marker for AD-tauopathy. The aim of this study is to investigate the role of plasma p-tau181 as a potential biomarker for AD pathology in early stages of the disease.
Methods: We included 26 Subjective Cognitive Decline (SCD), 32 Mild Cognitive Impairment (MCI) and 14 AD patients, who underwent plasma p-tau181 analysis with SiMoA assay and CSF biomarkers analysis (Aβ1-42, Aβ1-42/1-40, p-tau, t-tau). According to the A/T(N) system, patients were classified as carrier of AD pathology (AP+) when A+ was associated with T+ and/or N+, or non-carriers (AP-) when they were A- or A+/T-/N-.
Results: Plasma p-tau181 levels were correlated with CSF p-tau in SCD (rho=0.779, p<0.001) and in MCI (rho=0.674, p<0.001). Plasma p-tau181 levels were higher in SCD AP+ than in SCD AP- (2.85±0.53 vs 1.73±0.64, p<0.001), and in MCI AP+ than in MCI AP- (4.03±1.07 vs 2.04±0.87, p<0.001). In a multivariate linear regression analysis, AP status was the only variable that influenced plasma p-tau181 (B=1.670 [95%CI 1.097:2.244], p<0.001). ROC curve analysis showed that plasma p-tau181 was highly accurate for discriminating between AP+ and AP- patients (AUC=0.910), with a cut-off level of 2.69 pg/mL which may distinguish between AP+ and AP- (accuracy=84.21%, sensibility=86.36%, specificity=82.50%, PPV=75.00%, NPV=90.32%)

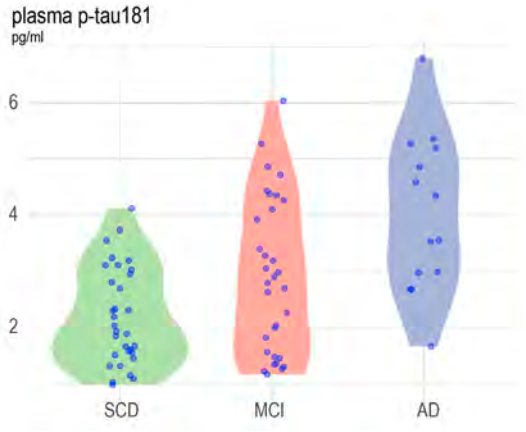

Figure 1: Plasma p-tau181 levels in SCD, MCI and AD patients

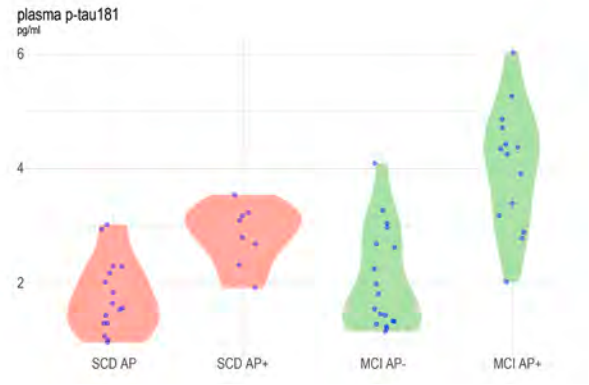

Figure 2: Plasma p-tau181 levels in SCD and MCI patients, stratified according to AP status

Conclusion: Plasma p-tau181 levels showed a high accuracy in differentiating SCD and MCI patients who were carriers of AD pathology from non-carriers. Plasma p-tau181 might be a promising non-invasive biomarker of AD pathology at very early stage.
Disclosure: The authors have nothing to disclose.

EPR-005

Aquaporin 4 modulation regulates intracerebral Abeta amyloid deposition in a mouse model of Alzheimer's disease

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Background and aims: Aquaporin 4 (AQP4) is the most important water channel in the CNS, and drives the clearance of the interstitial fluid in the paravascular pathways. We aimed here to assess if AQP4 modulation would change the way amyloid Abeta is deposited in the brain in a mouse model of Alzheimer's disease.
Methods: Double transgenic PS1/APP mice (1 month old, the age around which they start to deposit amyloid plaques) were treated daily for 1 month, with an AQP4 inhibitor (TGN-020) or a facilitator (TGN-073), as 200 mg/kg (N= 10/group). Their brains processed for immunohistochemistry for Abeta, astrocytes and blood vessels. Untreated PS1/APP animals were included as control group (N=10). On whole scanned slides, the number/density of amyloid plaques, and the distance to the nearest blood vessel were counted and analyzed.
Results: Our study showed that AQP4 facilitator drastically decreased the total Abeta burden compared to the untreated group, while AQP4 inhibitor increased the total Abeta, also increasing the average plaque optical density (IOD), especially for cortical and thalamic areas. Average and maxim plaque diameters did not change significantly,

however complexity of the plaques (Fractal Dimension) decreased for facilitator-treated animals, translating in less diffuse and more compact plaques. Very interesting, AQP4 facilitator significantly decreased plaque-vessel association compared to controls in cortical areas.

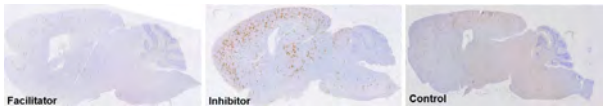

Figure 1 Exemplary whole brain images showing an important Abeta burden reduction in AQP4 Facilitator treated-animals and an increase in the Inhibitor-treated animals.

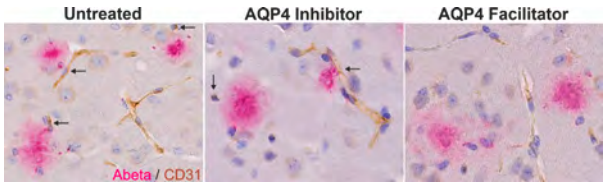

Figure 2 Plaque-vessel association analysis reveals a clear-cut decrease in the number of vessels associated with amyloid deposits for the AQP4 facilitator compared to control and inhibitor-treated animals (arrows indicate proximity vessels).

Conclusion: These results support the hypothesis that the functional deficiency of AQP4 that occurs with age-related vascular changes favors the accumulation of Abeta in patients with Alzheimer's disease, and an AQP4 facilitator accelerates clearing and decreases total Abeta burden.
Disclosure: Nothing to disclose.

EPR-006

Unmet needs and behavioral and psychological symptoms of dementia (BPSD) in large cohort of 10,405 patients

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Background and aims: Behavioral and psychological symptoms of dementia (BPSD) are common and complex during the course of dementia. With the progression of cognitive decline, the individuals' ability to accommodate and communicate their needs decreases. There is a variety of factors influencing the manifestation of individual symptoms.
Methods: We analysed unmet needs and BPSD in 10,405 individuals with Alzheimer's disease (AD), Lewy body disease (LBD), vascular dementia (VaD), frontotemporal dementia (FTD), and other dementias from SveDem and the Swedish BPSD registry, during 2010 - 2016. Multivariable linear regression models were applied to the whole cohort and each dementia diagnosis to evaluate the association between selected unmet needs and the total Neuropsychiatric Inventory (NPI) score. All models were adjusted for age, sex, severity of cognitive impairment and time.
Results: Pain was the most common unmet need in the whole cohort, followed by sleeping disturbances, impaired hearing and impaired vision. In linear regression analyses, we found a significant association between the total NPI score and sleeping problems (beta=17.75, t=31.74, $p<0.001$), social isolation (beta=10.32, t=13.84, $p<0.001$), food and fluid intake (beta=7.84, t=13.13, $p<0.001$), pain (beta=5.75, t=13.09, $p<0.001$), abnormal excrement (beta=3.52, t=5.68, $p<0.001$), sensory impairment (beta=1.68, t=13.3, $p<0.001$).
Conclusion: The results indicate that BPSD increases in the presence of physical or psychological unmet needs and pain was the most common, potentially treatable unmet need. The short and simple strategies for personal with repetitive assessments and treatment of needs in patients with dementia are discussed in BPSD registry education.
Disclosure: Nothing to disclose.

EPR-007

Enlarged perivascular spaces are correlated with CSF AQP4 and tau levels in patients with neurodegenerative dementia

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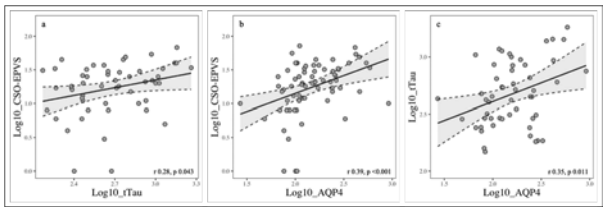
Background and aims: Perivascular spaces (PVS) are fluid-filled compartments that dilate in response to many different conditions. A high burden of enlarged PVS (EPVS) in the centrum semiovale (CSO) has been linked to neurodegeneration. Moreover, an increase in cerebrospinal fluid (CSF) levels of aquaporin-4 (AQP4), a water channel expressed on PVS-bounding astrocytes, has been described in patients with neurodegenerative dementia. Our aim was to investigate the relationship between neurodegenerative diseases and two putative glymphatic system biomarkers: AQP4 and EPVS.

Methods: We included 70 individuals, 54 patients with neurodegenerative diseases and 16 subjects with non-degenerative conditions. EPVS were visually quantified on MRI-scans according to Paradise et al. All subjects underwent lumbar puncture for the measurement of AQP4 levels in the cerebrospinal fluid (CSF). CSF levels of amyloid-β-1-42, phosphorylated and total tau (tTau) were also measured. Linear regression analyses were adjusted for age, sex, education and disease duration.
Results: CSF-AQP4 levels were independent predictors of total ($\beta = 0.33$, standard error [SE] = 0.09, $p < 0.001$), basal ganglia ($\beta = 0.29$, SE = 0.08, $p = 0.006$) and centrum semiovale EPVS ($\beta = 0.53$, SE = 0.17, $p = 0.002$). tTau levels predicted CSO-EPVS ($\beta = 0.40$, SE = 0.19, $p = 0.046$). Moreover, increased levels of AQP4 were strongly associated with higher levels of tTau in the CSF ($\beta = 0.36$, SE = 0.13, $p = 0.006$).



Scatterplots showing the correlation between: (a) CSO-EPVS number and CSF-tTau; (b) CSO-EPVS number and CSF-AQP4; (c) CSF-tTau and CSF-AQP4

Conclusion: We provide evidence that CSO-EPVS and CSF-AQP4 might be clinically meaningful biomarkers of neurodegeneration secondary to glymphatic dysfunction.
Disclosure: Nothing to disclose.

EPR-008

Dynamic reconfiguration of metabolic brain connectivity during progression from MCI to Alzheimer's disease dementia

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Background and aims: In the present study, we investigate brain connectivity reconfigurations along the progression from mild cognitive impairment (MCI) to Alzheimer's disease (AD) dementia, using a unique longitudinal design based on molecular information provided by positron emission tomography at three time points.
Methods: We longitudinally analysed the FDG-PET images of patients with AD according to ATN classification in the stages of MCI (AD-MCI, N=31), mild dementia (mild-AD, N=31) and full-blown dementia (AD-D, N=20). A group of age and sex-matched healthy controls (HC) was longitudinally evaluated for comparison. Grey matter parcellation was applied to the AAL atlas for whole-brain network construction. Pearson correlations were calculated between each pair of regions across subjects to obtain adjacent matrices. We evaluated between-group metabolic connectivity changes at each time point by applying a z-test to the correlation coefficients. The extent of connectivity changes for each region was quantified by means of summary indices, which served as input for a k-means (KM) cluster analysis, for each time point.
Results: KM analysis identified two clusters, an "alteration cluster" and a "spared cluster", at each time point. In AD-MCI, the alteration cluster involved subcortical and limbic regions, occipito-parietal cortices and cerebellum. At mild-AD and AD-D stages, the alteration cluster involved occipito-parietal cortices and cerebellum.
Conclusion: The current study describes metabolic connectivity changes along the disease course from prodromal to full-blown dementia. The connectivity alterations initially involved subcortical and AD-prototypical cortical regions. As disease progressed, the most altered regions were limited to the cortical associative regions and cerebellum only
Disclosure: Nothing to disclose.

EPR-009

Deep learning survival prediction in sporadic Creutzfeldt-Jakob Disease

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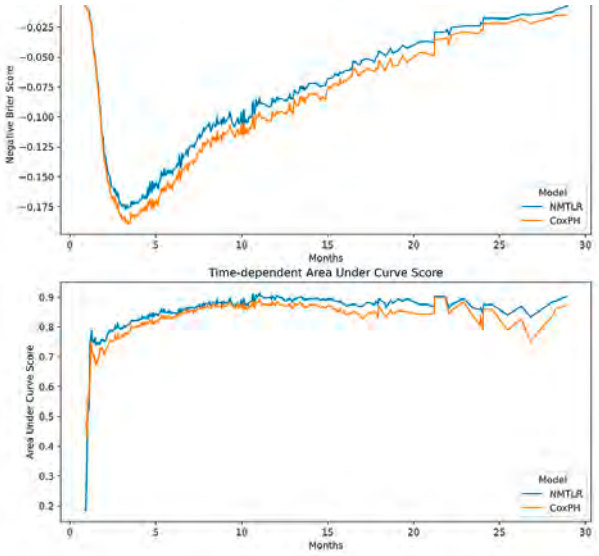
Background and aims: Sporadic Creutzfeldt-Jakob Disease (sCJD) is a rapidly progressive and fatal prion disease with significant public health implications. Survival is heterogenous, with some 'long survivors' posing challenges for prognostication and care planning. Using neural networks, we developed a survival model using highly phenotyped diagnostic data from comprehensive UK sCJD surveillance.
Methods: We evaluated 676 cases of probable or definite sCJD according to 2017 international consensus diagnostic criteria between 01/2017 and 01/2022. Data included symptoms at diagnosis, CSF RT-QuIC and 14-3-3, MRI and EEG findings, as well as sex, age, ethnicity, PRNP codon 129 polymorphism, CSF total protein and S100b. 15.6% of records were missing, and multiply imputed in 10 datasets. A neural network implementation of multitask logistic regression was used for survival analysis. Model optimisation and performance estimation were conducted using nested 5-fold cross validation. Performance was measured by integrated Brier score (IBS), concordance

index (c-index), time-dependent area under curve (AUC) scores and Brier scores.

Results: Our algorithm had c-index of 0.732, IBS of 0.073, and AUC at 6 and 12 months of 0.848 and 0.899. Our approach improves on standard cox proportional hazard model (c-index 0.719, IBS 0.082, AUC 0.833 and 0879). We will present clinical vignettes.



Time-dependent Brier scores and AUC scores for cox proportional hazard model and neural multitask logistic regression model.

Conclusion: We developed a clinically relevant and practical survival model for sCJD with statistical and performance advantages compared to both classical models and previous studies. Further development and clinical validation will facilitate improvements in prognostication and care planning, as well as inclusion criteria and outcome measures in future trials.

Disclosure: The UK NCJDRSU is funded by the Department of Health and Social Care Policy Research Programme and the Government of Scotland. ("The National CJD Research and Surveillance Unit (NCJDRSU)", PR ST 0614 00008_18). The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health and Social Care or the Government of Scotland. The work conducted by the NCJDRSU depends heavily on the cooperation of neurologists and other referring clinicians as well as neuropathologists throughout the UK. We are grateful for their cooperation while delivering an altered service at this unusual time. We are particularly thankful to the families of patients for their cooperation. No competing interests to declare.

Autonomic nervous system diseases

EPR-010

Autonomic cardiovascular impairment in adult SMA patients: towards the understanding of multisystem involvement in SMA

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Background and aims: Systemic pathology is emerging in spinal muscular atrophy (SMA) with the advent of new disease-phenotypes due to survival motor neuron protein (SMN)-rescue therapies. Previous reports of a defective autonomic nervous system (ANS) in preclinical models of SMA and severely-affected patients suggested an involvement of the ANS in the disease, which remains to be elucidated. In this single center observational study, we aimed to evaluate whether adult SMA patients present a cardiovascular autonomic dysfunction.
Methods: Two type-2 and 14 type-3 adult SMA patients underwent cardiovascular autonomic tests (CATs) (10 min head-up tilt after 10 min supine rest, Valsalva manoeuvre (VM), deep breathing, sustained handgrip, cold face test, mental stress), and the COMPASS-31 autonomic assessment. Heart rate variability (HRV), baroreceptor sensitivity, sympatho-vagal balance, were continuously evaluated during the CATs. Results were compared with aged and sex matched controls and normative data.
Results: Cardiovascular reflexes indices were significantly more affected in SMA population compared with healthy subject, with a peculiar pattern characterized by increased bradycardic drive during deep breathing ($p<0.00002$), increased variability of blood pressure during rest and head up tilt test ($p<0.0001$) consistent with a baroreflex afferent branch hypofunction and unbalanced sympatho-vagal. Moreover, we found an adrenergic hypofunction during VM ($p<0.0001$). Finally, a relative increased of HR at rest was found in 14 of 16 patients (87.5%).
Conclusion: Our data suggest the presence of autonomic cardiovascular dysfunction in adult SMA patients, probably related to impaired inhibitory drive on sympathetic outflow and sympato-vagal unbalance, contributing to properly define SMA phenotypic expression.
Disclosure: I received honoraria for advisory board activities, and compensation for travel and congress participation from Sanofi Genzyme, Biogen and Roche.

EPR-011

Long-term treatment outcomes of immunotherapy in autoimmune autonomic ganglionopathy

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Background and aims: The efficacy of long-term treatment in patients with AAG is still unknown. We aimed to evaluate the response to immunotherapy, and the degree of residual autonomic impairment in our UK cohort.
Methods: We longitudinally characterised patient response to immunotherapy with a multimodal autonomic biomarker assessment before and after treatment. All results are shown as average ± SD.
Results: 23 patients (9 F, 53 ± 13 years old) were followed for 4,95 ± 3,1 years. 3 patients with paraneoplastic AAG died during follow-up. Before immunotherapy, 18 patients were on anti-hypotensive medications, 11 needed catheterisation and 18 laxatives. deltaSBP during HUT was -68 ± 29 mmHg, time tolerated on HUT was 4,9 ± 4 minutes and the orthostatic intolerance ratio (OIR, deltaSBP/time on HUT) was 13,8. RSA was reduced (6 ± 5 bpm), and absent in 11 subjects. 18 patients had positive anti-gAChR antibodies. 10 patients received PLEX only, 1 IVIg only, and 12 a combination of both. 13 patients received steroids, 11 needed further immunosuppression. At last follow-up, 18 patients were on anti-hypotensive medications, 4 patients still needed catheterisation and 11 laxatives. The severity of OH improved (deltaSBP = -53 ± 40 mmHg, time on tilt = 9 ± 4 minutes, OIR = 5,8). RSA improved in 10 patients (8 ± 9 bpm). 4 patients with initially severe autonomic failure and high anti-gAChR antibodies titre seroconverted.
Conclusion: A stepwise, prolonged immunosuppression improves the severity of autonomic failure in AAG over time. A degree of residual impairment remains in more refractory patients.
Disclosure: Nothing to disclose.

EPR-012

Association of autonomic dysfunction with disease progression and survival in Amyotrophic Lateral Sclerosis

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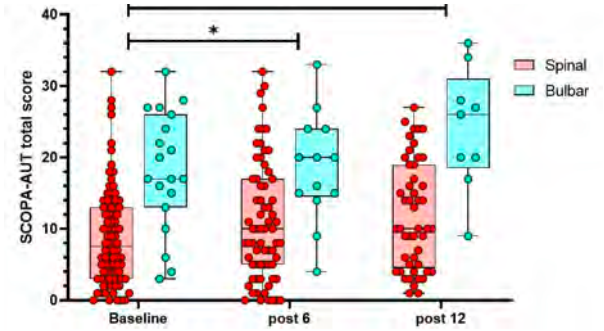
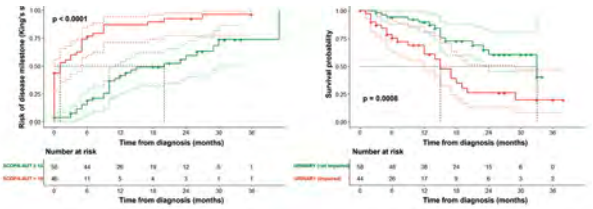
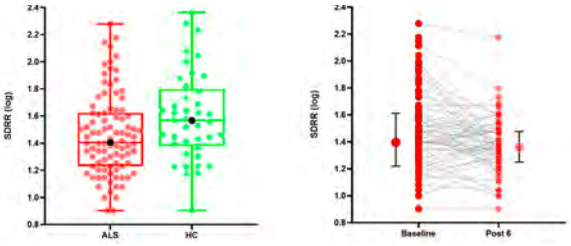
Background and aims: Aim fo this study was to examine the association of Autonomic dysfunction with disease progression and survival in ALS.
Methods: We enrolled newly diagnosed ALS patients and a healthy control group (HC). Patients with dementia at enrolment, genetic forms of ALS, comorbidities and treatment potentially affecting autonomic functions, were excluded. Autonomic dysfunction was assessed by the SCOPA-AUT questionnaire evaluating the following domains: gastrointestinal, urinary, sudomotor, cardiovascular, sexual and pupillomotor. Longitudinal assessment of parasympathetic and sympathetic cardiovascular activity was performed by the heart rate variability (HRV) and heart-rate at rest.
Results: A total of 102 patients (36.3% female; age at diagnosis, 62.5 [54-71] years; diagnostic delay, 13.5 [8-22] months) and 41 HC (53.7% female; age: 60 [52-67] years) were studied. Autonomic dysfunction in at least one domain occurred in 68% of patients at diagnosis and progressed over time (all p<0.02), especially in patients with bulbar onset (p<0.001). A higher overall autonomic dysfunction score was independent marker of faster development of King's stage 4 (p= 0.022), whereas urinary disturbs were independent factor of a shorter survival (p= 0.018). Lastly, ALS patient, compared with HC, complained more frequently gastrointestinal, urinary, sudomotor and pupillomotor symptoms and displayed a significant reduction of HRV (p=0.018) and increase of heart-rate (p= 0.032); in the longitudinal study patients showed a significant decrease of HRV at 6 months of follow-up (p=0.009) without any difference for heart-rate (p=0.532).



Longitudinal assessment of autonomic symptoms by SCOPA-AUT questionnaire in ALS patients with spinal and bulbar onset.



Kaplan-Meier curves of cumulative probability of disease milestone (King's stage 4) and survival probability among patients with ALS stratified by median value of total SCOPA-AUT score (A) and by urinary impairment (B).



Heart rate variability indexed by SDRR in ALS patients and healthy controls (A) and its significant reduction after 6 months (B).

Conclusion: Autonomic dysfunction and urinary impairment at diagnosis are associated with more rapid disease progression and shorter survival in patients with ALS.
Disclosure: Nothing to disclose.

EPR-013

Autonomic small nerve fibre pathology in Fibromyalgia: new insights from the skin.

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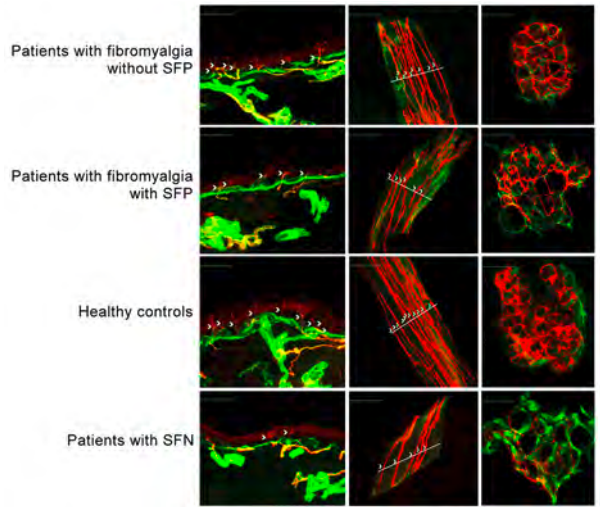
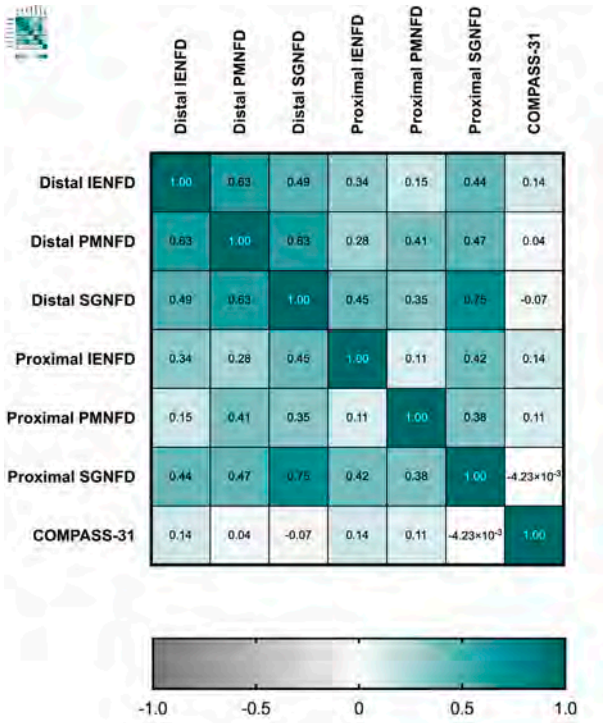
Background and aims: Fibromyalgia syndrome is a clinical condition characterized by widespread pain associated with multiple symptoms like fatigue and autonomic symptoms. Small fibre pathology (SFP) is described in nearly half of patients with fibromyalgia, although its impact on the clinical picture is still controversial. Investigation of dermal structures as piloerector muscles and sweat glands is increasingly recognized as a reliable method to quantify post-ganglionic small autonomic nerve fibres on skin biopsy. We aimed to verify whether in patients with fibromyalgia, SFP also implies a dermal autonomic damage.
Methods: Using skin biopsy, we investigated intraepidermal (IENFD), piloerector muscle (PMNFD), and sweat gland nerve fibre density (SGNFD) in 138 participants – 58 patients with fibromyalgia syndrome, 48 healthy subjects, 32 patients with small-fibre neuropathy (SFN). In fibromyalgia patients we also investigated how the different skin biopsy variables correlated with autonomic symptoms, as assessed with COMPASS-31 questionnaire. We used

non-parametric Mann-Whitney test to compare skin biopsy variables between patients and control groups.
Results: In fibromyalgia patients with-SFP, PMNFD and SGNFD was lower than that in healthy subjects ($p<0.0001$). However, the autonomic small-fibre damage had no correlation with autonomic symptoms severity ($p=0.6843$). In patients with SFP the IENFD, PMNFD and SGNFD was higher than that in patients with SFN ($p=0.0108$).



Representative skin biopsy images from fibromyalgia patients with SFP, with no SFP, healthy controls, and SFN, showing nerve fibre counting examples for intraepidermal nerve fibre density (IENFD), piloerector muscle (PMNFD), and sweat gland (SGNFD) nerve



Correlation matrix showing p values and Spearmans's r coefficients for the main diagnostic test variables and COMPASS-31 score in fibromyalgia patients. IENFD: intraepidermal nerve fibre density; PMNFD: piloerector muscle nerve fibre density; SGNFD: sweat

Conclusion: Fibromyalgia patients have a reduction of dermal autonomic small fibres paralleling the intraepidermal nerve fibre loss, indicating that SFP also implies autonomic small nerve fibre damage. However, autonomic small fibre damage had no correlation with the severity of autonomic symptoms, thus its clinical impact is still undetermined.
Disclosure: No disclosure.

EPR-014

Level of agreement between sudoscan and sympathetic skin response on small fiber neuropathy

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Background and aims: Small fiber neuropathy (SFN) can be assessed by Sudoscan, which measures electrochemical skin conductance (ESC) through reverse iontophoresis, or by sympathetic skin response (SSR), which measures skin potentials. The level of agreement between ESC and SSR remains unclear.
Methods: From 31st December 2021 to 31st December 2022, 71 patients (mean age of 54 years old; 42 women) were assessed by ESC and by SSR. We calculated the inter-rater reliability assessing SFN between both tests by Cohen's kappa coefficient. We also calculated Cohen's kappa coefficient for SFN in hands and SFN in feet.
Results: According to both tests: 12 patients had SFN and 32 did not have SFN. 22 patients had SFN by ESC with normal results by SSR. 5 patients had SFN by SSR with normal results by ESC. Cohen's kappa coefficient was 0.22 (Figure 1). For hands, Cohen's kappa coefficient was 0.16 (Figure 2). For feet, Cohen's kappa coefficient was 0.26 (Figure 3).

			SUDOSCAN		
			SFN	NORMAL	
	SYMPATHETIC SKIN RESPONSE	SFN	12	5	17
		NORMAL	22	32	54
			34	37	71

Observer agreement: 12+32/71= 0.62

*Agreement chance: (34/71) *(17/71) +(37/71) *(54/71) = 0.51*

Kappa: OA – AC/1-AC= 0.22

Fig.1: Results of both tests and estimation of Cohen´s kappa coefficient.

			SUDOSCAN		
	SYMPATHETIC SKIN RESPONSE		SFN IN HANDS	HANDS NORMAL	
		SFN IN HANDS	5	4	9
		HANDS NORMAL	18	44	62
			23	48	71

Observer agreement: 5+44/71= 0.69

	SYMPATHETIC SKIN RESPONSE		SFN IN FEET	FEET NORMAL	
		SFN IN FEET	11	5	16
		FEET NORMAL	19	36	55
			30	41	71

Observer agreement: 11+36/71= 0.66

*Agreement chance: (30/71) *(16/71) +(41/71) *(55/71) = 0.54*

Kappa: OA – AC/1-AC= 0.26

Fig.3 : Results of both tests and estimation of Cohen's kappa coefficient related to feet results.

Conclusion: Our study showed that ESC and SSR had a minimal level of agreement on SFN, with more level of agreement for feet that for hands. Thus, both tests cannot be replaced by the other. Further studies need to be performed in order to clarify the reliability and the efficiency of these test to assess SFN.

Disclosure: The author declares no conflict of interests.

EPR-015

A complex interplay between autonomic symptoms and symptoms of depression, anxiety, and stress

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Background and aims: We evaluated the influence of symptoms of depression, anxiety, and stress on the results of COMPASS-31 in a large population of people referred to tilt-table testing and healthy controls (HC).

Methods: 959 consecutive patients referred to tilt-table testing and 518 HC were enrolled. All participants completed Composite Autonomic Symptom Score-31 (COMPASS-31). Stress symptoms were evaluated by Depression, Anxiety and Stress-21 (DASS-21) questionnaire. We corrected the result of the COMPASS-31 with the independent predictors in order to improve the specificity of the test.

Results: In both patients and HC, COMPASS-31 was higher in participants with depression, anxiety, and stress symptoms (all $p<0.001$). In a multivariable linear regression analysis, HC was negative, while female sex, symptoms of depression, anxiety, and stress were independent positive predictors of COMPASS-31. In HC COMPASS-31 had a median of 7.913, and this value differentiated between HC and patients with a high sensitivity of 87% and low specificity of 50%. In order to adjust the value of COMPASS-31 with the parameters that were significant in the multivariable linear regression model, we calculated the new corrected COMAPSS-31 (cCOMPASS-31), which had comparable sensitivity of 77%, but an increased specificity of 73%.

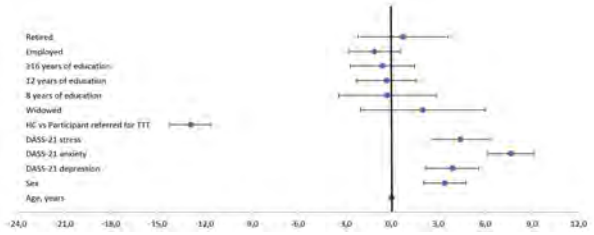

Figure 1. Multivariable linear regression model for predicting COMPASS-31

Conclusion: This study has shown that symptoms of depression, anxiety, and/or stress worsen the perceived severity of autonomic symptoms in people with symptoms of orthostatic intolerance and healthy population. cCOMPASS-31 is a valuable tool that can help clinicians in discerning the true autonomic background of patients' complaints.

Disclosure: MKS: received consultation and/or speaker fees from: Sanofi Genzyme, Roche. AJ: Nothing to disclose. MSH. Nothing to disclose. IA: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals. AK: Nothing to disclose. MH: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPR-016

Testing of quality indices for electrocardiogram and blood pressure signals using real world monitoring data

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Background and aims: For the analysis of large datasets, and especially artifact prone real-word datasets, quality indices are an important tool to quantify the noise and artifacts in bio signals. Quality indices (QI) using a modulation-spectrum-based approach are already in use for ECG. For continuous arterial blood pressure monitoring (ABP), quality indices are still missing. Due to increasing demand in baroreflex analysis, a quality measurement analogous to already established quality measures of ECG is needed for combined signals of ECG and ABP.
Methods: We programmed MS-QI and PD-QI using Matlab R2020b. The initial continuous bio signal is transformed using a short-time Fourier transformation until a modulation spectrum is achieved and a power modulation spectrum can be calculated. MS-QI is given by the ratio of the power of R-peaks in comparison to the remaining power of the modulation spectrum. PD-QI, on the other hand, is based on the peak distance of R-peaks in the modulation spectrum. We further computed the MS-QI and PD-QI for ECG and continuous BP. Both quality indices were applied on real-world monitoring data of patients, treated at a stroke and intermediate care unit.
Results: We are analyzing a correlation between MS-QI and PD-QI for ECG and ABP in comparison with percentage of artifacts and signal to noise ratio. Correlations between ECG PD-QI and MS-QI and between ECG PD-QI and ABP PD-QI were observed (corr. coeff. 0.74 and 0.8 respectively).
Conclusion: Modulation of both ECG and ABP spectral analysis is feasible for applying QI on noise and artifacts in real world data.
Disclosure: This work was supported by the research time out of the Karl Landsteiner University of Health Sciences.

EPR-017

Peripheral and autonomic neuropathy in AL amyloidosis detected by gold standard and screening tests

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Background and aims: Amyloid light-chain (AL) amyloidosis is a rare multisystemic disease with aggregation of immunoglobulin deposits in organ systems throughout the body with progressive organ damage. Autonomic involvement has been shown to worsen prognosis. We aimed to evaluate peripheral and autonomic neuropathy among patients with systemic AL amyloidosis using screening and gold standard tests.
Methods: All patients with systemic AL amyloidosis followed at Aarhus University Hospital, DK were invited to participate. We examined patients for peripheral small and large fiber neuropathy with neurological examination, patient history and small fiber gold standard test. We screened for cardiovascular autonomic neuropathy (CAN) with the Vagus-device, where two or more abnormal tests indicate definite CAN. We used gold standard autonomic function tests to evaluate cardiovagal, adrenergic and sudomotor function and divided into no, mild, moderate, and severe autonomic failure according to Composite Autonomic Scoring Scale.
Results: We included 21 patients with systemic AL amyloidosis. Definite small fiber neuropathy was found in 7/20. Probable large fiber neuropathy was found in 11/21. On autonomic screening, definite CAN was found in 7/17. On gold standard testing, almost all examined patients had autonomic affection: 10/16 had mild and 5/16 had moderate autonomic failure. The sudomotor domain was affected in 17/20, the cardiovagal domain in 8/15, and the adrenergic domain in 5/16.
Conclusion: Both peripheral and autonomic neuropathy were common in this cohort of patients with systemic AL amyloidosis and may to some degree be diagnosed with both screening and gold standard tests.
Disclosure: I have no disclosures.

EPR-018

Autonomic regulation correlates with cognitive performance in patients after traumatic brain injury

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Background and aims: Traumatic brain injury (TBI) may afflict brain areas contributing to both cardiovascular-autonomic regulation and cognitive performance. To evaluate possible associations between both functions in patients with a history of TBI (post-TBI-patients), we determined correlations between cardiovascular autonomic regulation and cognitive-executive function in post-TBI-patients.
Methods: In 86 post-TBI-patients (33.1±10.8 years old, 22 women, 36.8±28.9 months after injury), we monitored RR-intervals, systolic, diastolic blood pressures (BPsys, BPdia), and respiration (RESP) at rest. We calculated parameters of total cardiac-autonomic modulation [RRI-standard-deviation (RRI-SD), RRI-coefficient-of-variation (RRI-CV), RRI-total-powers], sympathetic [RRI-low-frequency-powers (RRI-LF), Bpsys-LF-powers] and parasympathetic cardiac modulation [Root-Mean-Square-of-Successive-RRI-Differences (RMSSD), RRI-high-frequency-powers (RRI-HF)], sympathetic-parasympathetic balance (RRI-LF/HF-ratios), and baroreflex-sensitivity (BRS); we moreover calculated normalized (nu) LF- and HF-powers of RRI. We used Mini-Mental State Examination and clock-drawing test (CDT) to screen the general global and visuospatial cognitive function, and assessed executive function using the standardized Trail-Making-Test (TMT) A assessing visuospatial abilities and TMT-B assessing executive function, with higher TMT-values indicating poorer function. We calculated correlations between autonomic and cognitive parameters (Spearman-rank-correlation-test; significance: $p<0.05$).
Results: CDT-values correlated only positively with age (coefficient=0.267, P=0.013). TMT-A inversely correlated with RRI-HF-powers (coefficient=-0.233, P=0.033) and BRS (coefficient=-0.221, P=0.043), TMT-B positively correlated with RRI-Lfnu-powers (coefficient=0.265, P=0.015), RRI-LF/HF-ratios (coefficient=0.230, P=0.036), BPsys-LF-powers (coefficient=0.236, P=0.030), but negatively with RRI-Hfnu-powers (coefficient=-0.265, P=0.015).
Conclusion: In post-TBI-patients, decreased cognitive performance is associated with reduced parasympathetic modulation and baroreflex sensitivity, and increased sympathetic predominance. These cardiovascular-autonomic changes are in turn associated with increased long-term cardiovascular risk.
Disclosure: Nothing to disclose related to the study.

Cerebrovascular diseases 1

EPR-019

External validation of clinical risk prediction score for mechanical thrombectomy in the elderly

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[1]Department of Neurology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, [2]Division of Radiology and Nuclear Medicine, Oslo University Hospital, Oslo, Norway, [3]Stroke Center Rigshospitalet, Department of Neurology, Rigshospitalet, Copenhagen, Denmark, [4]Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark, [5]Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Background and aims: Researchers in Denmark recently developed a clinical risk prediction score (CRPS) for functional outcome after anterior circulation mechanical thrombectomy (MT) in patients ≥80. The aim of this study was to assess predictors of functional outcome and validate the prediction model.

Methods: Consecutive patients from the Oslo Acute Stroke Reperfusion registry (OSCAR) treated with emergent MT were assessed. Clinical, procedural and radiological parameters and functional outcome measures after 3 months were used to calculate the CRPS. We performed univariate, bivariate, logistic regression and receiver-operating curve (ROC) analyses to find outcome predictors and evaluate the scoring system.

Results: Of 1028 consecutive patients treated with MT, 223 with anterior circulation occlusion were ≥80 years. Fair outcome, defined as modified Rankin scale ≤3 (mRS) was found in 51.6%. Female sex was significantly associated with poor outcome, mRS≥4 (p=0.014), as well as increasing age (p=0.014). Poor outcome was associated with baseline National Institute of Health Stroke Scale (NIHSS, p<0.001), pre-stroke mRS (p<0.001) and low Alberta Stroke Program Early Computed Tomography score (ASPECTS, p=0.003) in bivariate analyses. Significant predictors for outcome in regression analyses were: Pre-stroke mRS, adjusted odds ratio, aOR= 0.59 (95% CI: 0.46–0.77). NIHSS, aOR= 0.90 (95% CI: 0.85–0.95). ASPECTS aOR= 1.2 (95% CI: 1.02–1.42). The area under the curve (AUC) using the calculated CRPS was 0.75.

Conclusion: The CRPS can be a useful tool in the clinical decision making for MT in the elderly. Other variables may still be included in the model to increase its accuracy.

Disclosure: All authors declares no conflicts of interest.

EPR-020

Transient ischemic attacks in patients with active cancer

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Background and aims: Paraneoplastic coagulopathy in stroke patients is associated with specific biomarker changes. It can be the initial manifestation of an unknown occult cancer. Identifying a paraneoplastic coagulopathy is essential in guiding secondary prevention. An early cancer detection potentially improves patient outcomes. However, unlike ischemic stroke, it remains unclear whether a paraneoplastic coagulopathy is associated with transient ischemic attacks (TIA). This study assessed the presence of cancer-related biomarkers in TIA patients and evaluated long-term mortality rates in patients with and without active cancer.

Methods: Active cancer was retrospectively identified in consecutive TIA patients treated at a comprehensive stroke center between 2015 and 2019. An association between the presence of cancer and cancer-related biomarkers was assessed using multivariable logistic regression. Long-term mortality after TIA was analyzed using multivariable cox regression.

Results: From the 1436 TIA patients included, 72 had active cancer (5%), of which 17 were occult (1.2%). Cancer-related TIA was associated with male gender (adjusted odds ratio [aOR] 2.29, 95% CI 1.12-4.68), history of smoking (aOR 2.77, 95% CI 1.34-5.7), elevated D-dimer (aOR 1.77, 95% CI 1.26-2.49) as well as lactate dehydrogenase, lower leukocyte count and lower hemoglobin (FIgure 1). Long-term mortality was associated with both active cancer (adjusted hazard ratios [aHR] 2.47, 95% CI 1.58-3.88, Figure 2) and occult cancer (aHR 3.08, 95% CI 1.30-7.32).

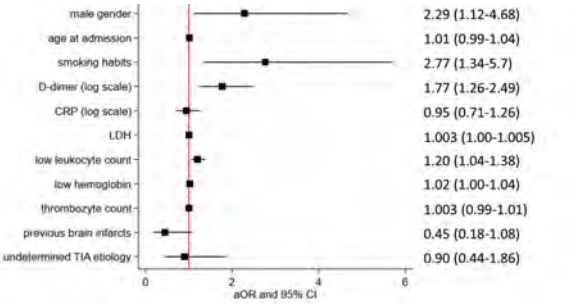

Figure 1 – Association between active cancer in TIA patients and demographics, relevant risk factors and blood biomarkers in the multivariate logistic regression model.

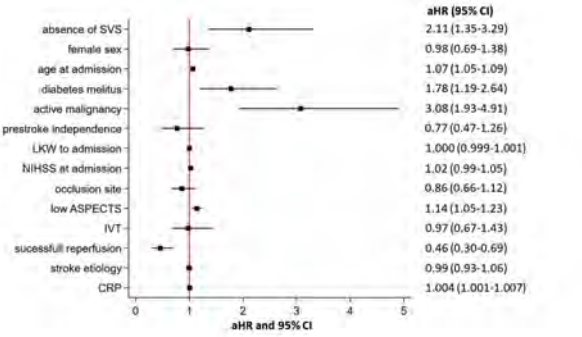

Figure 2 – Predictors of occult cancer in TIA-patients in the multivariable logistic regression.

Conclusion: Cancer-related TIA is not uncommon. Biomarkers known to be associated with cancer-related stroke also seem to be present in TIA patients. Early identification might help to adapt treatment strategies and improve outcomes in this patient population.

Disclosure: Dr. Beyeler reports research support from the "Kurt und Senta Hermann-Stiftung". Dr. Kaesmacher reports grants from the Swiss Academy of Medical Sciences/Bangerter Foundation, Swiss Stroke Society, and Clinical Trials Unit Bern during the conduct of the study. Dr. Fischer reports grants during the conduct of the study from Medtronic, Stryker, and CSL Behring, unrelated to the submitted work. Dr. Arnold reports personal fees from Bayer, Bristol-Myers Squibb, Medtronic, Amgen, Daiichi Sankyo, Nestlé Health Sciences, Boehringer Ingelheim, and Covidien during the conduct of the study. Dr. Meinel reports research support from the Bangerter Rhyner Foundation, Swiss National Foundation, and the Swiss Heart Foundation. Dr. Jung reports grants from the Swiss National Science Foundation and the Swiss Heart Foundation. None of the other authors report any conflicts of interest.

EPR-021

Cerebral small vessel white matter disease and its role in "Dizziness".

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Background and aims: Falls are the second leading cause of accidental or unintentional injury deaths worldwide. In the elderly population, one of the most common reasons for falling is dizziness. It is a highly disabling symptom, recognized by Bárány Society. The current evidence regarding the Cerebral Small-Vessel, White-Matter Disease (SVD) suggests a relevant role in the pathogenesis of dizziness.

Methods: Four participant groups, 50 persons each, are prospectively assessed at four sites: 1) patients suffering SVD and Dizziness, 2) patients with SVD, but without Dizziness, 3) patients without SVD, but with Dizziness, and 4) age-matched healthy participants. It is a prospective study, but a few examinations can be included retrospectively. The neurological, neuro-ophthalmological and neuro-otological examinations, neuropsychological assessment (MoCA), number of near-falls and falls, general check-up, laboratory testing, psychiatric/behavioural/sleep scales, video-oculography, video-head impulse test (v-HIT), ocular and cervical vestibular evoked myogenic potentials, posturography, gait assessment are performed. Two experienced neuroradiologists blindly grade the burden of SVD in cerebral 3T-MRI scans.

Results: The recruitment at four examination sites is ongoing. Fifty participants have been involved so far. The interim analysis will take place in May 2023.

Conclusion: This is the first clinical study to compare participants with and without SVD and dizziness, respectively, looking for the key factors that lead to falls, thus increased morbidity and mortality of the elderly. The results of this study can name the predictors for falls that can be prevented in the clinical practice in the future.

Disclosure: Dr. Tatiana Bremova-Ertl received speaker`s honoraria and travel funding from Actelion and Sanofi-Genzyme.

EPR-022

Short-term prognosis of reperfusion therapies in ≥90 years old acute ischemic stroke patients

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University of Health Sciences, Istanbul Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Rurkey

Background and aims: Intravenous thrombolytic therapy and mechanical thrombectomy are known to have benefits in patients with acute ischemic stroke. However, studies showing the results and efficacy of these treatments in patients over the age of 90 are limited in the literature.
Methods: The data of 63 patients who were followed up in the stroke unit of our hospital between 2018 and 2022, who underwent only tPA, only mechanical thrombectomy, both treatments were applied together, and no reperfusion treatment was applied, were analyzed. Data were statistically analyzed with Kruskall Wallis, Chi-Square, Friedman and Wilcoxon tests.
Results: The age value ranged between 90 and 101, with an average of 92.7±2.4. It was found statistically significant that the Arrival NIHSS score of the patients who underwent only tpa was higher than at the 24th hour, 7th day and 1st month. It was found statistically significant that the Arrival NHISS score of the patients who were administered TPA and MT together was higher than at the 24th hour, 7th day and 1st month ($p=0.001$; $p<0.01$). The higher 24th hour NHISS compared to the 7th day and 1st month was found to be statistically significant ($p=0.001$; $p<0.01$). The higher NHISS score on the 7th day compared to the 1st month was found to be statistically significant ($p=0.001$; $p<0.01$).
Conclusion: A significant decrease in NIHSS scores with treatment was observed in the short-term in patients who received TPA and MT treatments together. A significant increase in the discharge MRS score was observed in all patients who received reperfusion therapy.
Disclosure: There are no conflicts of interest.

Tablo 1: Gruplara Göre Ölçümlerin Karşılaştırılması

		n	Ort±Ss	Min-Max (Median)	p
Yaş	Sadece TPA	17	92,18±1,38	90-95 (92)	0,641
	Sadece MT	12	92,83±2,82	90-98 (91,5)	
	TPA+MT	16	92,25±2,05	90-97 (92)	
	Kontrol	18	93,5±3,03	90-101 (93)	
Yatış Süresi (Gün)	Sadece TPA	17	7,76±3,46	2-16 (7)	0,078
	Sadece MT	12	16,08±15,73	4-60 (11)	
	TPA+MT	16	16,44±21,37	2-90 (9,5)	
	Kontrol	18	6,44±5,18	1-26 (6)	
TPA Saati (Dk)	Sadece TPA	17	186,41±53,14	90-270 (180)	0,295
	Sadece MT	0	0±0	- (0)	
	TPA+MT	16	165,75±45,79	75-240 (168,5)	
	Kontrol	0	0±0	- (0)	
MT Saati	Sadece TPA	17	0±0	- (0)	0,870
	Sadece MT	12	203,33±73,03	90-270 (217,5)	
	TPA+MT	16	204,69±48,22	135-290 (202,5)	
	Kontrol	0	0±0	- (0)	
Giriş MRS	Sadece TPA	17	1,88±0,93	1-4 (2)	0,346
	Sadece MT	12	1,67±0,65	1-3 (2)	
	TPA+MT	16	1,31±0,87	0-3 (1)	
	Kontrol	18	1,44±0,92	0-3 (1)	
Çıkış MRS	Sadece TPA	17	2,43±1,4	1-5 (2)	0,013*
	Sadece MT	12	4±1,16	2-5 (4)	
	TPA+MT	16	2,75±1,49	1-5 (2,5)	
	Kontrol	18	1,8±1,01	0-3 (2)	
NHISS Geliş	Sadece TPA	17	11±5,2	4-20 (11)	0,001**
	Sadece MT	12	14,58±2,47	9-18 (15)	
	TPA+MT	16	14,06±4,93	7-22 (13,5)	
	Kontrol	18	5,33±5,08	1-23 (4)	
NHISS 24. Saat	Sadece TPA	17	6,82±5,69	1-18 (6)	0,004**
	Sadece MT	12	12,58±4,5	2-18 (13,5)	
	TPA+MT	16	10,19±6,59	1-24 (9,5)	
	Kontrol	18	5,5±5,06	2-23 (4)	
NHISS 7.Gün	Sadece TPA	17	4,73±4,76	0-14 (4)	0,090
	Sadece MT	12	10,33±5,77	0-16 (13)	
	TPA+MT	16	6,62±5,5	0-20 (5)	
	Kontrol	18	5,46±6,13	2-24 (3)	
NHISS 1.Ay	Sadece TPA	17	2,67±2,12	0-6 (3)	0,007**
	Sadece MT	12	14±1,63	12-16 (14)	
	TPA+MT	16	5,4±3,36	1-9 (6)	
	Kontrol	18	3,75±2,6	1-10 (3)	

Kruskall Wallis Test

EPR-023

Reperfusion time in stroke and long term cognitive performance

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Background and aims: Cognitive changes that result from cerebrovascular disease contribute to reduced quality of life and greater dependence. Among patients undergoing endovascular therapy (EVT), to our knowledge, there are no comparative studies that assess cognitive outcomes according to the degree and time for recanalization. We aim to assess cognitive function and evaluate the impact of reperfusion time and extent of ischemic injuries in cognitive performance.

Methods: We evaluated 44 patients with acute right anterior circulation strokes that underwent EVT between January 2018 and August 2020. Modified treatment in cerebral ischemia score (mTICI) was used for evaluation of level of recanalization. Cognitive evaluation was assessed using the Addenbrooke´s Cognitive Examination revised (ACE-R). Multiple linear regression analyses were used to determine the association between time for recanalization and ACE-R. The level of significance adopted was 0.05.
Results: The median age of participants was 71,5 (IQR 62,0-78,25) years, and 50% (22) were women. All patients in our sample had a successful recanalization with EVT (mTICI ≥2b). Time for recanalization and mRS at 3 months showed an inverse association with the ACE-R (b=-0.0207, P=0.0203; b=-5,2803, p=0.0095). Level of education had a strong and direct relationship with cognition (b =3,0869, p < 0,0001).
Conclusion: Longer time between stroke symptoms and recanalization with EVT in patients with right hemisphere ischemic stroke lead to lower ACE-R scores. Measures to improve door-to-recanalization time are important for cognitive performance after ischemic stroke.
Disclosure: Nothing to disclose.

EPR-024

rTPA plus thrombectomy versus thrombectomy alone in acute ischemic stroke using RAPID-AI.

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Background and aims: We studied a population of patients with large vessel occlusion stroke in a broader time window in order to verify the superiority of endovascular thrombectomy (EVT) preceded by intravenous thrombolysis (IVT). Furthermore we compared overall outcomes in the early and late time window.
Methods: This is a real world multicenter prospective cohort study of large vessel occlusion strokes in patients arriving within a 24-hour window from stroke onset. Patients received a unified prespecified imaging evaluation (CT, CT angiography, and CT Perfusion with Rapid-AI processing software mismatch determination). Outcomes were symptomatic intracranial hemorrhages, mRS 0-2 and deaths at three months.
Results: The patients selected to EVT using RAPID-AI were 194, in 96 patients EVT was preceded by IVT (bridging therapy, BDG), while 98 patients underwent EVT alone. Patients treated with bridging therapy have 17% more probability to have good functional outcome at three months (mRS0-2) then those treated with EVT alone. Numbers of symptomatic intracerebral hemorrhages (SICH) were 2% lower in BDG group and BDG patients have 9% less probability to die in comparison to EVT alone. Respectively 38% and 36% of the overall population reached a good function outcome in early and late time windows.
Conclusion: In this study bridging therapy within a 24-hour time window is associated with better survival, better functional outcomes at 3 months and similar sympthomatic hemorrhagic complications. EVT, either with or without rTPA, was associated with improvement in functional disability in the early and late time windows.
Disclosure: Nothing to disclose.

EPR-025

Influence of pre-hospital triage scale Madrid-direct in patients with cerebral haemorrhage

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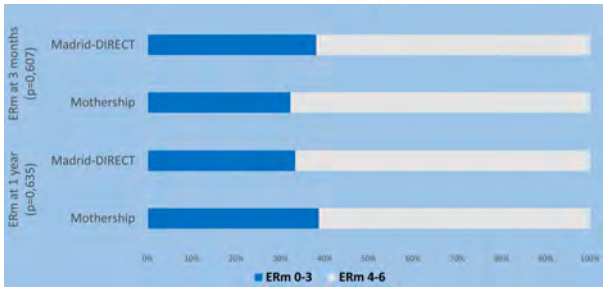
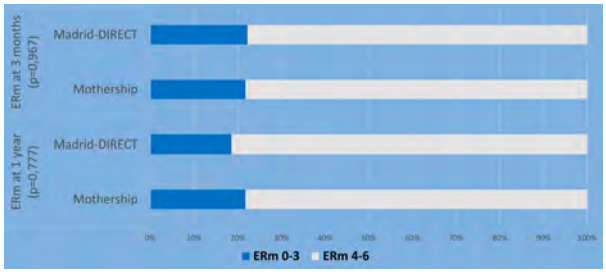
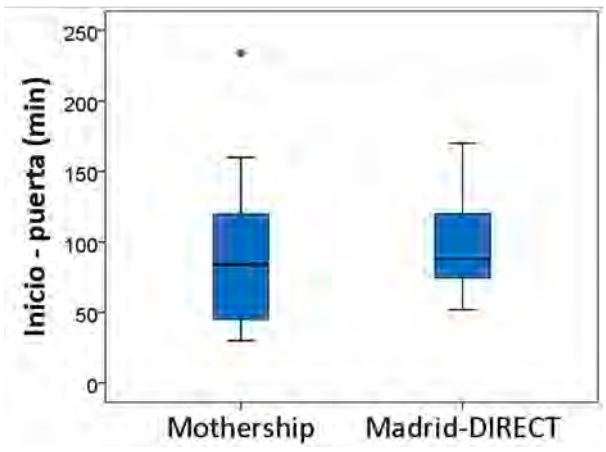
Background and aims: Prehospital stroke scales have shown to reduce onset-to-treatment times in patients with large vessel occlusion (LVO). However, patients with severe intracerebral hemorrhage (ICH) are usually classified as LVO. Blood pressure evaluation in the Madrid-DIRECT scale has shown to reduce false positives due to ICH. We aimed to assess the influence of Madrid-DIRECT triage in the outcomes of patients with ICH.
Methods: Post-hoc analysis of the Madrid-DIRECT study, including ICH patients. We compared demographic characteristics, stroke severity (initial NIHSS) and proportion of favourable outcomes (modified Rankin Scale ≤3) at 3 months and at 1 year between Mothership ─ direct transfer to thrombectomy hospital (TH) ─ and Madrid-DIRECT cohorts (direct transfer to TH for score ≥2, or to non-TH for <2). The subset of patients with severe ICH (NIHSS≥10) was analysed.
Results: Of 541 Stroke Code patients, 73 (13.5%) had an ICH, 50 of them (68%) severe. Baseline characteristics were similar in both cohorts. In the Mothership cohort, all 23 patients with severe ICH were directly transferred to TH. In the Madrid-DIRECT cohort, 16 out of 27 (59%) patients with severe ICH scored ≥2 and were directly transferred to TH. We found no significant differences in the proportion of favourable outcomes at 3 months between mothership and Madrid-DIRECT cohorts (32.3% vs 38.1%) nor among patients with severe ICH (21.7% vs 22.2%), neither at 1 year.







Conclusion: Madrid-DIRECT scale allows to rule out a significant proportion of patients with severe ICH and does not seem to compromise their outcomes in our Network.
Disclosure: The researchers declare no conflicts of interest.

EPR-026

Early recurrent intracerebral haemorrhage is associated with cerebral amyloid angiopathy and shows temporal clustering

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Background and aims: Patients with intracerebral haemorrhage (ICH) may have an elevated risk of early recurrent ICH, especially in cerebral amyloid angiopathy (CAA), but few studies have systematically investigated this phenomenon.
Methods: We investigated early recurrent ICH in consecutive ICH survivors classified by baseline MRI; patients with secondary causes of ICH other than small vessel disease (SVD) were excluded. Probable CAA was defined according to the Boston v2.0 criteria. Recurrent ICH was determined using electronic health records and confirmed by neuroimaging.
Results: Of 443 patients with ICH (mean age 67±13 years, 59% male, median follow-up period 5.7 years), 23.0% had CAA, 36.7% mixed SVD, 23.6% arteriolosclerosis and 16.7% were cryptogenic. Of 59 patients with a recurrent ICH, 21 (5%) had an early recurrent ICH within 90 days (median occurrence after 40 days). Those patients predominantly had CAA (17/21, arteriolosclerosis: 2, mixed SVD: 2, $p<0.001$). The 90-day-risk of recurrent ICH in patients with CAA was 12% (95% CI:7-20%), while the one-year-risk was 16% (95% CI:11-25%), i.e., an eight-fold increased recurrence risk in the first three months. Early recurrent ICH were frequently clustered in space; 13/17 (76%) were in the same or directly adjacent location as the index ICH. Patients with CAA and early recurrence frequently had both acute and previous leptomeningeal haemorrhage (convexal subarachnoid haemorrhage, cortical superficial siderosis).
Conclusion: Patients with ICH due to CAA have a high early recurrence risk with evidence for spatial and temporal clustering followed by quiescent periods; associations with leptomeningeal haemorrhage suggest "activation" of leptomeningeal disease as a possible explanation.
Disclosure: Nothing to disclose.

EPR-027

Strict blood pressure control after mechanical thrombectomy is associated with neuronal loss and poor functional outcome

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Background and aims: Mechanical thrombectomy (MT) has become standard treatment in acute ischemic stroke due to large vessel occlusion (LVO). However, optimal blood-pressure (BP) management following successful recanalization remains unclear. We aim to investigate the association of strictly achieving BP targets of ≤160/90mmHg with the extent of neuronal loss and functional outcome.
Methods: In patients prospectively enrolled in the Gutenberg-Stroke Study (May 2018-November 2019), BP was measured half-hourly for 24 hours following MT. Based on achieving BP-target of ≤160/90mmHg, patients were divided into 'low-BP' group (BP≤160/90mmHg) or 'high-BP' group (BP>160/90mmHg). Neuronal loss was quantified by serum-based measurement of neurofilament light chain (sNfL) after three days. BP-groups and association of BP parameters with sNfL were investigated by correlation analyses and multiple regression modelling.
Results: Of 253 enrolled patients (mean age 73.1±12.9 years, 53.4% female), 165 met inclusion criteria. 21.2% (n=35) strictly achieved 'low-BP' target. 'Low-BP' was associated with unfavorable functional outcome at 90 day follow-up (aOR[95%CI]: 6.418[2.141-19.240], p=0.001) and decreased health-related quality of life (mean EQ-5D-index 0.449±0.283 versus 0.633±0.312, p=0.009). sNfL levels were increased in 'low-BP' patients (median[IQR] 239.7[168.4-303.4] versus 118.8[52.5-220.5]pg/ml , p=0.026). Hypotensive episodes were more frequent in the 'low-BP' group (57.1% versus 32.3%, p=0.007). sNfL level could identify patients who had experienced hypotensive episodes with high discriminative ability (AUC[95%CI]: 0.690[0.572-0.791], p=0.003)
Conclusion: Strict BP control (≤160/90mmHg) within 24 hours following successful recanalization of LVO by MT is associated with increased neuronal injury, displayed by higher sNfL levels, and poorer functional outcome, potentially indicating hypotension-induced neuronal loss during post-MT phase.

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Child neurology/developmental neurology

EPR-028

Modern principles of diagnostics of cerebral disorders in children and adolescents with sugar type 1 diabetes

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Background and aims: Diabetes mellitus (DM) is considered one of the most urgent health problems, as it seems to be the cause of many complications of various organs and systems. On the part of the brain in DM, complications in the form of cognitive impairment are 20–70% more than in healthy people.
Methods: We examined 33 patients with diabetes mellitus aged 7-18 and 23 healthy children matched by sex and age. The activities carried out included the collection of anamnestic data, neuropsychological testing, the study of memory and attention functions, the state of the autonomic nervous system was assessed, and neurospecific proteins were determined to identify early markers of cognitive impairment, protein S100 and neuron-specific enolase (NSE).
Results: Despite the presence of optimal and suboptimal metabolic control of the pathology under study, all the examined children and adolescents with type 1 DM, according to the examinations, were found to have clinical manifestations of cerebral disorders: small-focal neurological symptoms, autonomic dysfunction, cephalgic and asthenic syndromes, as well as high incidence of cognitive dysfunctions, which are the main brain disorders in type 1 diabetes in children.
Conclusion: The results of neuropsychological testing showed a rather high incidence of cognitive disorders in children with diabetes, this fact is confirmed by an increased content of S-100 and NSE proteins in the blood serum. In addition, an increase in creatine and creatine phosphate, as well as a change in their ratios in hippocampal cells, demonstrates an increase in intracellular metabolism.
Disclosure: There is no conflict of interest.

EPR-029

Motor outcome of spinal muscular atrophy pediatric patients treated with nusinersen in COVID-19 times

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Background and aims: Nusinersen is the first oligonucleotide-based therapy approved for treating SMA of all types and has been available in Romania since 2018. The COVID-19 pandemic represents an ongoing challenge and the aim of our study was to evaluate the motor outcome of SMA patients during the COVID-19 pandemic.
Methods: All the patients aged 0-18 who received intrathecal nusinersen therapy for at least 15 months in our clinic were included in our study (19 patients). We have neurologically examined the patients and motor function was assessed using standardized clinical scales, including Hammersmith Functional Motor Scale - Expanded (HFMSE), which was the most widely used among our patient group. We categorized the patients relative to the COVID-19 pandemic timeline in Romania. We noted the functional scores obtained at each of the injections administered and analysed the data to find out whether the restrictions imposed by the pandemic influenced the results of the functional scores.
Results: HFMSE showed a statistically relevant tendancy to increase even during the pandemic. Internationally speaking, there were centers where nusinersen administration needed to be delayed due to the COVID-19 pandemic. In our center, all the patients received the nusinersen injection in a timely manner.
Conclusion: The access to gene-modifying therapy has dramatically changed the course of the disease in SMA patients, which otherwise had a natural evolution towards motor decline. The fact that the treatment was administered without delay influenced the positive motor outcome of the patients despite of the challenge represented by the pandemic.
Disclosure: Nothing to disclose.

EPR-030

Paramagnetic rim and core sign lesions in pediatric multiple sclerosis patients

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Background and aims: Paramagnetic rim lesions (PRL) are considered relatively specific for multiple sclerosis (MS), are present across all adult MS phenotypes and predict a more severe disease evolution. Conversely, core sign lesions have been observed at the earliest phases of adult MS, tended to shrink over a 3-year period follow-up, and only a minority of them evolved in PRLs. Given the relevant diagnostic and prognostic implications of PRLs and core sign white matter lesions (WML) in MS, we explored their prevalence in pediatric MS patients.
Methods: Using a 3.0 T MRI, a three-dimensional (3D) T1- weighted turbo field echo, 3D T2 fluid-attenuated inversion recovery and 3D SWI with magnitude and phase images. On phase images, two reviewers independently assessed PRLs, defined as a complete/incomplete rim of hypointense signal, and core sign WML, defined as paramagnetic hypointense core.
Results: Of 1256 WMLs, 1058 WMLs (84%) were assessed for SWI hypointensity; 198 WMLs were excluded because of size (<3 mm) or poor visibility. Twenty-seven (2.6%) PRLs and 185 (17.5%) core sign WMLs were identified. Ten pediatric MS patients (77%) had ≥1 PRL and all patients had ≥1 core sign WMLs. The median numbers of PRLs and core sign WMLs per patient were 1 (range=0-8) and 5 (range=1-43).
Conclusion: Our findings suggest that SWI sequence can be useful to characterize WMLs having acute or chronic inflammation and demyelination also in pediatric MS patients. Future longitudinal studies are needed to shed light on the diagnostic and prognostic values of these lesions in this peculiar population.
Disclosure: The authors have nothing to disclose.

EPR-031

KIF1A-dependent disorders in a group of first Polish patients

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Background and aims: KIF1A (Kinesin family member 1A)- related disorders encompass a variety of diseases. KIF1A variants are responsible for autosomal recessive and dominant spastic paraplegia 30 (SPG, OMIM610357), autosomal recessive hereditary sensory and autonomic neuropathy type 2 (HSN2C, OMIM614213), autosomal dominant neurodegeneration and spasticity with or without cerebellar atrophy or cortical visual impairment (NESCAV syndrome) formerly named mental retardation type 9 (MRD9) (OMIM614255).
Methods: The authors present first nine Polish patients with confirmed heterozygous pathogenic and potentially pathogenic KIF1A variants. All the patients were of Caucasian origin. A consanguineous background was absent. Female to male ratio=1,25).
Results: Exome sequencing identified seven different de novo variants and one variant which occurred to be inherited from mosaic parent (paternal origin) from 9 independent patients. Every variant found in our patients causes change of one aminoacid (missense type). Among 9 patients one variant, previously described, was detected in two patients: c.815A>G, p.(Asn272Ser). Remain 7 variants include 4 already reported: (c.38G>A, p.(Arg13His; c.646C>T, p.(Arg216Cys); c.946C>T, p.(Arg316Trp); c.296C>T, p.(Thr99Met) and 3 novel variants: c.442G>A, p.(Glu148Lys); c.609G>C, p.(Arg203Ser); c.218T>G, p.(Val73Gly). Only one c.442G>A has ClinVar annotation as likely pathogenic, two other seems to be variants of uncertain significance, although they are predicted in silco to be probably pathogenic. All three novel variants are located within highly conserved regions of the kinesin motor domain.
Conclusion: Analyzing the clinical symptoms of our patients, we have noticed that the phenotypic variation of KIF1A mutations is much broader than previously described.
Disclosure: Nothing to disclose.

EPR-032

Quindecim, a Phase II, double-blind, randomized, placebo-controlled trial of basmisanil in children with Dup15q syndrome

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Background and aims: Dup15q Syndrome is a rare genetic neurodevelopmental disorder with an incidence of ~1:14,000 caused by copy number gains of 15q11-13, which includes three GABA-A receptor subunit genes (GABRA5,GABRB3,GABRG3) and UBE3A, among others. We present a pioneering study (NCT05307679) testing the hypothesis that decreasing GABA-A α5 subunit-containing receptor signaling can improve adaptive behavior in Dup15q Syndrome.
Methods: A translational qEEG biomarker of GABA-A receptor function was developed to enable assessment of pharmacodynamic effects on GABA-A related disease

pathology. Clinical experts, patient advocacy groups and a patient council of Dup15q Syndrome caregivers were consulted to best target and incorporate the needs of patients.

Results: In the Quindecim global phase II, randomized, double-blind, placebo-controlled study, approximately 90 children with Dup15q syndrome, ages 2 to 11 years, will be treated for 52 weeks with basmisanil, a GABA-Aα5 negative allosteric modulator. Due to the lack of longitudinal natural history data in this rare disorder, a placebo arm remains essential. The primary efficacy endpoint is the Vineland-3 adaptive behavior composite after one year of treatment. In addition, an interim analysis based on a GABA-A related qEEG biomarker in the first 30 participants will provide an early assessment of basmisanil effects on abnormal EEG/GABA-A signaling.

Conclusion: In the rare disease Dup15q Syndrome, with limited trial and natural history experience, this placebo-controlled Phase 2 study innovates beyond investigation of clinical safety and efficacy. By employing a physiological biomarker of disease pathologic processes, Quindecim will enable both timely decision making and potential future studies in Dup15q Syndrome.

Disclosure: The authors are employed by Roche. This study (NCT05307679) is sponsored by Roche.

EPR-033

Hearing stimulation is important to hearing loss children before auditory sensitivity period: A graph theory analysis

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Background and aims: Sensorineural hearing loss (SNHL) has far-reaching, lifelong consequences for children and their families. However, children receiving cochlear implants at a younger age have faster and more age-appropriate development than those who received implants later. Considering the auditory system is still developing sensitively between the ages of 2-4, a graph theory analysis on SNHL children grouped by the auditory sensitivity period is aiming to provide an imaging foundation for the pathophysiological mechanisms related to ages. We hypothesize that older SNHL children show more white matter structural network alterations than the younger ones.

Methods: We gather diffusion tensor imaging data from 95 SNHL children and 50 control children. Depending on their ages, all participants were split into Group A (12 to 47 months) and Group B (48 to 120 months). We Create a structured brain network for graph theory analysis and analyze the topological properties.

Results: Group A only experienced a slight decrease in nodal topological parameters while no difference was found in the Global topological parameters or structural connections. Conversely, Group B showed obvious topological alterations of the structural network, reflected in the decrease in the global efficiency of the whole brain, the randomization of the small world attribute, and the decrease in connectivity between key brain regions. Most of the brain regions mentioned in this experiment are associated with higher-order cognitive functions.

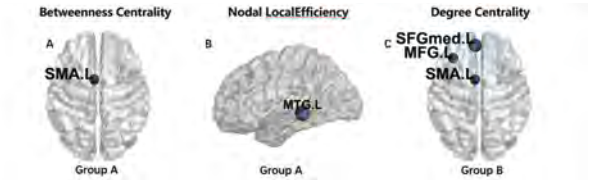

Figure 1. Nodal topological parameters : Decreased models are represented in blue. Fig A&B: Middle temporal gyrus(MTG.L) in NodalLocalEfficiency and Supplementary motor area (SMA.L) in BetweennessCentrality of Group A decrease. Fig C: Supplementary motor

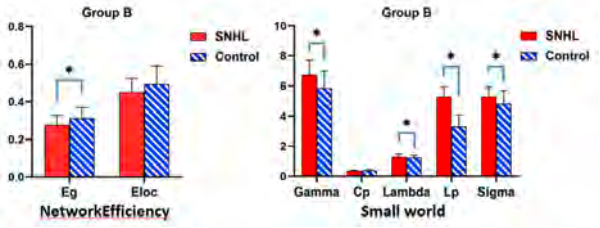

Figure 2. Global topological parameters: Eg in NetworkEfficiency represents global efficiency decrease.. All of the Small-world attribute increase except Cp in Group B.

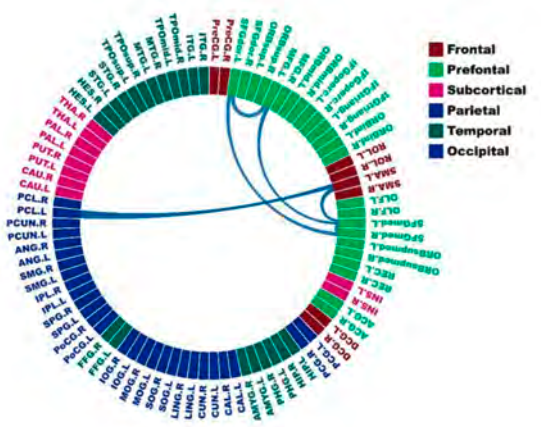

Figure 3. Structural connection : In Group B, we found that 6 nodes constituted 6 connections lower than those in the normal group, and there were no elevated brain area connections.

Conclusion: Children with SNHL should introduce hearing stimulation as early as possible before the sensitive period of hearing development to avoid malformed brain remodelling.

Disclosure: This study was funded by the Joint Research Fund for Enterprise and basic and applied basic research Programs of Guangdong Province of China (NO. 2021A1515 220112) and the Special Funds of the Department of Science and Technology of Guangdong Province (NO. 2020ST102).

Cognitive neurology/neuropsychology

EPR-034

The Consciousness 'Hubs': a study in stroke patients

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Background and aims: Despite extensive research, the neurophysiological mechanisms of Consciousness are still largely unknown. Presumably, some brain regions are involved in its genesis, such as the posterior cingulate cortex, the precuneus and, in particular, the thalamus and the claustrum. Of note, subcortical areas seem to be the most relevant, but their precise contribution has not yet been defined.
Methods: In this case-control study, we investigated possible correlations between stroke-induced lesions in specific brain regions and alterations in self-awareness, subjectively perceived or assessed by means of neuropsychological tests, i.e. the Mindful Attention Awareness Scale (MAAS). Our initial hypothesis was that alterations in subcortical regions were the most implicated in causing these alterations. Patients with first brain stroke and Mini Mental State Examination >27 admitted to our University Hospital were recruited. Cases were identified on the basis of subjective and/or objective alterations in self-awareness (MAAS < 45), whereas the controls had no alterations in self-awareness.
Results: 31 cases and 23 controls were enrolled. The study of the relationship between mean MAAS score and brain lesion sites showed a significant difference for diencephalic lesions (i.e., the thalamus) (p=0.002), which was maintained even after correction for age, education and cerebrovascular risk factors. Correlations between alterations in self-awareness and lesions in other brain regions were not significant.
Conclusion: Despite the small sample size and low specificity of neuropsychological tests in an acute setting, consistent with our initial hypotheses, self-awareness was mainly reduced in patients with lesions in sub-cortical sites (in particular, the thalamus), critically involved in its genesis.
Disclosure: No disclosures.

EPR-035

Time perception in stroke: a case-control study

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Background and aims: Time perception is crucial in everyday life, but its neurophysiological mechanisms are still largely unknown. Several studies suggested an involvement of the cerebellum and basal ganglia, with different roles depending on the considered time interval. We studied the functional consequences of injuries in these areas caused by brain stroke.
Methods: 19 stroke patients and 28 healthy controls were included. Four tasks were administered, two (A-B) for explicit time (participants were explicitly informed to process temporal information) and two (C-D) for implicit time processing (participants were not explicitly asked to process time). All participants also underwent a neuropsychological evaluation.
Results: • Time bisection (A): cerebellar patients were more variable than controls (p=.042); • Finger tapping (B): with free intervals, healthy older adults were slower than all patients (p=.005), but less variable than cerebellar ones (p=.015); also at fixed intervals of 1 second, older adults were less variable than patients (p=.009); • Rhythmic task (C): participants were faster when the target was preceded by a regular compared to irregular rhythm (p=.001); • Temporal orienting (D): participants were faster when the cue predicted the target and when the time interval was long (foreperiod effect). Moreover, patients were faster for long time intervals, while controls did not present a foreperiod effect (p=.001). Eventually, healthy older adults and basal ganglia patients used the cue to predict the target (p=.008).

	Healthy older adults N=28	Cerebellar patients N=14	Basal ganglia patients N=15	p
Age	63.18 (11.23)	68.29 (17.01)	63.27 (9.76)	0.590
Education	12.50 (4.29)	10.54 (3.71)	10.80 (4.51)	0.277
Mini-Mental State Examination (MMSE)	29.36 (0.68)	28.50 (1.51)	29.14 (1.21)	0.343
Token test	35.08 (0.95)	33.31 (1.03)	33.43 (2.51)	**0.007**
Memory - Prose test (immediate recall)	6.39 (1.26)	5.01 (2.25)	5.37 (2.19)	0.228
Memory - Prose test (delayed recall)	6.19 (1.77)	4.66 (1.55)	4.30 (1.99)	0.070
Memory - Rey words (immediate recall)	44.82 (9.32)	36.13 (11.11)	36.33 (4.08)	**0.010**
Memory - Rey words (delayed recall)	9.36 (3.38)	6.75 (3.88)	7.00 (1.41)	**0.041**
Rey figure (immediate recall)	33.16 (3.87)	29.61 (5.52)	34.25 (1.67)	0.137
Rey figure (delayed recall)	14.30 (6.58)	13.83 (10.99)	16.58 (2.89)	0.436
Trail Making Test (TMT) part A	61.46 (26.26)	80.88 (40.95)	81.83 (22.57)	0.154
TMT part B	117.89 (41.44)	167.67 (125.51)	211.00 (110.79)	0.222
Frontal Assessment Battery (FAB)	17.29 (0.85)	16.38 (1.77)	17.14 (0.90)	0.412
Phonemic verabl fluency (FAS)	38.21 (12.21)	27.88 (6.22)	35.43 (8.06)	**0.017**

Table 1: demographic characteristics and neuropsychological assessments of participants

Conclusion: Patients were more variable in explicit tasks and as accurate as controls in implicit timing, supporting the different involvement of the cerebellum and basal ganglia in the explicit time processing.
Disclosure: No disclosures.

EPR-036

Functional and structural MRI changes associated with cognitive worsening in multiple sclerosis: a 3-year study

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Background and aims: Heterogeneous processes may contribute to cognitive impairment in multiple sclerosis (MS). We applied a multiparametric MRI approach to identify mechanisms associated with cognitive worsening in MS.
Methods: Brain dual-echo, 3D T1-weighted, diffusion-weighted imaging, and resting state (RS) functional MRI scans were acquired at baseline and after median follow up of 3.4 years in 35 MS patients and 22 healthy controls (HC). Associations between cognitive worsening and longitudinal changes in T2-hyperintense lesion location, WM microstructural damage, gray matter (GM) atrophy and RS functional connectivity (FC) were explored.
Results: Fifteen (43%) MS patients were cognitively impaired at baseline and 10 (29%) deteriorated at follow-up. At baseline, compared to HC, MS patients showed widespread WM damage and GM atrophy, and decreased RS FC in some clusters of executive control (ECN) and working memory networks (WMN). At follow-up, annualized volume loss of caudate nucleus was significantly higher in MS patients with vs without cognitive deterioration (-1.2% vs -0.2%, $p<0.05$). Compared to stable MS patients, worsened patients showed decreased RS FC in right hippocampus of right WMN and in right insula of default mode network. In the opposite comparison, increased RS FC in left insula of ECN was found.
Conclusion: While cognitively-stable MS patients showed increased RS FC in left insula, possibly reflecting a compensatory mechanism, cognitive deterioration in MS patients was associated with decreased RS FC in several functional brain networks. In MS patients already characterized by structural damage, cognitive deterioration might be secondary to functional network collapse.
Disclosure: This study received no financial support.

EPR-037

Age of onset effect on cognitive disability progression in multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) onset typically occurs in young adulthood. However, there is a minority of pediatric- (i.e. before age 18 years) and late-onset (i.e. after age 50 years) patients, who might experience faster cognitive decline, according to recent evidence. Our aim was to explore the progression pattern of cognitive decline in pediatric-, adult-, and late-onset MS patients.
Methods: From a cross-sectional cohort of 1243 MS patients evaluated with Rao's Brief Repeatable Battery and Stroop Color Word Test, we identified 134 pediatric-, 1056 adult- and 53 elderly-onset patients. By using the Subtype and Stage Inference (SuStaIn) unsupervised machine learning algorithm.
Results: In all three groups, cognitive decline started – on average – from impairment in semantic fluency. This was followed by verbal memory impairment in adult- and elderly-onset patients, and by executive function impairment in pediatric-onset patients. The temporal sequence of impairment in the remaining domains was, from earlier to later: for adult-onset, attention, information processing speed (IPS), executive functions, visuo-spatial memory; for pediatric-onset, attention, verbal memory, IPS, visuo-spatial memory; for late-onset, IPS, attention, executive functions, visuo-spatial memory.

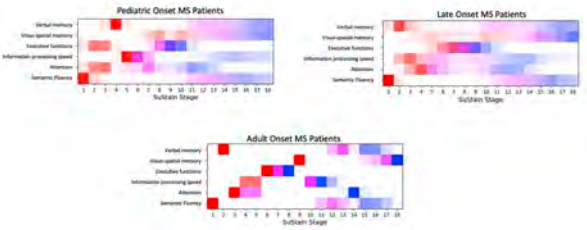

Figure 1. Summary of cognitive impairment progression over time in the pediatric, adult and late onset multiple sclerosis patients

Conclusion: By applying a machine learning algorithm on neuropsychological data, we identified a different effect of MS on brain function based on age at onset, possibly due to modifications induced by brain (and immune system) development and ageing. Our results underscore the need of targeted rehabilitation strategies, taking into account age at onset.
Disclosure: The authors have no competing interests related to the present manuscript.

EPR-038

Evaluation of the diagnostic quality of Alzheimer's disease after including the amyloid-β 42/40 ratio as a biomarker

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[1]Department of Neurology, Virgen de las Nieves Hospital, Granada, Spain, [2]Department of Neurology, Torrecárdenas Hospital, Almería, Spain, [3]Fidyan Neurocenter, Granada, Spain

Background and aims: Following the NIA-AA 2018 recommendations for the diagnosis of Alzheimer's disease (AD) with biomarkers in living persons, we aimed to apply the ATN classification and evaluate the improvement in diagnostic quality of AD in our center after including the amyloid-β 42/40 ratio in cerebrospinal fluid (CSF) as a diagnostic biomarker.
Methods: We included 193 patients from our department of cognition and behavior neurology who had baseline CSF with AD biomarkers, collected between July 2019 and July 2022. We compared the final diagnostic classification with and without including amyloid-β 42/40 ratio.
Results: The mean age was 68,3 ± 6,8 years old, with 113 (58,5%) women. 51 patients (26,4%) meet the NIA-AA 2018 criteria for AD (A+T+), with low of both β-42 and Aβ 42/40 ratio; 62 patients (32,1%) would meet criteria for Suspected Non-Alzheimer's Pathology (SNAP) (A-T+) using Aβ-42 as the only biomarker for amyloid deposit, but after including Aβ 42/40 ratio, only 13 patients (6,7%) meet criteria for SNAP (A-T+); 80 patients (41,4%) had normal AD biomarkers (A-T-). Using both, Aβ 42 and Aβ 42/40 ratio, AD diagnosis increased by 25,3% ($p<0.0001$) in our sample.
Conclusion: 25,3% of the patients in our cohort obtained a diagnosis of biologically defined AD after incorporate Aβ 42/40 ratio, what it means an improvement in diagnostic quality of AD.
Disclosure: All authors declare that they have no conflicts of interest.

EPR-039

Time-varying hippocampal functional connectivity is associated with cognitive performance in multiple sclerosis patients

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Background and aims: The hippocampus has a key role in cognition. Here, we explored hippocampal static (sFC) and time-varying functional connectivity (TVFC) and assessed their association with cognition in multiple sclerosis (MS).
Methods: Neuropsychological and 3T structural/functional MRI assessments were performed in 108 MS patients and 63 healthy controls (HC). Sliding-window correlation analysis using the left (L) and right (R) hippocampus as seed regions assessed TVFC, quantified by the standard deviation of connectivity across windows. Mean connectivity indicated sFC.
Results: MS patients had decreased sFC/TVFC vs HC between L hippocampus and temporo-parietal regions. Conversely, they had increased sFC between bilateral hippocampus and thalamus, precuneus and superior frontal cortex (SFC), as well as increased TVFC between bilateral hippocampus and occipital, sensorimotor, orbitofrontal and temporal cortices. In MS patients, better global cognition correlated with higher TVFC between L hippocampus and L pre-/post-central gyri (r=0.21-0.28; p=0.04-0.006). Better verbal memory correlated with higher TVFC between L hippocampus and L precentral gyrus (r=0.21, p=0.03), and better visuospatial memory correlated with higher TVFC between bilateral hippocampus and L cuneus, pre-/post-central and temporal cortices (r=0.19-0.23, p=0.02-0.04). Better information processing speed correlated with higher TVFC between L hippocampus and L postcentral gyrus (r=0.21, p=0.03), while better attention correlated with higher TVFC between L hippocampus and L temporal cortex (r=0.24, p=0.01). Finally, better information processing speed/attention correlated with higher sFC between R hippocampus and L SFC (r=0.21/0.20, p=0.03/0.05, respectively).
Conclusion: Increased hippocampal connectivity contributed to explain better cognition in MS, with peculiar association between higher hippocampal TVFC and better memory scores.
Disclosure: This study received no funding.

EPR-040

A regional FDG-PET approach to identify sub-threshold bvFTD in subjects with isolated apathy.

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Background and aims: As subtle behavioral deficits are a common presentation of behavioral variant frontotemporal dementia (bvFTD), we decided to evaluate if FDGPET findings, using a region of interest approach (ROI) could identify among subjects with isolated apathy those that will progress to develop bvFTD.
Methods: Inclusion criteria: (i) development of significant apathy confirmed at the neuropsychiatric inventory, (ii) lack at baseline of other behavioral symptomatology, (iii) insufficient clinical features at baseline to fulfill bvFTD criteria (iv) availability of a FDGPET brain scan and clinical follow-up of at least 18 months. Normalized regional metabolism, expressed in z-scores based on a group of 24 age-matched controls, was computed for the following ROIs: dorsolateral PFC ventromedial PFC, orbitofrontal cortex, temporal pole and basal ganglia. The anterior cingulate was not assessed given its association with apathy.
Results: 32 subjects with isolated apathy were included. At baseline none of these subjects fulfilled the possible bvFTD diagnostic criteria, while at the end of the follow-up 18 subjects were diagnosed with a possible FTD. There were no significant differences between FTD-converters and non-converters in cognition at baseline. Regarding regional metabolism, the number of ROIs with a z-score lower than -1.5, was significantly different between the two groups (chi-square p=0.006).
Conclusion: in subjects with isolated apathy the assessment of FDG signal as assessed with a ROI approach, is able to point towards those patients who will convert to possible bvFTD before the clinical progression of symptoms. A regional FDGPET approach to identify sub-threshold bvFTD in subjects with isolated apathy.
Disclosure: Nothing to disclose.

EPR-041

Disability impact on sexual dysfunction relies on illness perception: a multicenter study in multiple sclerosis

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Background and aims: Sexual dysfunction (SD) is a common but under-explored issue in people with multiple sclerosis (pwMS). Here, we assessed how disease severity, illness perception, and depressive symptoms relate to SD in pwMS.

Methods: In this multicenter Italian study, 1,010 pwMS (336 M; 40.57±10.61 years) responded to an online survey. Illness perceptions was assessed with the Brief Illness Perception Questionnaire, depressive symptoms with the Neuro-QoL and SD with the MS Intimacy and Sexuality Questionnaire. Data about disease severity (global disability measured with the Expanded Disability Status Scale) were provided by each participating center. A model considering negative illness perception and depressive symptoms as serial mediators of the relationship between disease severity and SD was built in SPSS PROCESS Macro with bias-corrected bootstrapping (5,000 samples) (Fig.1).

Results: Disease severity did not exert a direct effect on SD (β = 0.450; 95%CI = −0.158, 1.058). The first indirect path (disease severity→illness perception→SD) was significant (β = 0.315; 95%CI = 0.039, 0.590). The second indirect path (disease severity→depressive symptoms→SD) was not significant (β = −0.030; 95%CI = −0.116, 0.042). The third indirect path (disease severity→illness perception→depressive symptoms→SD) was significant (β = 0.182; 95%CI = 0.074, 0.309) (Fig.2). These results suggest that higher disease severity, rather than exerting a direct effect on SD, increases its magnitude by enhancing negative illness perception, that, in turn, affects SD both directly and through depressive symptoms.

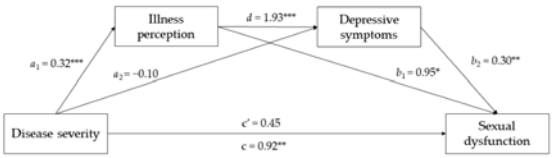

Figure 2. The mediated effects of illness perception and depressive symptoms on the relationship between disease severity and sexual dysfunction. *p<0.05 **p<0.01 ***p<0.001

Conclusion: Modulating the effect of illness perception by favoring adaptive coping strategies might represent a valid approach to mitigate SD symptoms in MS.

Disclosure: The Authors have no relationships/activities/interests related to the manuscript.

EPR-042

Topography of real space navigation deficits in focal epilepsy

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Background and aims: Spatial navigation requires a complex brain network with the hippocampus being one of the main hubs. However, it remains unclear, how the topography and laterality of focal brain dysfunction affects navigation performance and strategy in real space. The objective of this study was to examine the specific effects of lateralized hippocampal against extrahippocampal dysfunction in patients with focal epilepsy on route planning and target finding in a real space navigation paradigm.

Methods: 16 patients with right-sided mesial temporal lobe epilepsy (rTLE), 16 patients with left-sided mesial temporal lobe epilepsy (lTLE), 15 patients with frontal lobe epilepsy (FLE) and 24 healthy controls (HC) conducted a real space navigation paradigm, which required recall of known and recombination of so far unknown novel routes. Patients wore a gaze-controlled head-fixed camera, which allowed detailed post-hoc analysis of visual exploration behaviour and navigation trajectories.

Results: TLE-patients (both rTLE and lTLE) performed significantly worse than FLE-patients and HC on the entire real space navigation paradigm ($F=37.1$; $p<0.001$). TLE-patients exhibited particular deficits on creating and recombining novel routes ($F=43.3$; $p<0.001$). Specifically, rTLE-patients exhibited insufficient navigation trajectories with significantly less usage of a possible short-cut routes ($F=5.5$; $p=0.003$).

Conclusion: This study underpins the prominent role of the right hippocampus for efficient goal-oriented allocentric navigation in real environments in humans. Differential navigation deficits may be considered as localizing and lateralizing signs in focal epilepsies.

Disclosure: Nothing to disclose.

Headache and Pain 1

EPR-043

Abstract withdrawn.

EPR-044

Ketogenic Diet in resistant chronic migraine with failure to anti-CGRP monoclonal antibodies (KETOMIGRAINE)

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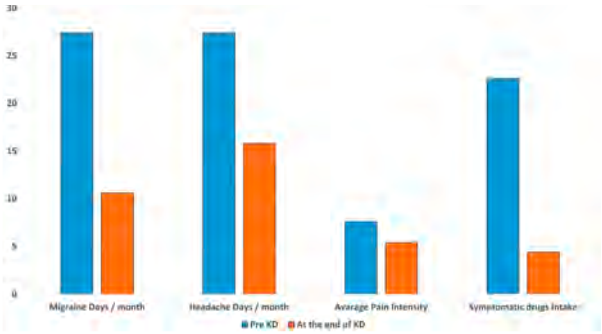
Background and aims: Chronic Migraine (CM) is a common and very disabling disorder. Prophylactic treatments are used to reduce frequency and intensity of headache; between them a prominent role is occupied by the innovative and effective monoclonal antibodies targeting CGRP pathway (mABs). Unfortunately, 30-40% of chronic migraineurs do not improve with mABs. The development of new therapeutical approaches, also non-pharmacological, is essential. In this pilot study, we propose Ketogenic Diet (KD) as an additional treatment option for resistant CM who also failed mABs (KETOMIGRAINE).
Methods: The study foresees the enrollment of 20 subjects with resistant CM, without a clinical improvement after mAbs, followed at IRCCS Mondino Foundation of Pavia (Italy). Subjects are prescribed a KD lasting 3 months, followed by a transitional diet (TD) and a follow-up period. Twelve patients have been enrolled in the study, and five subjects completed KD phase. They will be the focus of the interim analyses.
Results: Monthly migraine days, average pain intensity, disability and total pain burden significantly decreased during KD phase when compared to baseline ($p<0.05$ for all comparison). Headache days, symptomatic intake, impact of headache and quality of life showed a trend toward reduction during the KD phase, but did not reach the statistical significance.



Comparison between average values of the main headache features at baseline and at the end of KD

Conclusion: KD seems a promising alternative/complementary therapeutic option for highly disabled CM patients who did not respond to mABs. From the interim analyses of our data, we obtained encouraging results that need further validation in a larger cohort of patients.
Disclosure: I have no disclosure to declare.

EPR-045

Real-world effectiveness & safety of fremanezumab in migraine: 3rd interim analysis of the pan-European PEARL study

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Background and aims: PEARL (EUPAS35111) is an observational, prospective, Phase IV study of fremanezumab effectiveness and safety for episodic and chronic migraine (EM, CM) prevention. This third interim analysis was conducted when all patients had completed ≥6 months of treatment.

Methods: Participants are adults with EM or CM receiving fremanezumab treatment for migraine prevention, who maintain a daily headache diary prior to and throughout the 24-month observational period. Primary endpoint: proportion of patients with ≥50% reduction in monthly migraine days (MMD) during the 6 months post-fremanezumab initiation. Secondary endpoints: mean change from baseline across Months 1–12 in MMD, days of acute migraine medication use and headache-related disability (MIDAS and HIT-6). Safety was measured through adverse events (AEs) reported in clinical practice.

Results: Of 1140 patients enrolled, 968 were included in the effectiveness analysis (EM, 33.1%; CM, 66.9%). In patients with available data, 428/732 (58.5%) achieved ≥50% MMD reduction during the 6 months post-fremanezumab initiation (Figure 1). The proportions of patients reaching ≥50% reduction in MMD were sustained at Months 1–12 (Figure 2), as were reductions in mean MMD (Figure 3), days of acute medication use and headache-related disability. Overall, 267/1140 (23.4%) patients reported AEs relating to treatment, 2/1140 (0.2%) reported serious AEs relating to treatment and 33/1140 (2.9%) reported AEs that led to discontinuation.

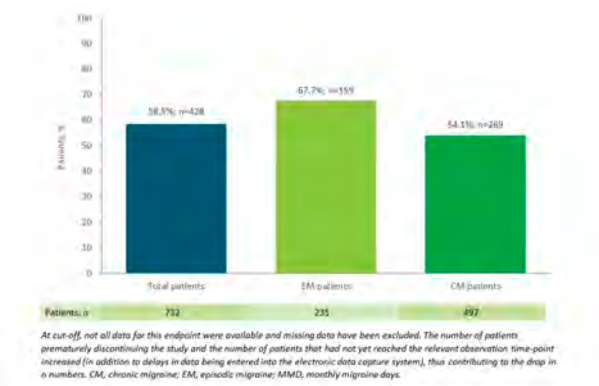

Figure 1: Proportion of patients reaching ≥50% reduction in MMD from baseline by migraine type during the 6 months after fremanezumab initiation (primary endpoint).

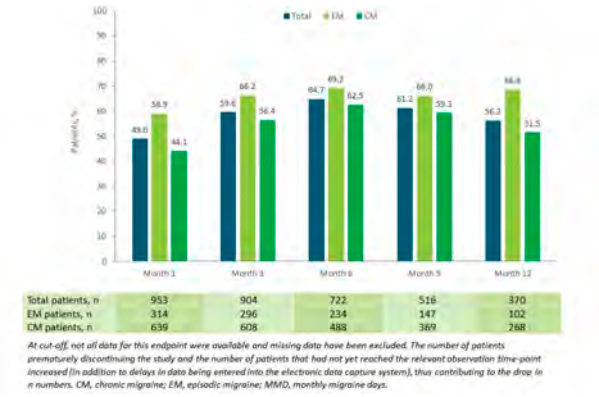

Figure 2: Proportion of patients reaching ≥50% reduction in MMD from baseline by migraine type at Months 1, 3, 6, 9 and 12.

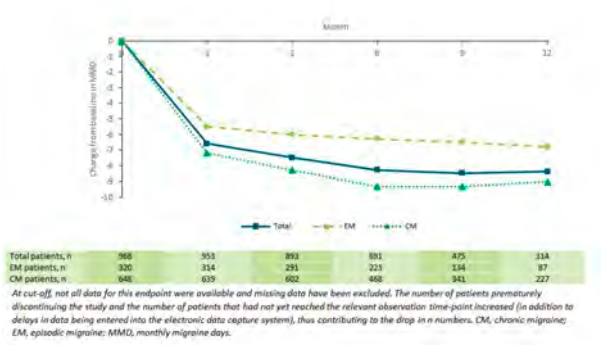

Figure 3: Mean change from baseline in MMD at Months 1, 3, 6, 9 and 12 after fremanezumab treatment initiation, by migraine type.

Conclusion: Over half of patients achieved ≥50% MMD reduction with fremanezumab, with sustained reductions in acute medication use and disability, and few AEs leading to discontinuation reported. Outcomes from this large, real-world population can guide informed migraine management.
Disclosure: Funded by Teva Pharmaceuticals.

EPR-046

Reversion from CM to EM with anti-CGRP mAbs: a prospective, multicenter study on 1109 patients (the I-NEED study)

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Background and aims: Randomized clinical studies documented that monoclonal antibodies (mAbs) to calcitonin gene-related peptide (CGRP) shift chronic migraine (CM) to episodic migraine (EM) at weeks 12 in ~50% of patients. We investigated antiCGRP mAbs efficacy in remitting CM to EM in real life, in patients with >3 preventive medications classes failure.
Methods: Multicenter (n=29), prospective, cohort, real-life study across 10 Italian regions. We considered all consecutive CM patients who had received >1 anti-CGRP mAbs dose from 01/02/2019 to 28/12/2022. All patients had previously failed >3 preventive medications classes. Primary endpoint: remission from CM to EM at week 12. Secondary endpoints: remission from CM to EM at weeks 4, 24 and 48 and reversion from medication overuse (MO) to no-MO at weeks 4, 12, 24 and 48.
Results: 1109 CM patients (MO:1003/1109, 90%) received >1 antiCGRP mAbs dose (erenumab/fremanezumab/galcanezumab: 676/295/138 patients). Remission from CM to EM and from MO to no-MO were monitored at weeks 12, 24 and 48 in all centers, conforming to Italian Medicines Agency regulations. Eight centers monitored treatment effects monthly, according to their routine practice. The table summarize results.

Table

Week	Patients (n)	Remission from CM to EM, n (%)	Remission from MO to no-MO, n (%)
4	769	461 (59.9)	372 (81.9)
12	800	**574 (71.8)**	444 (81.5)
24	632	487 (77.1)	390 (82.9)
48	364	294 (80.8)	232 (83.7)

(Primary endpoint in **BOLD**)

Conclusion: In real-life, antiCGRP mAbs reverse CM to EM in ~60% of patients at week 12, and in ~80% at week 48. Remission form MO to no-MO occurs at week 4 in >80% of subjects. AntiCGRP mAbs effectiveness is better than efficacy.
Disclosure: P. Barbanti received grants and honoraria from Alder, Allergan, Angelini, Assosalute, Bayer, ElectroCore, Eli-Lilly, GSK, Lundbeck, Lusofarmaco, 1MED, MSD, New Penta, Noema Pharma, Novartis, Stx-Med, Teva, Visufarma, Zambon. C. Aurilia received grants from FB-Health, Lusofarmaco, Almirall, Eli-Lilly Novartis and Teva; G. Egeo received grants and honoraria from Eli-Lilly, Novartis, New Penta and Ecupharma; P. Torelli received grants and honoraria from Allergan, Teva, Eli-Lilly and Novartis. C. Finocchi received grants and honoraria from Novartis, Eli Lilly, TEVA, AIM group F. d'Onofrio received grant and honoraria from Novartis, Teva, Neopharmed Gentili, Qbgroup srl, K link srl and Eli-Lilly L. d'Onofrio has no disclosures to declaire L. Di Clemente has no disclosures to declare. A. Ranieri received speaker honoraria from Teva, Lilly. F. Zoreddu has no disclosures to declare F. Frediani has received fees from Angelini, Cristalfarma, Ecupharma, IBSA, Lundbeck, Novartis, PIAM, Teva G. Fiorentini has no disclosures to declare. B. Orlando has no disclosures to declare. S. Proietti has no disclosures to declare. S. Bonassi has no disclosures to declare.

EPR-047

Investigating the CGRP-mediated changes in activation of trigeminal ganglion neurons using microfluidic cultures

N. Bhatti[1], R. Raouf[2]
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Background and aims: Growing research has implicated the role of Calcitonin Gene related Peptide (CGRP) in the sensitisation of Trigeminal Ganglion (TG) neurons leading to allodynia and hyperalgesia in migraine headache. However, the mechanisms behind the sensitisation, especially the axons of these neurons where pain signals are transduced and transmitted, remain elusive. We developed a microfluidic culture model to examine CGRP mediated changes in TG neuron excitability.

Methods: We utilised microfluidic cell cultures from P2-P4 mice preparations to investigate the changes in responsiveness of TG axons to depolarising stimuli following treatment with CGRP and CGRP receptor antagonists. We assessed axonal responses through applying stimuli to the axonal compartment and used calcium imaging at the somal compartment (Figure 1). Unpaired Students t-test was used to compare the fold changes between the groups. Paired Students t-test was used to compare change in F ratio between applications of 15mM KCl.

Results: Application of CGRP did not enhance the KCl-mediated depolarisation of isolated TG axons (Figure 2). Acute application of 500nM BIBN 4096, a selective CGRP antagonist, to the culture did not significantly alter the fold change between depolarising stimuli intervals. The inclusion of 1μM BIBN 4096 completely abolished all axonal and somal responses (Figure 3).

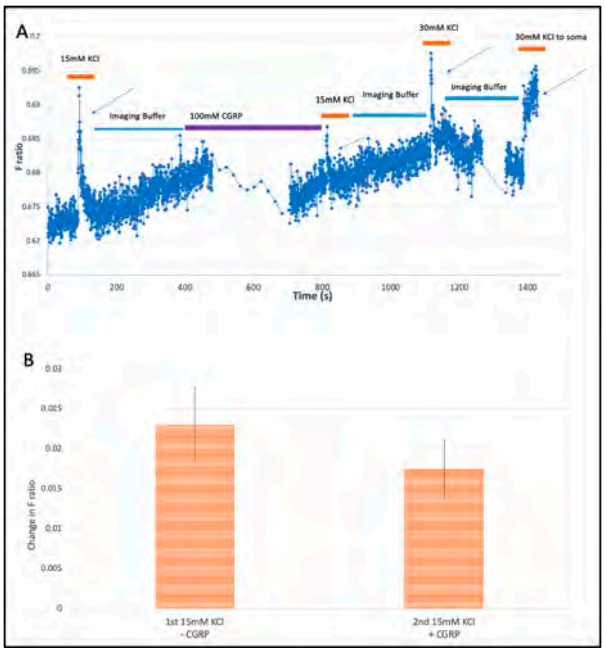

Figure 2: Fura-2 trace recorded from the somal compartment (arrows denote Ca response) after stimulation with 15 mM and 30mM KCl in the axonal compartment. B) The average change in F ratio between 15mM KCl additions

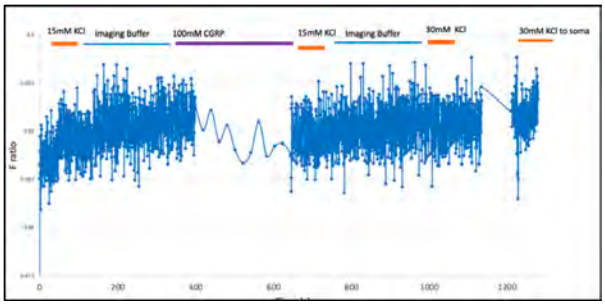

Figure 3: Fura-2 trace of Trigeminal ganglia cultures pre-treated with 1μM BIBN 4096. There was no observed response to axonal, or somal stimulation with KCl.

Conclusion: Our data indicates that CGRP does not cause sensitisation of TG axons and instead may have a role in neuroprotection. The use of migraine prevention strategies based on CGRP antagonism should be approached with greater caution.

Disclosure: This research has no commercial or institutional support.

EPR-048

Brain connectivity modifications induced by anti-CGRP mAbs in migraine patients: a prospective HD-EEG study

F. Bighiani[1], M. Corrado[1], R. De Icco[1], F. Cammarota[1], G. Vaghi[1], M. Semprini[2], D. Martinelli[1], G. Sances[1], C. Tassorelli[1]

[1]Headache Science and Neurorehabilitation Center, IRCCS Mondino Foundation, Pavia, Italy, [2]Rehab Technologies, Istituto Italiano di Tecnologia, Genoa, Italy

Background and aims: Monoclonal antibodies targeting the CGRP pathway (mAbs) proved effective and safe as migraine preventive treatment. mAbs act outside of the blood brain barrier, namely in the peripheral component of the trigeminovascular system. Nonetheless, a reduced sensitization of the first order neuron in the trigeminal ganglion may induce secondary effects at central level.
Methods: We plan to perform 5 resting state high-density electroencephalography (HD-EEG) recordings before mAbs treatment and then every 3 months for one year. Here we present data regarding 16 migraine patients (age 44.7±10.6, 14 females, 11 with CM) who completed the first three months of mAbs treatment (T3). We aim to study the connectivity changes in the nodes of the default mode network (DMN): the right and left angular gyrus (RANG and LANG), the medial pre-frontal cortex (MPC) and the posterior cingulate cortex (PCC)
Results: At T3, mAbs treatment induced an inter-nodal connectivity reduction between MPC-PCC (p=0.025), MPC-LANG (p=0.020), MPC-RANG (p=0.043), and PCC-LANG (p=0.005). By contrast, the connectivity was enhanced between PCC-RANG (p=0.005) and LANG-RANG (p=0.003). At T3, 7 patients qualified as "Responder" to mAbs (reduction in monthly migraine days of at least 50% when compared to baseline). Responders were characterized by a baseline enhanced connectivity between MPC-PCC (p=0.042) and MPC-RANG (p=0.032), and by a reduced connectivity between LANG-RANG (p=.016)
Conclusion: We hypothesize that a reduced sensitization of the peripheral component of the trigeminovascular system may account for the observed findings. In addition, Responder patients showed a specific baseline brain connectivity pattern.
Disclosure: Nothing to disclose.

EPR-049

Role of the default mode network in episodic cluster headache: cerebral connectivity analysis with HD-EEG

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[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy, [2]IRCCS Mondino Foundation, Pavia, Italy, [3]Italian Institute of Technology, Genoa, Italy

Background and aims: The pathophysiological mechanisms underlying episodic cluster headache (eCH), and shift between active and remission phases, are still not fully understood. We aimed to define specific internodal connectivity patterns of the default mode network (DMN) in eCH patients, through advanced brain connectivity analyses with high-density EEG (HD-EEG).
Methods: Twenty-four patients with eCH and 19 healthy controls (HCs) were enrolled. Patients with eCH were evaluated during both the active (T0) and the remission (T1) phases of disease. Of these 24 patients, 8 were registered only at T0, 10 only at T1, while 6 completed both registrations. The DMN areas considered for the analysis were: the right and left angular gyrus (RANG and LANG), the medial pre-frontal cortex (MPC) and the posterior cingulate cortex (PCC).
Results: The study of internodal brain connectivity in patients showed lower connectivity at T1 (remission) when compared to T0 between PCC and MPC (T0=0.078±0.009 vs. T1=0.049±0.006, p=0.022) and between PCC and RANG (T0=0.076 ± 0.008 vs. T1=0.052±0.005, p=0.024). Furthermore, connectivity at T1 was lower when compared to HCs, specifically between PCC and MPC areas (CHe-T1=0.049±0.005 vs. HS=0.067±0.005, p=0.028).
Conclusion: eCH patients evaluated during a remission phase of disease showed lower brain connectivity between specific areas of the DMN when compared with either eCH patients tested during an active phase and HCs. This finding may represent a biological marker of disease, while the fluctuation in PCC connectivity may reflect pathophysiological mechanisms involved in the shift from one phase of disease to the other.
Disclosure: Nothing to disclose.

EPR-050

Is there a sustained response following discontinuation of long-lasting anti-CGRP monoclonal antibodies treatment?

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Background and aims: Previous studies showed progressive migraine deterioration after 3-month discontinuation of anti-CGRP monoclonal antibodies (mAbs). In this real-life study we aimed to investigate whether long-lasting treatment with mAbs could lead to a sustained clinical response after treatment discontinuation.

Methods: One-hundred fifty-two migraine patients were enrolled: 72 received mAbs for 12 months (A-group), while 80 were treated for more than one year (B-group). Demographical data were collected at baseline. Clinical variables, including monthly headache days (MHD) and migraine days (MMD), monthly acute medication pills (AMP) and days (AMP), headache intensity on NRS, HIT-6, MIDAS and ASC-12 scores were recorded at baseline (T0), after one year or more of therapy (T1) and after minimum 3-month discontinuation period (T2). Within-group changes of clinical outcomes from T0 to T1 (T0-T1) and from T1 to T2 (T1-T2) were assessed using Wilcoxon test. Between-group differences were investigated using mixed-effect ANOVA tests.

Results: At T0-T1 both groups showed a significant reduction of all observed variables. Even if between-group comparison was not statistically significant, we observed a higher reduction of all clinical variables in B-group. At T1-T2, both groups showed a significant clinical worsening for all outcomes. We observed a worse clinical deterioration in B-group compared to A-group, even if differences were not statistically significant.

Conclusion: Long-lasting therapy with mAbs leads to a slight higher clinical improvement during treatment, as well as a more pronounced rebound effect during discontinuation. Further real-life studies with a larger sample size are needed.

Disclosure: The authors declare no competing interests related to this work.

EPR-051

The Impact of tDCS on Perceived Pain and Pain Processing in Parkinson's Disease Patients

Y. González Zamorano[1], F. Sánchez Cuesta[2], J. Fernández Carnero[1], A. Arroyo Ferrer[2], M. Moreno Verdú[2], L. Valenzuela López[2], J. Romero Muñoz[2]

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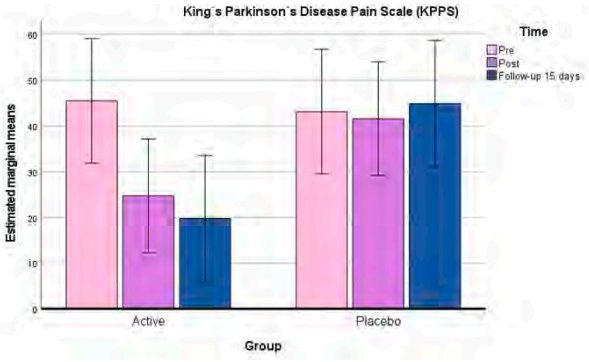
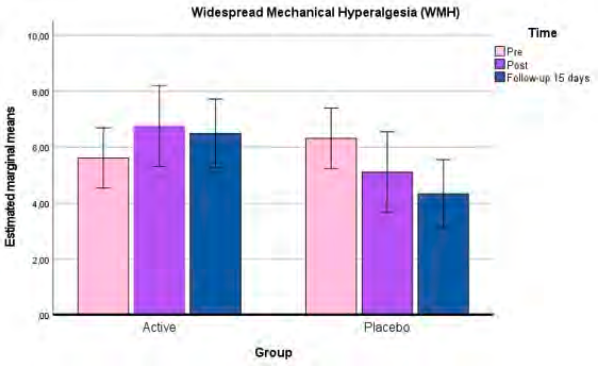
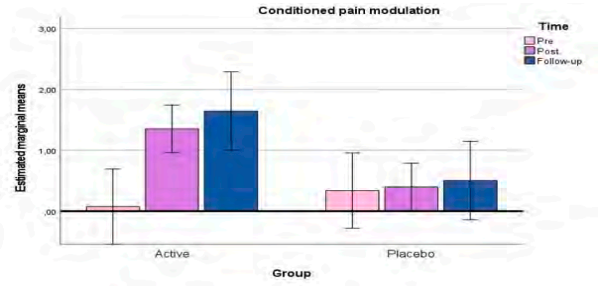
Background and aims: Pain is common among Parkinson's patients, affecting 85%. It negatively impacts quality of life, likely caused by brain changes in pain processing due to degeneration of dopamine and non-dopamine pain regulating pathways. Both pain and PD reduce activity in the primary motor cortex. TDCS applied to the M1 has been shown to reduce pain in other chronic pain conditions by increasing activity in brain regions involved in pain processing, but its effectiveness for PD-related pain has not been studied. We aim to assess the effectiveness of tDCS on PD-associated pain.

Methods: This is a randomized, triple-blinded, parallel-design study with 22 subjects (63.23±12.07). They were randomly assigned to one of two intervention groups: active-tDCS vs sham-tDCS. Active-tDCS group received 10 consecutive sessions of 20 min of tDCS with active anode on M1 at 2 mA intensity. The sham group followed the same protocol, but the tDCS stimulator was turned off at 30 seconds. King's Parkinson's Disease Pain Scale (KPPS), Pain Expansion, and Conditioned Pain Modulation (CPM) were evaluated pre, post, and 15 days post-intervention.

Results: Active-tDCS group showed significant improvement in KPPS and pain expansion compared to sham-tDCS group at 15 days follow-up (p=0.014, p=0.017). CPM also improved significantly in active-tDCS group post-intervention and at 15 days (p=0.002, p=0.017).







Conclusion: TDCS may alleviate PD-related pain by activating brain pathways that control pain. Results show that pain reduction and central pain desensitization require 15 days post-treatment while conditioned pain modulation improves faster.

Disclosure: The present project was funded by the Spanish Ministry of Science and Innovation grant (PID2020-113222RBC21/AEI/10.13039/501100011033). The authors have nothing to declare because the beforementioned institution did not participate in the development nor the design of the study.

Coma and chronic disorders of consciousness

EPR-052

Progression of auditory processing in acute coma: changes in neural synchrony

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Background and aims: The integrity of auditory processing in coma after cardiac arrest (CA), assessed via electroencephalography (EEG) is informative of coma severity. In the first 24 hours of coma, neural synchrony of auditory responses is predictive of coma outcome. It remains unknown what is the optimal temporal window for assessing auditory responses in coma. We hypothesised that neural synchrony of patients that later survive remains stable and that outcome prediction is more optimal early in time.
Methods: We studied 132 post-CA coma patients, presented with sounds, with two EEG recordings each, between the first and third coma day. The phase-locking value (PLV) was calculated to measure neural synchrony.
Results: In a pilot group (N=65 patients), the PLV of the first EEG recording was higher for survivors than non survivors (Fig. 1). Non survivors had a significant increase in PLV from first to second EEG ($p<0.01$; Fig. 2). The PLV was predictive of coma outcome on the first EEG, with a positive predictive value (PPV) of predicting awakening of 0.84. Results were confirmed in the test cohort (N=66), with a PPV of 0.79.

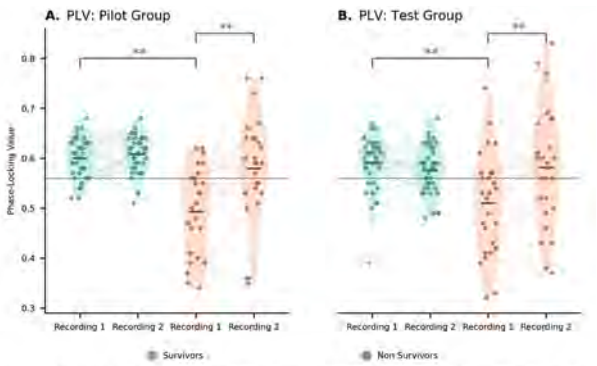

Figure 1: Phase-Locking values. PLV values for the pilot (left) and test (right) groups. All panels show values for both recordings and survivors (always left, green) and non survivors (always right, orange). **A.** PLV value for the pilot group, showing significant differences with regard to outcome ($p<0.01$), recording time ($p<0.01$) and interaction between factors ($p<0.01$). Post-hoc tests showed significant differences for the first recording between survivors and non survivors ($p_{corr}<0.01$) and between first and second recording for non survivors ($p_{corr}<0.01$). **B.** PLV values for the test group, showing significant differences with respect to outcome ($p<0.05$), recording time ($p<0.05$) and interaction ($p<0.01$). Also for this cohort post-hoc tests showed significant differences between survivors and non survivors ($p_{corr}<0.01$) in the first recording and for non survivors between first and second recording ($p_{corr}<0.01$).

Phase-Locking values for pilot and test group.

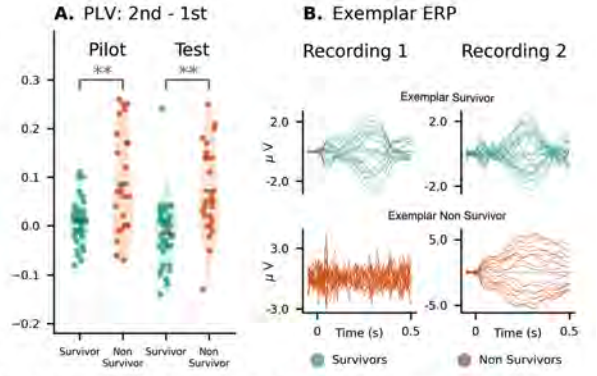

Figure 2: Change in PLV from first to second recording and exemplar ERP traces.
A. Difference in PLV values for second versus first recording, for both the pilot (left) and test (right) groups, for survivors (green) and non survivors (orange). A positive value implies an increase in neural synchrony from first to second recording. We find a significant difference between survivors and non survivors, for the pilot ($p<0.01$) and test ($p<0.01$) cohort. **B.** Exemplar ERP traces of a survivor (top, green) and non survivor (bottom, orange) for both recordings.

Change in PLV from first to second recording and exemplar ERP traces.

Conclusion: Neural synchrony changed for non survivors over the first days of coma, but remained stable for survivors. The predictive value of PLV was lost on the second recording. Our results highlight the importance of selecting the optimal temporal window for probing auditory responsiveness in the comatose brain.
Disclosure: Authors have no conflict of interest to disclose.

EPR-053

An Italian multicentre validation study of the Simplified evaluation of CONsciousness disorders: Preliminary data

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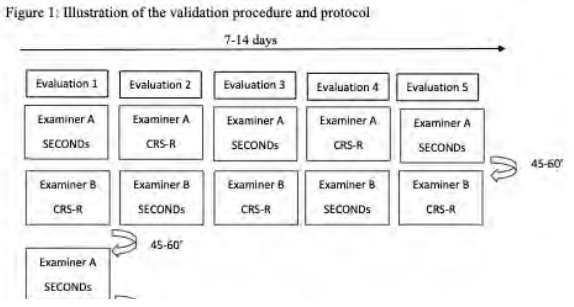
Background and aims: The Coma Recovery Scale-Revised (CRS-R) is the gold standard to assess consciousness in patients with disorders of consciousness. However, its time requirements limit its administration. A short-term assessment tool has been validated: the Simplified Evaluation of CONsciousness Disorders (SECONDs)1. This multicentre study aims at carrying out a cross-cultural translation of the SECONDs into Italian language and validating it between operators of different professions.

Methods: The translation and backtranslation of the scale into Italian language was completed with the contribution of the authors of the original version. Patients with diagnosis of Unresponsive Wakefulness Syndrome (UWS) or Minimally Conscious State (MCS) admitted to 3 Italian rehabilitation units were enrolled. The CRS-R / SECONDs were performed by 3 blinded examiners in each center (Figure 1). Weighted Fleiss' kappa coefficients were used to assess inter-/intra-rater reliability and concurrent validity.

Figure 1: Illustration of the validation procedure and protocol



Results: Twenty-two adult patients have been assessed [16 (72.7%) UWS, 8 (27.3%) MCS, 12 (54.5%) females; mean age: 54±19.6years; 6 (27%) trauma; 2 [2.75] months post-onset; Table 1]. The comparison of CRS-R vs SECONDs on the best assessments showed a "high" positive correlation for the total score (ρ =.844; p<.001) and a "substantial" agreement for the diagnosis (k =.779; p<.001). Intra-/inter-rater reliability showed a "high"-"very high" positive correlation on the total score [0.823< ρ < 0.923; p<0.001] and a "substantial"-"almost perfect" agreement on diagnosis [0.795< k<0.932; p<0.001; "Table2].

Table 1: Clinical and demographic characteristics of the study sample

Overall *n*=22	*n* (%) mean±SD median [IQR]
Center:	
Florence	13 (59.1%)
SA Lombardi	4 (18.2%)
Milan	5 (22.7%)
TPO (months)	2 [2.75]
TPO Florence (months)	2 [1.50]
TPO SA Lombardi (months)	10.5 [23]
TPO Milan (months)	9 [35]
Consciousness state (according to CRS-R)	
UWS	16 (72.7%)
MCS-	4 (18.2%)
MCS+	2 (9.1%)
Age (years)	54±19.6
Sex (F)	12 (54.5%)
Etiology:	
Traumatic	6 (27.3%)
Anoxic	5 (22.7%)
Ischemic	2 (9.1%)
Haemorrhagic	5 (22.7%)
Other	4 (18.2%)

SD: standard deviation; IQR: interquartile range; TPO: time post onset; CRS-R: Coma Recovery Scale-Revised; UWS: Unresponsive Wakefulness Syndrome; MCS: Minimally Conscious State; F: females.

Table 2: Correlation and agreement inter-/intra-rater and between SECONDs and CRS-R

Correlation between continuous total score **ρ=.844; *p*<.001**		Best CRS-R			
		UWS	MCS-	MCS+	
Best SECONDs	Coma	2	0	0	**k=.779; *p*<.001**
	UWS	14	0	0	
	MCS-	0	4	1	
	MCS+	0	0	1	

Correlation between continuous total score **ρ=.894; *p*<.001**		SECONDs (examiner 1 - assessment 1)				
		Coma	UWS	MCS-	MCS+	
SECONDs (examiner 1 - assessment 2)	Coma	2	0	0	0	**k=.932; p<.001**
	UWS	0	13	0	0	
	MCS-	0	1	5	0	
	MCS+	0	0	0	1	

Correlation between continuous total score **ρ=.823; *p*<.001**		SECONDs (examiner 1 - assessment 1)				
		Coma	UWS	MCS-	MCS+	
SECONDs (examiner 2)	Coma	2	1	0	0	**k=.795; p<.001**
	UWS	0	12	0	0	
	MCS-	0	1	5	1	
	MCS+	0	0	0	0	

Correlation between continuous total score **ρ=.923; *p*<.001**		SECONDs (examiner 1 - assessment 2)				
		Coma	UWS	MCS-	MCS+	
SECONDs (examiner 2)	Coma	2	1	0	0	**k=.867; *p*<.001**
	UWS	0	12	0	0	
	MCS-	0	0	6	1	
	MCS+	0	0	0	0	

CRS-R: Coma Recovery Scale-Revised; UWS: Unresponsive Wakefulness Syndrome; MCS: Minimally Conscious State; SECONDs: Simplified Evaluation of CONsciousness Disorders.

Conclusion: These preliminary data suggest that the Italian version of the SECONDs can be administered reliably and could differentiate successfully UWS from MCS. 1 Aubinet C. 2020

Disclosure: The authors report no disclosure.

EPR-054

Visual Response and Cortical Reactivity: best Predictors of Recovery of Consciousness in the Subacute Phase

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Background and aims: According to the lates international recommendations, the diagnosis of consciousness in patients with prolonged Disorder of Consciousness (pDoC) should include both clinical (Coma Recovery Scale-Revised, CRS-R) and instrumental evaluations (e.g. Electroencephalography, EEG). The study aim was to identify which CRS-R subscale and which EEG pattern at admission were associated with emergence from pDoC at discharge from the Intensive Rehabilitation Unit (IRU).

Methods: This analysis has been made in the framework of the PRABI study [1] including patients with pDoC referred to the IRCCS Don Gnocchi in Florence. At admission, the consciousness was assessed via repetitive CRS-R and the EEG reported according to the classification of the American Clinical Neurophysiology Society, [2]. Age, sex, time post-onset (TPO) and etiology were included as correlates. The outcome was the emergence from pDoC.

Results: Eighty-eight patients were included: female: 39 (44.3%), Age: 67 years [interquartile range=21]; traumatic: 20; TPO: 39 days [22]; Unresponsive Wakefullness State: 31(35.2%), Minimally Conscious State minus 23(26.1%) and plus 34 (38.6%). Multivariate analyses including only clinical variables (A) and only EEG variables (B) showed that the visual subscale and cortical reactivity were significantly correlated with outcome (R2: 0.460, 0.390 for A and B respectively) (Table I). Both remained independently significant when combined (EEG/CRS-R (C: $p<0.001$, R2 :0.657). R2 increases to 0.554 when only visual subscale and reactivity were considered (D).

Conclusion: The study suggests that the visual scale and cortical reactivity of admission are the best predictors of emergence from altered consciousness at discharge from IRU. [1] 10.3389/358fneur.2022.711312 [2] 10.1097/WNP.0000000000000806

Disclosure: The authors report no disclosure.

Model A: CRS and clinical correlates			
Nagelkerke's R^2 = 0.460	**OR**	**95%CI**	**p-value**
CRS-R auditory	0.766	0.358-1.638	0.492
CRS-R visual	3.650	1.870-7.122	**<0.001**
CRS-R motor	0.928	0.570-1.511	0.764
CRS-R oro-motor	3.001	0.768-11.728	0.114
CRS-R communication	0.762	0.100-5.790	0.793
CRS-R arousal	1.117	0.384-3.247	0.839
Age, *years*	1.008	0.969-1.049	0.692
Sex, *female*	0.622	0.191-2.028	0.431
Etiology, *Traumatic*	1.273	0.595-2.722	0.534
TPO, *days*	0.986	0.962-1.010	0.248
Model B: EEG and clinical correlates			
Nagelkerke's R^2 = 0.390	**OR**	**95%CI**	**p-value**
Background frequency, *θ*	1.125	0.171-7.424	0.902
APG, *present*	1.395	0.421-4.624	0.587
Cortical reactivity, *present*	12.202	3.593-41.438	**<0.001**
Symmetry, *present*	0.916	0.291-2.885	0.881
Background voltage, *low-voltage*	0.557	0.149-2.074	0.383
Age, *years*	0.996	0.959-1.034	0.834
Sex, *female*	0.440	0.141-1.376	0.158
Etiology, *Traumatic*	1.518	0.732-3.145	0.262
TPO, *days*	0.987	0.963-1.011	0.285
Model C: CRS, EEG and clinical correlates			
Nagelkerke's R^2 = 0.657	**OR**	**95%CI**	**p-value**
CRS-R auditory	0.518	0.191-1.404	0.196
CRS-R visual	5.355	1.965-14.589	**0.001**
CRS-R motor	0.737	0.382-1.425	0.364
CRS-R oro-motor	5.537	0.800-38.346	0.083
CRS-R communication	0.936	0.083-10.540	0.958
CRS-R arousal	1.029	0.261-4.066	0.967
Background frequency, *θ*	1.386	0.127-15.177	0.789
APG, *present*	1.428	0.259-7.886	0.683
Cortical reactivity, *present*	21.997	3.958-32.254	**<0.001**
Symmetry, *present*	0.907	0.171-4.813	0.908
Background voltage, *low-voltage*	1.053	0.172-6.429	0.955
Age, *years*	1.016	0.966-1.069	0.540
Sex, *female*	0.392	0.088-1.755	0.221
Etiology, *Traumatic*	1.616	0.581-4.491	0.358
TPO, *days*	0.977	0.946-1.008	0.146
Model D: selected predictors			
Nagelkerke's R^2 = 0.554			
CRS-R visual	3.019	1.756-5.191	**6E-5**
Cortical reactivity, *present*	9.261	2.813-30.494	**2E-4**

Table I. Multivariate logistic regressions with outcome presence/absence of a pDoC at discharge from the IRU. Absence of pDoC is coded as 0, thus OR > 1 indicates that higher values of the independent variable lead to exiting from the state of altered consciousness.

Table I. Multivariate logistic regressions with outcome presence/absence of a pDoC at discharge

EPR-055

Clinical evolution of post-anoxic prolonged Disorders of Consciousness: an individual patient data meta-analysis

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Background and aims: Prognosis of patients with severe anoxic brain injury and prolonged Disorders of Consciousness (pDoC) is usually considered poor, but solid prognostic indications for long-term clinical evolution are still lacking. We present a systematic review and meta-analysis aimed at evaluating long-term outcome of anoxic pDoC, and at identifying possible demographic and clinical predictors.

Methods: We evaluated the rates of mortality and of recovery of full consciousness at least 6 months after the injury. A cross-sectional approach searched for differences in baseline demographic and clinical characteristics between deceased vs. survivors and patients who recovered full consciousness vs. not-recovered.

Results: Data from 23 publications and 345 patients (Unresponsive Wakefulness Syndrome, UWS=272; Minimally Conscious State, MCS=73) were extracted and included in the meta-analysis. We found a pooled mortality rate of 30% and a rate of full consciousness recovery of 14%, within a median time of 12 months after injury. Younger age, diagnosis of MCS vs. UWS, and higher Coma Recovery Scale-Revised total score at study entry were associated with a lower likelihood of mortality. These same variables, together with shorter time from injury, were associated with recovery of full consciousness.
Conclusion: Although anoxic aetiology usually leads to a poor outcome, patients with pDoC have a relatively low mortality rate and a chance of late recovery of consciousness 6 months after injury. Specific predictive factors may guide the long-term management of anoxic patients with pDoC.
Disclosure: This study was supported by Italian Ministry of Health-Ricerca Corrente 2019-2021 and by European Union's HORIZON2020-MSCA n°778234-DoCMA project.

EPR-056

Global Neurophysiological Measures in Disorders of Consciousness: a Meta-Analysis

M. Meys[1], Z. Wang[1], S. Abagnale[1], B. Kaan OK[1], N. Alnagger[1], M. Bardiau[2], C. Beaudart[3], S. Laureys[1], O. Gosseries[1], A. Thibaut[1], A. Sala[1], J. Annen[1]
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Background and aims: Here, we aim to quantitatively synthesise existing electroencephalography (EEG), magnetoencephalography (MEG) and functional near-infrared spectroscopy (fNIRS) findings in patients with disorders of consciousness (DoC), including the unresponsive wakefulness syndrome (UWS) and minimally conscious state (MCS).
Methods: In January 2022, we searched MEDLINE, Scopus and Embase for resting-state studies, involving adults with prolonged DoC, diagnosed with a validated behavioural scale. Two referees independently screened studies and extracted useful statistics. Separate random effect meta-analyses were conducted to compare global metrics between controls and DoC patients. The full protocol is available on PROSPERO (CRD42022327151).
Results: As of January 2023, from 3563 unique studies, 21 EEG studies were eligible for inclusion, spanning 240 controls, 499 UWS and 508 MCS patients (Figure 1). We here report only measures appearing in three or more studies. Power and connectivity in delta and alpha bands consistently differed between controls and DoC, along with power in the beta band. Still, studies' heterogeneity was considerable and larger for UWS than MCS. Power in delta and alpha bands, as connectivity in alpha band, also differed between UWS and MCS with medium effect sizes (Figure 2). UWS and MCS showed different power and participation coefficient in theta and connectivity in beta bands, all with small effects.

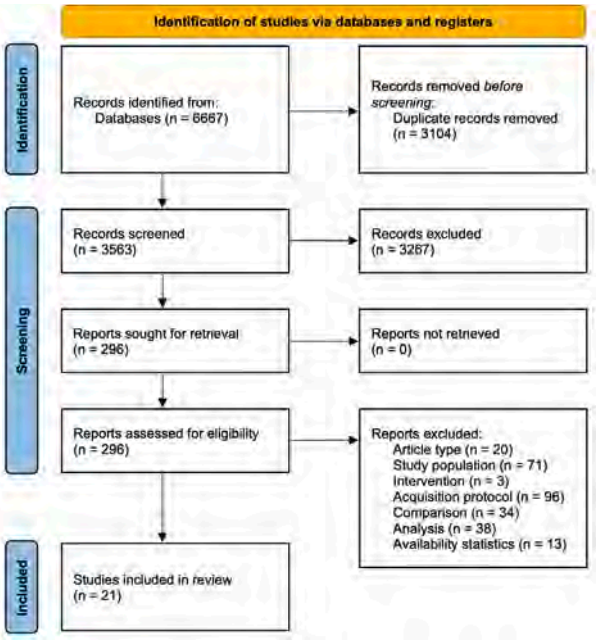

Figure 1: PRISMA flow diagram. Journal articles and conference papers were considered in the literature search, excluding case-studies.

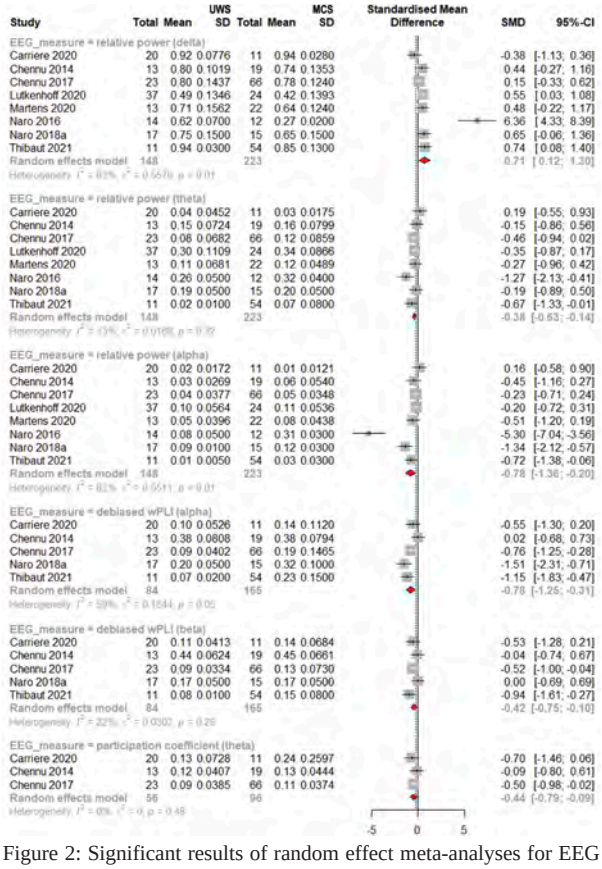

Figure 2: Significant results of random effect meta-analyses for EEG measures, investigating differences between UWS and MCS.

Conclusion: Delta and alpha measures consistently differed between UWS and MCS, indicating these as possibly interesting measures for diagnostic purposes. The large variability observed in UWS studies supports the notion of UWS heterogeneity, with part of UWS patients likely presenting residual brain activity, more similar to MCS.
Disclosure: Nothing to disclose.

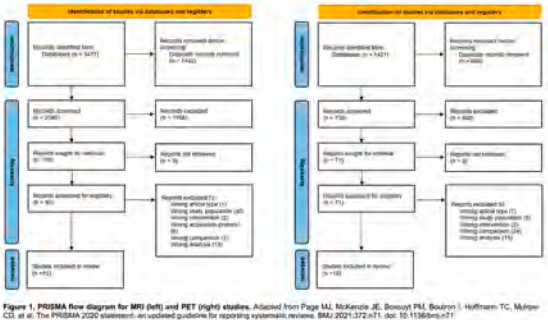

Fig. 1

EPR-057

Brain alterations in disorders of consciousness: a coordinate-based meta-analysis

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Background and aims: We aim to shed light on the localization of brain alterations in Disorders of Consciousness (DoC), by quantitatively synthesizing existing structural, functional and molecular evidence in patients with unresponsive wakefulness syndrome (UWS) and minimally conscious state (MCS).
Methods: In January 2022, we used MEDLINE, Scopus and Embase to search for resting-state magnetic resonance and positron emission tomography studies, involving adults with prolonged DoC, diagnosed based on a validated behavioural scale. Two referees independently screened studies and extracted coordinates of whole-brain, voxel-based comparisons between groups of patients and controls or patients subgroups. Coordinate-based meta-analysis was performed via activation likelihood estimation. The full protocol is available on PROSPERO (CRD42022327151).
Results: As of January 2023, of the resulting 2798 studies, 33 studies met criteria for inclusion, for a total of 454 UWS and 572 MCS patients and 277 controls (Fig. 1). The primary analysis, including studies comparing DoC patients vs. controls, revealed brain alterations in cortical regions, medially (precuneus, posterior/middle cingulate gyrus) and laterally (angular gyri, inferior parietal lobules), and in subcortical regions (dorsomedial thalami and head of caudate nuclei) (Fig. 2). Contrast analysis of UWS and MCS results revealed stronger brain alterations in UWS in the precuneus, posterior/middle cingulate gyrus, right angular gyrus and inferior parietal lobule, and dorsomedial thalami.

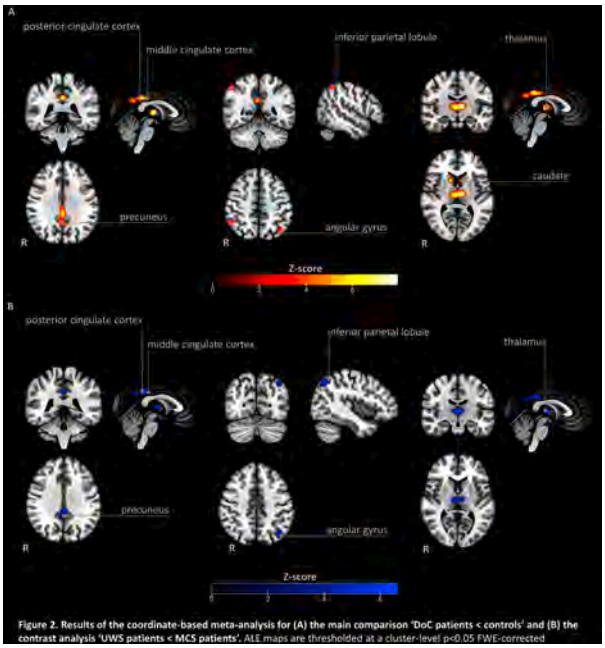

Fig. 2

Conclusion: This meta-analysis provides the most extensive evidence to date on brain alterations in DoC, pointing at a specific set of regions, at cortical and subcortical level, as anatomical basis for DoC, with stronger alterations in UWS compared to MCS.
Disclosure: Nothing to disclose.

EPR-058

Vagal nerve stimulation to treat severely brain-injured patients: a placebo-controlled randomized clinical trial

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Background and aims: Patients with disorders of consciousness (DOC) are a challenging population prone to misdiagnosis and lacking effective treatment options. Among neuromodulation techniques, trans-auricular vagal nerve stimulation (taVNS) may act trough a bottom-up manner to modulate thalamo-cortical connectivity and promote patients' recovery.

Methods: We will conduct the first randomized placebo-controlled double-blind clinical trial in DOC patients with taVNS. Forty-four patients in the acute phase will randomly receive 5 days of either active bilateral vagal stimulation (45 min duration; 3mA; 200-300μs current width, 25Hz.) or sham stimulation. Behavioural (i.e., Coma Recovery Scale-Revised, CRS-R) and neurophysiological (i.e., high-density electroencephalography, EEG) measures will be collected at baseline and at the end of the treatment.

Results: Improvements in the CRS-R total score will be our primary outcome. As secondary outcomes, we expect that the clinical changes in responders will be correlated with the EEG metrics. Fourteen patients (i.e., 7 patients in each group) have already been included in the trial. Preliminary results show that following the 5-day treatment phase, 3 patients from the active group were considered clinical responders to taVNS (i.e., showing new signs of consciousness that were never displayed at baseline nor during the screening phase) and showed enhanced CRS-R total scores compared to baseline. Moreover, among them, 2 patients improved diagnosis at the end of the treatment. No patient from the sham group showed any improvement at that stage.

Conclusion: These results will contribute to define the role of taVNS for the treatment of these challenging conditions and identify the neural correlates of its action.

Disclosure: Authors have no conflict of interest to disclose.

Education in neurology

EPR-059

Is Virtual Reality an effective educational tool to enhance patient-physician dialogue? ENGAGE learning intervention.

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Background and aims: Myasthenia gravis (MG) is a rare, chronic, heterogenous, unpredictable autoimmune disease characterised by dysfunction and damage at the neuromuscular junction.1 A recent, patient-led analysis identified a sense of disconnect with healthcare professionals as one of five overarching themes that reflect the lived experience of MG from the patient's perspective.2 ENGAGE aims to explore the hypothesis that immersive learning using virtual reality (VR) is an effective educational tool for neurologists to bridge this sense of disconnect by increasing physician understanding of the patient experience and thereby improving patient-physician dialogue and shared decision making (SDM) in MG.

References
1. Juel VC, Massey JM. Orphanet J Rare Dis. 2007.
2. Law N et al. Neurol Ther. 2021;10:1103–1125.

References

Methods: ENGAGE is a three-phase, educational pilot programme to design and evaluate an immersive learning intervention using VR. ENGAGE is co-designed with a steering committee including neurologists and patients living with MG. Phase 1: Needs assessment of the current reality for physicians and patients Phase 2: Design and trial of the VR educational intervention Phase 3: Comprehensive outcome evaluation to assess the impact of the educational intervention.
Results: The needs assessment is ongoing. To date, 10 interviews with neurologists from 5 educational sites and 10 interviews with patients have been analysed. Preliminary findings indicate that MG symptoms are overlooked in certain cases and learning interventions are required to increase physician understanding of MG. The educational intervention and outcome evaluation will follow.
Conclusion: ENGAGE aspires to better understand what drives current behaviour and to evaluate immersive learning as an educational tool for neurologists to improve patient-physician dialogue and SDM in MG. Funded by UCB Pharma.
Disclosure: Sophie Barry, Natasha Monin and Marc De Backer are employees of UCB Pharma. Ina Weisshardt is president of LLH Concepts. Cornelia Reyes works for LLH Concepts as a senior researcher. LLH Concepts has been commissioned by UCB Pharma to design and implement the ENGAGE project.

EPR-060

Use of the four-component instructional design model in the neurology rotation at the Medical School, Univ.Minho

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Background and aims: The neurology rotation aims to prepare students for the diagnosis and initial management of patients with neurological presentations. This requires the integrated mastery of multiple competencies, better acquired using the four-component instructional design model (4C/ID). This strategy is based in the use of authentic real-life learning tasks, complemented by a variety of learning tools (supportive and procedural information, part-task training) to facilitate the acquisition of knowledge, skills and attitudes.
Methods: In 2021 we started a new rotation according to the 4C/ID model, and assessed student satisfaction and its feasibility after the first 2 years.
Results: The rotation has 4 weeks and 6 core learning tasks, organized by symptom (lower limb weakness, upper limb difficulties, headache, cognitive complaints) or diagnosis (stroke, epilepsy). Each task consists of supervised practice in the hospital (20h/week), collection of a portfolio of cases, solving virtual patients, team-based learning sessions and simulations in the clinical skills laboratory. This is complemented by a curated collection of materials available for on-demand study (videos, lecture notes, annotated references and more). There is also a part-task training on the neurological examination in special occasions. Students are highly satisfied with the changes and most (88%) rate the sessions as useful or very useful. Tutors are also satisfied with student motivation and preparedness for practice and improved their average student rating (0,9 in a scale of 1 to 9).
Conclusion: Use of the 4C/ID in a neurology rotation is feasible and improves student and tutor satisfaction.
Disclosure: Nothing to disclose.

EPR-061

Structured, modular and competency-based postgraduate curriculum for RND

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Background and aims: Comprehensive European standards of knowledge in rare neurological diseases (RND) are lacking. To counteract this situation, the European Reference Network for Rare Neurological Diseases (ERN-RND) launched a procedure to compile and define educational requirements resulting in structured catalogue of competencies, Body of Knowledge (BoK) for best medical practice in RND. The target 'persona' is a clinician within 5 years after obtaining the Board Certificate in Neurology living in EU.

Methods: An existent BoK in epilepsies has been used as a blueprint to compile likewise structured BoKs for RND. Additionally, relevant competencies and learning objectives from other existent curricula such as EAN, ESHG, EPNS, UEMS have been evaluated, selected and supplemented to the core BoK. This procedure has been carried out for each of the 6 disease groups (DG) covered in ERN-RND. The draft BoKs were reviewed by 6-8 distinguished experts from different member institutions of ERN-RND including the patient representatives. In a final consenting step, the reviewers could give a final appraisal of the learning objective formulation without interpersonal bias and earmark each learning objective to a basic or an advanced knowledge.
Results: ERN-RND has compiled, reviewed and consented 6 structured catalogues of competencies, one per each DG. Each BoK is built of five domains: 1. General, 2. Diagnosis, 3. Disease management 4. Treatment, 5. Communicating with patients/family members.

Body of Knowledge (BoK)	
Domain	**Specification**
General/Theory	Competencies and learning objectives
Diagnosis/Neurogenetics	Competencies and learning objectives
Disease Management	Competencies and learning objectives
Treatment/Therapy	Competencies and learning objectives
Communicating with and counsulting RND patients and family members	Competencies and learning objectives

Body of knowledge (BoK)- structured catalogue of competencies

Conclusion: The compiled BoKs reflect a comprehensive set of educational requirements for neurologists involved in care of patients with RND from different perspectives: human genetics, paediatric and adult neurology and patient needs.
Disclosure: S.H., C.R. and H.G. are part of the coordination team of ERN-RND.

EPR-062

MS Nurse PROfessional 2012–2023: A Vision of MS Nursing Excellence

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Background and aims: Nurses play a critical role in MS patient care. The Multiple Sclerosis Nurse Empowering EDucation (MS-NEED) survey reported disparate nursing standards across Europe. One-fifth of the MS Nurses surveyed cited lack of training, skill and knowledge to provide expert MS nursing care.
Methods: To address this inconsistency, the European MS Platform developed MS Nurse PROfessional using a collaborative model with key MS organisations. An online platform was developed to create and host relevant learning materials and to allow the community to connect and share best practices. An expert faculty develops all learning materials and a community manager animates the community.
Results: MS Nurse PROfessional offers a free, multi-lingual, internationally accredited, foundation level e-learning programme providing five courses that support the evolving role of nurses caring for people with MS. Furthermore, it offers two advanced e-learning programmes focusing on rehabilitation and nursing research respectively. Actively promoted in 16 countries, MS Nurse PROfessional organises annually two international and one national live educational sessions, publishes six blogposts and two e-newsletters on relevant topics. To date, the programme welcomed 8000+ users, of which on average 1300 are active on the platform per year, with +800 courses completed annually.

Leaflet MS Nurse PRO_Front

Leaflet MS Nurse PRO_Front

Conclusion: Impact analysis shows MS Nurse PROfessional meets user needs, exerting positive influence on clinical practice, resulting in (self-reported) increased self-confidence to answer patients' questions, improved dialogues with colleagues, and an improved relationship with people with MS.

Disclosure: The authors have nothing to disclose. MS Nurse PRO received funding in 2022 from Biogen, Bristol Myers-Squibb, Coloplast, ECTRIMS, Janssen, Merck, Novartis, Roche.

EPR-063

Anti-Tr/DNER Cerebellar Ataxia after Immune-checkpoint inhibitors therapy in a patient with a SCA2 family history.

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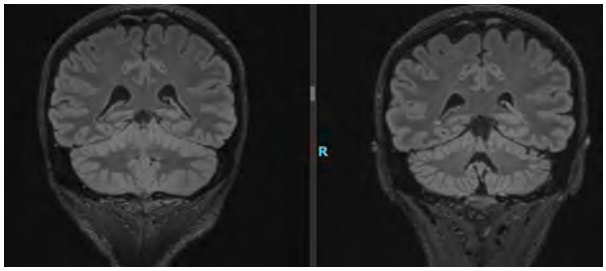
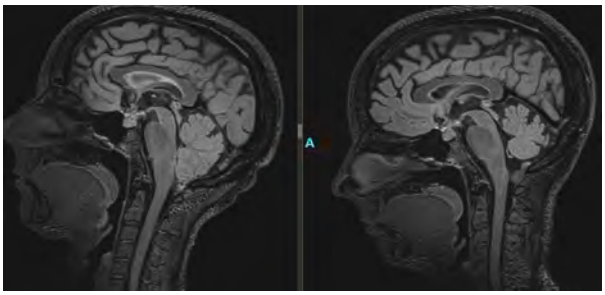
Background and aims: Anti-Tr/DNER Antibody-Associated Cerebellar Ataxia is a classical paraneoplastic neurological syndrome (PNS) associated with Hodgkin lymphoma (HL).
Methods: Describe a case of a paraneoplastic cerebellar ataxia associated with the use of Immune-checkpoint Inhibitors (ICI) that was initially misdiagnosed as being hereditary.
Results: A 39-year-old woman presented to the ER complaining with a one-week history of unstable walking and diplopia. Her past medical history revealed a HL diagnosis at 30 years of age successfully treated with first-line chemotherapy that relapsed 5 years later. She didn't respond to second-line chemotherapy and joined an experimental protocol with ICI, stopped 6 months before the onset of neurological symptoms. Her mother was affected by spinocerebellar ataxia type 2 (SCA2). At the first evaluation she presented with minor neurologic signs; brain MRI was normal, so she was discharged with a diagnosis of suspected SCA2. In the next few days she noted worsening of symptoms, therefore she came to our attention. A new brain MRI showed increased volume of the cerebellar cortex. Laboratory analysis showed mild CSF pleocytosis and serum anti-Tr/DNER positivity. Total body FDG-PET/CT didn't show HL relapses, so we treated her with steroids and IVIg without benefit. Now she is being treated with Rituximab and is slowly getting better. Genetic testing proved negative.



Midline MRI before and after treatment

Conclusion: This case highlights the importance of excluding acquired and treatable causes of cerebellar ataxia before thinking of familial degenerative forms. Furthermore, it could represent the first described case of neurologic Delayed immune-related adverse event (nDIRE) of ICI therapy.
Disclosure: Nothing to disclose.



EPR-064

Objective Structured Mimed Examination (OSME): an innovative method to teach neurology.

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Background and aims: Medical students fear neurology because they struggle to integrate clinical examination with theoretical knowledge. To try and address this issue, we developed the Objective Structured Mimed Examination (OSME), a clinical reasoning workshop that requires learners to simulate neurological signs and collaborate to solve clinical scenarios. OSME stations use a social-constructivist learning approach and are well suited to integrate competency-based medical curricula. The objective of this study was to assess student's satisfaction with an OSME station.
Methods: In 2021, we developed and administered a 2-hour OSME station to 195 4th year medical students at the Lausanne University medical school. At the end of the workshop, we administered a questionnaire to a group of 62 students to get feedback about this new learning approach. Questions focused on the following dimensions: structure, active learning, active reasoning and overall impression. Students could also comment on the strengths and weaknesses of the activity using free text fields.

Results: The vast majority of students highly appreciated the OSME station. Satisfaction regarding structure, active learning and active reasoning were 100%, 97%, and 100% respectively. In free text comments, students especially valued the interactivity, the discussions and the possibility to link theoretical and practical knowledge. Proposals for improvement mostly suggested having OSME stations more frequently and earlier in the curriculum.
Conclusion: OSME represents an innovative and well accepted teaching method for neurology. Further studies are needed to evaluate the effect on learning.
Disclosure: The authors declare that they have no conflict of interest.

EPR-065

A nationwide survey on neurophobia and its implications for the willingness to pursue a career in neurology

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Background and aims: The "fear of neurology" – neurophobia – makes the field less attractive for medical students. We investigated the prevalence of neurophobia in Lithuania and its association with the will to choose neurology residency.
Methods: From September 2021 to March 2022, undergraduate medical students in both Lithuanian medical schools received an online questionnaire about the knowledge, confidence, interest, and teaching quality of various medical specialties (including neurology), as well as the intent to choose neurology for residency. Neurophobia was defined as combined low confidence and perceived high difficulty in neurology.
Results: The survey was completed by 852 students (77.2% female, 236 (27.7%) already exposed to the course of neurology). Neurology was perceived more difficult than other specialties and respondents reported less confidence and knowledge in this area ($p<0.001$). The prevalence of neurophobia among respondents was 58.9%. Neurophobia was lower in those reporting positive professor influence on their outlook of neurology (OR=0.383, 95% CI=0.223-0.658). Neuroanatomy (202, 85.6%), insufficient practical skills (174, 73.7%) and wide differential diagnostics (158, 67.0%) were cited as major contributors to the complexity of neurology. Low scores of neurophobia (OR=1.785, 95% CI=1.152-2.767) and having conducted neurology research (OR=2.072, 95% CI=1.145-3.747) increased the odds of a student being willing to pursue a career in neurology.
Conclusion: Our findings indicate that neurophobia is frequent among undergraduate medical students and may be impactful for their future career choices. However, improvements in the student experience of clinical neurology teaching should be investigated as a potential area to remediate neurophobia.
Disclosure: The authors disclose no conflicts of interest.

Movement disorders 1

EPR-066

Relative bioavailability of levodopa given as a subcutaneous infusion with ND0612 versus oral IR levodopa/carbidopa

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Background and aims: ND0612 is in development as a continuous 24-hour subcutaneous infusion of levodopa/carbidopa for patients with Parkinson's disease experiencing motor fluctuations. In this study we determined the relative bioavailability of levodopa when administered as a subcutaneous infusion with ND0612 versus levodopa derived from oral immediate-release LD/CD (IR-LD/CD) tablets in healthy volunteers.
Methods: Single-center, single-dose, open-label, sequence-randomized, 3-period, 2-way crossover PK study in 16 healthy volunteers (11M, 5F; 18-50y) (NCT02726386). Volunteers randomized (1:1) to receive either ND0612 infused over 16h (to a total LD/CD dose of 360/45mg) followed by oral IR-LD/CD 100/25 mg QID over 15h (given every 5h to a total dose of 400/100mg), or vice versa with an intervening 6-day washout period.
Results: ND0612 subcutaneous infusion reached a steady level compared to a fluctuating plasma concentration profile characterized by multiple peaks and troughs observed throughout the day with oral IR-LD/CD given QID due to the relatively short plasma half-life of levodopa. Geometric LS mean ratios [90% CI] of both AUClast and AUCinf for ND0612 compared to oral IR LD/CD were 1.30 [1.24, 1.36]. This profile resulted in a 6-fold lower levodopa fluctuation index with ND0612 vs oral IR-LD/CD.
Conclusion: Treatment with ND0612 may provide a continuous and stable levodopa level, avoiding the peaks and deep troughs associated with oral IR-LD/CD delivery that are associated with motor fluctuations. Subcutaneous delivery of levodopa with ND0612 (360mg) showed a 1.3-fold higher bioavailability with a 6-fold lower fluctuation index as compared to oral IR-LD/CD delivery (400mg).
Disclosure: Funded by NeuroDerm. Liat Adar and Natalia Vostokova are employed by NeuroDerm.

EPR-067

Impact of GBA variants on clinical outcome of Deep brain Stimulation in a large Italian cohort of Parkinsonian patients

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Background and aims: GBA mutations are a well-known genetic risk factor for PD. We aim to explore the impact of GBA variants on the long-term outcome of deep brain stimulation (DBS) in a cohort of PD subjects who underwent DBS-surgery.
Methods: We retrospectively analysed clinical data from a multicentric Italian cohort of DBS-PD patients upon stratification for the presence/absence of GBA variants. Motor and non-motor features were recorded before surgery and after 1, 3 and 5 years.
Results: We recruited 296 DBS-PD patients, of whom 65 (22%) carried GBA variants (severe=29, mild=12, risk=16, unknown=8). Mean age at onset was 57.1±12.4yrs, mean disease duration 13,9±5.8 yrs. At pre-DBS evaluation, GBA-PD had earlier age at onset and shorter disease duration than non-mutated PD (NM-PD) but showed similar clinical features except dyskinesias (more prevalent in GBA-PD). At 3 to 5 years post-DBS, both groups showed motor improvement with satisfactory control of fluctuations and dyskinesias; all non-motor symptoms were also comparable except cognition, which worsened significantly faster in GBA-PD than NM-PD, already at 3 years from DBS. Analysis on GBA-PD stratified by mutation type are ongoing.

Conclusion: This is the first report addressing the impact of GBA variants on DBS clinical outcomes in a large well-characterized Italian PD cohort with a relatively long follow-up. Our data, although preliminary, suggest that GBA-PD patients benefit from DBS as much as NM-PD, as the frequency of motor complications is similar between the two groups. Cognitive performance, although progressively worsening in both groups, shows a more rapid deterioration in GBA-PD.
Disclosure: Nothing to disclose.

EPR-068

The Effect of non-invasive Brain Stimulation on Sense of Agency Network in Functional Neurological Disorder

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Background and aims: Disrupted sense of agency (SoA) - the sense to be the agent of own's actions - has been demonstrated in patients with Functional Neurological Disorder (FND) and a key area of the corresponding neuronal network is the right temporoparietal junction (rTPJ).Several functional-magnetic-resonance-imaging (fMRI) studies have found hypoactivation of the rTPJ in FND. Our aim was to test whether transcranial magnetic stimulation (TMS) over the rTPJ could restore this abnormal activity.
Methods: We conducted a randomized, cross-over, single-blinded trial using TMS over the rTPJ (MNI [62 -34 30]) in 23 FND patients and 19 healthy controls with 3 experimental interventions (inhibitory cTBS, excitatory iTBS and sham TMS over the vertex). During fMRI, participants played a visuomotor task manipulating the SoA (baseline vs. turbulence), repeated after each neurostimulation. We compared brain activity and behavioral SoA (subjective judgement of agency after each trial) before and after TMS.
Results: At baseline, patients showed decreased accuracy in detecting low agency compared to controls (figure 1), and lower brain activation in the rTPJ in the contrast baseline

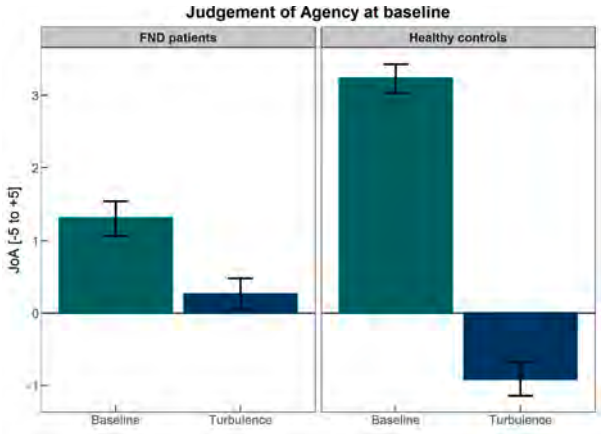

Figure 1. Baseline Comparison; Judgement of Agency. FND patients vs. healthy controls, divided according to condition (baseline vs. turbulence). Significant interaction of group and condition ($\beta = -3.10$, $t = -10.19$, $p < 0.001$). Error bars indicating SE.

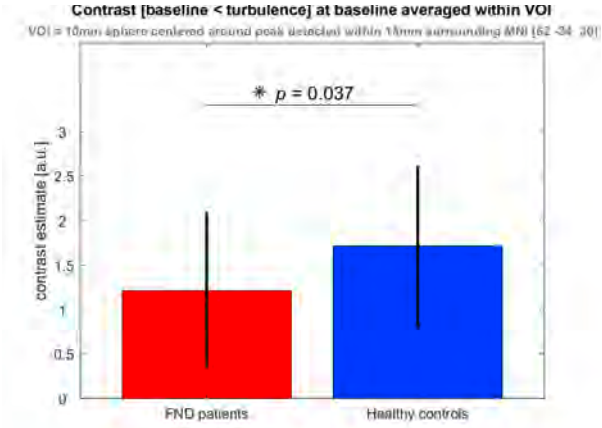

Figure 2. Baseline Comparison; VOI-Analysis. Mean contrast estimate extracted from individual VOI (rTPJ). Comparing FND patients vs. healthy controls in one-tailed 2-sample t-test ($t(40) = -1.83$, $p = 0.037$). Error bars indicating standard deviation.

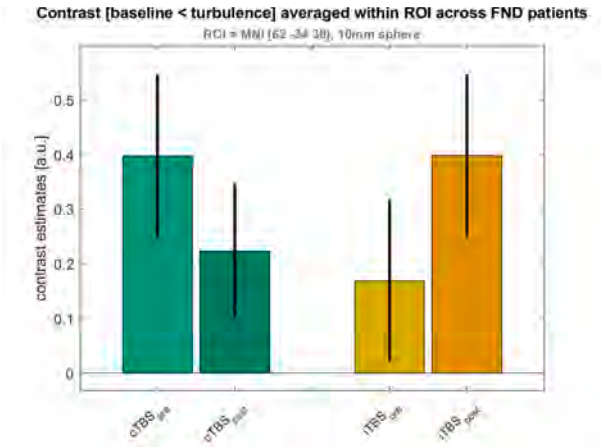

Figure 3. Stimulation Effect; ROI-Analysis. Mean contrast estimate extracted from ROI (rTPJ). Significant interaction of timepoint and stimulation ($F(1, 88) = 4.915$, $p = 0.029$). Error bars indicating standard deviation.

Conclusion: Aberrant processing of agency in FND was confirmed at baseline, reflected in self-reported judgements and in lower activity in the rTPJ. Excitatory TMS over this key-region elicited neuronal changes in patients, showing a potential to restore the abnormal processing of SoA in FND.
Disclosure: Nothing to disclose.

EPR-069

Transient resting-state salience-limbic co-activation patterns in functional neurological disorders

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Background and aims: Patients suffering from functional neurological disorders (FND) experience neurological symptoms that were historically regarded as the manifestation of a dynamic brain lesion without anatomical changes. Analysing large-scale brain network dynamics at rest offers the opportunity to explore temporal fluctuations in aberrant brain functions associated with functional neurological symptoms.
Methods: Using a two-step hierarchical approach, we first computed static functional connectivity between 17 resting-state networks in 79 FND patients and 74 healthy controls (HC). We identified increased functional connectivity between the salience-limbic networks in patients as compared to HC. These networks include two key regions - the insula and the amygdala - involved in interoception and emotion regulation, which have previously been linked to FND pathology. Second, we examined dynamic network alterations in the salience-limbic networks using co-activation pattern analysis based on the seed activity of the insula and the amygdala.
Results: Overall, we identified insular co-(de)activation patterns related to the default mode network (DMN), the somatosensory and the interception network, as well as amygdalar co-deactivation patterns with the DMN. Patients and HC differed regarding how often they visited the state characterized by the insular co-activation of the interoceptive network, and the state characterized by the amygdalar co-deactivation with the DMN (patients less frequently than HC). Insular-interoception network and amygdalar-DMN temporal dynamics negatively correlated with symptom severity.
Conclusion: Functional alterations involving salience-limbic network interactions play a role in the pathophysiology of FND and longitudinal studies should verify if this is a trait or state-marker of the disorder.
Disclosure: Nothing to disclose.

EPR-070

Association between dopamine depletion of striatal sub-regions and motor dysfunction in Parkinson's disease

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Background and aims: The association between putaminal dopamine depletion and motor dysfunction is well documented in Parkinson's disease (PD), but not for other striatal regions. This study aimed to explore how dopamine depletion of different striatal regions (putamen, caudate, ventral striatum [VS]) differentially contribute to motor impairments in prodromal and clinical PD.
Methods: Data of 223 prodromal and 250 clinical PD patients were downloaded from the Parkinson's Progression Marker Initiative (PPMI.org). Standardized uptake value ratios (SUVRs) were extracted from dopamine transporter SPECTs using the Oxford-GSK-Imanova structural striatal atlas. MDS-UPDRS-III scores were used to quantify motor dysfunction. First, regional SUVRs were compared between groups and correlated with motor scores. Next, the groups were matched according to putamen SUVR and correlation analyses were repeated in the sub-cohort. Finally, moderation analyses were conducted to assess whether caudate or VS SUVR mitigate the association between putaminal dopamine depletion and motor dysfunction in the prodromal and clinical group.
Results: SUVRs of all three striatal sub-regions significantly decreased with disease progression. Reduced putaminal SUVRs were related to worse motor scores. In the entire and matched groups, neither the caudate nor the VS SUVRs were significantly related to motor scores. Moreover, no significant moderation effect of either caudate or VS SUVRs was found regarding the relationship between putamen SUVRs and motor scores in the prodromal or clinical cohort.
Conclusion: Dopamine loss in the putamen seems to be closely connected to motor dysfunction in PD, whereas this does not seem to apply for the caudate or VS.
Disclosure: Project was supported by the German Research Foundation. ID: 431549029—SFB 1451.

EPR-071

Cerebrospinal fluid synaptic biomarkers in AT(N)-based subgroups of Lewy body disease

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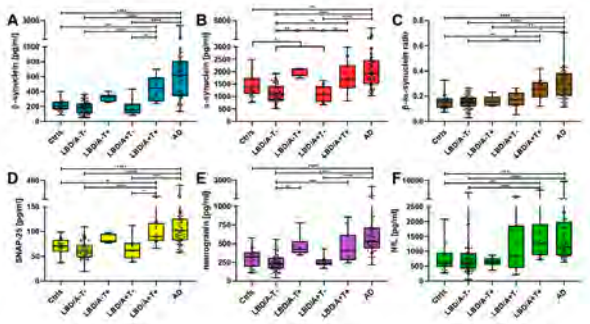
Background and aims: We aimed to investigate whether CSF biomarkers of synaptic and neuro-axonal damage are correlated with the presence of AD co-pathology in LBD and can be useful to differentiate LBD patients with different AT(N) profiles.
Methods: We retrospectively measured CSF levels of AD core biomarkers (Aβ42/40 ratio, p-tau, t-tau) and of synaptic (β-synuclein, α-synuclein, SNAP-25, neurogranin) and neuro-axonal proteins (NfL) in 28 cognitively unimpaired participants with non-degenerative neurological conditions and 161 participants with a diagnosis of either LBD or AD (at both mild cognitive impairment, AD-MCI, and dementia stages, AD-dem). We compared CSF biomarker levels in clinical and AT(N)-based subgroups.
Results: CSF β-synuclein, α-synuclein, SNAP-25, neurogranin and NfL levels did not differ between LBD (n=101) and controls and were increased in AD (AD-MCI n=30, AD-dem n=30) compared to both groups ($p<0.001$ for all comparisons). In LBD, we found increased levels of synaptic and neuro-axonal degeneration biomarkers in patients with A+T+ (LBD/A+T+) than with A-T- profiles (LBD/A-T-) ($p<0.01$ for all), and β-synuclein showed the highest discriminative accuracy between the two groups (AUC=0.938, 95%CI: 0.884-0.991). CSF β-synuclein ($p=0.0021$), α-synuclein ($p=0.0099$) and SNAP-25 concentrations ($p=0.013$) were also higher in LBD/A+T+ than in LBD/A+T- cases, which had synaptic biomarkers



CSF biomarkers across AT(N)-based subgroups of LBD.

Conclusion: LBD/A+T+ and AD cases showed significantly increased CSF levels of synaptic and neuro-axonal biomarkers compared to LBD/A-T- and control subjects. LBD patients with AD co-pathology might, thus, experience similar degrees of synaptic dysfunction than pure AD cases.
Disclosure: Nothing to declare.

EPR-072

Detection of non-motor fluctuations in PD using the electrodermal activity

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Background and aims: Multiple biosignals are used to assess, treat, and monitor the status of people with Parkinson's disease (PD). To evaluate the sympathetic activation, the most used biomarker is the electrodermal activity (EDA). Previous studies have found a relationship between EDA and motor fluctuations in PD (Nene et al. 2019), but its usefulness to accurately detect them remains unexamined. This study has the purpose of determining the ability of EDA measures to detect non-motor fluctuations in people with PD by assessing changes of EDA values in ON and OFF states.
Methods: In this observational study, 18 people with PD participated (13 females, mean age = 60.12±12.41 years, Hoehn and Yahr (H&Y) 1-3). EDA was captured using the Empatica E4 device, placed on the wrist, and was continuously recorded in ON and OFF states. The cleaned signal was analyzed with 3 different approaches.
Results: In the time domain, there were trends for higher EDA values in OFF state in comparison to ON state (mean = 2.07±2.2 μS vs 1.27±1.66 μS,) only in people with H&Y ≥ 2 (n=13). Similarly, in the frequency domain, higher power average values were found in OFF state in comparison to ON state (mean = 5.16±10.98 μS2/Hz vs. 10.77±19.84 μS2/Hz), only in people with moderate and severe PD.
Conclusion: Sympathetic activation changes assessed with EDA measures could be of great value for the detection of non-motor fluctuations in PD and potentially could also be used to rate the evolution of the disease.
Disclosure: Nothing to disclose.

EPR-073

A systematic analysis of minipolymyoclonus in a cohort of patients with various neurological disorders

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Background and aims: Minipolymyoclonus is specific type of myoclonus, which is defined as intermittent, arrhythmic involuntary movements that involve only fingers or, more rarely, the entire hand at the beginning of a posture or movement. In this study, we aimed to evaluate frequency, clinical and electrophysiological features of minipolymyoclonus.

Methods: We retrospectively evaluated the medical records of cases who underwent polymyographic analysis in our laboratory between 2010 and 2022. Among them, we identified clinical and electrophysiological features of patients with irregular, jerky, involuntary movements in the fingers or hands and myoclonic discharges at different amplitudes in the distal hand muscles on clinical examination and polymyography.

Results: Minipolymyoclonus was detected in 25 patients among 163 patients (mean age: 56±20.2 years; age range 17 and 84 years; 6 women). There were patients with multisystem atrophy (n=6), Parkinson's disease (n=3), other movement disorders (n=3), amyotrophic lateral sclerosis (n=1), hereditary polyneuropathy (n=5), chronic inflammatory polyneuropathy (n=4) and acute inflammatory polyneuropathy (n=3). EMG bursts were in sequential patterns. EMG burst durations were between 50-100 ms. and often discharged simultaneously in several muscles of the same limb. C reflex was detected in three patients. Giant SEP was not detected.

Conclusion: Our findings suggest that minipolymyoclonus is a non-specific phenomenon that can accompany many neurological manifestations. Detection of the C reflex in only 3 patients suggests that the cortical component is rarer.

Disclosure: Nothing to disclose.

EPR-074

Efficacy and safety of foslevodopa/foscarbidopa subcutaneous infusion in patients with prior deep brain stimulation

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Background and aims: In advanced Parkinson's disease (PD), chronic oral levodopa therapy often leads to motor fluctuations and dyskinesia. In patients with suboptimal control despite optimized oral medications, device-aided therapies like deep brain stimulation (DBS) or foslevodopa/foscarbidopa subcutaneous infusion can alleviate motor fluctuations.

Methods: This post-hoc analysis of a 52-week, open-label, single-arm foslevodopa/foscarbidopa clinical trial (NCT03781167) evaluated baseline characteristics, various outcomes, and the safety profile of patients with or without prior DBS therapy. Trial eligible patients were ≥30 years of age with idiopathic levodopa-responsive PD and an average daily "Off" time ≥2.5 hours. An analysis of covariance (ANCOVA) model was utilized to compare outcomes change from baseline to final available visit (least squares mean).

Results: Of 244 total patients, 24 (9.8%) had been previously treated with DBS while 220 (90.2%) had not. Patient demographics, outcomes, and safety are shown in Tables 1-3, respectively. Patients with prior DBS had a longer disease duration and more impaired speech and gait (single items of the Movement Disorders Society-Unified Parkinson's Disease Rating Scale [MDS-UPDRS] Parts II and III) at baseline. MDS-UPDRS Part II score (Activities of Daily Living) and the speech-related item improved significantly more in the non-DBS group, while other outcomes including "Off" time and "On" time without troublesome dyskinesia measured at the final available visit did not differ significantly based on prior DBS treatment. Safety profiles of the two groups were generally similar.

Table 1 - Summary Demographics and Baseline Characteristics Between Patients With and Without Prior DBS Treatment (FAS)

Parameter	Prior DBS (N=24)	No Prior DBS (N=220)	P Value[a]
Age, years, mean (SD)[b]	64.33 (6.391)	63.86 (9.441)	0.8124
Parkinson's Disease Duration Group, n (%)[c]			
<10 years	4 (16.7)	127 (57.7)	0.0001*
≥10 years	20 (83.3)	93 (42.3)	
Average Normalized "Off" Time, hours, mean (SD)[b]	5.56 (2.128)	5.95 (2.258)	0.4309
Average Normalized "On" Time With Troublesome Dyskinesia, hours, mean (SD)[b]	1.12 (1.447)	0.94 (1.758)	0.6212
Average Normalized "On" Time Without Troublesome Dyskinesia, hours, mean (SD)[b]	9.31 (2.671)	9.12 (2.488)	0.7151
MDS-UPDRS Part II Score, mean (SD)[b]	16.63 (7.383)	15.67 (7.390)	0.5475
Speech, mean (SD)[d]	1.92 (0.929)	1.41 (1.105)	0.0351*
Walking and Balance, mean (SD)[d]	2.00 (1.022)	1.57 (1.060)	0.0533
MDS-UPDRS Part III Score, mean (SD)[b]	26.38 (12.860)	23.18 (11.291)	0.1957
Speech Problems, mean (SD)[d]	1.04 (0.624)	0.83 (0.705)	0.1252
Gait, mean (SD)[d]	1.33 (0.917)	0.95 (0.869)	0.0283*
PDQ-39 Summary Index Total Score, mean (SD)[b]	36.99 (14.008)	34.23 (15.117)	0.3935

DBS, deep brain stimulation; FAS, full analysis set; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale; N, number of patients in the treatment category; n, number of patients in the individual parameter; PDQ-39, Parkinson's disease questionnaire 39 item; SD, standard deviation
[a] Statistical comparisons between the Prior DBS and No Prior DBS groups are limited by the sample size imbalance of the two groups
[b] Continuous variables compared using a t-test
[c] Fisher's exact test was used for categorical variables
* Statistically significant difference between patients with Prior DBS versus No Prior DBS
[d] P value for the MDS-UPRDS Part II and Part III single item scores is based on Wilcoxon rank-sum test

Table 2 - Outcomes of Summary and Model-Based Statistics in Patients With and Without Prior DBS Treatment (FAS)

	Summary Statistics				Model-Based Statistics[a]				
Parameter	Prior DBS (N=24) Mean (SD) Difference from Baseline	No Prior DBS (N=220) Mean (SD) Difference from Baseline	Prior DBS (N=24) Within Group P Value[bc]	No Prior DBS (N=220) Within Group P Value[bc]	Prior DBS (N=24) LS Mean (SE)	No Prior DBS (N=220) LS Mean (SE)	LS Mean of Difference (SE)	95% CI	Two-Sided P Value[b]
MDS-UPDRS Part II Score	**0.83 (6.211)**	**-2.27 (6.850)**	**0.5175**	**<0.0001***	**1.13 (1.29)**	**-2.30 (0.43)**	**3.43 (1.36)**	**(0.76, 6.11)**	**0.0122***
Speech	0.13 (0.992)	-0.32 (0.951)	0.5430	<0.0001*	0.33 (0.17)	-0.35 (0.06)	0.67 (0.18)	(0.32, 1.03)	0.0002*
MDS-UPDRS Part III Score	5.08 (12.303)	3.61 (12.602)	0.0551	<0.0001*	5.49 (2.56)	3.57 (0.84)	1.93 (2.69)	(-3.38, 7.23)	0.4752
Average Normalized "Off" Time, hours[d]	-1.96 (3.435)	-2.45 (3.824)	0.0102*	<0.0001*	-2.21 (0.70)	-2.42 (0.24)	0.21 (0.74)	(-1.25, 1.68)	0.7756
Average Normalized "On" Time With Troublesome Dyskinesia, hours[d]	-0.60 (1.914)	-0.26 (2.209)	0.1356	0.0877	-0.50 (0.37)	-0.27 (0.12)	-0.22 (0.39)	(-0.99, 0.54)	0.5705
Average Normalized "On" Time Without Troublesome Dyskinesia, hours[d]	2.57 (3.328)	2.71 (3.939)	0.0010*	<0.0001*	2.68 (0.74)	2.70 (0.25)	-0.02 (0.78)	(-1.57, 1.52)	0.9751
PDSS-2 Total Score*	-2.62 (9.271)	-6.26 (10.976)	0.2102	<0.0001*	-4.36 (1.94)	-6.06 (0.66)	1.70 (2.05)	(-2.35, 5.75)	0.4089
PDQ-39 Summary Index Total Score*	-2.34 (13.758)	-5.68 (13.957)	0.4447	<0.0001*	-1.23 (2.89)	-5.81 (0.99)	4.58 (3.05)	(-1.44, 10.61)	0.1349

CI, confidence interval; DBS, deep brain stimulation; FAS, full analysis set; LS, least squares; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale; N, number of patients in the treatment category; PDQ-39, Parkinson's disease questionnaire 39 item; PDSS-2, Parkinson's disease sleep scale-2; SD, standard deviation; SE, standard Error
[a] Analysis of Covariance (ANCOVA) was used to compare change from baseline to final available visit (LS Mean), and ANCOVA model: change = DBS – group baseline
[b] Statistical comparisons between the Prior DBS and No Prior DBS groups are limited by the sample size imbalance of the two groups
[c] Within group P value comes from one-sample t-test
* P value ≤0.05
[d] Average Normalized "Off" Time, Average Normalized "On" Time With Troublesome Dyskinesia, and Average Normalized "On" Time Without Troublesome Dyskinesia summary and model-based statistics for No Prior DBS were calculated based on n=209 patients
* PDSS-2 and PDQ-39 summary and model-based statistics were calculated based on n=21 patients for Prior DBS and n=179 patients for No Prior DBS

Table 3 - Summary of Safety Analyses in Patients With and Without Prior DBS (SAS)

AE Category, n (%)	Prior DBS (N=24)	No Prior DBS (N=220)
Premature discontinuation of the study	8 (33.3)	87 (39.5)
Premature discontinuation of foslevodopa/foscarbidopa	8 (33.3)	99 (45.0)
Any TEAE	21 (87.5)	209 (95.0)
Any severe TEAE	11 (45.8)	52 (23.6)
Any serious TEAE	8 (33.3)	55 (25.0)
Any TEAE considered associated with study drug	20 (83.3)	204 (92.7)
Any TEAE leading to premature discontinuation of study drug	4 (16.7)	60 (27.3)
Any TEAE leading to death	0 (0)	3 (1.4)

AE, adverse event; DBS, deep brain stimulation; SAS, safety analysis set; TEAE, treatment-emergent adverse event

Conclusion: Overall, the efficacy and safety profile of foslevodopa/foscarbidopa in patients with or without prior DBS was similar.

Disclosure: Abstract support provided by AbbVie Inc.

Epilepsy

EPR-075

Number of seizure-free days with adjunctive cenobamate: post-hoc analysis of an open-label extension study

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Background and aims: Cenobamate, an antiseizure medication (ASM), is approved in Europe as adjunctive therapy for adults with inadequately controlled focal seizures. Study NCT01866111 (C017) was an international double-blind, placebo-controlled clinical trial with an open-label extension (OLE) that evaluated adjunctive cenobamate in adults with uncontrolled focal seizures. Long-term efficacy of cenobamate was evaluated by percent seizure frequency reduction and responder rates. Reduction in seizure burden measured as the percentage of seizure-free days provides an additional characterization of cenobamate efficacy.
Methods: Adults with focal seizures despite treatment with 1-3 concomitant ASMs completed the double-blind treatment period with ≥1 year of follow-up. A post-hoc analysis of seizure-free days in the OLE phase of study C017 compared baseline and postbaseline percentage of seizure-free days.
Results: As of June 2020, 206 participants who entered the C017 OLE had completed ≥4 years of follow-up. Patients taking cenobamate experienced 86.3% seizure-free days compared with 64.4% at baseline. Overall, for participants taking cenobamate throughout the OLE, the odds ratio for having seizure-free days was 3.47 compared to baseline. Results remained consistent throughout the OLE period. The percentage of seizure-free days at year 1 was 83.7% (N=354); year 2, 86.2% (N=272); year 3, 87.3% (N=237); year 4, (87.8% (N=221); and year 5, 88.6% (N=206).
Conclusion: This post-hoc analysis of seizure-free days during the C017 OLE study further supports the efficacy of cenobamate by demonstrating sustained improvement in the percentage of seizure-free days compared to baseline. Treatment with cenobamate can reduce the day-to-day seizure burden in patients with inadequately controlled focal seizures.
Disclosure: The original study (NCT01866111) was supported by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini S.p.a. (Rome, Italy).

EPR-076

First seizure event: high yield of long-term EEG and MRI

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Background and aims: To establish how an advanced work-up including long-term EEG (LT-EEG) and brain MRI increases the accuracy in the diagnosis of first seizure events (FSE) in new onset epilepsy (NOE) when compared to a routine work-up (standard EEG and brain CT).
Methods: Retrospective analysis of adult patients presenting with FSE in the ED between 1.3.2010 and 1.3.2017. MRI and/or LT-EEG were carried out as part of the initial work-up. We excluded patients with obvious non-epileptic or acute symptomatic seizures. Patients were followed for 2 years.
Results: Using the comprehensive battery of exams, 90% of a total of 1010 patients obtained a definite diagnosis (NOE 49.4%). LT-EEG within the first week after the index event, compared to a later time-point, was associated to better interictal epileptiform discharges (IED) identification (p=0.08). LT-EEG and MRI provided an additional yield to routine work-up of 50% and 19%, respectively. The combination of MRI and LT-EEG was the most powerful and only 2.5% NOE patients would have been missed. False negative findings were noted in only 0.8% of patients.
Conclusion: Our results suggest an excellent yield of advanced work-up of FSE both for the presence and of absence of NOE. The use of this advanced workup, together with specialist consultations outside neurology whenever necessary were strongly associated to final diagnosis during the first 2 years. Our findings suggest the benefit of first-seizure units, similar to stroke units, active upon admission in the ED.
Disclosure: Nothing to disclose.

EPR-077

Cenobamate in real-life setting: Final outcomes of an expanded access program

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Background and aims: Early real-life experience of antiseizure medication (ASM) is provided by Expanded Access Program (EAP). This work reports final outcomes of EAP with cenobamate (CBM) in a large series of patients with epilepsy.

Methods: This is a multicenter, retrospective, observational study in 14 Spanish hospitals. Inclusion criteria were: ≥18 years; focal seizures; EAP authorization. Data source was clinical records. Time-points analyzed were baseline, 3, 6, and 12 months. Patients with ≤3 months of follow-up were excluded.

Results: We included 170 patients. At baseline, mean epilepsy duration was 26 years, mean seizures/month was 23, mean(range) of prior ASM was 12,1 (4-20) and mean of concomitant ASM was 3,2. Mean dosage/day was 175,8 mg (3 months) , 200,2 mg (6 months), and 250 mg (12 months). Retention rate was 98,2% [3 months (167/170)], 94,5% [6 months (120/127)] and 87% [1 year (40/46)]. At last visit seizure-freedom was 13.3%, ≥90% responder 27,9%, ≥75% responder 45.5% and ≥50% responder 63%. Responses were maintained regardless of prior or concomitant ASM. Number of concomitant ASM was reduced in 44,7% of patients. Cumulative percentage of patients with adverse events (AE) and those that led to discontinuation were 68,2% and 3.5% at 3 months, 74,1% and 4.1% at 6 months and 74,1% and 4.1% at 12 months. Most frequent AE were somnolence, dizziness, memory disturbances and ataxia.

Conclusion: Outcomes in a refractory population with epilepsy treated with CBM showed a high response regardless of prior and concomitant ASM. AE were reported in high proportion of patients but few led to discontinuation.

Disclosure: This study has been supported by Angelini Pharma España, S.L.U.

EPR-078

A prospective population-based study of the incidence of status epilepticus according to the new definition.

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Background and aims: Until 2008, the definition of SE included an epileptic seizure lasting more than 30 minutes or a series of seizures without complete recovery of consciousness. Based on that definition, the incidence was given with 17,1/100 000 for Germany. It is now recommended in appropriate guidelines that consistent treatment of generalized SE should be started after five minutes of clinical seizure activity.

Methods: According to the study in 2001, a prospective population-based study was conducted from 2018 to 2020. 181 adult patients were included who lived in the postal code area 35xxx, which can be considered representative for Germany, as well as a selected urban area “A”, due to its population structure and suffered a seizure of at least 5 minutes duration or repeated seizures without recovery. A follow-up was performed approximately 30 days after discharge.

Results: The incidence of SE in urban area A was 28.1/100 000. It was higher in men than in women and higher in persons > 60 years than < 60. Most patients (43%) had an acute etiology, mainly acute cerebrovascular (17.16%). The 30-day lethality in area A was 5.6%. The overall 30-day lethality in the 35xxx zip code area studied was 11.6%.

Conclusion: This study provides the first epidemiological data on the new definition of SE in Germany. Compared to the incidence using the old definition in 2001, an increase in the incidence in adults occurred. It is likely that the change in definition plays an important role in the increasing incidence.

Disclosure: Nothing to disclose.

EPR-079

Clinical practice guidelines in the field of rare and complex epilepsies

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Background and aims: The EU-funded EpiCARE network aims to develop guidelines (CPGs) for diagnosis and management of rare and complex epilepsies in collaboration with the International League Against Epilepsy, European Academy of Neurology and European Pediatric Society. In this study, we aimed to identify the quality of existing guidelines and areas were guidleine development is needed.
Methods: A standardized questionnaire was distributed to 32 centers of the EpiCARE network across 17 European countries. Quality of selected guidelines were assessed by using Appraisal of Guidelines Research and Evaluation (AGREE) II instrument. Cutoff of 70% for each AGREE II standardized domain score was set. Guidelines were considered of high quality if a score was more than 70% across all domains.
Results: Complete responses were received from 27/32 (84%) centers. Overall, 80 documents were collected. The 21 (12 in English and 9 in 6 different languages) guidelines were included in AGREE II assessment. Only 5/21 guidelines were classified as high quality guidelines. The overall assessment of guidelines ranged between 2 to 7 on the 7-point scale. Most of included guidelines scored low in Applicability and half of these guidelines failed to report appropriate conflict of interest disclosures. Of the 21 guidelines, 6 were recommended for use.
Conclusion: Our study shows that very few of collected documents actually meet the criteria of a clinical practice guideline. Furthermore methodological rigor and reporting quality of existing guidelines often fail to fulfil the AGREE II criteria. Thus, the need for standardized guidelines and recommendations is particularly high.
Disclosure: Nothing to disclose.

EPR-080

Long-term outcomes of autoimmune encephalitis with NORSE presentation

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Background and aims: New-onset refractory status epilepticus (NORSE) can be the presenting symptom in about half of the patients with autoimmune encephalitis (AE). In this study, we assessed predictors for developing chronic epilepsy as the outcome in the long-term of definite or probable AE with NORSE presentation.
Methods: Patients with definite or probable AE with NORSE as the presenting symptom were enrolled in this retrospective observational multicenter cohort study.

Results: Sixty-six patients (22 children, 44 adults) were selected and followed up for a median time of 32.5 months (range: 12-192). Six patients died during the SE. At the final follow-up, epilepsy was present in 46% with a prevalence in probable antibody-negative AE (p=0.001) and patients with older age at SE onset (p=0.04). Early immunotherapy (p=0.006) and the administration of second-line agents (p=0.01) were associated with seizure freedom. A poor response to immunotherapy during the acute phase (p=0.004), and a longer duration of SE (p=0.01) were significantly related to the development of autoimmune-associated epilepsy. Most patients developing epilepsy (85.71%) had neuropsychiatric symptoms (p=0.005). In the multivariate analysis, the independent predictor of developing autoimmune-associate epilepsy was probable antibody-negative AE (p=0.02).
Conclusion: Patients with defined or probable AE may develop autoimmune-associated epilepsy in 43.73% of cases. Clinical presentation with NORSE is an unfavorable prognostic factor, with the risk of developing epilepsy in approximately half of the cases. Early identification of the etiology of the status epilepticus and the prompt institution of tailored treatment is associated with a more favorable outcome.
Disclosure: Nothing to disclose.

EPR-081

Manegement of Non-Convulsive Status Epilepticus: data from the STatus Epilepticus project in Emilia-Romagna, Italy.

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Background and aims: Status Epilepticus (SE) is a neurologic emergency with high mortality and morbidity rates. The aim of our study was to evaluate the clinical features and outcomes of Non-Convulsive SE (NCSE) in Emilia-Romagna, northern Italy.
Methods: Prospective multicentric observational study of adults patients with NCSE. Data collection occurred from October 2019 to October 2021 in 17 Italian neurology units. The diagnosis and classification of NCSE were done accordingly to the 2015 ILAE proposal. Categorial variables were analysed with X2 test, whereas parametric or non-parametric tests were used to analyse continuous variables, as appropriate.
Results: 285 NCSE episodes were included (64% female; mean age: 71.6 ± 14.9 y/o), 157 of whom occurred outside the hospital setting. Cerebrovascular diseases (80/285; 28%), brain tumors (25/285; 9%) and anoxic brain injury (21/285; 7%) were the most frequent causes of NCSE. Median times from NCSE onset to EEG execution and treatment initiation were 11.1 and 10.3 hours, respectively. Even if 47% of cases were refractory to first- and second-line agents, SE finally resolved in all but 15 cases. On the other hand, 30-day mortality rate was 24% and it significantly increased in case of in-hospital onset (p=0.0001), severe consciousness impairment (p<0.0001), acute symptomatic aetiologies (p=0.01) and SE refractoriness (p=0.009).
Conclusion: Our prospective multicentric study confirmed that the diagnosis and treatment of NCSE are challenging with extremely prolonged time-to-evaluation and treatments times. NCSE aetiology and clinical features, as well as treatment refractoriness, are confirmed to be strong predictors of short-term outcome.
Disclosure: This study was funded by the grant "STEPPER–bando 2016 Ricerca finalizzata ordinaria RF-2016-02361365" by the Italian ministry of Health. STEPPER Study Group: M. Zanello, S. Mazzoni, MC. Casadio, A. Zini, E. Pasini, M. Tappatà, M. Romoli, C. Coniglio, R. Rinaldi, P. De Massis, I. Naldi, , G. Turchi, A. Marudi, G. Monti, A. Pignatti, R. Rizzi, M. Russo, I. Florindo, L. Zinno, V. Tontini, E. Picetti, C. Giorgi, E. Fallica, E. Cesnik, M. Pugliatti, E. Marchesi, C. Bomprezzi, Y. Bartolini, G. Bini, C. Leta, D. Passarelli, A. Guidi, FD. Baccarini, M. CurròDossi, G. Bernabè, F. Ceccaroni, M. Volpini.

EPR-082

Perampanel as only add-on epilepsy treatment in elderly patients: real-world data from multicenter study

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Background and aims: Management of epilepsy in elderly individuals represent a common situation in daily practice due to the rapid growing of this segment of population. Older people with epilepsy (PWE) show peculiar characteristics compared with younger ones. The aim of this study was to assess 12-month effectiveness and tolerability of adjunctive perampanel (PER) in elderly PWE (≥65 years of age) treated in a real-world setting.
Methods: This study was a subgroup analysis of elderly PWE included in a previous 12-months multicenter study including PWE receiving PER as only add-on treatment. Seizure response (≥50% reduction of frequency), seizure-freedom, retention rate, incidence of adverse events (AEs) and rate of treatment discontinuation were recorded at 3.6

and 12 months after PER introduction.
Results: The sample included 64 subjects (34 female, 53.1%; median age: 74.6 years), with focal (87.5%), generalized (10.9%) and undetermined (1.6%) epilepsy. Median daily doses of PER at 3, 6, and 12 months were 4, 6, and 8 mg, respectively. At 12 months, 18/27 (66.7%) patients had at least 50% reduction of seizure frequency, with a seizure freedom rate of 9/27 (33.3%). Retention rate was 89.1%, 80.8%, and 70.3% after 3, 6, and 12 months, respectively. The reasons of treatment withdrawal were insufficient efficacy in 3 (4.7%) patients and poor tolerability in 7 (10.9%) patients. AEs were reported by 27 (42.2%) patients, but only one serious AEs was noticed.
Conclusion: Adjunctive PER was efficacious and generally well tolerated in elderly PWE in clinical practice and can represent a suitable therapeutic option.
Disclosure: Nothing to disclose.

EPR-083

Random Forests algorithm predicts two-year seizure recurrence after Status Epilepticus

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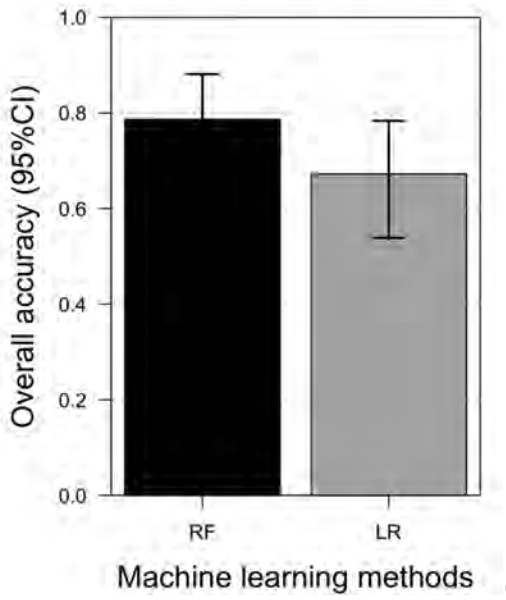
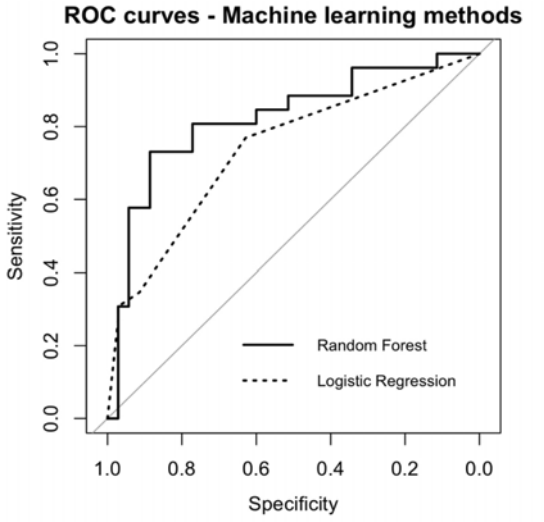
Background and aims: Tools to predict seizure recurrence after Status Epilepticus (SE) are lacking. Random Forests (RF) is a Machine Learning (ML) technique that, from an input feature, generates multiple bifurcating decision trees to return an expected output from the ensemble. In this study, we explored the ability of RF algorithm to predict two-year seizure recurrence after SE.
Methods: Consecutive SE episodes in patients aged ≥16 years without previous history of seizures admitted to Vall d'Hebron Hospital (Barcelona, Spain) from 2011 to 2021 were reviewed. Random Forests technique was trained to predict two-year seizure recurrence. 70% of the sample was randomly selected to train the model; the remaining 30% was used for validation. Its predictive capability was compared to Logistic Regression (LR) model prediction using the area under the receiver operating characteristic curve (AUROC) with 95% confidence interval (95%CI).
Results: From 846 total patients, 268 were included, of which 88 (32.8%) developed a new unprovoked seizure within two years. Factors significantly associated with seizure recurrence were progressive symptomatic SE etiology ($p<0.001$), EEG pattern ($p=0.047$), and time to SE treatment >1.5 hours ($p=0.001$). The RF algorithm showed an overall accuracy of 78.7% in the validation dataset, compared to 67.2% in LR model. The RF was accurate in predicting seizure recurrence, with an AUROC of 0.822 (95%CI = 0.709–0.935), compared to the LR model (AUROC 0.738, 95%CI = 0.618–0.858).



Graphic showing the superior overall accuracy of Random Forests (RF) algorithm compared to logistic regression (LR) in predicting two-year seizure recurrence after Status Epilepticus (RF overall accuracy 78.7%, LR overall accuracy 67.2%).



Area Under the Receiver Operating Carachteristic Curve (AUROC) with 95% confidence interval (95%CI) of Random Forests and of Logistic Regression models of two-year seizure recurrence after Status Epilepticus prediction.

Conclusion: In our study, the RF algorithm was superior to the LR model in predicting two-year seizure recurrence after SE in adults without previous history of seizures.
Disclosure: The authors report no disclosures.

Neuro-ophthalmology/ neuro-otology 1

EPR-084

Visual fixation-induced hemi-seesaw nystagmus

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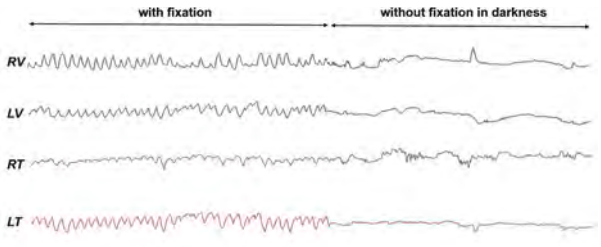
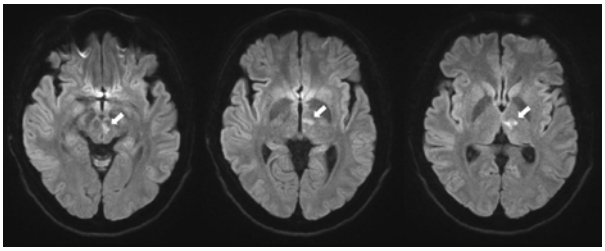
Background and aims: Seesaw nystagmus is a conjugate torsional nystagmus with dissociated vertical components. The jerky seesaw nystagmus may be related to the ocular-tilt reaction or an imbalance in the vestibular pathways. We report a patient with hemi-seesaw nystagmus due to unilateral meso-diencephalic infarction that becomes apparent during visual fixation only.
Methods: A 36-year-old male presented with acute dizziness, diplopia and dysarthria.
Results: Ocular motor examination revealed bilateral upward gaze palsy with partial impairment of downward gaze, which were not overcome by the doll's head maneuver. Horizontal gaze was intact and pupils were equal and reactive to the light. Eye movement recording using three-dimensional video-oculography showed hemi-seesaw nystagmus during visual fixation, consisting of intorsional upbeat nystagmus in the right eye synchronous with extorsional downbeat nystagmus in the left eye (counterclockwise from the patient's perspective). The frequency of the nystagmus was consistently 2 Hz. The amplitudes of torsional component was larger in the left eye than the right eye, but vertical component was opposite. The slow phases of the nystagmus mostly showed exponentially decreasing waveforms, except for the vertical component of the left eye with linear waveforms. The nystagmus disappeared completely in darkness when visual fixation was removed. MRI of the brain exhibited an acute infarction at the left medial thalamus and upper midbrain. The hemi-seesaw nystagmus resolved a day later.



Three-dimensional video-oculography shows hemi-seesaw nystagmus during visual fixation, consisting of counterclockwise torsional nystagmus (from the patient's perspective) with upbeat nystagmus in the right eye and downbeat nystagmus in the left eye



MRI scans of the brain reveal an acute infarction at the left medial thalamus and upper midbrain.

Conclusion: In our patient, damage of the dorsoterminal nucleus could have blocked the transmission of retinal error signals caused by binocular vertical misalignment, leading to the visual modulation of hemi-seesaw nystagmus.
Disclosure: We have no disclosure of any competing interest.

EPR-085

Retinal degeneration in MOG antibody Associated Disease (MOGAD): a longitudinal OCT (Optical Coherence Tomography) study

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Background and aims: We analysed longitudinal dynamics of MOG antibodies and OCT parameters(Ganglion Cell Layer GCL and Retinal Nerve Fibre Layer RNFL thicknesses) in MOGAD patients. We compared GCL and RNFL thicknesses and dynamics between MOGAD and relapsing remitting multiple sclerosis(RRMS) patients.
Methods: Prospective and retrospective monocentric study(IRCCS Mondino Foundation, Pavia). 16 MOGAD patients(mean age 38 years, EDSS 1.8, FU duration 49 months, 8/16 with relapsing disease, 11/16 with history of optic neuritis ON+). 21 RRMS patients(mean age 34 years, EDSS 1, FU duration 40 months).
Results: In 5/8 MOGAD relapsing patients, clinical relapse occurred in concomitance with an increasing in MOGab titres. No significant correlation between MOGab titres at baseline and mean GCL and RNFL thicknesses, and between MOGab titres and OCT thicknesses variation rates was found. A strong positive association between annualized GCL variation rate and the relapsing course of MOGAD(p-value=0.01) and with disability progression(p-value=0.03) was found. In ON- patients, a significantly higher annualized GCL variation rate in the group of MOGAD patients was found(p-value=0.03).

Conclusion: In MOGAD, the occurrence of a clinical relapse is often preceded by an increasing in MOGab titres and retinal degeneration is higher in all-cause relapsing patients; all patients experiencing disability progression showed increased MOGab titres at the end of FU and faster GCL thinning rates; thus, retinal degeneration and disability progression could be the result of recurrent relapses. In ON-patients, retinal degeneration seems to be higher in MOGAD than in RRMS, allow us to question if a pure neurodegenerative process could exist in MOGAD.
Disclosure: Nothing to disclose.

EPR-086

Acute Vestibular Symptoms in Supratentorial Stroke

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Background and aims: To investigate the prevalence, clinical characteristics, and anatomical correlation of acute vestibular symptoms in supratentorial stroke.
Methods: We conducted a prospective multicenter observational study that had recruited patients with supratentorial stroke presenting acute vestibular symptoms from referral-based 4 university hospitals in Korea. All patients received a constructed neuro-otological evaluations, and neuroimaging.
Results: Of 1,301 patients with supratentorial stroke, 48 (3.7%) presented with acute vestibular symptoms, and 13 of them (1%) had the vestibular symptoms in isolation. In 48 patients with acute vestibular symptoms, abnormal findings included spontaneous nystagmus (5%), impaired horizontal smooth pursuit (41%), and abnormal tilt of the subjective visual vertical (SVV) (20%). Video head impulse and caloric tests were normal in all the patients. Patients had lesions in various cortical or subcortical areas responsible for vestibular information processing without lateralization (48% in the right), even in patients with vertigo (42% in the right). The 13 patients with isolated vestibular symptoms showed ipsilesional spontaneous nystagmus (n=1), impaired horizontal smooth pursuit (n=5), or abnormal contralesional SVV tilt (n=1).
Conclusion: Acute vestibular symptoms may be reported in 3.7%, and may be isolated in 1% of supratentorial stroke. The widespread lesions responsible for acute vestibular symptoms implicate diffuse vestibular cortical-subcortical networks in the cerebral hemispheres without a lateralization.
Disclosure: There is no disclosure.

EPR-087

Loss of Torsional Quick Phases During Head Oscillation in the Roll Plane in Progressive Supranuclear Palsy

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Background and aims: To determine the diagnostic value of decreased torsional quick phases during head oscillations in the roll plane in patients with progressive supranuclear palsy (PSP).
Methods: Using video-oculography, we recorded the head and eye motion during passive head oscillations in the roll plane and determined the decrease of torsional quick phases in patients with PSP (n = 13) in comparison to normal controls (n = 13) and those with multiple system atrophy (MSA, n = 17), idiopathic Parkinson's disease (PD, n = 6).
Results: Torsional quick phases were absent during the torsional vestibulo-ocular reflex (VOR) in 78.6% (11/13) of the patients with PSP, but only in 11.8% (2/17) of those with MSA and none with idiopathic PD or of normal controls (Chi-square tests, $p < 0.001$) while gains of the torsional VOR did not differ among the groups (Chi-square tests, $p > 0.05$). Furthermore, the torsional quick phases were smaller even when observed in patients with PSP.
Conclusion: Loss of torsional quick phases is a biological marker for diagnosis of PSP, and may be ascribed to degeneration of the rostral interstitial nucleus of the medial longitudinal fasciculus that contains the burst neurons for torsional as well as vertical saccades.
Disclosure: Dr. J-S Kim serves as an Associate Editor of Frontiers in Neuro-otology and on the editorial boards of the Journal of Clinical Neurology, Frontiers in Neuro-ophthalmology, Journal of Neuro-ophthalmology, Journal of Vestibular Research, Medicine, and Clinical and Translational Neuroscience. The other author has nothing to disclose.

EPR-088

Clinical significance of square-wave jerk in Parkinson's disease

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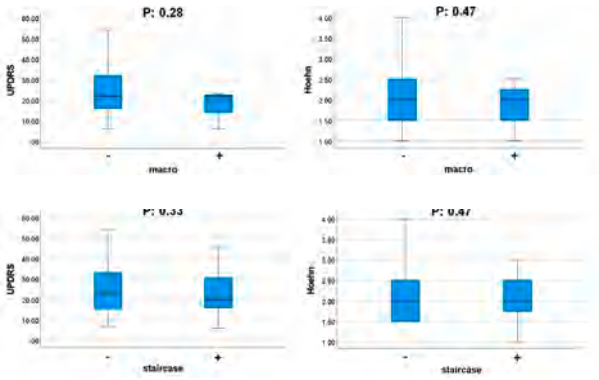
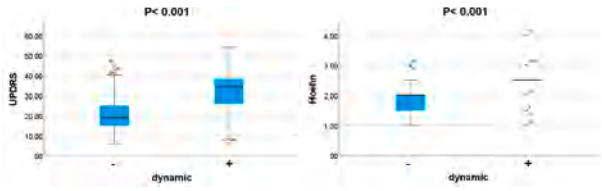
Background and aims: Square-wave jerks (SWJs) are pairs of small horizontal saccades (typically < 2°) that take the eye away from the target and then return it within 200 ms. They may be common in normal elderly subjects, but a prominent clinical finding in neurodegenerative disorders such as Parkinson's disease. This study aimed to determine the clinical significance of SWJ in idiopathic Parkinson's disease.

Methods: We retrospectively recruited 79 patients with idiopathic Parkinson's disease in Pusan National University Yangsan Hospital. We assessed the frequency, amplitude and shape of SWJ documented by video-oculography, and compared their characteristics with clinical scales such as Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn-Yahr scale.

Results: 79 patients showed SWJ with a mean frequency of 26.5 per minute. The amplitudes ranged between 0.2° and 8.0° (mean amplitude 0.7°), and 3 patients (3.8%) had macro-SWJ (> 5°). A staircase SWJ was observed in 33 patients (41.8%) with high frequency SWJ. 19 patients (24.1%) had SWJ with a dynamic overshoot after each primary saccade, whom they showed higher UPDRS (p<0.001) and Hoehn-Yahr scale (p<0.001) compared to patients without a dynamic overshoot. There was a weak correlation between SWJ frequency and UPDRS (r=0.271, p=0.018), but no significant correlations between macro- or staircase SWJ and clinical scales.





Conclusion: The present study showed that SWJ with a dynamic overshoot appear to reflect motor severity in idiopathic Parkinson's disease.

Disclosure: We have no disclosure of any competing interest.

EPR-089

Long-term efficacy of idebenone in patients with LHON according to sex and disease phase: Results from the LEROS study

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Background and aims: Leber hereditary optic neuropathy (LHON) is a mitochondrial disease resulting in bilateral vision loss. For individuals carrying a causative mitochondrial DNA mutation, disease penetrance can vary, with male sex considered a risk factor. In LEROS, a Phase IV, open-label interventional study (ClinicalTrials.gov NCT02774005), visual acuity (VA) outcomes following 24 months of idebenone treatment were compared to those of an external Natural History (NH) cohort. Here, we report the results of sub-analyses according to sex and disease phase.

Methods: LEROS included patients with LHON aged ≥12 years and with a disease onset ≤5 years prior. Data from 181 patients were compared to retrospective data from the NH cohort (N=372), matched by time since symptom onset. Patients were stratified by time since symptom onset in the most recent eye: subacute/dynamic (≤1 year) and chronic (>1 year). Outcome measures (from baseline) included clinically relevant recovery (CRR): improvement from "off-chart" VA to at least 1.6 logMAR, or a ≥0.2 logMAR improvement if already "on-chart"; and clinically relevant worsening (CRW): a deterioration of ≥0.2 logMAR or from "on"- to "off-chart".

Results: Rates of CRR and CRW at Month 24 in eyes of idebenone treated patients and in the matched NH groups are summarised in Table 1, stratified by sex and disease phase.

	Idebenone	Natural History	*p*-value
Females			
Subacute/dynamic eyes			
CRR, % (n/N)	27.0 (10/37)	9.1 (1/11)	0.2162
CRW, % (n/N)	42.3 (11/26)	80.0 (4/5)	0.0482
Chronic eyes			
CRR, % (n/N)	35.0 (7/20)	0.0 (0/18)	0.0002
CRW, % (n/N)	0.0 (0/14)	46.2 (6/13)	0.0004
Males			
Subacute/dynamic eyes			
CRR, % (n/N)	57.1 (48/84)	37.5 (24/64)	0.1383
CRW, % (n/N)	19.4 (13/67)	47.7 (21/44)	0.0271
Chronic eyes			
CRR, % (n/N)	31.3 (30/96)	20 (15/75)	0.0318
CRW, % (n/N)	3.7 (2/54)	12.8 (6/47)	0.0328

Rates of CRR and CRW at Month 24 by sex and disease phase.

Conclusion: Idebenone improved the ratio of positive to negative VA outcomes in a large proportion of patients with LHON. Treatment with idebenone significantly increased recovery in chronic female and male eyes and reduced the frequency of VA worsening in both sexes irrespective of disease phase.

Disclosure: This study was funded by Santhera Pharmaceuticals. TK, PYWM, and VC received research support and/or personal compensation from Santhera Pharmaceuticals, Chiesi GmbH, and GenSight Biologics. CLM has acted as a consultant for Chiesi Farmaceutici, Regulatory PharmaNet, and Thenewway srl and has also received speaker honoraria and/or financial support for meetings from these companies, as well as from First Class srl and Biologix. CLM has also acted as a principal or study investigator for clinical trials sponsored by GenSight Biologics, Santhera Pharmaceuticals, Stoke Therapeutics, and Reneo Pharmaceuticals.

EPR-090

Can the neuro-ophthalmology service cope with the growing use of OCT in clinic and in the community?

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Background and aims: Neuro-ophthalmology services are seeing an increasing number of urgent referrals for suspected disc pathology seen on optical coherence tomography(OCT) imaging. This has challenged the capacity of the service. We conducted an audit with an objective to assess the clinical diagnostic accuracy of disc pathology on OCT scans with a focus on disc swelling/ peripapillary hyperreflective ovoid mass-Like structures(PHOMS) & to identify strategies to improve accuracy.

Methods: We reviewed the diagnostic accuracy of 100 OCT images of the optic disc of normal controls & pathology. In the absence of a gold standard, we used the level of agreement(kappa) between 5 neuro-ophthalmologists and implemented the Delphi technique over 3 repeated rounds. After round 1, participants undertook training which included a combination of self-study in recommended references, a teaching presentation & received feedback on their round 1 scan reviews. Only those participants who passed the predefined 80% threshold agreement in round 2 participated in round 3.

Results: The level of agreement in round 1(100 OCT images, 5 raters) was slight with kappa = 0.149. In round 2 (100 images, 5 raters) it was moderate with kappa = 0.48 and in round 3 (60 images, 4 raters) it was substantial with kappa = 0.689. Only 4 of 5 participants from round 2 met the predefined 80% threshold of agreement & therefore participated in round 3.

Conclusion: A quantifiable threshold of agreement(~80%) with a validated gold standard needs to be set & Individual raters should be trained to achieve this to avoid diagnostic errors.

Disclosure: Srikirti Kodali is funded by the UCL-CCL Clinical Research Fellowship.

MS and related disorders 1

EPR-091

Cladribine tablets in people with relapsing multiple sclerosis: a real-world multicentric, multinational study

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Background and aims: The aim of this study was to provide real-world evidence of cladribine's efficacy in people with multiple sclerosis (pwMS).

Methods: This was a retrospective observational multi-center, multi-national study. Electronic data records were analyzed for clinical and radiological activity 12 months prior to cladribine initiation with a follow-up of up to 24 months.

Results: We identified 320 pwMS treated with cladribine tablets. There were 75.3% (241) females, mean age was 41.6±10.6 years. In 12 months prior to cladribine initiation 84.2% experienced relapses and 64.2% had active lesions on brain MRI. Data for 12-month follow-up was available for 245 and for 24-month follow-up for 129 pwMS. After 12 months 91.6% did not have EDSS worsening, 86.9% were relapse free and 72.9% did not have MRI activity. At month 24, 90.2% did not experience EDSS worsening, 86.5% were relapse free and 75.5% did not have MRI activity. NEDA-3 was present in 58.0% pwMS at month 12 and in 54.2% at month 24. According to univariable logistic regression analysis age was a predictor of achieving NEDA-3 at 12 months (exp(B) 1.066, 95%CI 1.033-1.101, p<0.001). At 24-months age (exp(B) 1.047, 95%CI 1.004-1.091, p=0.031) and disease duration (exp(B) 1.075, 95%CI 1.006-1.149, p=0.032) were predictors of NEDA-3. Age was a predictor of being relapse free during both years of follow-up (exp(B) 0.947, 95% CI 0,919-0.976, p p<0.001). In a multivariable logistic regression model age positively predicted NEDA-3 at 12 months of follow-up.

Conclusion: Our results provide real-world data on the efficacy of cladribine tablets in treating relapsing multiple sclerosis.

Disclosure: BB: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals. IA: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals. TG: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals. MKS: received consultation and/or speaker fees from: Sanofi Genzyme, Roche. MH: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPR-092

Adding the optic nerve region assessed by optical coherence tomography to the diagnostic criteria for multiple sclerosis

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Background and aims: The optic nerve has been recommended as an additional region for demonstrating dissemination in space (DIS) in diagnostic criteria for multiple sclerosis (MS). We investigated adding the optic nerve region as determined by optical coherence tomography (OCT) to DIS criteria to improve the 2017 diagnostic criteria.

Methods: From a prospective observational study, we included patients with a first demyelinating event who had a spectral-domain OCT scan obtained within 90 days. Modified DIS criteria (DIS+OCT) were constructed by adding the optic nerve to the current DIS regions based on validated thresholds for OCT inter-eye differences.

Results: We analyzed 267 MS patients (mean age 31.3 years [SD 8.1], 69% female) during a median observation period of 59 months (range: 13 - 98). Adding the optic nerve as a fifth region improved the diagnostic performance by slightly increasing accuracy (DIS+OCT 81.2% vs. DIS 65.6%,) and sensitivity (DIS+OCT 84.2% vs. DIS 77.9%) without lowering specificity (DIS+OCT 52.2% vs. DIS 52.2%). Fulfilling DIS+OCT criteria (≥2 of 5 DIS+OCT

regions affected) indicated a 3.6-fold risk increase of a second clinical attack (HR 3.6, CI 1.4 – 14.5) compared to a 2.5-fold increased risk when fulfilling the 2017 McDonald DIS criteria (HR 2.5, CI 1.2 – 11.8). When the analysis was conducted according to topography of the first demyelinating event, DIS+OCT criteria performed similarly in both optic neuritis and non–optic neuritis.

Table 1. Risk for a second clinical attack according to dissemination in space.

	Absolute number (%)	Second clinical attack (n, %)	Hazard ratio (95% CI)
Number of regions affected			
1	50 (18.7)	12/50 (24.0)	5.9 (1.7 – 18.3)
2	35 (13.1)	14/35 (40.0)	9.8 (2.4 – 33.1)
3	59 (22.1)	28/59 (47.5)	11.6 (3.8 – 35.3)
4	43 (16.1)	23/43 (53.5)	13.1 (4.0 – 38.2)
5	31 (11.6)	21/31 (67.7)	16.5 (5.7 – 54.5)
Only optic nerve affected	22 (8.2)	8/22 (36.4)	8.9 (2.0 – 25.2)
2017 DIS fulfilled (≥2/4)[1]	147 (55.1)	75/147 (51.0)	2.5 (1.2 – 11.8)[c]
2017 DIS+OCT fulfilled (≥2/5)[2]	168 (62.9)	86/168 (51.2)	3.6 (1.4 – 14.5)[c]

[1]DIS criteria as defined in McDonald criteria 2017: at least 1 lesion in at least 2 of 4 regions (periventricular, cortical or juxtacortical, infratentorial, spinal cord)
[2]Modified DIS criteria (DIS+OCT) were constructed by adding the optic nerve region (defined by abnormal intereye asymmetry in OCT): at least 1 lesion in at least 2 of 5 regions (periventricular, cortical or juxtacortical, infratentorial, spinal cord, optic nerve)
[c]with reference to not fulfilling 2017 DIS criteria
[d]with reference to not fulfilling 2017 DIS+OCT criteria

CI: confidence interval, DIS: dissemination in space, OCT: optical coherence tomography

Table 1

Table 2. Risk for a second clinical attack according to dissemination in space criteria in optic neuritis vs. non-optic neuritis

	Absolute number (%)	Second clinical attack (n, %)	Hazard ratio (95% CI)
Optic neuritis (n=81)			
2017 DIS fulfilled (≥2/4)[1]	38 (46.9)	15/38 (39.5)	2.4 (1.1 – 11.5)[c]
2017 DIS+OCT fulfilled (≥2/5)[2]	45 (55.6)	18/45 (40.0)	4.0 (1.5 – 16.2)[d]
Non-optic neuritis (n=186)			
2017 DIS fulfilled (≥2/4)[1]	115 (61.8)	63/115 (54.8)	2.6 (1.3 – 12.3)[c]
2017 DIS+OCT fulfilled (≥2/5)[2]	130 (69.9)	72/130 (55.4)	3.3 (1.4 – 13.8)[d]

[1]DIS criteria as defined in McDonald criteria 2017: at least 1 lesion in at least 2 of 4 regions (periventricular, cortical or juxtacortical, infratentorial, spinal cord)
[2]Modified DIS criteria (DIS+OCT) were constructed by adding the optic nerve region (defined by abnormal intereye asymmetry in OCT): at least 1 lesion in at least 2 of 5 regions (periventricular, cortical or juxtacortical, infratentorial, spinal cord, optic nerve)
[c]with reference to not fulfilling 2017 DIS criteria
[d]with reference to not fulfilling 2017 DIS+OCT criteria

CI: confidence interval, DIS: dissemination in space, OCT: optical coherence tomography

Table 2

Conclusion: Addition of the optic nerve, assessed by OCT, as a fifth region in the current DIS criteria improves diagnostic performance by increasing sensitivity without lowering specificity.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPR-093

Real-world safety and effectiveness of ocrelizumab in different treatment lines in RMS - CONFIDENCE interim analysis

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Background and aims: CONFIDENCE (ML39632, EUPAS22951) is a German non-interventional, post-authorization safety study including MS patients newly treated with ocrelizumab (OCR) and other disease-modifying therapies. This analysis includes patients treated with OCR up to 4.5 years.

Methods: Data cut-off was 14/10/2022. Safety and effectiveness were described in treatment-naïve patients (TN-patients) and patients with 1, 2 or ≥ 3 prior MS-specific therapies (pwPMST). Safety analysis included patients with ≥ 1 dose; effectiveness analyses for patients with ≥ 1 follow up visit evaluated annual relapse rate (ARR), 24-week confirmed disease progression (CDP), 24-week confirmed disease improvement (CDI) and Treatment Satisfaction Questionnaire for Medications© (TSQM).

Results: Mean (SD) observation time for safety was 2.43 (1.16) years with 2241 patients (402 TN-patients, 771 pwPMST≥3). Adverse events (AEs) occurred in 51.0/100 patient years (PY) in TN-patients (88.5/100PY in pwPMST≥3), 19.3/100PY classified as SOC "Infections and infestations" (28.9/100PY in pwPMST≥3). No new safety signals with extended exposure time to OCR were observed. Mean (SD) observation time for effectiveness was 2.46 (1.13) years with 2214 patients; overall ARR was 0.12 (0.35, n=2112). Over 36 months, 83.9% and 80.2% of TN-patients (n=320) and pwPMST≥3 (n=662), respectively, were without CDP; 16.5% of TN-patients vs 10.6% of pwPMST≥3 reached CDI; TSQM was stable (total Score (SD): 68.92 (26.94)). Over 48 months overall persistence rate was 80%.

Conclusion: Subgroup analyses will be presented supporting the early use of OCR.

Disclosure: MB received honoraria for lecturing, consulting and/or travel expenses for attending meetings from Bayer, Biogen, Boehringer, Bristol-Myers Squibb, Coloplast, Daiichi-Sankyo, Das Fortbildungskolleg, Merck, Novartis, RG Ärztefortbildung, Roche, Sanofi and Teva

EPR-094

MRI Biomarkers in Multiple Sclerosis are Associated with Clinical Scales: Results from the Phase-3 OPTIMUM Study

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Background and aims: The Phase-3 OPTIMUM study demonstrated superiority of ponesimod (20 mg) over teriflunomide (14 mg) with respect to the annualized relapse rates, active lesions, ventricular, deep gray-matter volumes, white matter (WM) myelin content and NFL. We quantified associations between MRI biomarkers and clinical outcomes at baseline and after 108 weeks of treatment.
Methods: Each patient's MRI feature set consisted of 1010 measures (figure 1) at baseline and week 108. Clinical assessments included FSIQ-RMS, T25FW, SDMT, PASAT, EDSS, MSFC, 9-HPT. Patients were randomly assigned to two groups, A (n=427) and B (n=428). Baseline data from A was used to derive regression models for each of the clinical scales as a function of the first three principal components of each MRI feature group (volume, myelination, and tract damage). Resultant models were tested on data from groups B_baseline, A_Wk108 and B_Wk108.

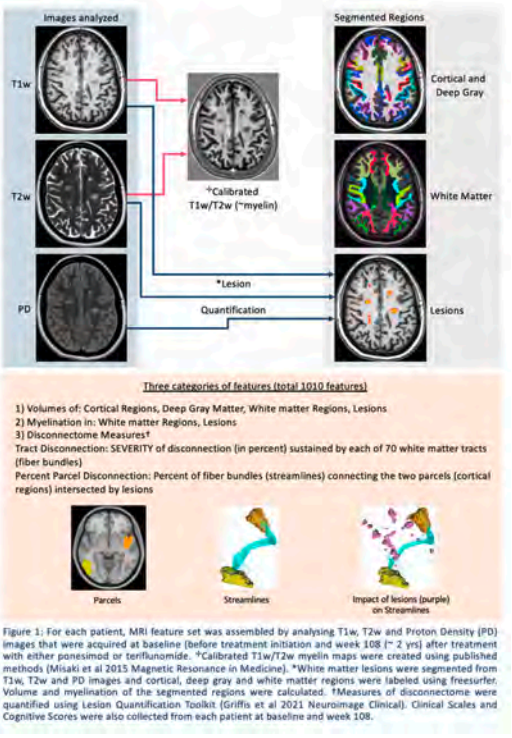

Figure 1: For each patient, MRI feature set was assembled by analysing T1w, T2w and Proton Density (PD) images that were acquired at baseline (before treatment initiation and week 108 [~ 2 yrs] after treatment with either ponesimod or teriflunomide. *Calibrated T1w/T2w myelin maps were created using published methods (Misaki et al 2015 Magnetic Resonance in Medicine). *White matter lesions were segmented from T1w, T2w and PD images and cortical, deep gray and white matter regions were labeled using freesurfer. Volume and myelination of the segmented regions were calculated. †Measures of disconnectome were quantified using Lesion Quantification Toolkit (Griffis et al 2021 Neuroimage Clinical). Clinical Scales and Cognitive Scores were also collected from each patient at baseline and week 108.

Results: MRI features were associated with all clinical scales except FSIQ ($p<10^{-2}$). The largest associations with the MRI features were seen in 9-HPT, MSFC and SDMT. For both groups, the amount of variance (r^2) in the clinical scale explained by the MRI features were 0.1-0.33 at baseline and 0.01-0.27 at week 108 (figure 2). No association was found between change in MRI features and change in clinical scores.
Conclusion: We found significant associations between MRI features at baseline and clinical functions such as upper limb dexterity, mobility, cognition, and disability but not fatigue. These findings support the relevance of MRI biomarkers in MS.
Disclosure: Authors Ritobrato Datta, Tina Wang, Ibrahim Turkoz, Maria Ait-Tihyaty, Ziad S. Saad and Hartmuth C. Kolb are or were employees of Janssen Pharmaceuticals and may own stock or Stock in Johnson & Johnson Author L. Kappos' institution (University Hospital Basel and RC2NB) received research support for steering committee, advisory board, consultancy fees from AbbVie, Actelion, AurigaVision AG, Biogen, Celgene, Desitin, Eli Lilly, EMD Serono, Genentech, Genzyme, GlaxoSmithKline, Janssen Pharmaceuticals, Japan Tobacco, Merck, Minoryx, Novartis, Roche, Sanofi, Santhera, Senda, Shionogi, Teva Pharmaceuticals, and Wellmera; speaker fees from BMS, Janssen, Merck, Novartis, and Roche; license fees for Neurostatus products; and grants from European Union, Innosuisse, Novartis, Roche Research Foundation, Swiss MS Society, and Swiss National Research Foundation.

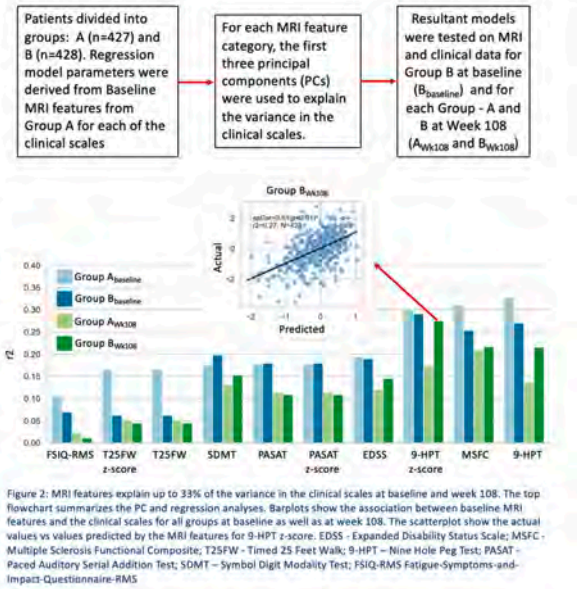

Figure 2: MRI features explain up to 33% of the variance in the clinical scales at baseline and week 108. The top flowchart summarizes the PC and regression analyses. Barplots show the association between baseline MRI features and the clinical scales for all groups at baseline as well as at week 108. The scatterplot show the actual values vs values predicted by the MRI features for 9-HPT z-score. EDSS - Expanded Disability Status Scale; MSFC - Multiple Sclerosis Functional Composite; T25FW - Timed 25 Feet Walk; 9-HPT – Nine Hole Peg Test; PASAT - Paced Auditory Serial Addition Test; SDMT – Symbol Digit Modality Test; FSIQ-RMS Fatigue-Symptoms-and-Impact-Questionnaire-RMS

Figure 2

EPR-095

Baseline Whole Brain Volume and Disability Progression in Ozanimod-Treated Patients With Relapsing Multiple Sclerosis

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Background and aims: In people with multiple sclerosis (MS), brain volume loss correlates with long-term disability progression. This secondary analysis assessed disability progression over 5-7 years of ozanimod treatment stratified by high or low baseline whole brain volume (WBV).

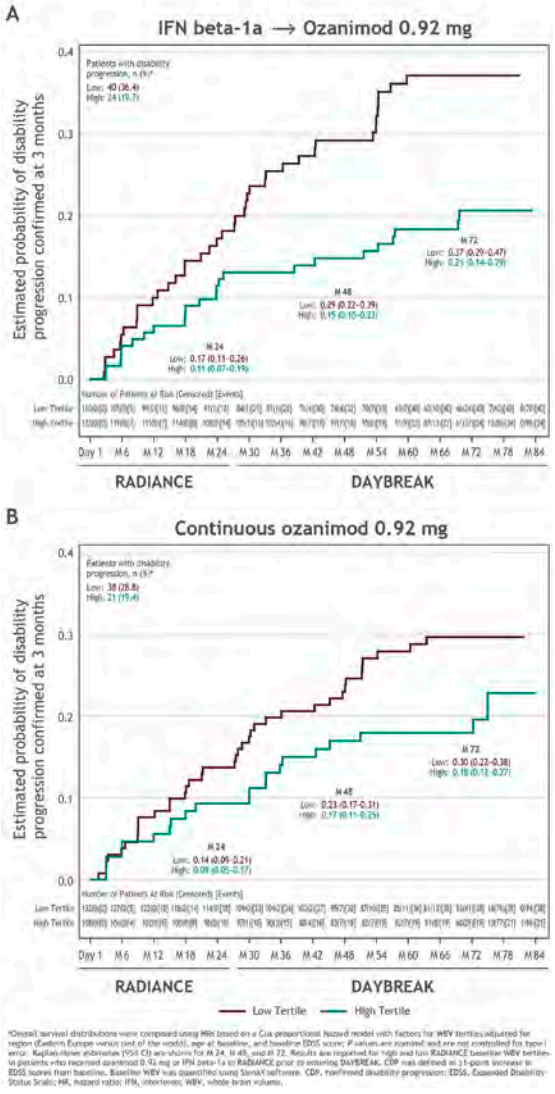
Methods: In the 24-month phase 3 RADIANCE (NCT02047734) trial, patients with relapsing MS (RMS) were randomly assigned ozanimod 0.46 or 0.92 mg/d or IFN beta-1a 30 µg/wk; completers were eligible to enrol in DAYBREAK (NCT02576717) and receive ozanimod 0.92 mg. Kaplan-Meier analyses of 3-month confirmed disability progression were performed for patients with high versus low RADIANCE baseline WBV.

Results: At the February 2, 2021, data cutoff (5-7 years of ozanimod treatment), high baseline WBV was associated with a lower proportion of patients with and slower rates to disability progression when compared with the low baseline WBV group in those who switched from IFN beta-1a to ozanimod 0.92 mg (high/low hazard ratio (HR) [95% CI]: 0.56 [0.32–0.96], nominal P=0.0365; Fig 1A). A relatively similar numerical trend was observed for patients who received continuous ozanimod 0.92 mg (high/low HR [95% CI]: 0.85 [0.49–1.47], nominal p=0.5587; Fig 1B).

Conclusion: In RADIANCE and DAYBREAK, high baseline WBV was associated with numerically less disability progression over 5-7 years of ozanimod treatment compared with low baseline WBV in patients with RMS; however, these subgroup analyses assessed a small sample size and are hypothesis generating rather than declarative.

Disclosure: MF: Editor-in-Chief of the Journal of Neurology, Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology; received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, and Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and Teva; participation in advisory boards for Alexion, Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, and Takeda; scientific direction of educational events for Biogen, Bristol Myers Squibb, Celgene, Lilly, Merck, Novartis, Roche, and Sanofi-Genzyme; and receives research support from ARiSLA (Fondazione Italiana di Ricerca per la SLA), Biogen Idec, Fondazione Italiana Sclerosi Multipla, Italian Ministry of Health, Merck-Serono, Novartis, and Roche. All author disclosures will be included in the presentation. This study was supported by Bristol Myers Squibb.

Figure 1. Time to onset of sustained disability progression: 3-month CDP during RADIANCE and DAYBREAK by baseline normalized WBV in patients who switched from IFN beta-1a after 24 months in RADIANCE to ozanimod 0.92 mg in DAYBREAK (A) or received continuous ozanimod 0.92 mg (B)



EPR-096

Neurofilament light chain and JCV index monitoring in a positive JCV pregnant patient treated with natalizumab

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Background and aims: Pregnant patients usually keep natalizumab treatment during pregnancy until week 32. Very high JCV antibodies are a risk for suffering from PML. Some studies proposed serum neurofilaments light chain (sNfL) to detect PML in a preclinical phase

Methods: A 37-year-old woman was diagnosed with highly active RMS in March 2021. Baseline cranial MRI showed more than 20 gadolinium-enhanced lesions (Figure 1) and the spinal MRI a C4-enhanced lesion. JCV index was 2.52. They started treatment with natalizumab every 4 weeks in April 2021

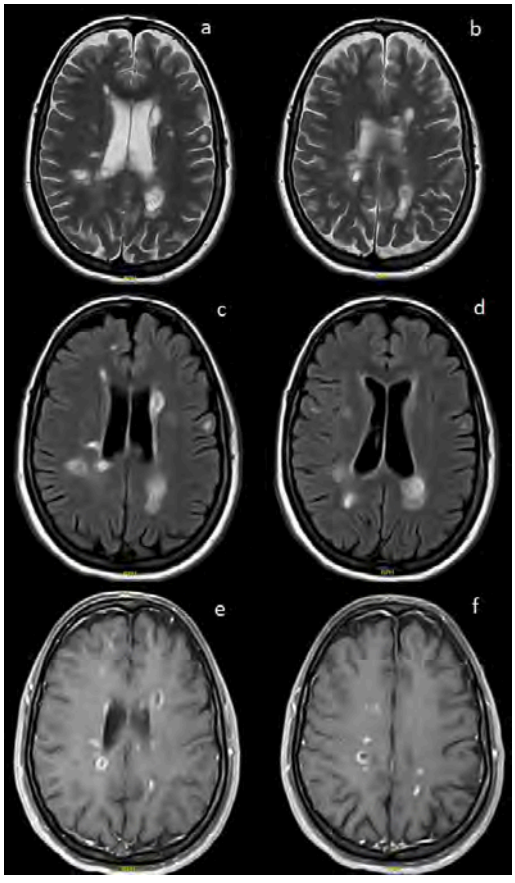
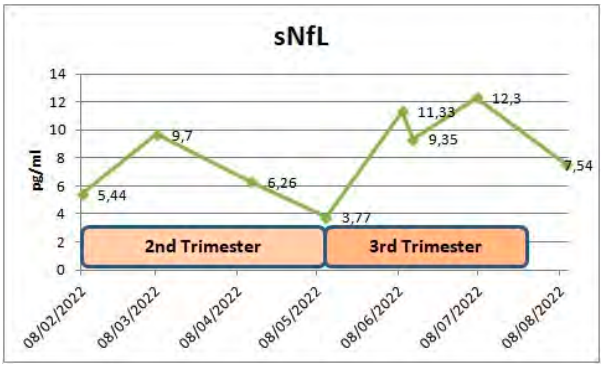


Figure 1. First brain MRI (March 2021): Axial T2-weighted (a, b), FLAIR sequence (c, d), T1 post-gadolinium sequence (e, f). Multiple T2-hyperintense lesions (periventricular, juxtacortical, subcortical), some of them with contrast enhancement

Results: Three months later the patient was referred to our center for the follow-up. We extended the natalizumab dose to every 6 weeks. In November 2021 she became pregnant and natalizumab was continued until the 33rd gestation week. Due to the risk of PML, JCV antibodies and sNfL were monitored monthly. JCV index remained stable in the first trimester, with a decrease in the second and third trimester of pregnancy (JCV index prior to delivery: 1.25). Baseline sNfL levels were 5.44 pg/ml and were slowly increasing until 12.30 pg/ml. In the 19th gestation week, due to a suden increase of sNfL (from 5.44 pg/ml to 9.7 pg/ml), an urgent MRI was performed, with no evidence of PML or enhanced T2 lesions. At 39 gestation week, a healthy baby was born. A new MRI scan after the delivery showed no new T2 lesions and treatment with Ocrelizumab was started.



Graphic 1. Monitoring of sNfL levels

Conclusion: JCV and sNFL monitoring could be useful in natalizumab treated patients during pregnancy to minimize the risk of PML

Disclosure: Nothing to disclose.

EPR-097

Five-Year Efficacy Outcomes of Ofatumumab in Relapsing MS Patients: Insights From ALITHIOS Open-label Extension Study

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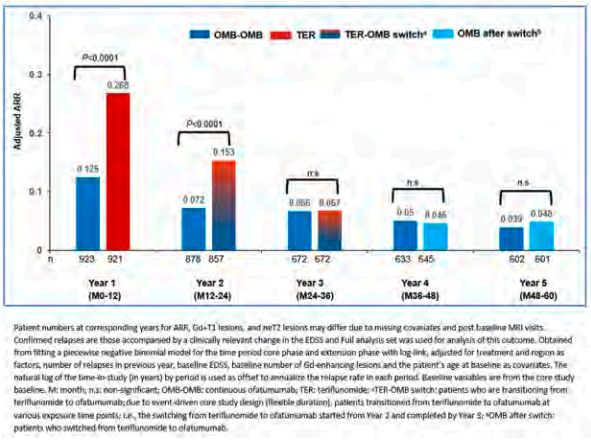
Background and aims: In the Phase 3 ASCLEPIOS I/II trials, ofatumumab reduced clinical and MRI disease activity versus teriflunomide in relapsing multiple sclerosis (RMS) patients; sustained reductions were observed with extended treatment (up to 4 years) in the ongoing, open-label ALITHIOS extension study. Here, we report ofatumumab efficacy outcomes for up to 5 years.

Methods: This analysis included participants randomised to ofatumumab/teriflunomide in the ASCLEPIOS I/II trials (core study) and who received ofatumumab in ALITHIOS extension study (data cut-off: 25-Sep-2022). Endpoints analysed by year included annualized relapse rates (ARR), MRI lesion activity (Gd+T1 and new/enlarging T2 lesions) and NEDA-3 for up to 5 years in the continuous (ofatumumab [core+extension]; N=690) and switch (teriflunomide [core]/ ofatumumab [extension]; N=677) groups.

Results: Patients in the continuous group maintained a low ARR over Years 1–5; while in the switch group, a marked reduction was observed from Year 2–3 (0.15–0.07) and maintained through Years 3–5 (0.05). Profound suppression of MRI lesion activity was maintained in the continuous group up to Year 5; while in the switch group, suppression was observed from Year 3–5. In the continuous group, the odds of achieving NEDA-3 increased from Year 2 (80%) and reached maximum at Year 5 (93.4%) (Figures 1-3).

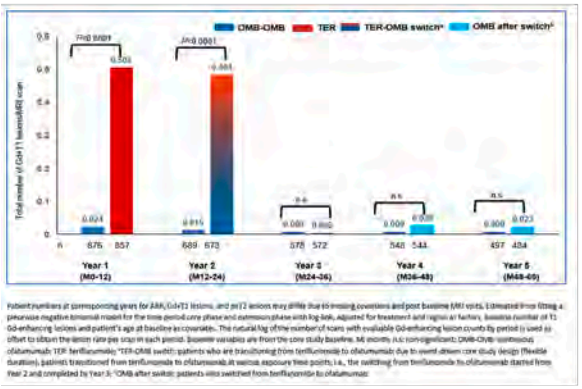
Conclusion: Continuous ofatumumab showed sustained efficacy on relapses and an almost complete suppression of MRI lesion activity for up to 5 years. Teriflunomide-to-ofatumumab switch resulted in pronounced reductions in these outcomes through Years 3–5. Ofatumumab treatment showed higher odds of achieving NEDA-3 over time in both groups.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

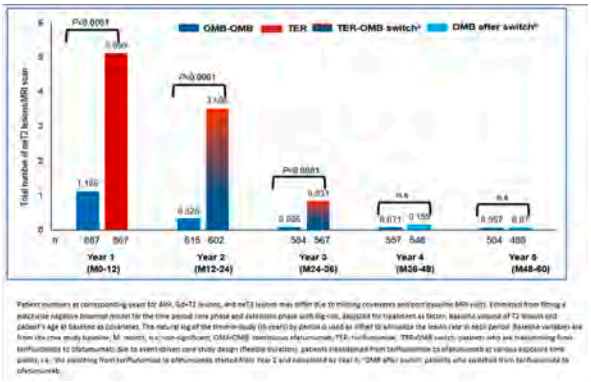


Annualized relapse rate (ARR) in ASCLEPIOS I/II (Year 1-2) and ALITHIOS extension phase (Year 3-5)

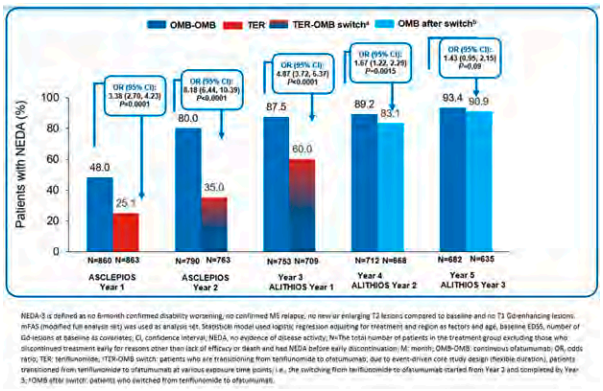
2a. Gd+T1 lesions in ASCLEPIOS I/II and ALITHIOS extension phase



2b. neT2 lesions in ASCLEPIOS I/II and ALITHIOS extension phase



MRI lesion activity in ASCLEPIOS I/II (Year 1-2) and ALITHIOS extension phase (Year 3-5)



NEDA-3 status in ASCLEPIOS I/II (Year 1-2) and ALITHIOS extension phase (Year 3-5)

EPR-098

Long-term safety outcomes from Tysabri Observational Program (TOP) in relapsing-remitting MS patients

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Background and aims: The Tysabri Observational Program (TOP) is the largest ongoing real-world observational study to inform on long-term safety and effectiveness of Biogen's natalizumab (NTZ) in relapsing-remitting multiple sclerosis (RRMS) in clinical practice.
Methods: Safety data collected between 29 June 2007 and 26 May 2022 from 6321 patients was analysed and summarised for the serious adverse events of progressive multifocal leukoencephalopathy (PML), serious herpes infections, malignancies and deaths. Interim safety data was compared between May 2022 and May 2014 data cuts.
Results: A total of 1107 patients (17.5%) had at least 1 serious adverse event (SAE) in TOP. The cumulative incidence rate (CIR) of at least 1 SAE per 1000 patient-years was 38.82 (95% confidence interval [CI]: 36.10, 40.65) in 2022 vs. 43.87 (95% CI: 40.27, 47.69) in 2014. The CIR of confirmed PML cases was 1.81 (95% CI: 1.37, 2.34) per 1000 patient-years in 2022 vs. 2.07 (95% CI: 1.35, 3.04) in 2014. Less than 1% of patients were diagnosed with serious herpes infection in 2022 and 2014. The CIR of malignancies was 3.34 per 1000 patient-years (95% CI: 2.73, 4.03) in 2022 vs. 4.78 (95% CI: 3.65, 6.15) in 2014. The cumulative rate of treatment related deaths was comparable in 2022 (0.1% (10/6321) vs. 2014 (0.1% (6/5623).
Conclusion: The results demonstrate that the cumulative incidence of PML, serious herpes infections and malignancies are comparable between 2022 and 2014 interim analyses. Overall, these safety findings are consistent with the known safety profile of NTZ.
Disclosure: This study is supported by Biogen. LK institutions: Abbvie, Actelion, Auriga Vision AG, Bayer HealthCare, Biogen, Bristol Myers Squibb, Celgene, Desitin, df-mp Monia & Pohlmann, Eli Lilly, EMD Serono, European Union, Genentech, Genzyme, Glaxo Smith Kline, Innosuisse, Janssen, Merck, Minoryx, Neurostatus, Novartis, Roche, Sanofi, Santhera, Senda Biosciences, Shionogi, Swiss MS Society, Swiss National Research Foundation, Teva, and Wellmera AG. TS: Biogen, Novartis. MT: Biogen, Merck, Novartis, Roche, Sanofi, and Teva; MT institution: Biogen, Merck, Novartis and Roche. HB: Oxford Health Policy Forum; HB institution: Biogen, Merck, Novartis, Roche, UCB Pharma. HW: AbbVie, Actelion, Alexion, argenx, Biogen, Biologix, Bristol Myers Squibb, Cognomed, EMD Serono, Evgen, F. Hoffmann-La Roche, Gemeinnützige Hertie-Stiftung, Genzyme, GlaxoSmithKline GmbH, Idorsia, IGES, Immunic, Immunovant, Janssen, Johnson & Johnson, MedDay, Merck Serono, Novartis, Roche, Sanofi Genzyme, Swiss MS Society, Teva, UCB, WebMD Global. JL, LD, ZS, AR, AD: employees of and may hold stock and/or stock options in Biogen.

EPR-099

Paramagnetic rim lesions are associated with peripapillary retinal nerve fiber layer thinning in multiple sclerosis

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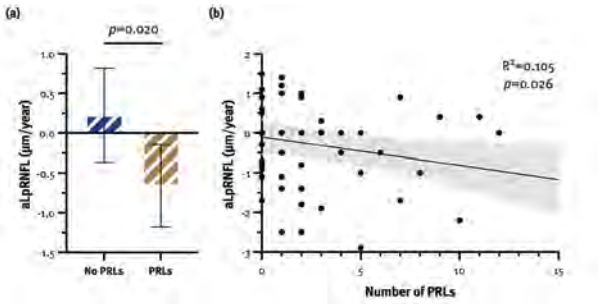
Background and aims: Paramagnetic rim lesions (PRLs) are chronic active lesions that are associated with a more severe disease course in multiple sclerosis (MS), also reflected by lower retinal layer thickness measured by optical coherence tomography (OCT).
Methods: In this longitudinal retrospective study, we included pwMS who underwent a 3T brain MRI between 2015 and 2021, and had at least one OCT scan +/– 6 months from MRI with a follow-up OCT scan at least one year apart. A linear regression model was calculated with aLpRNFL as the dependent variable, and the number of PRLs as the independent variable, adjusted for age, sex, disease duration and Expanded Disability Status Scale (EDSS) at baseline.
Results: We analyzed data from 62 pwMS (mean age 36.3 years [SD 10.3], 74.2% female, median disease duration 3 years [IQR 0–11], median EDSS 2.0 [0–3.0], median follow-up 1.2 years [1.0–2.1]). Baseline median number of PRLs was 1 (0–3.3), 24 (38.7%) pwMS had no PRLs. Mean pRNFL thickness at baseline was 94.1 µm (11.8). PwMS with PRLs had higher median aLpRNFL compared to patients without PRLs (–0.5 µm [–1.8, 0.4] vs. 0.0 µm [–0.6, 1.1], p=0.020). In a multivariable model, higher number of PRLs was associated with higher aLpRNFL (β= –0.28; 95% CI –0.14, –0.01; p=0.026), explaining 10.5% of its variance.



Patients with PRLs had significantly higher aLpRNFL (a). In a multivariable model, higher number of PRLs was associated with higher aLpRNFL (b).

Conclusion: The association between the number of PRLs and aLpRNFL provides additional evidence that pwMS with PRLs are affected by a more pronounced neurodegenerative process.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

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ePresentations

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Infectious diseases

EPR-100

Toscana virus meningitis, an emergent disease in southern Spain. A descriptive analysis of seven cases.

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Background and aims: Toscana virus (TOSV, genus Phlebovirus, family Bunyaviridae), is an arbovirosis endemic in Mediterranean countries, transmitted to humans by the bite of phlebotomine sand flies. It typically causes aseptic meningitis, although encephalitis has also been described. This study attempts to emphasise the importance of considerating TOSV as an etiology for aseptic meningitis in southern Spain.
Methods: We perform a descriptive analysis of a case series that includes seven patients admitted to Neurology Department between 2007 and 2022 in Hospital Virgen de La Arrixaca in Murcia, located in the Southeast of Spain, with diagnosis of acute meningitis due to Toscana virus infection.
Results: Seven patients were studied with a mean age of 49.7 years. All patients started with headache as initial symptom. Five patients (71.4%) developed fever. The analysis of cerebrospinal fluid (CSF) showed pleocytosis in all patients, with a mean of 296 leukocytes/µl. Only in one patient predominance of polymorphonuclear leukocytes was found. The microbiological study of CSF showed positive IgM antibodies against TOSV in all patients, despite of TOSV polymerase chain reaction in CSF tested negative in three of them. The course was benign in all patients, with only a case of sensorineural hearing loss as a sequela.
Conclusion: TOSV should be considerated as a potential etiology for aseptic meningitis in Europe, especially in southern countries. Despite the number of reported cases has increased markedly in recent years, TOSV neurological infection may be underdiagnosed since few laboratories include this virus in their portfolio.
Disclosure: All authors declare they have no conflicts of interest.

EPR-101

Infective endocarditis and its neurological complications. Descriptive study of a series of patients with endocarditis.

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Background and aims: Infective endocarditis(IE) is a rare cause of stroke with high mortality. The objective of this study is to describe the demographic and clinical characteristics of patients with endocarditis in our setting, neurological complications, and clinical prognosis.
Methods: 478 patients with IE from our center were evaluated during 2007-2021.
Results: 33 patients(7%) presented neurological complications (90%ischemic stroke, 9%hemorrhagic stroke, 0.42%meningitis and 0.62%seizures). 69.7% of the patients were men, mean age 65+/-13.6 years. The majority had native mitral valve involvement(40%). 43% of the patients had a stroke as the first manifestation of IE. Stroke patients had a baseline NIHSS of 3[0.6]. 30% of the patients received surgical treatment, although in no case it was performed in the acute phase (first 2-4 weeks). Mortality was 37% and in all cases during hospital admission, none of the operated patients died. 47.1% of the patients had a good prognosis at 3 months(mRS 0-2). Microorganisms were isolated in 87.8%, S.Aureus being the most frequent(23.5%), being associated with a higher mortality (24%vs.62.5%, p=0.04). Endocarditis due to S. Epidermidis was associated with a worse functional prognosis with mRS 0-2 at 3 months (10.3%vs89.7% p<0.01), as well as the number of vegetations (1.07±0.3 vs2±2, p<0.001). No differences in mortality or functional dependence were detected depending on the affected valve.
Conclusion: Endocarditis is associated with high mortality, especially in those patients with endocarditis due to S. Aureus, with a greater number of vegetations and without surgical treatment.
Disclosure: There is no conflict of interest. Informed consent was obtained from the patients participating in this study and a favorable report from the CEIm of our center.

EPR-102

Progressive Multifocal Leukoencephalopathy in a non-immunosuppressed patient successfully treated with pembrolizumab

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is an opportunistic brain infection caused by JC virus (JCV), without specific antiviral treatment, and fatal outcome unless cellular immune function can be restored. PML in non-immunosuppressed patients is extremely rare. Pembrolizumab, a PD-1 blocker, targets pathways involved in immune exhaustion and can reinvigorate antiviral immunity. It has shown restoration of anti-JCV activity of T cells, with associated clinical and radiological improvement in some patients with PML.
Methods: A 77-year-old man without known immunosuppression presented with subacute left-arm weakness and cognitive impairment. Over three months he progressively developed left-side spastic hemiparesis, focal motor seizures, and encephalopathy. Brain MRI showed right frontal-parietal subcortical T2/FLAIR hyperintesities suggesting PML, and JCV PCR was positive in CSF. HIV infection, malignancies, and immune deficiencies were discarded. A right frontal lobe biopsy showed lymphocytic encephalitis without cellular atypia, but with immunohistochemical evidence of neuronal and glial inclusions, and positive JCV PCR 4.763.718 copies). He was treated on a compassionate-use basis with pembrolizumab 2 mg/Kg intravenously.
Results: A follow-up MRI 2 weeks later showed mild radiological improvement. IFN-gELISpot assays, performed 1 week before and 4 weeks after pembrolizumab, did not detect effector T lymphocyte response against BK virus (high sequence homology with JCV). Six weeks after the infusion, the encephalopathy had improved, and the spastic hemiparesis was stable, so he received a second dose of pembrolizumab. Subsequent clinical, MRI, and immunological assessments are pending.
Conclusion: Immune reconstitution with PD-1 blockade can be considered in patients with PML and no immunosuppression.
Disclosure: The authors do not have disclosures related to this work.

EPR-103

Bacterial load in csf predicts unfavourable outcome in pneumococcal meningitis in adults

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Background and aims: Bacterial meningitis is a severe disease with high mortality and morbidity, which is caused by S.pneumoniae in 70% of adult cases. The objective of this study is to determine whether bacterial load in cerebrospinal fluid (CSF) at admission correlates to disease severity and outcome in pneumococcal meningitis.
Methods: Bacterial DNA load was quantified using PCR targeting the LytA gene in CSF samples of adults with community-acquired pneumococcal meningitis included in a nationwide prospective cohort. We determined the association with clinical characteristics and outcome, based on the Glasgow Outcome Scale (GOS) score. Unfavourable outcome was defined as GOS 1–4.
Results: A total of 49 CSF samples from pneumococcal meningitis patients were included. Median age of the patients was 61 years (IQR 53-67). Almost half of the patients was female (23/49, 47%) and 6/48 patients (13%) received antibiotics pre-admission. Unfavourable outcome occurred in 33% (16/49) of the cases, and the overall case fatality rate was 14% (7/49). Median bacterial load was 1.27x10^4 DNAcopies/ml (IQR 2.47x10^3 – 8.69x10^4), and was not significantly correlated with CSF leukocytes count or CSF protein. Bacterial load was higher in patients with an unfavorable outcome (5.25x10^4 copies/ml [IQR 6.70x10^3–1.07 x 10^5] vs. 6.17x10^3 copies/ml [IQR 3.60x10^2–7.64x10^4], p<.001). High CSF bacterial load was identified as a significant predictor of unfavourable outcome (OR 2.5 per logarithmic increase, CI95% 1.2-5.9, p = 0.018), after correcting for antibiotics pre-admission.
Conclusion: High CSF bacterial load is an important predictor of unfavourable outcome in pneumococcal meningitis, suggesting an important role for bacterial load in the pathophysiology.
Disclosure: Nothing to disclose.

EPR-104

Increasing incidence of community-acquired adult group A streptococcal meningitis in the Netherlands

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Background and aims: Streptococcus pyogenes (GAS) is an uncommon causative pathogen of bacterial meningitis. Recently, an increasing incidence of childhood invasive GAS infections has been reported in the Netherlands.
Methods: We assessed the incidence, clinical characteristics, and outcome of patients with GAS meningitis included in a nationwide cohort study of adults with community-acquired bacterial meningitis in the Netherlands (MeninGene) between June 2006 and Oct 2022. Outcome was scored at discharge using the Glasgow Outcome Scale (score of 1-4 was considered unfavourable outcome).
Results: The causative pathogen was GAS in 66 of 2931 episodes of community-acquired bacterial meningitis (2.3%). The incidence rose from 1.5 in 2006 to 8.8 per 10 million adults in 2022. Extra-meningeal infection foci were present in 61 of 66 patients (92%), most commonly otitis (89%). Neurological complications occurred in 49 of 66 patients (74%): subdural empyema in 15 of 66 (23%) and cerebral infarction occurred in 11 patients (18%). Unfavourable outcome occurred in 27 patients (41%) and 12 patients died (18%). The risk of unfavourable outcome tended to be higher in the patients with meningitis occurring in 2022 as compared to the period 2006-2021 (9 of 15 [60%] vs. 18 of 51 [35%]; p=0.09).
Conclusion: We observed an increase of group A streptococcal meningitis in adults in 2022. GAS meningitis is associated with otitis and has a high rate of unfavourable outcome. The rate of unfavourable outcome of GAS meningitis observed in 2022 tended to be higher than preceding years.
Disclosure: Increasing incidence of community-acquired adult group A streptococcal meningitis in the Netherlands.

EPR-105

Abstract withdrawn.

EPR-106

Clinico-radiological profile and outcomes of children with CNS tuberculosis presenting to a tertiary care center

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Background and aims: CNS Tuberculosis accounts for approximately 1% of all cases. It carries a high mortality rate and a distressing level of neurological morbidity due to multiple factors persistent or progressive hydrocephalus, multiple cranial nerve involvement, vasculitis leading to cerebral infarcts.
Methods: An ambispective study was done for children one month to 18 years diagnosed with CNS tuberculosis who presented to our tertiary care center for a period of 4 years. A retrospective review was done and clinic-radiological profile and outcomes were determined.
Results: 34 children were diagnosed with CNS TB. 21 (62%) children had disseminated tuberculosis, and 13 (38%) had primary CNS TB. The mean age of the children was 8±5.5 years. 33 patients had tubercular meningitis (TBM), 18 had tuberculomas, and one had spinal TB. 3 (10%), 20(60%), and 10(30%) children had stages 1,2, and 3 of TBM, respectively. Neuroimaging findings of basal exudates (24), arachnoiditis (8), vasculitic infarcts (21), hydrocephalus (24), and cranial nerve enhancements (12) were seen. 21/24 (87.5%) with hydrocephalus underwent CSF diversion procedures. 18/34 had a microbiological confirmation of TB. The mortality rate in our cohort was 29% (10 patients). 11(32%) had completed anti-tubercular treatment. The degree of disability in our cohort assessed with the Modified Rankin Scale(mRS) are – 17 (mRS – 0), 2 (mRS – 2), 2 (mRS – 3), 1 (mRS – 4) and 1 (mRS – 5), 10 (mRS – 6).
Conclusion: Timely diagnosis and prompt management of complications will be rewarding in children with CNS tuberculosis.
Disclosure: There is no conflict of interest. Project didn't require any funding.

EPR-107

Clinical, laboratory and neuroimaging profile of herpes simplex virus encephalitis: a 12-year retrospective case series

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Background and aims: To describe cases Herpes simplex virus (HSV) type 1 and 2 encephalitis over a span of 12 years, in an area of 450,000 inhabitants, and focus on factors that can predict the outcome.

Methods: Cases were found through microbiological confirmations in CSF by PCR and codified diagnosis in the electronic medical history.
Results: We obtained 26 patients. Six (67% women) presented HSV encephalitis type 2 (HSV2E), with a median age of 41 years (interquartile range- IQR of 33-46). Twenty (65% women) presented HSV type 1 (HSV1E) with a median age of 64 years (IQR 50-76). Previous immunosuppression was present in 35% of HSV2E cases and 17% of HSV1E cases. Up to 40% of HSV1E presented with acute neurological deficit. Initial CT scan was altered in 37% of HSV1E, and 5 had haemorrhagic lesions (figure 1). Mortality was of 20% in HSV1E patients, and 75% of the deceased had previous immunosuppression. In HSV1E patients, after a median follow-up of 4 months the modified Rankin Scale (mRS) was a median of 2(IQR 1-3). During the follow-up, only 1 patient developed an anti-NMDA encephalitis. We found a significant negative correlation between the pleocytosis in CSF and mRS at follow-up, in those with no previous immunosuppression (p=-0,6; p=0,04) (Figure 2).

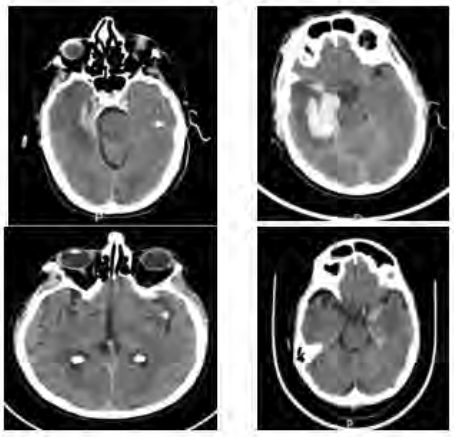

Figure 1. CT scan of patients with HSVE with haemorrhagic lesions in neuroimage. In total, 7 of 20 people who had HVS1E presented with initial alterations in the CT scan, 5 of them with haemorrhagic lesions (A) Hypodensity within the right temporal lobe, with haemorrhagic signs at temporal medial level. (B) Right temporal haematoma with signs of herniation. (C) Hyperdense lesion within the cortico-subcortical left insular region. (D) SAH on both left temporal and sylvian fissure with intracerebral

Figure 1

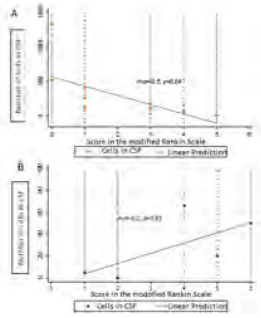

Figure 2. Association between cellularity in CSF and functional scale after encephalitis process mediated by mRS (after finalisation of treatment and posterior medical assessment) in patients without a history of immunosuppression (A) and with a history of

Figure 2

Conclusion: HSV1 is a severe condition with worse outcome in immunosuppressed patients. Likewise, in our case series, an initial lower cellularity in CSF was associated with a worse functional outcome in immunocompetent patients. This indicates the importance of a low diagnostic threshold for this condition.
Disclosure: None of the authors have any conflicts of interest to declare.

EPR-108

Progressive multifocal leukoencephalopathy: biomarkers for early diagnosis and response to targeted therapy

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is a rare and potentially fatal demyelinating infection of the brain, caused by JC-polyomavirus (JCPyV). This devastating complication no longer only concerns the patients historically at risk, including those with hematological malignancies or HIV-infected. PML is also observed as adverse event during therapy with modern immune suppressive treatments for immune-mediated disease, especially multiple sclerosis. Diagnosis and treatment remain even 65 years after the description of the first cases complex matter. For successful therapy studies, there is medical need for optimized biomarkers for earlier PML diagnosis, and for evaluating the response to therapy.
Methods: Clinical samples of 30 patients at particular risk for PML and 5 healthy controls (serum, urine) as well as 15 PML patients (cerebrospinal fluid (CSF) and brain biopsy) were collected, and different quantitative molecular assays, including real-time (RT-PCR), as well as droplet digital PCR (ddPCR), applied for the detection of JCPyV DNA. Tissue-specific viral genetic changes in the non-coding control region and viral protein-1 of JCPyV were analyzed by Sanger sequencing and next-generation sequencing (NGS).
Results: Pre-analytical conditions (DNA extraction method) greatly influenced PCR sensitivity. However, no significant difference between RT-PCR and ddPCR sensitivity could be detected. Viral strains isolated from CSF and brain biopsy samples showed various PML-associated genetic changes.
Conclusion: Further studies are needed to implement sensitive tools for the detection of JCPyV DNA and the characterization of tissue-specific viral variation into clinical practice, also to be used as surrogate markers of response to therapy in pivotal treatment studies.
Disclosure: CW has received institutional support from Novartis, Alexion, Sanofi Genzyme, Biogen, Merck, and Roche

Motor neurone diseases

EPR-109

Apitegromab in SMA: An Analysis of Additional Efficacy Endpoints in the TOPAZ Study at 36 Months

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Background and aims: In SMA, a decrease in SMN protein expression results in progressive denervation weakness, muscle atrophy, and progressive loss of motor function. Apitegromab is an investigational, fully human, monoclonal antibody that specifically binds and inhibits proforms of myostatin, a negative regulator of skeletal muscle growth, directly targeting the muscle atrophy in patients with SMA. The TOPAZ phase 2 trial (NCT03921528) provided proof-of-concept that apitegromab has the potential to be the first muscle-directed therapy, complementary to SMN-augmenting therapy, in patients with SMA.

Methods: TOPAZ was conducted in subjects with Type 2 or Type 3 SMA (age 2-21 years). Patients received IV apitegromab Q4W, alone or with nusinersen. 58 patients were dosed in 3 cohorts. Assessment of motor function improvements via the Hammersmith scale and RULM scores and safety results from TOPAZ were previously reported over 24 months. Following the initial treatment period in TOPAZ, participants were offered the opportunity to enter 3 successive open label 12-month extension periods.

Results: The TOPAZ study showed improved motor function scores over 24 months. Incidence and severity of AEs were consistent with the underlying patient population and background therapy. Multiple efficacy endpoints and safety analyses over 3 years of apitegromab treatment will be presented.

Conclusion: The ongoing TOPAZ extension B is ongoing and will provide further long-term efficacy and safety data of apitegromab in SMA patients. This information will deepen our understanding of latent myostatin dynamics and inform future studies.

Disclosure: Dr Crawford: Consultant/ad boards: Biogen; Roche/Genentech; Avexis / Novartis; Pfizer; Study site investigator: Biogen; Avexis; Cytokinetics; Parexel; Catalyst; Scholar Rock; Patient Organizations: CureSMA; SMA Foundation; Muscular Dystrophy Association; Ataxia Telangiectasia Children's Project.

EPR-110

Arable lands proximity influenced risk and age at onset in Amyotrophic Lateral Sclerosis

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Background and aims: Amyotrophic lateral sclerosis (ALS) incidence and phenotypic heterogeneity is due to an interaction between genetic background and differently distributed environmental factors. We investigated the effect of living near specific croplands on ALS risk, site of onset, age at onset and progression rate.

Methods: In a population-based dataset of ALS patients (PARALS registry), diagnosed between 2007 and 2014, we recover the historical residence in the 20 years before disease onset. We gather data on the geographical distribution of croplands in the same period. For all the municipalities we calculated the percentages of area covered by each crop, comparing them to patients smoothed incidence using linear regression. Then, we calculated proximity scores by assessing the percentage of area covered by each crop enclosed in a circle centered on the residence address (radii range 100-2,000 meters, Figure 1), using historical residence data, weighting each exposure by the residence period.

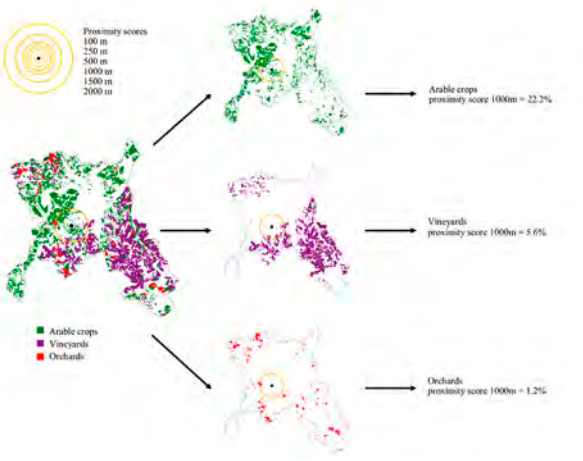

Figure 1: Proximity score

Results: ALS cases incidence increased according to the percentage of area covered in each municipality by arable crops, ranging from 0.75 to 1.81 cases/100.000/year (R=0.191, p<0.001, Figure 2). Using historical residential data, arable crops and vineyards proximity significantly influenced age at onset, even considering different radii (for arable lands 100-1,500 meters, for vineyards 500-2,000

meters) and stratifying for sex, site of onset and genetic status. We found no significant effect on progression rate or site of onset.

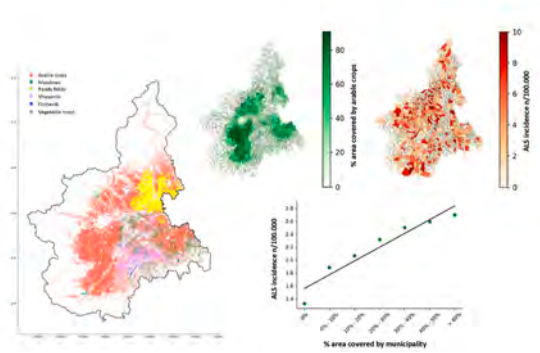

Figure 2: Smoothed incidence

Conclusion: We confirmed a higher ALS risk in municipality with high percentage of arable crops. Arable crops and vineyards proximity significantly reduced median age at onset.

Disclosure: The authors declared no significant disclosures related to the presented data.

EPR-111

Assessing Primary Model Assumptions in CENTAUR Trial of Sodium Phenylbutyrate and Ursodoxicoltaurine in ALS

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Background and aims: An oral, fixed-dose combination of sodium phenylbutyrate and ursodoxicoltaurine slowed functional decline in people living with amyotrophic lateral sclerosis in the 24-week randomised, placebo-controlled phase of the CENTAUR trial. The prespecified primary model evaluated rate of progression on the Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised (ALSFRS-R) using a shared-baseline, linear, mixed-effects model in the modified intention-to-treat (mITT) population. Here, we report analyses assessing assumptions made in the primary model and methods for handling missing data.

Methods: Sensitivity analyses that removed the shared baseline and linearity assumptions were performed. To assess the impact of missing data, a placebo-based multiple imputation for missing data was also performed. A mortality-adjusted progression (MAP) model was utilised to account for deaths prior to week 24. All sensitivity analyses were performed in the intention-to-treat (ITT) population.

Results: Primary analysis results were consistent in the mITT and ITT populations (Table 1). When both the shared baseline and linearity assumptions were removed, the ALSFRS-R estimated treatment effect was 2.15 (P=.03) as compared to 2.32 (P=.03) using the prespecified model. The placebo-based imputation analysis reduced the treatment effect slightly, but remained consistent with the primary result. The MAP model resulted in a death-adjusted treatment difference for ALSFRS-R (2.37; P=.04) that was similar to the point estimate observed in the primary model (2.32; P=.03).

Conclusion: All sensitivity analyses returned consistent findings, demonstrating that the primary estimate of treatment effect is robust.

Disclosure: LM, YW, RK, MK, and JT are employees of and have stock option ownership in Amylyx Pharmaceuticals. SP was the PI for the CENTAUR trial and received research grants from Amylyx Pharmaceuticals, The ALS Association, and ALS Finding a Cure applicable to the trial presented.

Table 1. Week 24 ALSFRS-R Treatment Difference

End Point Time Point	Estimate (SE or 95% CI)		Estimated Difference	95% CI	*P* value
Primary Model					
ALSFRS-R Total Change from Baseline (mITT[a], linearity assumed)					
	Placebo+SOC[b] (N=48)	**AMX0035+SOC[b] (N=89)**			
Week 24	−9.18 (0.880)	−6.86 (0.660)	2.32	0.18–4.47	.0340
Sensitivity Analyses					
ALSFRS-R Total Change from Baseline (ITT[c], linearity assumed)					
	Placebo+SOC[b] (N=48)	**AMX0035+SOC[b] (N=89)**			
Week 24	−9.19 (0.880)	−6.87 (0.659)	2.32	0.18–4.47	.0340
ALSFRS-R Total Change from Baseline (ITT[c], without linearity assumption)					
Week 24	−8.83 (−10.4 to −7.25)	−6.68 (−7.87 to −5.50)	2.15	0.17–4.13	.0335
ALSFRS-R Total Change from Baseline (ITT[c], without linearity assumption, placebo-based imputation for missing data)					
Week 24	−8.87 (−10.46 to −7.27)	−6.90 (−8.13 to −5.68)	1.96	−0.02 to 3.94	.05
Mortality-adjusted progression (ITT[c] population)					
Week 24			2.37	0.17–4.57	.035

ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; ITT, intention-to-treat; MAR, missing at random; mITT, modified intention-to-treat; MMRM, mixed model for repeated measures; SE, standard error; SOC, standard of care.

EPR-112

SUNFISH Parts 1 and 2: 4-year efficacy and safety data of risdiplam in Types 2 and 3 spinal muscular atrophy (SMA)

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Background and aims: Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier, approved in more than 90 countries worldwide.
Methods: SUNFISH (NCT02908685) is a multicentre, two-part, randomized, placebo-controlled, double-blind study in patients with Types 2 and 3 SMA (inclusion criteria: aged 2–25 years at enrolment). Part 1 (N=51) assessed the safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam dose levels in patients with Types 2 and 3 SMA (ambulant and non-ambulant). Part 2 (N=180) assessed the efficacy and safety of the Part 1-selected dose versus placebo in Type 2 and non-ambulant Type 3 SMA. In Part 2, participants were treated with risdiplam or placebo for 12 months; participants then received risdiplam in a blinded manner until Month 24. At Month 24, patients could enter the open-label extension phase.
Results: The primary endpoint (Part 2) of change from baseline in 32-item Motor Function Measure (MFM32) total score in patients treated with risdiplam (n=120) versus placebo (n=60) was met at Month 12. These increases in motor function were sustained in the second and third year after risdiplam treatment, as measured by MFM32, Hammersmith Functional Motor Scale – Expanded, and Revised Upper Limb Module. At Month 36 (data-cut: 6 September 2021), there were no treatment-related safety findings leading to withdrawal from SUNFISH Part 1 or 2. Here we present 4-year efficacy and safety data.
Conclusion: SUNFISH is ongoing and will provide further long-term efficacy and safety data of risdiplam in a broad population of children, teenagers and adults with SMA.
Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by Chrysalis Medical Communications, in accordance with Good Publication Practice (GPP2022) guidelines (https://www.ismpp.org/gpp-2022), and funded by F. Hoffmann-La Roche Ltd.

EPR-113

Association of APOE genotype and CSF Aβ and tau biomarkers with cognitive and motor phenotype in ALS

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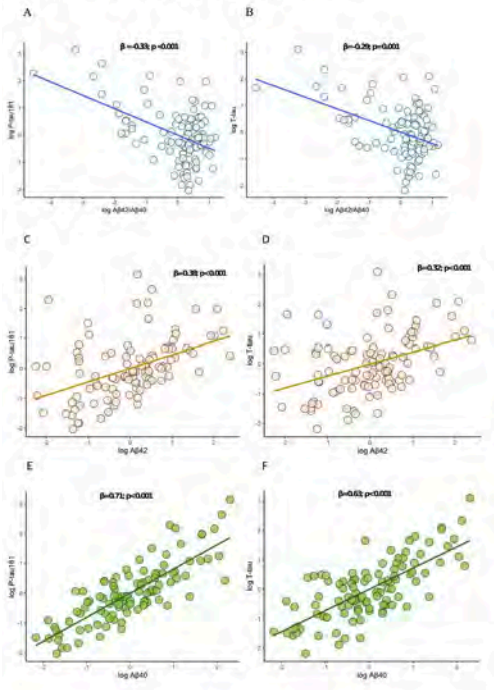
Background and aims: Little is known about ALS-nonspecific cognitive deficits –most notably memory disturbance– and their biological underpinnings. We investigated the associations of the Alzheimer's disease (AD) genetic risk factor APOE and CSF biomarkers Aβ and tau proteins with cognitive and motor phenotype in ALS.
Methods: APOE haplotype was determined in a cohort of 281 ALS patients; for 105 of these, CSF levels of Aβ42, Aβ40, total tau (T-tau), and phosphorylated tau (P-tau181) were quantified by CLEIA. The Edinburgh Cognitive and Behavioural ALS Screen (ECAS) was employed to evaluate the neuropsychological phenotype.
Results: The APOE E4 allele was associated with worse ECAS memory score (median, 14.0 in carriers vs 16.0 in non-carriers) and lower CSF Aβ42 (-0.8 vs 0.1, log-transformed values) and Aβ42/40 ratio (-0.1 vs 0.3). 37.1% of ALS patients showed low Aβ42 levels, possibly reflecting cerebral Aβ deposition. While lower Aβ42/40 correlated with lower memory score (β = 0.20), Aβ42 positively correlated with both ALS-specific (β = 0.24;) and

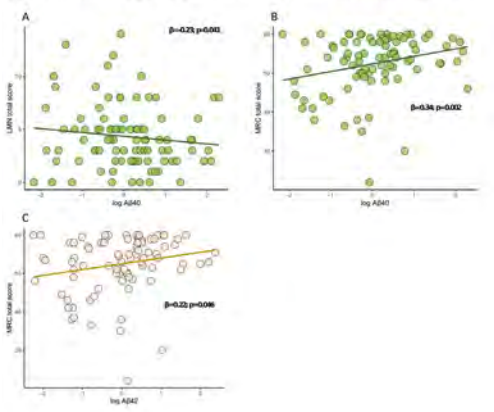
-nonspecific (β = 0.24) scores. Although Aβ42/40 negatively correlated with T-tau (β = -0.29) and P-tau181 (β = -0.33), we found an unexpected positive association of Aβ42 and Aβ40 with both tau proteins (β between 0.32 and 0.71). Regarding motor phenotype, both Aβ species were inversely associated with lower motor neuron (LMN) signs (for Aβ42, β = 0.22).

Figure 3: Correlation between β-amyloid isoforms and tau proteins



simple dispersion with adjustment curve displaying significant negative correlations of CSF values of Aβ42/40 ratio with T-tau and P-tau181 (A-B) and significant positive correlations of CSF Aβ42 (C-D) and Aβ40 (E-F) with T-tau and P-tau181

Figure 4: Correlation of $A\beta_{40}$ and $A\beta_{42}$ with clinical indexes of lower motor neuron impairment



Simple dispersion with adjustment curve illustrating significant correlations of Aβ40 and Aβ42 with clinical indexes of LMN impairment, namely LMN (A) and MRC scores (B and C), respectively. Abbreviations: LMN = lower motor neuron; MRC

Conclusion: APOE haplotype and CSF Aβ biomarkers are associated with cognitive deficits in ALS and particularly with memory impairment. This might partly reflect AD-like pathophysiological processes, but additional ALS-specific mechanisms could be involved.

Figure 7: Hypothesized biologic pathway leading to intracellular amyloid accumulation/extracellular Aβ plaque deposition from ALS-induced neuronal damage.

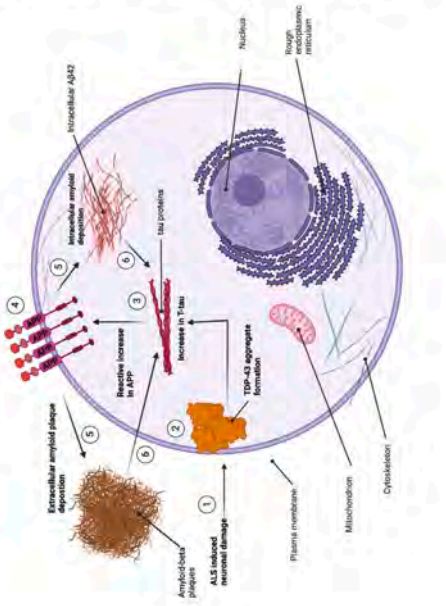


Illustration of proposed biological interplay between classic ALS-related mechanisms of damage and Aβ pathways. Neuronal damage caused by ALS (1) resulting in TDP-43 accumulation (2) is associated with progressive increase of T-tau protein (3).

Disclosure: Alessio Maranzano, Federico Verde, Antonella Dubini, Silvia Torre, Eleonora Colombo, Alberto Doretti, Francesco Gentile, Arianna Manini, Ilaria Milone, Alberto Brusati, Silvia Peverelli, Serena Santangelo, Erminio Torresani, Davide Gentilini, Stefano Messina, Claudia Morelli, Barbara Poletti and Antonia Ratti report no disclosure. Vincenzo Silani received compensation for consulting services and/or speaking activities from AveXis, Cytokinetics, Italfarmaco, LiquidWeb, Srl and Novartis Pharma AG. He receives or he has received research support from the Italian Ministry of Health, AriSla, and E-Rare Joint Translational Call. He is on. the Editorial Board of Amyotrophic Lateral Sclerosis and Frontotemproal Degeneration, European Neurology, American Journal of Neurodegenerative Disease and Frontiers in Neurology. Nicola Ticozzi received compensation for consulting services from Amylyx Pharmaceutical and Zambon Biotech SA. He received research funding from the Italian Ministry of Health and AriSLA. He is associate editor of Frontiers in Aging Neuroscience.

EPR-114

FIREFISH Parts 1 and 2: 4-year efficacy and safety of risdiplam in Type 1 spinal muscular atrophy (SMA)

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Background and aims: Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier, approved in more than 90 countries worldwide.

Methods: FIREFISH (NCT02913482) is a multicentre, open-label, two-part study of risdiplam in children with Type 1 SMA and two SMN2 gene copies (inclusion criteria: 1–7 months old at enrolment). FIREFISH Part 1 assessed the safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam doses. Pivotal Part 2 assessed the safety and efficacy of risdiplam over 24 months at the dose selected from Part 1. Thereafter, children entered a 3-year open-label extension phase and continue to receive risdiplam at the pivotal dose.

Results: Pooled safety and efficacy data were available from 58 enrolled infants who received risdiplam treatment (Part 1 high-dose cohort, n=17; and Part 2, n=41). As of the cut-off date (23 November 2021), there were no treatment-related adverse events leading to withdrawal, no additional deaths and no additional children meeting the definition of permanent ventilation since Month 24. At Month 36, 84% of children were alive and did not require permanent ventilation. Children either maintained or improved their motor skills in terms of developmental milestones and motor function between Months 24 and 36, which is not observed in natural history. Here we present longer-term pooled safety and efficacy data from children who have received risdiplam at the pivotal dose for ≥48 months.

Conclusion: FIREFISH Parts 1 and 2 are ongoing globally and will provide further safety and efficacy data of risdiplam in Type 1 SMA.

Disclosure: This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance was provided by Chrysalis Medical Communications, in accordance with Good Publication Practice (GPP2022) guidelines (https://www.ismpp.org/gpp-2022) and funded by F. Hoffmann-La Roche Ltd.

EPR-115

ALS serum-induced motoneuron degeneration in slow and fast progressing disease groups

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Background and aims: Amyotrophic lateral sclerosis (ALS) is characterized by the progressive loss of motoneurons (MN). Systemic inflammatory changes have been implicated to contribute to the pathogenesis of ALS, including elevated serum cytokine levels and presence of anti-MN antibodies. We have previously shown that passive transfer of ALS serum induces MN loss in mouse. Here we aim to characterize the degeneration induced by the transfer of serum from slow and fast progressing ALS patients.
Methods: Blood serum was collected from 15 ALS patients, who were sorted into slow (n=7) and fast progression (n=8) subgroups based on the annual decrease in the ALS functional rating scale. Balb/c mouse received ALS serum in the form of intraperitoneal injections over 4 weeks. Denervation of neuromuscular junctions (NMJs) was evaluated in the tibialis anterior (TA), and soleus (SOL) muscles based on morphological and electrophysiological analysis. Cell counting was performed to determine MN loss in the spinal cord.
Results: Compared to intact animals, ALS serum induced atrophy of the axon terminals and robust denervation of NMJs in the fast progression ALS group, while in the slow progression subgroup only moderate denervation was observed. In the TA, the number of motor units decreased in both groups, but in the SOL only the progressive group showed significant reduction of motor units. In the spinal cord the serum injection resulted in moderate MN loss in both groups.
Conclusion: Here we showed that ALS serum from patients with progressive clinical phenotype induces more prominent alterations at the level of NMJs, indicating a dying-back process.
Disclosure: The project was financially supported by the OTKA FK_22 143326 grant of the National Research, Development and Innovation Office of the Hungarian government.

EPR-116

Structural and functional connectome alterations across King's stages in amyotrophic lateral sclerosis

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Background and aims: This study aims to explore the rearrangements of structural and functional connectivity within and among brain networks underlying the clinical spreading of ALS, as described by the King's staging system, to suggest objective, continuous measures mirroring disease progression.
Methods: 104 patients with amyotrophic lateral sclerosis (ALS) and 61 age- and sex-matched healthy controls underwent clinical evaluation and brain magnetic resonance imaging (MRI) on a 3T scanner. Patients were stratified into four groups, according to the King's staging system. No patient had comorbid frontotemporal dementia. Structural and functional connectivity values within and between different brain regions were obtained using diffusion tensor and resting-state functional MRI data.
Results: Compared with controls, a progressive reduction of structural connectivity within brain nodes of the sensorimotor network was observed in ALS patients across King's stages 2, 3 and 4 ($p<0.006$). Stage 3 and 4 patients also showed loss of structural connectivity between frontal and sensorimotor regions ($p=0.001$). Disruption of functional connectivity within frontotemporal regions was found only in stage 4 ($p=0.025$). Sensorimotor structural connectivity showed a strong correlation with ALSFRS-r scores ($r=0.31$, $p=0.001$).
Conclusion: Brain MRI allows to demonstrate and quantify increasing disruption of structural connectivity involving the sensorimotor and frontal networks in ALS, mirroring disease progression. Frontotemporal functional disconnection seems to characterize only advanced disease stages. MRI connectomics can stratify patients and stage brain pathology in ALS in a reproducible way, which mirrors clinical progression.

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EPR-117

Abstract withdrawn.

Cerebrovascular diseases 2

EPR-118

Long-term ECG monitoring in patients after ischaemic stroke

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Background and aims: Atrial fibrillation (AF) is a frequent cause of ischaemic stroke. Long-term ECG monitoring is used to detect a paroxysmal form of AF. Biomarkers can predict paroxysmal AF detection. The study aimed to describe the effectiveness and patient tolerance of long-term ECG monitoring in detecting paroxysmal AF in ischaemic stroke patients. A secondary aim was to identify biomarkers of paroxysmal AF detection.
Methods: An interim analysis of a retrospective multicenter study on ischaemic stroke patients with unknown AF hospitalized at 19 stroke centers within the Czech Stroke Research Network (STROCZECH) from 2015 to 2020 who underwent subsequent long-term ECG monitoring (continuous Holter ECG monitoring or event-loop monitor).
Results: 1896 patients (mean age 67 years, 56% men, mean NIHSS at admission 4, 82.2% with cryptogenic stroke) were so far included in the study (55% remaining). The mean length of ECG monitoring was 22 days. The monitoring was terminated early in 0,8% of patients. AF was detected in 7.9% of patients. Patients with AF were older (73.5 vs. 65.3 years, $p<0.001$), had higher CHA2DS2-VASc score (2.8 vs. 1.7, $p<0.001$), higher levels of NT-proBNP (1200 vs. 252 ng/l, $p=0.005$), hs-troponin I (11.1 vs. 8.4 ng/l, $p=0.002$), lower eGFR (1.2 vs. 1.4 ml/s, $p=0.004$) and had more frequently old ischaemic lesions on MRI (44.3% vs. 31.2%, p=0,008).
Conclusion: Using long-term ECG monitoring, paroxysmal AF was detected in 7.9% of ischaemic stroke patients. Patients with AF detection were significantly older, had higher levels of NT-proBNP and hs-troponin I, lower eGFR, and more frequently old ischaemic lesions on MRI.
Disclosure: Nothing to disclose.

EPR-119

Trends in Incidence of Ischemic Stroke and Oral Anticoagulant Use in Patients with Atrial Fibrillation in Korea

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Background and aims: Atrial fibrillation (AF) is the most common cardiac arrhythmia that causes ischemic stroke (IS). After the introduction of non-vitamin K antagonist oral anticoagulants (NOACs), the use of OAC has been increased. It remains uncertain whether the increased use of OAC at the population level will result in a lower incidence of IS related to AF and the changes in the OAC prescription around ischemic stroke.
Methods: The data source for this study was the Korean Nationwide Health Insurance System. We included patients with AF from the database. The inclusion criteria were as follows: (1) patients diagnosed with AF from January 1, 2015, to December 31, 2019. (2) Patients with CHA2SD2-VASc score ≥ 2 in men, 3 in women.
Results: A total of 140,597 patients were included in this study. Of the 140,597 patients, 9,265 patients (6.59%) had an IS after the diagnosis of AF. Among patients with acute IS, the preadmission use of NOAC increased from 1.6% in 2015 to 27.8% in 2019. The use of NOAC increased particularly after 2015 due to the NOAC approval in Korea, while the use of warfarin declined between 2015 through 2019.
Conclusion: In conclusion, the proportion of ischemic stroke related to AF remains high although the increased use of OAC among AF patients. The use of NOAC particularly increased after 2015 in Korea. However, there are still a large proportion of eligible but insufficiently treated AF patients, which leaves room for improvement with regard to preventing stroke and improving stroke incidence.
Disclosure: Nothing to disclose.

EPR-120

Anatomical higher risk appearance and carotid stenting

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Background and aims: Carotid artery stenting (CAS) is currently performed as an alternative interventional treatment option to carotid endarterectomy (CEA). However, pre-procedural consideration and anatomical risk factor analysis are still not enough. Thus, we investigate the anatomical higher risk appearance of CAS such as CCP from the standpoint of neurointerventionist which predict periprocedural complications.

Methods: Patients with carotid stenosis who underwent CAS in a comprehensive stroke center from January 2012 to December 2021 were reviewed retrospectively. Patients with modified Rankin Scale of 2 or less who underwent CAS for atherosclerotic stenosis of the proximal internal carotid artery (ICA) were included in the analysis. Curved-centered plaque (CCP) was defined as the stenotic segment with a plaque located middle of the severe curvature vascular appearance. Patients were divided into two groups, those with complications and those without complications, for periprocedural complication risk factor analysis.
Results: A total of 148 patients (64 women [43.2%]; median age, 73.0 [inter-quartile range, 65.5-79.0]) were analyzed. Complications occurred in 39 of 148 patients, mostly was minor and transient. The complication group showed high initial National Institutes of Health Stroke Scale, and a higher proportion of symptomatic stenosis and CCP of proximal ICA than the without complication group. By multivariate logistic analysis, CCP was an independent risk factor for complications of CAS.

	Univariable analysis Odds ratio (95% CI)	*P* - value	Multivariable analysis Adjusted odds ratio (95% CI)	*P* - value
Age>80	1.76 (0.76–3.98)	0.18		
Symptomatic stenosis	2.89 (1.34–6.62)	0.009	2.29 (1.01–5.41)	0.052
Initial NIHSS	1.09 (1.00–1.19)	0.038		
Curved-centered plaque	2.62 (1.25–5.61)	0.012	2.23 (1.02–4.88)	0.044
Carotid bulb stenosis or Suprabulb	1.16 (0.48–2.65)	0.733		
Puncture to final angiography time, min	1.02 (1.00–1.04)	0.017	1.01 (1.00–1.03)	0.143
Length of stenosis >15mm	0.85 (0.40–1.78)	0.672		
Ostial centered lesion	1.16 (0.48–2.65)	0.733		

Table. Factors associated with any complications of carotid stenting

Conclusion: High-risk vascular anatomical appearance, such as CCP, showed an association with the high frequency of periprocedural complications of CAS. Tailored patient selection in carotid stenosis is a crucial strategy for preventing periprocedural complications.
Disclosure: Nothing to disclose.

EPR-121

Risk of MRI-detected cerebral infarction and effect on cognitive functions after CEA and carotid stenting over a decade

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Background and aims: Advances in medical management of carotid endarterectomy (CEA) and new materials used in carotid stenting (CAS) should improve the prognosis of patients with carotid stenosis. The aim of the study was to compare the safety of CEA and CAS over one decade.
Methods: The first 50 patients treated by CEA and 50 patients treated by CAS in 2 time periods (2008–2012 and 2018–2022) were included. New ischemic lesion on control brain magnetic resonance, vascular event or death and changes in cognitive functions within 30 days were compared between CEA and CAS in individual periods and between individual interventions in two periods.
Results: Totally 400 patients (274 males; age 66.9±7.3 years) with carotid stenosis ≥70% (mean 80.7±9.1%) were included. New ischemic lesions on control brain magnetic resonance were detected significantly less frequently in patients underwent CEA compared to CAS in both periods ($p<0.001$ and $p=0,017$, resp.); in CAS group in period 2 compared to period 1 ($p=0.004$); and in all patients in period 2 compared to period 1 ($p=0.002$). In the period 1, there was significant decline in cognitive functions only in asymptomatic patients undergoing both CEA ($p=0.049$) and CAS ($p=0.015$). No significant cognitive decline in any test was detected in period 2 in both groups.
Conclusion: Changes in interventional techniques and patients' management during a decade led to decrease of risk of new brain infarction on magnetic resonance and risk of cognitive decline in patients with asymptomatic carotid stenoses.
Disclosure: Supported by grants NV19-04-00270, NU22-04-00389.

EPR-122

Real-life experience using tenecteplase versus alteplase in acute ischemic stroke outside conventional indications

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Background and aims: Current guidelines establish the use of intravenous tenecteplase (TNK) for acute ischemic stroke (AIS) treatment in the context of less than 4,5 hours since the beginning of symptoms and before mechanic thrombectomy (MT). Our objective is to determine the efficacy and security of TNK use versus alteplase (rTPA) in the real-world setting outside this indication.
Methods: From a prospective database, we retrospectively evaluated patients with AIS treated with rTPA (0,9mg/kg) or TNK (0,25mg/kg) from November 2020 to January 2022 in other scenarios: unknown onset, wake-up stroke, more than 4,5 hours of symptoms and patients not receiving MT. Clinical and radiological characteristics, functional and safety outcomes, and mortality were compared.
Results: 29 patients received TNK and 41 patients rTPA, with no significant differences in the baseline characteristics between groups. 12 patients had unknown onset, 24 wake-

up stroke, 10 had more than 4,5 hours of symptoms, and 35 did not receive MT. TNK use was associated with significant clinical improvement at 24 hours (reduction of NIHSS 8 points or greater; OR 18, p<0,001), functional excellence at 3 months (mRS 0-1; OR 3,46, p=0,042) and functional independence at 3 months (mRS 0-2; OR 5,06, p=0,038; Figure 1), without increasing the risk of intracranial bleeding (OR 0,28, p=0,269) or death (OR 0,32m p=0,362).

Figure 1. mRS score at 90 days distribution between groups.

Conclusion: Tenecteplase use was associated with better functional outcomes, without increasing the risk of intracranial bleeding or death, also in real-world practice settings and in conditions not yet included in the clinical guidelines.
Disclosure: The authors did not receive funds, grants, or other support from any organization for the submitted work.

EPR-123

Overcoming barriers on the way to reperfusion therapy implementation in ischemic stroke patients in Kyrgyzstan

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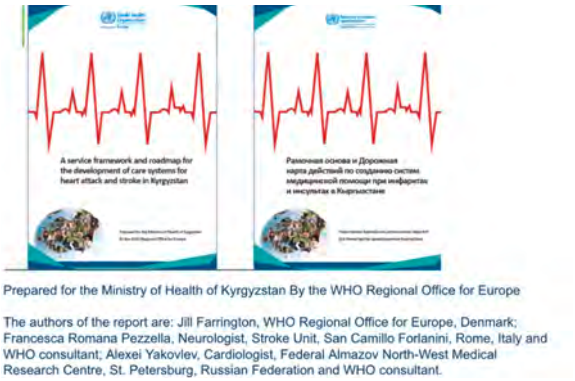
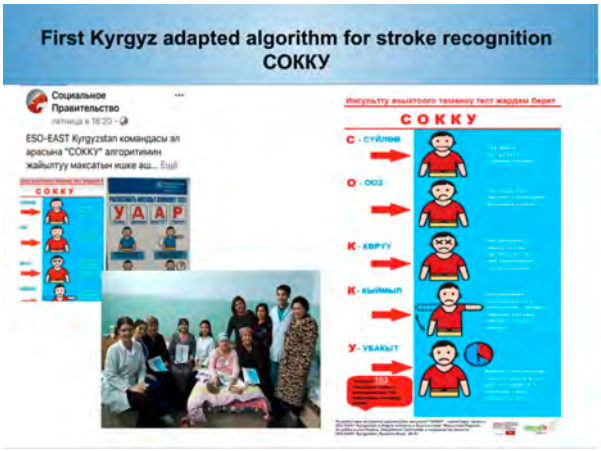
Background and aims: In Kyrgyzstan, a low income country, stroke affects individuals in the most productive years of their lives: the median age of ischemic stroke patients is 67 years and poststroke disability is high (mRs = 3). Insurance-covered reperfusion therapy was absent in Kyrgyzstan due to a high cost and limited resources.
Methods: A stroke Roadmap in Kyrgyzstan was designed in collaboration with WHO and ESO leaders and was implemented in action in 2019 aimed to reduce the gap in evidence-based stroke treatment and prepare the neurologists and paramedics for reperfusion therapy implementation and consists of the structured plan for all the healthcare levels for 10 years.



Stroke Roadmap in Kyrgyzstan

Results: We used three strategies according to the Roadmap: 1) facilitated the unified electronic stroke registry usage in all regions of Kyrgyzstan, 2) trained paramedics and stroke physicians in stroke recognition, NIHSS and mRs use, translating them in Kyrgyz language, and detecting the early neuroimaging patterns on CT in ischemic stroke patients and 3) influenced the stroke logistics, prioritizing the early admission of stroke patients into hospitals.



First algorithm for stroke recognition SOKKU in Kyrgyzstan

Conclusion: Next stage will be implementation of the CT-scans into the governmental hospitals as all the neuroimaging is now located in the private centers surrounding the stroke hospitals, enlargement the network of stroke units and stroke ready hospitals training the personnel in the thrombolysis use and stroke patients monitoring.
Disclosure: Nothing to disclose.

EPR-124

Reduced expression of BIN1 and VEGFA genes in patients with cerebral small vessel disease and cognitive impairment

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Background and aims: Cerebral small vessel disease (cSVD) is one of the leading causes of dementia in an aging population. The mechanisms underlying this disease are not completely clear. The aim of the study was to determine the role of the functional activity of genes that converged in cerebrovascular pathology and Alzheimer's disease according genome-wide association studies (GWAS) in the development of cSVD with cognitive impairment (CI).
Methods: The study included 34 cSVD patients (61.7+/- 8.95; women 63.6%) with white matter hyperintensity grade Fazekas 3 and CI, and 11 healthy participants (HP) (57.3+/- 9.7, women 64.7%). Gene expression was determined using an individual NanoString nCounter panel (NanoString Technologies, USA), created at our request and including 56 genes that reflect inflammation, permeability, cytoprotection, amyloidogenesis, and regulation of the cell cycle. RNA was isolated using a "miRNeasy Mini Kit ("Qiagen")" and placed in a digital analyzer nCounter Analysis System. Processing of the obtained "raw" data was performed using the "nSolver 4.0", statistical processing – "SPSS Statistics v.26".
Results: CSVD patients had reduced expression in BIN1 (3.6 [2.3; 5.5] versus 8.7 [4.3; 12.7], p=0,019) and VEGFA (2.9 [2.2; 5.8] vs 9.5 [2.9; 13.4], p=0,007) genes (figure). The significance of the genes was confirmed by real-time PCR. BIN1 gene expression correlated with VEGFA gene expression (r=0.489), Montreal Cognitive Assessment Scale scores (r=0.354) and brain gray matter volume (r=0.421).

Figure. Differences in expression levels of BIN1 and VEGFA genes in cSVD and HP.

Conclusion: Reduced expression of the VEGFA and BIN1 genes is associated with the progression of cSVD and CI, suggesting a role for angiogenesis and demyelination/ inflammation, respectively, according to the literature.
Disclosure: Nothing to disclose.

EPR-125

Detection of right-to-left shunt with transoccipital approach of transcranial Doppler.

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Background and aims: Right-to-left shunt (RLS) represents an important cause of cryptogenic stroke (CS). Transcranial Doppler (TCD) with an agitated saline bubble study is a highly sensitive modality for RLS diagnosis with a transtemporal approach (TCD-TT). However, a minority of patients has insufficient temporal windows. Our aim was to evaluate the accuracy of transoccipital TCD (TCD-TO) for RLS diagnosis.
Methods: Prospective, single-centre, observational study including patients with CS or transient ischemic attack (TIA) who were included in a standard protocol for RLS diagnosis between January 2022 and January 2023. We compared TCD-TT and TCD-TO approaches. We also evaluated the concordance of RLS grade between TCD-TO and transesophageal echocardiogram (TEE) through kappa index.
Results: Eighteen patients were included (66.7% men, median age: 49 years old, IQR: 43-53,75). The most frequent diagnosis was hemispheric stroke (55.6%). RLS was found in ten patients (55.6%) after the Valsalva maneuver with TCD-TT, and nine with TCD-TO (50%). Sensitivity and specifity of TCD-TO reached 90% and 100% respectively, whereas positive predictive value was 89% and negative predictive value was 79%. Moreover, the concordance of RLS grade between TCD-TT and TCD-TO was 0.76 (p<0.001). All nine positive-RLS screened by TCD-TO were confirmed by TEE, with medium or large RLS. Only one patient with negative screening for RLS underwent TEE, where a small RLS was shown. The concordance between TCD-TO and TEE was 0.688 (p<0.004).
Conclusion: TCD-TO is a sensitive and specific test for RLS diagnosis, with a substantial concordance with TEE, especially for medium and large RLS.
Disclosure: Nothing to disclose.

EPR-126

Non-stenosing intracranial atherosclerotic lesions in embolic stroke of undetermined source: a vessel wall MRI study

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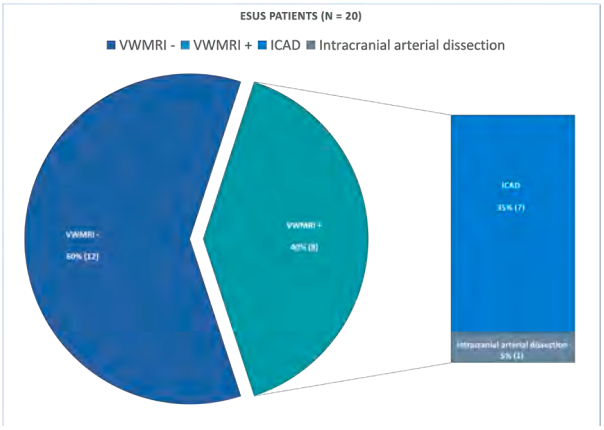
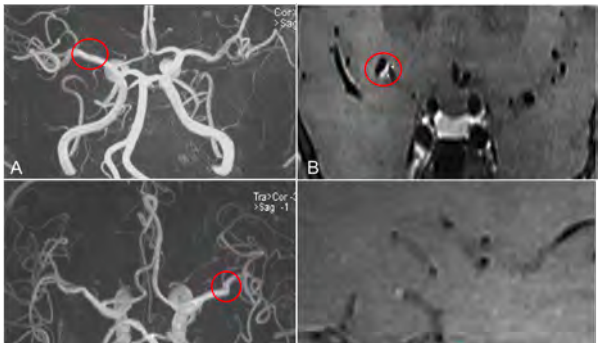
Background and aims: Despite standard diagnostic approach, 30% of ischemic strokes remain cryptogenic, and the 50% of them can be classified as embolic stroke of undetermined source (ESUS). Artery to artery embolization from non-stenosing complicated atherosclerotic intracranial plaques has been suggest as a potential aetiology of ESUS, often undetected by conventional imaging. Vessel wall MRI (VWMRI) can identify high-risk atherosclerotic plaques and other culprit arterial lesions. However, prospective studies of VWMRI in ESUS patients are lacking. The aim of our study was to define the proportion of ESUS caused by intracranial arteries lesions undetected by luminal-based imaging, clarifying the role of VWMRI in ESUS.
Methods: We prospectively evaluated all consecutive patients with acute ischemic stroke admitted to IRCCS Mondino Stroke Unit from July 2022. All patients underwent standard diagnostic workup including CT angiography of intracranial and epiaortic vessels, transthoracic echocardiogram and 72 h ECG monitoring. Patients with multi-territory strokes were excluded. All patients respecting ESUS criteria without contraindication to MRI were included in the study and underwent VWMRI with gadolinium contrast agent administration within 1 month.
Results: The first 20 patients have been enrolled in the study. VWMRI revealed culprit intracranial vessels lesions in the involved vascular territory in 40% (n=8) of patients. Particularly, 7 patients had non-stenosing complicated atherosclerotic plaques with contrast enhancement; 1 patient had a dissection of the intracranial vertebral artery.



VWMRI findings in patients with uniterritorial ESUS.



TOF MRI angiography did not show any significant stenosis of intracranial arteries in the two ESUS patients (A,C). VWMRI reveals culprit atherosclerotic plaques with contrast enhancement in both of them (B,D).

Conclusion: VWMRI revealed culprit lesion in a significant proportion of ESUS patients with a single vascular territory involvement. Our preliminary data suggest the importance of VWMRI in the diagnostic workup of ESUS.
Disclosure: Authors report no disclosures.

Muscle and neuromuscular junction disorder

EPR-127

A real world experience with Efgartigimod in generalized Myasthenia Gravis in a national reference center

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Background and aims: Inhibition of the neonatal Fc receptor (FcRn) is a new treatment strategy for antibody mediated disorders. We report our real life experience with Efgartigimod (EFG) in 19 patients with generalized MG along a clinical follow-up of 13 months.
Methods: EFG was administered according to the GENERATIVE protocol (consisting of a Fixed period of 2 treatment cycles of 4 infusions at weekly intervals, followed by a Flexible period during which EFG was given in case of clinical worsening). 8 pts were AChR-Ab+, 4 MuSK+, 2 LRP4+, and 5 were seronegative. Clinical outcomes were evaluated by means of the MG-ADL, QMG, and MGC scales.
Results: 53% of patients needed 3 treatment cycles, 26% 4 and 21% 5 cycles along the follow-up (Nov 2021-Dec 2022). Meaningful improvement was observed at the end of each treatment cycle with all the scores adopted. Along the year before EFG, 8/19 patients (42%) were hospitalized, and 15/19 (79%) needed treatment with Plex/IVIG; 3/19 (16%) were admitted to the ICU. During EFG, none of them was hospitalized and only 1 patient required immunomodulation. No major side effects or infusion related reactions occurred.
Conclusion: Our results confirm the efficacy of EFG as reported by RCTs and extend the observation along a follow up of 13 months during which EFG modified significantly the course of the disease. A longer follow-up will be available at the time of the meeting. Our experience strengthens the role of FcRn inhibition as a new effective tool in the management of MG.
Disclosure: R. Mantegazza received funding for travel, meeting attendance or Advisory Board participation from Alexion, Argenx, Biomarin, Catalyst, Sanofi, Regeneron and UCB. C. Antozzi received funding for meeting attendance from Biogen and Sanofi. L. Maggi received funding for travel, meeting attendance or Advisory Board participation from Sanofi Genzyme, Roche, Alexion, AmicusTherapeutics and Biogen. S. Bonanno received funding for travel, meeting attendance or Advisory Board participation from Sanofi Genzyme, Biogen and Roche

EPR-128

Safety Profile Overview of Efgartigimod Clinical Trials in Participants With Diverse IgG-Mediated Autoimmune Diseases

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Background and aims: Efgartigimod is a first-in-class human IgG Fc fragment that inhibits the neonatal Fc receptor and outcompetes endogenous IgG binding. This results in reduced recycling and increased degradation of IgGs, including pathogenic IgG autoantibodies. This study assessed the safety profile of efgartigimod across IgG-mediated disorders.
Methods: Intravenous efgartigimod safety was assessed in generalized myasthenia gravis (gMG) in phase 2 and 3 (ADAPT) trials and a 3-year open-label extension (ADAPT+) trial. It was also evaluated in a phase 3 (ADVANCE) trial in primary immune thrombocytopenia (ITP) and an open-label phase 2 trial in pemphigus. These studies examined different dosing regimens of efgartigimod (10–25 mg/kg), including cyclical dosing in gMG and continuous weekly dosing in ITP and pemphigus.
Results: Across all indications and doses studied, efgartigimod demonstrated a consistent safety profile, with comparable treatment-emergent adverse event (TEAE) rates to placebo (ADAPT 77.4% efgartigimod/84.3% placebo; ADVANCE 93.0% efgartigimod/95.6% placebo; and 85% in the open-label pemphigus study). Most TEAEs across studies were mild to moderate in severity. Discontinuation rates due to adverse events were consistently low (3.6% efgartigimod/3.6% placebo in ADAPT; 3.5% efgartigimod/2.2% placebo in ADVANCE; and 3% of pemphigus study participants). Efgartigimod was well tolerated in ADAPT+, with no increase in TEAE incidence rates or infections with additional efgartigimod dosing (≤19 cycles). Efgartigimod treatment did not reduce albumin or increase cholesterol levels.
Conclusion: Efgartigimod was well tolerated across indications and doses studied. Most TEAEs, including infections, were mild or moderate in severity and did not increase in frequency with recurrent dosing.

Disclosure: This work was supported by argenx BVBA, who designed and funded the analysis. AB: Consultant: Alexion Pharmaceuticals, argenx BVBA, Sanofi-Aventis, Ultragenyx Pharmaceuticals; Honoraria: Alexion Pharmaceuticals, argenx BVBA, Sanofi-Aventis, UCB. KG: Consultant: Alexion Pharmaceuticals, argenx BVBA, Strongbridge, UCB; Honoraria: Alexion Pharmaceuticals. CB: Honoraria: Alexion Pharmaceuticals, argenx BVBA, Apellis, Sanofi. MG: Consultant: argenx BVBA, Almirall; Honoraria: Biotest, GSK, Janssen, Leo Pharma, Lilly, Novartis, UCB. HM: Consultant: argenx BVBA, Alexion Pharmaceuticals, UCB, Roche; Honoraria: Japan Blood Products Organization, Chugai; Research funding: Ministry of Health, Labour and Welfare, Japan. ZBC: Consultant: Sanofi-Genzyme Hungary; Honoraria: Orvostovábbképzo Szemle; Research funding: NKFI Hungary. AN: Consultant: Amgen, Angle, argenx BVBA, Dova, Novartis, Ono, Rigel, Shionogi; Honoraria: Amgen, Angle, argenx BVBA, Dova, Novartis, Ono, Rigel, Shionogi; Research funding: Amgen, Novartis, Rigel; Paid expert testimony: argenx BVBA, Rigel. JFH: Honoraria: Alexion Pharmaceuticals, argenx BVBA, F. Hoffman-LaRoche Ltd., Immunovant Inc., Ra Pharmaceuticals, Regeneron Pharmaceuticals, Sanofi US, Viela Bio Inc., Research Funding: Alexion Pharmaceuticals, argenx BVBA, Cartesian Therapeutics, Ra Pharmaceuticals, Takeda Pharmaceuticals. PE, RK, JTG, SA, MJ: Employees of argenx BVBA and may own stock/options in the company.

EPR-129

Natural variability in myocytes oxidative deficiency and homogenate mitochondrial genetics in m.3243A>G-related myopathy

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Background and aims: Mitochondrial DNA (mtDNA) undergoes continuous replication and degradation in post-mitotic tissues allowing clonal expansion of pathogenic variants over their disease-threshold and accumulation of oxidative phosphorylation (OXPHOS)-deficient fibres prior to clinical mitochondrial myopathy in patients. Mitosis-dependent mtDNA replication-segregation cycles, initially during muscle embryogenesis and later during satellite cell proliferation in adult muscle, may introduce further intra-individual molecular variability. We aimed to assess, for the first time to our best knowledge, the natural intra-individual variability in OXPHOS deficiency, mtDNA copy number (CN) and mutation heteroplasmy, which are increasingly used in clinical research into mitochondrial myopathies.
Methods: We analysed 50 post-mortem samples of tibialis anterior (TA) and quadriceps (QD) muscles from five individuals with m.3243A>G-related muscle disease. Single-fibre OXPHOS deficiency was quantified in three serial sections per sample using quadruple-immunofluorescence for NDUFB8 and MTCO1 OXPHOS markers and VDAC1 mitochondrial mass marker. We also quantified CN, using real-time PCR, and mutation heteroplasmy, using pyrosequencing, in homogenates per sample.
Results: Using bootstrapping and Bayesian inference we were able to quantify within-patient variability in proportions of OXPHOS-deficient fibres within and between samples and between muscles, as well as variability between samples and between muscles for CN and heteroplasmy in sample homogenates.
Conclusion: Over time, cell-specific differences in mtDNA dynamics induce variation in molecular markers of mtDNA-related disease between cells and ultimately between muscles. Quantifying the variability within samples and within muscles is essential to design longitudinal experiments with repeated muscle sampling from participants as required in studies of disease progression and the response to interventions in mitochondrial myopathies.
Disclosure: No conflict of interest to disclose.

EPR-130

Eculizumab in adolescents with refractory gMG: A sub-analysis of a phase 3 study by chronic IVIg use at study entry

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Background and aims: Chronically administered intravenous immunoglobulin (IVIg) is commonly used to treat refractory generalized myasthenia gravis (gMG) in adolescents. Eculizumab, a terminal complement C5 inhibitor, was efficacious and well-tolerated in a phase 3 study of adolescents with refractory anti-acetylcholine receptor antibody-positive gMG (AChR Ab+ gMG), of whom >50% were receiving chronic IVIg at study entry. This analysis evaluated response to eculizumab in adolescents who were or were not receiving chronic IVIg treatment.

Methods: Sub-group analysis of a phase 3, open-label, single-arm multicenter study (NCT03759366), assessed clinical response to eculizumab in adolescents aged 12–17 years receiving or not receiving IVIg at baseline. Changes from baseline to Weeks 12 and 26 in multiple parameters, including Quantitative Myasthenia Gravis (QMG; primary endpoint) and Myasthenia Gravis-Activities of Daily Living (MG-ADL) total scores were descriptively summarized. Myasthenia Gravis Foundation of America Post-Intervention Status (MGFA-PIS) was also assessed.
Results: Of 11 enrolled adolescents (mean age 14.8 [standard deviation 1.8] years), 6 were receiving chronic IVIg at baseline. The magnitude of improvement in QMG and MG-ADL total scores from baseline to Weeks 12 and 26 was similar between patients receiving and not receiving chronic IVIG (Table). At Week 12, 3/6 patients receiving and 5/5 patients not receiving IVIg at baseline had improved on MGFA-PIS; all 10 completing patients had improved at Week 26.

Conclusion: Adolescents with refractory AChR Ab+ gMG treated with eculizumab achieved clinical improvement, irrespective of whether or not they were receiving chronic IVIg at baseline.
Disclosure: This study was funded by Alexion, AstraZeneca Rare Disease.

Time point	Receiving chronic IVIg at baseline (n=6)	Not receiving chronic IVIg at baseline (n=5)	All patients (N=11)
	Mean (SE) change from baseline in QMG		
Week 12	-5.2 (2.36)	-5.4 (1.03)	-5.3 (1.31)
Week 26	-5.8 (2.96)[a]	-6.4 (0.75)	-6.1 (1.44)[b]
	Mean (SE) change from baseline in MG-ADL		
Week 12	-1.3 (0.99)	-2.0 (0.84)	-1.6 (0.64)
Week 26	-2.8 (0.80)[a]	-2.2 (0.86)	-2.5 (0.56)[b]

[a]n=5. [b]n=10
MG-ADL, Myasthenia Gravis-Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; SE, standard error

EPR-131

Shared B cell receptor repertoire between thymus and peripheral blood in patients with myasthenia gravis

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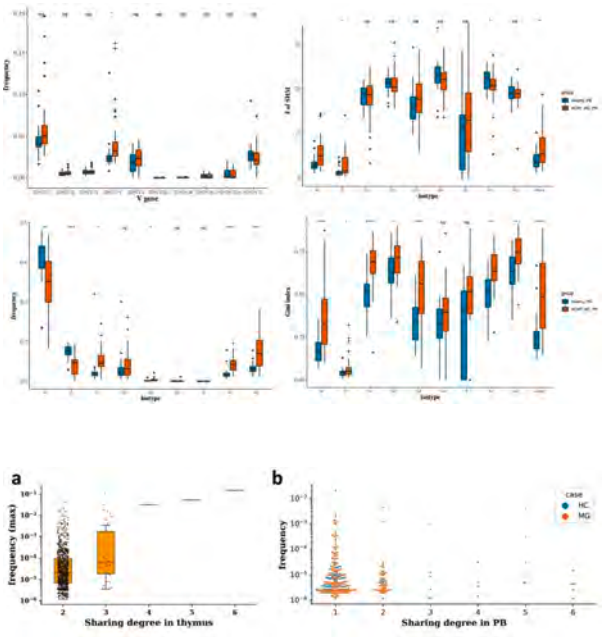
Background and aims: Little attempts were made to compare the disease-specific B cell repertoire between thymus and peripheral blood in patients with MG. We assessed whether the clones shared between thymi obtained from different MG patients are more likely to be observed in peripheral blood B cell repertoire.

Methods: Fifteen thymi and 34 peripheral blood mononuclear cells collected from patients with AChR Ab-positive MG were analyazed. B cell receptor (BCR) repertoire of peripheral blood and thymus were analyzed using the NovaSeq platforms. The peripheral blood BCR repertoires were compared between MG patients and healthy controls.
Results: IGHV3-74 was more abundantly used in MG patients ($p \leq 0.05$). Isotypes distribution was more biased to the functional isotypes, including IgG1 ($p \leq 0.05$), IgG3 ($p \leq 0.05$), IgA1 ($p \leq 0.0001$), and IgA2 ($p \leq 0.0001$) in MG patients. The number of SHMs in naïve isotypes (IgM/D) was increased in MG patients. A total of 1,054 clonotypes were found to be shared between ≥2 thymus samples. Of 1,054 clonotypes, 169 clonotypes were mapped in peripheral blood BCR repertoire of MG patient, whereas only 36 were mapped in that of healthy controls. The clonotypes which were shared between higher number of thymus tended to exist in peripheral blood samples of larger number of MG patients.
Conclusion: MG patients showed some different distributions in V gene usage, isotypes, and the number of SHMs. Some clonotypes were shared between thymus from different MG patients. These clonotypes were more frequently found in peripheral blood of MG patients than of healthy controls.
Disclosure: This work was supported by the National ResearchFoundation of Korea (NRF) grant funded by the Koreagovernment (MSIP) (2019R1C1C1009875).



EPR-132

Response to zilucoplan in the Phase 3 RAISE study in patients with generalised myasthenia gravis

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Background and aims: RAISE (NCT04115293) was a Phase 3, randomised, multicentre, double-blind, placebo-controlled study of zilucoplan, a macrocyclic peptide complement C5 inhibitor with a dual mechanism of action, in patients with generalised myasthenia gravis (gMG). RAISE demonstrated statistically significant and clinically meaningful improvements in MG-specific outcomes. Here, we assessed the proportion of Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) responders and a post hoc analysis of baseline characteristics of responders.

Methods: Adult patients with acetylcholine receptor antibody-positive gMG (MGFA Disease Class II–IV) were randomised 1:1 to receive daily subcutaneous zilucoplan 0.3 mg/kg or placebo for 12 weeks. Responders were defined as achieving a ≥3-point improvement in MG-ADL score, or a ≥5-point improvement in QMG score.

Results: Overall, 174 patients were randomised to zilucoplan (n=86) or placebo (n=88). At Week 12, responder rates for MG-ADL (73% vs 46%, p<0.001) and QMG (58% vs 33%, p=0.0012) were significantly higher for the zilucoplan group compared with placebo. Furthermore, 45% and 32% of zilucoplan patients met the MG-ADL and QMG responder criteria, respectively, at Week 1 (placebo: 30% and 8%). There were no meaningful differences in baseline disease characteristics of MG-ADL responders and non-responders at Week 12 (Figures 1 and 2).

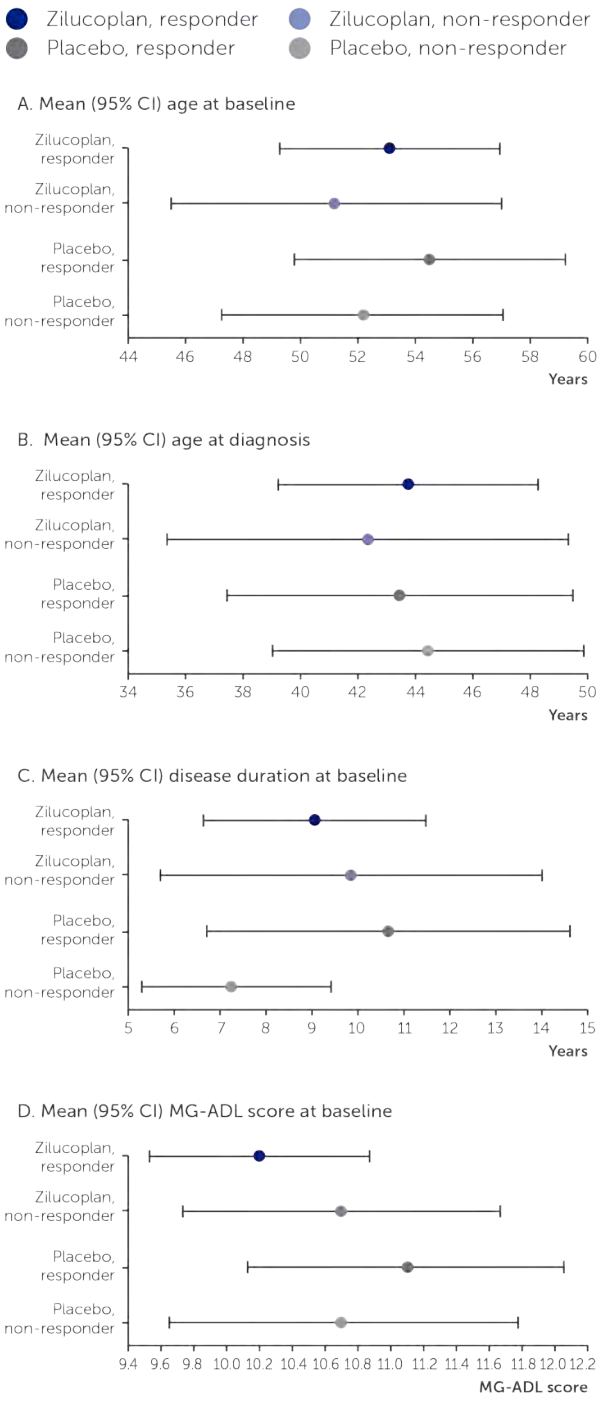
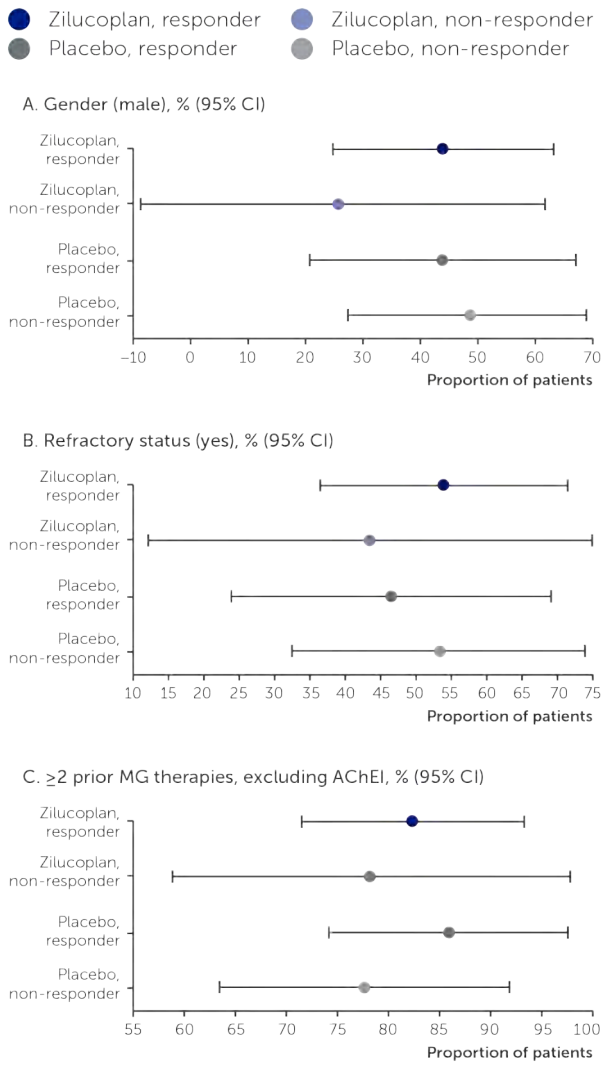


Figure 1. Baseline characteristics for MG-ADL responders and non-responders at Week 12 (zilucoplan responders n=63, zilucoplan non-responders n=23, placebo responders n=43, placebo non-responders n=45); continuous characteristics.



CIs are not adjusted for covariates or multiple testing.
AChEI, acetylcholinesterase inhibitor; CI, confidence interval; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living.

Figure 2. Baseline characteristics for MG-ADL responders and non-responders at Week 12 (zilucoplan responders n=63, zilucoplan non-responders n=23, placebo responders n=43, placebo non-responders n=45); categorical characteristics.

Conclusion: Zilucoplan showed a rapid onset of efficacy, with nearly half of patients being MG-ADL responders at Week 1. Responder rates for MG-ADL continued to increase up to the study completion at 12 weeks, regardless of patient baseline disease characteristics. Funding: UCB Pharma.
Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation.

EPR-133

Long-Term Safety, Tolerability, And Efficacy of Efgartigimod In Patients With gMG: Final Analyses From The ADAPT+ Study

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Background and aims: Efgartigimod is a human IgG1 antibody Fc-fragment that reduces total and pathogenic IgG autoantibody levels through neonatal Fc receptor blockade. ADAPT was a 26-week, global, multicentre, randomised, placebo-controlled, phase 3 trial evaluating efgartigimod in patients with generalised myasthenia gravis (gMG). Patients who completed ADAPT could enroll in the ADAPT+ open-label extension. ADAPT+ evaluated long-term safety and tolerability of efgartigimod in patients with gMG.
Methods: Efgartigimod (10 mg/kg intravenous) was administered in cycles of 4 weekly infusions, with subsequent cycles initiated based on clinical evaluation. Efficacy was assessed using Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scales.
Results: Of 167 patients from ADAPT, 151 (90%) entered ADAPT+ and 145 received ≥1 cycle as of January 2022. With 217.55 patient-years of follow-up (mean duration per patient: 548 days), the most common adverse events (AEs; mostly mild or moderate) were headache (25%), concomitant coronavirus 2019 (COVID-19) infection (15%), nasopharyngitis (14%), and diarrhoea (10%). These

AEs did not increase in frequency with subsequent treatment cycles (Table 1). AChR-Ab+ patients (ADAPT/ADAPT+ primary endpoint population) with ≥1 year of follow-up across ADAPT/ADAPT+ (n=95) received a median 5.0 (range, 0.4–7.6) cycles per year. AChR-Ab+ patients (n=111) demonstrated consistent improvements (mean change [SE], week 3 of cycle 1) in MG-ADL (-5.0 [0.33]; repeated up to 14 cycles) and QMG (-4.7 [0.41]; repeated up to 7 cycles) scores (Figure 1).

	ADAPT						ADAPT+		
	Placebo (n=83) [34.51 PY]			Efgartigimod (n=84) [34.86 PY]			Efgartigimod (n=145) [217.55 PY]		
	IR[a]	m	n (%)	IR[a]	m	n (%)	IR[a]	m	n (%)
AEs[b]	7.8	270	70 (84)	7.2	252	65 (77)	3.6	783	123 (85)
SAEs	0.3	10	7 (8)	0.1	4	4 (5)[c]	0.2	52	34 (23)[c]
≥1 Infusion-related reaction event	0.3	9	8 (10)	0.1	3	3 (4)	0.1	21	15 (10)
Infection AEs	1.2	42	31 (37)	1.6	56	39 (46)	0.8	164	80 (55)
Discontinued due to AEs	0.1	3	3 (4)	0.2	7	3 (4)	0.1	14	12 (8)
Severe AEs (grade ≥3)	0.4	12	8 (10)	0.3	10	9 (11)	0.3	72	38 (26)
Death[d]	-	0	0 (0)	-	0	0 (0)	<0.1	5	5 (3)
Most frequent AEs									
Nasopharyngitis	0.5	17	15 (18)	0.3	12	10 (12)	0.1	24	20 (14)
Upper respiratory tract infection	0.2	5	4 (5)	0.3	11	9 (11)	<0.1	7	6 (4)
Urinary tract infection	0.1	4	4 (5)	0.3	9	8 (10)	0.1	18	13 (9)
Headache	1.1	39	23 (28)	1.2	40	24 (29)	0.5	98	36 (25)
Nausea	0.4	15	9 (11)	0.2	7	7 (8)	0.1	13	9 (6)
Diarrhoea	0.4	14	9 (11)	0.2	6	6 (7)	0.1	19	14 (10)
COVID-19[e,f]	-	0	0 (0)	-	0	0 (0)	0.1	23	22 (15)

AEs, adverse events; COVID-19, coronavirus 2019; IR, incidence rate; m, number of events; PY, patient-years; SAEs, serious adverse events; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a]IR was calculated as number of events per total PYs of follow-up. [b]AEs were predominantly mild or moderate. [c]Only 1 SAE was considered treatment related per investigator. [d]None of the deaths in ADAPT+ were related to efgartigimod administration per the principal investigator. [e]Includes all preferred terms of COVID-19, COVID-19 pneumonia, Coronavirus infection, and SARS-COV-2 test positive. [f]The ADAPT study occurred prior to the start of the COVID-19 pandemic, while the ADAPT+ study occurred during the COVID-19 pandemic.

Table 1: Summary of AEs in the safety population.

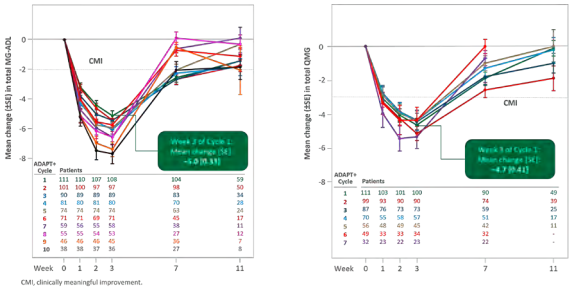

Figure 1: Mean change in MG-ADL (left) and QMG (right) total scores from cycle baseline in AChR-Ab+ patients.

Conclusion: These ADAPT+ analyses suggest long-term efgartigimod treatment is well tolerated and efficacious. Additional final data cut analyses will be presented at EAN 2023.

Disclosure: Multiple relationships financial and non-financial nature for authors AM, JLdB, JV, VB, TV, CK, SP, HM, SB, MP, SS, BVH, CT, KU, RM and JFH Jr. stated at point of presentation.

EPR-134

COMET: Patient-reported outcome measures in patients with late-onset Pompe disease after 145 weeks' avalglucosidase alfa

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Background and aims: Avalglucosidase alfa (AVAL), a recombinant human GAA ERT, has increased mannose-6-phosphate content for increased cellular uptake versus alglucosidase alfa (ALGLU). We evaluated patient-reported outcomes (PROs) in late-onset Pompe disease during the COMET (Phase 3; NCT02782741) open-label, extended-treatment period (ETP) following a 49-week, double-blind, randomised-controlled, primary analysis period (PAP).

Methods: PAP participants were treatment-naïve (n=100; age 16-78 years). Fifty-one received AVAL 20mg/kg every other week (qow) in the PAP, continuing this in the ETP (AVAL-arm). Of 49 receiving ALGLU 20mg/kg qow in the PAP, 44 entered the ETP receiving AVAL 20mg/kg qow (Switch-arm). Changes from baseline are reported after 145 total weeks (AVAL-arm: 145 weeks' AVAL; Switch-arm: 49 weeks' ALGLU, 96 weeks' AVAL).

Results: SF-12 PCS improved continuously until Week 145 in both arms; SF-12 MCS improved to Week 49 in both arms, plateauing at Week 145 (Fig1). Week 49 PGIC improvements stabilised at Week 145 in both arms; AVAL-arm improvements were larger (Fig1). PDSS/PDIS scores improved by Week 49 and were maintained at Week 145 (Fig2). Switch-arm PDIS mood and PDSS overall fatigue scores improved noticeably at Week 145. EQ-5D VAS improved continuously in the AVAL-arm and improved after switching in the Switch-arm. R-PAct summary score (Table1) continuously improved in the AVAL-arm and stabilised in the Switch-arm. No safety/immunogenicity concerns occurred to Week 145.

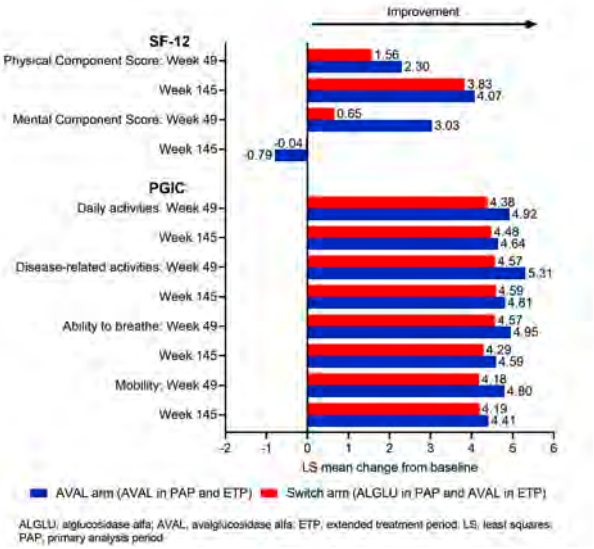

Figure 1 LS mean change in Short-Form-12 (SF-12) Physical and Mental Component Scores, and Patient Global Impression of Change (PGIC) measures from baseline (Week 0) to Week 49 (end of PAP) and Week 145 (during ETP). Data are for patients ≥18 years old.

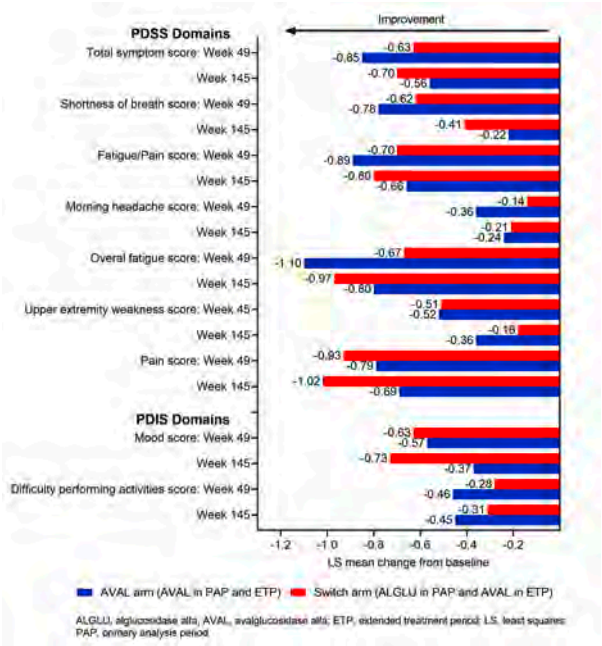

Figure 2 LS mean changes in the Pompe Disease Symptom Scale (PDSS) and Pompe Disease Impact Scale (PDIS) scores from baseline (Week 0) to Week 49 (end of PAP) and Week 145 (during ETP). Data are for patients ≥18 years old.

Parameter	Week	AVAL arm AVAL in PAP and ETP	Switch arm ALGLU in PAP; AVAL in ETP
EQ-5D-5L VAS, mean (SD)	49	8.80 (15.01) [n=50]	−0.33 (16.13) [n=42]
	145	9.45 (16.70) [n=47]	3.97 (14.71) [n=36]
R-PAct summary score, LS mean (SE)	49	2.46 (1.23) [n=19]	0.95 (1.16) [n=21]
	145	5.32 (1.37) [n=16]	−1.41 (1.23) [n=20]

ALGLU, alglucosidase alfa; AVAL, avalglucosidase alfa; ETP, extended treatment period; LS, least squares; PAP, primary analysis period; SD, standard deviation; SE, standard error. Higher scores denote improvement.

Table 1 Changes from baseline (Week 0) to Weeks 49 and 145 in Rasch-built Pompe-specific Activity (R-Pact) scale and EuroQoL 5 Dimension 5 Level Visual Analogue Scale (EQ-5D-5L VAS) scores. Data are for patients ≥18 years old.

Conclusion: Overall, PRO data show sustained benefit with AVAL post-PAP, and stabilisation of treatment effect post-switch from ALGLU to AVAL over 145 weeks; supporting long-term maintenance of clinically meaningful outcomes with AVAL.

Disclosure: Funding: Sanofi.

EPR-135

Ravulizumab in adults with generalised myasthenia gravis: Post hoc analysis of MG-ADL item score change in CHAMPION MG

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Background and aims: In the 26-week, randomised placebo-controlled period (RCP) of the phase 3 CHAMPION MG study (NCT03920293) in adults with anti-acetylcholine receptor antibody-positive (AChR Ab+) generalised myasthenia gravis (gMG), ravulizumab was associated with improvement versus placebo in the Myasthenia Gravis–Activities of Daily Living (MG-ADL) total score. This post hoc analysis evaluated changes in impairment severity for the eight MG-ADL items.

Methods: Patients scored MG-ADL item impairment as 0–3 (higher scores, more severe impairment) at baseline and Week 26. Proportions of patients with improved MG-ADL item scores during the RCP were calculated.

Results: Overall, 160/175 patients had score-shift data at Week 26. Greater proportions of ravulizumab-treated patients achieved improved scores (in 7/8 MG-ADL items) and complete resolution (score reduced to 0; 8/8 items) versus placebo by Week 26 (Figure). The two ocular items had the highest proportions of patients with severe impairment (score 3) at baseline. Proportions of patients with a score of 3 in the ravulizumab-treated group were reduced from baseline to Week 26 for eyelid droop (23.1% to 14.1%) and were similar at baseline and Week 26 for double vision (11.5% and 10.3%). With placebo, increases from baseline to Week 26 were observed for both eyelid droop (20.7% to 24.4%) and double vision (6.1% to 12.2%) (Table).

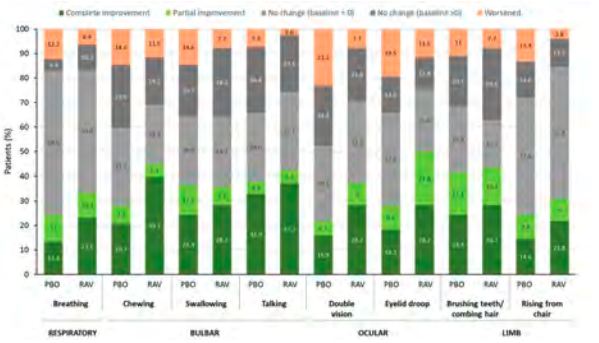

Figure: Changes in severity of muscle impairment from baseline to Week 26 based on MG-ADL item scores in patients receiving ravulizumab (n=78) or placebo (n=82).

MG-ADL item	Baseline score	Patients, n (%)							
		Ravulizumab (n=78)				Placebo (n=82)			
		Week 26 score: 0	1	2	3	0	1	2	3
Double vision	0	17 (21.8)	3 (3.8)	1 (1.3)	0	20 (24.4)	7 (8.5)	0	1 (1.2)
	1	14 (17.9)	8 (10.3)	1 (1.3)	1 (1.3)	9 (11.0)	12 (14.6)	5 (6.1)	1 (1.2)
	2	8 (10.3)	5 (6.4)	11 (14.1)	0	2 (2.4)	5 (6.1)	10 (12.2)	5 (6.1)
	3	0	0	2 (2.6)	7 (9.0)	2 (2.4)	0	0	3 (3.7)
Eyelid droop	0	10 (12.8)	2 (2.6)	0	0	12 (14.6)	1 (1.2)	0	0
	1	13 (16.7)	6 (7.7)	2 (2.6)	1 (1.3)	11 (13.4)	11 (13.4)	5 (6.1)	3 (3.7)
	2	5 (6.4)	9 (11.5)	8 (10.3)	4 (5.1)	4 (4.9)	1 (1.2)	10 (12.2)	7 (8.5)
	3	4 (5.1)	5 (6.4)	3 (3.8)	6 (7.7)	0	3 (3.7)	4 (4.9)	10 (12.2)

Worsened | No change (baseline>0) | No change (baseline=0) | Improvement (partial) | Improvement (complete)

Note: Percentages are calculated based on all patients with non-missing values at both baseline and Week 26 visits.
MG-ADL, Myasthenia Gravis–Activities of Daily Living

Table: Shift from baseline to Week 26 in MG-ADL ocular item scores for ravulizumab versus placebo

Conclusion: In patients with AChR Ab+ gMG, ravulizumab provided greater treatment benefit in reducing symptom severity than placebo in 7/8 MG-ADL items, including ocular items, which had the highest proportions of patients with severe impairment at baseline.

Disclosure: Study funded by Alexion, AstraZeneca Rare Disease.

Headache and Pain 2

EPR-136

Long-term efficacy and impact of erenumab treatment on quality of life of patients participating in the APOLLON study

H. Göbel[1], M. Koch[2], C. Weiss[3]
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Background and aims: The monoclonal antibody erenumab is an EMA and FDA approved anti-CGRP pathway treatment developed for the prevention of episodic and chronic migraine. German as well as international studies already found erenumab to be an effective treatment for the prevention of migraine with international data further confirming the long-term safety profile. However, long-term data regarding the treatment with erenumab is still limited for the German population.
Methods: APOLLON is a 128-week open-label study of erenumab treatment, assessing long-term safety and tolerability data of migraine patients in Germany who previously participated in a head-to-head trial comparing the tolerability of erenumab and topiramate (NCT03828539). Patients were allowed to pause the treatment after 12 weeks of continuous treatment with erenumab. Throughout the study, TSQM-II and HIT-6 questionnaires were completed. Monthly migraine days were collected in relation to the drug holiday.
Results: In total, 701 patients at 80 sites in Germany were included. An interim analysis (n=386, average exposure to erenumab 93.8 weeks excl. drug holidays) showed that treatment satisfaction increased over the course of the study in all observed areas: convenience, effectiveness, global satisfaction and side effects. HIT-6 data showed an improvement by more than 5 points within the first 24 weeks. The results will be completed by the final data at the end of the study in February 2023.
Conclusion: The results provide additional data on the long-term efficacy and impact on quality of life of erenumab-treated migraine patients in Germany, thus adding to the understanding of monoclonal antibody-based migraine prophylaxis.
Disclosure: H. Göbel received honoraria for consulting and lectures from Allergan, Almirall, Astra Zeneca, Bayer Vital, Berlin-Chemie, Bionorica, Bristol-Myers-Squibb, Elli Lilly, Fujisawa, GlaxoSmithKline, Grünenthal, Hermal, Hormosan, Ipsen-Pharma, Janssen-Cilag, Johnson&Johnson, Krewel-Meuselbach, Klosterfrau, Lichtwer, Menarini Pharma, Merz Pharmaceuticals, Minster Pharmaceuticals, MSD, Novartis Pharma, Pfizer, Pharmacia, Sandoz, Schaper und Brümmer, Schwarz-Pharma, Teva, Weber&Weber, Smith Kline Beecham. M. Koch is an employee of Novartis AG. C. Weiss is an employee of Novartis Pharma GmbH.

EPR-137

Atogepant for the Preventive Treatment of Migraine in Participants With Prior Treatment Failure: The ELEVATE Trial

P. Pozo-Rosich[1], K. Nagy[2], C. Tassorelli[3], M. Lanteri-Minet[4], S. Sacco[5], T. Nežádal[6], M. Finnegan[7], H. Guo[7], P. Gandhi[7], J. Trugman[7]
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Background and aims: Atogepant is an oral calcitonin gene-related peptide receptor antagonist indicated for the preventive treatment of episodic migraine (EM) in adults in the US. The ELEVATE trial evaluated the efficacy, safety, and tolerability of atogepant 60 mg once daily (QD) for the preventive treatment of EM in participants with prior treatment failure.
Methods: ELEVATE was a randomized, double-blind, placebo-controlled trial conducted in Europe and North America. Adults (18-80 years) who previously failed 2-4 classes of conventional oral medications for migraine prevention and reported 4-14 monthly migraine days (MMDs) during the 28-day screening period were randomized to atogepant 60 mg QD or placebo. The primary endpoint was change from baseline in mean MMDs across 12 weeks. Secondary endpoints included achievement of ≥50% reduction in MMDs across 12 weeks and change from baseline in Headache Impact Test-6 (HIT-6) and Migraine-Specific Quality-of-Life Questionnaire version 2.1 Role Function-Restrictive (MSQ v2.1 RFR) domain scores at week 12.
Results: The efficacy analysis population included 309 participants (placebo: n=155; atogepant 60 mg QD: n=154). Across the 12-week treatment period, atogepant-treated participants experienced a significantly greater decrease in MMDs than placebo-treated participants (Figure 1). Secondary endpoints of achievement of ≥50% reduction in MMDs, reduction in HIT-6 and improvement in MSQ v2.1 RFR scores also showed a statistically significant treatment effect for atogepant vs placebo (Table 1). The most commonly reported treatment-emergent adverse events are listed in Table 2.

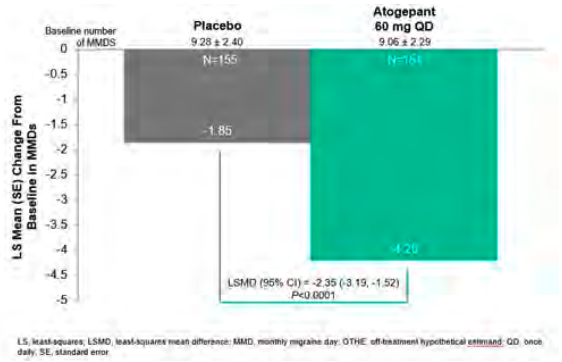


Figure 1. Change From Baseline in Mean MMDs Across 12 Weeks (OTHE Population)

	Placebo (n=155)	Atogepant 60 mg QD (n=154)
Achievement of >=50% reduction in MMDs across the 12-week treatment period, n (%)	28 (18.1)	78 (50.6)
Atogepant vs placebo odds ratio (95% CI)		4.82 (2.85, 8.14)
Adjusted P value		<0.0001
Change from baseline in HIT-6 total score at week 12, LS mean (SE)	−4.14 (0.795)	−10.56 (0.804)
Atogepant vs placebo LSMD (95% CI)		−6.42 (−8.22, −4.63)
Adjusted P value		<0.0001
Change from baseline in MSQ v2.1 RFR domain score at week 12, LS mean (SE)	15.38 (2.047)	33.26 (2.065)
Atogepant vs placebo LSMD (95% CI)		17.88 (13.34, 22.42)
Adjusted P value		<0.0001

HIT-6, Headache Impact Test-6; LS, least-squares; LSMD, least-squares mean difference; MSQ v2.1 RFR, Migraine-Specific Quality-of-Life Questionnaire version 2.1 Role Function–Restrictive; OTHE, off-treatment hypothetical estimand.

Table 1. Summary of Key Secondary Efficacy Endpoints (OTHE Population)

n (%)	Placebo (n=157)	Atogepant 60 mg QD (n=156)
TEAEs	84 (53.5)	81 (51.9)
Treatment-related TEAEs	14 (8.9)	31 (19.9)
TESAEs	0	4 (2.6)
Treatment-related TESAEs	0	0
Any TEAE leading to discontinuation	2 (1.3)	3 (1.9)
Common TEAEs in >=5%		
Constipation	4 (2.5)	16 (10.3)
COVID-19	15 (9.6)	13 (8.3)
Nausea	5 (3.2)	11 (7.1)
Nasopharyngitis	12 (7.6)	8 (5.1)

AE, adverse event; QD, once daily; TEAE, treatment-emergent AE; TESAE, treatment-emergent serious AE.

Table 2. Common (≥5%) Treatment-Emergent Adverse Events (Safety Population)

Conclusion: Atogepant 60 mg QD was efficacious, safe, and well-tolerated for the preventive treatment of EM in participants with prior treatment failure.

Disclosure: This study was supported by AbbVie.

EPR-138

Response Rates With Oral Atogepant in Participants With Prior Preventive Treatment Failure: Results From ELEVATE

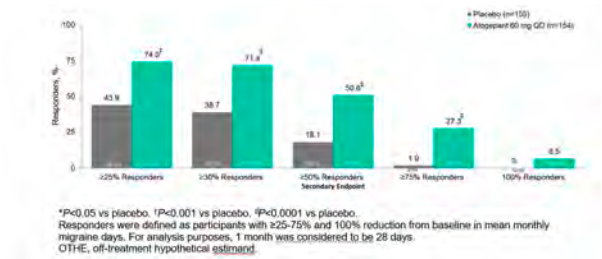
P. Pozo-Rosich[1], K. Nagy[2], C. Tassorelli[3], M. Lanteri-Minet[4], S. Sacco[5], T. Nežádal[6], M. Finnegan[7], L. Luo[7], P. Gandhi[7], J. Trugman[7]

[1]Vall d'Hebron University Hospital, Barcelona, Spain; Universitat Autonoma de Barcelona, Barcelona, Spain, [2]AbbVie, Budapest, Hungary, [3]Headache Science Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy, [4]Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France, [5]Director, Carolinas Headache Clinic, Matthews, NC, USA, [6]Neurology Department, Military University Hospital, 1st School of Medicine, Charles University, Prague, Czech Republic, [7]AbbVie, Madison, NJ, USA

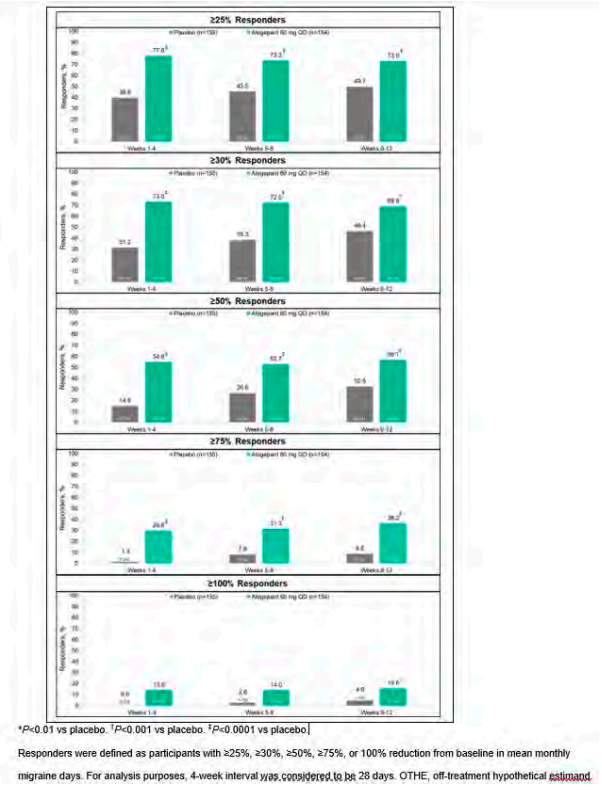
Background and aims: Atogepant is an oral calcitonin gene-related peptide receptor antagonist approved for the preventive treatment of episodic migraine in adults in the United States. The objective of this analysis was to evaluate monthly migraine day (MMD) responder rates to further characterize the efficacy profile of atogepant.

Methods: ELEVATE was a randomized, double-blind, placebo-controlled trial conducted in Europe and North America. Adults (18-80 years) with 4-14 MMDs on average in the previous 3 months and during baseline who had previously failed 2-4 classes of conventional oral medications for preventive treatment of migraine were randomized to atogepant 60 mg once daily (QD) or placebo. This analysis evaluated the proportions of participants achieving ≥25%, ≥30%, ≥50% (alpha-controlled secondary endpoint [across 12 weeks]), ≥75%, and 100% reductions in mean MMDs across 12 weeks and at each 4-week interval.

Results: A total of 309 participants were included in the analysis population (placebo: n=155; atogepant 60 mg QD: n=154). Across the 12-week treatment period, a ≥50% improvement was achieved by 50.6% of atogepant-treated participants vs 18.1% of placebo-treated participants (P<0.0001). Significant treatment effects were observed for the achievement of a ≥25%, ≥30%, ≥75%, and 100% reduction in MMDs across the 12-week treatment period (Figure 1). These significant treatment effects were observed as early as the first 4-week interval and maintained throughout the double-blind treatment period (Figure 2). No new safety concerns were identified.



Proportions of Participants Achieving ≥25%, ≥30%, ≥50%, ≥75%, and 100% Reductions in Mean Monthly Migraine Days Across the 12-Week Double-blind Treatment Period (OTHE Population)



*P<0.01 vs placebo. †P<0.001 vs placebo. ‡P<0.0001 vs placebo.

Responders were defined as participants with ≥25%, ≥30%, ≥50%, ≥75%, or 100% reduction from baseline in mean monthly migraine days. For analysis purposes, 4-week interval was considered to be 28 days. OTHE, off-treatment hypothetical estimand.

Proportion of Participants Achieving ≥25%, ≥30%, ≥50%, ≥75%, and 100% Reductions in Mean Monthly Migraine Days Across Each 4-Week Interval (OTHE Population)

Conclusion: Treatment with atogepant 60 mg QD significantly increased the proportions of participants achieving ≥25%, ≥30%, ≥50%, ≥75%, and 100% reductions in MMDs compared with placebo.

Disclosure: This study was supported by Allergan (prior to its acquisition by AbbVie).

EPR-139

Impact of Atogepant on Migraine-Specific QoL Among Individuals With Episodic Migraine and Preventive Treatment Failure

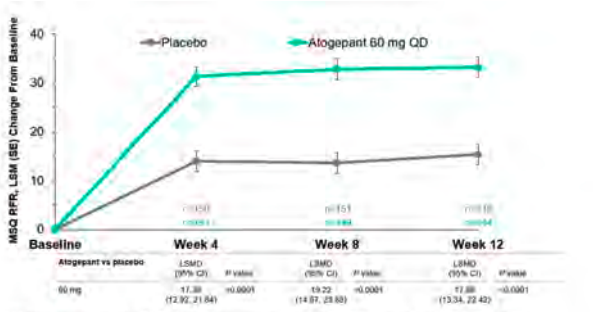
C. Tassorelli[1], P. Gandhi[2], S. Sacco[3], P. Pozo-Rosich[4], M. Lanteri-Minet[5], T. Nežádal[6], J. Trugman[2], L. Luo[2], J. Stokes[2], K. Nagy[7]

[1]Headache Science Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy, [2]AbbVie, Madison, NJ, USA, [3]Director, Carolinas Headache Clinic, Matthews, NC, USA, [4]Vall d'Hebron University Hospital, Barcelona, Spain; Universitat Autonoma de Barcelona, Barcelona, Spain, [5]Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France [6]Neurology Department, Military University Hospital, [1]st School of Medicine, Charles University, Prague, Czech Republic, [7]AbbVie, Budapest, Hungary

Background and aims: Atogepant is an oral calcitonin gene-related peptide receptor antagonist approved for the preventive treatment of episodic migraine (EM) in adults. This analysis evaluated the impact of atogepant on the Migraine-Specific Quality-of-Life Questionnaire version 2.1 (MSQv2.1) among participants with EM with prior preventive treatment failures.

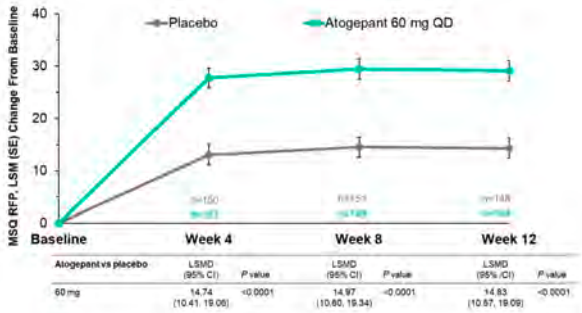
Methods: ELEVATE (NCT04740827) was a multicenter, randomised, double-blind, placebo-controlled, parallel-group, phase 3 study conducted in Europe and North America among participants with EM who previously failed 2-4 classes of conventional oral preventive migraine medications. Adults (18-80y) experiencing 4-14 migraine days/month on average in the previous 3 months and 28-day baseline period were treated with atogepant 60 mg once daily or placebo. Efficacy endpoints included change from baseline in MSQv2.1 Role Function-Restrictive (RFR), Role Function-Preventive (RFP), and Emotional Function (EF) domain scores at weeks 4, 8, and 12. Change from baseline in MSQv2.1 RFR domain score at week 12 was an alpha-controlled secondary endpoint to establish statistical significance.

Results: Of 315 randomised participants, 309 were included in the off-treatment hypothetical estimand population. Atogepant 60mg once daily demonstrated significant improvement vs placebo in MSQv2.1 scores at week 4 and the effect was maintained through week 12 (RFR, LSMD: 17.88 [P<0.0001]; RFP, LSMD: 14.83 [P<0.0001]; EF, LSMD: 13.22 [P<0.0001] Figures 1–3). Overall safety results were consistent with the known safety profile of atogepant.



LSM, least-squares mean; LSMD, least-squares mean difference; MSQ, Migraine-Specific Quality-of-Life Questionnaire version 2.1; OTHE, off-treatment hypothetical estimand; QD, once daily; RFR, Role Function–Restrictive; SE, standard error.
Change from baseline in MSQ v2.1 RFR at week 12 was an alpha-controlled secondary endpoint.
The OTHE included all randomised participants who received >=1 dose of atogepant, had an evaluable baseline period of eDiary data, and had >=1 evaluable post-baseline 4-week period of eDiary data. This population was used for the efficacy analysis in support of submissions in Europe.

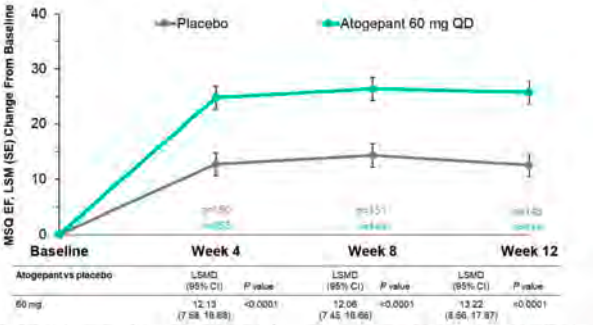
Changes From Baseline in Migraine-Specific Quality-of-Life Questionnaire v2.1 Role Function–Restrictive Domain Score (OTHE Population, see footnote for definition).



Atogepant vs placebo	LSMD (95% CI)	P value	LSMD (95% CI)	P value	LSMD (95% CI)	P value
60 mg	14.74 (10.41, 19.06)	<0.0001	14.97 (10.60, 19.34)	<0.0001	14.83 (10.57, 19.09)	<0.0001

LSM, least-squares mean; LSMD, least-squares mean difference; MSQ, Migraine-Specific Quality-of-Life Questionnaire version 2.1; OTHE, off-treatment hypothetical estimand; QD, once daily; RFP, Role Function-Preventive; SE, standard error.
The OTHE included all randomised participants who received >=1 dose of atogepant, had an evaluable baseline period of eDiary data, and had >=1 evaluable post-baseline 4-week period of eDiary data. This population was used for the efficacy analysis in support of submissions in Europe.

Changes From Baseline in Migraine-Specific Quality-of-Life Questionnaire v2.1 Role Function–Preventive Domain Score (OTHE Population, see footnote for definition).



Atogepant vs placebo	LSMD (95% CI)	P value	LSMD (95% CI)	P value	LSMD (95% CI)	P value
60 mg	12.13 (7.58, 16.68)	<0.0001	12.06 (7.45, 16.66)	<0.0001	13.22 (8.66, 17.87)	<0.0001

EF, Emotional Function; LSM, least-squares mean; LSMD, least-squares mean difference; MSQ, Migraine-Specific Quality-of-Life Questionnaire version 2.1; OTHE, off-treatment hypothetical estimand; QD, once daily; SE, standard error.
The OTHE included all randomised participants who received >=1 dose of atogepant, had an evaluable baseline period of eDiary data, and had >=1 evaluable post-baseline 4-week period of eDiary data. This population was used for the efficacy analysis in support of submissions in Europe.

Changes From Baseline in Migraine-Specific Quality-of-Life Questionnaire v2.1 Emotional Function Domain Score (OTHE, see footnote for definition)

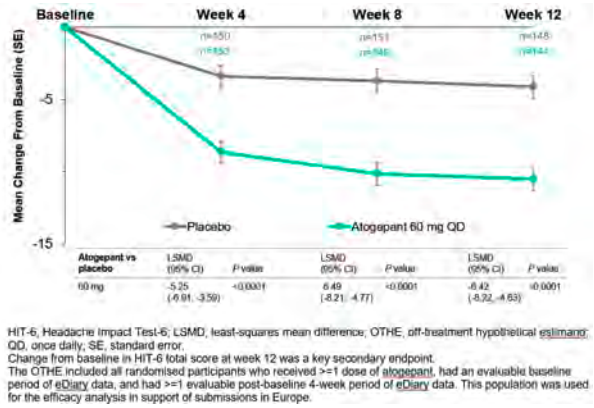
Conclusion: Participants with prior treatment failure who received atogepant 60mg once daily had statistically significant and clinically meaningful improvements in the ability to perform daily social and work-related activities and overall quality of life compared with placebo.
Disclosure: Study supported by AbbVie.

EPR-140

Effect of Atogepant on Headache Impact Test-6 Among Individuals With Episodic Migraine and Preventive Treatment Failure

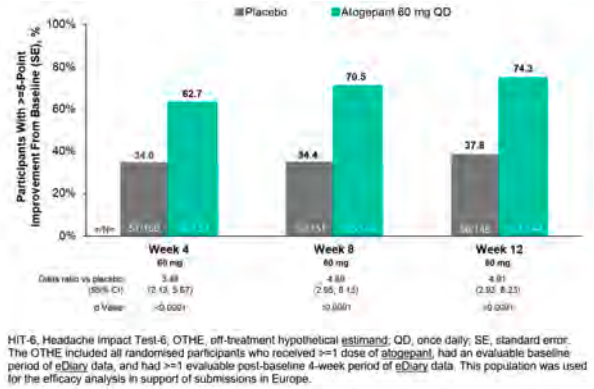
C. Tassorelli[1], P. Gandhi[2], S. Sacco[3], P. Pozo-Rosich[4], M. Lanteri-Minet[5], T. Nežádal[6], J. Trugman[2], L. Luo[2], J. Stokes[2], K. Nagy[7]
[1]Headache Science Centre, C. Mondino Foundation and University of Pavia, Pavia, Italy, [2]AbbVie, Madison, NJ, USA, [3]Director, Carolinas Headache Clinic, Matthews, NC, USA, [4]Vall d'Hebron University Hospital, Barcelona, Spain; Universitat Autonoma de Barcelona, Barcelona, Spain, [5]Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France [6]Neurology Department, Military University Hospital, 1st School of Medicine, Charles University, Prague, Czech Republic, [7]AbbVie, Budapest, Hungary

Background and aims: Atogepant, an oral calcitonin gene-related peptide receptor antagonist, is approved for the preventive treatment of episodic migraine (EM) in adults. This analysis assessed the effect of atogepant on headache-related impact among participants with EM who experienced prior preventive treatment failures.
Methods: ELEVATE (NCT04740827) was a multicenter, randomised, double-blind, placebo-controlled, phase 3 study conducted in Europe and North America among participants with EM who previously failed 2-4 classes of conventional oral preventive migraine medication. Adults (18-80y) experiencing 4-14 migraine days/month on average in the previous 3 months and the 28-day baseline period were included and treated with atogepant 60 mg once daily or placebo. The analysis measured the change from baseline in Headache Impact Test-6 (HIT-6) total score and the percentage of participants with ≥5-point improvement from baseline at weeks 4, 8, and 12 (responders). Change from baseline in HIT-6 total score at week 12 was an alpha-controlled secondary endpoint for the European Union.
Results: Of 315 participants randomised, 309 were included in the off-treatment hypothetical estimand population. Atogepant 60 mg once daily showed significant improvement in the change from baseline in HIT-6 total score at weeks 4, 8, and 12 ($p<0.0001$ vs placebo; Figure 1). Significantly greater proportions of atogepant- versus placebo-treated participants were HIT-6 responders at weeks 4, 8, and 12 ($p<0.0001$; Figure 2). Overall safety results were consistent with the known safety profile of atogepant.



HIT-6, Headache Impact Test-6; LSMD, least-squares mean difference; OTHE, off-treatment hypothetical estimand; QD, once daily; SE, standard error.
Change from baseline in HIT-6 total score at week 12 was a key secondary endpoint.
The OTHE included all randomised participants who received >=1 dose of atogepant, had an evaluable baseline period of eDiary data, and had >=1 evaluable post-baseline 4-week period of eDiary data. This population was used for the efficacy analysis in support of submissions in Europe.

Changes From Baseline in HIT-6 Total Score (OTHE Population, see footnote for definition).



HIT-6, Headache Impact Test-6; OTHE, off-treatment hypothetical estimand; QD, once daily; SE, standard error.
The OTHE included all randomised participants who received >=1 dose of atogepant, had an evaluable baseline period of eDiary data, and had >=1 evaluable post-baseline 4-week period of eDiary data. This population was used for the efficacy analysis in support of submissions in Europe.

HIT-6 Responder Rates (OTHE Population, see footnote for definition).

Conclusion: Atogepant 60 mg once daily significantly reduced headache-related impact versus placebo in participants who previously failed 2-4 classes of oral preventive treatment.
Disclosure: This study was supported by Allergan (prior to its acquisition by AbbVie).

EPR-141

Impact of community-based supported self-management pain program: Results of a practice-based research evaluation

N. Sharma, A. Mishra, U. Solanki, P. Shah
Aarogyam UK CIC, Leicester UK

Background and aims: Chronic pain is the leading cause of disability in the United Kingdom, affecting nearly half of the population. A community-based walk-in support initiative was set up for Asian and ethnic minority communities. The primary objective of the present study (based on practice-based outcome) was to determine the effectiveness of a personalized, integrative, culturally responsive pain management program in community-based walk-in support.
Methods: The retrospective study was conducted on 108 pain patients who participated in the walk-in pain management project between October 2019 and February 2020. The change in each patient was determined by comparing the pre- and post-program variables including pain severity, frequency, global impression of change (GIC), quality of life, and disability.
Results: Physical, mental, and social health outcomes showed statistically and clinically significant improvements following the intervention, with the GIC score improving substantially. Participants found the intervention to be effective in terms of self-efficacy and confidence in managing their own pain, and patients' pain related disability significantly decreased.
Conclusion: The results of the study indicated that a community-based supported self-management pain program could be a feasible and acceptable approach, particularly in populations with diverse cultural backgrounds. Integrative pain programs may sustainably improve pain, quality of life, and disability.
Disclosure: Nothing to disclose.

EPR-142

Interferon-beta produce analgesia through activating mu-opioid receptor

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Background and aims: Interferon (IFN)-beta is currently used as a therapy for multiple sclerosis and has been demonstrated to exert a direct protective effect against neurotoxic and inflammatory insults on neurons. However, little is known about the role of IFN-beta in regulating pain sensitivity and synaptic transmission in the spinal cord. Thus, we will study the role of IFN-beta in regulating pain sensitivity and mechanism of antinociception in this study.
Methods: Intrathecal injection of IFN-beta was performed in naïve rats and 2 days after injection of complete Freund's adjuvant (CFA). After behavioral test, spinal cords were harvested for western blot and immunohistochemical staining of IFN- beta, p-mu-opioid receptor, and type 1 IFN receptor. To determine the role of endogenous IFN-beta in pain control, we blocked the action of IFN-beta with an IFN-beta-neutralizing antibody and naloxone. The expression of the phospho-mu-opioid receptor and type-I IFN receptor (IFNR1) after administration of IFN-beta in the spinal cord were examined.
Results: Intrathecal administration of IFN-beta increased pain threshold in naïve rats and reduced CFA-induced inflammatory pain, whereas removal of endogenous IFN-beta by a neutralizing antibody induced hyperalgesia in naïve rats. Intrathecal injection of naloxone reversed the antinociceptive effect of IFN-beta on CFA-induced mechanical allodynia. Double staining further demonstrated that IFNR1 was co-localized with the mu-opioid receptor in

the lamina I-II. The expression of phospho-mu-opioid receptor was a significant increase after the administration of IFN-beta.
Conclusion: Our findings suggest IFN-beta is an endogenous pain inhibitor and provide an antinociceptive effect through binding and activating mu-opioid receptor in the spinal cord.
Disclosure: Nothing to disclose.

EPR-143

Clinical predictors of cranial autonomic symptoms in patients with chronic migraine

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Background and aims: Cranial autonomic symptoms, even though characteristic clinical signs of trigeminal autonomic cephalalgias, can be present in more than half of migraineurs
Methods: Chronic migraine cases were audited in a tertiary headache centre. A generalized linear model with a Poisson distribution and log link function, the total number of cranial autonomic symptoms was set as the dependent variable. Sex, the presence of aura, age at headache onset and pulsatility of the pain were examined as predictors.
Results: Three hundred and four cases were audited. The number of cranial autonomic symptoms were related to female sex (P=0.036), the presence of aura (P<0.001) and unilaterality of cranial autonomic symptoms (P<0.001). Age at headache onset and pulsatility were not significant predictors.
Conclusion: Females with migraine and any type of aura may develop more cranial autonomic symptoms during a migraine attack. The cranial parasympathetic outflow pathway has important cerebrovascular protective effects, which is consistent with enhanced activation during aura. The data suggests this group of patients could benefit more from therapies targeting the cranial autonomic pathway.
Disclosure: None of the authors have relevant disclosures for this abstract.

EPR-144

Effect of Plasmapheresis and Immunoadsorption in SPS

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Background and aims: Stiff person syndrome (SPS) is a chronic autoimmune disease which mainly affects the central nervous system. High-titer anti-GAD antibodies are characteristically seen in patients with stiff person syndrome (SPS). Studies suggest that plasma exchange may be useful as adjuvant therapy, mainly in patients with no other therapeutic response. In addition to plasmapheresis, immunoadsorption is another therapy option, in which auto-antibodies are washed out of the patient's bloodstream quickly and efficiently.
Methods: The effect of plasmapheresis (n=9) and immunoadsorption (n=5) on GAD-positive SPS patients is to be measured using various clinical parameters such as the walking speed and laboratory parameters like antibody titers and immunohistochemistry of patient serum in the hippocampus, cerebellum and spinal cord.
Results: With both therapies, the onset of effect was rapid after completion of exchange treatment. Walking velocity improved, antibody titer and immunohistochemistry binding was lower after treatment. The binding pattern showed lower binding of the small neurons after treatment, which was negatively correlated with lower pain score in the numeric rating scale (Fig. 1).

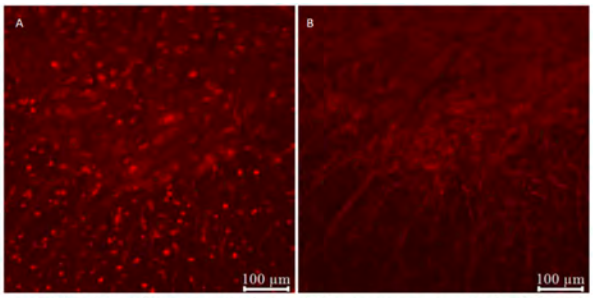

Figure 1: Effect of plasmapheresis. Immunohistochemistry of SPS patient serum on mouse spinal cord. A) before plasmapheresis, B) after plasmapheresis.

Figure 1: Effect of plasmapheresis. Immunohistochemistry of SPS patient serum on mouse spinal cord. A) before plasmapheresis, B) after plasmapheresis.

Conclusion: Plasmapheresis and immunoadsorption are effective therapies in patients with SPS. This study showed clinical and cellular effects of these immunotherapies. Whether these therapies also play a role in the other GAD-positive patients with neurological diseases or in SPS patients without GAD antibodies is not yet known.
Disclosure: I worked with Sabine Seefried and Claudia Sommer both members of the Department of Neurology, Universitätsklinikum Würzburg, Germany

Neuroimaging

EPR-145

White matter hyperintensities in first seizure patients

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Background and aims: MRI depicts potentially non-epileptogenic lesions (pNEL) after a first seizure. The SWISS FIRST study closed in December 2022. Here, we report on the interim results of white matter hyperintensities (WMH) in first seizure patients.
Methods: All patients underwent MRI with a dedicated epilepsy imaging protocol. Two in-house developed methods were used to automatically segment WMHs (Deep SCAN) on FLAIR images and to segment gray matter and the ventricles (DL+DiReCT). FLAIR and T1-weighted MRIs were co-registered to mask lesions > 5mm from the ventricles to < 1mm to the cortex. The segmentations were co-registered to the MNI152 atlas to visualize the lesion distribution.
Results: Eighty-three out of 615 patients received a final diagnosis up to now. Fifty-nine were diagnosed with established epilepsy, based on ILAE practical guidelines . Structural epileptogenic lesions (SEL) were present in 34%, pNEL in 49%, no image abnormality in 17%. Although WMHs were the most frequent pNEL (76%), the absolute WMH lesion load was higher in the SEL group, with iuxtacortical predominance (p<0.01).

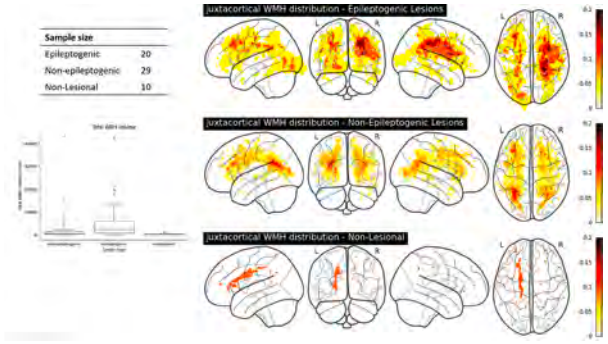

Figure: WMH distribution and volumes in SEL vs pNEL patients

Conclusion: WMH are common findings in patients with SEL and in pNEL after a first seizure. The majority of SEL patients presented with WMHs associated with remote brain lesions involving the iuxcortical white matter, potentially facilitating seizure generation.
Disclosure: This study was supported by the Swiss National Foundation Grant N° 180365

EPR-146

Identifying variants of posterior cortical atrophy using clinical classification or MR-based machine learning

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Background and aims: To detect variants of posterior cortical atrophy (PCA) using clinical classification or a data driven machine learning approach based on MRI network metrics.
Methods: We recruited 36 PCA patients and 69 healthy controls. All subjects underwent cognitive examinations, lumbar puncture and a 3T MRI. Patients were first categorized in ventral (vPCA,N=19) and dorsal (dPCA,N=17) variants based on the current diagnostic criteria. Sociodemographic, clinical, cognitive as well as topological brain network properties using graph analysis and connectomics were compared between groups. K-means clustering was performed on the whole group of patients considering both demographics and graph metrics of the occipital, temporal, and parietal lobes, as informative features. Sociodemographic, clinical, cognitive and CSF characteristics of the two clusters were compared.

Results: vPCA and dPCA were similar for sociodemographic, clinical and CSF features. Relative to controls, only vPCA patients showed alterations of all global, temporal, and parietal metrics. The k-means analysis identified two clusters of 26 and 10 subjects, similar for clinical and cognitive features. However, patients from Cluster 1 were significantly younger and had lower levels of CSF amyloid-beta compared to Cluster 2 patients.
Conclusion: Our findings suggest the potentially high sensitivity of graph-analysis and connectomic in capturing signs of neurodegeneration in PCA. The MRI-based machine learning approach, albeit unable to capture clinical phenotype differences, provided indications about underlying disease pathology. These findings offer potential biomarkers for non-invasive diagnosis of neurodegenerative conditions.
Disclosure: Supported by: Italian Ministry of Health (#GR-2010-2303035; #GR-2011-02351217), Philippe Chatrier and France Alzheimer Foundations, Fondation pour la Recherche sur Alzheimer.

EPR-147

Cortico-cortical signal transmission and brain connectivity in healthy individuals as a model for studying AD

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Background and aims: Signal following a transcranial magnetic stimulation (TMS) pulse can be tracked by electroencephalography (EEG). We wish to establish how contralateral time of signal transmission (STT), specifically the TMS-evoked potential (TEP)'s P20 latency, following a TMS pulse of specific brain nodes is related to the integrity of interhemispheric white matter (WM) fibers.
Methods: 28 healthy controls underwent an MRI and a TMS-EEG session. Resting-state fMRI maps were used to define default mode-DMN and executive control-ECN network nodes to be stimulated: left and right inferior parietal (IPL;DMN) and dorsolateral prefrontal (DLPFC;ECN). Fiber tracking of the main intra- and interhemispheric WM tracts was performed (probtrackx, FSL). TEP's P20 latency for each contralateral area of the stimulated node and DTI indices from each tract were obtained. The ability of WM measures to predict TEP's P20 latency were explored using multiple linear regression models.
Results: We observed that lower WM integrity of the splenium predicts lower TEP's P20 latency after left IPL stimulation. These findings were neither observed for intra-hemispheric connections nor within the ECN.
Conclusion: In healthy controls, we demonstrated that the WM integrity of the splenium predicts the interhemispheric P20 latency within the DMN following a TMS pulse of the left IP nodes. These findings reflect interhemispheric and network specificity. P20 latency is a promising measure of brain interhemispheric connectivity. After our initial validation, this approach could provide a novel single-subject marker of brain connectivity in early cases of Alzheimer's disease.
Disclosure: Supported by: Italian Ministry of Health (GR-2016-02364132). Foundation Research on Alzheimer Disease.

EPR-148

Sex-related differences in Amyotrophic Lateral Sclerosis: a brain 2-[18F]FDG-PET study

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Background and aims: The neuroanatomical correlates of sex in Amyotrophic Lateral Sclerosis (ALS) have been studied in animal models and human neuropathological series, but they remain unclear. This study is aimed at exploring the brain metabolic differences related to sex.
Methods: We collected two groups of male (m-ALS) and female ALS (f-ALS) patients (n=130 each), who underwent 2-[18F]FDG-PET at diagnosis. They were matched for site of onset (bulbar/spinal), cognitive status (normal/impaired), and King's stage. We included two groups of 84 male (m-HC) and 84 female (f-HC) age-matched healthy controls (HC). We compared m-ALS and f-ALS including age as covariate on one hand, and m-HC and f-HC on the other hand, employing the two-sample t-test model of SPM12. Then, a differential network analysis was performed. Starting from

each patient, 94 brain ROIs and metaROIs were extracted, along with their respective (normalized) metabolic levels. By building two correlation networks we assessed differences in connectivity between m-ALS and f-ALS.
Results: F-ALS showed clusters of relative hypermetabolism including bilateral medial frontal, parietal, and occipital cortices, and left temporal cortex, compared to m-ALS. No significant difference emerged between m-HC and f-HC. In node-wise comparison between m-ALS and f-ALS, 2 metaROIs showed significantly higher connectivity in f-ALS compared to m-ALS (right mid cingulate cortex and left superior and medial frontal gyrus).
Conclusion: Sex impacts brain metabolism in ALS and underlies differences in brain connectivity. Sex should be considered when evaluating results in clinical trials, since sex-related brain metabolic differences might be associated with a heterogeneity in treatment response.
Disclosure: No conflicts of interest to declare.

EPR-149

Multimodal Fusion Imaging in Dementia with Lewy Body: an original insight into routes leading to Neurodegeneration

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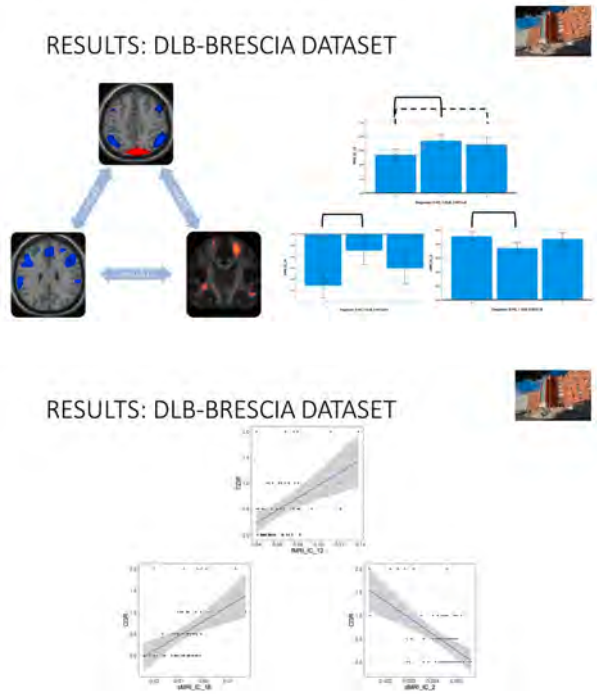
Background and aims: Data fusion analyses enable the integration of different modalities of MRI evaluating gray and white matter integrity as well as functional connectivity to find out possible alterations across modalities.
Methods: DLB patients, at prodromal (pDLB, n=15) and dementia stages (DLB-DEM, n=19), were included and compared to Healthy Controls (HC, n=27). Each participant underwent 3T MRI session and neurological assessment. A multivariate analysis (P-GICA) was carried using Structural, DTI and fMRI data to identify the maximally correlated components from each modality. The different distribution of components among d-DLB, p-DLB and HC groups and correlations with clinical features were then assessed.
Results: P-GICA detected 3 correlated components, describing a pattern of atrophy clustering in middle-inferior frontal gyrus, as well as superior and inferior parietal lobules in p-DLB and DLB-DEM. The linked fMRI ICs showed a reduced connectivity in hubs of Dorsal Attention Network and an overactivation in regions belonging to Ventral Attention Network in DLB. DTI analyses revealed reduced FA values in patients in superior and inferior longitudinal fasciculi. The integrative components significantly distinguish between HC and DLB-DLB,, with significative correlations with disease severity.



Conclusion: This study provided an original profile of DLB-related neurodegeneration, in which fronto-parietal atrophy is associated to DAN-VAN disconnection and WM disintegration in bundles underpinning their interactome. These results leverage strengths of a novel multimodal fusion approach pointing out a connectivity rearrangement in early stages of DLB, defining the combination of GM and WM structural changes driving to functional failure.
Disclosure: Nothing to disclose.

EPR-150

Multimodal fusion imaging reveals structural correlates of precuneus Hyperactivation in the early stages of in AD

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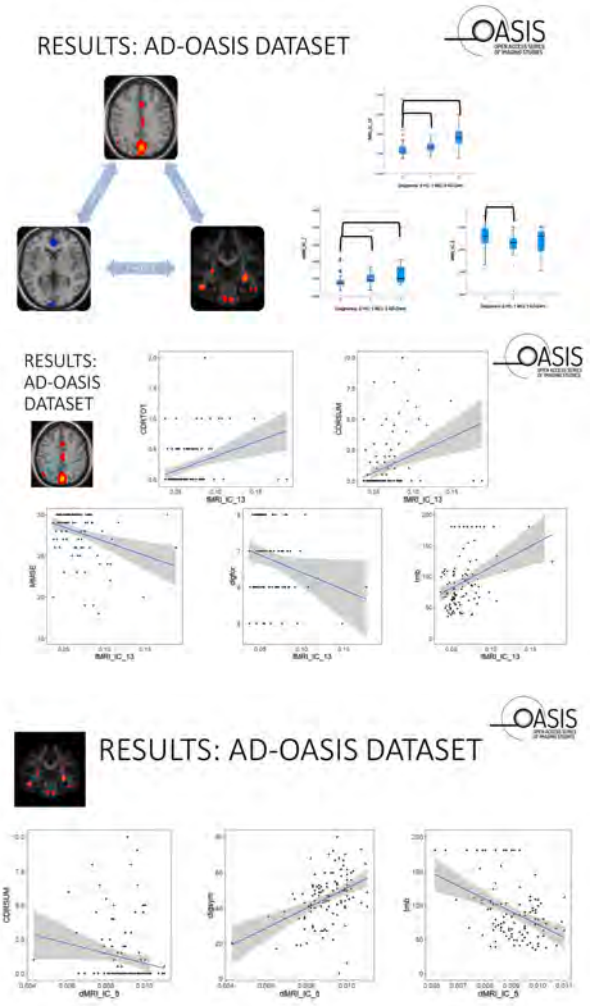
Background and aims: While different MRI modalities apport their own contribution to the comprehension of neurodegeneration, multimodal approach can integrate different structural and functional MRI data to find out changes across modalities.

Methods: Data were downloaded from the OASIS-3 brain project, and included healthy controls (HC, n=80) and AD (n=35), namely MCI (n=23) and mild AD-DEM (n=12) subjects. Each participant underwent MRI and neurological assessment. A multivariate analysis, based on a parallel-Group-guided Independent Component Analysis (P-GICA) was carried using Structural, DTI and fMRI data. This analysis returned a "Triangle", made of the maximally correlated components from each modality. A univariate model evaluated the different distribution of MRI components among patients groups and possible correlations with clinical features.
Results: P-GICA detected 3 maximally correlated components from Structural, DTI and fMRI images, describing a pattern of atrophy in the Anterior Cingulate Cortex (ACC), associated to increased activation of precuneus and reduced FA values in corpus callosum, superior and inferior longitudinal fasciculus (SLF, ILF) and uncinate fasciculus (UF). The integrative components showed a different distribution across groups, distinguishing MCI from HC, as well as AD-DEM from HC. Significative correlations emerged with disease severity and Neuropsychological scores.



Conclusion: This study showed greater atrophy within ACC correlating positively with enhanced connectivity of the posterior hub of DMN, associated to disintegration of UF SLF and ILF. This covariance pattern could explain pathways leading to AD-related neurodegeneration in the early stages, pointing out structural changes associated to dysfunctional connectivity of the precuneus and regions primarily affected by the amyloid spreading.
Disclosure: Nothing to disclose.

EPR-151

The remote effects of regional amyloid on tau pathology spread are mediated by functional connectivity

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Background and aims: Consistent with the amyloid-cascade-hypothesis, we assumed that i) regional components of amyloid burden are associated with tau pathology increases in spatially independent brain regions and that ii) functional connectivity serves as a mediator bridging the observed spatial gap between these pathologies.
Methods: Data of 98 amyloid-positive and 35 amyloid-negative subjects with baseline amyloid (18F-AV45) and longitudinal tau (18F-AV1451) PET were selected from ADNI. All images were z-transformed using the amyloid-negative subjects as reference. Annual tau change maps were computed. Z-maps of baseline amyloid and annual tau change were submitted to a parallel independent component analysis in GIFT, yielding six component pairs linking spatial patterns of baseline amyloid to longitudinal tau increase. Next, we used the region of maximum coefficient per component as seeds for functional connectivity analyses in a healthy control dataset. This resulted in six pairs of amyloid and tau seed-based networks (SBN). Subsequently, the spatial overlap between these SBNs and the independent components (amyloid OR tau change) and the combined component pairs (amyloid AND tau change) were quantified.
Results: Amyloid SBNs (green) presented greater spatial overlap with their respective amyloid (red) components (24%-54%) than tau SBNs with the respective tau change (blue) components (16%-40%). However, the spatial combination of amyloid and tau component pairs showed highest spatial overlap with the amyloid SBNs (up to 62% vs. 39% for the tau SBNs) suggesting that amyloid offsets tau spread within the same network.

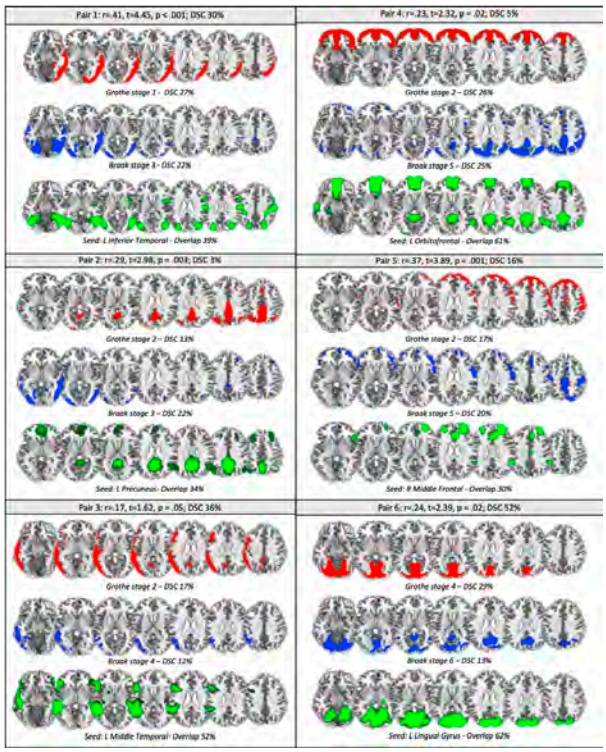

Figure 1 – Regional amyloid-tau associations and corresponding functional connectivity networks. The six component pairs of the pICA are depicted including the correlation coefficient, their spatial overlap in addition to the amyloid SBN.

Conclusion: Amyloid plaques may trigger local tau pathology which then spreads via functional connections to remote brain regions.
Disclosure: Nothing to disclose.

EPR-152

MRI features of idiopathic intracranial hypertension are not prognostic of visual and headache outcome

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Background and aims: In idiopathic intracranial hypertension (IIH), certain MRI features are promising diagnostic markers, but whether these have prognostic value is currently unknown.
Methods: We included patients from the Vienna-Idiopathic-Intracranial-Hypertension (VIIH) database with definitive IIH according to Friedman criteria and cranial MRI performed at diagnosis. Presence of empty sella (ES), optic nerve sheath distension (ONSD), optic nerve tortuosity (ONT), posterior globe flattening (PGF) and transverse sinus stenosis (TSS) was assessed and multivariable regression models regarding visual outcome (persistent visual impairment /visual worsening) and headache outcome (headache improvement/ freedom of headache) were fitted.
Results: We included 84 IIH patients (88.1% female, mean age 33.5 years, median body mass index 33.7). At baseline, visual impairment was present in 70.2% and headache in 84.5% (54.8% chronic). Persistent visual impairment occurred in 58.3%, visual worsening in 13.1%, headache improvement was achieved in 83.8%, freedom of headache in 26.2%. At least one MRI feature was found in 78.6% and 60.0% had ≥3 features with ONSD most frequent (64.3%) followed by TSS (60.0%), ONT (46.4%), ES (44.0%) and PGF (23.8%). In multivariable models, there was no association of any single MRI feature or their number with visual impairment, visual worsening, headache improvement or freedom. Visual impairment at baseline predicted persistent visual impairment (odds ratio 6.3, p<0.001), but not visual worsening. Chronic headache at baseline was significantly associated with lower likelihood of headache freedom (odds ratio 0.48, p=0.013), but not headache improvement.

Table 1

Table 2

Conclusion: MRI features of IIH are neither prognostic of visual nor headache outcome.
Disclosure: GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPR-153

Aging influences regional white-matter axonal density loss

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Background and aims: To investigate brain network structural alterations during aging using connectome-analysis with advanced diffusion-weighted metrics.
Methods: Forty-eight young (YC), 20-31 years, and 65 older controls (divided considering 60-years as cut-off: 21 middle-aged [MC] and 44 elderly [EC]), were enrolled and underwent multi-shell diffusion MRI and cognitive evaluation. Fractional anisotropy (FA) maps were computed. Intra-cellular Volume Fraction (ICVF) and Orientation Dispersion Index (ODI) maps were estimated using NODDI model. Graph analysis and connectomics assessed global and local network properties and regional connectivity. Correlations were tested between MRI and cognitive performances.
Results: EC subjects showed altered structural global network properties than YC. Widespread changes were observed in MC and EC relative to YC (decreased FA and increased ODI). Considering FA, ICVF and ODI, EC subjects showed altered local measures within frontal, basal-ganglia, and temporal areas relative to MC. EC were characterized by decreased FA relative to MC in the connections within mainly frontal, sensorimotor, parietal and temporal. Considering ICVF, differences between EC and MC were more focal than FA. In YC and EC subjects, altered MRI measures were related to worse cognitive performances (executive functions, non-verbal memory and visuospatial abilities). In addition, in EC, structural network disruption correlated to worse working memory. Interestingly, in MC only poor visuospatial abilities were related to MRI measures.
Conclusion: Connectome-analysis based on advanced diffusion-weighted models can be a more useful biomarker to evaluate initial structural brain disruptions of aging process than diffusion-derived measures.
Disclosure: Supported-by: European-Research-Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer's Disease.

Neuroimmunology

EPR-154

Influence of Beta-Fibrinogen 455G/A and Factor V 4070A/G polymorphisms on Multiple Sclerosis clinical course

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Background and aims: A growing body of evidence suggests a role of coagulation components in Multiple Sclerosis (MS) neuroinflammation. Fibrin(ogen) promotes inflammatory processes within perivascular lesions, and thereby contributes to neuronal damage, and inhibits tissue repair processes. Recently, we have showed that Beta-Fibrinogen 455G/A and Factor V 4070A/G polymorphisms may be associated with a higher risk of MS. To evaluate whether MS patients carrying the Beta-Fibrinogen 455A/A genotype, or the G allele of the Factor V 4070A/G polymorphism present a worse disease course.
Methods: We retrospectively collected demographic and clinical (age at onset, EDSS at onset) data at disease onset and after 2 and 5 years of follow up (EDSS and number of relapses). Patients were genotyped for the Beta-Fibrinogen 455G/A and Factor V 4070A/G polymorphisms. The association between the polymorphisms and the clinical data was analyzed by linear and Poisson regression models, as appropriate. The regression models were adjusted according to gender and disease-modifying therapies (first vs second line DMTs) over the follow-up period.
Results: We enrolled 176 RRMS patients. The Factor V 4070A/G genotype was associated with a higher MSSS score (p=0,021; CI: 0,16-1,9) and a higher number of relapses at two (p=0,013; IC: 0,11-0,98) and five (p=0,002; CI:0,19-0,8) years of follow-up. The Beta-Fibrinogen 455A/A genotype was associated with a higher number of relapses at two (p<0,001; CI: 0,57-1,55) and five (p=0,007; CI:0,15-0,99) years of follow-up.
Conclusion: Beta-Fibrinogen 455G/A and Factor V H1299R polymorphisms may influence MS disease course.
Disclosure: The authors declare no competing interests for this work.

EPR-155

Long-term follow-up after anti-NMDAR encephalitis, focusing on cognitive sequelae and quality of life.

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Background and aims: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a brain inflammation caused by NMDAR antibodies. Typical clinical symptoms include cognitive and behavioural changes, seizures and autonomic dysregulation. It is a severe disease, and many patients end up at the intensive care, but fortunately treatable: over 80% improve to a 'good outcome' on the modified Rankin Scale (mRS≤2). Nevertheless, many patients experience persistent cognitive and emotional sequelae, and a decreased quality of life years after treatment. We aim to capture the whole scope of potential sequelae of anti-NMDAR encephalitis.
Methods: As national reference centre for autoimmune encephalitis, we have invited all adult patients diagnosed in the Netherlands with anti-NMDAR encephalitis to cross-sectionally assess long-term outcomes: undergo a neurological examination, complete a comprehensive neuropsychological assessment and answer questionnaires.
Results: We included 84 anti-NMDAR encephalitis patients. In a preliminary analysis (n=55; median age 27 years, range 14-73; median follow-up 52 months, range 0-167), 53 patients (96%) scored below -1 standard deviation (SD) on one or more cognitive domains and 69% below -2SD. The largest impairments were shown for language (mean z-score=-1.22, SD=1.04) and verbal memory (z=-1.07, SD=1.29). At a group level, cognition improved over time (Figure 1). Cognition and mRS correlated poorly (R~0.3). Quality of life was decreased, measured by the WHO-5 well-being index (62.9 vs 73.0).

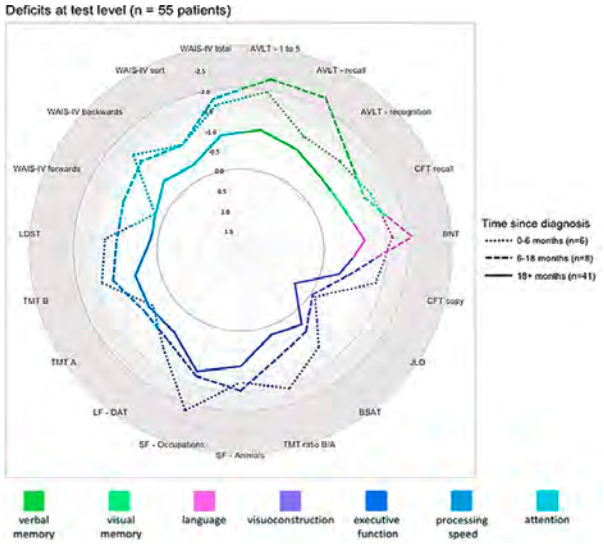

Figure 1: Cognitive sequelae over time after diagnosis of anti-NMDAR encephalitis.

Conclusion: Cognitive deficits and a diminished well-being may persist years after anti-NMDAR encephalitis. The used outcome measures exposed long-term sequelae well, and captured relevant changes over time, better than mRS).

Disclosure: The presented study is funded by Dioraphte (project number 20010403).

EPR-156

MRI characterization of whole brain atrophy and hippocampal volumetry in Limbic Encephalitis

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Background and aims: Limbic Encephalitis (LE) is a well characterized form of autoimmune encephalitis. Despite clear evidence of immune-mediated pathogenesis and known clinical specificities, few quantitative MRI data exist in terms of neuroradiological evolution over the long term (whole brain and hippocampal involvement) as well as MRI volumetric data in the different subforms.

Methods: Multicentric, retrospective, observational, longitudinal study including patients with definite LE and disease duration <6 month. Brain MRI scans were acquired at baseline and at one follow-up time point. Global brain atrophy (AR/y) were evaluated through advanced image analysis and compared to age-related normative values. Hippocampal volume at onset and at follow-up and hippocampal subfields volume change (PVC/y) were analysed in patients and in matched healthy controls. Data have been then stratified according to patient serostatus and compared among serogroups.

Results: 22 LE patients were included: 7 seronegative, 11 with anti-LGI1, 2 with anti-CASPR, 2 with anti-GAD Abs. Pathological AR/y rates were observed at follow up (median 21 months, range 6-80:) in patients compared to the age-related normative values ($p<0.01$). No difference in hippocampal volume at baseline was observed between patients and controls, but in patients hippocampal volumes resulted reduced at follow-up ($p<0.01$). Significant PVC/y of all hippocampal subfields were observed in patients compared to controls except for subiculum. Regardless of Ab-status, Hippocampal amygdaloid transition area (HATA) was the most severely involved subfield ($p=0.038$).

Conclusion: In LE, regardless of Ab status, a pathological global brain and hippocampal residual atrophy were observed. Regardless of Ab-status, HATA seems the most involved subfield.

Disclosure: Nothing to disclose.

EPR-157

Serum NfL levels and cognitive performance in persons with multiple sclerosis

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Background and aims: Serum neurofilament light (sNfL) is a robust biomarker to indicate neuro-axonal damage in various neurologic conditions including multiple sclerosis (MS). Cognitive impairment (CI) is a frequent feature in MS with a huge impact on quality of life and social functioning. It is still not clear if sNfL correlates with or even predicts CI in MS. This study aims to elucidate the association between sNfL and CI in persons with MS (pwMS).
Methods: 186 pwMS (112 female; mean age=39.6±10.4; mean disease duration=10.6 years; median EDSS=1.5 (IQR=2.75)) and 49 healthy controls (HC) (35 females; mean age=33.4±10.7) underwent clinical examination, neuropsychological (Brief Cognitive Assessment for MS-BICAMS) and 3T brain-MRI assessment, including T2-hyperintense lesion load and normalized brain volumes calculations. sNfL was quantified by single molecule array (Simoa SR-X). We calculated sNfL Z-scores corrected for age and body-mass-index; Symbol Digit Modalities Test (SDMT) Z-scores corrected for age and education; Verbal Learning Memory Test (VLMT) and Brief Visuospatial Memory Test (BVMT) T-scores corrected for age.
Results: In this cross-sectional analysis, 48 pwMS showed CI in at least one BICAMS test and 38 in SDMT (M=-0.2±1.1); 6 in VLMT (M=56.2±9.5) and 20 in BVMT (M=54.3±12.7) in comparison to no CI in HC ($p<0.001$). Baseline sNfL Z-scores (M=0.73±0.09) were unrelated to BICAMS sub-tests, including the SDMT, VLMT and BVMT (all $p>0.05$, n.s.) both in pwMS and HC.
Conclusion: In this cross-sectional analysis, sNfL was unrelated to CI in pwMS. Longitudinal analyses investigating the relation of sNfL dynamics and MRI metrics with cognitive decline are currently ongoing.

Disclosure: M. Khalil has received speaker honoraria from Bayer, Novartis, Merck, Biogen Idec and Teva Pharmaceutical Industries Ltd. and serves on scientific advisory boards for Biogen Idec, Merck Serono, Roche, Novartis, Bristol-Myers Squibb and Gilead. He received research grants from Teva Pharmaceutical Industries, Ltd., Biogen and Novartis. S. Wurth has participated in meetings sponsored by, received honoraria or travel funding from Allergan, Biogen, Ipsen Pharma, Merck, Novartis, Roche, Sanofi Genzyme, Teva and Bristol Myers Squibb. S. Hechenberger has received speaker honoraria from Bristol Myers Squibb and Roche. B. Helmlinger has received speaker honoraria from Roche. All other authors have nothing to disclose.

EPR-158

Longitudinal response to mRNA SARS-CoV-2 vaccines and breakthrough infection in autoimmune neurological disorders

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Background and aims: To investigate (a) the longitudinal durability of two-dose mRNA vaccine and the T cell response at 6 months; (b) the effects and safety of the booster dose; (c) the relationship between the immunological data and the frequency of breakthrough infections and their outcome in patients with autoimmune neurological conditions (ANC).
Methods: We included patients vaccinated with 2 doses of BNT162b2 or mRNA-1273 vaccines. Clinical status and anti-spike receptor binding domain antibody (anti-RBD IgG) levels were evaluated before, 3 and 6 months after the second dose and at three time points after the third dose. SARS-CoV-2-specific T cell immunity was determined in a subset of patients at T6.

Results: We included 295 ANC patients. Anti-RBD IgG titers progressively declined (p<0.0001) after the second dose, but most patients remained seropositive. However, fourteen patients, mostly on anti-CD20 mAb therapy (p<0.0001), become seronegative at T3. The third dose was safe and significantly increased antibody levels (p<0.0001). Nevertheless, 15 patients, all on anti-CD20 mAb therapy (p<0.0001), remained seronegative. A positive T-cell response against the S protein was found in 29/60(48.3%) patients and was associated with anti-CD20 mAb therapy (p<0.0001). During the 12-month study period, 90 (30.2%) patients reported a SARS-CoV-2 infection. Age (p=0.008) and antibody levels (p=0.007) were predictors of breakthrough infection. Symptomatic infections (p=0.035) and hospitalization (p=0.045) were more common in patients treated with anti-CD20 mAb.
Conclusion: Antibody responses vary across ANC patients receiving different immunotherapies and supports the need of immunomonitoring and individualized vaccination schedules in ANC patients.
Disclosure: Nothing to disclose.

EPR-159

Laboratory diagnostic strategies for the diagnosis of autoimmune encephalitis

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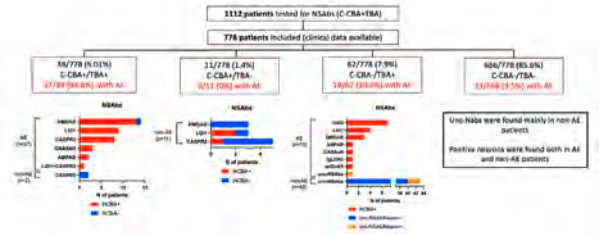
Background and aims: The detection of antibodies against neuronal synaptic proteins (NSAbs) is a crucial step in autoimmune encephalitis (AE) diagnosis, but different laboratory assays are available. We aimed to compare the performance of commercial and in-house assays for NSAbs detection and to define the relevance of uncharacterized NSAbs (unc-NSAbs) identified only on in-house rat brain tissue based assays (TBA).
Methods: We tested for NSAbs 1112 samples sent for suspect AE using commercial cell-based assay (C-CBA) and TBA. All positive patients on TBA and/or C-CBA were additionally tested using in-house CBAs (ih-CBA). Unc-NSAbs were tested on live rat neuronal cultures (LNC). We analysed the predictive relevance of TBA staining pattern using multivariate analysis.
Results: We included 778/1112 patients and 79/778 (10.2%) had AE (Fig.1). All C-CBA+/TBA+ patients diagnosed with AE, and none of the C-CBA+/ihTBA-. The TBA showed the highest negative Likelihood Ratio (Table 1). Forty-three/44 of unc-Nabs patients were not diagnosed with AE, and 3 of them were positive using LNC. Both CSF and serum were analyzed in 442/778 patients. Serum-only positivity in any assay occurred only in non-AE patients. The only TBA pattern predictor for AE diagnosis was a higher intensity of CSF staining (p<0.001).



Flow chart of the results of laboratory assays performed on the patients included in the study, according to the results of tissue-based assay (TBA), live neuronal cultures (LNC) and and both commercial (C-CBA) and 'in-house' (ihCBA) cell-based assay.

Assay	Sensitivity %(CI)	Specificity %(CI)	Accuracy %(CI)	Positive Likelihood Ratio (CI)	Negative Likelihood Ratio (CI)
C-CBA	46.3 (35.0-57.8)	98.1 (96.8-99.0)	92.8 (90.8-94.5)	24.8 (13.8-44.7)	0.5 (0.5-0.7)
TBA	71.3 (60.1-80.8)	93.7 (91.6-95.4)	91.4 (89.2-93.3)	11.3 (8.2-15.5)	0.3 (0.2-0.4)
ih-CBA	94.8 (85.6-98.9)	94.6 (84.9-98.9)	94.7 (88.8-98.0)	17.4 (5.8-52.3)	0.1 (0.0-0.2)
C-CBA+TBA	61.7 (48.2-73.9)	99.7 (98.9-99.9)	96.5 (94.8-97.7)	198.9 (49.1-804.9)	0.4 (0.3-0.5)
ih-CBA+TBA	100 (93.4-100)	100 (63.1-100)	100 (94.2-100)	-	-

The table shows the analytical performance of the tissue-based assay (TBA) and the commercial (C-CBA) and "in-house" (ihCBA) cell-based assay.

Conclusion: Commercial kits for NSAbs detection have lower accuracy compared to in-house assays. The best diagnostic strategy should combine TBA as a screening test, followed by ih-CBA, preferentially using both serum and CSF. In our study, Unc-NAbs were not clinically relevant, and NLC do not seem to increase the diagnostic accuracy.
Disclosure: Supported by the EAN research fellowship 2022.

EPR-160

Clinically-relevant increases in serum NfL and GFAP in patients with Susac Syndrome

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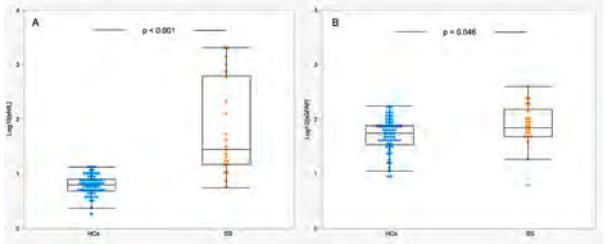
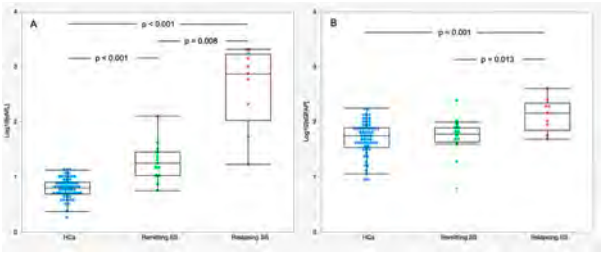
Background and aims: Serum levels of neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP) are promising biomarkers of neuronal damage and astrocytic activation, respectively. They have not yet been reported in Susac syndrome (SS) but could be useful as clinically relevant markers of tissue damage in patients with this disease. Our aim was to evaluate sNfL and sGFAP levels in patients with SS and assess their clinical relevance in the relapse and remission phase of the disease.

Methods: sNfL and sGFAP levels of 22 SS patients (9 during an acute disease relapse and 13 in remission) were assessed using SimoaTM assay Neurology 2-Plex B Assay Kit and compared to those of 59 age- and sex-matched healthy controls (HCs).

Results: sNfL levels were higher than those of HCs ($p < 0.001$) in the 22 SS patients and in both the subgroup of 9 relapsing-SS and 13 remitting-SS patients ($p< 0.001$ for both), with significantly higher sNfL levels in relapsing-SS than in remitting-SS ($p=0.008$). Levels of sGFAP were marginally significantly higher in the whole group of SS patients than HCs ($p=0.046$), and were higher in relapsing-SS than in remitting-SS ($p=0.013$) and in HCs ($p=0.001$).



log10-serum levels of neurofilament light chain (NFL) values (A), log10-glial fibrillary acidic protein (sGFAP) values (B) in healthy controls (HCs) and patients with Susac syndrome (SS).



log10-serum levels of neurofilament light chain (NFL) values (A), log10-glial fibrillary acidic protein (sGFAP) values (B) in healthy controls (HCs) and in remitting and relapsing patients with Susac syndrome (SS).

Conclusion: Both sNFL and sGFAP increase during the relapse phase of SS. sNFL seems to be more sensitive to clinical changes and can be a useful biomarker to monitor neuronal damage at different disease stages. Longitudinal studies are needed to establish whether sNfL and sGFAP can be reliable biomarkers for monitoring patients with SS in the clinical setting.

Disclosure: Nothing to report in relation to this study.

EPR-161

Development of brain-infiltrating B cells in multiple sclerosis: contribution of EBV and impact of BTK inhibition

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Background and aims: B cell-restricted pathways are likely disturbed by Epstein-Barr virus (EBV) and genetic risk variants in multiple sclerosis (MS). Here, we aimed to specify how B cells are shaped to become brain-infiltrating, antibody-secreting cells (ASC) that contribute to MS.

Methods: Protein expression was measured using FACS (primary B cells) and immunoblotting (EBV+/-BLCLs). Blood naive and memory B cells were cultured in IL-21/CD40L-containing media. Brain tissues were obtained post-mortem from the Netherlands Brain Bank. B-cell EBV load was determined using multiplex PCR. IgG levels in lesions were assessed using laser-capture microdissection and microarray.

Results: B cells carrying the risk variant IFNGR2 showed increased sensitivity to IFN-γ, probably due to IFNGR2 expression at the surface. The IFN-γ pathway was constitutively active in risk carriers with high B-cell EBV

load. EBV load positively associated with (IFN-γ-inducible) CXCR3 expression, particularly in IgG+ B cells. In vitro IgG switching was promoted by IFN-γ and TLR9 ligand. EBVhighCXCR3high IgG+ B cells of MS patients preferentially developed into ASC in vitro. These processes were attenuated by Bruton's tyrosine kinase (BTK) inhibition with evobrutinib. Enriched CXCR3high B cells displayed a prominent ASC phenotype in MS versus control brain tissues, which corresponded with IgG and T-cell presence within lesions.

Conclusion: This work reveals how triggers such as EBV and BTK induce CXCR3high B cells to enter and develop into ASC in the MS brain.

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EPR-162

CD8+ T cells expressing CD20 populate brain and cerebrospinal fluid in multiple sclerosis

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Background and aims: Circulating CD20dim CD8+ T cells have been implicated in multiple sclerosis (MS). We investigated the contribution of CD20dim CD8+ T cells to immune surveillance of the central nervous system (CNS) in MS.

Methods: We performed flow cytometry on and analysed the bulk-transcriptome of CD8+ T cells isolated from post-mortem brain tissue and blood of brain donors with and without MS. Additionally, T cells within the cerebrospinal fluid (CSF) were analysed with flow cytometry in CSF samples of patients with progressive MS with or without ocrelizumab treatment.

Results: The transcriptome of post-mortem brain grey and white matter CD69+CD103+/- CD8+ tissue-resident memory T (TRM) cells was enriched for MS4A1 (CD20) expression compared to circulating T cells. Brain CD20dim CD8+ TRM cells showed high presence of several chemokine receptors (CCR2, CCR5, CXCR6) and effector molecules (GrB, GrK, IFN-γ) but hardly expressed the integrin CD103. These findings were similar in brain donors with and without MS. In living people with MS, the CSF was enriched for GrK+ CD20dim CD69+ CD8+ T cells. In CSF, an EOMES+T-BET- transcriptional program characterized CD20dim CD8+ T cells, whereas these cells were predominantly EOMES-T-BET+/- in white matter. CSF CD20dim CD8+ T cells were depleted after treatment with ocrelizumab.

Conclusion: CD20 expression characterizes CNS-homing CD8+ T cells, which are depleted from the CSF by ocrelizumab treatment in progressive MS. The distinct transcriptional program of CSF versus brain CD20dim CD8+ T cells suggests a distinct phenotypic and functional profile between these compartments.

Disclosure: This work was supported by grants from Biogen, German Research Foundation, Nationaal MS Fonds, Stichting BeterKeten, and Stichting MS Research. The authors report no further disclosures relevant to this study.

Movement disorders 2

EPR-163

Weight, BMI, and Dyskinesia in Patients With Parkinson's Disease on Levodopa-Carbidopa Intestinal Gel

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Background and aims: Patients with Parkinson's disease (PD) with lower body weight or weight loss during the course of the disease (Park–weight phenotype) are at risk for dyskinesia, frailty, and poor quality of life. This post hoc analysis assessed the evolution of weight and associations of body weight, body mass index (BMI), and dyskinesia at baseline and change from baseline over 36 months (36M).
Methods: DUOGLOBE (DUOdopa/Duopa in Patients with Advanced Parkinson's Disease – a GLobal OBservational Study Evaluating Long-Term Effectiveness; NCT02611713) was an observational study evaluating the effectiveness of levodopa-carbidopa intestinal gel (LCIG) in patients with aPD. Clinical assessments occurred before treatment (baseline) and at scheduled visits for up to 36M of LCIG treatment. Dyskinesia was evaluated using the Unified Dyskinesia Rating Scale (UDysRS). Correlations were measured using Pearson's correlation coefficient tests.
Results: This analysis included 195 patients with a mean (SD) body weight of 72.9 (14.2) kg and BMI of 25.9 (4.1) kg/m2. From baseline to 36M, patients experienced a mean (SD) decrease in body weight of −3.1 (8.0) kg and BMI of −1.2 (2.8) kg/m2. Mean change from baseline to last study visit in body weight and BMI was lowest in patients with low BMI (Figure 1). Low body weight and BMI were correlated with more severe dyskinesia (higher UDysRS scores) at baseline (Figure 2 and Table 1).

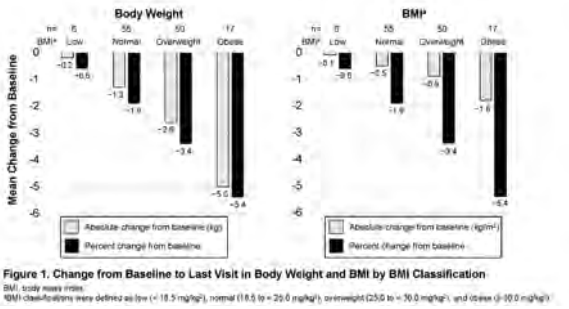

Figure 1. Change from Baseline to Last Visit in Body Weight and BMI by BMI Classification

Figure 1. Change from Baseline to Last Visit in Body Weight and BMI by BMI Classification

Table 1. Correlations Between Baseline Body Weight, BMI, and Dyskinesia

Characteristic	Pearson Correlation	*P* value
Body weight at baseline Dyskinesia[a] severity at baseline	−0.264	0009
BMI at baseline Dyskinesia[a] severity at baseline	−0.311	0013
BMI at baseline Change from baseline in BMI	−0.241	0062

BMI, body mass index; UDysRS, Unified Dyskinesia Rating Scale
[a]Evaluated using the UDysRS

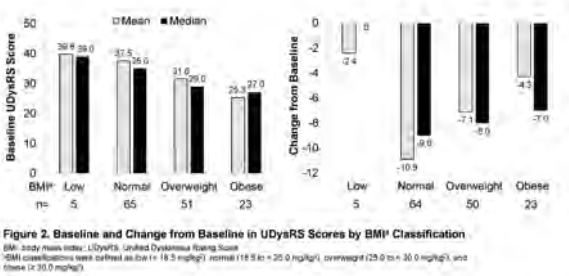

Figure 2. Baseline and Change from Baseline in UDysRS Scores by BMI* Classification

Figure 2. Baseline and Change from Baseline in UDysRS Scores by BMI Classification

Conclusion: Among patients treated in DUOGLOBE, lower baseline body weight or BMI were associated with lower weight loss and greater dyskinesia severity at baseline, consistent with the Park–weight phenotype.
Disclosure: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approving the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. All authors agreed to submit this abstract to the EAN 2023 Congress for consideration as an oral presentation or poster. AbbVie and authors thank all the trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Michael Dyle, PhD, of JB Ashtin, and funded by AbbVie.

EPR-164

Quantifying the effect of subthalamic stimulation on bradykinesia using digitized spiral drawings in Parkinson's disease

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Background and aims: The effect of subthalamic (STN) deep brain stimulation (DBS) on bradykinesia is usually analyzed when performing simple repetitive hand movement tasks. Instead, we aimed to investigate how the parameters of complex, visually controlled, voluntary movements, such as drawing a spiral, are influenced by adjusting the stimulation intensity.

Methods: Thirty-five patients with Parkinson's disease treated with bilateral STN-DBS were first prescreened while we selected four levels of contralateral stimulation (0: OFF, 1-3: decreasing symptoms to ON state) individually, based on kinematics. In the screening period, the patients drew spirals with the more affected hand on a digital tablet five times voluntarily, in each level of contralateral stimulation sequentially, in counterbalanced order. We calculated the average and peak values of tangential velocity and the sample entropy of tangential velocity representing irregularity in the temporal domain. Parameters of five spirals at each stimulation level were averaged for further statistical analysis.

Results: Both average and peak tangential velocity increased gradually with increasing stimulation intensity. In addition, the entropy of velocity diminished when turning the stimulation on but did not change parallel with increasing stimulation intensity.

Conclusion: Our result support earlier findings that contralateral STN-DBS exerts its best effect on the speed of movement. However, we show that improvement in the speed irregularity is limited and does not follow the increase in stimulation intensity. Analysis of complex, fine hand movements may result in a better understanding of the mechanism of action of STN-DBS.

Disclosure: The authors declare nothing to disclose.

EPR-165

Alteration of PI3/AKT/mTOR pathway related genes in the pathogenesis of GBA-associated Parkinson's disease

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Background and aims: Molecular mechanisms of Parkinson's disease (PD) associated with mutations in the GBA gene (GBA-PD), encoding the enzyme glucocerebrosidase (GCase), are unknown. Currently being discussed that dysfunction of the autophagy-lysosomal PI3/AKT/mTOR pathway represents a central pathogenic event in GBA-associated neurodegeneration. The aim of the current study was to estimate whether alteration of expression of genes associated with PI3/AKT/mTOR pathway contributes to GBA-PD pathogenesis.

Methods: 15 GBA-PD patients, 17 sporadic PD patients (sPD) and 35 controls were recruited for the current study. Expression of genes previously shown to be involved in PI3/AKT/mTOR pathway (ARL4D, ARL4C, SGK1, TRIM13, PDK4, BCL6, DUSP1) were analyzed in lymphocytes peripheral blood cells by real-time PCR with TaqMan assay.

Results: The main results were that GBA-PD patients were characterized to by decreased DUSP1, ARL4C and increased ARL4D expression levels compared to controls ($p=0.00011$, $p=0.03$, $p=0.047$, respectively) and also increased ARL4D, TRIM13 along with decreased BCL6 expression levels than in sPD patients ($p<0.0001$, $p=0.0019$, $p=0.0037$, respectively).

Conclusion: We revealed alteration of gene expression profile of PI3K-Akt-mTOR signaling pathway in the peripheral blood mononuclear cells of GBA-PD patients compared to controls and sPD patients. Influence on PI3/AKT/mTOR pathway maybe considered as a potential therapeutic target for GBA-PD.

Disclosure: This work was supported by the Ministry of Science and Higher Education of the Russian Federation (Project No 121060200125-2, "The study of molecular and cellular components of the pathogenesis of socially significant diseases for the development of methods for early diagnosis and treatment").

EPR-166

Pain in people with multiple system atrophy: a systematic review

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Background and aims: People with multiple system atrophy (MSA) often complain about pain. Its prevalence, characteristics and risk factors remain however poorly characterized to date.

Methods: To estimate pain prevalence and to collect information on its characteristics, risk factors and treatment strategies in people with MSA, the PubMED, Cochrane and Web of Science databases were systematically screened for papers published in English until September 2022, by using the following keywords: "pain" AND "multiple system atrophy" OR "MSA", olivopontocerebellar atrophy" OR "OPCA", "striatonigral degeneration" OR "SND", "Shy Drager", "atypical parkinsonism". Additional papers were retrieved by reference cross-check. Papers reporting information on pain prevalence in people with possible or probable MSA were included.

Results: Seven-hundred records were identified, 16 were included in the qualitative synthesis and 14 (7 cross-sectional, 1 retrospective, 6 prospective) were retained for final analysis, pooling data from 1319 individuals with MSA. Among them, 60% (n=797) reported pain, with prevalence of pain ranging from 40% to 88% across studies. Pain was reported by 67% of people with MSA-Parkinson (MSA-p) and by 47% of MSA-cerebellar phenotype (MSA-c) ($p<0.001$). According to two studies, 50% of the individuals with MSA had received any kind of pain-specific treatment. We found a high heterogeneity in pain prevalence, classification and assessment tools across studies.

Conclusion: Pain is a frequent, but still under-recognized and undertreated feature of MSA. A better characterization of pain prevalence, characteristics and predisposing factors in people with MSA will help tailoring its assessment and management.

Disclosure: Academic study supported by a grant from the MSA-Coalition. The authors declare no competing interest relevant to the abstract.

EPR-167

A Portuguese cohort of autosomal recessive spastic ataxia of Charlevoix-Saguenay

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Background and aims: Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is characterized by early-onset spastic ataxia and peripheral neuropathy. We aimed at performing a clinical-genetic analysis on a cohort of ARSACS patients.

Methods: Prospective study since 2017, according to a structured protocol; patients identified through an electronic database. Data collection/analysis performed on REDCap, at CHUPorto.

Results: Eleven patients from 8 families (4 consanguineous) were identified, with a median follow-up of 9 (IQR 0-11.5) years. Disease onset occurred in the first year of life in 5 patients, childhood/adolescence in 5 and adulthood in 1. First symptoms included motor delay (n=6), ataxia (2), spastic gait (2) and neuropathy (1). Ataxia and pyramidal signs were present in all, identified at age 12.5±11.0 and 9.2±8.4 years; 10 patients had neuropathy by age 26.1±17.1 years. Seven individuals were wheelchair-bound by age 27.4±9.9 years. Two died (at age 53 and 51 years). MRI (6) showed vermis atrophy in all and pontine hypointensities in 2. EMG (5) identified sensory-motor axonal neuropathy. Genetic diagnosis was achieved through Sanger sequencing (4), exome (4) or NGS panel (3): 8 were homozygous and 3 compound heterozygous at SACS. Pathogenic variants located mainly in exon 10, but two were on exon 8; 1 patient with spastic ataxia also carried two disease-causing variants in APTX.

Conclusion: We contribute to ARSACS characterization. There was an earlier onset of the disease in this cohort; but one case had onset in adulthood (pathogenic variants in APTX). Pyramidal signs tended to precede ataxia, while neuropathy had a later onset.

Disclosure: All authors declare that they have no conflicts of interest related to the manuscript.

EPR-168

Correlates of the discrepancy between objective and subjective cognitive functioning in non-demented patients with PD

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Background and aims: Subjective complaints of cognitive deficits are not necessarily consistent with objective evidence of cognitive impairment in Parkinson's disease (PD). We examined demographic, clinical, and behavioral factors associated with the objective-subjective cognitive discrepancy.
Methods: We enrolled 90 non-demented PD patients who completed PD-Cognitive Functional Rating Scale and Montreal Cognitive Assessment (MoCA), respectively subjective and objective cognitive measures, using them to classify patients as "Overestimators", "Accurate estimators" and "Underestimators". To identify the factors distinguishing these groups, we used chi-square tests or one way analyses of variance, completed by logistic and linear regression analyses.
Results: Forty-nine patients (54.45%) were classifed as "Accurate estimators", twenty-nine (32.22%) as "Underestimators", twelve (13.33%) as "Overestimators". "Underestimators" scored higher on the Fatigue Severity Scale (FSS), Beck Depression Inventory (BDI), and Parkinson Anxiety Scale ($p<0.01$). Logistic regression confirmed that FSS and BDI scores distinguished the "Underestimators" group from the others ($p<0.05$) and that FSS and BDI scores positively related to objective-subjective cognitive discrepancy ($p<0.01$). "Overestimators" scored lower than others on the MoCA's total score and attention and working memory subscores ($p<0.01$). In more than 45% of consecutive non-demented PD patients, we found a 'mismatch' between objective and subjective cognitive measures associated to the presence of fatigue, depressive symptoms and frontal executive impairment. This suggests caution in relying on patients' subjective reports, especially in the absence of objective testing.
Conclusion: Our findings highlight the importance of assessing and monitoring fatigue and depressive symptoms in PD, especially when patients' complaints of cognitive impairment are used as prognostic indicators of future objective cognitive deterioration.
Disclosure: Nothing to disclose.

EPR-169

Asymmetry of bradykinesia features in Parkinson's and interhemispheric inhibition imbalance

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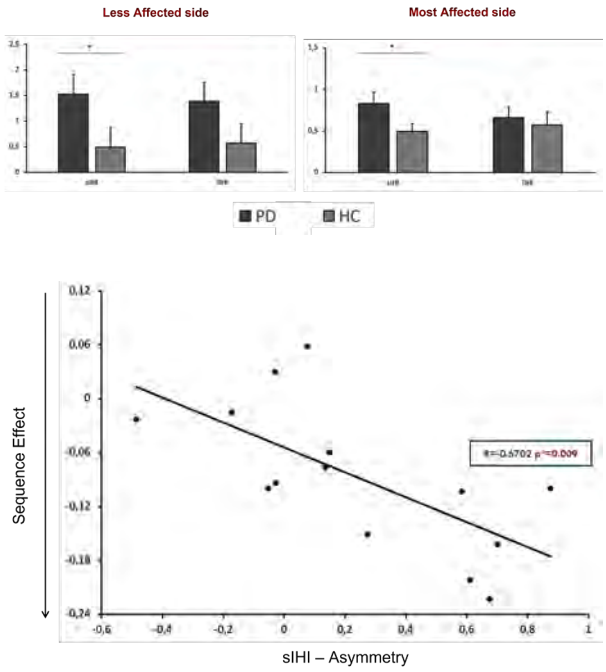
Background and aims: Bradykinesia and other motor symptoms in Parkinson's disease (PD) are predominantly asymmetric. An altered connectivity between the two primary motor cortices (M1) have been demonstrated in PD. The aims of our study was to investigate the relationship between the asymmetry of bradykinesia, quantified by kinematic analysis of finger tapping, and the asymmetry of the interhemispheric inhibitory connections in PD, tested by transcranial magnetic stimulation (TMS).
Methods: Twelve PD patients and 10 healthy controls (HCs) were enrolled. Objective bradykinesia measurements were obtained using a motion analysis system. Paired-pulse TMS was used to measure the interhemispheric inhibition (IHI) between the hand areas of the two M1, with an interstimulus interval (ISI) of 10 ms (short-latency IHI, sIHI) and 40 ms (long-latency IHI, lIHI). Asymmetry indices (AI) were calculated for all neurophysiological data. We then tested possible relationship between kinematic and TMS data.
Results: PD patients were slower than HCs during finger tapping ($p=0.01$). In PD there was a more severe progressive reduction of movement amplitude during movement repetition, i.e., sequence effect ($p=0.04$). When testing IHI (from the most affected to the less affected hemisphere), we found a reduced sIHI in patients. The amount interhemispheric disinhibition, i.e., interhemispheric imbalance quantified by the sIHI-AI, correlated with the sequence effect of the less affected side ($p<0.001$).
Conclusion: we here provided novel evidence on the role of interhemispheric disinhibition in the pathophysiology of bradykinesia asymmetry in PD. The results support the hypothesis that the sequence effect has pathophysiology mechanisms distinct from those underlying other bradykinesia features.
Disclosure: No conflict of interest.

	PD-MA	PD-LA	HC	p-value* PD-MA vs HC	p-value* PD-LA vs HC	p-value* PD(LA vs MA)
N° Mov	52,93±15,00	55,52±12,32	45,49±13,75	0,20	0,06	0,12
CV	0,14±0,10	0,13±0,07	0,10±0,03	0,14	0,17	0,38
Amplitude slope	-0,24±0,13	-0,11±0,11	-0,06±0,27	**0,04**	0,56	**0,003**
Amplitude	45,06±9,63	44,48±45,96	44,17±11,65	0,83	0,94	0,84
Velocity slope	6,34±2,32	3,93±2,52	6,48±5,22	0,93	0,12	0,05
Velocity	919,77±199,29	1017.24±222,33	1084,28±156,88	**0,03**	0,39	0,17



EPR-170

Motor neuron involvement in facial muscles as characteristic of ANO10 mutation

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Background and aims: Mutation in the ANO10 gene is causing a type of autosomal recessive ataxia named spinocerebellar ataxia 10 (SCAR10), a group of spastic ataxias, without neuropathy. Previously, motor neuron involvement was found in the muscles of the lower extremities, but the findings on electromyography (EMG) findings in other muscles were not mentioned in the literature. Here we want to present the phenotype of the patients carrying ANO10 mutation which included motor neuron involvement in facial muscles.
Methods: Group of 23 patients of Romani ancestry (11 previously reported) were diagnosed with pathogenic variant c.1150_1151 in the ANO10 gene. All patients were neurologically examined and EMG of the facial muscles was done in 6 patients, while EMG of the lower extremities in 11 patients.
Results: All patients had gait and limb ataxia, cerebellar dysarthria, and hyperreflexia. Additional signs in the form of spasticity and extensor plantar response had 82% and 61% of patients, respectively. During the oculomotor examination, 65% of patients had gaze-evoked nystagmus, 39% had downbeat nystagmus, while strabismus had 48% of patients. Other signs on clinical examination were semiptosis in 39%, head tremor in 26%, and facial myokymia in 13% of patients. On EMG analysis of LE, 54% of patients (6/11) had motor neuron involvement, and for the analysis of frontalis and orbicularis oculi muscles of the face 100% of patients (6/6).
Conclusion: SCAR10 belongs to the group of ARCAs without neuropathy, but with frequently present motor neuron involvement in the facial muscles which could precede involvement in the muscles of the extremities.
Disclosure: We have nothing to disclose.

EPR-171

Efficacy of deep brain stimulation in Parkinson's disease - age greater than or equal to 70 versus less than 70 years

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Background and aims: The age cutoff for subthalamic nucleus (STN) deep brain stimulation (DBS) in Parkinson's disease (PD) has been a matter of controversy. This study aimed to compare DBS efficacy outcomes in patients 70years old or older versus those younger than 70.
Methods: A retrospective, unicentric, cross-sectional, case-control study of PD patients undergoing STN-DBS between 2002-2019. The analysis included clinical and demographic variables related to neurostimulation parameters: MDS-UPDRS-III and IV; L-dopa equivalent daily dose (LEDD).
Results: Of 360 patients, 15 were 70 years old or older and met the inclusion criteria; [median age of 70 years [IQR:1,0]; mean disease duration of 13.4±5.3years]. Comparing the latter to a homogeneous group of 61 patients younger than 70 years old [median age of 61years [IQR:8,5] and mean disease duration of 13.0±2.3 years]. There were no significant statistical differences between the MDS-UPDRS-III scale in individuals 70years old or older versus younger than 70 years at the first assessment post-DBS[mean of 15.2±5.2 versus a median of 17.0[AIQ:9,0]](p=0.166) and at 36 months of follow-up [median of 23.0 [AIQ:19,0] versus mean of 19.8±7.9](p=0.123). In both groups, the post-DBS reduction in LEDD was similar (p=0.239), but in patients 70 years or older, the LEDD was higher at 36 months (p=0.003).

Conclusion: Our results suggest STN-DBS is effective in patients 70years or older, but a different adjustment of dopaminergic medication could be necessary after three years, with higher doses in the elderly group. This group of patients should be represented in future research studies for a better understanding of the cost-effectiveness of DBS in this population.
Disclosure: Nothing to disclose.

Neuro-oncology

EPR-172

Plasma beta-synuclein, GFAP and neurofilaments in patients with diffuse gliomas undergoing surgical and adjuvant therapy

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Background and aims: Blood neurofilaments (NfL and NfH) and glial fibrillary acidic protein (GFAP) are well-established neuronal and astrocytic biomarkers, respectively, however their potential application in diffuse gliomas has not been fully explored. Beta-synuclein (beta-syn) is a pre-synaptic protein, which is highly expressed in glioma tissues and might represent a candidate non-invasive biomarker in the neuro-oncological field. In the present study, we investigated the longitudinal concentrations and prognostic value of beta-synuclein, GFAP and neurofilament in patients with diffuse gliomas, who underwent surgical and adjuvant therapy.

Methods: We retrospectively evaluated plasma beta-syn, GFAP, NfL and NfH levels in longitudinal samples of 33 patients with diffuse gliomas (21 with glioblastoma, 12 other tumors). 16 and 17 patients underwent complete and incomplete resection, respectively. Radiotherapy was administered in 31 subjects at different total doses.

Results: Baseline GFAP and NfL levels were higher in patients with glioblastoma compared to subjects with other tumors (Fig. 1A). After surgery, beta-syn, NfL and NfH increased significantly whereas GFAP remained stable. GFAP decreased significantly after radiotherapy (Fig. 1B). Both beta-syn and neurofilament levels were influenced by the surgery type. Patients treated with a radiation total dose >54 Gy showed a significant reduction in beta-syn values. At univariate analysis, higher baseline GFAP and neurofilaments levels were associated with a shorter survival.

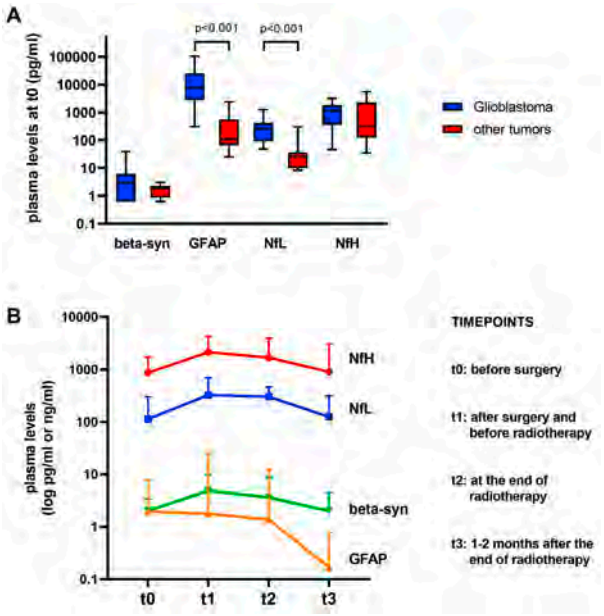

Figure 1

Conclusion: Plasma GFAP and NfL are differentially altered among diffuse glioma subtypes. According to our preliminary data, beta-syn and neurofilaments might be candidate markers for neurosurgical damage, whereas beta-syn and GFAP for evaluating the radicality of treatment and residual disease.

Disclosure: This research was supported by grants from the German Federal Ministry of Education and Research (projects: FTLDc 01GI1007A), the EU Joint Program-Neurodegenerative Diseases (JPND) network, the EU Moodmarker program (01EW2008), Roux program of the Martin Luther University Halle-Wittenberg, the Foundation of the State Baden-Württemberg (D.3830), Genfi-Prox (01ED2008A), the German Research Foundation/DFG (SFB1279), the Boehringer Ingelheim Ulm University BioCenter (D.5009) and the Thierry Latran foundation (D.2468).

EPR-173

Seizures in Patients with Brain Metastases from Breast Cancer: Results from a Retrospective Single-Centre Study

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Background and aims: Seizures may be a symptom of brain metastases (BrMs) from breast cancer. Gross-total resection (GTR) is known to correlate with a better seizure control, while the impact of radiotherapy (RT) and chemotherapy (CT) still remains uncertain. In this study, we aimed to explore which clinical and molecular factors might affect seizure control in a cohort of patients with BrMs from breast cancer.

Methods: We retrospectively included patients ≥18 with surgically resected BrMs from primary breast cancer treated in our Institution from 1991 to 2022.

Results: We included 79 patients in the analysis. Thirty-three (41.7%) had a history of seizures. Seizures prevailed in patients <50 vs ≥50 (59.0% vs 32.0%, p=0.021), and they were not associated with BrMs location, number, or morphology (cystic vs non-cystic; bleeding vs non-bleeding). Patients with low (score 0-1) vs high (score 2-3) STAT3 expression in the peritumoural reactive astrocytes (RAs) had a slightly higher incidence of seizures (50.0% vs 35.0%, p=0.337). Seizure incidence did not differ between HER2+, HR+/HER2- and TNBC patients. Seizures tended to be more common after non-GTR as compared with GTR (21.0% vs 11.0%, p=0.293). RT and CT did not affect seizure control.

Conclusion: Younger age was associated with a higher risk of seizures, whereas different molecular subgroups (HER2+, HR+/HER2-, TNBC) or STAT3 expression in the RAs were not. To our knowledge, this is the first real-life study investigating the correlation between seizures and clinical and molecular factors in patients with BrM from breast cancer.

Disclosure: I have nothing to disclose.

EPR-174

To predict the p53 Condon 72 polymorphism types of Glioblastoma Multiforme by brain MRI - Deep Learning Based Methods

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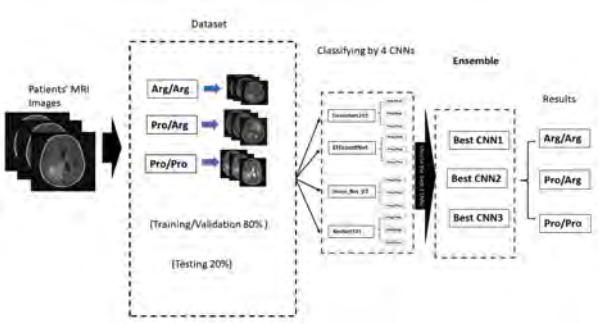
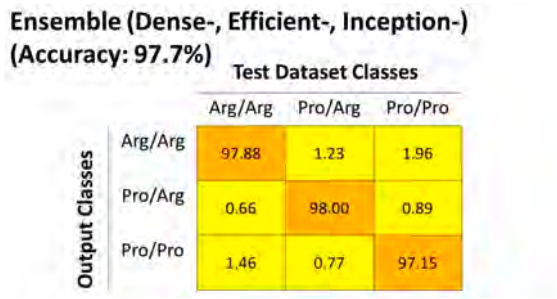
Background and aims: Adding bevacizumab on concurrent chemoradiotherapy might improve Glioblastoma Multiforme (GBM) patients' overall survival. The p53 codon72 polymorphisms are good for predicting the effectiveness of bevacizumab add-on therapy. The overall survival could be beneficial in both of the arginine homozygotes (Arg/Arg) and proline/arginine heterozygotes (Pro/Arg), while the proline/proline homozygotes (Pro/Pro) would not be improved. To get the gene information earlier, we designed a deep learning algorithm to detect the types of p53 codon72 polymorphisms in GBM patients by their brain MRI which noted their GBM tumors earliest.

Methods: We enrolled GBM patients with known p53 codon72 polymorphisms at Taichung Veterans General Hospital. The earliest brain MRI which noted their GBM tumors were collected and classified according to the gene types (Arg/Arg, Pro/Arg and Pro/Pro). The dataset was divided into 'Training/Validation' and 'Testing' datasets with 8:2 proportion. Four Convolutional Neural Networks (CNN):DenseNet201, EfficientNet82, Inception-ResNetV2 and ResNet101, were used to train/validation and test. The top three performed CNNs were put into an ensemble model for further testing.



Framework of our Algorithm

Results: 59 patients (Arg/Arg 23 patients, Pro/Arg 21 patients, Pro/Pro 15 patients) were included: Male/Female 31/28 (Arg/Arg 11/12, Pro/Arg 13/8, Pro/Pro 7/8, p=0.56), average age 55.8±12.8 years (Arg/Arg 60.0±10.4, Pro/Arg 54.6±13.3, Pro/Pro 51.8±14.0, p=0.14). The testing accuracies of the four CNNs (DenseNet201, EfficientNet82, Inception-ResNetV2 and ResNet101) were 96.9%, 91.9%, 97.4% and 88.9%. The DenseNet201, EfficientNet82 and Inception-ResNetV2 were used inour ensemble model and the final accuracy was 97.7%.



Confusion Matrix of Ensemble Model

Conclusion: Our algorithm might be a promising computer-aid approach for early detection and early treatment of the GBM patients.
Disclosure: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

EPR-175

Abstract withdrawn.

EPR-176

STAT3 expression in brain metastases from breast cancer: correlations with molecular subtypes and clinical outcome

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Background and aims: STAT3 expression in peritumoral reactive astrocytes (RA) of brain metastases (BM) from breast cancer (BC) may favor a pro-metastatic environment
Methods: Clinical, molecular data, and intracranial progression (i-PFS) were retrospectively retrieved from 85 BM specimens from BC. pSTAT3 expression was scored in RA according to Priego et al. Nat Med 2018.
Results: Median age was 54 years (range30-81). Immunohistochemistry for GFAP/pSTAT3 was feasible in 68/85 (80%). 15/68 patients (21.1%) had BM from luminal BC, 27 (39.7%) from HER2-positive BC, and 26 (39.2%) from TNBC. 56/68 (82.4%) showed positive staining of pSTAT3, of which 9 (13.3%) scored with 3, 26 (38.2%) with 2, 21 (30.9%%) with 1, and 12 (17.6%) with 0 (negative). High pSTAT3 expression (score 2-3) was observed in 17/27 (62.9%) HER2-positive BM and in 15/26 (57.7%) triple negative BM, while most of luminal like BM (12/15 – 80%) had low or absent pSTAT3 (score 0-1) (p=0.021). Overall i-PFS was 16 months (range 7-41): low pSTAT3 BM had a median i-PFS of 21 months versus 12 months for high pSTAT3 BM. A shorter median i-PFS was observed in high pSTAT3 BM from TNBC (4 months) as compared with low pSTAT3 BM (11 months). Conversely, i-PFS of high pSTAT3 BM (7 months) was similar to low pSTAT3 BM (6 months) in HER2-positive BC.
Conclusion: pSTAT3 expression in RA of BM from triple negative and HER2-positive BM is higher than in BM from luminal BC. High pSTAT3 BM from TNBC progressed earlier in comparison with low pSTAT3, suggesting an influence on the outcome.
Disclosure: Nothing to disclose.

EPR-177

Immune effector cell-associated neurotoxicity syndrome (ICANS) after CD19 CAR-T therapy. A real-world study.

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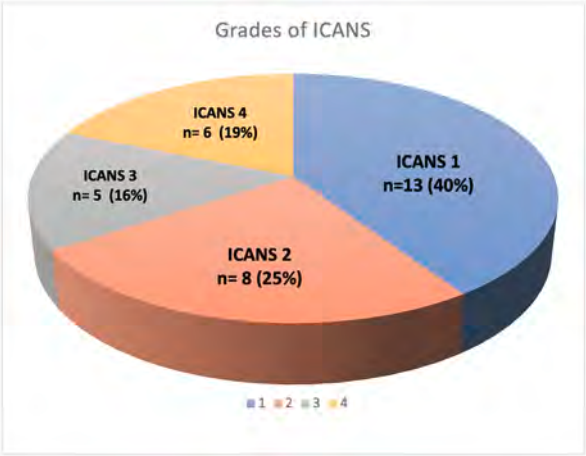
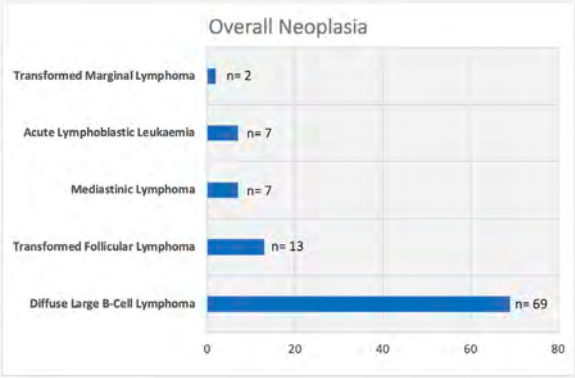
Background and aims: Immune activation therapies have been introduced as promising treatments for refractory cancer. However, many of these therapies have been related to emerging neurological toxicities. A chimeric antigen receptor (CAR) is an artificial T-cell receptor which grafts the specificity of a monoclonal antibody on to a T-cell. CD-19 directed CAR-T therapy were the first approved for B-cell haematological malignancies. CAR-T may induce a cytokine release syndrome (CRS). Some patients might develop a wide range of neurological symptoms, ICANS, which holds an uncertain prognosis. Herein we present our experience of ICANS after CD-19 CAR-T therapy.
Methods: An observational retrospective monocentric study was performed. Patients receiving Axicabtagene-ciloleucel (Axi-) or Tisagenlecleucel (Tisa-) were included. Demographic, tumor-related and ICANS evolution data were extracted from clinical records from June 2019-November 2022.
Results: 98 subjects were infused. 57% received Axi- vs 43% Tisa-. 33% of patients suffered ICANS. Most had encephalopathy (72%), 75% presented focal deficits and 69% associated a new-onset tremor. 3 patients suffered epileptic seizures, one fatal. Two patients presented a biphasic ICANS, following underlying tumoral progression. Median time to maximum ICANS was 7 days. All received corticosteroids, 47% high doses. 94% received tocilizumab, 66% siltuximab, 50% anakinra, 19% cytokine filters, 12% intrathecal therapy and 44% antiepileptics. Half of the 12 patients that required intensive-care Unit died while ICANS was active. Overall ICANS mortality was 19%.



Distribution of ICANS according to maximum reached grade according to ASTCT consensus.



B-cell haematological malignancies suffered by the infused population.

Conclusion: Despite ICANS is often considered as mild and reversible, one-third of our patients reached grades 3 or 4, with a 19% mortality. Requiring ICU showed a bad prognosis.

Disclosure: Presenting authors state no conflict of interest for this study. No funding was received.

EPR-178

An in-depth appraisal of cytokine-induced killer (CIK) cells in glioblastoma

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Background and aims: Cytokine-Induced Killer (CIK) cells, the immune cells obtained by incubating PBMC with IFN-gamma, OKT3 and IL-2, were demonstrated to improve PFS but not OS in Glioblastoma (GBM) patients when used as add-on therapy to temozolomide (TMZ). This study aims to optimize the CIK manufacturing process in GBM patients and evaluate the potential detrimental effect of the concomitant use of TMZ.

Methods: CIK cells were expanded from six healthy volunteers and three GBM patients. The use of 5% human serum (HS) or 5% platelet lysate (PL) was tested to optimize the culture protocol in GBM patients. CIK cells were treated with increasing doses of TMZ, comparable to concentrations observed in patients' plasma during the standard treatment, and the CIK viability was tested by flow cytometry.

Results: Preliminary data obtained from GBM patients showed a mean expansion rate of 12.2 folds with the standard protocol, 1653.53 in the presence of HS and 940.52 in the presence of a PL. Notably, we observed a significant cytotoxic effect on CIKs induced by both 0.05 mM and 0.1 mM TMZ ($p < 0.001$ and $p < 0.01$).

Conclusion: Our data suggest a potential role of HS and PLT in increasing the expansion fold of CIK manufacturing in GBM patients. Furthermore, our data showed the cytotoxic effect of TMZ on CIK cells, laying the ground for the application of CIK immunotherapy without the use of TMZ in GBM patients with unmethylated MGMT promoter, who are expected to have marginal benefit from TMZ.

Disclosure: All authors declare no conflicts of interest.

EPR-179

Neuropsychiatric sequels of lung cancers

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Background and aims: Our review aims to describe common neuropsychiatric sequels, incidence, and risk factors in patients with lung cancer to facilitate their recognition and proper management.
Methods: The literature search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched the PubMed for original research regarding neurological and neuropsychiatric symptoms in patients with lung cancer.
Results: We identified 1177 articles. Reviewing titles and/or abstracts, we selected 49 articles that met our requirements. Following the exclusion criteria, 34 full-text articles were excluded after the review. We included 14 studies: one study related to polyneuropathy, two studies to cognitive impairment, five studies to sleep disorders and six studies to psychological distress. All studies were observational; nine were cross-sectional, and five were longitudinal cohort studies. Ten studies evaluated non-small and small-cell lung cancer, and one focused on NSCLC patients. The most common neuropsychiatric sequel overall was insomnia, which affects up to 59 % of patients, closely followed by depression and anxiety (57 %), cognitive impairment (40 %), excessive daytime sleepiness (35%), and cognitive concerns (26 %). All described sequels were more common in patients treated with chemotherapy than radiotherapy or surgery. In addition, females at younger ages, current smoking status, socio-economic status and cancer-related physical symptoms were associated with depression and anxiety.
Conclusion: Neuropsychiatric sequels of lung cancers are common and affect every second patient. Therefore, we should actively search for them to improve patients' health and quality of life.
Disclosure: The authors declare no conflicts of interest in this work.

EPR-180

The Synergistic Effect of SIXAC and Chemotherapy on Glioma Cell Line Growth as a Potential Therapy for Glioblastoma

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Background and aims: This study focused on investigating a novel treatment for Glioblastoma (GBM), the most common and aggressive form of primary brain tumor, using a PAR-1 inhibitor named SIXAC in combination with standard chemotherapy. GBM remains difficult to treat despite surgical, radiation, and chemotherapy approaches. The thrombin, a coagulation factor, has been found to play a major role in GBM pathogenesis through its activation of Protease Activated Receptors (PARs) and enhancement of nerve growth factors in glial cells. PAR-1, the major thrombin receptor expressed in the brain, is upregulated in GBM and its inhibition has been proposed as a potential treatment.
Methods: The treatments tested were SIXAC, a novel compound designed by our group based on the thrombin binding-site sequence of PAR-1, a specific PAR-1 antagonist, and Temozolomide (TMZ), a standard alkylating agent for GBM treatment. The cells were grown in a specific culture medium, treated with the different compounds at varying concentrations, and the cell proliferation was monitored using an Incucyte Live-Cell Analysis System, which quantified cell surface area coverage, over a period of 3 days.
Results: The study found that SIXAC alone did not show a significant effect on CNS-1 cells at concentrations ranging from 10nM to 10uM, suggesting it may not be a suitable monotherapy. However, the study observed a synergistic effect when combining TMZ and SIXAC on starvation cells, which was not present on non-starving cells.

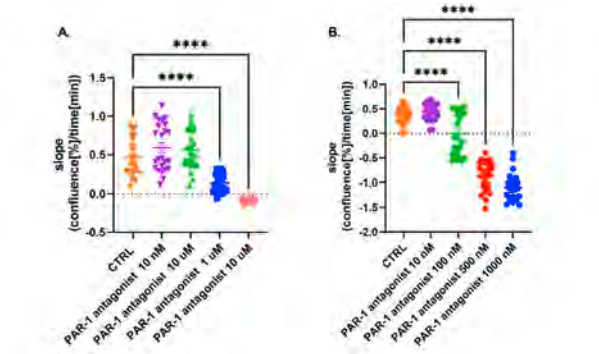

Figure 1. (A). PAR-1 antagonists significantly decreased growth of CNS-1 cells. The effect was seen from a concentration of 1 uM. (B). The inhibitory effect of PAR-1 antagonist was measured at a lower concentration following starvation (100 nM). ****p < 0

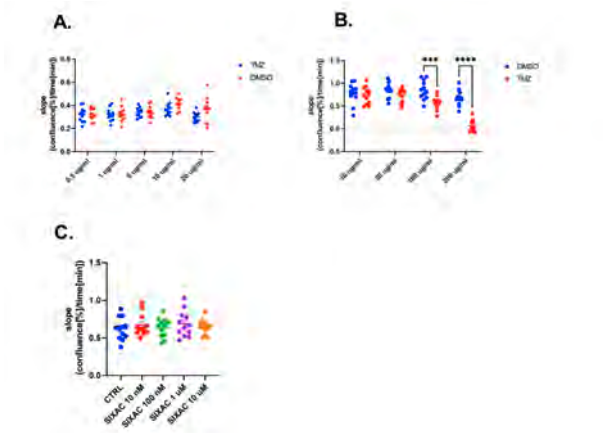

Figure 2. (A). No significant effect on growth with low dosage of TMZ (0.5-2- ug/ml). (B). effect on growth reduction was seen with a TMZ concentration from 100 ug/ml. (C). No significant effect on growth of CNS-1 cells with SIXAC concentration from 10 nM

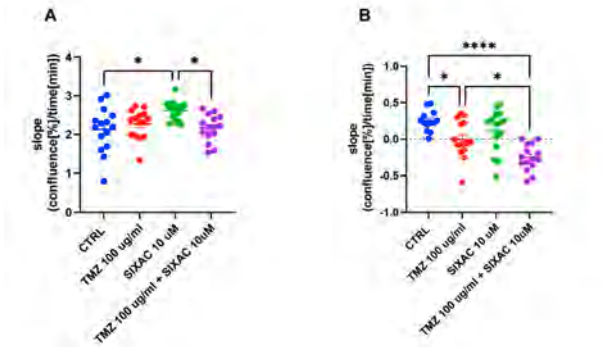

Figure 3. (A). Neither TMZ nor its combination with SIXAC showed an effect on cell growth when medium was added to the cells. A higher growth was weakly significant with SIXAC alone and a decreased growth of CNS 1 cells confluence when comparing the effec

Conclusion: The study's conclusion is that SIXAC may have potential as an add-on therapy to increase the efficacy of conventional therapy for GBM treatment.
Disclosure: Nothing to disclose.

Neuro-ophthalmology/neuro-otology 2

EPR-181

Balancing with eyes closed: conventional and advanced sway features of the Romberg test in patients and controls

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Background and aims: The Romberg test is commonly applied as a screening tool for sensory ataxia. Although simple to perform, it lacks standardization needed for reliable diagnostics. Here we assessed the diagnostic sensitivity of the classical Romberg test and its vestibular variant using conventional and advanced stabilometric analyses.
Methods: Static balance was assessed in 30 patients with pure sensory neuropathy and 30 healthy controls while standing on firm surface or foam with eyes open or closed. Postural sway was analyzed by means of linear (sway area and standard deviation) and nonlinear (Shannon entropy) time and frequency domain metrics. The latter was based on comparisons of the percentage of energy in each of three frequency bands: low (0-0.5 Hz), middle (0.05-2 Hz) and high frequency (2-20 Hz).
Results: Romberg quotients (eyes closed / eyes open on firm support) of linear sway metrics differed significantly between patients and controls. Moreover, The Shannon entropy of body sway was significantly more pronounced in patients whilst standing with eyes closed on firm support. Vestibular Romberg quotients (eyes closed / eyes open on foam), on the other hand, were similar in patients and controls. In this latter condition, however, sensory neuropathy patients exhibited increased power in the high frequency range. ROC analysis showed that the above parameters did discriminate sensory neuropathy above change but with relatively low AUC (between 0.6 and 0.7).
Conclusion: The Romberg test in pure sensory neuropathy exhibits distinct linear, nonlinear and spectral postural sway changes which can be detected by static posturography.
Disclosure: Nothing to disclose.

EPR-182

Reliability of transorbital sonography and MRI measuring the opticus nerve sheath diameter in idiopathic intracranial

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Background and aims: The purpose of this study was to evaluate the performance of magnetic resonance imaging (MRI) in measuring the optic nerve sheath diameter (ONSD) compared to the established method transorbital sonography (TOS) in patients with idiopathic intracranial hypertension (IIH).
Methods: 23 patients with IIH were prospectively included applying IIH diagnostic criteria. All patients received a lumbar puncture with assessment of the CSF opening pressure to assure the IIH diagnosis. Measurement of ONSD was performed 3 mm posterior to inner sclera surface in B- TOS by an expert examiner, while three independent neuroradiologists took measurements in axial T-weighted MRI examinations. The sella turcica with the pituitary gland (and potential presence of an empty sella) and the trigeminal cavity were also assessed on sagittal and transversal T1-weighted MRI images by one independent neuroradiologist.
Results: The means of ONSD between ultrasound (US) and MRI measurements were 6.3 mm (SD 0.6 mm) and 6.2 mm (SD 0.8 mm). The interrater reliability between three neuroradiologists showed a high interclass correlation coefficient (CI: 0.573).
Conclusion: MRI can reliably measure ONSD and yields similar results compared to TOS in patients with IIH. Moreover, patients with empty sella showed significantly larger ONSD than patients without empty sella.
Disclosure: Nothing to disclose.

EPR-183

Acute vertical pendular nystagmus: eye-movement analysis and review of the literature

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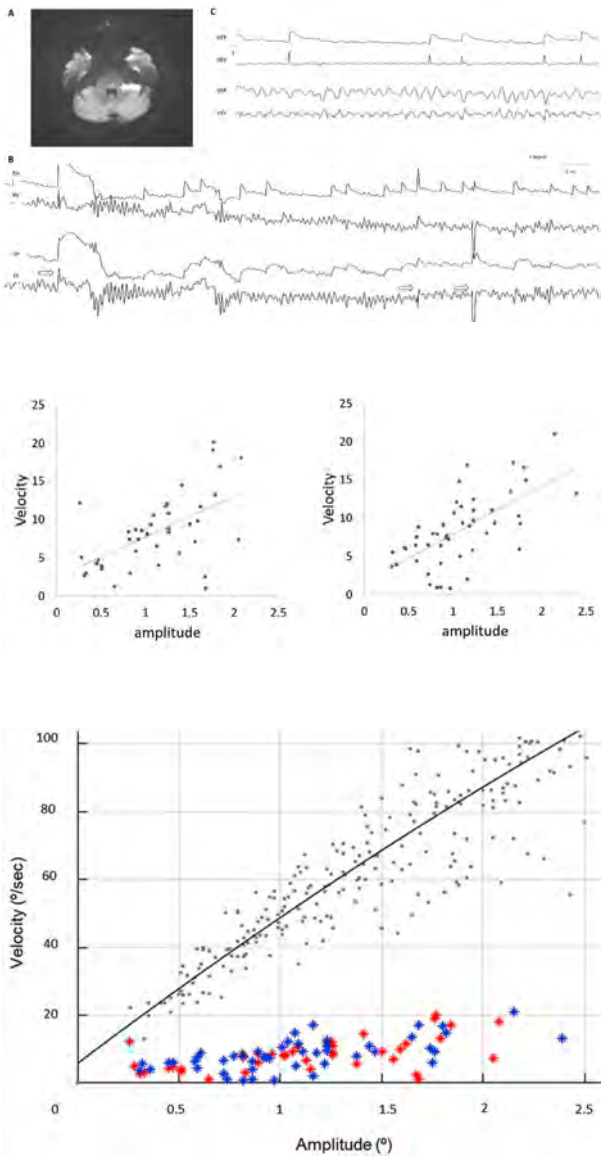
Background and aims: Vertical pendular nystagmus (PN) rarely occurs acutely with pontine lesions. The pathophysiology of acute vertical PN may differ from that of typical oculopalatal tremor. This study aimed to investigate the mechanism of acute vertical PN using quantitative eye-movement recording.
Methods: We analyzed the clinical characteristics and quantitative eye-movement recordings of one new case with acute vertical PN and an additional 11 patients from the literature.
Results: Most patients had extensive pontine lesions causing either the locked-in syndrome or unresponsiveness, but two conscious patients had focal lesions restricted to the paramedian caudal pontine tegmentum. All patients presented a complete or partial horizontal gaze palsy, and about half showed ocular bobbing before or during the appearance of vertical PN. The vertical oscillations were

conjugate at a frequency of 1-5 Hz, and the amplitudes were variable, ranging from 0.2 to 40º. The peak velocities were asymmetric in some patients, faster with downward movements. About half of the patients developed palatal tremor several weeks or months after presenting with acute vertical PN.

Conclusion: Based on the location of the lesions and results of eye-movement recordings, we suggest two possible mechanisms for acute vertical PN; oscillations originating in the inferior olives due to disruption of the central tegmental tract or low-velocity saccadic oscillations caused by omnipause neuron damage.

Disclosure: We have no disclosure of any competing interest.



EPR-184

Serum markers of neuronal and glial damage in patients with hereditary optic atrophy.

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[1]Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy, [2]Università Cattolica del Sacro Cuore, Rome, Italy

Background and aims: Non syndromic hereditary optic neuropathies are a group of mitochondrial related neurodegenerative disorders of the optic nerve associated to loss of central vision and characterized by significant optic atrophy (OA). The most common forms are the autosomal dominant optic atrophy (ADOA) due to mutations in the nuclear gene OPA1 and Leber hereditary optic neuropathy (LHON) caused by pathogenic variants in mtDNA and maternally inherited. Neurofilament light chain (NfL) and glial fibrillar acidic protein (GFAP) are established biomarkers of neuroaxonal and glial injury. The aim of this study is to evaluate if serum NfL (sNfL) and sGFAP levels in a cohort of 13 patients with OA (6 LHON,7 ADOA) and compared them with a cohort of 11 remitting multiple sclerosis patients with previous optic neuritis (MSON) and 59 age-and BMI-matched healthy controls (HCs).

Methods: sNfL and sGFAP levels were assessed in each serum sample of patients and controls. We used the commercially available immunoassay kits for GFAP and NfL run on the ultrasensitive SR-X™ Biomarker Detection System (Quanterix).

Results: Age and BMI-corrected sNfL were higher in both OA patients [median sNfL(pg/ml)=43.51;min=9.71; max=148.37] and MSON patients [median sNfL(pg/ml)=44.51;min=15.50;max=100.35] than HCs [median sNfL(pg/ml)=6.45;min=1.85;max=13.53](p<0.001 for both). Age and BMI-corrected sGFAP levels were higher in OA patients [median sGFAP(pg/ml)=76.64;min=47.17; max=271.17] compared to HCs [median sGFAP(pg/ml)=57.04;min=8.89;max=176.20,p=0.031], whereas there was no significant difference between MSON patients [median sGFAP(pg/ml)=75.96;min=38.90;max=224.38] and HCs,nor with AO patients.

Conclusion: The results of this preliminary study show that neuronal and glial degeneration are distinctive features of ADOA and LHON with levels almost comparable to those observed in MSON patients.

Disclosure: Nothing to report in relation to the current study.

EPR-185

Diagnosis of vestibular disorders via APP - automatic analysis of ocular motor and vestibular function: the study design

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Background and aims: A detailed patient history and assessment of vestibular function and eye movements are the keys to the diagnosis of vertigo and dizziness. We here present VertifyMed, a mobile phone-based app for the differential diagnosis of vestibular disorders based on a pre-specified questionnaire, systematic examination of eye movements and vestibular function, and machine-learning algorithms. VertifyMed's technology is a simulation-based end-to-end system that analyses head and eye movements directly from the camera or video feed.
Methods: Trial design: We are planning a prospective open study with at least 110 patients at the Department of Neurology, Medical University of Vienna and optionally with the Department of Neurology, LMU, Munich. Participants: Inclusion criteria: patients must be older than 18 years and suffer from dizziness/vertigo. Exclusion criteria are infantile nystagmus, strabismus, and dioptres >10. Interventions: Symptoms are systematically assessed by means of a special questionnaire. Eye movements will be video-recorded using a mobile smart device. Function of the vestibulo-ocular reflex will also be quantified. Data collection process: The diagnosis made by VertifyMed is compared with the diagnosis made clinically in a standardized way and laboratory testing of ocular motor and vestibular function (videooculography, video-HIT, calorics).
Results: The objective of this study will be to evaluate whether VertifyMed can distinguish between different causes of vertigo/dizziness.
Conclusion: This diagnostic tool has the potential to optimize early diagnosis of vestibular diseases. The major target group will be general practitioners. Increased diagnostic accuracy will help to improve outcomes and reduce healthcare costs.
Disclosure: The authors declare no competing financial interests. M. Strupp is Joint Chief Editor of the Journal of Neurology, Editor in Chief of Frontiers of Neuro-otology and Section Editor of F1000. He has received speaker's honoraria from Abbott, Auris Medical, Biogen, Eisai, Grünenthal, GSK, Henning Pharma, Interacoustics, J&J, MSD, NeuroUpdate, Otometrics, Pierre-Fabre, TEVA, UCB, and Viatris. He receives support for clinical studies from Decibel, U.S.A., Cure within Reach, U.S.A. and Heel, Germany. He distributes "M-glasses" and "Positional vertigo App". He acts as a consultant for Abbott, AurisMedical, Bulbitec, Heel, IntraBio, Sensorion and Vertify. He is investor and share-holder of IntraBio.

EPR-186

Treatment effects of vestibular noise stimulation on imbalance in patients with bilateral vestibulopathy

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Background and aims: Previous studies indicate that imbalance in patients with bilateral vestibulopathy (BVP) may be reduced by treatment with low intensity noisy galvanic vestibular stimulation (nGVS). This study aimed to elucidate the potential mechanisms underlying this therapeutic effect. In particular, we determined whether nGVS-induced balance improvements in patients are compatible with stochastic resonance (SR) – a mechanism by which weak noise stimulation can paradoxically enhance sensory signal processing.
Methods: Effects of nGVS of varying intensities (0–0.7mA) on body sway were examined in 19 patients with BVP standing with eye closed on a posturographic force plate. We assumed a bell-shaped response curve with maximal sway reductions at intermediate nGVS intensities to be indicative of SR. An established SR-curve model was fitted on individual patient outcomes and three experienced human raters had to judge whether responses to nGVS were consistent with the exhibition of SR.
Results: nGVS-induced reductions of body sway compatible with SR were found in 12 patients (63%) with optimal improvements of 31±21%. In 10 patients (53%), nGVS-induced sway reductions exceeded the minimally important clinical difference, indicative of strong SR. This beneficial effect was more likely in patients with severe vestibular loss (i.e., lower video head impulse test gain; R=0.663; p=0.002) and considerable postural imbalance (baseline body sway; R=0.616; p=0.005).
Conclusion: More than half of the assessed patients showed robust improvements in postural balance compatible with SR when treated with nGVS. In particular patients with a higher burden of disease may benefit from the non-invasive and well-tolerated treatment with nGVS.
Disclosure: No conflicts of interest to disclose.

EPR-187

A hierarchical multimodal diagnostic algorithm for prediction of cognitive impairment in elderly patients with dizziness

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Background and aims: The routine diagnostic workup for chronic dizziness in elderly patients mostly is based on testing of sensory and motor function, balance control and gait pattern. Cognitive impairment as a primary source of perceived dizziness is often neglected. This study intended to establish a hierarchical prediction model for cognitive impairment in patients with chronic dizziness based on data sources, which are routinely collected in a tertiary referral center.

Methods: Ninety-four patients (age: 75.5±7.2 years, 48.1% women), who presented to the German Center for Vertigo and Balance Disorders (LMU Munich) with chronic dizziness were prospectively characterized by 1) neuro-otological testing, 2) in-laboratory quantitative gait assessment, 3) evaluation of routine brain MR images, and 4) MoCA test for cognitive screening. For the statistical analysis, we calculated a multiple regression model with four hierarchical levels (level 1-demographics, level 2-vestibular testing, level 3-quantitative gait parameters, level 4-imaging scales) and the MoCA score as the dependent variable.

Results: The mean MoCA score was 24±4 points (range: 15-30 points). All model levels depicted a significant contribution for prediction of cognitive performance ($p<0.005$, ANOVA). The r^2-values for each hierarchical level were as follows: level 1-demographics: 0.131; level 2-vestibular testing: 0.274, level 3-gait analysis: 0.368, level 4-imaging: 0.438.

Conclusion: The most important predictors of cognitive impairment in elderly dizzy patients are normal peripheral vestibular test results, a worsening of the gait pattern on dual-task conditions and a focal insular brain atrophy. Cognitive testing in chronic dizziness should especially be considered if one or more of these indicators are found.

Disclosure: Nothing to disclose.

MS and related disorders 2

EPR-188

NfL levels and disease activity during long-term treatment of relapsing MS with the BTK inhibitor evobrutinib

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Background and aims: The efficacy of evobrutinib (highly selective, CNS-penetrant, covalent BTK inhibitor) observed in the double-blind phase (DBP) of a phase II trial (NCT02975349) in patients with RMS (PwRMS), was maintained in the open-label extension (OLE; beginning at W48 from DBP baseline). Moreover, evobrutinib treatment led to reductions in NfL levels up to W144. Here, we evaluated NfL levels as a prognostic and a potential surrogate marker of evobrutinib treatment response in PwRMS.
Methods: NfL levels were measured over time in the pooled OLE safety population and reported as control-adjusted Z-scores (expression of standard deviations away from mean NfL level in a control population [participants without evidence of CNS disease]). The number of T1 Gd+ and new/emerging T2 lesions at W96 and W144 and qualified relapses over W96-144 were assessed, stratified by W96 Z-scores (<1;≥1). MRI outcomes at W48 and W96 and relapses over W48-96 were also assessed using stratified W48 Z-scores.
Results: Stratified by W96 Z-scores (<1[N=66]; ≥1[N=34]), the proportions of patients with no T1 Gd+ lesions, no new/enlarging T2 lesions (both at W144) and no relapse between W96-144 were 84.5% (n=49/58) vs 57.1% (n=16/28), 65.5% (n=38/58) vs 28.6% (n=8/28) and 95.4% (n=62/65) vs 94.1% (n=32/34), respectively. Similar findings were observed in patients stratified by W48 Z-scores (Figure 1).

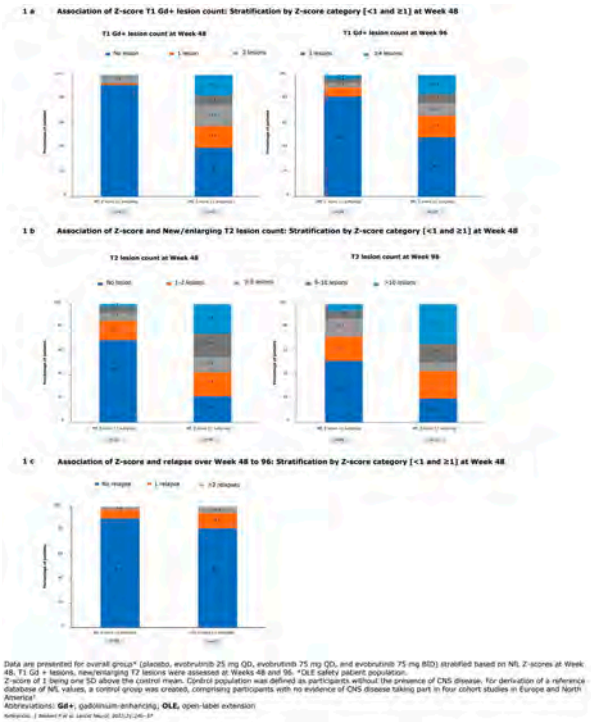

Figure 1: Association of Z-score and T1 Gd+ lesion count, New/enlarging T2 lesion count, and relapses (stratification by Z-score category [<1 [N=84] and ≥1 [N=40] at Week 48)

Conclusion: Evobrutinib reduced NfL levels in a sustained manner (up to W144). Low NfL levels were associated with improved MRI and relapse outcomes, supporting the role of NfL as a prognostic marker of disease activity and a potential surrogate marker for evobrutinib's treatment effect.
Disclosure: This study was sponsored by EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA (CrossRef Funder ID: 10.13039/100004755), Detailed author disclosures will be included in the presentation.

EPR-189

The prognostic value of CSF CXCL13 and CHI3L1 levels in people with Multiple Sclerosis treated with Dimethyl fumarate.

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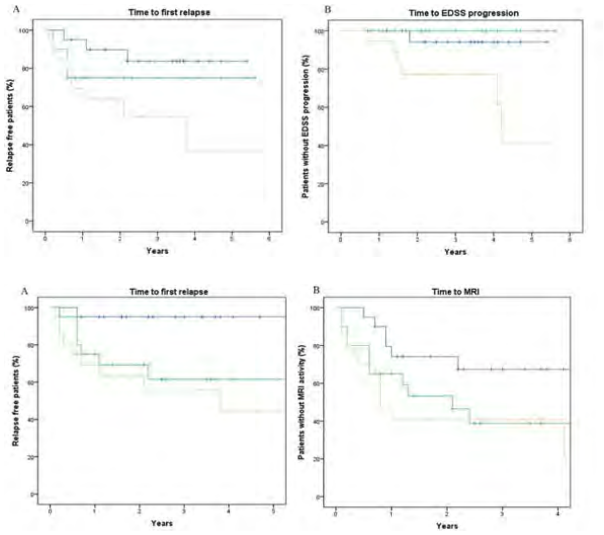
Background and aims: Cerebrospinal fluid(CSF) levels of CHI3L1 and CXCL13 were found to be elevated in people with Multiple Sclerosis(MS) compared to healthy subjects. Recently, we demonstrated that CSF CXCL13 e CHI3L1 levels, at the time of diagnostic evaluation, represent very good prognostic biomarkers in an unselected cohort of RMS patients. In this study, we assessed CHI3L1 and

CXCL13 CSF concentration in RMS patients treated with dimethyl fumarate(DMF) as the first-line treatment.
Methods: We measured the CSF concentration of CHI3L1 and CXCL-13 through a Luminex Assay. MS patients were prospectively evaluated, and clinical and radiological activity data were recorded. We then divided our cohort into three groups based on CSF biomarkers' level(high, intermediate, and low groups) and compared them through a log-rank test.
Results: We enrolled 60 RMS patients with a mean disease duration of 1.3 years and a median EDSS score of 1.5. After a mean follow-up of 3.1 years, 17(28.3%) patients had at least one relapse, while we found radiological activity in 29(48.3%). Only 7(11.7%) patients had confirmed EDSS worsening. The high-CHI3L1 group presented a significantly higher risk of relapse(p=0.023) and EDSS worsening(p=0.007) compared to the low-CHI3L1 group. Moreover, the low-CXCL13 group had a significantly lower risk of further relapse(p=0.018) or radiological activity(p=0.022) with respect to the high-CXCL13 group.



Conclusion: We found that higher CSF levels of CHI3L1 and CXCL13 at diagnosis are associated with a higher risk of further clinical and radiological disease activity. Therefore, they can represent a reliable prognostic biomarker identifying patients at risk of first-line treatment failure.
Disclosure: Nothing to disclose.

EPR-190

Non-inferiority efficacy analysis of natalizumab (TYSABRI) subcutaneous versus intravenous administration.

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Background and aims: The REFINE study explored the effects of multiple natalizumab administration regimens in relapsing-remitting (RR) multiple sclerosis (MS). In this posthoc analysis, non-inferiority efficacy analysis of the subcutaneous (SC) versus the intravenous (IV) administration arm was carried out in the same data set for the 300mg Q4W approved dosing regimen.
Methods: Outcomes: new MRI brain lesions (primary); Annualized Relapse Rate (ARR; secondary). Non-inferiority of SC vs IV administration was analyzed using the REFINE study data set. Three clinically meaningful non-inferiority margins (M) were a priori defined for each outcome as the 25%, 33%, and 50% fraction of the effect size of 300mg IV versus placebo arm on the outcome measures observed in the AFFIRM study.
Results: The mean effect of the SC administration vs the IV was close to 0, both for the number of new lesions and the ARR, with the lower 95% confidence intervals (CI) resulting respectively -0.148 (3.5% of the whole effect size of natalizumab vs placebo; $p< 0.00001$ for all the M values) and -0.119 (25% of the whole effect size vs placebo; $p= 0.02$). These results were confirmed by a sensitivity analysis accounting for some patients in the SC arm meeting rescue criteria and receiving IV treatment.
Conclusion: This posthoc analysis of the two arms of the REFINE study indicates that natalizumab 300mg Q4W SC treatment is not inferior to the 96.5% and the 75% of the IV treatment efficacy, respectively on the MRI and the ARR outcomes at a 2.5% significance level.
Disclosure: Professor Luca Massacesi received the following: - educational unrestricted support from: Biogen; Sanofi-Genzyme; Novartis Roche and Merck-Serono; - honoraria for scientific lectures, scientific consultation, or participation in advisory boards from Biogen; Novartis; Sanofi-Genzyme; Roche; Mylan; Merck- Serono. - research grants (recipient: University Dept.) from Sanofi-Genzyme; Biogen; Roche; Merck-Serono; Novartis

EPR-191

Clinical outcomes with evobrutinib in relapsing MS up to 4 years of treatment: an ongoing Phase 2 open-label extension

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Background and aims: Evobrutinib is a highly selective. central nervous system-penetrant. covalent Bruton's tyrosine kinase inhibitor. In a Phase 2 trial. the evobrutinib efficacy and safety profile in patients with relapsing multiple sclerosis (PwRMS) in the double-blind period (DBP) remained stable over 3.5 years of treatment (DBP and openlabel extension [OLE]: NCT02975349). Here. we elucidate further the long-term effect of evobrutinib on annualised relapse rate (ARR). time to first qualified relapse (OR). Expanded Disability Status Scale (EDSS) and functional system scores (FSS).

Methods: In the 48-week (W) DBP, PwRMS (n=267) received placebo (switched to evobrutinib 25mg once-daily [QD] after W24), evobrutinib 25mg QD, 75mg QD, or 75mg twice-daily (BID), or open-label dimethyl fumarate (120mg BID first week, 240mg BID thereafter) fasted. At W48, patients could enter the OLE (n=213) and received evobrutinib 75mg QD (mean[±SD] duration 49.8W[±6.2]), before switching to 75mg BID (n=190). Data cut-off 28-Jan-2022; EDSS/FSS reported to W192 (OLE W144).

Results: Of 164 DBP evobrutinib-treated patients that entered the OLE, 128 (78.0%) reached OLE ≥144W. The lowest ARR (0.11) was with the evobrutinib 75mg BID dose during both the DBP and OLE (pre-switch 75mg QD: 0.20 [95% CI:0.14–0.28]; post-switch 75mg BID: 0.11 [0.07–0.15]). The estimated time when 25% of patients initiated on DBP evobrutinib 75mg BID experienced a first QR had a>3-fold delay versus placebo/evobrutinib 25mg QD (Figure 1). Overall, EDSS stability was consistently mirrored across all underlying FSS (Figure 2).

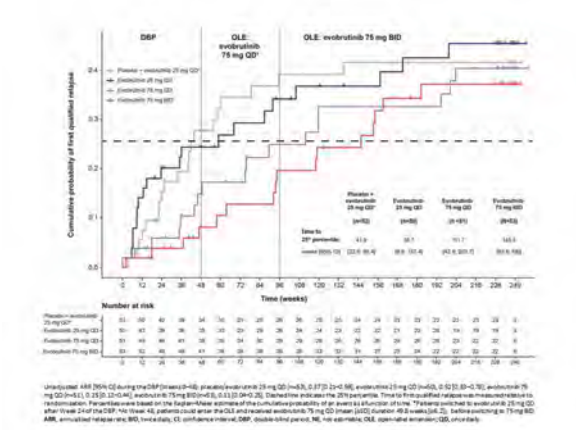

Figure 1. Estimated time to first qualified relapse

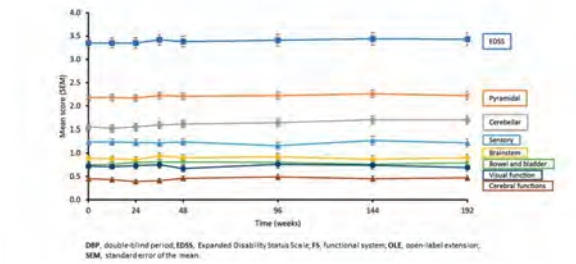

Figure 2. Mean (SEM) EDSS and FS scores during the DBP and OLE (Week 0 to Week 192) across pooled evobrutinib treatment groups

Conclusion: These results indicate that long-term evobrutinib treatment maintains a low relapse rate with no increase in disability (EDSS and FSS).

Disclosure: This trial was funded by Merck Healthcare KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945), detailed author disclosures will be included in the presentation.

EPR-192

Superficial Capillary Plexus alterations in MS patients with optic neuritis detected by OCT-Angiography

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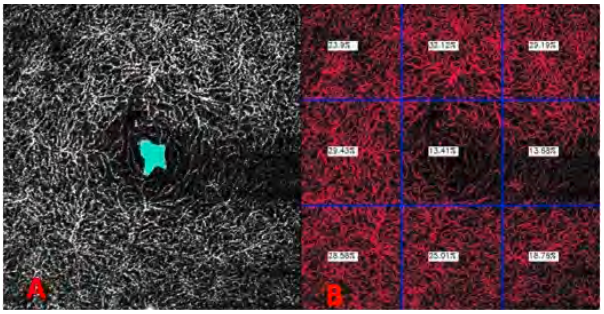
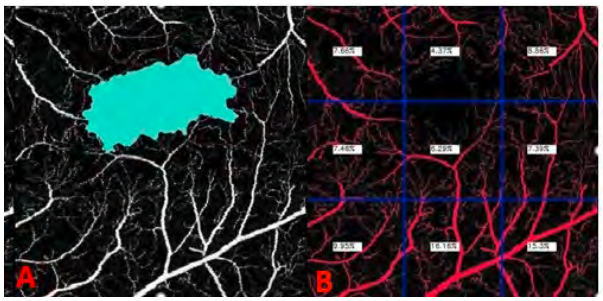
Background and aims: Optical coherence tomography angiography (OCT-A) is a new imaging method that allows quantification of retinal vascular density in neurodegenerative and inflammatory diseases. Objective: To analyze vascular changes in macular and peripapillary regions detected by OCT-A in RRMS patients with and without optic neuritis.

Methods: RRMS patients were examined. We compared patients with (NO) and without optic neuritis (non-NO).A complete ophthalmological study was carried out, assessing

retinal microvasculature (Superficial Capillary Plexus (SCP) and Deep Capillary Plexus (DCP)). Foveal avascular Zone (FAZ) and Capillary Vessel Density (CVD) were measured using the OCTA Heidelberg Spectralis device.
Results: 56 eyes of 28 patients (20 females, mean age 47 years old, mean EDSS 2.5) were analysed. Eighteen eyes suffered from an optic neuritis in the past. Visual acuity (1,25%) was 0.14±0.11 for NO patients and 0.19±0.08 for non-NO patients and visual acuity (2,50%) was 0.22±0.14 for NO patients and 0.32±0.09 for non-NO patients. In the superficial capillary plexus, FAZ was significantly increased in ON patients (749,16 ± 66,38 µm) in comparison with non-ON patients (593,83 ± 64,81 µm) and CVD was statistically significant lesser in ON patients (18,27±3,57 %) than in non-ON patients (22,28±4,78 %). There were no statistically significant differences regarding the deep capillary plexus between both groups (FAZ 286,13±133 µm, 278,53±152 µm; CVD 24±4,60%, 26,17±4,46%).



Patient without optic neuritis. A.FAZ B. Superficial Capillary Plexus



Patient with optic neuritis. A.FAZ B. Superficial Capillary Plexus

Conclusion: MS patients with ON have a significant retinal superficial vascular loss compared without previous neuritis. Therefore, retinal vascular density could represent a novel biomarker for the differential diagnosis and to monitor the evolution of the disease.
Disclosure: Nothing to disclose.

EPR-193

Evaluation of specific unmet medical needs in relapsing MS patient care: Final results from the PROFILE RMS study

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Background and aims: Patients with relapsing multiple sclerosis (RMS) differ by individual necessities and courses of disease. Although treatment options are manifold, unmet medical needs may persist. To identify these needs, PROFILE RMS (ML39348) captured real-world data on five pre-defined RMS patient subgroups.
Methods: PROFILE RMS was a prospective, non-interventional study enrolling patients aged ≥18 years with RMS (relapsing remitting or relapsing secondary progressive MS) according to the McDonald 2010 criteria at ~100 centres in Germany. Patients were treatment-naïve or formerly/currently treated with disease-modifying treatments (DMTs) according to local labels. Patients were analysed in five predefined subgroups: 1. Disease activity on current DMT 2. Significant adverse effects or safety concerns 3. Low treatment satisfaction 4. Treatment-naïve patients 5. Previously treated with DMT but without current treatment The primary outcome was the 48-week failure rate (confirmed relapse, EDSS progression, MRI activity or treatment change). Secondary outcomes comprised the percentage of patients with treatment change, patient-reported outcomes, and MS signs and symptoms.
Results: From 960 patients enrolled, 776 completed the study (763 RRMS and 13 rSPMS). The overall mean (range) patient age was 43.6 years (18–85) and 79.0 percent of patients were female. Further baseline characteristics are presented in Table 1. Treatment failure rates, therapy changes, adverse events and other outcomes for the five profiles will be presented at the congress.

	Profile 1 (n=248) Disease activity on current DMT in the past 12 months	Profile 2 (n=186) Significant side effects or findings of theoretical safety concerns	Profile 3 (n=69) Low treatment satisfaction	Profile 4 (n=215) Treatment-naïve	Profile 5 (n=242) Previously treated with a DMT but without current treatment
Age (years), mean (range)	41.7 (19–74)	43.2 (20–70)	45.1 (19–68)	44.3 (18–85)	45.0 (21–75)
Female, n (%)	195 (78.6)	146 (78.5)	46 (66.6)	170 (79.1)	200 (82.6)
Time since first MS symptoms					
n	232	177	65	205	216
years, mean (range)	9.84 (0.2–58.9)	13.28 (0.1–40.1)	12.01 (1.8–36.6)	10.67 (0.0–60.0)	14.42 (0.7–42.3)
Time since first MS diagnosis					
n	241	180	69	210	237
years, mean (range)	8.14 (0.0–38.2)	11.31 (0.1–37.4)	9.03 (0.0–30.5)	7.16 (0.0–40.2)	12.34 (0.3–42.0)
Affected functional systems at first MS symptoms, n (%)					
Pyramid	46 (18.5)	22 (11.8)	10 (14.5)	28 (13.0)	35 (14.5)
Visual acuity	68 (27.4)	50 (26.9)	24 (34.8)	61 (28.4)	74 (30.6)
Sensibility	113 (45.6)	99 (53.2)	37 (53.6)	97 (45.1)	102 (42.1)
Ambulatory acuity	35 (14.1)	14 (7.5)	5 (7.2)	24 (11.2)	22 (9.1)
Affected functional systems at first MS diagnosis, n (%)					
Pyramid	55 (22.2)	26 (14.0)	10 (14.5)	40 (18.6)	41 (16.9)
Visual acuity	80 (32.3)	52 (28.0)	20 (29.0)	66 (30.7)	69 (28.5)
Sensibility	121 (48.8)	105 (56.5)	43 (62.3)	101 (47.0)	116 (47.9)
Ambulatory acuity	37 (14.9)	19 (10.2)	5 (7.2)	26 (12.1)	27 (11.2)

DMT, disease-modifying treatment; MRI, magnetic resonance imaging; MS, multiple sclerosis; SD, standard deviation. Profile 1, disease activity on current DMT in the past 12 months (occurrence of confirmed relapse, new/enlarged MRI lesions, or disease progression); Profile 2, significant side effects (infections, injection problems) or findings of theoretical safety concerns as assessed by the treating physician; Profile 3, low treatment satisfaction (measured by the Treatment Satisfaction Questionnaire for Medication version 1.4 Global, score <75). If more than one profile was applicable, profile 1 was given the highest priority followed by profile 2. Profile 3 was given the lowest priority and did not include disease activity nor safety issues.

Table 1. Baseline characteristics of the five predefined subgroups in PROFILE

Conclusion: PROFILE was designed to elucidate RMS patient care and unmet medical needs in Germany. In-depth final analysis of safety and effectiveness data from PROFILE RMS will be presented at the congress.
Disclosure: All authors received support for their contribution to this study as well as medical writing support for the development of this congress abstract from Roche Pharma AG, Grenzach-Wyhlen, Germany. IK Penner: Adamas Pharma, Almirall, Bayer Pharma, Biogen, Celgene, Genzyme, Merck, Novartis, Roche, Teva (2,3); the German MS Society, Celgene, Novartis, Roche, Teva (7); H Schreiber: Almirall, Biogen, Genzyme, Merck, Novartis, Roche, Teva (2,3,5); Biogen, Novartis, Teva (7); Biogen, Novartis, Roche (9); T Maier: Roche (10); J Leemhuis: Roche (10, 11); S Hieke-Schulz: Roche (10); T Ziemssen: Bayer (2,11), Biogen (2, 3, 9, 7), Genzyme/Sanofi (2, 3, 9, 7), Novartis (2, 3, 9, 7), Roche (2, 3, 9, 7, 11), Teva (2); Celgene (2, 3), Almirall (2), Merck (2,3, 9) 1 Royalties; 2 speakers bureau or advisory board; 3 consulting fees; 4 board of trustees; 5 travel reimbursement; 6 writing assistance; 7 research grants; 8 data and safety monitoring boards; 9 data monitoring or steering committees; 10 employee; 11 shareholder, or financial interests.

EPR-194

Guidelines for the critical reading of phase III and IV clinical trials on disease modifying drugs for MS

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Background and aims: In recent years there has been an increase in the number of disease-modifying drugs (DMDs) approved for multiple sclerosis (MS). The evidence of their safety and efficacy has been obtained through several phase III and IV clinical trials. The objective of this study is to develop a document with recommendations to help neurologists in the critical reading of these trials.
Methods: A two-round Delphi study was carried out. In the preparatory phase, a multidisciplinary expert panel was established using a purpose sampling. Its members were selected based on their scientific credentials and experience, seeking to include people involved in MS diagnosis, treatment and research. A semi-open questionnaire was developed based on key generic and MS-specific methodological instruments identified through a scoping bibliographic search (such as "RoB2" or the EMA guidelines on MS clinical research), plus the information provided by the experts. Consensus was defined a priori as items rated as "essential" by at least 70% and of "limited importance" by less than 15% of the respondents.
Results: The expert panel consisted of nine independent leading national experts with long-standing experience with MS (five neurologists, a neuroradiologist, a pharmacologist, a methodologist and a MS community representative), all of which completed both rounds. The Delphi study resulted in consensus for 76 items across five domains (internal validity, selection of participants, outcome measures, study results and transparency).
Conclusion: This study resulted in the development of a document intended to help in the critical reading of phase III and IV clinical trials on DMDs for MS.
Disclosure: The authors have no conflict of interest to report.

EPR-195

Monoaminergic functional connectivity modifications occur in fatigued MS patients treated with fampridine and amantadine

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Background and aims: Fatigue is common and disabling in multiple sclerosis (MS). Here, we investigated modifications of fatigue severity and resting state (RS) functional connectivity (FC) in monoaminergic networks in 45 fatigued MS patients after different symptomatic treatments.
Methods: Patients were randomly, blindly assigned to treatment with fampridine (n=15), amantadine (n=15) or placebo (n=15). Clinical, fatigue and 3T RS fMRI assessments were performed at baseline (T0) and after four weeks (W4) of treatment. Fifteen matched healthy controls (HC) were enrolled. Dopamine-, noradrenaline- and serotonin-related RS FC patterns were derived by independent component analysis, constrained to PET atlases for dopamine, noradrenaline and serotonin transporters.
Results: At T0, MS patients showed decreased monoamine-

related RS FC in temporal, occipital, insular and cerebellar regions, and increased RS FC in frontal, parietal and subcortical areas in all three networks. At W4, fatigue scores decreased in all patients' groups. At W4, fampridine and amantadine patients showed increased dopamine- and noradrenaline-related RS FC in the insula, as well as increased serotonin-related RS FC in the precuneus/posterior cingulate cortex. Amantadine patients also showed increased dopamine- and noradrenaline-related RS FC in the anterior cingulate cortex (ACC). Conversely, placebo patients showed increased noradrenaline-related RS FC in the precuneus and middle cingulate cortex. In fampridine and placebo, there were trends towards significant correlations between RS FC modifications and fatigue improvements (r=-0.49:-0.52, p=0.07-0.08).
Conclusion: Fatigue improved in all groups, concomitantly with RS FC modifications in insular, ACC and parietal regions for fampridine and amantadine MS patients, and in medial parietal regions for placebo patients.
Disclosure: The authors have nothing to disclose.

EPR-196

PAS-positive lymphocytes vacuoles possible markers of impaired autophagy in multiple sclerosis

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Background and aims: Autophagy is mechanism essential to maintain the cellular steady-state in both physiological and stress conditions as well as in innate and adaptative immunity. Several microorganisms such as Epstein Barr (EBV) can impair the autophagy process impeding autophagosome/lysosome fusion. Here we investigated the presence of PAS-positive/LC3-II labelled vacuoles in lymphocytes of MS patients at diagnosis and their possible relationship with disease activity, progression and previous infection with EBV.
Methods: Blood smears were studied with PAS to evidence autophagy vacuoles. PAS-positive (PAS-plv) lymphocytes were counted in 3 adjacent microscopic fields at 40x magnification. The percentage of PAS-plv on the total number of lymphocytes was calculated. Immunofluorescence with anti-LC3B-Cy3 marked antibodies was performed to label impaired autophagosomes in lymphocytes.
Results: 25 confirmed MS patients were all EBV IgG positive and all showed PAS-plv. LC3-II labelling of PAS positive-lymphocyte vacuoles suggest therefore that autophagy is impaired in our patients. Only 2/20 healthy controls had a few PAS-plv also presented a previous EBV infection. 16/25 patients had a progressive form of disease and 12/25 patients had clinical or instrumental activity. A higher proportion of a PAS-plv was observed in patients with a progressive phenotype.

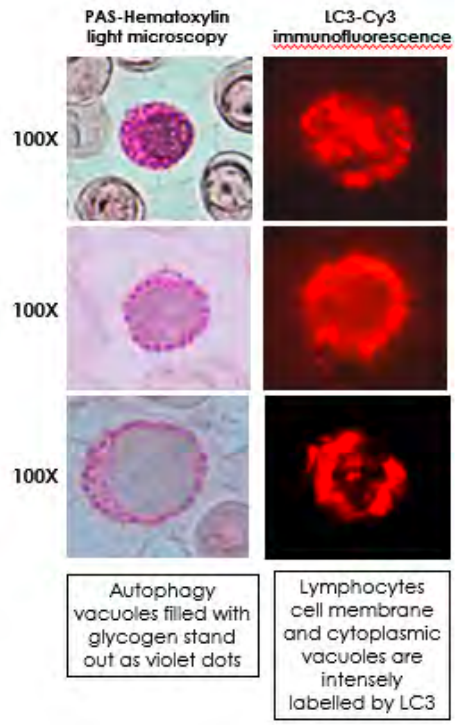

Figure 1 PAS-plv on lymphocytes of MS patients

	Patients N=25	Controls N=20
Age, mean (SD)	39.6 (11.1)	38.4 (12.1)
Females, n(%)	64.2%	50.0%
Years from symptom onset, median (IQR)	15.8 (2.5-1265)	
Years from diagnosis, median (IQR)	9.94 (2.0-10.3)	
Baseline EDSS, mean (SD), range	1.75 (1.72), 0-6	
ARR previous year, mean (SD)	0.33 (0.44)	
Disease course (remitting %)	88%	
Active lesions at baseline, n(%)	25.3	
PAS-plv on total lymphocytes n (%)	100%	10%
DBS (umol/L/h: normal >2)	4.3	4.9
EBV IgG presence n (%)	100%	10%
Mean number of PAS-plv lymphocytes	3.08 (0.8)	

Table 1 Demographic and clinical features of MS patients and healty controls

Conclusion: EBV encodes proteins able to inhibit autophagosome/lysosome fusion, as a result it finds in blocked autophagosomes oligonucleotides, amino acids, glycoproteins and lipids useful for replication and assembly of their cycle. This is the first study to investigate and highlight altered autophagy in MS. Possible links between EBV infection and slowing of autophagy in lymphocytes deserve further investigation.
Disclosure: Nothing to disclose.

ePresentations

Monday, July 03 2023
Sleep-wake disorders

EPR-197

Disentangling the complex landscape of sleep-wake disorders with data-driven phenotyping: A study of the Bernese center

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Background and aims: The diagnosis of sleep-wake disorders (SWD) is challenging because of the existence of only few accurate biomarkers, the frequent co-existence of multiple SWD and comorbidities. The aim of this study was to assess in a large cohort of SWD patients the potential of a data-driven approach in the identification of single SWD.
Methods: The data set analyzed consists of 6,958 patients included over 16 years in the Bernese Sleep registry and a total of 300 variables/biomarkers including questionnaires, results of polysomnography/vigilance tests, and clinical diagnoses according to international criteria. Unsupervised machine learning was used and a pipeline was created to extract and cluster the clinical data.
Results: A first analysis focused on a cohort of patients with central disorders of hypersomnolence (CDH) and revealed four patient clusters: two with narcolepsy type 1 (NT1) patients and two with NT2 and idiopathic hypersomnia. In the full cohort of SWD nine clusters were found: four contained patients with obstructive and central sleep apnea, one with NT1 and four with all the remaining diagnoses intermixed. In the cohort of patients without coexisting SWD an additional cluster of patients with chronic insomnia was identified.
Conclusion: This study confirms the existence of clear clusters of NT1 in CDH, but mainly intermixed groups in the full spectrum of SWD, with the exception of sleep apneas and NT1. New biomarkers are needed for a better phenotyping and diagnosis of SWD.
Disclosure: No conflicts of interest.

EPR-198

Cardiovascular autonomic dysfunction is a marker of progression and conversion in isolated REM Sleep Behavior Disorder

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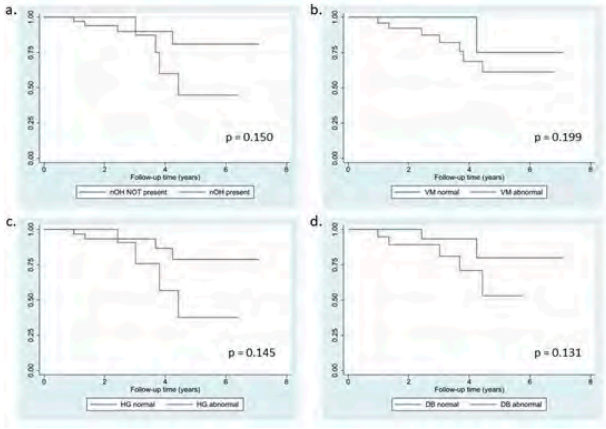
Background and aims: Cardiovascular autonomic dysfunction is a common marker of neurodegeneration in iRBD, with greatest impairment in sympathetic function. However, prospective data are limited. Our objective was to assess cardiovascular autonomic function in patients with isolated REM sleep behavior disorder (iRBD), its longitudinal progression and value for conversion.
Methods: We enrolled 34 consecutive videopolisomnography-confirmed iRBD patients and followed them longitudinally for a mean of 2,35±1,27 years. Each patient underwent Ewing's battery of cardiovascular reflexes tests. Procedures were performed at baseline, and annually for a total of 103 observations (range 2–6 per patient).
Results: Patients (40 males – 73%) had a mean age of 68.23±6.67 years. At baseline 27 iRBDs (50%) showed a pathologic Valsalva Manoeuvre, of them 10 showed neurogenic orthostatic hypotension (nOH). Blood pressure (BP) responses were the most blunted in relation to CTRs, and, to a lesser extent, also heart rate changes (HR). Cold face, handgrip and deep breathing and tests were abnormal in 19, 14 and 19 patients respectively, the latter two more in iRBDs than CTRs (p=0.034 and 0.009). At follow-up BP responses to test stimuli prevalently deteriorated, nOH increased (yearly OR: 1.45 [1.02–2.07] – p=0.040). Eight patients converted to an alpha-synucleinopathy, patients with nOH at baseline (p=0.012) and with poorer BP responses had a higher risk of conversion.

	iRBD (n = 55)	HC (n = 57)	p-value
Sex M/F (number - %)	40 – 72.7% 15 – 28.3%	38 – 66.7% 19 – 33.3%	0.312
Age at T0 (years) (Mean ± SD)	68.23 ± 6.67	66.83 ± 7.49	0.300
Age of Onset (years) (Mean ± SD)	61.78 ± 7.74	/	/
Duration RBD T0 (years) (Mean ± DS)	6.45 ± 5.00	/	/
Height (m) (Mean ± SD)	1.68 ± 0.10	1.69 ± 0.10	0.688
Weight (Kg) (Mean ± SD)	77.29 ± 12.75	74.43 ± 11.49	0.186
BMI (Kg/m²) (Mean ± SD)	27.12 ± 3.47	26.07 ± 3.58	0.084

Demographic data of the two groups of subjects examined.



Survival (Kaplan-Meier) curves for conversion towards an overt α-synucleinopathy depending on a) presence of nOH, b) abnormal VM, c) abnormal HG or d) abnormal DB test.

Conclusion: Not only cardiovascular autonomic impairment in iRBD in already manifest, but it also worsens over time impacting for conversion, justifying its value as a marker of progression.

Disclosure: The authors report no conflict of interest.

EPR-199

Hippocampal atrophy in Parkinson´s disease with obstructive sleep apnoea

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Background and aims: Parkinson´s disease (PD) is a neurodegenerative disorder characterized by dopaminergic denervation of multiple brain regions. Obstructive sleep apnoea (OSA) is manifested by recurrent obstructions of upper airways, resulting in episodic oxygen desaturation and arousals from sleep. The severity of OSA is indicated by apnoea/hypnoea index (AHI), which measures the number of apnoeas/hypnoeas per hour. Since PD and OSA have each been associated with changes in brain morphology, our study aimed to investigate the interaction of early-stage PD and OSA (AHI>15 or AHI<15) on subcortical brain volumes.

Methods: The study included 86 subjects: 1) PD with AHI>15 [n=21, age 62.9±(SD)8.5 years]; 2) PD with AHI<15 [n=24, age 60.2±8.6y]; 3) healthy controls (HC) with AHI>15 [n=20, age 61.1±8.3y); 4) HC with AHI<15 [n=21, age 60.6±8.7y]. T1- and T2-weighted high-resolution images and FreeSurfer v7.1.0 were used to estimate volumes of the following structures: hippocampus (head, body, tail), amygdala, striatum and pallidum. The effect of factors GROUP (PD, CON), AHI (<15,>15) and GROUP*AHI interaction on the selected volumes was performed using a general linear model.

Results: Only the interaction of GROUP and AHI proved significant for the hippocampal body of the left (F=9.213, pFDRcor<0.05) and right (F=13.702, pFDRcor<0.01) hemisphere. PD with AHI>15 had significantly smaller volumes of hippocampal body (p<0.05) compared to all other groups in post-hoc Fisher´s LSD.

Conclusion: This study shows that OSA in PD is associated with reduced hippocampal volume, suggesting that dopaminergic denervation in this region increases vulnerability to hypoxia.

Disclosure: Funding: AZV NV19-04-00233 and projects NINR (LX22NPO5107), Cooperatio Neuroscience.

EPR-200

Circadian phase tailored light therapy in primary chronic insomnia. A randomised control trial study.

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Background and aims: Our study aims to investigate the effects of a tailored light therapy protocol on sleep and mood parameters in patients with primary chronic insomnia (PCI).
Methods: Twenty-four drug-free PCI patients (M/F: 7/9; mean age 49.06 (11.86) years) were investigated for subclinical mood related symptoms (STAY, Beck, Fatigue severity scale), subjective chronotype (MEQ) ,subjective nocturnal sleep parameters (PSQI, ISI, SCI), 7-day/night actigraphy and circadian phase (by in-home salivary Dim Light). The measurements were compared before and after a single-blind 5-weeks tailored light therapy versus sham protocol (Luminette/Sham group: 12/12 patients).
Results: Sixteen patients completed the protocol (Luminette/Sham: 8/8 patients). In Luminette group 43% patients showed a DLMO time shift in accordance to light delivery time. Sham group failed to present an analogous shift. In Luminette group sleep efficiency (SE) remained stable after active light treatment with respect to pre treatment condition (SE pre median 84.95% [76.25–88.59], SE post mean 85.12%±3.76) while in the Sham group it showed a decremental trend (SE pre median 85.78% [77.25–89.5], SE post mean 81.22%±7.91). Insomnia severity index (ISI) mean score improved nearly significantly in the Luminette group (pre mean 16.38±5.48, post mean 11.5±6.05) but not in the sham group. Anxiety (STAY mean score) significantly improved in the Luminette group (pre mean 42.14±14.08, post mean 35.88±12.67), while remained stable in the sham group.
Conclusion: Light therapy protocol tailored on the circadian phase proved to improve both sleep and mood in drug-free patients with primary chronic insomnia.
Disclosure: In October 2020 this study protocol won FIDIA 2020 award and grant in sleep and chronobiology field at the “XXX Italian sleep congress (AIMS)”.

EPR-201

Development, assessment and application of home ambulatory sleep polysomnography in sleep-related motor behaviours

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Background and aims: For most sleep behaviour-disorders, in-laboratory polysomnography (PSG) is currently the diagnostic gold standard. However, a need for more handy diagnostic tools has been underlined. In the study of nocturnal behaviours, video analysis along with EEG evaluation is still essential to perform a correct diagnosis. We aim to describe the experience of Bologna Sleep Centre in the evaluation of sleep-related motor behaviours by means of home-based video ambulatory recording.
Methods: We analysed consecutive home-based video ambulatory recordings from April 2016 to November 2022 of patients afferent for different suspected sleep-related motor behaviours including REM and NREM parasomnias, sleep-related epilepsy, psychogenic non-epileptic seizures. The patients were equipped in the sleep lab by expert sleep technicians, who also provided the instructions to carry on with the recording in the home setting.
Results: We included 314 consecutive home-based video ambulatory recordings of 242 patients. Overall, 84.1% of recordings were diagnostic (either confirming or excluding the clinical suspicion), while 15.9% of recordings were not diagnostic (insufficient evidence to confirm a diagnosis or technical problems). An accurate technical evaluation of quality of polygraphic tracings on the first 50 recordings disclosed artifacts in 8% of channels.
Conclusion: Home-based PSG tracings provided a good diagnostic accuracy (85% of cases). The recording in the patient’s natural environment might increase the likelihood to capture the habitual episodes. Home-based PSG showed a good quality, with lack of artifacts in 92% of channels. In conclusion, home-based recordings seem a promising approach with lesser costs and faster waiting time than in-lab PSG.
Disclosure: Nothing to disclose.

EPR-202

The role of melanin-concentrating hormone (MCH) neurons in gating REM sleep and cataplexy in narcolepsy

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Background and aims: The melanin-concentrating hormone (MCH) neurons regulate REM sleep and dynamically modulate its expression during thermoneutral ambient temperature (Ta) warming (Komagata et al., 2019). Given the reciprocal inhibition between the hypocretin (Hcrt) and MCH systems, we hypothesize that Hcrt loss may disinhibit MCH activity inducing the increased REM sleep propensity characteristic of narcolepsy, whereas MCH hypoactivity may exacerbate boundary state instability and favor cataplexy.
Methods: First, we investigate the occurrence of cataplexy and REM sleep as a function of ambient temperature in narcoleptic Hcrt-KO mice. Then, we evaluate the role of the MCH system in REM sleep and cataplexy in narcoleptic MCH:cre/Hcrt-KO mice both at constant Ta and upon Ta manipulation by using fiber photometry and optogenetic approaches.
Results: Interestingly, we found a temperature-dependent dynamic dissociation of REM sleep and cataplexy. Specifically, during the warming phase we observed an increase in REM sleep and a significant decrease in cataplexy, whereas an opposite dynamic modulation occurred during the cooling phase. Fiber photometry experiments revealed that MCH activity increases both during REM sleep and cataplexy, but then it decreases at the transition to the wake state. Importantly, MCH tone is elevated prior to NREM to REM sleep transitions but remains lower prior to cataplexy onset. Finally, MCH optosilencing promotes cataplexy but Ta warming reversed the response, suggesting that the warming effect on cataplexy reduction is independent of the MCH system.
Conclusion: Taken together, these results suggest that an absence of MCH activity promotes state instability and increases the probability of cataplexy expression.
Disclosure: Nothing to disclose.

EPR-203

Telemedicine for innovative multidisciplinary care of people with narcolepsy, the TENAR randomized controlled trial

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Background and aims: Narcolepsy is a rare central hypersomnia associated with endocrine and psychosocial problems, requiring a multidisciplinary approach. We report preliminary data from the non-inferiority trial of telemedicine vs in-office management of people with narcolepsy.
Methods: People with narcolepsy aged >14 years were eligible for inclusion in a randomized controlled trial that compared multidisciplinary management (neurological, endocrinological, and psychosocial care) performed via telemedicine versus office visit for one year. Primary outcome was control of sleepiness (according to the Epworth Sleepiness Scale, ESS) at 12 months, with a non-inferiority margin of 1.5 points. Secondary outcomes were control of other symptoms, treatment compliance, metabolic control, quality of life, feasibility, patient and family satisfaction with care, safety, and disease-related costs.
Results: 208 patients were randomized and 202 completed the study at 12 months. At baseline, clinical and outcome variables were well balanced in the two groups. ESS score (primary outcome) improved by 1.3 mean points in both groups (no statistical difference between groups). The secondary outcome BMI improved in both groups (0.58 in outpatient, 0.40 in telemedicine, no statistical difference between groups).

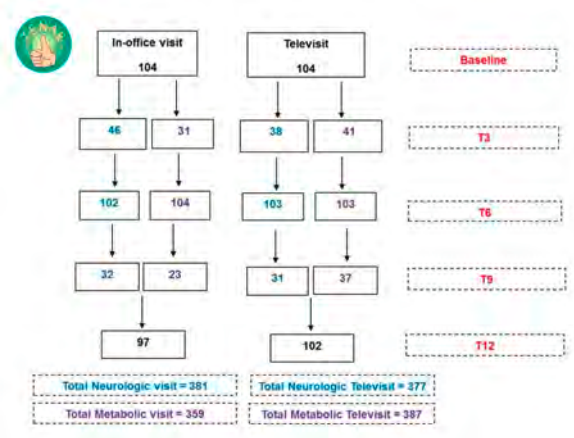

Figure 1. TENAR RCT patient flow.

Baseline Variables	In-office visit n = 104	Televisit n = 104	p-value
Sex (%) – Female	52 (50.0)	54 (51.9)	0.890
Education (%) – elementary school	1 (1.0)	4 (3.8)	0.440
secondary school	28 (26.9)	30 (28.9)	
high school	54 (51.9)	57 (54.8)	
degree or more	21 (20.2)	13 (12.5)	
Narcolepsy type (%) 1	93 (89.4)	89 (85.6)	0.530
2	11 (10.6)	15 (14.4)	
Orexina (%) – positive	68 (65.4)	69 (66.4)	0.574
negative	10 (9.6)	14 (13.5)	
missing	26 (25.0)	21 (20.2)	
Cataplexy (%) – yes	91 (87.5)	82 (78.9)	0.137
Age (mean) – years	28 (20 – 43)	33 (20 – 47)	0.279
Age onset (mean) – years	15 (11 – 23)	16 (10 – 22)	0.660
Age diagnosis (mean) – years	21 (14 – 32)	27 (13 – 39)	0.201
Body Mass Index (mean) – Kg/m²	25.0 (22.3 – 28.2)	26.1 (22.1 – 31.0)	0.216

Figure 2. Baseline characteristic of patients at baseline, by intervention group (.in-office visit vs televisit).

Conclusion: Preliminary data indicate the viability in terms of feasibility, effectiveness and safety of multidisciplinary telemedicine care procedures for narcolepsy in adults and teenagers.
Disclosure: Nothing to disclose. The study was funded by the Italian Ministry of Health (RF-2016-02364742).

EPR-204

Nocturnal Hypoxemia is Associated with White Matter Hyperintensities in Stroke

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Background and aims: Sleep-disordered breathing (SDB) is highly prevalent in stroke and associated with an increased risk of white matter hyperintensity (WMH). Apnea-hypopnea index (AHI), the universal metric of sleep apnea severity, poorly captures the key aspects of SDB. Therefore, we sought to investigate the prognostic value of nocturnal hypoxemic burden for WMH in stroke.
Methods: The samples were derived from two cohorts: the SAS-CARE 1 trial (ClinicalTrials.gov identifier: NCT01097967) and the Post-stroke Biomarkers Of Sleep disorders study to determine the number of episodic desaturations per hour (oxygen desaturation index, ODI) and time spent below 90% oxygen saturation (T90). Patients with an MRI at admission and a Polysomnography at 3 months following stroke were analyzed. WMH were assessed by two independent raters, using the Fazekas and the Wahlund score. Multivariate regression models were used to investigate the impact of SDB on WMH severity and localizations.

Results: 276 ischemic stroke/TIA patients, predominantly male (73.9%), with a mean age of 63.3±12.1 years, and mostly with mild-to-moderate stroke/TIA (mean admission NIHSS 4.9±5.3) were finally analyzed. Multivariate logistic regression models show that ODI (OR 1.07, p=0.036), but not T90 (OR 0.998, p=0.227) was significantly associated with WMH severity when adjusting for age, sex, hypertension, and AHI. Obstructive sleep apnea is associated with the frontal (OR 2.35, p=0.045) and basal ganglia WMH (OR 3.15, p=0.007).

	WMH Q1(n=92)	WMH Q1(n=92)	WMH Q1(n=92)	Total (N=276)	p value
Age	57.5 (13.5)	63.8 (10.9)	68.7 (8.8)	63.3 (12.1)	< 0.001
Male	72 (78.3%)	73 (79.3%)	59 (64.1%)	204 (73.9%)	0.032
Current smoker	15 (16.5%)	17 (18.5%)	15 (16.3%)	47 (17.1%)	0.910
Alcohol consumption	5 (5.5%)	5 (5.5%)	9 (9.8%)	19 (6.9%)	0.419
AHI	17.4 (15.9)	17.0 (16.8)	22.1 (19.5)	18.9 (17.6)	0.089
ODI	2.0 (4.9)	2.0 (4.0)	3.7 (6.6)	2.6 (5.3)	0.051
T90	355.4 (82.3)	362.9 (84.4)	328.5 (78.0)	348.9 (82.7)	0.012
OAI	2.0 (4.9)	2.0 (4.0)	3.7 (6.6)	2.6 (5.3)	0.051
CAI	1.7 (3.2)	2.4 (7.2)	1.5 (3.8)	1.9 (5.0)	0.416
Arousal index	20.4 (14.0)	21.4 (15.4)	26.8 (18.3)	22.9 (16.2)	0.015
Sleep efficiency	79.8 (15.5)	79.6 (14.5)	75.8 (14.2)	78.4 (14.8)	0.117
NIHSS admission	5.9 (6.4)	4.3 (4.7)	4.6 (4.5)	4.9 (5.3)	0.088
Hypertension	28 (30.8%)	49 (53.3%)	69 (75.8%)	146 (53.3%)	< 0.001
Diabetes	8 (8.9%)	15 (16.3%)	10 (10.9%)	33 (12.0%)	0.281
Dyslipidemia	34 (37.8%)	44 (47.8%)	40 (43.5%)	118 (43.1%)	0.390

Table: Baseline and stroke characteristics stratified by White Matter Hyperintensity severity. Data are presented as mean±SD unless otherwise stated. AHI: apnea-hypopnea index; ODI: oxygen desaturation index; T90: time spent below 90% oxygen saturation

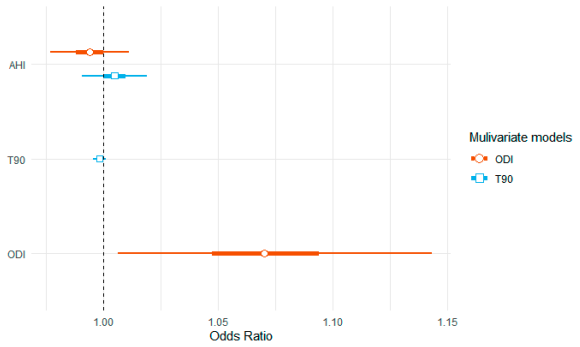

Figure: Odds ratio of white matter hyperintensity severity measured by the Wahlund score divided into tertiles. Confounders: age, sex, known hypertension, and apnea-hypopnea index.

Conclusion: In stroke, ODI is an independent predictor of WHM severity. WMH in frontal and basal ganglia areas showed significant associations with obstructive sleep apnea but not central sleep apnea.
Disclosure: This work was supported by a grant from the Swiss National Science Foundation ((SNF-320000-122031)

and a Ph.D. fellowship from China Scholarship Council. All authors declare no conflict of interest related to the current work.

EPR-205

Vigilance and attention in patients enrolled to the Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (SPHYNCS)

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Background and aims: The ongoing multicenter SPHYNCS study aims to find sensitive biomarkers to establish diagnostic criteria for narcolepsy and its borderland (NBL). The central disorders of hypersomnolence (CDH) are frequently accompanied by cognitive dysfunction, in particular an inability to maintain vigilance. Cognition has been investigated in narcolepsy type 1 (NT1) while the other CDH remain poorly assessed. The objective of this study is to identify peculiarities of attentional impairment in CDH.
Methods: SPHYNCS participants performed sustained attention to response test (SART) and psychomotor vigilance test (PVT) 3 times over the course of 2 following days respectively. SART and PVT metrics (reaction time (RT), number of total errors, standard deviation of mean reaction time (SD), commission and omission errors for SART) were used as primary outcomes. Circadian modulation was taken into account.
Results: SART results were available in 84 patients and 9 healthy controls (HC). PVT was performed by 76 patients and by 9 HC. In SART, NT1 had more omission errors than HC ($p<0.05$) irrespectively of the time of the day; SD was positively correlated with the total errors ($p<0.0001$), most obviously in NT1. In PVT all metrics significantly differed between NT1 as well as NBL versus HC. Our primarily analysis suggests, that there are no substantial differences of SART and PVT metrics between the trials.
Conclusion: This preliminary report suggests significantly disturbed vigilance in CDH. Further analysis will be performed to identify patterns of cognitive dysfunction in NBL.
Disclosure: The study is supported by the Swiss National Science Foundation.

Neurogenetics

EPR-206

Autoimmune Comorbidities in Multiple Sclerosis: prevalence estimation through epidemiological approach and genetic data

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Background and aims: This study aims to test the risk of Autoimmune Diseases (ADs) as comorbidities in Multiple Sclerosis (MS) using an epidemiological innovative approach based on Electronic Administrative Health Databases (EAHD), and to link the EAHDs with genetic data to evaluate the role of AD-associated genes with AD comorbidity risk in MS.
Methods: From EAHD of Piedmont (Italy) population (over 4 million people), we constructed several algorithms to identify MS and 15 other ADs. We designed a cumulative Genetic Risk Score (GRS) for the 15 ADs previously identified and a GRS specific for MS and each AD, using known genetic variants associated with each AD.
Results: We ascertained 8,850 MS cases, 16.2% of whom had at least one of the 15 tested ADs. Compared to non-MS cases, we found a statistically significant positive association of MS comorbidity with 8 ADs, and a protective effect for Inflammatory Bowel Disease. In the sub-set of MS-cases with EAHD and available genetic data (n=792), MS-patients with AD co- morbidity (n=105), showed a statistically significant higher cumulative GRS ($p=0.043$) than those without (n=688). The mean GRS specific for each AD was significantly ($p<0.04$) different between MS patients with/without AD comorbidity only considering GRS for MS itself, Type-1 diabetes, Celiac Disease, and Hashimoto's Thyroiditis.
Conclusion: EAHDs can be successfully used to test genotype-phenotype associations in MS. We confirmed a risk for AD comorbidity in MS analysing one of the largest population-based cohort until now. Our preliminary data showed that a genetic background shared by different ADs increases the risk for ADs in MS.
Disclosure: Nothing to disclose.

EPR-207

Natural history of adult-onset Metachromatic Leukodystrophy: findings from a large retrospective multicentric cohort

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Background and aims: Metachromatic Leukodystrophy (MLD) is a neurodegenerative autosomal recessive disease caused by the deficient activity of arylsulfatase A. The aim of this study was to describe the characteristics and outcomes of the rare adult-onset form of MLD.
Methods: We retrospectively collected clinical data of patients with MLD disease and first clinical manifestations beyond 15 years-old, through a standardized survey, from several centers worldwide (n=36). We additionally included patients from the literature (n=28).
Results: We included 64 patients (F/H=55%) with adult-onset MLD, median age at first symptoms 26 years-old [15–62]. MLD manifestations were behavioral changes (84% of patients/ present at onset 59%), cognitive disorder (92%/47%), psychotic symptoms (34%/17%), seizures

(27%/11%), gait disorder (42%/9%), upper-limb difficulties (28%/8%) or sphincter dysfunction (41%/5%) (Fig.1). Among the 13 patients (median age 23[19–38]) treated with hematopoietic stem cell transplantation (HSCT), 2 patients improved (follow-up 5 and 22 years), 5 stabilized (median follow-up 9[5–20]), 6 worsened (median follow-up 7[3–29]) and 1 patient died of toxic complication. After disease onset (median follow-up 10 years [1–44]), 15/57 (26%) patients lost the ability to speak, 12/57 (21%) lost the ability to walk and 8/57 (14%) died. After 25 years of evolution, only 2 patients were still able to speak and walk, 10 patients had lost the ability to walk, 11 had lost the ability to speak and 6 had died (Fig.2).

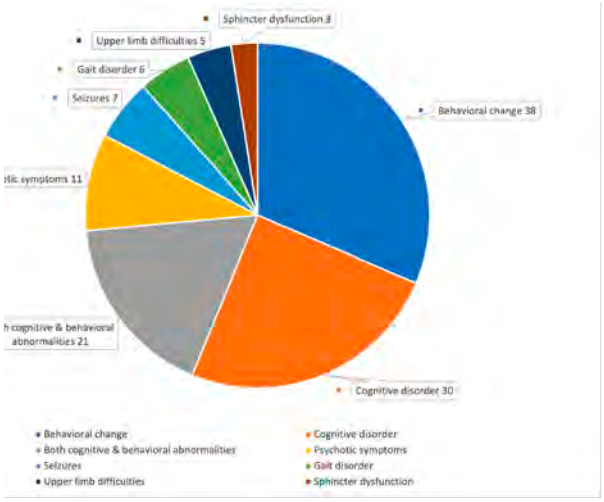

Figure 1. First clinical manifestations of the disease

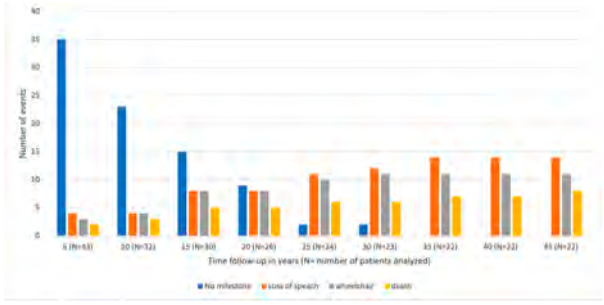

Figure 2. Milestones evolution during the course of the disease

Conclusion: Behavioural abnormalities and cognitive impairment are the main presenting symptoms of adult-onset MLD. Adult-onset MLD is a severe neurological disease still without established treatment, even though HSCT is a possible therapeutic option.
Disclosure: Nothing to disclose.

EPR-208

Phenotype and natural history of mitochondrial -membrane protein-associated neurodegeneration (MPAN)

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Background and aims: Mitochondrial membrane protein-associated neurodegeneration (MPAN) is an ultraorphan neurogenetic disease from the group of Neurodegeneration with Brain Iron Accumulation (NBIA) disorders. Here we report cross-sectional and longitudinal data to define the phenotype and to assess disease progression.
Methods: We enrolled patients with genetically confirmed MPAN from the Treat Iron-Related Childhood-Onset Neurodegeneration (TIRCON) registry and cohort study, and from additional sources. Linear mixed-effect modelling (LMEM) was used to calculate annual progression rates for Unified Parkinson's Disease Rating Scale (UPDRS), Barry-Albright Dystonia (BAD) Scale, and Schwab and England Activities of Daily Living (SE-ADL) scale. Growth mixture modelling (GMM) was used to test for unobserved subpopulations based on longitudinal trajectories.
Results: Between Feb 11, 2010, and May 05, 2022, we investigated 86 MPAN patients, with functional outcome measures collected in 36. Median age at onset was 9 years. The most common findings were gait disturbance, pyramidal involvement, dysarthria and visual disturbances. LMEM showed an annual progression rate of 4.6 points in total UPDRS, mostly driven by part II subitems freezing while walking, turning in bed and dressing, and part III subitems hand grips and arising from chair. The annual worsening of the total BAD scale was 0.18 points, and of the SE-ADL scale 4.45%. GMM found no distinct subpopulations of patients based on longitudinal trajectories.
Conclusion: Our cross-sectional results define order of onset and frequency of symptoms in MPAN. Our longitudinal findings define the natural history of MPAN and reveal the most responsive outcomes.
Disclosure: The current study was performed within the TIRCON project, a multinational collaborative project, funded by the European Commission 7th Framework Programme (FP7/2007-2013, HEALTHF2-2011; Grant Agreement No.277984, TIRCON) from 2011 to 2015 and maintained after 2015 through continuous donations from patient advocacies (NBIA Alliance and its members, www.nbiaalliance.org) as well as through single donations from pharmaceutical companies including ApoPharma Inc. (Toronto, Canada), CoA Therapeutics (San Francisco, CA; USA) and Retrophin, Inc. (San Diego, CA; USA).

EPR-209

Systemic and intracellular iron starvation response in Friedreich´s Ataxia

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Background and aims: Friedreich´s Ataxia (FA) is a devastating neurogenetic disorder caused by biallelic GAA expansions in the frataxin gene. Iron accumulation is believed to contribute to disease progression in FA. The main regulator of systemic iron metabolism is the hormone hepcidin. In condition of iron excess, the liver synthetizes hepcidin, which induces the degradation of ferroportin, the only cellular iron-exporting protein. Data on the state of the hepcidin-ferroportin axis in FA patients are lacking.
Methods: We measured 1) systemic iron parameters and regulatory hormones (hepcidin, endogenous erythropoietin, erythroferrone) in blood as well as 2) frataxin, ferroportin and intracellular iron metabolism parameters in PBMCs of genetically confirmed FA patients (n=40) and controls (n=40). We quantified iron content in liver, pancreas and spleen using MRI R2*-mapping.
Results: FA patients displayed reduced serum iron levels and transferrin saturation compared to controls; serum ferritin and mean corpuscular volume showed a significant inverse correlation with the length of the shorter GAA expansion (GAA1). Serum values of iron regulatory hormones were comparable in FA and controls. MRI R2*-mapping demonstrated lower iron storages in the liver and spleen of FA. Liver and spleen R2* values showed a significant inverse correlation with the GAA1 length. FA PBMCs displayed an upregulation of transferrin receptor and downregulation of ferritin, hepcidin and lipocalin-2. Moreover, the expression of HIF1α was downregulated in FA PBMCs and directly correlated with the frataxin levels.
Conclusion: FA features an iron starvation signature, both at a systemic and cellular level, whose degree correlates with the underlying genetic severity.
Disclosure: The present work was supported by a postdoctoral research grant funded by the Friedreich´s Ataxia Research Alliance (FARA), FARA Ireland and FARA Australia and awarded to Elisabetta Indelicato.

EPR-210

Whole exome sequencing in Serbian patients with hereditary spastic paraplegia

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Background and aims: Hereditary spastic paraplegia (HSP) is a neurodegenerative disease with a high genetic and clinical heterogeneity. Numerous HSP patients remain undiagnosed despite screening for known genetic causes of HSP. Therefore, identification of novel variants is needed.
Methods: Our first study analyzed 74 Serbian adult HSP patients from 65 families using the next-generation sequencing panel of the 13 most common HSP genes (L1CAM, PLP1, ATL1, SPAST, CYP7B1, SPG7, KIF5A, SPG11, ZYFVE26, REEP1, ATP13A2, DYNC1H1, and BICD2) in combination with a copy number variation analysis for three genes (SPAST, SPG7, and SPG11). Conclusive genetic findings were established in 23 patients from 19 families (29%). In the present study, nine patients from nine families negative on the HSP gene panel were selected for the whole exome sequencing (WES) – cohort 1. Besides, 44 newly diagnosed adult HSP patients from 44 families were sent to WES directly – cohort 2.
Results: WES analysis of cohort 1 revealed a likely genetic cause in five (56%) of nine HSP families, including variants in the ETHE1, ZFYVE26, RNF170, CAPN1,and WASHC5 genes. Only the ZFYVE26 gene was in the panel. In cohort 2, possibly causative variants were found in seven (16%) of 44 patients, comprising six different genes: SPAST, SPG11, WASCH5, KIF1A,KIF5A, and c9orf12.
Conclusion: These results expand the genetic spectrum of HSP patients in Serbia and the region with implications for molecular genetic diagnostics and future causative therapies. WES can be the first step in HSP diagnosis in well selected cohorts, especially in populations with yet non-defined HSP genetic background.
Disclosure: Whole exome sequencing, analysis and variant interpretation were performed at 3billion, Inc, Seoul, Republic of Korea as a part of 3billion's research funding program granted to DSP, VRS and SP.

EPR-211

Biallelic variants in ACER3 cause infantile and childhood-onset neurodegeneration

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Background and aims: Biallelic variants in ACER3 have recently been linked to early-onset leukodystrophy in 4 case reports describing 3 families with 7 affected members. Here we describe previously unreported 35 affected individuals from 32 unrelated families with biallelic variants in ACER3 and delineate the phenotypic spectrum of ACER3-related disease.

Methods: Exome sequencing, data sharing, screening the genetic databases of several international genetic laboratories, and GeneMatcher were used to identify the affected individuals reported here. The levels of the major glycerophospholipids, neutral lipids, and sphingolipids from control and ACER3 fibroblasts were determined by lipidomics.

Results: The cohort is composed of 35 affected individuals from 32 independent families including 20 females and 15 males. Twenty-one individuals are currently alive with a mean age of 5.6±4.1 years (range 1.4–15). Eleven patients (31%) died between the ages of 3 and 6.3 years due to the rapidly progressive disease course. The manifesting symptoms frequently included global developmental delay (GDD), motor regression, lower limb spasticity with gait impairment, frequent falls and loss of ambulation, dysarthria, and dysphagia. Among the frequent neurological findings were GDD/Intellectual disability (30/35), axial hypotonia (24/35), appendicular spasticity in (27/35), muscle weakness (21/35), feeding difficulties (16/25), and limb dystonia (15/29). Brain MRI available from 15 cases showed generalized brain cortical atrophy and leukodystrophy (Figure 1). ACER3 variants are presented in Table 1. The major change in lipidomics was a 2.19-fold increase in the level of sphingomyelin (SM), the major sphingolipid in eukaryotic cells (Table 2).

Clinical-demographic features	Frequency (overall=35)
Sex	20F, 15M
Current age	5.6±4.1 years (range 1.4-15)
Congenital microcephaly	3/11 (27%)
GDD/ID	32/32 (100%)
Type of progression (rapid, moderate, slow)	Rapid -9, Moderate-13, slow- 2, NA- 11
Motor regression	26/26 (100%)
Seizures	5/22 (23%)
Breathing difficulties	7/13 (53%)
Feeding difficulties	14/23 (61%)
Microcephaly at the last examination	5/22 (23%)
Dysmorphism	11/29 (38%)
Multiple contractures	12/26 (46%)
Hypotonia (truncal)	22/27 (81%)
Spasticity/ hypertonia (appendicular)	25/30 (83%)
Dystonia	15/29 (52%)
Peripheral neuropathy on EMG	2/14 (14%)
Increased DTRs	27/28 (96%)
Mortality	11/35 (31%)

Figure 1. Clinical features of the cohort. Description: A. Patients have generalized spastic dystonia. B. Representative Brain MRIs show generalized cerebral cortical and cerebellar atrophy, periventricular white matter abnormalities. C. Clinical features

Family	Variant type	c.DNA (NM_018367.7)	Protein	ACMG classification
F1	Missense	c.193G>C	p.(Ala65Pro)	VUS
F1, F32	Splicing	c.751-5A>G	4bp insertion	P
F2	Nonsense	c.234G>A	p.(Trp78Ter)	LP
F3	Missense	c.398 C>T	p.(T133I)	VUS
F3	Splicing	c.600-1 G>C	?	VUS
F4, F14, F26-F28, F30, F31	Missense	c.587 G>A	p.(Cys196Tyr)	P
F5, F16	Missense	c.53T>C	p.(Leu18Pro)	LP
F6	Nonsense	c.607C>T	p.(Arg203Ter)	P
F7	Missense	c.608G>C	p.(Arg203Pro)	VUS
F8	Missense	c.73T>C	p.(Tyr25His)	VUS
F8	Frameshift	c.474delT	p.(Arg159DfsTer33)	LP
F9	Missense	c.631G>T	p.(Gly211Cys)	VUS
F10	Missense	c.227G>A	p.(Gly76Glu)	VUS
F10, F22	Nonsense	c.475C>T	p.(Arg159*)	P
F11, F21, F24	Missense	c.264G>C	p.(Met88Ile)	P
F12	Missense	c.107A>G	p.(Asn36Ser)	VUS
F13	Missense	c.608G>A	p.(Arg203Gln)	VUS
F15	Deletion	c.598_705-539del4077	?	LP
F15	Missense	c.505C>T	p.(Pro169Ser)	VUS
F17	Frameshift	c.399delC	p.(Thr133Tfs)	LP
F18	Missense	c.238T>C	p.(Phe80Leu)	VUS
F19	Missense	c.599G>A	p.(Arg200Lys)	VUS
F20,	Stop gain	c.233G>A	p.(Trp78Ter)	P
F25	Missense	c.464A>G	p.(Asp155Gly)	VUS
F29	Missense	c.232T>C	p.(Trp78Arg)	VUS

VUS, variant of unknown significance; P, pathogenic, LP, likely pathogenic.

Table1. ACER3 variants identified in the cohort

Table 2. Fold change in major lipid classes in *ACER3* fibroblasts versus control

Lipid	Median fold change	P-value
SM	2.19	0.000001
Cer	1.25	0.559
PC	1.04	0.951
PE	0.91	0.173
PS	0.73	0.312
PI	1.41	0.181
PG	1.37	0.078
DG	1.19	0.129
TG	1.33	0.007

SM, sphingomyelin; Cer, ceramide; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PS, phosphatidylserine; PI, phosphatidylinositol; PG, phosphatidylglycerol; DG, diacylglycerol; TG, triacylglycerol

Table 2. Fold change in major lipid classes in ACER3 fibroblasts from patients versus control

Conclusion: Biallelic variants in ACER3 are associated with infantile and childhood-onset neurodegeneration.
Disclosure: Nothing to disclose.

EPR-212

Epidemiology and genotype-phenotype correlation of the Hungarian C9orf72 positive cases

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Background and aims: The intronic G4C2 hexanucleotide repeat expansion in the C9orf72 gene is the most common genetic cause of the familial form of frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). Recently, the mutation has been detected in other neurodegenerative diseases, such as Parkinson's disease and Huntington's like phenotype.
Methods: Patients (n=1,030) with different neurodegenerative conditions were investigated. The hexanucleotide repeat expansion in the C9orf72 gene was analyzed with repeat primed PCR technique. All reported patients carried a repeat longer than 30 hexanucleotide units.
Results: Altogether 76 patients harboured pathogenic repeat expansion. Out of the patients 39 showed the symptoms of pure ALS, 2 cases ALS-FTD overlap, 2 cases ALS-Parkinson overlap and 18 cases Parkinson's disease (three with concomitant dementia). In 3 cases with Huntington's disease phenocopy pathogenic expansion was detected. The age at onset of the patients with C9orf72 repeat expansion was significantly lower than in case of the sporadic forms of the conditions. In the ALS cohort the bulbar onset was significantly enriched. C9orf72 repeat expansion positive cases showed a more rapid progression and often were accompanied by psychiatric symptoms, such as severe anxiety, delusions or hallucinations.
Conclusion: The testing of the C9orf72 gene has an important role in the diagnostic pathway of neurodegenerative disorders. Understanding the phenotype - genotype correlation may help us to identify the right follow-up parameters in a natural history study which can support the development of new therapy which hopefully are on the horizon.
Disclosure: Nothing to disclose.

EPR-213

Harmonizing genetic testing for early onset Parkinson's disease: results of the PARKNET multicentric study

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Background and aims: Patients with early onset Parkinson's disease (EOPD) are often addressed to diagnostic genetic testing based on next-generation sequencing (NGS) multigene panels. However, the interpretation of NGS results can be challenging in a diagnostic setting, and few studies have addressed this issue so far.
Methods: We retrospectively collected data from 648 EOPD patients (age-at-onset, AO≤55y) who underwent NGS of a minimal panel of 15 PD-related genes and PD-MLPA in eight Italian genetic diagnostic laboratories, including report's outcomes. Patients were further stratified based on AO≤40y (vEOPD subgroup, n=157). All variants were re-classified according to the latest ACMG criteria and diagnostic outcomes pre- and post-harmonization were compared.

Results: In 186/648 EOPD (29%) and 71/157 vEOPD (45%) patients, the diagnostic report listed at least one single nucleotide variant (SNV) or copy number variation (CNV). In 105/648 (16%) patients, the testing outcome was considered diagnostic. After harmonization, the genetic diagnosis changed in 20/186 (11%) patients, with six reports shifting from non-diagnostic to diagnostic and 14 former diagnostic reports being re-classified as inconclusive. A definite diagnosis was reached in 97 (15%) EOPD patients (39 vEOPD, 25%), of whom the majority carried either GBA variants (58, 9%; 14 vEOPD, 9%) or biallelic PRKN SNVs/CNVs (17, 3%; 12 vEOPD, 8%). In 89 (14%) cases (32 vEOPD, 20%), the genetic report was inconclusive.
Conclusion: This study provides a successful attempt to harmonize diagnostic reporting of PD genetic testing across several labs, highlighting the current difficulties in interpreting genetic variants emerging from NGS multigene panels, with relevant implications in terms of counselling.
Disclosure: This work was supported by grants of the Italian Ministry of Health (Ricerca Corrente Reti 2021-2022 - PARKNET project). A.D.F. reports advisory board fees from Sanofi and speaking honoraria from Sanofi and Zambon. None of the other authors reports any conflict of interest.

EPR-214

Pooled analysis of patients with inherited prion disease caused by 2- to 7-octapeptide repeat insertions in PRNP gene

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Background and aims: Inherited prion diseases caused by two- to seven-octapeptide repeat insertions (OPRI) in the prion protein gene (PRNP) have a phenotype similar to sporadic Creutzfeldt-Jakob disease. This pooled analysis summarizes all cases reported in literature to date and describes the relation between survival, age of onset, number of OPRI and codon 129 polymorphism.
Methods: MEDLINE and Google Scholar were queried from database inception up to December 31, 2022. Age of onset was compared per number of OPRI and per codon 129 polymorphism using the Kruskal-Wallis and Wilcoxon-Mann-Whitney tests, respectively. Survival was modelled non-parametrically by a Kaplan-Meier model and semi-parametrically by a Cox model.
Results: This study comprised 113 patients. Baseline characteristics are presented in Table 1. Age of onset was significantly different (p<0.001) per number of OPRI and was higher in patients with lower number of repeats (Figure 1). Survival was significantly different (p<0.001) per number of OPRI, with lower survival in patients with two- to four-OPRI (Figure 2). Patients with valine (cis-V) vs. methionine (cis-M) on codon 129 of the mutated allele were significantly older (median age of 59.0 vs. 43.0 years, p=0.005) and had lower survival (HR 2.32, 95% CI 1.03-5.19, p=0.041). Survival was, however, not significantly different (HR 1.39, 95% CI 0.61–3.18, p=0.429) between patients with cis-V vs. cis-M on codon 129 after adjustment for age of onset.

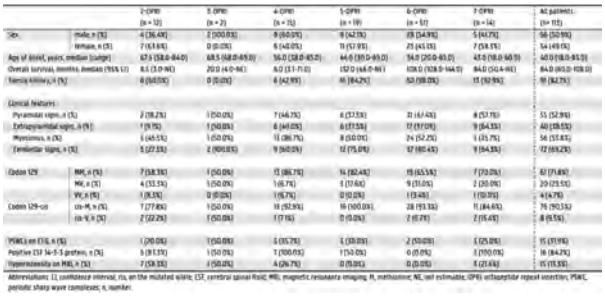

Table 1: Clinical characteristics of all 2- to 7-OPRI patients

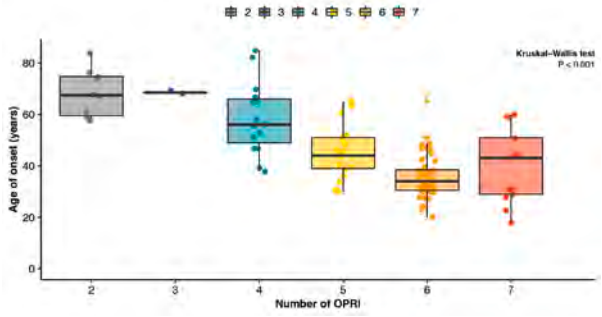

Figure 1: Age of onset per number of OPRI

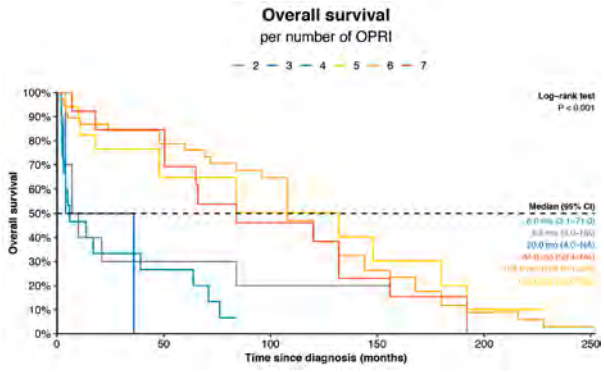

Figure 2: Survival per number of OPRI

Conclusion: This study summarized the largest cohort of patients with two- to seven-OPRI to date. Number of OPRI and codon 129 polymorphism were significantly associated with age of onset and survival.
Disclosure: Nothing to disclose.

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EPR-215

Epileptic seizures on Stroke Fast Track Protocol: frequency and aetiological characterization

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Background and aims: Epileptic seizures (ES), though unusual initial stroke symptom, are known as an important stroke mimic. Its recognition has vital diagnostic and prognostic implications. Our study want to investigate the ES frequency as a stroke mimic in Stroke Fast Track Protocol (SFTP) patients and its clinical and aetiological characterization.
Methods: Descriptive and retrospective study, about SFTP´s admissions classified as ES, from a tertiary hospital in Portugal, between January 2012 and December 2021. Patients with acute symptomatic seizures (ASS) and acute stroke were excluded.
Results: From 5,038 SFTP´s activations, 1,071 patients (21.3%) were stroke mimics, of which 182 (17.0%) with ES. They were 82 men (56.9%), median age of 72 years. Motor focal onset seizure was the most frequent (58.3%) seizure type. 76 patients (52.8%) were in post ictal state. Status epilepticus was identified in 24 patients (16.7%). 29 ASS were diagnosed, of which, ten by infectious nature and six by hyponatremia. 81 new epilepsy diagnosis were made, of which, 65 patients by structural causes: 40 by vascular causes (35 due to past stroke); 18 by tumoral nature; and seven posttraumatic related. Vascular structural aetiology was found in 20 of 34 patients with known history of epilepsy.
Conclusion: ES are a frequent stroke mimic on SFTP, as already found on literature. Vascular epilepsy was the most frequent aetiology, especially due to past stroke, possibly explained by the high prevalence of stroke in Portugal. ES in already diagnosed epileptic patients, highlight the need of a proper medication and monitorisation.
Disclosure: Nothing to disclose.

EPR-216

Cerebral Microinfarction are significantly common in patients with overt epithelial cancer

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Background and aims: Cerebral microinfarcts (CMI) are the most common type of brain ischemia, and can be detectable only for 2 weeks approximately on Magnetic-resonance-diffusion-weighted-imaging (MRI-DWI). CMI are related to increased stroke risk and cognitive impairment. Incidence and effect of CMI on population with malignancy is unknown. We aimed to examine whether CMI are more common in patients with malignancy, as a possible prediction marker for cognitive impairment or cancer related stroke.
Methods: We used the computerized database of Clalit health services (with approximately 5 million members representing over half of the Israeli population both inpatients and community care) to identify adults with a diagnosis of lung cancer and compared to a group of breast, pancreas or colon cancer patients (NLCCG) who underwent brain MRI scan in the 5 years following cancer diagnosis between 2014–2020. We looked for CMI incidence and total CMI number in this populations.
Results: 3,662 MRI scans of 2,463 patients were scanned. A total of 143 CMI were found in 73/2,056 (3.5%) MRI scans of lung cancer group, compared to a total of 29 CMI in 22/1,606 (1.4%) MRI scans of NLCCG, $p<0.01$. Multivariate analysis showed that Cancer type (e.g., Lung vs. NLCCG) was the only associated factor with CMI incidence

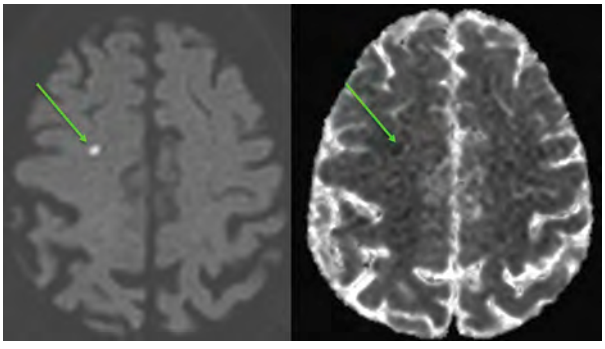
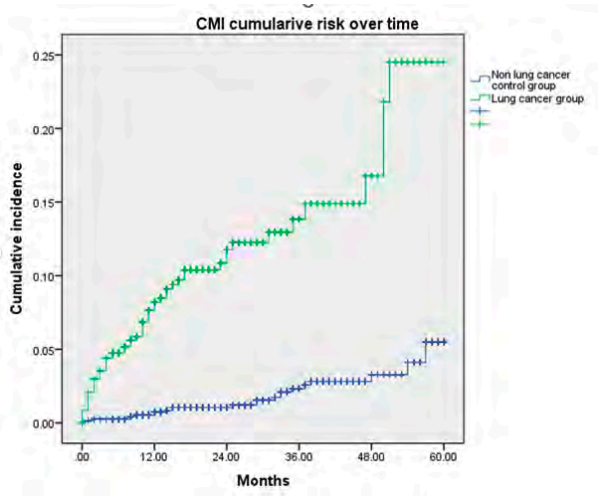


Figure 1: Cerebral micro-infraction in DWI-MRI and ADC

		Positive CMI (95 MRI scans in 95 patients)	Negative CMI (3567 MRI scans in 2341 patients)	p. value – univariate	p. value – Multivariate analysis
Demographic data					
Age (mean ± SD)		65± 11	61± 17	0.04	0.34
Gender – female (n, %)		45 (47%)	1418 (60%)	0.02	0.87
Comorbidities					
Hypertension (n,%)		41 (43%)	955 (41%)	0.57	
Diabetes mellitus (n,%)		25 (26%)	513 (22%)	0.28	
Smoking (n,%)		63 (66%)	1250 (53%)	0.01	0.57
Obesity (n,%)		25 (26%)	619 (26%)	0.96	
Atrial fibrillation (n,%)		8 (8%)	121 (5%)	0.16	
Congestive heart failure (n,%)		4 (4%)	50 (2%)	0.18	
Myocardial infraction (n,%)		14 (15%)	192 (8%)	0.02	0.19
Stroke (n,%)		9 (9%)	160 (7%)	0.3	
Chronic obstructive pulmonary disease (n,%)		10 (10%)	274 (12%)	0.75	
Peripheral vascular disease (n,%)		4 (4%)	133 (6%)	0.56	
Carotid artery disease (n,%)		0 (0%)	75 (3%)	0.08	0.99
Aortic aneurysm (n,%)		0 (0%)	29 (1%)	0.28	
MRI scans	**lung cancer patients (n,%)**	**73 (77%)**	**1983 (55%)**	**<0.01**	**<0.01**
	Non lung cancer patients (n,%)	**22 (23%)**	**1576 (45%)**		

Comparison between positive cerebral microinfarcts in DWI-MRI to negative DWI-MRI scans for CMI in all cohort.



Cumulative risk for cerebral microinfarcts in lung cancer group vs. No lung cancer control group

Conclusion: CMI are far more common in patients with lung cancer comparing to other cancers. This finding can imply that these patients are prone to ischemic stroke and cognitive decline. Future studies need to evaluate whether lung cancer patients with incidental finding of CMI can benefit from preventive anti thrombotic treatment.

Disclosure: The authors declare that they have no competing interests, and this study received no funding.

EPR-217

Cerebrovascular reactivity assessment during Spreading Depolarization in a swine model of Intracerebral Hemorrhage

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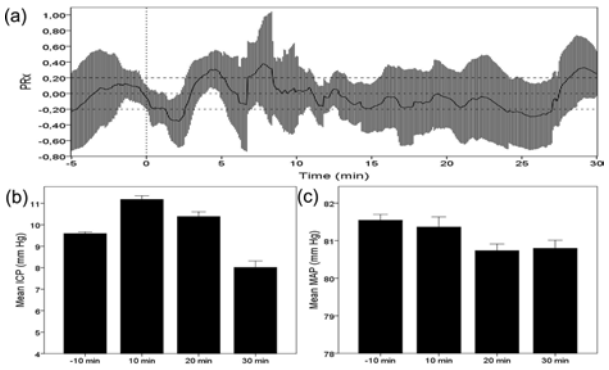
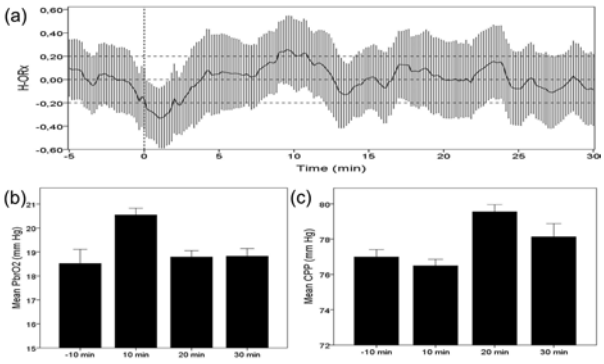
Background and aims: Spreading Depolarization (SD) has been detected in a significant portion of patients after intracerebral hemorrhage (IHC). Following SD, an impairment of cerebrovascular reactivity has been observed. The pressure reactivity index (PRx) and the oxygen pressure reactivity index (ORx) have been used as predictors of neurological outcomes after ICH. This study aimed to evaluate the PRx and ORx indices during the early phase of the post-SD period in a swine model of autologous ICH.

Methods: Nine male swine were craniotomized and continuously monitored for mean arterial blood pressure (MAP), intracranial pressure (ICP), cerebral perfusion pressure (CPP), and partial pressure of brain tissue oxygen (PbrO2). An electrocorticography (ECoG) subdural recording strip was placed for SD detection. Under systemic arterial pressure, autologous blood was injected to produce ICH. The PRx and the high-frequency ORx (H-ORx) were simultaneously calculated and measurements before and after SD occurrence were compared.

Results: Following ICH, 22 SDs events evolved spontaneously in 2/3 of the animals. During the period that followed SD, significant fluctuations of preserved-impaired autoregulation in both PRx (p=0.008) and H-ORx (p=0.043) were observed in 40.9% and 86.4% of the SDs events, respectively. These autoregulatory changes were associated with a significant increase in ICP (15.4%) and PbrO2 (10.8%), as well as a reduction in MAP (0.7%) during the first 10 min after SD.



(a) Time course of pressure reactivity index (PRx) during the early phase of 9 SD events. (b) Changes observed in intracranial pressure (ICP) and (c) mean arterial pressure (MAP) before and during SD occurrence. Values are expressed as mean and 95% CI



(a) Time course of high-frequency ORx (H-ORx) during the early phase of 19 SD events. (b) Changes observed in partial pressure of brain tissue oxygen (PbrO2) and (c) cerebral perfusion pressure (CPP) before and during SD occurrence

Conclusion: Changes in cerebral autoregulation can be detected through the PRx and H-ORx indices during the early phase after SD in a swine model of autologous ICH, showing an intermittent pattern of preserved-impaired autoregulation.
Disclosure: Nothing to disclose.

EPR-218

Moving from CT to MRI in acute ischemic stroke: feasibility, effects on misdiagnosis, stroke etiology, long-term outcome

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Background and aims: The relative value of CT and MRI in acute ischemic stroke (AIS) is debated. In May 2018, we switched from MRI to CT as first line imaging for suspected AIS. Here, we aimed to retrospectively assess the effects of this paradigm change on diagnosis and disability outcomes.
Methods: We compared all consecutive patients in the Acute STroke Registry and Analysis (ASTRAL) during the MRI-period (05/2018-08/2022) with an identical number of patients during the preceding CT-period, performing univariate and multivariate analyses.
Results: The median age of the 2,972 included consecutive AIS patients was 76 (IQR=65–84) years, and 1,361 (46%) were female. In the MRI-period, 80% underwent MRI as first acute imaging. The proportion of patients requiring a second acute imaging modality for diagnostic ± revascularization reasons increased from 2.3% to 6.9% (puniv<0.01). The rates of initially missed AIS diagnosis was similar (3.8% vs 4.4%, padj=0.44). Thrombolysed stroke mimics decreased by half (8.6% vs 4.3%, padj<0.01). Rates of unidentified stroke mechanism at hospital discharge was higher in the MRI period: 22.8% vs 28.1% (padj<0.01). The length of hospitalisation decreased from 9 (IQR=6–14) to 7 (IQR=4–12) days (padj< 0.01). Disability at 3 months was similar (common adjusted odds ratio for favourable Rankin shift 1.12 (95% CI=0.96–1.30); padj=0.138).
Conclusion: The paradigm shift from CT to MRI as first-line imaging for AIS in a comprehensive stroke centre seems feasible. MRI was associated with reduced thrombolysis of stroke mimics, but not with rates of missed AIS diagnosis, identification of stroke mechanism or long-term outcome.
Disclosure: Costanza Maria Rapillo received the EAN Research Fellowship Grant to conduct her project in Lausanne University Hospital - CHUV.

EPR-219

Automated pupillometry predicts three-month stroke outcome: an observational, prospective, cohort study.

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Background and aims: Automated pupillometry (AP) is a non-invasive tool that can reliably evaluate the pupillary light reflex. The prognostic role of AP in patients with traumatic brain injury is well known. The aim of the study was to analyze the prognostic role of AP in patients with ischemic stroke.

	Abbreviation	Unit	Definition	ANS branch involved
Baseline Pupil Diameter	BPD	mm	Pupillary diameter at baseline, before the light stimulus	Both
Minimum Pupil Diameter	MIN	mm	Pupillary diameter at the peak of constriction	Parasympathetic
Reflex Latency	LAT	s	Time delay between the light stimulus and the onset of pupillary constriction	Parasympathetic
Average Constriction Velocity	CV	mm/s	Average velocity of the pupil constriction	Parasympathetic
Maximum Constriction Velocity	MCV	mm/s	Maximum velocity of the pupil constriction	Parasympathetic
Constriction Index	CH	%	Obtained by applying the sequent formula: (BPD-MIN)/BPD	Parasympathetic
Dilatation Velocity	DV	mm/s	Average velocity of the pupil dilatation	Sympathetic
NeuroPupillary Index	Npi	N/A	A composite measure obtained by the combination of all the aforementioned parameters	Both

Table 1. A list of the pupillary parameters obtained through automated pupillometry, their abbreviations, their meaning, and the branch of the autonomic nervous system involved. Abbreviations: ANS, Autonomic Nervous System; N/A, Not Applicable.

Methods: In this observational, cohort study, we included consecutive adult patients admitted to our Stroke Unit for a diagnosis of ischemic stroke. Exclusion criteria included: eye diseases, bilateral strokes, and previous neurological disorders. AP was performed within 72 hours of stroke onset and parameters of the eye ipsilateral and contralateral to the cerebral lesion were considered. Stroke outcome was assessed through 3-month modified Rankin Scale (mRS). Statistical analyses were performed through univariate and multivariate logistic regression. Optimal thresholds for AP parameters were obtained via Receiver Operating Characteristic (ROC) curves.

Results: 157 patients were included in the study. Several AP parameters were found to be prognostic predictors in univariate analysis, such as dilatation velocity in the eye ipsilateral to the ischemic lesion (DVi), contralateral DV, contralateral constriction index. A DVi reduction was a predictor of poor prognosis in all the outcome models analyzed (mRS≤1 vs mRS>1: p=0.007; mRS≤2 vs mRS>2: p=0.007; mRS≤3 vs mRS>3: p=0.001) and an independent predictor in the model mRS≤3 vs mRS>3 (p=0.022). A DVi<0.875 mm/s predicted an unfavorable outcome with 65% specificity and 56% sensibility.

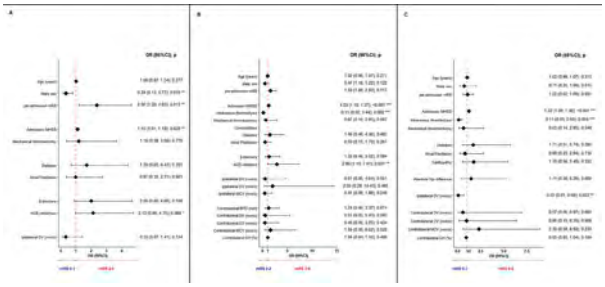

Figure 1. The forest plots of the multivariate analyses. In PANEL A, B, and C are represented, respectively, the results of the mRS≤1 vs mRS>1, mRS≤2 vs mRS>2, and mRS≤3 vs mRS>3 comparisons.

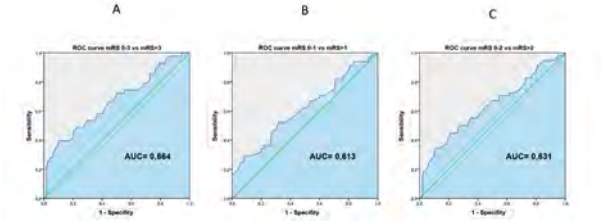

Figure 2. A graphic representation of the ROC curves obtained by analyzing the DV in the eye ipsilateral to the ischemic lesion respect to the various 3-month mRS dichotomizations (A: mRS ≤3 vs mRS>3, B: mRS ≤1 vs mRS>1, C: mRS ≤2 vs mRS>2).

Conclusion: A DVi reduction is associated with poor stroke outcome. AP is a useful tool to predict the prognosis of stroke patients.

Disclosure: Nothing to disclose.

EPR-220

Comparison of signal and biophysical diffusion modeling results in cerebral small vessel disease.

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Background and aims: Cerebral small vessel disease (CSVD) is one of the main causes of cognitive impairment, ischemic and hemorrhagic strokes. The pathological mechanisms of disease progression are largely unclear. The purpose of the study was to assess the microstructural integrity of the corpus callosum using signal and biophysical diffusion modeling in patients with CSVD.
Methods: The study included 167 patients (60.3±6.3 y.o., 52.1% men) The control group consisted of 44 volunteers (55.5±5.5 y.o., 65.9% men). The study was carried out on 3T scanner. The tract profile method (based on DIPY algorithm) was used to evaluate diffusion measures along the large and small forceps, the middle part of the corpus callosum for several diffusion models: diffusion tensor and kurtosis, neurite orientation dispersion and density imaging, white matter tract integrity, multi-compartment spherical mean technique.
Results: The most significant changes in the microstructural integrity were selected using binary logistic regression and appeared to be an increase in extra-axonal axial diffusivity (AE, p=0.003) and transverse diffusion coefficient for extra-axonal water (ETR, p<0.001), a decrease in fractional anisotropy (FA, p<0.001) and axonal water fraction (AWF, p<0.001).
Conclusion: An increase in the volume of extracellular fluid in the white matter in terms of longitudinal (ETR) and transverse (AE) diffusion with a decrease in FA, which characterizes the disorganization of the microstructure, and AWF, indicating a decrease in the density of axons, indicates the determining importance of the accumulation of extracellular fluid in demyelination and axonal death of the white matter.
Disclosure: Supported by the Russian Foundation for Basic Research, project no.22-15-00183.

EPR-221

Iatrogenic cerebral amyloid angiopathy (iCAA): a case series

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Background and aims: The number of patients with CAA neuroimaging features, younger than usual, who had a neurosurgical procedure at a young age is increasingly reported. These cases are defined as iatrogenic CAA (iCAA). A possible transmission of amyloid-β (Aβ) by exposure to Aβ proteopathic seeds has been hypothesised as a pathogenic mechanism.
Methods: We recruited 9 patients who met the Boston Criteria 2.0 for probable CAA and had undergone neurosurgical brain intervention in the early 1980s for removal of an expansive lesion or for treatment of haemorrhage from head trauma. All underwent brain MRI, amyloid PET (a-PET) and neuropsychological tests. Lumbar puncture and genetic analysis were performed in part of the cohort.
Results: Average age at surgery and at symptoms onset were respectively 12 (±9.2) and 46 (±8.5). From the brain operation, potential pathogenic trigger, to the clinical epiphenomenon, an average time of 34.3 (± 5.6) years elapsed (Table 1). First manifestations were headache, transient focal neurological deficits, and vision problems (Table 2). All a-PET showed pathological amyloid load deposition. Eight patients underwent lumbar puncture, with findings confirming an excessive aβ deposition (Table 3). Average age at diagnosis was 51. At an average follow-up of 20 months we observed exclusively radiological worsening. None experienced new symptomatic ICH or the development of cognitive impairment.

Patient	Year of birth	Surgery year (age)	Onset year (age)	Latency	Diagnosis year (age)	Follow-up (months)
PT1 (M)	1984	1984 (0)	2020 (36)	36	2020 (36)	35
PT2 (M)	1955	1981 (26)	2012 (57)	31	2021 (66)	23
PT3 (M)	1981	1984 (3)	2018 (37)	34	2019 (38)	36
PT4 (M)	1975	1983 (8)	2015 (40)	32	2020 (45)	29
PT5 (M)	1970	1987 (17)	2022 (52)	35	2022 (52)	7
PT6 (F)	1962	1982 (20)	2004 (42)	22	2022 (60)	2
PT7 (M)	1958	1980 (22)	2020 (62)	40	2022 (64)	20
PT8 (F)	1974	1985 (11)	2021 (48)	36	2022 (48)	8
PT9 (M)	1969	1969 (0)	2012 (43)	43	2020 (51)	18
				34.3 (± 5.6)		19.7 (± 11.6)

Table 1. Biographical characteristics and clinical history timeline. Abbreviation: PT, patient; M, male; F, female.

Patient	lobar ICH	cSS	WMH	CSO-PVS	CMBs	Onset symptoms
PT1	0	+	0	+	+	speech disorder
PT2	+	+	0	0	+	vision problems
PT3	+	+	+	0	+	transient dysestesia / hyposthenia
PT4	0	0	0	+	+	transient dysestesia / hyposthenia
PT5	0	+	+	+	+	transient dysestesia / hyposthenia
PT6	0	+	0	0	+	dizziness, headache
PT7	+	0	0	0	+	vision problems
PT8	+	+	+	+	+	headache
PT9	+	+	+	+	+	speech disorder

Table 2. Radiological and clinical characteristics. Abbreviation: PT, patient; ICH, intracerebral haemorrhage; cSS, cortical superficial siderosis; CSO-PVS, centrum semiovale perivascular spaces; WMH, white matter hyperintensities; CMBs, microbleeds.

Patient	Aβ40	Aβ42	42/40	T-tau	P-tau	PSEN1	PSEN2	APP	D-APP	APOE	TTR	PNRP	CST3
PT1	NE	NE	NE	NE	NE	E318G (Benign)	WT	WT	n=2	E3/E3	WT	WT	WT
PT2	3909	442	0.11	396	72.4	WT	WT	WT	n=2	E3/E3	WT	WT	WT
PT3	4935	312	0.06	288	24	WT	R62H (Benign)	WT	n=2	E3/E3	WT	WT	WT
PT4	9171	321	0.03	769	113.2	WT	S236S (Bening)	WT	n=2	E3/E3	WT	WT	WT
PT5	7166	642	0.08	832	59.5	WT	WT	WT	n=2	E2/E3	WT	WT	WT
PT6	5949	383	0.06	202	25.7	WT	WT	WT	n=2	E3/E3	WT	WT	WT
PT7	6898	504	0.07	452	66.5	WT	WT	WT	n=2	E2/E3	WT	WT	WT
PT8	4355	270	0.06	337	38.4	WT	WT	WT	n=2	E2/E3	WT	WT	WT
PT9	2035	10	0.01	213	23	WT	WT	WT	n=2	E3/E3	WT	WT	WT

Table 3. CSF values of aβ40, aβ42, p-tau and t-tau and genetic analysis. Abbreviation: PT, patient; NE, not executed; WT, wild type; D-APP, duplication of APP gene

Conclusion: Our experience leads us to hypothesise a less pronounced clinical deterioration in iCAA comparison to sporadic CAA cases. Certainly, international registers will allow a better definition of the disease and its severity in the future.
Disclosure: Nothing to disclose.

EPR-222

Diagnostic accuracy of plasma biomarkers in predicting cardioembolic stroke

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Background and aims: Plasma biomarkers have shown some potential in identifying cardioembolic stroke, which is essential to ascertain the right course of treatment. In this study, we aim to evaluate the accuracy of brain natriuretic peptide (BNP), N-terminal-proBNP (NT-proBNP) and troponin I in predicting atrial fibrillation (AF).
Methods: We included 717 consecutive patients admitted to our Stroke Unit with a diagnosis of ischemic stroke between January 2020 and January 2022. We evaluated retrospectively ECG monitoring≥48h and troponin I, BNP and NT-proBNP levels available in the acute phase.
Results: From our sample of 717 patients, 583 had no previous diagnosis of AF. From these, 23.7% had a high troponin on admission (120/507), 38.0% had high BNP (164/432) and 35.8% had high NT-proBNP (24/68). From those with high troponin at admission, 35.8% were found to have AF (RR=2.2; 95% CI=[1.6;3.0]), with a specificity of 81.0% and a sensitivity of 40.1%, with area under the ROC curve (AUC) of 0.69. From those with high BNP, 41.5% were found to have AF (RR=4.8; 95% CI=[3.1;7.4], with a specificity for AF detection of 71.8%, and a sensitivity of 74.7%, with AUC of 0.73. From those with high NT-proBNP, 47.5% were found to have AF (RR=4.5; 95% CI=[1.6;12.8], with a specificity for AF detection of 73.6%, and a sensitivity of 71.8%, with AUC of 0.72.
Conclusion: These biomarkers can be useful for early identification of cardioembolic stroke, with BNP and NT-proBNP having a higher sensitivity but lower specificity than troponin I.
Disclosure: Nothing to disclose.

EPR-223

Neutrophil-to-Lymphocyte Ratio as a predictor for poor functional outcome three months after an ischemic stroke

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Background and aims: Neutrophil-to-lymphocyte ratio (NLR) has been associated with poor long-term functional outcome in patients with acute ischemic stroke (AIS).
Methods: The study included 235 adults without signs of infection on admission divided in the following groups: 141 with a diagnosis of AIS (48 with intravenous thrombolysis and 93 with conservative treatment), and 94 stroke-free controls. Blood samples were obtained at admission to calculate NLR. Clinical data, including NIHSS was also registered on admission, and the long-term outcome was defined as 3 months post-stroke by the modified Rankin Scale (mRS).
Results: In all three patient groups we examined the mean NLR ratio, as it was significantly higher in the intravenous thrombolysis group (IvTG) and in the conservative treatment group (CTG) in comparison with the control group (CG) ($p<0.001$) (Table 1). Receiver operating characteristic curve (ROC) analysis was performed to determine optimal cutoffs of NLR as predictor of therapy outcomes. Elevated NLR was significantly associated with worse clinical outcome and functional dependency (mRS:3-5) in the whole group with AIS and in the IvTG subgroup ($p<0.05$). The ROC curve analysis revealed an optimal NLR cutoff value of 2.61 with 82.1% sensitivity and 59.7% specificity, as for the IVTG group it was 80.0% and 72.7% respectively (Figure 1).

Study Groups	Neutrophil lymphocyte ratio		ANOVA	
	Range	Mean ± SD	F	P-value
Conservative treatment group (CTG)(n=93)	0.63 – 13.12	4.26 ± 2.74	11.342	< 0.0001
Intravenous thrombolysis group (IvTG)(n=48)	1.09 – 12.11	4.33 ± 2.56		
Control group (CG)(n=94)	0.90 – 8.16	2.84 ± 1.50		
TUKEY'S TEST				
CTG vs IvTG	CGT vs CG		IvTG vs CG	
P = 0.982	P < 0.0001		P = 0.0008	

Table 1: Comparison between groups regarding neutrophil to lymphocyte ratio (NLR).

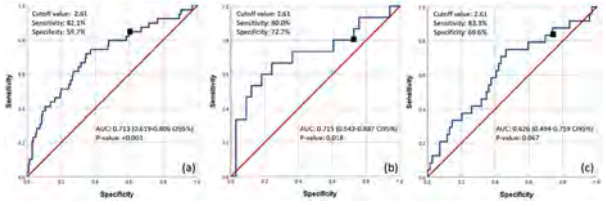

Figure 1: NLRvalues predicting functional dependence (mRS 3-5) in all patients with AIS (a), in the IvTG group (b) and in the CTG group (c) at 3 months post-stroke.

Conclusion: NLR is widely available and reliable marker for poor functional outcome at 3 months in both general AIS population and in patients treated with intravenous thrombolysis with high sensitivity and specificity.
Disclosure: Nothing to disclose.

Neuropathies

EPR-224

Inter-laboratory validation of a serum Fibroblast Growth Factor Receptor 3 (FGFR3) antibody test in sensory neuropathies

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Background and aims: Since their first description in patients with sensory neuronopathy in 2015, anti-fibroblast growth factor receptor 3 (FGFR3) antibodies have been reported in various forms of mostly sensory large fibre neuropathy as well as in small fibre neuropathy. So far, no standardized protocols for antibody testing are available. Here, we aim at validating a previously established anti-FGFR3 ELISA protocol in an inter-laboratory comparison. This protocol may serve as a standard for anti-FGFR3 diagnostic assessment.
Methods: We performed anti-FGFR3 ELISA using an identical protocol in two independent centres in France (centre 1) and Germany (centre 2) with two repeated assays each. In total, 42 serum samples of patients with sensory neuronopathy (n=18), small fibre neuropathy (n=18), and healthy controls (n=6) were assessed. These sera had been considered seropositive (n=18) or seronegative (n=24) in previous diagnostic assessment.
Results: Overall concordance of positive/negative results was 34/42 (81.0%, Cohen's kappa=0.61, substantial agreement). Although overall optical densities (OD) were lower when tested at centre 2 (median=0.076 vs 0.293, $p<0.0001$), the mean OD from two independent tests showed a strong correlation in all sera ($r=0.68$, $p<0.0001$).
Conclusion: The previously established anti-FGFR3 ELISA protocol reliably detects seropositive patients in most cases, while showing weakness at low OD levels. As the clinical significance, specificity, pathogenicity and relevance for treatment decisions of anti-FGFR3 antibodies remain unclear, this validation study paves the way for standardized assessment, analysis and interpretation of anti-FGFR3 antibodies.
Disclosure: Nothing to disclose.

EPR-225

Neurofilament light chain as a potential biomarker in patients with hereditary ATTR-polyneuropathy in NEURO-TTRansform

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Background and aims: Neurofilament light chain (NfL) is a biomarker of neuroaxonal damage. A small but growing body of evidence suggests that NfL may be a sensitive biomarker of polyneuropathy in patients with hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN) (Kapoor 2019; Luigetti 2022; Maia 2020; Ticau 2021). In one observational study, NfL increased over time in untreated patients, but decreased with TTR gene silencer treatment (Ticau 2021). The effect of silencer treatment on NfL levels warrants further study. We evaluated NfL levels in patients with ATTRv-PN treated with the TTR gene silencer eplontersen in the phase 3 NEURO-TTRansform study (NCT04136184; EudraCT 2019-001698-10).
Methods: NEURO-TTRansform enrolled 168 adults with ATTRv-PN, defined by Coutinho Stage 1-2, a documented TTR sequence variant, and signs/symptoms consistent with polyneuropathy (Neuropathy Impairment Score $\geq$10 and $\leq$130). Patients were assigned 6:1 to eplontersen 45 mg subcutaneously every 4 weeks (n=144) or inotersen 300 mg once weekly (n=24) until Week 35, after which all patients received eplontersen 45 mg subcutaneously every 4 weeks. Serum NfL (sNfL) levels were measured using the Protein Simple ELLA NfL assay at baseline, Day 1, and regular intervals through Week 85.
Results: Preliminary results in a subset of the NEURO-TTRansform study population show that baseline sNfL levels were, on average, elevated compared with healthy populations. There was a trend towards decreasing sNfL levels among patients receiving eplontersen through Week 85. Full results will be presented.
Conclusion: Results from this analysis will provide longitudinal data on sNfL as a potential biomarker in patients with ATTRv-PN treated with eplontersen.

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EPR-226

Prevalence and Characteristics of Peripheral Neuropathy in Patients with Psoriasis and Psoriatic Arthritis

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Background and aims: To assess the prevalence and clinical features of peripheral neuropathy in patients with psoriasis and psoriatic arthritis.

Methods: Patients with psoriasis or psoriatic arthritis (n=100) control subjects (n=100) were consecutively enrolled. Clinical neuropathy was diagnosed when symptoms and signs of peripheral sensory or motor involvement were present. Nerve conduction study was performed to confirm the diagnosis. Patients with a confirmed peripheral neuropathy also underwent laboratory and nerve ultrasound investigations.

Results: One hundred patients with psoriasis or psoriatic arthritis and 81 controls were enrolled so far. Polyneuropathy was found in 9 (9%) patients (4 with psoriasis, 5 with psoriatic arthritis) and in none controls (p=0.0056). Polyneuropathy was axonal, length-dependent, symmetric, sensory or sensorimotor in all patients. Polyneuropathy was significantly prevalent in both patients with psoriasis and psoriatic arthritis (p=0.0016 and p=0.0004, respectively). When excluding patients with an alternative cause for the polyneuropathy, the frequency of polyneuropathy in patients with psoriasis or psoriatic arthritis still remained significantly increased (p=0.045). In multivariate analysis, none of the factor examined (comorbidities, disease duration, medications) were significantly associated with an increased risk of polyneuropathy. Frequency of carpal tunnel syndrome did not differ between patients with psoriasis or psoriatic arthritis and controls.

Conclusion: Preliminary results of our study show that psoriasis and psoriatic arthritis are associated with an increased risk of polyneuropathy. The risk seems to be partly secondary to the comorbidities frequently encountered in psoriasis and psoriatic arthritis and partly attributable to direct mechanisms.

Disclosure: No potential competing interest was reported by the authors.

EPR-227

Cerebrospinal-fluid tau levels as a marker of axonal damage in Guillain-Barré syndrome

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Background and aims: Inflammatory neuropathies (INs) are acquired disorders of peripheral nerves. Since these diseases usually affect the proximal nerve roots, the pathogenic process may lead to cerebrospinal fluid (CSF) biomarker alterations. High CSF levels of neurofilament light chain have been reported in Guillain-Barré syndrome (GBS) and in chronic inflammatory demyelinating polyneuropathy (CIDP), while the role of other biomarkers, including the CSF total-tau (t-tau), is still uncertain. We aimed to investigate the value of CSF t-tau levels in revealing neuronal damage in INs.
Methods: We included n=17 patients with INs diagnosed at the Neurology Unit of the Sant'Andrea Hospital, Vercelli, Italy. Patients were classified according to the clinical presentation, and evidence of albumin-cytologic dissociation, in GBS (n=12) and CIDP (n=5). Nerve conduction studies (NCS) were conducted in the upper and lower limbs. T-tau levels were measured in the CSF.
Results: GBS and CIDP groups were similar for age and sex. NCS studies showed a predominant demyelinating involvement in 67% of GBS patients. T-tau levels were significantly higher in the GBS than in the CIDP (218.4±90.9 vs. 125.3±59.6 pg/ml). Also, in the GBS, CSF t-tau levels were inversely correlated with the ulnar compound motor action potential (cMAP) amplitude.
Conclusion: The higher CSF t-tau levels in GBS compared to CIDP suggest a greater neuronal damage in acute INs than in chronic ones, possibly related to a temporary higher permeability of the blood-brain barrier. The correlation with the cMAP amplitude supports the hypothesis of an acute axonal damage, even in predominantly demyelinating forms.
Disclosure: Nothing to disclose.

EPR-228

A family with subclinical Charcot-Marie-Tooth Disease associated with a mutation in the MPZ gene

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Background and aims: There are now over 100 genes that are known to be responsible for various forms of Charcot–Marie–Tooth disease (CMT), among which the MPZ gene is one of the commonest. Mutations in this gene are mostly associated with CMT 1B but they are also a well-known cause of more severe and early-onset phenotypes, such as Congenital Hypomyelinating Syndrome and Dejerine-Sottas Syndrome.
Methods: An apparently healthy 26-year-old woman undertook an electromyography due to minor unrelated symptoms. Nerve conduction studies (NCS) were highly suggestive of a hereditary polyneuropathy, more specifically an intermediate type of CMT. There were no symptoms attributable to a neuropathy, nor there were any abnormal findings in the neurological examination (e.g. pes cavus, weakness or atrophy foot intrinsic muscles). Deep tendon reflexes were normal throughout.
Results: Her father - also asymptomatic - displayed similar results in NCS. After negative screening for PMP22 gene duplication, a gene panel identified a novel frameshift (c.275dup) heterozygous mutation in MPZ gene. After a 5-year follow-up, both subjects remain without signs of CMT.
Conclusion: To the best of our knowledge, this is the first documented case of MPZ gene-associated CMT without clinical signs of the disease. This is particularly intriguing because this mutation probably results in a premature stop codon which should translate into a truncated and non functional protein. This case broadens the phenotypical spectrum of neuropathies associated with the MPZ gene. Moreover, it suggests that phenotypic expression of MPZ gene mutations might be co-determined by other genetic or epigenetic factors.
Disclosure: The authors deny having a conflict of interest.

EPR-229

A prospective open-label trial with rituximab in patients with CIDP not responding to conventional immune therapies

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) often responds to immune therapies including steroids, intravenous immunoglobulins or plasma exchange. These therapies needs to be continued for a long period of time to avoid deterioration after therapy suspension.
Methods: We performed and open-label prospective study with intravenous rituximab (1 gram, day 1 and 15) on 20 patients with CIDP not responsive to adequate dose of at least two conventional therapies including steroids, immunoglobulins or plasma exchange. The primary end-point was the proportion of patients improving by at least one point on the INCAT scale or two points on the MRC force scale or four points on the RODs scale, 6 months after therapy with rituximab. Secondary endpoints included the proportion of patients that: improved 12 months after therapy; improved after 6 and 12 months in electrophysiological parameters; discontinued rituximab due to side effects; improved the quality of life after 6 and 12 months. The median duration of clinical improvement after therapy was also analyzed
Results: 19 patients were included two of whom retired their consent before treatment due to concern related to COVID-19. All the 17 treated patients (9 male, 8 female, median age 54 years, range 49–70, median disease duration 75 months, range 39–192) completed the treatment and will complete the 6-month follow-up by March 2023. None of the treated patients retired for side effects or voluntary withdrawal.
Conclusion: Rituximab was a safe therapy in patients with CIDP. Data on the efficacy of rituximab therapy will be presented at the congress.
Disclosure: Supported by Italian Ministry of Health, Ricerca Finalizzata, Grant RF-2016-02361887

EPR-230

Charcot-Marie-tooth disease and sport activities: a worldwide survey

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Background and aims: Charcot-Marie-Tooth (CMT) disease is the most common genetic neuromuscular disease. The symptomatology involves distal muscle weakness, provoking different degrees of disability. The practice of recreational activities could promote wellness and quality of life. The aim of this study is to investigate sport practice among the CMT population.
Methods: We designed an online questionnaire for CMT patients to investigate sport practice and recreational activities and we spread it worldwide with the support of many patient advocacy groups. We included all hereditary neuropathies.
Results: A total of 290 CMT people responded to the survey. The most frequent age-range was 46 to 55 years (30%). 46,9% of them were from Italy, the remaining were from Europe, United States and Australia. The most of them stated to practice home exercises (28,3%) or individual physical therapy (23,8%). Only the 3,8% stated to not practice any activity. The frequency of the exercises was 2,8±1,9 days per week. No significant differences have been observed among age range.
Conclusion: TThe majority of CMT persons stated to practice many different wellness activities. If we consider that the OMS guidelines suggest a minimum of 150 minutes of a moderate aerobic activity per week, most of them does not reach the minimum of practice. Since literature lacks of studies about sport practice in people with CMT, we need further study to understand what kind of activity is beneficial and raise awareness in CMT population.
Disclosure: Nothing to disclose.

EPR-231

Expanding the phenotype of GARS1 mutations

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Background and aims: Glycyl-TRNA Synthetase 1 (GARS1) mutations have been described as a cause of sensory and motor axonal neuropathy, as well as an exclusively motor distal neuropathy.
Methods: This cross-sectional retrospective observational study includes patients with GARS1 mutations evaluated in a neuropathy reference center in Spain. We reviewed the clinical, examination findings, as well as nerve conduction and muscle magnetic resonance imaging (MR) of the lower limbs. Six patients underwent a skin biopsy.
Results: We identified ten patients (two families) with the same c.794C>T (p. Ser265Phe) missense mutation in GARS1. All affected individuals developed a distal hereditary motor neuropathy, affecting the intrinsic hand muscles before or at the same time as the distal leg musculature. Nerve conduction studies revealed a reduction in compound muscle action potentials (CMAP) in all nerves, being more prominent in the median and peroneal nerves. In 4 patients we could evidence a 'split hand' phenomenon with reduction ulnar nerve CMAP to the first interosseous compared to the abductor digiti minimi. Most patients referred distal pinprick sensory loss on examination but all had normal sensory nerve conductions on electrophysiological testing. Muscle MR was consistent with a length dependent neuropathy, with fatty muscle infiltration in lower limb muscles. Skin biopsies revealed a reduction of intraepidermal nerve fiber density in 5/6 patients.
Conclusion: Mutations in GARS1 may produce a distal motor phenotype with a 'split hand' and sensory disturbances even with normal nerve conduction studies, which may in part be explained by a small nerve fiber reduction.
Disclosure: Nothing to disclose.

EPR-232

DRP2 mutations as a cause of Charcot Marie Tooth in Spain

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Background and aims: Dystrophin related protein 2 (DRP2) mutations have been described as a rare cause of intermediate X-linked Charcot-Marie-Tooth (CMT) disease
Methods: This study includes CMT patients with DRP2 mutations evaluated in 5 centers throughout Spain. We collected a standardized history and symptom questionnaire. Nerve conduction studies, muscle magnetic resonance imaging (MR), and nerve echography were performed. Two patients underwent a skin biopsy destined for immunofluorescence and electron microscope techniques, and another a sural nerve and muscle biopsy.
Results: We identified seven symptomatic CMT patients with 4 different novel DRP2 variants, two missense and two deletions. The variants were classified as probably pathogenic according to ACMGcriteria. Skin pathology revealed absence of DRP2 in myelinated fibers, as well as decompaction of myelin, axonal vacuoles and inclusion bodies near the Cajal bands (Figure 1). All affected males were symptomatic except a young adult with unequivocal findings in ancillary testing and the five carrier women evaluated were normal. Symptom onset was in the third-fifth decade, with distal lower limb weakness, unsteadiness and tripping. Progression was mild in four patients, but the other three developed prominent distal weakness and sensory loss leading to important disability. Nerve conduction studies were consistent with intermediate-CMT and muscle MR with length dependent fatty muscle infiltration. Nerve echography revealed an homogeneous increase in the cross sectional area of cervical nerve roots, but not in more distal nerves (Figure 2).

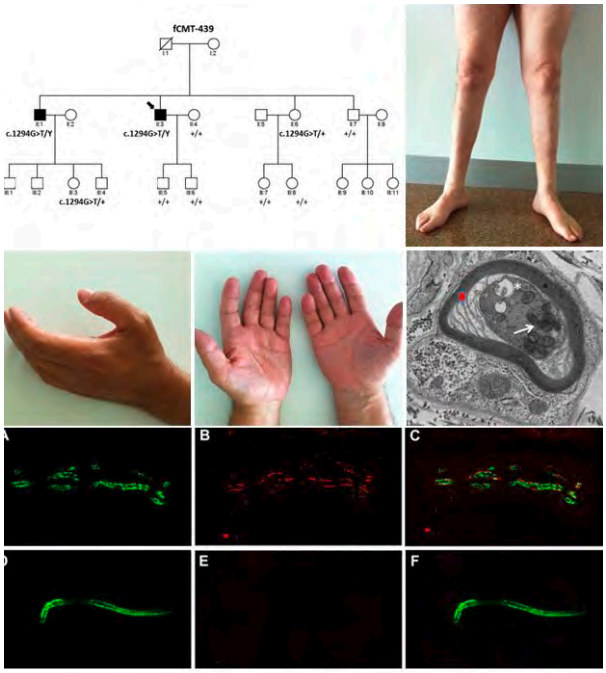

Figure 1: Pedigree, photographs of the hands and distal legs, and skin biopsy of family fCMT-459

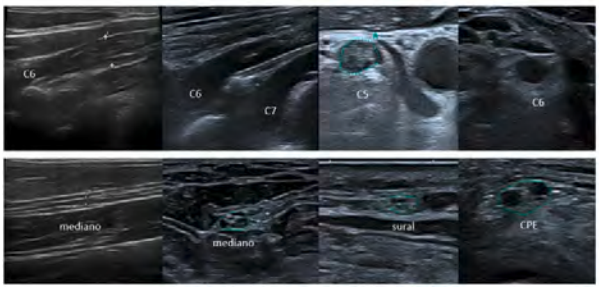

Figure 2: Nerve echography of cervical nerve roots and distal nerves

Conclusion: The description of this series confirms the pathogenic role of DRP2 in CMT and expands the known phenotype

Disclosure: Nothing to disclose.

Neurorehabilitation; Spinal cord and root disorders

EPR-233

The positive effects of aerobic capacity on fatigue are mediated by thalamic nuclei in people with multiple sclerosis

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Background and aims: Fatigue is a common symptom in people with multiple sclerosis (pwMS) affecting mental and physical domains. Aerobic capacity (AC), disability and cognitive impairments contribute to fatigue perception. The thalamus, with its nuclei related to motor and cognitive processes, has been consistently involved in fatigue pathogenesis. The aim of the study was to identify associations between thalamic nuclei volumes and fatigue and to explore whether the effect of AC on this symptom is mediated by the thalamus in pwMS.
Methods: In this cross-sectional study, Modified Fatigue Impact Scale (MFIS), Expanded Disability Status Scale (EDSS), Symbol Digit Modalities Test (SDMT), maximal oxygen uptake (VO2max) and brain MRI data of thalamic volumes were collected from 74 pwMS. A group of 47 sex- and age-matched healthy controls (HC) was included for MRI comparison, with a subgroup of 10 presenting VO2max values.
Results: In pwMS, fatigue was associated with atrophy of left latero-dorsal nucleus (left-Dor) (r-value=-0.278; p≤0.018), with a stronger association with cognitive rather than physical fatigue. More severe disability (r-value=0.355; p=0.004) and worse cognitive processing speed (r-value=-0.353; p=0.003) were associated with more severe fatigue and diffuse thalamic atrophy. In contrast, higher aerobic capacity was associated with less severe fatigue (r-value=-0.263; p=0.027) and atrophy of the left-Dor (r-value=-0.288; p=0.015). A mediation model showed that in pwMS there was a significant indirect effect of VO2max on fatigue through the left-Dor nucleus (b =-0.305, CI [-0.678;-0.005]) (Figure 1).

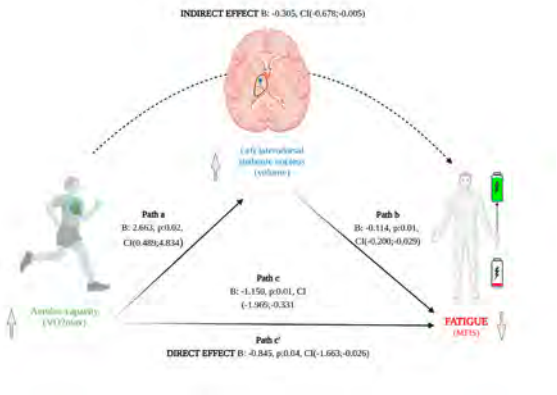

Figure 1. Direct and indirect pathway of aerobic capacity on fatigue, mediated by left laterodorsal thalamic nucleus. B: b-value, CI: confidence interval, VO2max: maximal consumption of oxygen, p: p-value, MFIS: modified fatigue impact scale.

Conclusion: AC exerts a positive effect on fatigue in MS, which is mediated by a preserved volume of the left-Dor.
Disclosure: Funding. The study has been partially supported by Italian Ministry of Health (GR-2019-12369599).

EPR-234

Ultrasound-Guided Percutaneous electroneurostimulation in treatment of Meralgia paresthetica

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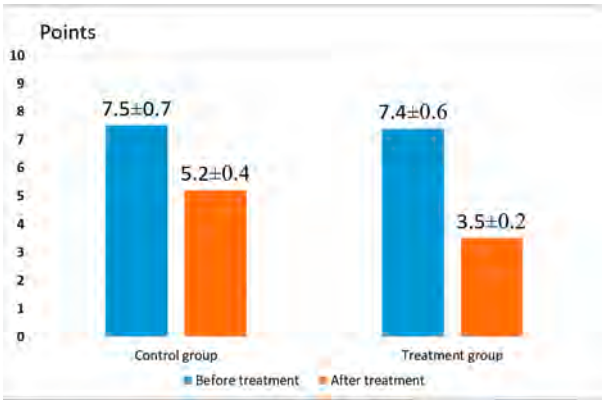
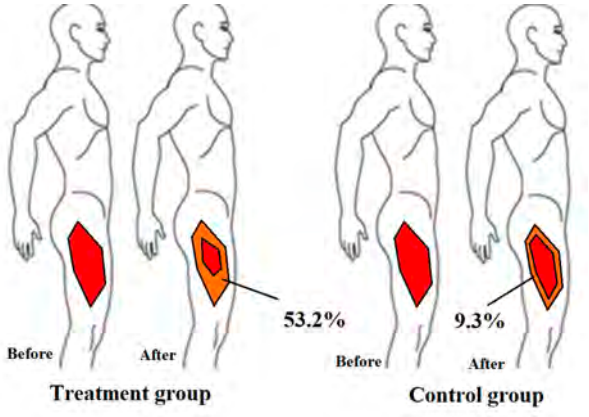
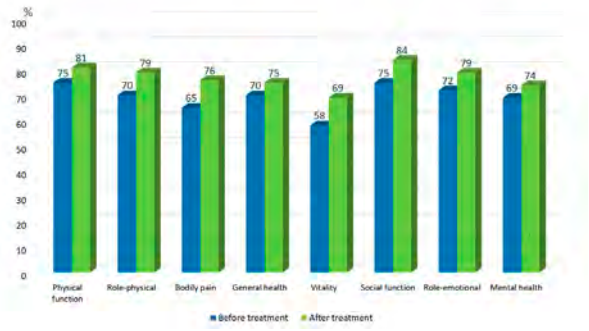
Background and aims: Meralgia Paresthetica (MP) is caused by damage to the Lateral Femoral Cutaneous Nerve almost at the level of the inguinal ligament.
Methods: Our study included 20 patients with MP, aged 30 to 50 years (mean 39±0.4 years) with a disease duration of 2 to 5 years (mean 3.7±0.2years). All patients were obese with a mean body mass index of 32±0.7. All patients were treated with ultrasound-guided percutaneous electro-neurostimulation (UGPE) of the lateral femoral cutaneous nerve (LFCN). The needle form cathode was inserted next to the nerve and the anode was fixed over the anterior superior iliac spine. All patients underwent standard medical therapy. In addition to drug therapy, 10 patients underwent electrical stimulation using 1 Hz and 100 Hz current (main group) and 10 patients underwent a course of sham stimulation (control group).
Results: After treatment, the severity of pain syndrome decreased in the main group by 30.7% and in the treatment group by 52.7%. The area of hypoesthesia decreased in the control group by 9.3% and in the treatment group by 53.2%. SF-36 quality of life improved in the treatment group by 11.1% on physical health scales and by 11.7% on mental health scales. At the same time, there was no significant improvement in quality of life in control group.



The intensity of positive sensory symptoms on a visual analogue scale before and after treatment in the control and treatment groups



Percentage reduction in the area of hypoesthesia after treatment in control and treatment groups



Dynamics of the quality of life with the use of SF-36 after UGPE of LFCN in treatment group

Conclusion: UGPE of LFCN is highly effective in the treatment of MP and leads to a reduction in pain and positive sensory symptoms, restoration of sensory deficits and a significant improvement in the quality of life.
Disclosure: Nothing to disclose.

EPR-235

A dangerous method to have a laugh: subacute combined degeneration related to nitrous oxide abuse

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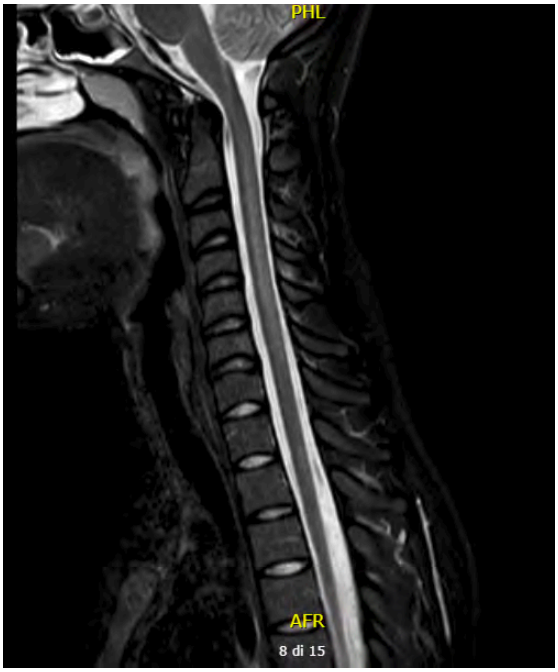
Background and aims: Subacute combined degeneration (SCD) of the spinal cord is a rare acquired myelopathy caused by vitamin B12 deficiency. Herein we describe a case of 20-year-old female who developed SCD after a prolonged recreational use of nitrous oxide.

Methods: The patient complained a history of acroparaesthesia started 3 months before the admission. Subsequently, she also developed an impaired and unsteady gait needing support to walk. At the admission the neurological examination showed ataxic features at the lower limbs with absent deep tendon reflex; gait was wide and uncertain, Romberg test was positive. Upper limbs were unremarkable except for distal paraesthesia. Strength was normal. After a deep interview she admitted to have started a recreational use of laughing gas of at least 20 balloons per day for almost eight months. We performed blood tests, electroneurography, sensitive evoked potentials and brain-spinal MRI.

Results: Laboratory testing showed mild anemia associated with Vitamin B12 deficiency (149 pg/ml) and high level of homocysteine and iron deficiency. Infective, celiac, autoimmune gastritis screening were negative. Electroneurography confirmed a sensory-motor axonal PNP at lower limbs with normal electromyography. SEPs showed reduced N20 and P40 amplitude and increased central conduction time. Cervical spinal MRI showed a C1-C7 T2 hyperintensity of dorsal columns with the inverted "V" sign confirming SCD. Supplementation of high dose of Vitamin B12 was promptly started.



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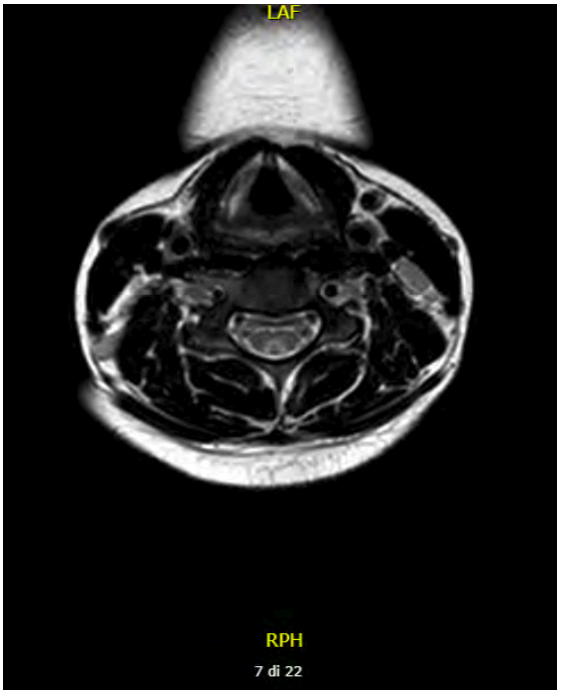

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Conclusion: Nitrous oxide is a rising cheap, not routinely detectable and available recreational drug among young with euphoric properties. It irreversibly inactivates cobalamin with serious neurological sequelae. Drug abuse must be carefully investigated.

Disclosure: Nothing to disclose.

EPR-236

Depression moderates the effect of rehabilitation on recovery of autonomy in daily life activities after stroke

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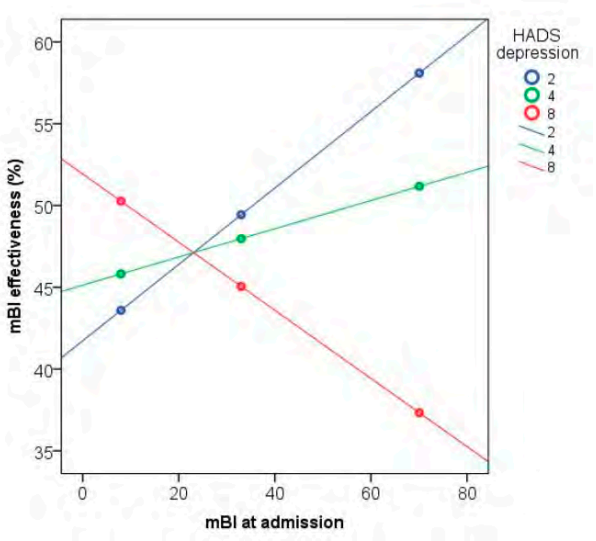
Background and aims: Previous studies showed that depression acts as an independent factor in functional recovery after stroke1. We aimed to test depression as a moderator of the effectiveness of rehabilitation on recovery of physical disability.
Methods: From a dataset of individuals admitted in a rehabilitation unit of IRCCS Don Gnocchi and enrolled in a multicenter prospective observational study (RIPS)2 we considered 81 patients who had assessment of depression by HADS. All patents underwent a comprehensive evidence-based Integrated rehabilitation Care Pathway. Clinical and neurological data were collected at the admission (T0) and discharge (T1). As outcome of our analysis, we considered the effectiveness of recovery on the modified Barthel Index (mBI), measured as actual improvement divided by potential improvement. Moderation analysis was performed by using the PROCESS macro for SPSS using the bootstrapping procedure (Hayes 2013).
Results: The relationship between the functional status at admission and the functional recovery after rehabilitation was moderated by the presence of depression (p=0.047). This association was independent by age, NIHSS score at admission. When analyzing our data by the JN approach (Hayes 2013), the effect of depression on the relationship between mBI at admission and mBI effectiveness at discharge was significant only in absence of depression. In particular, the HADS score up to which the moderator had a significant moderating effect was 5.9.



Moderation effect of the Hospital Anxiety and Depression Scale (HADS) on the relationship between modified Barthel Index (mBI) at admission and mBI effectiveness at discharge.
Conclusion: Correlation between mBI at baseline and mBI effectiveness is valid only for non-depressed patients. This evidence support the opportunity to screen stroke patients for depression.
Disclosure: The authors declare no commercial or financial relationships that could be construed as a potential conflict of interest.

EPR-237

Brain-Computer Interface for Lower Extremity Rehabilitation in Chronic Stroke

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Background and aims: Brain-computer interfaces which trigger functional electrical stimulation (FES) have been shown to be effective in facilitating motor recovery of the upper extremity after stroke. Here we investigated whether a BCI based on motor imagery, FES and avatar feedback is able to facilitate lower extremity motor function improvements in chronic stroke patients.
Methods: Ten chronic stroke patients with hemiparesis in the lower extremity participated in 25 BCI sessions. During the BCI therapy patients performed dorsiflexion motor imagery of their paretic ankle and healthy wrist and received FES and avatar feedback. Assessments were carried out, before the first and after the last therapy session to evaluate the patients' motor function. The 10-meter walk test (10MWT), and the Timed Up and Go test (TUG).
Results: All ten patients improved in their self-selected 10MWT performance by 1.8 [1.4; 4.1] seconds in median [IQR] (p=0.002) and patients who were able to perform the fast velocity 10MWT improved by 1.3[0.7; 2.2] seconds (p=0.030). Furthermore, all ten patients improved their TUG performance by 5.6 (6.2) seconds in mean (SD) (p=0.027). One patient was not able to perform the TUG test before the BCI treatment but was able to do so after. Patients' 10MWT and TUG test performance did not deteriorate one month after the BCI treatment.
Conclusion: These results provide preliminary evidence for the feasibility and efficacy of MI and FES-based BCIs in lower extremity treatment in chronic stroke patients. Furthermore, patients' improvements did not deteriorate one month after the BCI treatment.
Disclosure: SS, MS-R, WC, RO and FF are employed at g.tec medical engineering. CG is the CEO of g.tec medical engineering, who developed and sells the BCI system used in this study.

EPR-238

Atypical Hirayama Syndrome with dorsal spinal epidural lipomatosis and lateral detachment of the dural sac

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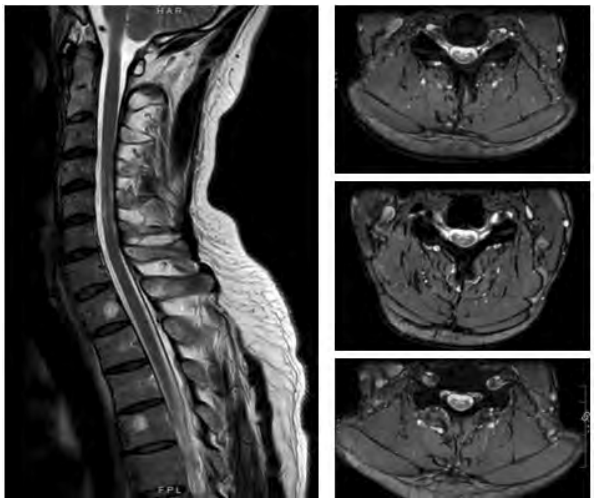
Background and aims: Hirayama disease (HD) is a flexion-induced myelopathy, characterized by the juvenile onset of unilateral or asymmetric weakness and amyotrophy of the hand and ulnar forearm, predominantly affecting C8–T, most commonly seen in males in Asia(1,2). The spinal epidural lipomatosis (SEL) is characterized by an overgrowth of unencapsulated adipose tissue in the extradural space(3).

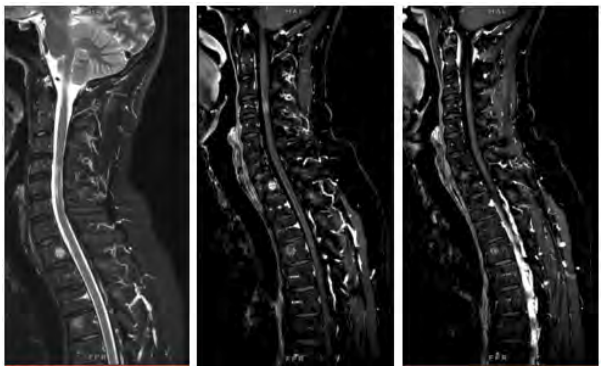
Methods: We report a case of HD associated to dorsal SEL, who had focal weakness and wasting confined to scapular and proximal upper muscles. Dynamic flexion magnetic resonance imaging (DfMRI) is the imaging modality of choice to diagnose HD(4), revealing forward migration of dura with enlargement of posterior epidural space(2,5).

Results: The patient experienced repeated disease relapse with an interval of clinical stability, as occasionally reported(8). DfMRI revealed a segmentary detachment between the posterior dural sac and the subjacent lamina at the C3–C5 section. A "snake-eye appearance" was found as a symmetrical bilateral high-signal-intensity lesion enhanced by cervical flexion(7). Electromyography revealed a progressive neuronopathic impairment, mainly involving both the upper limbs.



Cervical and dorsal MRI. On T2-weighted imaging (T2WI), there is a markedly hyperintense signal, in the C4-C6 section of the medullary cord. The lesion involves predominantly the front horns of the gray matter, with the "snake-eye appearance".

Conclusion: The current case fulfils the recent Huashan diagnostic criteria for HD(1). The prominent shifting of dural sac in C3-5 segment by dfMRI may explain the unusual distribution of the disease, with the atypical involvement of the proximal upper limb(6). Adipose deposition may cause mass effect or venous engorgement, and could explain the unusual direction of the epidural detachment(9). Both neurophysiological and neuroimaging findings confirmed the diagnosis and indicated an irreversible lesion, a poor prognosis, and the need for timely surgical intervention (7,8).



In the dorsal area, there is a discrete increase in the representation of the posterior epidural adipose tissue and significant blockage of the epidural venous plexus, in the posterior and postero-lateral in the two sides (contrast-enhanced T1 sequences).

Disclosure: The authors reveal no competing interests.

EPR-239

Efficacy of home based-restorative cognitive training on cognitive impairment in MS patients

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Background and aims: The benefits of home-based restorative cognitive training (R-CT) on different levels of cognitive impairment (CI) and their duration over time are still unclear in multiple sclerosis (MS) and were investigated in the present study.

Methods: We recruited 38 MS patients, 23 with mild CI (MS-MCI, patients with 1 altered cognitive test) and 15 with severe CI (MS-SCI, patients with ≥2 altered cognitive tests). They completed a three-month home-based R-CT consisting of daily online training sessions. Outcome measures included neuropsychological assessment (BRB-N, Proceed Speed Test, and Wisconsin Card Sorting Test), anxiety and depression (HADS), fatigue (MFIS) and quality of life (QoL; MSQoL-54) investigations. The set of assessments was performed at baseline, month 3 (end of treatment), and at month 6 (end of observation period).

Results: Compared to baseline, patients with MS-SCI improved memory and attention functions at month 3 ($p=0.002$ and $p=0.027$, respectively) and 6 (both $p<0.001$), while patients with MS-MCI patients showed no significant improvement of memory, attention and executive abilities at month 3 ($p<0.05$), but significantly improved at month 6 ($p=0.021$, $p<0.001$ and $p=0.010$). At month 3 and 6, both groups reported reduced cognitive fatigue ($p<0.001$ and $p=0.012$), while MS-SCI patients showed lower anxiety levels ($p=0.016$), and MS-MCI indicated improved QoL ($p=0.032$).

Conclusion: Home based R-CT improves cognitive functions in both MS-SCI and MS-MCI patients, with a more rapid effect in MS-SCI. In both groups, R-CT associated benefits were not limited to the trained cognitive domains, but also extend to emotional-behavioural functioning.

Disclosure: Ente Ospedaliero Cantonale (employer) received compensation for C.Z.'s and C.G.'s speaking activities, consulting fees, or research grants from Almirall, Biogen Idec, Bristol Meyer Squibb, Lundbeck, Merck, Novartis, Sanofi, Teva Pharma, Roche. G.C. R. receives research grant compensation from Biogen Idec. This study was supported by Biogen.

EPR-240

Action observation and motor imagery improve motor imagery abilities in Parkinson's disease – a functional MRI study

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Background and aims: To assess motor imagery (MI) changes and brain functional reorganization after 6 weeks of action observation training (AOT) and MI associated with increasingly difficult gait/balance exercises in Parkinson's disease patients with postural instability and gait disorders (PD-PIGD).

Methods: 25 PD-PIGD patients were randomized into two groups: the DUAL-TASK+AOT-MI group performed 6 weeks of gait/balance exercises including dual-tasks combined with AOT and MI; DUAL-TASK group performed the same exercises combined with watching landscape videos. MI was assessed using the Kinesthetic and Visual Imagery Questionnaire (KVIQ). 23 healthy controls were included. All subjects performed a MI functional MRI task: subjects were asked to watch first-person perspective videos representing challenging gait/balance tasks and mentally simulate to move themselves in each condition.

Results: At baseline, during MI fMRI task, PD-PIGD patients showed reduced activity of sensorimotor cortex, temporal and cerebellar areas relative to controls. After training, both groups showed an improvement of kinesthetic MI. DUAL-TASK+AOT-MI group showed improvement also of visual MI and total KVIQ score together with increased activity of cerebellum VIII-IX, anterior cingulate and fronto-temporal areas and reduced recruitment of cerebellum VI and crus-I. DUAL-TASK group showed increased recruitment of hippocampal/parahippocampal and occipital areas and reduced activity of cerebellum crus-I. DUAL-TASK+AOT-MI relative to DUAL-TASK group had increased activity of cerebellar lobules VIII-IX. In DUAL-TASK+AOT-MI group, KVIQ improvement correlated with increased activity of cerebellum IX and anterior cingulate, and reduced activity of crus-I.

Conclusion: AOT-MI improves MI abilities in PD-PIGD patients, promoting the functional plasticity of brain areas involved in MI processes and gait/balance control.

Disclosure: Nothing to disclose.

EPR-241

Influence of cognition and fatigue on the correlation between objective and subjective upper limb measure in pwMS

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Background and aims: Small correlation between 9-Hole Peg Test (9-HPT), Box and Block test (BBT),Hand Grip Strength (HGS) and Manual Ability Measure36(MAM-36) was reported.The study aimed at evaluate influence of cognition and fatigue on correlations between objective and subjective upper limb(UL) measures.

Methods: Assessments: 9-HPT, BBT, HGS, MAM-36, Modified Fatigue Impact Scale (MFIS) and Symbol Digit Modalities Test(SDMT).

Results: Sample consisted of 200 PwMS: 132F; age 51.66(13.60); disease duration 14.75(10.91); 105RRMS, 39PPMS, 56SPMS, EDSS 4.89 (1.92). Tests scores: 9-HPT-R 36.41(30.24)s, 9-HPT-L 40.86(37.35)s, BBT-R 45.48(15.87)b, BBT-L 44.70(15.39)b, HGS-R 20.01(9.91), HGS-L 18.11(8.94), SDMT 38.02(14.07), MFIS 33.01(18.43).Fatigue showed correlations with 9-HPT (L:r=0.167, $p<0.05$), BBT (R: r=-0.208, $p<0.01$; L:r=-0.216, $p<0.01$) and HGS (R:r=-0.178, $p<0.05$; L:r=-0.228, $p<0.01$) on both arms, and with MAM36 (r=-0.490, $p<0.01$). SDMT correlated with MAM-36 (r=0.170, $p<0.05$), BBT for both arms(R:r=0.214, $p<0.01$; L:r=0.261, $p<0.01$), and 9HPT on both arms (R: r=-0.235, $p<0.01$; L: r=-0.307, $p<0.01$). No correlations between HGS and SDMT. Correlation between MAM-36 and objective UL measures showed minor variations based on the level of cognitive impairment and fatigue. Correlations between 9-HPT and MAM36 were stronger among patients without cognitive impairment (SMDT>48) (i: R: r=-0.310, p=0.000; L:r=-0.271, p=0.01; n-i: R: r=-0.592, p=0.000; L:r=-0.531, p=0.000; p-value<0.001).

Conclusion: No significant differences across the groups in the correlation between the MAM-36, HGS and BBT. Stratifying the sample for MFIS cut-off (MFIS>38) no significant differences across the groups between MAM-36 and objective UL measures were observed. Cognitive function were evaluated only using SDMT, cognition, but not fatigue, may influence correlation between objective and subjective UL measure.

Disclosure: Nothing to disclose.

Peripheral nerve disorders

EPR-242

Immune-related neuropathies: different phenotypes require different therapeutic approaches?

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Background and aims: Immune checkpoint inhibitors (ICIs) are associated with a broad spectrum of neurotoxicities. ICI-related neuropathies are estimated to occur in 0.1-1.2% of patients. Guidelines recommend prompt discontinuation of the ICIs, and steroids depending upon the severity of the adverse event. However, the management of severe and steroid-refractory cases is less standardised, and IVIg have been suggested in patients with demyelinating polyradiculoneuropathies.
Methods: We report a retrospective series of patients with an ICI-related neuropathy, addressed to our department between 2016 and 2021, with the intent to describe their clinical and para-clinical features and the outcome after ICI discontinuation and steroids.
Results: We identified 12 cases. The most common neuropathy phenotypes were a length-dependent sensory(motor) axonal neuropathy (n=5 patients) and a meningo-radiculoneuritis (n=5 patients). The delay of symptoms onset from ICI initiation was significantly longer in length-dependent axonal neuropathy cases compared with meningo-radiculoneuritis ones. A higher level of disability was reported in the majority of patients with meningo-radiculoneuritis (4 out of 5) and only in one patient with peripheral neuropathy. ICIs were stopped in all patients and steroids started in 7 patients, leading to a favorable outcome (complete recovery=7, partial recovery=4, stable disability=1).
Conclusion: We identified two main phenotypes of ICI-related neuropathy: length-dependent sensory(motor) axonal neuropathies and meningo-radiculoneuritis, the latter characterized by an earlier onset and a more severe clinical presentation. The favorable outcome of this series underlines the necessity of the ICI discontinuation and suggests the efficacy of corticosteroids for all types of neuropathies, and do not support the requirement for IgIV.
Disclosure: Yes

EPR-243

Assessment of clinical diagnostic criteria for CIDP variants: what to expect from the 2021 EAN/PNS clinical criteria

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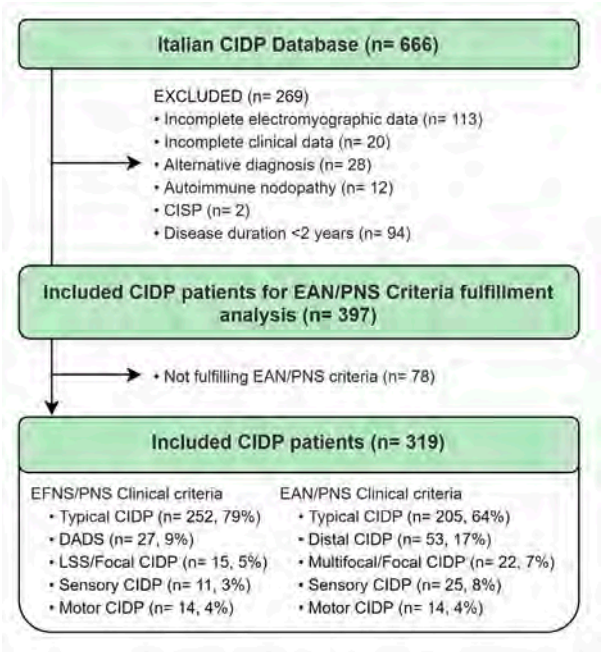
Background and aims: There are different criteria for the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) variants in the literature. This led to conflicting results across studies on their frequency, clinical presentation, outcome, and treatment response.

Methods: We compared the clinical criteria for CIDP variants of the 2021 EAN/PNS guidelines with the criteria for atypical CIDP of the 2010 EFNS/PNS guidelines in 319 patients included in the Italian CIDP database who fulfilled the EAN/PNS electrodiagnostic criteria for CIDP.

Results: The EAN/PNS criteria increased the prevalence of CIDP variants from 21% to 36%. When compared to corresponding typical CIDP group, the 2010 EFNS/PNS and 2021 EAN/PNS criteria equally identified distinct patient populations. Multifocal, distal, and sensory CIDP had milder impairment and symptoms. Additionally, multifocal CIDP displayed male predominance, lower rate of hyperproteinorrachia, lower response to treatment and intravenous immunoglobulins. Distal CIDP patients were older at onset but showed similar treatment response. Sensory CIDP patients were older at onset and presented lower rates of distal latency prolongation and reduced conduction velocity, but a higher rate of prolonged F-wave latency. Motor CIDP presented a relapsing-remitting history and higher rates of prolonged F-wave latency.



Case selection flow-chart. LEGEND: CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CISP, chronic immune sensory polyradiculopathy; DADS, distal acquired demyelinating symmetric neuropathy; LSS, Lewis-Sumner syndrome.

Conclusion: The 2021 EAN/PNS clinical criteria enlarge the cohort of CIDP patients defined as variants but still identify distinct CIDP populations compared to the EFNS/PNS criteria. Since the EAN/PNS guidelines provide more definite criteria for the diagnosis of CIDP variants they better help to identify CIDP variants and should be used in future studies on patients with CIDP.

Disclosure: The study was supported by a Grant from Regione Lombardia, Italy, and by a Grant from Ministero della Salute, Ricerca Finalizzata (Progetto RF-2016-02361887). The study was also supported by unrestricted grants from Kedrion Biopharma (Italy), CSL Behring (Italy), Humanitas Clinical and Research Institute (Milan, Italy), and GBS-CIDP Foundation International (USA). The funders had no role in study design, data collection and analysis, decision to publish, or in the preparation of the manuscript.

EPR-244

Facilitated subcutaneous immunoglobulin 10% for CIDP: interim results from a long-term safety and tolerability study

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Background and aims: This prespecified interim analysis of ADVANCE-CIDP 3 evaluates long-term safety and efficacy of facilitated subcutaneous immunoglobulin (fSCIG; human immunoglobulin G [IgG] 10% with recombinant human hyaluronidase) in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Methods: ADVANCE-CIDP 3 (NCT02955355) is a long-term extension of ADVANCE-CIDP 1 (NCT02549170), a Phase 3, double-blind, randomized, placebo-controlled study that evaluated efficacy and safety/tolerability of fSCIG as maintenance therapy for CIDP. Patients completing 6 months without relapse in ADVANCE-CIDP 1 could enter ADVANCE-CIDP 3 and receive open-label fSCIG treatment. The primary outcome is safety. Efficacy is an exploratory outcome including evaluation of CIDP relapse (≥1-point increase from baseline at two consecutive timepoints in Inflammatory Neuropathy Cause and Treatment score).

Results: This interim analysis included 79 patients (mean age 53.9 years, 54.4% male) with total follow-up of 169 patient-years; 2,595 infusions were administered. Median exposure was 23 months (range: 0–61 months). Most AEs were mild or moderate, local and/or self-limiting, and consistent with the established fSCIG safety profile. Overall, 1,166 adverse events (AEs; 40 severe and 18 serious) occurred in 70 (88.6%) patients. Of these, 661 AEs (19 severe and 2 serious) were related to fSCIG. Systemic AEs (e.g. hemodynamic alterations) were infrequent. Overall, 5 patients relapsed; the 6-month relapse rate was 1.5%.

Conclusion: ADVANCE-CIDP 3 demonstrates favourable long-term safety and tolerability of fSCIG, and a low relapse rate, supporting its use as a maintenance treatment for CIDP.

Disclosure: Study/writing support funder: Takeda Development Center Americas, Inc./Takeda Pharmaceuticals International AG.

EPR-245

A comparative study of imaging parameters in patients with chronic inflammatory demyelinating polyneuropathy

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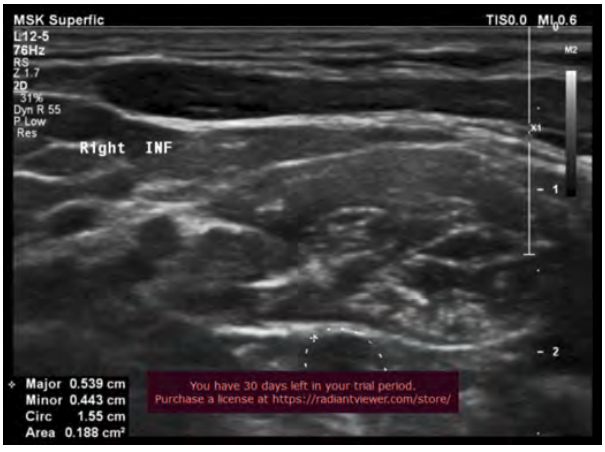
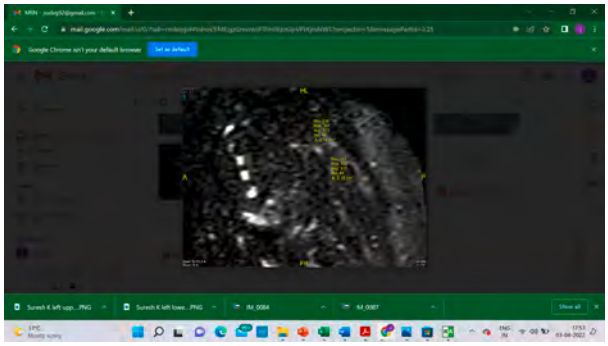
Background and aims: This study was conducted to systematically compare High-Resolution Ultrasound and Magnetic Resonance Neurography findings in patients with chronic inflammatory demyelinating polyneuropathy (CIDP). We also tried to find a correlation between imaging parameters, disease severity, and electrophysiological parameters in patients with CIDP.

Methods: In a prospective, observational, cross-sectional, monocentric study, twenty patients with typical features of CIDP by fulfilling the EFNS/PNS criteria for CIDP who were admitted to our hospital underwent High-Resolution Ultrasonography (HRUS) and Magnetic Resonance Neurography (MRN) of the brachial plexus by using standard protocols.

Results: Cross-sectional areas of the trunks of the brachial plexus through HRUS varied from 0.07 cm^2 to 0.21 cm^2, whereas they ranged from 0.08 cm^2 to 0.21 cm^2 using MRN. Spearman's correlation test was used to correlate the findings of HRUS and MRN. The correlation coefficient was high in all the correlations. There was a positive correlation between all the respective trunks which was statistically significant. Overall, electrophysiologically, there was a negative correlation between the CMAP and SNAP findings with the HRUS and MRN findings. Using Spearman's correlation test there was a positive correlation between the MRC sum score and imaging findings, and a variable correlation between INCAT disability score imaging findings, both of which were not statistically significant.



Cross-sectional area of the right inferior trunk through high-resolution ultrasound of patient "A"



Cross-sectional area of the right superior and middle trunk through M R Neurography of patient “A”

Rho and p-value (*)	MRN of right superior trunk	MRN of right middle trunk	MRN of right inferior trunk	MRN of left superior trunk	MRN of left middle trunk	MRN of left inferior trunk
HRUS of right superior trunk	0.945 (<0.001)	0.713	0.667	0.487	0.732	0.706
HRUS of right middle trunk	0.525	0.950 (<0.001)	0.609	0.323	0.569	0.579
HRUS of right inferior trunk	0.684	0.634	0.992 (<0.001)	0.508	0.622	0.755
HRUS of left superior trunk	0.720	0.469	0.699	0.890 (<0.001)	0.682	0.767
HRUS of left middle trunk	0.681	0.697	0.514	0.593	0.931 (<0.001)	0.731
HRUS of left inferior trunk	0.790	0.720	0.826	0.657	0.779	0.984 (<0.001)

Spearman’s rho test for correlation between high-resolution ultrasound and magnetic resonance neurography in cases

Conclusion: Brachial plexus sonography could complement MRI in the diagnostic work-up of patients with CIDP. Our results indicate that brachial plexus sonography can be useful as a bedside diagnostic tool to assess plexus enlargement in patients with CIDP.
Disclosure: Nothing to disclose.

EPR-246

IgA-related neuropathies in a cohort of IgA monoclonal gammopathy: red flags for the diagnosis of treatable conditions

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Background and aims: IgA-related neuropathies (IgA-PN), mainly AL amyloidosis and POEMS syndrome, are severe conditions whose prognosis depends on early diagnosis. They remain a diagnostic challenge. Clues are needed to distinguish them from IgA-unrelated neuropathies in everyday practice. Our objective is to identify the key features of IgA-PN.
Methods: We retrospectively analyzed the neurological and hematological features in a bicentric cohort of patients diagnosed with monoclonal IgA and peripheral neuropathy between 2016 and 2022. After excluding multiple myeloma chemotherapy-induced neuropathies, we classified the patients into two groups: IgA-PN and IgA-unrelated neuropathies. We compared their clinical, neurophysiological, and biological characteristics using keywords.
Results: There were 29 patients with IgA-PN (14 AL amyloidosis, 14 POEMS syndrome, one vasculitis) and 58 with IgA-unrelated neuropathies [main etiologies: diabetes (23), hereditary (8), alcoholic (7), and uremic (5)]. IgA-PN presented a faster course (<6 months: 70% vs. 24%, p<0.001), more frequent motor deficit (50% vs. 18%, p<0.01), autonomic manifestations (41% vs. 9%, p<0.001), walking disability (62% vs. 32%, p<0.01), and demyelinating pattern on nerve conduction studies (41% vs. 10%, p<0.001). The IgA blood level was not significantly higher in IgA-PN. Multivariate analysis showed three independent features related to IgA-PN: younger age at diagnosis (mean 58 vs. 66 years, p=0.001), impaired general condition (62% vs. 14%, p<0.001), and a lambda light chain (93% vs. 51%, p<0.001).
Conclusion: Younger age at onset, impaired general condition, rapidly progressive disabling neuropathy, and lambda light chain are easily identifiable red flags pointing to IgA-PN, potentially eligible for disease-modifying treatments.
Disclosure: Nothing to disclose.

EPR-247

Serum neurofilament light chain in chronic inflammatory demyelinating polyneuropathy – the limitations of a biomarker

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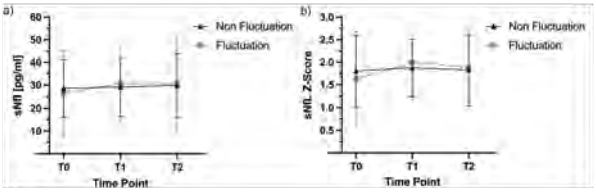
Background and aims: Serum neurofilament light chain (sNfL) is a marker for axonal degeneration and is associated with disease activity in different neurological disorders. Patients with CIDP often report a fluctuation of symptoms throughout one treatment cycle with intravenous immunoglobulins (IVIG). The aim of this study was to determine whether sNfL is a suitable biomarker to detect patient reported symptom fluctuations.
Methods: 29 patients with the diagnosis of CIDP or a CIDP-variant and current treatment with IVIG were recruited in this prospective cohort study and underwent examination before IVIG infusion (T0), in the middle (T1) and before their treatment cycle (T2). Patients were surveyed regarding symptom fluctuations at the last visit. Patients were divided into two groups: with and without fluctuations of symptoms. At the first visit sociodemographic as well as disease specific data (initial diagnosis, therapy etc.) were collected. Multiple clinical scores were assessed at every examination. sNfL values were compared between both groups after conversion into Z-Scores – adapted for age and BMI.
Results: Patients with CIDP show elevated Z-Scores (Median T0: 2.14, IQR: 1.40–2.39). There was no significant change of Z-Scores or questionnaire scores within the treatment cycle in either group. Patient reported symptom fluctuation did not correlate with changes in sNfL-levels.



Longitudinal analysis of sNfL and sNfL Z-Scores

Conclusion: CIDP patients show elevated sNfL levels. sNfL is not suitable to reflect patient reported fluctuations of symptoms. This indicates that symptom fluctuations during treatment cycles with IVIGs are not caused by a neuroaxonal injury. Furthermore, repeated sNfL measurements within one treatment cycle with IVIGs show no benefit for symptom-monitoring.
Disclosure: Nothing to disclose.

EPR-248

Early therapy initiation is crucial in chronic inflammatory demyelinating polyneuropathy - prospective multimodal data

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Background and aims: Clinical disability in later disease stages of chronic inflammatory demyelinating polyneuropathy (CIDP) mostly depend on secondary axonal damage as a result of chronic inflammation. Since early disease stages have rarely been described, the impact of delayed treatment initiation is elusive. Here, we multimodally describe in a prospective cohort early disease stage of CIDP in order to dissect predictors of disease progression.
Methods: Patients with first diagnosis of CIDP within one year before inclusion were systematically selected from the German prospective "Immune-mediated Neuropathies Biobank" (INHIBIT) registry. Within the registry, demographic data, clinical presentation, nerve conduction study (NCS), and nerve and muscle ultrasound were obtained at inclusion and 12 months afterwards.
Results: We identified 30 early CIDP patients (mean time from diagnosis to study inclusion: 22±50w). The most common therapy was repeated intravenous immunoglobulins (n=9). 26% of the patients received rituximab as a second-line therapy. Delayed therapy initiation resulted in significantly disability progression in regression analysis. Low compound muscle potential amplitudes in NCS and high echogenicity in muscle ultrasound, both as a sign for axonal damage, correlated positively with clinical disability. All patients with ameliorated axonal damage in the disease course received a second-line therapy.
Conclusion: Early therapy initiation is crucial for the disease course in CIDP patients. Second-line therapy might improve long-term outcome. In addition to NCS, ultrasound examinations aid to identify axonal damage which itself is the main driver for functional disability even in early disease stages.
Disclosure: Nothing to disclose.

EPR-249

Immune events preceding neuralgic amyotrophy

D. Sparasci[1], L. Schilg-Hafer[2], B. Schreiner[3], O. Scheidegger[4], A. Peyer[5], A. Lascano[6], A. Vicino[7], B. Décard[8], P. Tsouni[9], A. Humm[10], E. Pianezzi[11], G. Zezza[11], T. Hundsberger[2], A. Dietmann[4], H. Jung[3], T. Kuntzer[7], E. Wilder-Smith[5], G. Martinetti-Lucchini[11], S. Fontana[12], C. Niederhauser[13], C. Gobbi[1], P. Ripellino[1]
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Background and aims: Infections and vaccinations have been identified as potential triggers preceding neuralgic amyotrophy (NA), but the exact type and frequency of the different agents in Europe is largely unknown.
Methods: Swiss multicentre prospective study over a 3-year period (09.2019–09.2022). NA was diagnosed by neuromuscular experts according to existing criteria and electrodiagnostic studies. Clinical data and biological samples of NA patients were collected in the acute phase of the disease (within 90 days from onset). Serological tests were all performed in one reference microbiology laboratory.
Results: Disease onset was preceded by an identifiable immune trigger in 23/42 patients (54.8%) (Figure 1). Infection in 16/42 (38%) and COVID vaccination in 7/42 (16.7%). Viral infections were the most common (n=13, 31%). Identified (mostly by RT-PCR methods) viral agents were hepatitis E virus (HEV, n=6), Epstein-Barr virus (EBV, n=1), SARS-COV-2 (n=2), influenza virus (n=2), human immunodeficiency virus (HIV, n=1) and Parvovirus B19 (n=1). A bilateral involvement of NA was found in 7/42 (16.7%) patients and was always associated with a preceding systemic viral infection.

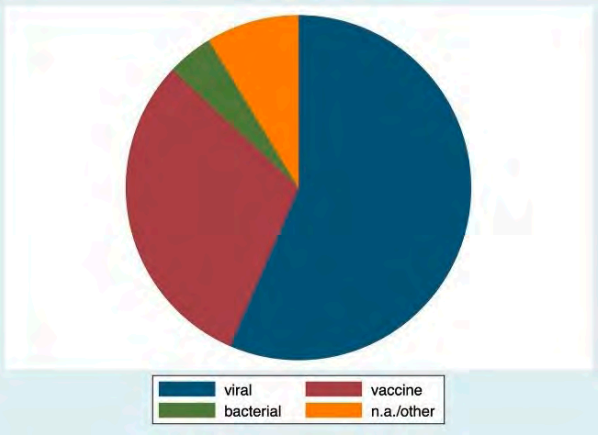

Figure 1

Conclusion: Our data support a para-infectious pathogenesis of NA in the majority of cases. A bilateral involvement in NA could serve as a clinical marker for preceding viral infection.
Disclosure: Nothing to disclose.

EPR-250

Clinical and pathology characterization of small nerve fibers neuropathy in RFC1-related disease

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Background and aims: Disease manifestations of biallelic mutation/expansion of the gene RFC1 evolved from complex presentations as Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS) to encompass also limited forms as sensory ataxia due to isolate sensory neuronopathy. The aim of the present study was to describe the frequency and characteristics of small fiber neuropathy (SFN) in RFC1-related disease.
Methods: We enrolled 40 patients with RFC1-related disease referred to our Clinic, irrespective of clinical presentation. Neuropathic Pain Symptom Inventory (NPSI) and Composite Autonomic Symptom Score-31 (COMPASS-31) questionnaires were administered to investigate SFN symptoms. Clinical and instrumental data were collected to evaluate large and small fiber sensory function. Available skin biopsy samples were reassessed to investigate somatic and autonomic innervation.
Results: Patients frequently reported mild-to-moderate positive symptoms (median NPSI score 12.1/50.0, IQR 5.0–23.0) and autonomic disturbances (median COMPASS-31 score 38.6/100.0, IQR 17.7–45.1) and largely independent to disease duration. The pattern of impairment in nociception was non-length-dependent in most patients, at odds with the apparent length-dependent distribution of tactile sensory loss. Accordingly, pathology revealed an extreme somatic denervation both at proximal and distal sites (fibers/mm RFC1-cases vs HC: proximal 0.0 vs 20.5, $p<0.0001$; distal 0.0 vs 13.1, $p<0.0001$). Interestingly, only a limited loss of autonomic innervation was observed.
Conclusion: A severe and widespread afferent SFN is characteristic of RFC1-related disease, and could represent its earliest clinical and pathology feature.
Disclosure: Nothing to disclose.

COVID-19

EPR-251

The Correlates of Subjective Brain Fog in 25796 UK Participants

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Background and aims: "Brain fog" has gained increasing attention after COVID-19. However, the heterogeneity of this subjective state has not been systematically characterised.
Methods: We systematically studied the associations between 29 variables with that of the self-reported presence of "brain fog", via univariate and machine learning methods. We used a peer-review validated smartphone application for remote data collection (Mindstep) between September 15th to November 18th, 2022. The studied variables encompassed clinical comorbidities, lifestyle factors, symptoms, functional deficits, and cognitive scores. We set Bonferroni-corrected statistical significance at 5%.
Results: There were 25,796 users of the digital application Mindstep, of which 7,280 (28.2%) reported experiencing brain fog. The following were significantly associated with brain fog (Table 1): • Demographics: older age (mean 35.7 vs 32.8 years p<0.0001), and female sex (OR=1.2, p<0.001). • Comorbidities: anxiety, depression, lower cognitive scores, migraine scores, long COVID-19 (OR=3.8), and concussions (OR=2.4) (all p<0.0001). • Symptoms: difficulty focusing or concentrating (OR=3.3), difficulty following conversations (OR=2.2) (both p<0.0001). • Lifestyle: less exercise (p<0.001), and lower sleep quality (p<0.0001). Extreme gradient boosting algorithms achieved a training accuracy of 84% with cross-validated accuracy of 74%.

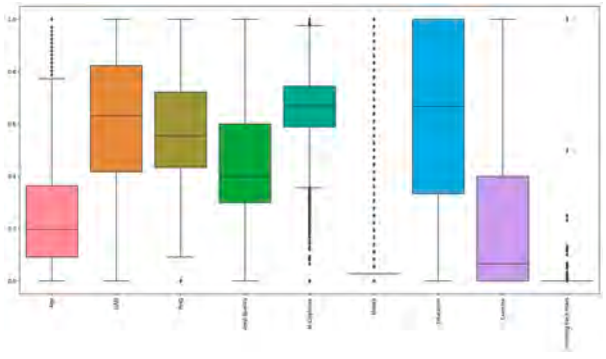

Figure 1: The distribution of non-Boolean variables after minmax normalisation. MIDAS: Migraine Disability Assessment Test. GAD: Generalised Anxiety Disorder Assessment (GAD-7). PHQ: Patient Health Questionnaire Test for Depression (PHQ-9).

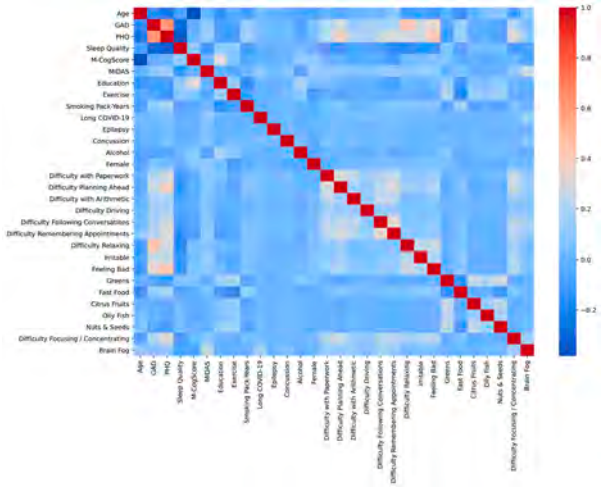

Figure 2: Heatmap of correlations between variables

Variable	Total	Brain Fog	No Brain Fog	p value (Chi-square)
Long COVID-19	5.0%	10.4%	2.9%	<0.0001
Epilepsy	1.1%	1.2%	1.1%	0.77
Concussion	2.2%	3.8%	1.6%	<0.0001
Alcohol	57.0%	56.0%	57.4%	0.04
Female	89.2%	90.4%	88.8%	<0.001
Difficulty with Paperwork	36.8%	46.8%	32.9%	<0.0001
Difficulty Planning Ahead	47.5%	57.0%	43.7%	<0.0001
Difficulty with Arithmetic	29.7%	39.1%	25.9%	<0.0001
Difficulty Driving	10.1%	12.5%	8.8%	<0.0001
Difficulty Following Conversations	47.8%	61.8%	42.3%	<0.0001
Difficulty Remembering Appointments	37.7%	48.9%	33.3%	<0.0001
Difficulty Relaxing	76.9%	79.2%	76.1%	<0.0001
Irritable	65.0%	80.9%	63.5%	<0.0001
Feeling Bad	76.2%	80.1%	74.6%	<0.0001
Greens	56.1%	56.7%	55.9%	0.23
Fast Food	41.8%	43.0%	41.4%	0.019
Citrus Fruits	28.9%	29.0%	28.9%	0.91
Oily Fish	15.1%	16.1%	14.6%	<0.001
Nuts & Seeds	28.5%	30.5%	27.8%	<0.0001
Difficulty Focusing / Concentrating	86.4%	94.3%	83.3%	<0.0001

Proportion of Boolean variables in Brain Fog vs not Brain Fog. Bold = significant after Bonferroni correction.

Conclusion: This is the first large-scale digital study of the correlates of subjective brain fog. Difficulty focusing, concentrating, and trouble following conversations characterised brain fog well, which was associated with objectively worse cognitive performance, and higher levels of anxiety, depression, and migraines. With further prospective data, extreme gradient boosted algorithms show promise in identifying individuals at risk of subjective brain fog.
Disclosure: Funding for this paper was provided by Mindset Technologies Ltd. All authors are, or were, employees and/or shareholders of Mindset Technologies Ltd.

EPR-252

Unveiling the cognitive and neurological consequences of COVID-19: A pretest-posttest study

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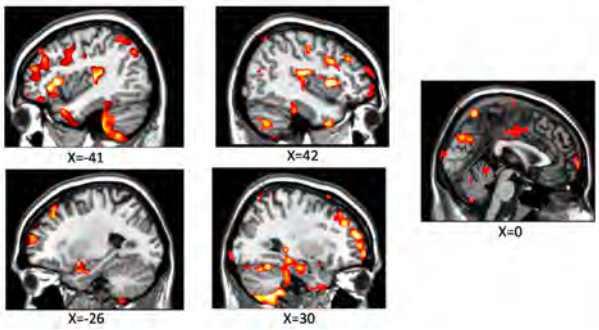
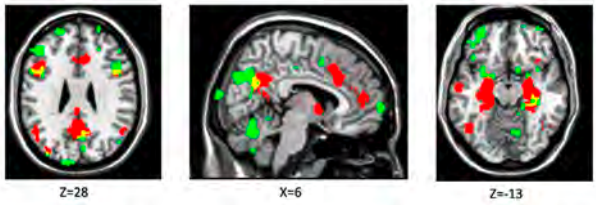
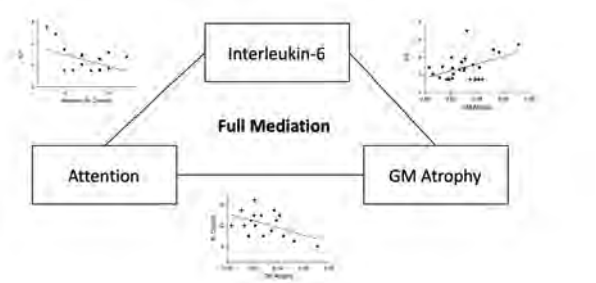
Background and aims: This project aims to overcome the caveats of previous research assessing the inflammatory mechanisms supporting the direct effects that COVID-19 has in promoting cognitive impairment and inducing neural damage.
Methods: We recruited a cohort of 160 individuals who contracted COVID-19, and for whom we have access to prepandemic structural neuroimaging data. Selected patients participated in a follow-up session at least 6 months and no later than two years after surviving COVID-19. In this post-COVID-19 session participants underwent extensive cognitive behavioral testing,brain MRI, and blood extraction to quantify chronic inflammation (CRP,MMP-9,glutamate and IL-6 among others).
Results: 35 patients met all the inclusion criteria. We identified significant worsening of grey matter (GM) measures in a posttest vs.pretest comparison. There was an overlap between the regions showing structural damage in COVID-19 survivors and those showing abnormalities in Alzheimer's Disease. Also, those patients who had greater GMatrophy, showed problems in short and long term visual memory, selective attention, and executive functions (R=-0.58, p<0.02; R=0.52, p<0.04; R=0.48, p<0.05; R=0.6, p<0.01, respectively). Moreover, higher levels of inflammation markers were also correlated with higher GMatrophy (IL-6:R=0.45, p<0.02; CRP:R=0.4, p<0.05). A mediation analysis showed that the correlation between increased GMatrophy and worse attentional skills was fully explained by increased levels of IL-6.



Worsening of grey matter measures in a posttest vs. pretest comparison



Overlap between the regions showing structural damage in COVID-19 survivors and those showing abnormalities in Alzheimer's Disease



Full mediation analisis

Conclusion: In our cohort we found structural damage in patients who suffered COVID-19, as evidenced by a worsening of grey matter measures in a posttest vs. pretest comparison. The amount of damage induced by COVID-19 correlates both with behavioral measures of cognitive decline and biomarkers of inflammation.
Disclosure: Study supported by TMcity.

EPR-253

Muscle manifestations and CK levels in COVID infection

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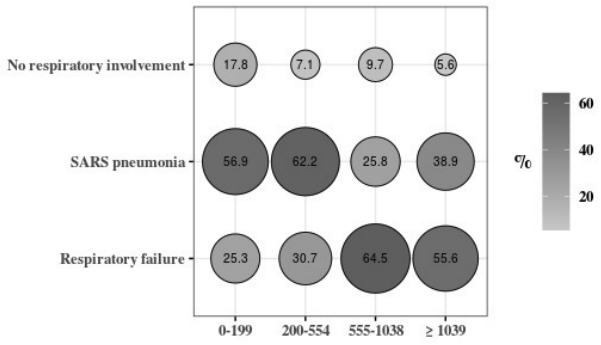
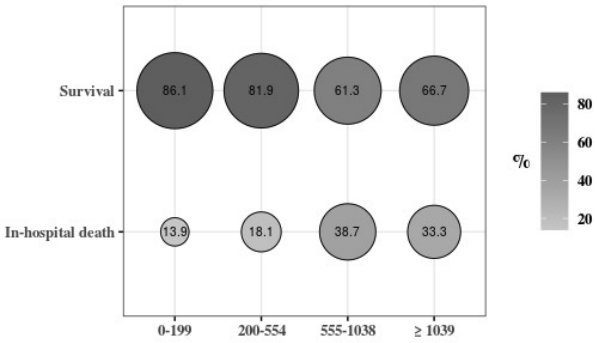
Background and aims: Although COVID-19 involves pulmonary system in the first place, it can also cause symptoms affecting the skeletal muscle. The primary aim of our study was to investigate both muscular manifestations and CK levels of a large cohort of patients with COVID infection in order to find a possible correlation among them. The secondary aim was to identify the association among CK levels, respiratory failure and in-hospital death.
Methods: Data of 615 patients discharged from ASST Ovest Milanese (Milan, Lombardy, Italy) with final diagnosis of COVID-19 infection were retrospectively extracted from electronical medical records from 21 February to 1 May 2020. Patients were descriptively analyzed with respect to the following variables: sex, age, muscular manifestations, fatigue, respiratory involvement and history of falls. Association between patients' characteristics and CK levels was investigated. In addition, the proportion of patients who died following access to the ER was calculated. Finally, the effect of CK levels and other patients' features on mortality was estimated using a logistic regression model.
Results: 176 (28.6%) patients had raised serum CK levels. CK levels were significantly associated with history of falls, male gender, SARS pneumonia, respiratory failure and in-hospital death. No correlation was found between hyperckemia and muscular manifestations.



Percentage distribution of respiratory involvement according to CK levels.



Percentage distribution of in-hospital death according to CK levels.

Conclusion: Our study provides preliminary evidence that hyperckemia is associated with respiratory failure and fatal outcome in patients with COVID-19 infection. In these patients, among other testing, CK dosage is recommended.
Disclosure: Nothing to disclose.

EPR-254

Neurological cues of COVID-19 and non-COVID-19 Acute Respiratory Distress Syndromes (ARDS)

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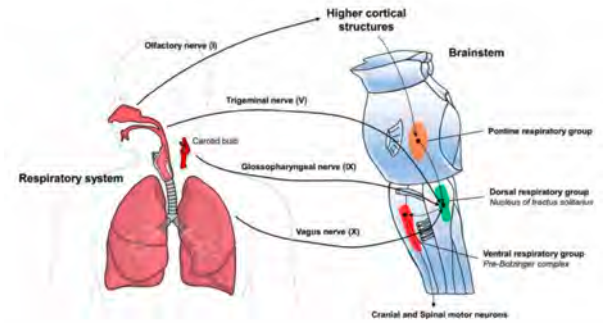
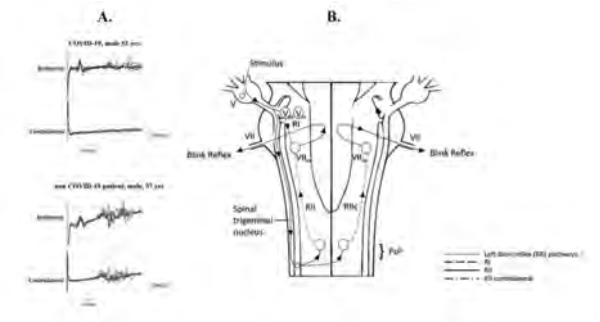
Background and aims: The aim of the study was to explore the function of the brainstem in patients with COVID-19 and non-COVID-19 Acute Respiratory Distress Syndrome (ARDS), by neurophysiologically assessing the Blink Reflex (BR) and the Masseter Inhibitory Reflex (MIR), which share quite similar brainstem pathways involved in respiratory control. To date, a comprehensive neurophysiological approach to the respiratory function of the brainstem is still lacking in humans.

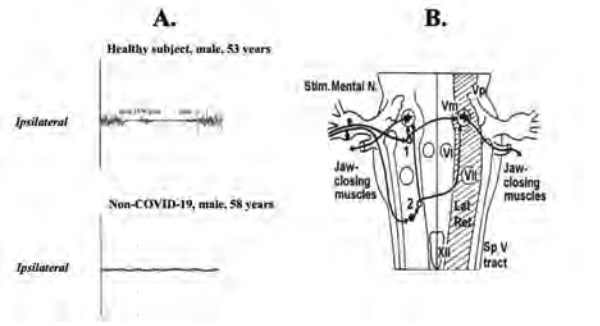


Anatomy of the lung–brain axis

Methods: 25 healthy volunteers, 9 COVID-19 and 6 non-COVID-19 ARDS patients were enrolled in the study. Bayesian and parametric comparisons of BR latencies (RI and RII) were performed in healthy volunteers undergoing different experimental conditions: normal breathing, maximal inspiration and expiration. Differences in RI and RII latencies, and in silent periods (SPI and SPII) onset latencies and durations of the MIR, were assessed among the three groups enrolled.
Results: Among healthy subjects, a significant value emerged from the comparison between basal condition and maximal expiration for ipsilateral RII (BF10>3). A remarkable number of RII and SPII responses were absent between ARDS patients. Almost all the values of the BR among healthy volunteers and COVID-19 ARDS patients were statistically significant (p-values<0.05). There was no statistical evidence between the two groups of ARDS patients, nor among healthy patients and non-COVID-19 ARDS subjects (except for RI latencies, p-value=0.019).



A: COVID-19 patient and non-COVID-19 patient. In the first case, ipsilateral RII responses had prolonged latencies, and contralateral RII were non-recordable. B: Schematic representation of BR pathways.



A: Ipsilateral response of the MIR in healthy subject and non-COVID-19 ARDS patient. Silent periods of the MIR (ES1 and ES2) were unrecordable in the second patient, while they are both present in the first one. B: Schematic representation of MIR pathways

Conclusion: Our data provide a neurophysiological involvement of the brainstem function in patients with ARDS due to COVID-19, thereby playing a possible role in causing neurogenic acute respiratory failure, not as relevant in non-COVID-19 ARDS.
Disclosure: Nothing to disclose.

EPR-255

Neurological manifestations of SARS-CoV-2 infection in solid organ transplant: a single centre retrospective study

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Background and aims: No studies evaluated the risk of neurological manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in solid organ transplant (SOT) recipients. Central nervous system involvement, during coronavirus infection, may be related to cytokine storm [1]. Our aim is to understand if immunosuppression may reduce hyper-inflammatory status [2] and protect against neurological outcomes of SARS-CoV-2 infection in SOT recipients.
Methods: We performed a single centre retrospective study on a cohort of n°99 adult SOT recipients with a diagnosis of SARS-CoV-2 infection. Patients were excluded if informed consent or data were not available (n=26). Data were collected using medical charts and phone interviews. To compare continuous and categorical variables, Wilcoxon tests and Chi-Square tests were used. Level of significance were set with $p<0.05$.
Results: Demographic and clinical data of the final cohort (n=73), as well as of the two categorized patients according to the primary end-point (neurological manifestations occurrence), were reported in Table 1. Headache and hyposmia/hypogeusia were the most common neurological symptoms, respectively 37% and 36,9%. Patients with neurological symptoms were more likely to receive oxygen -therapy (p=0.0344) and be hospitalized (p=0.0552).

Table 1: demographic and clinical data of SOT patients with a history of SARS-CoV-2 infection

Baseline Features	All Patients (n=73)	Patients with neurological manifestations (n= 54)	Patients without neurological manifestations (n=19)	P_value
Age in years, mean (SD)	53.43 (15.87)	53.15 (14.89)	54.21 (18.81)	0.5845
Male sex, n (%)	46 (63%)	34 (62,9%)	12 (63,1%)	0.9879
Organ transplant, n (%)				
KTx	33 (45,2%)	26 (48,1%)	7 (36,8%)	
CLTx	31 (42,5%)	21 (38,9%)	10 (52,6%)	
LTx	5 (6,8%)	3 (5,6%)	2 (10,5%)	0.5684
HTx	1 (1,4%)	1 (1,8%)	0	
Combined transplant	3 (4,1%)	3 (5,6%)	0	
Time from transplant to infection in years, median (IQR)				
BMI, mean (SD)	27.56* (4.92)	28.03**(5.38)	26.24***(3.04)	0.2758
Last tacrolimus blood level before infection (ng/ml), mean (SD)	5,78****(2,91)	6,02*** (3,01)	4,66* (2,09)	0.2016
Outcomes, n (%)				
Hospitalized	20 (27,4%)	18 (33,3%)	2 (10,5%)	**0.0552**
Oxygen (O_2-therapy)	18 (25,3%)	17 (31,5%)	1 (5,9%) ***	**0.0344**
No-hospitalization/No-O_2-therapy	49 (69,0%)	33 (61,1%)	16*** (94,1%)	
No-hospitalization/non-invasive O_2-therapy	3 (4,2%)	3 (5,6%)	0	
Hospitalization/without O_2-therapy	5 (7,0%)	4 (7,4%)	1*** (5,9%)	0.1146
Hospitalization with non-invasive O_2-Therpy	13 (18,3%)	13 (24,1%)	0	
ICU admission/mechanical ventilation	1 (1,4%)	1 (1,8%)	0	
Neurological comorbidities	24 (33,3%)	17 (31,5%)	7 (38,9%)*****	0.5637
Immunosuppresion regimen including steroids	37 (51,4%)	31 (57,4%)	6 (33,3%) *****	0.0768

Table 1: demographic and clinical data from all SOT patients, with a history of SARS-CoV-2 infection, and from categorized patients as having (n= 54) or not (n=19) at least one neurological symptom (primary endpoint) are presented in order to detect specific risk factors. Values in bold indicate statistically significant differences

*8 missing values
**6 missing values
***2 missing values
****10 missing values
*****1 missing values

Table 1: demographic and clinical data from all SOT patients, with a history of SARS-CoV-2 infection, and from categorized patients as having (n= 54) or not (n=19) at least one neurological symptom (primary endpoint) are presented in order to detect specific risk factors.

Table 2: Clinical features of SOT patients with SARS-CoV-2 infection and at least one neurological symptom cohort (n=54)

Neurological symptoms/signs/syndromes	% neurological cohort (54)	% of whole cohort (73)
Headache	27 (50%)	37,0%
Hyposmia Hypogeusia	27 (50%)	37,0%
Myalgia	42 (77,8%)	57,5%
Cognitive impairment	17 (31,5%)	23,3%
Affective & behavioural impairment	10 (18,5%)	13,7%
Visual impairment	2 (3,7%)	2,7%
Ataxia	0	
Seizures	0	
Status epilepticus	0	
Meningoencephalitis	0	
Delirium	0	
Coma	1 (1,8%)	1,4%
Ischemic stroke	0	
Intracranial bleeding	0	
Weakness	1 (1,8%)	1,4%
Impaired sensation	2 (3,7%)	2,7%
Neuropathic pain	0	
Dizziness	5 (9,3%)	6,8%

Table 2: neurological symptoms were self-reported; neurological signs and syndromes were considered when reported in medical charts and evaluated by physicians.

Conclusion: Frequency of headache was comparable with the same self-reported symptom in the general population, hyposmia/hypogeusia was more frequent in our cohort [3]. No risk factor for neurological manifestations was found in SOT patients; higher level of tacrolimus as well as being on steroids did not result protective against neurological manifestations; neurological symptoms were more frequent in more severe cases of infection.
Disclosure: Nothing to disclose.

EPR-256

Clinical phenotype of Post-COVID Neurological Syndrome: 2 year follow-up

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Background and aims: Coronavirus disease 2019 (COVID-19) poses a global hazard to the nervous system. We characterized two-year post-COVID neurological syndrome (PCNS) in a cohort of patients diagnosed in an outpatient and inpatient setting.
Methods: Prospective cohort of 732 COVID-19 patients diagnosed between March-June 2020. Follow-up was performed face-to-face or by phone at 3-, 12- and 24-months post-infection.
Results: 24 months post-infection, 450/732 patients were evaluated: 71.3% presented at least one sign or symptom of neurological dysfunction, compared to 68.2% at 12-months and 59.2% at 3-months. Male patients were more likely to present PCNS (77.7% vs. 61.4%). There was no association between PCNS and age upon acute infection or symptoms severity at onset. The most prevalent neurological complaints were cognitive (49.6%) and sleep dysfunction (34%), followed by visual (22.4%), new onset headache (16.2%), sensory (15.6%) vertigo (14.9%), hyposmia (13.6%) and hypogeusia (10.2%). In comparison with 12-months PCNS, there was an increase in all of the symptoms apart from sleep complaints. When compared to 3-months, only hyposmia and hypogeusia declined. Reinfection was reported in 20% of patients. All these cases had mild disease and did not present significant differences in PCNS frequency or phenotypes. Vaccination was > 95% in the cohort.
Conclusion: The prevalence of PCNS remains high 24 months post-infection. Cognitive complaints persist as the most frequent with an increasing tendency. Impact on patient health and quality of life reinforces the need for healthcare-providers to promote long-term solutions for PCNS.
Disclosure: Nothing to disclose.

EPR-257

SARS-CoV-2 and auto-antibodies in the cerebrospinal fluid of COVID-19 patients: prospective multicenter cohort study

V. Nersesjan[1], M. Amiri[1], A. Nilsson[2], C. Wamberg[3], S. Storm[4], V. Jensen[5], C. Petersen[6], A. Hejl[6], A. Lebech[7], A. Theut[5], C. Jørgensen[5], M. Blaabjerg[4], M. Benros[8], D. Kondziella[1]
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Background and aims: Disease-mechanisms underlying neurological and neuropsychiatric complications after COVID-19 (neuro-COVID) are poorly understood. Therefore, we evaluated CSF from neuro-COVID patients for presence of SARS-CoV-2 RNA and antibodies, and autoantibodies against neuronal surface antigens.
Methods: CSF and blood were prospectively collected in individuals with neuro-COVID from 05/2020 to 12/2021 at Copenhagen University hospitals. Outcomes were presence of 1) SARS-CoV-2 RNA via PCR and antibodies using the Euroimmun-antibody-assay; and 2) anti-neuronal autoantibodies using commercial cell-based (CBA) and tissue-based (TBA) assays as well as inhouse TBA and live neuronal-based (NBA) assays.
Results: We included 38 COVID-19 patients (mean age ±SD 56.5±19.2, 53% female), with neurological or neuropsychiatric complications. CSF pleocytosis (>5cells) was observed among 23.7%, elevated CSF protein (>0.50g/L) in 34.2% and elevated CSF/serum albumin-ratio in 34.3%. PCR for SARS-CoV-2 RNA in CSF was negative in all. SARS-CoV-2 CSF antibodies were detected in 44.1% which positively correlated with corresponding serum levels ($R=0.93$, $p<0.001$), blood-brain-barrier permeability ($R=0.47$, $p=0.006$), and peripheral inflammation ($R=0.51$, $p=0.002$), and associated with critical COVID-19 requiring admission to the ICU (OR: 17.65; 95%CI: 1.18–264.96; $p=0.04$). Commercial CBA detected weakly positive NMDAR-, LGI1- and CASPR2-antibodies in serum (11.8%) but none in CSF. However, CNS-reactivity was more prevalent with inhouse tissue- (serum: 90.0%; CSF: 10.5%) and neuronal-based assays (serum: 38.2%; CSF: 10.5%).
Conclusion: Active SARS-CoV-2 infection in the CSF was absent, but SARS-CoV-2 antibodies were prevalent

(44.1%); probably due to an impaired blood-brain-barrier. Anti-neuronal antibodies measured by commercial assays were rare; nevertheless, TBA and NBA measured autoreactivity could indicate autoimmunity in a subset of neuro-COVID patients.

Disclosure: This work was supported by unrestricted grants from the Lundbeck Foundation (grant number R349-2020-658 and R268-2016-3925), by the Novo Nordisk Foundation (grant number NNF21OC0067769) and the Research Fund of the Mental Health Services - Capital Region of Denmark.

EPR-258

Abstract withdrawn

EPR-259

COVID-19 associated cerebral microbleeds in the general population

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Background and aims: Cerebral microbleeds (CMB) are frequent incidental findings on brain magnetic resonance imaging (MRI) and have previously been shown to occur in COVID-19 cohorts of critically ill patients. We aimed to determine the risk of having microbleeds on medically indicated brain MRI and comparing non-hospitalized COVID-19 infected patients with non-infected controls.

Methods: In this retrospective case control study, we included patients over 18 years of age, having an MRI with a susceptibility weighted sequence, between January 1, 2019, and July 1, 2021. Cases were identified based on a positive reverse transcriptase polymerase chain reaction test for SARS-CoV-2, and matched with three non-exposed controls, based on age, sex, body mass index and comorbidities, whereafter the number of CMB on each scan was determined by use of artificial intelligence.

Results: We included 73 cases and 219 matched non-exposed controls and found that COVID-19 is associated with significantly greater odds of having CMB on MRI; OR 2,66 (1,23–5,76, 95% confidence interval), increasingly when patients with dementia, and hospitalized patients were excluded.

Conclusion: Our findings indicate that CMB may associate with COVID-19 infections, which may shed light on pathophysiological considerations, as well as provide a potential explanation in the case of incidental CMB in subjects with previous COVID-19.

Disclosure: This project has received funding from VELUX FONDEN and Innovation Fund Denmark under grant number 1063-00014B, and Pioneer Centre for AI, Danish National Research Foundation, grant number P1.

Clinical neurophysiology

EPR-260

Exploring the use of proximally recorded C-reflex in myoclonus

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Background and aims: C-reflex, a long-loop reflex recorded in patients with cortical myoclonus, reflects sensorimotor cortex hyperexcitability. It is typically recorded from abductor pollicis brevis (APB), but it is possible to record from more proximal muscles. We aimed to investigate presence of C-reflex from proximal muscles in patients with myoclonus.
Methods: We retrospectively analyzed a cohort of patients with upper extremity myoclonus admitted to our clinic between 2010–2022. First, all patients underwent polymyographic analysis from APB, extensor and flexor muscles of wrist, and biceps brachii. Then, to detect C-reflex, we stimulated the median nerve at the wrist and recorded responses from the same muscles of upper extremity. We classified patients with C-reflex into two groups: epilepsy (group 1) and movement disorders (group 2), and compared the characteristics of C-reflex between the two groups.
Results: Out of 260 patients with upper extremity myoclonus, 45 had cortical myoclonus and C-reflex. There were 21 (46.7%) patients with epilepsy (PME in 17, JME in 3, and Rasmussen encephalitis in 1) and 24 (53.3%) with movement disorders (Parkinson's disease and parkinson-plus syndromes in 19, Creutzfeldt-Jakob disease in 4 and Lance-Adams syndrome in 1). The C-reflex was recorded from the proximal muscles of seven patients in Group 1 and three patients in Group 2 (p=0.09).
Conclusion: Proximally recorded C-reflex was more common in patients with epilepsy than in patients with other etiologies of cortical myoclonus. Sensorimotor cortex hyperexcitability in epilepsy tends to follow motor homunculus, which is relatively rare in other etiologies despite the presence of cortical myoclonus.
Disclosure: Nothing to disclose.

EPR-261

Thalamocortical dysrhythmia in patients with delirium: an EEG possible marker of prodromal DLB

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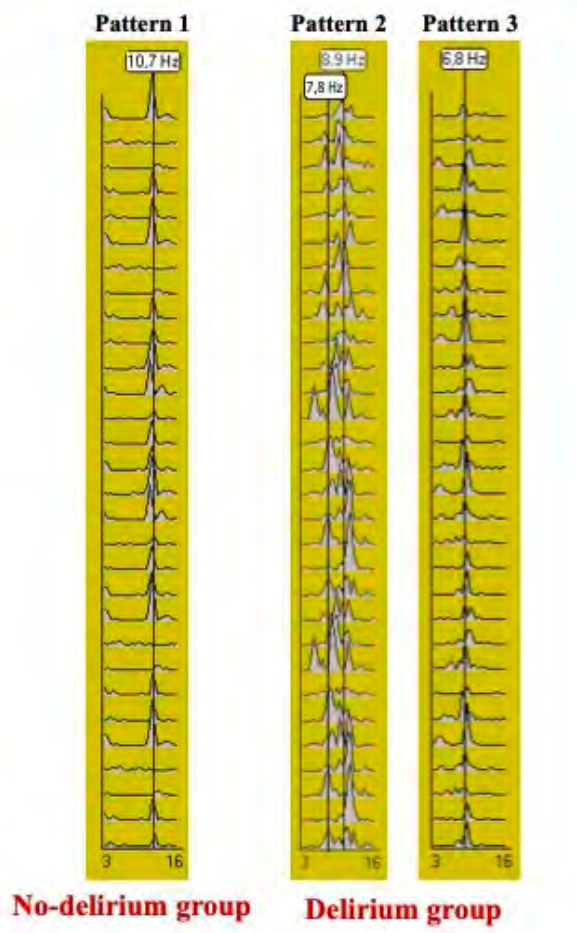
Background and aims: EEG in DLB is characterized by pre-alpha dominant frequency (DF) [6–7.5] Hz. The prealpha rhythmis linked to a dysfunctional thalamocortical connection, thalamocortical dysrhythmia (TCD). TCD is implicated in DLB as demonstrated by structural, functional, and molecular imaging studies. TCD is implicated in the appearance of altered conscious states, including fluctuating cognition (core feature of DLB) and delirium, which is a symptom of prodromal DLB. We aimed to assess if specific EEG abnormalities typical of TCD and DLB, are present in the delirium-type prodromal stage of DLB.
Methods: cross-sectional multicentre cohort study and longitudinal prospective study, nested in the multicentre. EEG was compared in hospitalized patients with delirium vs. patients without delirium. In a subset of delirium. patients, EEG was also recorded at resolution of symptom and and at 1-month follow-up. DF and DF variability (DFV) were analysed.
Results: Cross-sectional multicentre study 65 subjects with acute delirium were matched for age/sex with 41 controls. Abnormal EEGs were found in 100% delirium patients vs.34% no-delirium patients. DF was lower and DFV was higher in delirium group (p<0.001), which showed pre-

alpha DF. Single-centre longitudinal study After delirium resolution, 21 patients had EEG normalization. 2 patients had abnormal EEG and were respectively diagnosed as DLB and MCI.



Different CSA patterns from occipital derivations in three illustrative patients included in no-delirium group and delirium group.

Conclusion: Delirium was characterized by pre-alpha DF, expression of TCD. In most patients EEG normalized after resolution, making EEG a state marker of acute delirium, when the thalamocortical system becomes unstable, but it is still able to recover. TCD may become unrecoverable when the neurodegenerative process of DLB progresses.
Disclosure: Nothing to disclose.

EPR-262

Side-Dependent Subthalamic Local Field Potential Dynamics in Parkinson's Disease.

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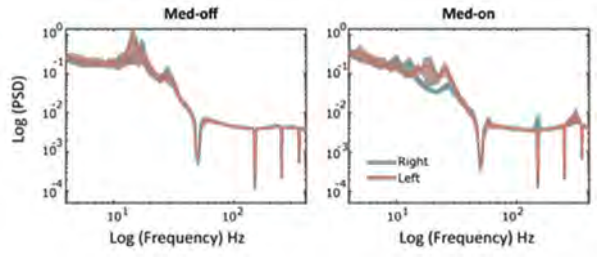
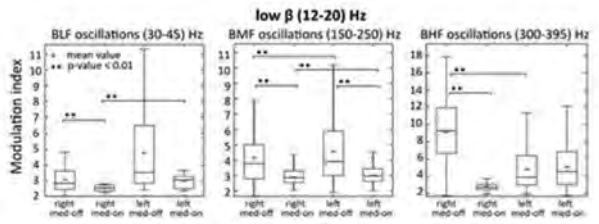
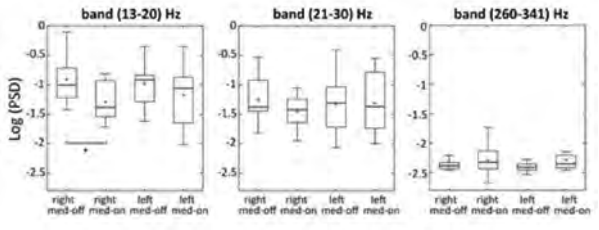
Background and aims: Parkinson´s disease (PD) is associated with pathological beta band (11–30 Hz range) oscillatory activity in the subthalamic nucleus (STN). As proof of that beta activity is suppressed by levodopa. Asymmetry of frontal cortex beta activity was correlated with disease severity. STN oscillations were investigated in patients affected by PD. Local field potentials (LFP) were obtained by implanted DBS electrodes and analyzed by a phase-amplitude coupling (PAC) approach. Right and left STN activity was compared.
Methods: 24 patients previously implanted with DBS underwent bilateral LFPs recordings at rest, both on L-dopa administration and 12 h after L-dopa withdrawal. STN oscillations at rest were quantified by standard LFP power spectral analysis. PAC determined whether interactions across these frequency ranges occurred and if those were lateralized.
Results: A significant difference between Off an On group conditions was found in the low-beta frequency band in the right STN. PAC provided statistical differences in the ranges 12–20 Hz (low) and 21–30 Hz (high). Interestingly the pharmacological treatment reduced in the right hemispheres with respect to the left both the level of low and high beta coupling frequencies for amplitude. No significant differences were found in the other considered frequency bands.



Group averaged (dotted line) PSDs and 95% confidence interval of the mean (shaded area) are plotted for both left (light blue) and right (peach color) STN during both Med-Off (left) and Med-On (right) conditions



Boxplot representing averaged PSD values in the low, high and high frequencies between both the two hemispheres and the two pharmacological treatments. Statistical differences are denoted with *(p<0.05)



Boxplot representing averaged phase of coupling for both low (left) and high (right) between both the two hemispheres and pharmacological treatments. Statistical differences are denoted with ** (p<0.01).

Conclusion: Data are consistent with studies showing that the two sides of the brain are distinctly involved in PD. Hemispherical differences were independent on the clinical phenotype or the side of onset. The lateralization of cortical/subcortical activity may predict response to treatment and new pathophysiological insights of PD.
Disclosure: Nothing to disclose.

EPR-263

Factors influencing successful intraoperative visual evoked potentials during transsphenoidal pituitary tumor surgery

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Background and aims: One major obstacle to using intraoperative visual evoked potential (VEP) monitoring is the low success rates in achieving successful baseline potentials. This study analyzed several extrinsic and intrinsic factors to determine which variables are associated with successful baseline potentials.
Methods: A retrospective review of medical records from 124 patients undergoing transsphenoidal pituitary tumor surgery with VEP monitoring was performed. Patient data, such as pre- and postoperative magnetic resonance images, histopathological diagnoses, the results of VEP monitoring, and pre- and postoperative examination of visual functions were evaluated. The association between these factors and the success rate of obtaining baseline VEPs analyzed. The effect of achieving successful baseline VEP on postoperative visual outcome was also studied.
Results: A successful baseline recording of VEPs was obtained in 190 eyes (76.6%). The use of a high-intensity light-emitting diode (LED) stimulator, application of electroretinography (ERG), tumor size, tumor location, and preoperative visual function showed significant association with successful obtaining baseline VEPs (p<0.05). All the other parameters such as patient age, sex, history of diabetes mellitus, hypertension, hyperlipidemia, smoking, and history of eye surgery did not show significant association with successfully obtaining baseline VEPs. The ability to monitor VEPs also significantly associated with favorable visual outcomes.
Conclusion: High-intensity LED and ERG should be applied to optimize the chances of obtaining intraoperative VEPs. By identifying the factors influencing inadequate baseline VEP signals, the neurophysiologist may be better prepared for the monitoring. The ability to monitor VEPs also significantly associated with favorable visual outcomes.
Disclosure: There is no potential conflict of interest to be disclosed.

EPR-264

Investigating the mechanism of action of tDCS by means of TMS-EMG

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Background and aims: Transcranial Direct Current Stimulation (tDCS) is used to modulate neuronal activity, but its exact mechanism of action is unclear, hampering its clinical applicability. This study investigates whether the effects of tDCS are established through a 'direct' effect on cortical neuronal structures inducing neurophysiological changes, or rather through an 'indirect' mechanism, where the effects are caused by stimulation of cranial and/or peripheral nerves located in the vicinity of the tDCS electrodes.
Methods: In a randomized cross-over study, 4 experimental conditions were compared in healthy volunteers: (1) anodal tDCS (a-tDCS) on the motor cortex, (2) a-tDCS on the motor cortex with locally applied anesthetic on the scalp, (3) a-tDCS on the cheeks and (4) sham a-tDCS on the motor cortex. TMS-EMG was applied before and repeatedly after tDCS to evaluate the tDCS-induced effects on corticospinal excitability.
Results: An interim analysis of 10 participants (5 males, 5 females) demonstrated a higher peak-to-peak MEP amplitude in the conditions with motor cortex a-tDCS and with a-tDCS on the cheeks. No tDCS-induced motor evoked potential (MEP) modulation was found when a-tDCS was delivered with a local anesthetic applied on the scalp or after sham tDCS.
Conclusion: These preliminary results show a trend toward the indirect mechanism of tDCS, as there was a MEP amplitude increase observed after stimulating peripheral/cranial nerves, but not after applying a-tDCS on a locally anesthetized scalp. This trend is not statistically significant yet, thus further analysis of the full study cohort (n=20) is needed to confirm our preliminary results.
Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPR-265

Does nerve conduction study improve better in IVIg/PLEX treated Guillain – Barre syndrome than those on natural course

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Background and aims: Intravenous immunoglobins (IVIg)/Plasmapheresis (PLEX) is the standard treatment of Guillain Barre syndrome (GBS). There is paucity of information about the nerve conduction changes in the IVIg/PLEX treated GBS patients compared to those without. To compare the serial nerve conduction studies (NCS) between IVIg/PLEX treated GBS patients compared to those without IVIg/PLEX or Natural course(NC). We also correlated NCS changes with clinical improvement between the two groups.
Methods: Patients with GBS, diagnosed based on clinical, CSF and NCS were included. They were treated with IVIg/PLEX in the affording patients and the non-affording patients were on NC. The peak disability was assessed using 0-10 Clinical Severity Grading Scale (CSGS) and repeated at 1 and 3 months. Motor NCS including compound muscle action potentials(CMAPs), conduction velocities, conduction block and F latencies were serially followed and change in NCS at 1 and 3 month were compared between IVIg/PLEX and NC group, and correlated with outcome
Results: 54 patients received IVIg (44) or PLEX (10), and 18 were in NC. At 3month, 31 had complete recovery (CSGS<2), 25 had partial (CSGS 3,4,5,6) and 13 had poor clinical outcome (CSGS>6). The NCS revealed significant improvement in F latency in IVIg/PLEX group compared with NC (p=0.03). There was no difference in CMAP, nerve conduction velocities and conduction blocks between the two groups despite clinical improvement in both the groups.
Conclusion: The improvement in NCS is independent of IVIg/PLEX treatment. There is no correlation in clinical improvement and NCS parameters except F latency.
Disclosure: Nothing to disclose.

EPR-266

Relationship between interlimb transfer of a visuomotor learning task and interhemispheric inhibition in healthy humans

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Background and aims: The 'interlimb transfer' phenomenon consists of improved performance of the trained and untrained contralateral limb after unilateral motor practice. We here assessed whether a visuomotor learning task can be transferred from one hemisphere to the other, whether this occurs symmetrically, and the cortical neurophysiological correlates of this phenomenon, with a focus on interhemispheric connectivity measures.
Methods: We enrolled thirty-three healthy subjects (age range: 24–73 years). Participants underwent two randomized sessions, which investigated the transfer from the dominant to the non-dominant hand and vice versa. Measures of cortical and intracortical excitability and interhemispheric inhibition were assessed through transcranial magnetic stimulation before and after a visuomotor task.
Results: The execution of the visuomotor task led to an improvement in motor performance with the dominant and the non-dominant hand, and induced a decrease in intracortical inhibition in the trained hemisphere. Participants were also able to transfer the visuomotor learned skill. The interlimb transfer, however, only occurred from the dominant to the non-dominant hand, and positively correlated with individual learning-related changes in interhemispheric inhibition.

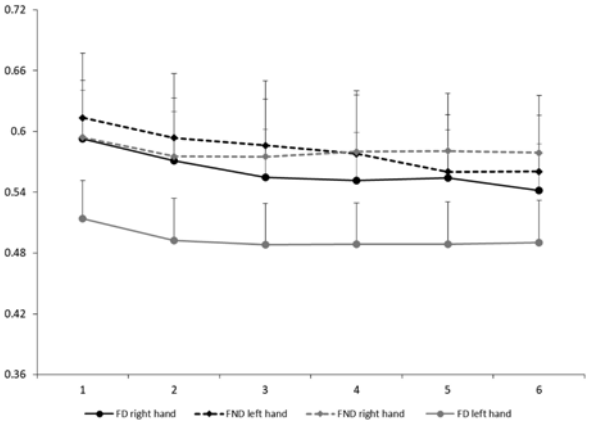

Fig. 1 Motor skill acquisition across the visuomotor tasks

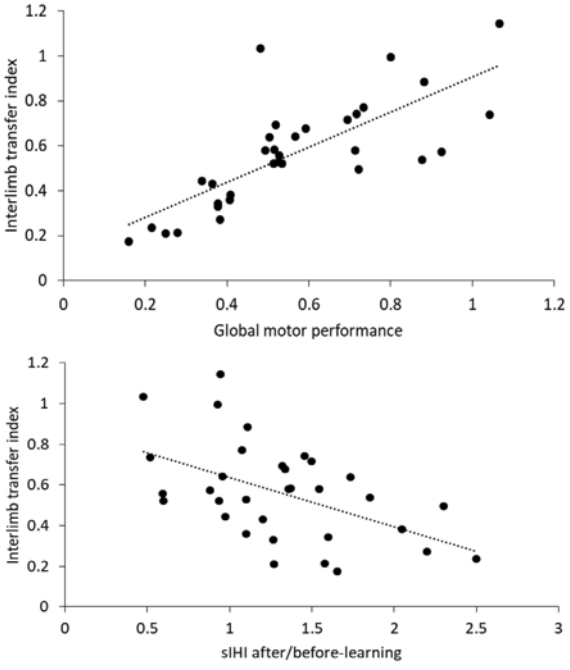

Fig. 2 Correlation analysis

Conclusion: We here demonstrated that the interlimb transfer of a visuomotor task occurs asymmetrically and relates to the modulation of specific inhibitory interhemispheric connections. The study results have pathophysiological, clinical and neuro-rehabilitative implications.
Disclosure: Nothing to disclose.

EPR-267

Critical illness neuromyopathy (CIPNM): highly variable temporary reversibility of motor nerve conduction abnormalities

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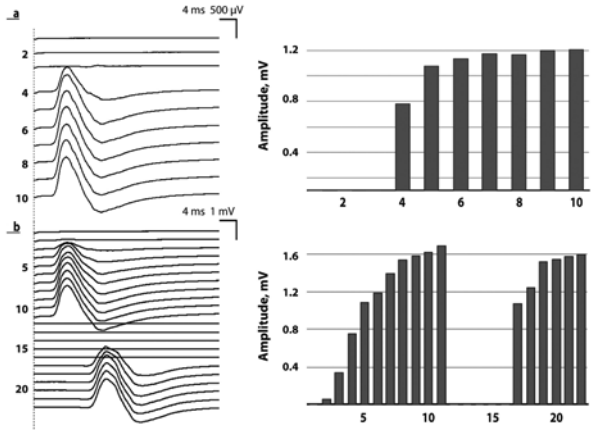
Background and aims: In CIPNM slow serial electrical stimulation of peripheral motor nerves induces a marked temporary increase of motor responses termed facilitation phenomenon (FP)(Clin Neurophys 2022;142:244–253). We investigated reproducibility and variability of FP in motor nerves.

Methods: In six patients with sepsis and CIPNM defined by muscle weakness and absent / small compound muscle action potentials (CMAPs) FP was followed by repeated series of slow electrical stimuli in motor nerves. Nerve conduction velocities (NCV) could be analysed once CMAPs were facilitated. Needle EMG was done in all patients. Serum electrolytes were and corrected before the examinations if needed.

Results: Slow serial motor nerve stimulation induced FP. FP was induced and could be reproduced several times with a huge variability in the same and in different nerves in all patients. Facilitated CMAPs looked normal and CMAPs increased temporarily to normal values in 4/6 patients but reached only 1 or 2 mV in 2/6 patients. NCVs were in the low normal range utilizing the facilitated CMAPs for analyses. Neither conduction block nor CMAP dispersion was present. Needle EMG showed no (3/6), mild (2/6) or moderate (1/6) spontaneous activity.



Slow serial electrical stimulation of the peroneal nerve initially induces no motor responses; after a variable numbers of stimuli rising CMAPs are seen (FP) from distal and proximal stimulation

Conclusion: The huge variability of FP patterns despite identical stimulus strength suggest striking fluctuations of the underlying dysfunctional processes. The nerve conduction data obtained with facilitated CMAPs argue against a predominant axonal or mixed neuropathy. These observations add a new facet to the current hypotheses on the still enigmatic pathophysiology challenging the relative contribution of a predominant neuropathy in these patients.

Disclosure: None; Supported by the binational doctorate degree program of the German Academic Exchange Service (DAAD) and by the University Research Funds of the Universities of Leipzig and Würzburg.

EPR-268

Comparison between SFEMG-v and SFEMG-s in patients with suspected neuromuscular junction disease

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Background and aims: Single fiber electromyography with voluntary activation (SFEMG-v) is one of the main electrophysiologic techniques used for the diagnosis of neuromuscular junction disorders. However SFEMG-v may be poorly tolerated for its extensive duration or for the difficulty of maintaining constant voluntary contraction. The SFEMG with near-nerve stimulation (SFEMG-s) may have some advantages, though there is lack of evidence regarding its diagnostic accuracy. The aim of this study was to compare the results of these two techniques in a cohort of patients with suspected neuromuscular junction disease.

Methods: This study involved 26 patients with suspected neuromuscular junction disorder. All patients underwent a clinical examination and an electrophysiological assessment consisting of repetitive nerve stimulation, and SFEMG-v and SFEMG-s by using a concentric needle electrode. We tested the right orbicularis oculis in all patients.

Results: In almost all patients the results matched between SFEMG-v and SFEMG-s. In particular, the differences between the percentage of potential pairs with pathological jitter values were not statistically significant. Moreover, no differences were observed between the percentage of patients with pathological mean MCD values when comparing these two methods. In 10 patients a neuromuscular junction disorder was diagnosticated with consistent results between the two techniques.

Conclusion: This study shown that SFEMG-s is a reliable diagnostic technique compared to the traditional SFEMG-v due to the consistency of results in our cohort of patients. This method might be an effective alternative to the SFEMG-v in patients who have difficulty maintaining constant voluntary activation of the muscle or are poorly compliant.

Disclosure: Nothing to disclose.

Movement disorders 3

EPR-269

Effects of continuous subcutaneous infusion of foslevodopa/foscarbidopa on quality-of-life in Parkinson's patients

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Background and aims: Foslevodopa/foscarbidopa is a soluble formulation of levodopa/carbidopa prodrugs delivered as a 24-hour/day continuous subcutaneous infusion for the treatment of motor fluctuations in patients with advanced Parkinson's disease (aPD). An open-label, 52-week, single-arm clinical safety/tolerability trial on foslevodopa/foscarbidopa treatment (NCT03781167) also evaluated improvement in patient-reported quality of life via the Parkinson's Disease Questionnaire-39 items (PDQ-39), which measures quality of life aspects relevant to patients with aPD via a summary index total score and 8 domain scores.

Methods: Eligible patients had levodopa-responsive idiopathic PD, were ≥ 30 years of age, and had ≥ 2.5 hours of average daily "Off" time prior to study enrollment. This interim analysis included PDQ-39 domain data. A paired sample t-test was used to compare change from baseline. All P-values are nominal and not corrected for multiplicity. All participants receiving foslevodopa/foscarbidopa infusion composed the Safety Analysis Set.

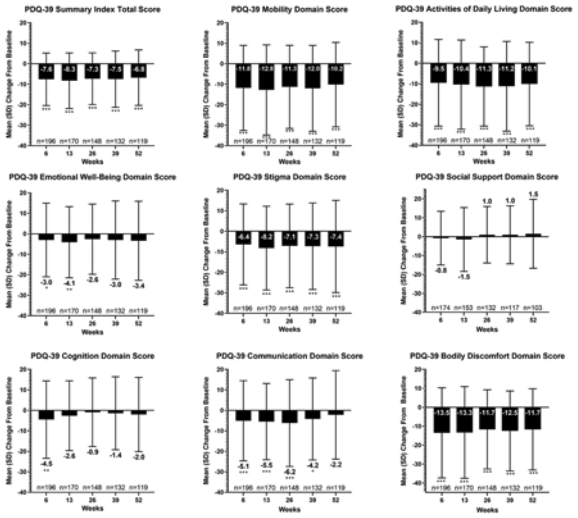
Results: The PDQ-39 mean (SD) summary index score change from baseline to Week 52 (n=119) was -6.8 (13.56; p≤0.001). Significant improvements through 52 weeks were found for the subdomains of mobility, activities of daily living, stigma, and bodily discomfort (Table 1 and Figure 1). Foslevodopa/foscarbidopa safety data were previously presented (Aldred et al. EAN, 2022) and foslevodopa/foscarbidopa was generally safe and well tolerated, with infusion site events being among the most commonly reported adverse events (infusion site erythema [51.2% of patients], nodule [27.9%], cellulitis [23.0%]).

Table 1 – Parkinson's Disease Questionnaire-39 Items (PDQ-39) Summary Index and Domain Scores at Baseline, Week 52, and Change From Baseline

PDQ-39 Domain	N	Baseline Mean (SD)	Week 52 Visit Mean (SD)	Mean (SD) Change From Baseline	P Value[a]
Summary Index Total Score	**119**	**33.5 (14.75)**	**26.7 (16.51)**	**-6.8 (13.56)**	**≤ 0.001***
Mobility Domain Score	119	43.2 (24.20)	33.0 (25.25)	-10.2 (20.63)	≤ 0.001*
Activities of Daily Living Domain Score	119	40.2 (21.33)	30.1 (21.32)	-10.1 (20.35)	≤ 0.001*
Emotional Well-being Domain Score	119	30.5 (20.00)	27.1 (19.66)	-3.4 (19.32)	0.0575
Stigma Domain Score	119	23.3 (21.76)	15.9 (20.04)	-7.4 (22.47)	≤ 0.001*
Social Support Domain Score	103	12.9 (15.95)	14.3 (20.19)	1.5 (18.21)	0.4188
Cognition Domain Score	119	27.0 (17.88)	25.0 (18.45)	-2.0 (18.12)	0.2201
Communication Domain Score	119	28.4 (22.08)	26.2 (21.84)	-2.2 (21.63)	0.2758
Bodily Discomfort Domain Score	119	39.8 (22.09)	28.1 (22.99)	-11.7 (21.49)	≤ 0.001*

PDQ-39, Parkinson's disease questionnaire 39 items; SD, standard deviation
[a] P value is obtained from two-sided paired-sample t-test
* P value ≤ 0.001

Figure 1 – The Change from Baseline in PDQ-39 Summary Index and Individual Domain Scores over the 52-week Treatment Period



* P ≤ 0.05, ** P ≤ 0.01, *** P ≤ 0.001 vs. the baseline value from the same visit; P value is obtained from a two-sided paired-sample t-test

Conclusion: Foslevodopa/foscarbidopa demonstrated significant improvements in quality of life as measured by the PDQ-39 summary index as well as 4 subdomains.

Disclosure: Abstract support provided by AbbVie Inc.

EPR-270

Results of tremor treatment with HIFU with direct coordinates obtained by tractography

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Background and aims: Tractography is a novel MRI method that allows us to locate neural tracts. Classically, for the treatment of tremor by HIFU, the theoretical coordinates of the VIM are used, but with tractography we locate the dentato-rubro-thalamo-cortical tract as a target. We present the results of patients treated with this technique in our hospital.

Methods: The demographic and clinical characteristics, data of the procedure, clinical results at 6 months of treatment and side effects of the patients done till June-2022 have been collected. A descriptive analysis has been carried out.

Results: 31 patients with refractory essential tremor. 35% men and 65% women. Average age 67,5 years. Mean of SDR was 0,53 (0,72–0,36). A mean of 7,5 (4–13) sonications per procedure were performed. The average maximum energy used was 11.956J. Side effects during the procedure: 9% (paresthesia, dysmetria, facial paresis), 95% transient headache and 40% transient vertigo. At one month and six-month 19% y 6% of mild adverse events was presents. Average reduction in the scale of the tremor CRST-A was 89,3 % and CRST-B was of 73% in the treated hand. The mean of reduction in CRST-C was 85%.

Conclusion: Tractography allows individualizing the target in each patient. Clinical results are equal to or slightly better than with the indirect VIM target. This lesions avoid motor and sensory areas associated with the risk of secondary effects. Reduces the number of sonications per procedure.

Disclosure: I do not have any conflict of interest with the content of this abstract.

EPR-271

Assessment of quality of life in Polish patients with cervical dystonia

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Background and aims: The aim of the study was an assessment of quality of life in patients with cervical dystonia with regard to the severity of dystonic symptoms, level of depression, quality of sleep and other clinical factors.

Methods: The study group included patients with cervical dystonia treated with botulinum toxin. On the day of administration, examinees were asked to complete questionnaires: Craniocervical Dystonia Questionnaire (CDQ-24), Beck Depression Inventory (BDI-II) and Pittsburgh Sleep Quality Index (PSQI). Intensity of dystonic symptoms was measured using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). Other clinical data was extracted via questionnaire and medical record.

Results: The study comprised 33 patients with cervical dystonia (23 women, 10 men, average age – 55.6±11.9 years, average disease duration – 14.1±9.3 years, average botulinum toxin treatment duration – 8.6±5.1 years). The highest CDQ-24 score, advocating the lowest quality of life was observed for subscales 'pain' and 'stigma' (tab.1). Significant correlations between the gravity of dystonia according to TWSTRS (tab.2), severity of depression according to BDI-II (tab. 2), sleep disorders according to PSQI (tab.3) and lower total quality of life and particular CDQ-24 subscales were revealed. The duration of botulinum toxin treatment correlated significantly with the result of 'pain' subscale of CDQ-24. Notable parallels between the concomitance of other disorders, especially mental and lower quality of life were observed.

CDQ-24	**Average** (0-100) ±SD
total	51,0 ± 20,2
stigma	57,1 ± 24,2
emotional wellbeing	48,6 ± 25,7
pain	62,9 ± 29,1
activities of daily living	54,7 ± 25,0
social/family life	29,8 ± 25,8

Tab. 1 Results of CDQ-24 (SD – standard deviation)

CDQ-24	TWSTRS				BDI-II
	total	severity	disability	pain	
total	**p=0,003 R=0,50**	**p=0,014 R=0,42**	**p=0,013 R=0,43**	**p=0,008 R=0,46**	**p=0,000 R=0,73**
stigma	p=0,196 R=0,23	p=0,091 R=0,30	p=0,527 R=0,11	p=0,284 R=0,19	**p=0,006 R=0,47**
emotional wellbeing	**p=0,015 R=0,42**	p=0,072 R=0,32	**p=0,019 R=0,41**	**p=0,037 R=0,36**	**p=0,000 R=0,82**
pain	**p=0,001 R=0,54**	**p=0,046 R=0,35**	**p=0,005 R=0,48**	**p=0,000 R=0,58**	**p=0,004 R=0,49**
activities of daily living	**p=0,006 R=0,47**	**p=0,029 R=0,38**	**p=0,014 R=0,42**	**p=0,017 R=0,41**	**p=0,007 R=0,46**
social/family life	**p=0,027 R=0,39**	p=0,057 R=0,34	p=0,058 R=0,33	p=0,057 R=0,34	**p=0,000 R=0,70**

Tab. 2 Correlation between CDQ-24 and TWSTRS and BDI-II results (R – Pearson's correlation coefficient)

CDQ-24	PSQI			
	global	subjective sleep quality	sleep latency	sleep duration
total	**p=0,00045 R=0,58**	**p=0,00006 R=0,64**	**p=0,0177 R=0,41**	**p=0,0333 R=0,37**
stigma	**p=0,0238 R=0,39**	**p=0,00979 R=0,44**	p=0,216 R=0,22	p=0,0600 R=0,33
emotional wellbeing	**p=0,00802 R=0,45**	**p=0,00142 R=0,53**	p=0,0633 R= 0,33	p=0,304 R=0,18
pain	**p=0,00010 R=0,62**	**p=0,00017 R=0,61**	**p=0,00120 R=0,54**	p=0,0650 R=0,32
activities of daily living	p=0,0906 R=0,30	**p=0,0303 R=0,38**	p=0,279 R=0,19	p=0,0760 R=0,31
social/family life	**p=0,0171 R=0,41**	**p=0,00410 R=0,49**	p=0,0786 R=0,31	p=0,489 R=0,12
CDQ-24	**PSQI**			
	sleep efficiency	sleep disturbance	use of sleep medication	daytime dysfunction
total	p=0,782 R=0,05	**p=0,00086 R=0,55**	p=0,0700 R=0,32	**p=0,00013 R=0,62**
stigma	p=0,899 R=-0,02	**p=0,0277 R=0,38**	p=0,323 R=0,18	**p=0,0156 R=0,42**
emotional wellbeing	p=0,870 R= 0,03	**p=0,00444 R=0,48**	**p=0,0323 R=0,37**	**p=0,00167 R=0,53**
pain	p=0,483 R= 0,13	**p=0,00346 R=0,49**	p=0,0705 R=0,32	**p=0,00296 R=0,50**
activities of daily living	p=0,585 R=-0,10	**p=0,0190 R=0,41**	p=0,969 R=0,01	**p=0,0491 R=0,35**
social/family life	p=0,723 R=-0,06	**p=0,0383 R=0,36**	**p=0,0417 R=0,36**	**p=0,00037 R=0,58**

Tab. 3 Correlation between CDQ-24 and PSQI results (R – Spearman's rank correlation coefficient)

Conclusion: Patients with cervical dystonia declare low quality of life, especially concerning pain and stigma. The severity of dystonia, level of depression and sleep disorders significantly affect the quality of life in these patients.
Disclosure: Nothing to disclose.

EPR-272

A study of dopaminergic pathway in neurologic Wilson disease with movement disorder

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Background and aims: Movement disorder (MD) is an important manifestation of neurologic Wilson disease (NWD), but there is a paucity of information on dopaminergic pathways. To evaluate dopamine and its receptors in patients with NWD, and correlate the changes with MD and MRI changes.
Methods: Twenty patients with NWD having MD were included. The severity of dystonia was assessed using BFM (Burke-Fahn-Marsden) score. The neurological severity of NWD was categorized as grade I to III based on the sum score of 5 neurological signs and activity of daily living. Dopamine concentration in plasma and CSF was measured using Liquid Chromatography Mass Spectrometry, and D1 and D2 receptor expression at mRNA by reverse transcriptase polymerase chain reaction in patients and 20 matched controls.
Results: The median of the patients was 15 years and 7(35%) were females. 18(90%) patients had dystonia and 2(10%) chorea. The CSF dopamine concentration (0.08± 0.02 vs 0.09±0.017pg/ml; p=0.42) in the patients and controls was comparable, but D2 receptor expression was reduced in the patients (0.41±0.13 vs 1.39 ±1.04; p=0.01). Plasma dopamine level correlated with BFM score (r= 0.592, p<0.01) and D2 receptor expression with severity of chorea (r=0.447, p<0.05). The neurological severity of WD correlated with plasma dopamine concentration (p=0.006). Dopamine and its receptors were not related to MRI changes.
Conclusion: Central nervous system dopaminergic pathway is not enhanced in NWD, which may be due to structural damage to the corpus striatum and /or substantia nigra.
Disclosure: Nothing to disclose.

EPR-273

Fluid biomarkers for differential diagnosis and clinical disease severity in atypical parkinsonian syndromes

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Background and aims: Currently, there are no established in-vivo biomarkers available for differential diagnosis of Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP) against Parkinson's Disease (PD) or assessment of clinical disease severity in these disease entities. Here, we investigate biomarkers representing neurodegeneration (neurofilament light chain, NfL), astrocytosis (glial fibrillar acidic protein, GFAP) and microglial activation (soluble triggering receptor expressed in myeloid cells 2, sTREM2) for their value in MSA and PSP.
Methods: Plasma samples of 25 MSA, 45 PSP, 25 PD patients (diagnosed using clinical consensus criteria) and 21 healthy controls (HC) were analyzed for NfL and GFAP (Quanterix Simoa®). CSF samples of a subset of patients were analyzed for NfL, GFAP and sTREM2. sTREM2 analysis was performed using a previously published ELISA. Biomarker levels were cross-sectionally compared between groups and correlated to clinical disease severity in MSA and PSP.
Results: NfL in CSF and plasma was significantly elevated in MSA and PSP compared to PD and HC ($p<0.05$). For MSA, GFAP in CSF and plasma and sTREM2 in CSF showed positive correlation with clinical disease severity (UMSARS score, $p<0.05$), while NfL in CSF and plasma correlated well with clinical disease severity in PSP (PSPRS score, $p<0.05$).
Conclusion: NfL shows promise as biomarker for differential diagnosis of MSA and PSP against PD. While NfL also seems to serve as biomarker for clinical disease severity in PSP, in MSA both GFAP and sTREM2 seem to reflect clinical disease severity. Longitudinal investigations are needed to investigate the dynamic of these biomarkers throughout the disease course.
Disclosure: Nothing to disclose.

EPR-274

Inter-software variation in post-operative localization of deep brain stimulation electrodes

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Background and aims: Tools and pipelines for the exact post-operative localization of deep brain stimulation (DBS) electrodes may be of major benefits in the evaluation of the stimulation area. However, little is known about their accuracy and inter-software agreement. This study is comparing 3 different software packages used for DBS electrode localization. The primary aim was to evaluate the distances between the calculated electrode positions and overlap between the estimated volumes of tissue activated (VTAs).
Methods: T1-weighted MRI images before and after implantation of the electrodes to the subthalamic nucleus for DBS in 106 Parkinson's disease patients (age 59,5±8,26 years; disease duration 13.5±6,1 years) were processed using Lead-DBS (LDBS), SureTune (ST), and Brainlab (BL). Afterwards, Euclidean distance between the active contacts and Dice coefficient for VTA overlap were calculated.
Results: Euclidean distance between the calculated positions of the active contact in individual software packages (median [10th–90th percentile]): 1. LDBS vs. ST: 1.92 mm (0.83–3.73) 2. LDBS vs. BL: 2.27 mm (0.93–3.90) 3. ST vs. BL: 1.98 mm (0,84–3.84) Dice coefficient (LDBS vs ST): 0,32(0–0,6). BL does not calculate VTA, so no relevant data is presented.
Conclusion: Since the presented median distances between the calculated electrode position in individual software packages approach the size of the target area, one must exercise extreme caution when utilizing these outputs for any clinical decision making. Better objectivization and more accurate tools are still needed for this field to achieve bigger impact.
Disclosure: This research was financed by the Ministry of Health, project Clinical, imaging and biological predictors of effects associated with deep brain stimulation in Parkinson's disease (CLIMABI), grant no. NV19-04-00233.

EPR-275

The effect of APOE ε4 on striatal vesicular monoamine transporter-2 density in Parkinson's disease

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Background and aims: Vesicular monoamine transporter-2 (VMAT2) is considered to be an objective biomarker of presynaptic dopaminergic nerve terminals in the striatum of Parkinson's disease (PD) patients. The Apolipoprotein E ε4 (APOE ε4) is associated with the risk of early PD, and whether it has a direct effect on dopaminergic system is unclear. The aim of this study was to evaluate the effect of APOE ε4 on striatal VMAT2 density in PD.
Methods: Longitudinal data were obtained from 19 PD patients who were classified as APOE ε4 carriers (n=7) and non-carriers (n=12) in the Parkinson's Progression Marker Initiative. The availability of VMAT2 in the caudate, anterior and posterior putamen was assesed using 18F-AV-133 PET at baseline and the 1- and 3-year follow-up. 18F-AV-133 striatal binding ratio (SBR) was calculated as (target region/reference region)-1 using the occipital lobe as the reference region. Independent-samples t-test and linear mixed model were used to assess the effect of APOE ε4.
Results: At beasline, APOE ε4 carriers showed lower 18F-AV-133 SBR than non-carriers in the caudate, anterior and posterior putamen, but not statistically significant ($p > 0.05$). At 1- and 3-year follow-up, APOE ε4 carriers exhibited greater magnitude of longitudinal changes in straital 18F-AV-133 SBR than non-carriers, but again not statistically significant.
Conclusion: APOE ε4 has no significant effect on dopaminergic system in patients with PD.
Disclosure: Nothing to disclose.

EPR-276

Feasibility of Deep Learning in Predicting Phenotype Conversion of REM Sleep Behaviour Disorder

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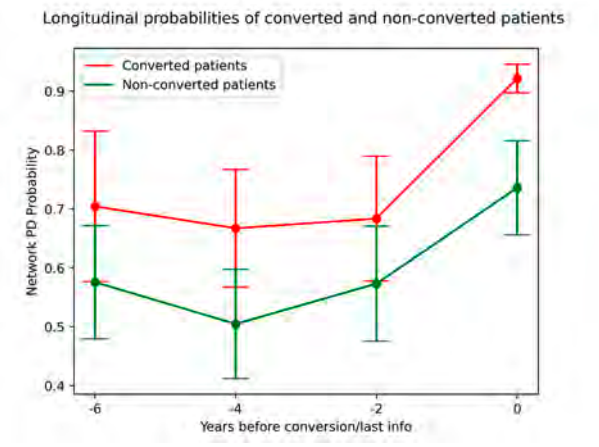
Background and aims: Isolated rapid-eye-movement sleep behavior disorder (iRBD) is considered an early stage of alpha-synucleinopathies such as Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy. There is no available biomarker to predict phenoconversion to overt α-synucleinopathy. Our goal was to investigate the feasibility of deep learning(DL) in predicting disease progression and phenoconversion in patients with iRBD.
Methods: The study was conducted in 18F-FDG PET scans of 38 iRBD patients with a follow-up of 2–10 years. A previously developed convolutional neural network for parkinsonism differential diagnosis was adapted to derive deep metabolic imaging indices, which were used as predictive scores of longitudinal data. The network was trained with 769 parkinsonian and 863 non-parkinsonian subjects. Differences in predictive scores of scans taken more than 6 years and less than 6 years before conversion were assessed by Mann-Whitney U test.
Results: The predictive scores increased with disease progression in patients that converted to PD/DLB and that did not convert. The scores were higher in converted than in non-converted subjects, although differences were only statistically significant at conversion year (p=0.004). The predictive scores of scans less than 6 years before conversion were higher than those acquired more than 6 years before conversion p=0.001).



Average longitudinal DMI indices of converted to PD/DLB (n=11/n=4) and non-converted (n=16) subjects at 6, 4, 2, and 0 years before conversion or last clinical information. Error bars represent the standard error of the mean (SEM).

Conclusion: Despite the limited sample size in this pilot study, the results confirmed the feasibility of DL for phenoconversion prediction of iRBD. The potential of DL in extrapolating to the prodromal stage may accelerate the development of early diagnostic methods for disease progression in alpha-synucleinopathies.
Disclosure: KS receives research grants from Novartis and Siemens Healthineers.

EPR-277

Effects of probiotics on clinical symptoms in Parkinson's disease: a pilot, randomized, placebo-controlled study

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Background and aims: Parkinson's disease (PD) is a common neurodegenerative disease whose pathophysiology has not yet been fully understood. Alpha synuclein may also accumulate in the gut accounting for the frequently reported gastrointestinal symptoms. This gut-brain-axis can be modulated by probiotics, which exert known anti-inflammatory activity. The aim of this study is to evaluate the suitable clinical impact of probiotics in a group of PD patients compared to placebo.
Methods: Patients were enrolled and blindly randomized to receive active probiotics (composed by Bifidobacterium animalis subsp. lactis BS01, Bifidobacterium longum 03, Bifidobacterium adolescentis BA02, Fructo-oligosaccharides and Maltodextrin) or placebo. Clinical evaluations included motor (with the UPDRSIII), non-motor (with NMSS, Compass-31, PaC-Qol, CAS, Wexner, Zung and BDI-II) and cognitive (with MOCA) assessment and were performed at enrolment, after 6 and 12 weeks. Anti-parkinsonian therapy was stable during the study.
Results: 40 PD patients were recruited (20 for each group, which did not differ for clinical and demographic data). After 12 weeks, the "active" group had a significant improvement of the motor (UPDRS III: 13.89±4.08 vs 12.74±4.57, p=0.028) and non-motor symptoms (NMSS: 34.32±21.41 vs 30.11±19.89, p=0.041), particularly in the gastrointestinal subitem (3.79±4.14 vs 1.89±2.54, p=0.021). A positive trend was also detected in the CAS, MoCA, Compass-31 e PaC-Qol tests.
Conclusion: Though on a small group of patients, our data demonstrate that probiotics may constitute an important add-on therapy to conventional anti-parkinsonian drugs in order to improve motor, non-motor and cognitive symptoms in PD patients.
Disclosure: Nothing to disclose.

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EPR-278

Opicapone's Effects on Progression Scales in Relation to the 9-Symptom Wearing-off Questionnaire: the OPTIPARK Study

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Background and aims: In clinical trials, opicapone (OPC) was effective for end-of-dose motor fluctuations (MF) in Parkinson's disease (PD) patients; however, real-world studies are necessary to complement evidence from these trials. The OPTIPARK study aimed to evaluate OPC-50 mg as adjunct to levodopa in PD patients in everyday clinical practice.

Methods: OPTIPARK was a prospective, open-label, single-arm study conducted in the UK and Germany. PD patients with MF received OPC 50-mg as add-on to current antiparkinsonian treatment. Primary efficacy endpoint was Clinician's Global Impression of Change after 3 months. Secondary endpoints included Unified Parkinson's Disease Rating Scale (UPDRS), Non-motor Symptoms Scale (NMSS), Parkinson's Disease Questionnaire (PDQ-8) and Symptom Wearing-off Questionnaire (WOQ-9). This study evaluated changes in UPDRS, NMSS and PDQ-8 after 3 months of OPC treatment in patients who reported improvements in WOQ-9 versus those who did not.

Results: 393 (82.4%) completed the 3-month endpoint (Completers Set; Table). Compared to patients without WOQ-9 improvements, those with WOQ symptoms at baseline that had improved at 3 months had greater improvement in: UPDRS (particularly for anxiety/panic attacks, reduced dexterity and pain/aching); NMSS score, except for mood changes (particularly for cloudy mind/slowness of thinking and anxiety/panic attacks); and PDQ-8, except for tremor and any stiffness (particularly for slowness of movement, pain/aching and muscle cramping) (Figure).

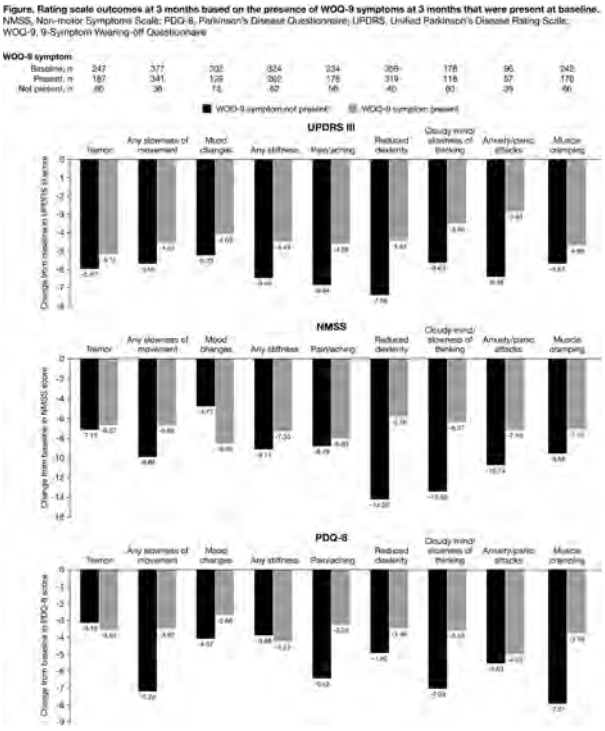

Figure. Rating scale outcomes at 3 months based on the presence of WOQ-9 symptoms at 3 months that were present at baseline. NMSS, Non-motor Symptoms Scale; PDQ-8, Parkinson's Disease Questionnaire; UPDRS, Unified Parkinson's Disease Rating Scale; WOQ-9, 9-Symptom Wearing-off Questionnaire

Conclusion: OPC treatment improved 'wearing-off' symptoms including those with a high impact on patients' life, such as pain and reduced dexterity. Even for patients still experiencing 'wearing-off' symptoms at 3 months, improvements in motor/non-motor symptoms and quality of life were reported.

Disclosure: Supported by BIAL.

EPR-279

Dopaminergic medication affects smooth pursuit but not saccadic eye movements in Parkinson's disease

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Background and aims: PD is characterised by brady-hypokinesia, tremor, rigidity, and balance impairments. Other abnormalities, such as changes in eye-movements, also occur. The effect of dopaminergic medication on eye-movements is however not clear. The objective of this study was to assess the effect of dopaminergic medication on eye movements in PD.
Methods: 21 healthy subjects (HS) and 20 PD patients tested on medication (PD-ON); 17 were also tested off medication (PD-OFF). Reflexive saccades, antisaccades, and smooth pursuit with three different velocities of the moving target (low, medium, and high) in horizontal and vertical plane were evaluated with an eye-tracking system.
Results: Compared to HS, PD-ON showed greater latency in horizontal smooth pursuit tasks when the target was moving at high (p=0.004) and medium (p=0.043) veisclose. locities. Compared to HS, PD-ON (p=0.010) and PD-OFF (p=0.017) were less accurate in tracking the target moving with high velocity in the vertical direction. PD-OFF had greater latency in vertical smooth pursuit at medium target velocity compared to their latency ON medication (p=0.035) as well as compared to HS (p=0.022). PD-OFF needed more time to perform antisaccades compared to PD-ON (p=0.044).
Conclusion: Compared to HS, patients with PD had prolonged latencies in horizontal and vertical smooth pursuit. Similarly, PD patients were less accurate in vertical smooth pursuit. Dopaminergic medication affected the latency of vertical smooth pursuit and the time needed to perform antisaccades. There were no significant differences in the latency of reflexive saccades and in the number of errors in antisaccades between the groups.
Disclosure: Nothing to disclose.

EPR-280

Divergent sex-specific functional striatal connectivity in drug-naïve patients with Parkinson's disease

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Background and aims: Sex-specific pattern within the nigrostriatal and striatocortical pathway may underlie clinical divergences observed in male and female patients with Parkinson's disease (PD) over the disease course. The aim of this study is to investigate the potential effect of sex on the regional striatal functional connectivity (FC) in drug-naïve PD patients applying a region-of-interests (ROIs)-based approach to resting-state functional MRI (rs-fMRI).
Methods: 147 drug-naive PD patients (83 male and 64 female) and 38 healthy controls (HCs) were enrolled. Motor, non-motor, neuropsychological assessments and rs-fMRI were performed.
Results: Both male and female PD patients showed decreased FC between the sensorimotor ROI and the substantia nigra compared to HCs. The sensorimotor ROI showed decreased FC with the superior frontal gyrus (SFG) in female PD patients compared to male PD and HCs and decreased FC with the cingulate gyrus in male PD patients compared to female PD and HCs. The limbic ROI showed increased FC with the insula in male PD patients and increased FC with the hippocampus in female PD patients compared to HCs. The cognitive ROI showed increased connectivity with the insula and decreased connectivity with the SFG in female PD patients compared to HCs.
Conclusion: Our findings revealed the presence of a disease-related, sex-specific divergent functional striatal connectivity in PD patients even in the early stages.
Disclosure: Nothing to disclose.

EPR-281

Effect of Continuous Subcutaneous Foslevodopa/foscarbidopa Treatment on Falls, Posture and Freezing of Gait

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Background and aims: Foslevodopa/foscarbidopa (LDP/CDP) is a soluble formulation of levodopa/carbidopa (LD/CD) prodrugs administered as a 24-hour continuous subcutaneous infusion (CSCI). This post hoc analysis evaluates falls, posture and freezing of gait (FOG) in patients with Parkinson's disease treated with LDP/CDP.

Methods: This 12-week, phase 3, randomised controlled trial (RCT) (NCT04380142) and 52-week, phase 3, single-arm, open-label trial (NCT03781167) included patients aged ≥30 years with idiopathic, LD-responsive Parkinson's disease and ≥2.5 hours of "Off" time/day despite optimized therapy. Falls, posture and FOG were assessed using individual items of the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Quality of life (QoL) was assessed with the 39-item Parkinson's Disease Questionnaire.

Results: Overall, baseline item scores were low, making detection of improvement challenging. There were significant differences from baseline to months 3 and 12 in MDS-UPDRS related items scores (Table 1). In the RCT, there were no significant differences in item score changes between groups. In the open-label trial, changes in walking and balance and in freezing were positively correlated with changes in QoL (Spearman r=0.417 and 0.3163, respectively, p<0.001). Baseline characteristics were similar between patients who had vs had not experienced adverse events with falls or fall-associated injuries, except for significant differences in baseline MDS-UPDRS Part III (RCT) and walking and balance scores (open-label trial) (Table 2). Safety was reported elsewhere.

Table 1. Change from baseline to 3 months[†] or 12 months in gait- and freezing-of-gait-related items

	RCT (Week 12)						Open-label Trial (Week 13)			Open-label Trial (Week 52)		
	Oral LD/CD			CSCI			CSCI			CSCI		
Variable	LS mean (SE)	95% CI	*P* value	LS mean (SE)	95% CI	*P* value	LS mean diff. *P* value	LS mean (SE)	95% CI	*P* value	LS mean (SE)	95% CI	*P* value
Walking and balance	−0.05 (0.12)	−0.28, 0.19	.6919	0.26 (0.10)	0.06, 0.46	.0128*	.0647	0.35 (0.06)	0.22, 0.48	<.0001***	0.27 (0.07)	0.13, 0.41	.0002***
Freezing	0.21 (0.10)	0.00, 0.41	.0490*	0.46 (0.12)	0.22, 0.70	.0003***	.1419	0.52 (0.08)	0.37, 0.68	<.0001***	0.40 (0.09)	0.23, 0.57	<.0001***
Gait	0.19 (0.08)	0.02, 0.35	.0257*	0.27 (0.11)	0.05, 0.49	.0184*	.4724	−0.04 (0.06)	−0.16, 0.07	.4736	−0.15 (0.06)	−0.28, −0.03	.0152*
Freezing of gait	0.04 (0.08)	−0.12, 0.20	.6564	0.26 (0.12)	0.03, 0.49	.0267*	.1800	0.02 (0.06)	−0.10, 0.14	.7010	−0.06 (0.07)	−0.19, 0.07	.3410
Postural stability	0.07 (0.09)	−0.11, 0.24	.4403	0.11 (0.14)	−0.16, 0.38	.4326	.9774	−0.01 (0.07)	−0.15, 0.12	.8243	−0.17 (0.07)	−0.31, −0.03	.0211*
Posture	0.11 (0.08)	−0.06, 0.28	.2032	0.16 (0.11)	−0.05, 0.37	.1355	.9197	−0.02 (0.06)	−0.13, 0.10	.7887	−0.16 (0.06)	−0.28, −0.03	.0137*

[†]Assessed at week 12 for the RCT and week 13 of the open-label trial.
*$P<.05$; ***$P<.001$.
CD, Carbidopa; CSCI, continuous subcutaneous infusion; diff., difference; LD, levodopa; LS, least squares; RCT, randomized, controlled trial.

Table 1. Change from baseline to 3 months or 12 months in gait- and freezing-of-gait related items

Table 2. Comparison of baseline characteristics in patients with AEs of falls or fall-associated injuries and without AEs of falls or fall-associated injuries

	RCT CSCI			Open-label Trial CSCI		
Characteristic, mean (SD) unless otherwise specified	AE with falls or falls associated with injuries at baseline (n = 7)	AE without falls or falls associated with injuries at baseline (n = 67)	*P* value	AE with falls or falls associated with injuries at baseline (n = 45)	AE without falls or falls associated with injuries at baseline (n = 263)	*P* value
Sex, n (%) male	4 (57.14)	46 (68.66)	.536	20 (48.78)	126 (62.07)	.113
Race, n (%) White	7 (100.00)	63 (94.03)	.506	32 (78.05)	175 (86.21)	.184
Age, years	69.57 (9.52)	65.93 (9.18)	.322	66.27 (8.78)	63.43 (9.20)	.071
Years since PD diagnosis, n (%) < 10 years	5 (71.43)	46 (68.66)	.880	26 (63.41)	105 (51.72)	.171
LED from LD-containing medication and COMT inhibitors, mg/day	1051.33 (613.72)	1082.08 (598.04)	.803	1051.59 (612.30)	1067.50 (580.90)	.724
Baseline normalized "Off" time, hours	7.48 (1.24)	6.22 (2.33)	.164	5.92 (2.11)	5.91 (2.28)	.974
MDS-UPDRS Part II Score	18.43 (5.53)	14.99 (7.01)	.213	17.78 (7.54)	15.35 (7.30)	.055
MDS-UPDRS Part III Score	43.57 (21.07)	27.97 (13.55)	.008**	26.20 (11.71)	22.95 (11.37)	.099
Walking and balance (Item 2.12)	1.43 (1.13)	1.51 (1.02)	.922	1.95 (1.07)	1.54 (1.05)	.032*
Freezing (Item 2.13)	1.57 (1.27)	1.18 (1.23)	.415	1.44 (1.27)	1.19 (1.23)	.224
Gait (Item 3.10)	1.57 (0.79)	1.21 (0.86)	.222	1.12 (0.95)	0.97 (0.86)	.322
Freezing of gait (Item 3.11)	0.29 (0.76)	0.49 (1.01)	.531	0.54 (1.05)	0.29 (0.75)	.062
Postural stability (Item 3.12)	1.29 (1.38)	0.72 (1.10)	.234	0.95 (1.18)	0.66 (1.02)	.128
Posture (Item 3.13)	1.71 (0.95)	1.21 (0.88)	.147	1.32 (1.06)	1.08 (0.97)	.198

*$P<.05$; **$P<.01$. *P*-values are based on Wilcoxon rank-sum test for LD-containing medication and COMT inhibitors, and for MDS-UPDRS.
AE, adverse events; COMT, catechol-O-methyltransferase; CSCI, continuous subcutaneous infusion; LD, levodopa; LED, levodopa equivalent dose; MDS-UPDRS, Movement Disorders Society Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; RCT, randomized, controlled trial.

Table 2. Comparison of baseline characteristics in patients with AEs of falls or fall-associated injuries and without AEs of falls or fall-associated injuries

Conclusion: Modest improvement in walking, balance and freezing were observed with LDP/CDP after 3 and 12 months of treatment. Improvement in gait and freezing items were associated with improvement in QoL.

Disclosure: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approving the abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract. No honoraria or payments were made for authorship. All authors agreed to submit this abstract to the European Academy of Neurology (EAN) 2023 Congress for consideration as an oral presentation or poster. Medical writing support was provided by Michael Dyle, PhD, of JB Ashtin, and funded by AbbVie.

EPR-282

Continuous subcutaneous levodopa/carbidopa infusion for Parkinson's disease: 3-year data from the BeyoND study

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Background and aims: Primary data from the BeyoND study showed continuous, subcutaneous levodopa/carbidopa infusion with investigational ND0612 was generally safe and well-tolerated and provided sustained ≥2h improvement in 'Good' ON-time (ON without troublesome dyskinesia) and a corresponding reduction in OFF-time through 12-months of treatment. Here we evaluate 3-year outcomes.
Methods: BeyoND is an ongoing open-label study (NCT02726386) evaluating the long-term safety of ND0612 in PD patients experiencing ≥2h daily OFF-time. The primary endpoint was assessed at Month-12 followed by an open label extension of up to 108 months.
Results: Of the 114 patients who continued into the OLE, 94 (82.5%) completed ≥2 years and 76 (66.7%) completed ≥3 years of ND0612 treatment. Of those patients who started the OLE, treatment-related adverse events decreased from being reported by 73.7% of patients in Yr1, to 36.9% in Yr2 and 39.4% in Yr3. While 54,7% of patients reported adverse events of infusion-site reactions (ISRs), these led to early discontinuation in 4.4%. The incidence of infusion-site infection decreased from 19.3% in Yr1 to 9.9% in Yr2, and 11.7% in Yr3, while the incidence of other ISRs decreased from 60.5% in Yr1 to 26.1% in Yr2, and 27.7% in Yr3. Dyskinesia was reported in 3.5% of patients in Yr1, 0% in Yr2, and 1.1% in Yr3. At Month-36, the mean reduction in OFF-time was -2.8h and the increase in Good ON-time was 2.8h.
Conclusion: These data support the long-term safety, tolerability, and efficacy of ND0612.
Disclosure: Study funded by NeuroDerm. Werner Poewe, Fabrizio Stocchi, and Nir Giladi report consultancy for NeuroDerm. Liat Adar, Sophia Sopromadze, and Tami Yardeni are employed by NeuroDerm.

EPR-283

Dysphagia and mortality in levodopa/carbidopa intestinal gel: a retrospective analisys

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Background and aims: Dysphagia is a common feature in advanced phases of Parkinson's disease (PD), representing a significant risk factor for aspiration pneumonia, which is the first cause of death in PD. The impact of dysphagia in advanced PD patients treated with levodopa-carbidopa intestinal gel (LCIG) has been poorly investigated.
Methods: We retrospectively evaluated data from 95 consecutive PD patients treated with LCIG in two Italian movement disorder centers. Kaplan-Meier survival analysis and log-rank test were used to compare the survival between patients developing dysphagia (PD-Dys) or not (PD-NDys). A Cox regression was used to estimate the influence of age, disease duration, Hoehn and Yahr (H&Y) at LCIG implantation, and presence of dysphagia on mortality. We used univariate and multivariate regression analysis to estimate the association between dysphagia and age, disease duration, H&Y, hallucinations, and dementia at last evaluation.
Results: The survival analysis showed a significant higher mortality in PD-Dys vs. PD-NDys group. Dysphagia was the only variable significantly associated with mortality (95%CI 2.780–20.609; p<0.001). Univariate analyses showed a significant correlation between dysphagia and dementia (OR=0.387; p=0.033), hallucinations (OR=0.283; p=0.009), and H&Y score (OR=2.680; p<0.001). In the multivariate analysis, only the H&Y stage survived (OR=2.357; p=0.003).

Table 1. Baseline demographic and clinical features of included patients

		Overall (N = 86)	PD-NDys (N = 44)	PD-Dys (N = 42)	P value
Sex	M	58 (67%)	29 (66%)	29 (69%)	.936[b]
	F	28 (33%)	15 (34%)	13 (31%)	
Age at LCIG start (years)		67.7 ± 7.1	67.8 ± 6.9	67.7 ± 7.3	.900[a]
H&Y at LCIG start		3 (2-3)	2.75 (2-3)	3 (2-3)	.213[a]
Disease duration at LCIG start (years)		13.0 ± 5.1	13.4 ± 5.5	12.6 ± 4.6	.845[a]
Follow-up duration		3.01±2.20	3.56±2.54	2.38±1.62	**.016[a]**
Age at dysphagia onset (years)		-	-	70.5 ± 6.9	
H&Y at dysphagia onset		-	-	3 (2-4)	
Disease duration at dysphagia onset (years)		-	-	15.4 ± 5.0	
MDS-UPDRS item 2.3 at dysphagia onset		-	-	3.5 (3-4)	

Results are reported as average ± standard deviation (range) or absolute values (percentage), as appropriate. a Mann-Whitney test b Chi-square test Bold indicates the significant value of p-value: statistical significance H&Y: Hoehn and Yahr stage; LCIG:

Table 2. Univariate and multivariate analysis of the association between patients' characteristics and dysphagia

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	OR (95%CI)	P value
Age	1.030 (0.971-1.092)	.324	-	-
Disease duration	1.025 (0.953-1.102)	.504	-	-
Hoehn &Yahr stage at last evaluation	2.680 (1.608-4.468)	**<.001**	2.357 (1.330-4.180)	**.003**
Hallucinations	0.283 (0.109-0.732)	**.009**	0.346 (0.194-1.778)	.346
Dementia	0.387 (0.162-0.924)	**.033**	0.839 (0.312-2.575)	.839

Results are reported as Odds Ratio (OR); 95% Confidence Interval (CI) is reported in brackets. Bold indicates the significant value of p-value: statistical significance

Conclusion: Dysphagia significantly increased the risk of death in PD patients treated with LCIG, independently from the presence of dementia and hallucinations. These findings confirm the management of this symptom as a priority in the advanced PD stages, especially in people with PD who underwent LCIG.
Disclosure: Nothing to disclose.

EPR-284

Local Field Potentials in Parkinson's Disease: Effect of Lead Type and Target, Peak Detection, and Contact Selection

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Background and aims: The objective was to determine differences in local field potentials (LFP) between targets (i.e., globus pallidus internus (GPI), subthalamic nucleus (STN)), lead type (i.e., directional vs cylindrical), determine real-world peak detection, and the association of peak contact pairings to stimulation contact selection.
Methods: Real-world LFP data from 48 PwPD (age: 65.1[56.3–71.8] years, sex: 19 female, disease duration: 12.0[7.8–15.0] years) and 96 nuclei recordings were collected as part of a prospective, post-market study. Peak characteristics and band power amplitude averages were calculated for each nucleus.
Results: Peaks were detected in a total of 76(81.7%) nuclei with a recording and at least 1 peak was detected in 93.3% of patients with bilateral recordings. Peaks were detected in 30/36 directional nuclei and 46/60 cylindrical nuclei (p=0.288). Peak amplitude (p=0.577) and frequency (p=0.962), as well as band power in the low-beta (p=0.104) and high-beta (p=0.213) ranges were similar between lead types. No differences were found in peak detection (p=0.078), amplitude (p=0.281), and frequency (p=0.506), as well as band power in the alpha (p=0.073), high-beta (p=0.314), and gamma (p=0.464) between targets. Therapeutic contact selection fell in between or on the lower contact of the peak bipolar contact pairing in 94.1% of cases.
Conclusion: Lead type and target appear to have minimal effect on peak detection and LFP characteristics when deployed in a real-world setting. Importantly, LFP peaks are prominently detectable in real-world settings and demonstrate association to stimulation contact selection in PwPD. These data provide key insights into the real-world feasibility and interpretation of LFPs in PwPD.
Disclosure: A. Singer, C. Sannelli, N. Morelli are employees of Medtronic, Minneapolis, MN, USA. A. Fasano, T. Witt, S. Bick, M. Schiess, H. Mure, G. Oyama and K. Kimura are Principal Investigators of the Medtronic Product Surveillance Registry.

EPR-285

Parkinson's Disease (PD) and predictors of Driving Cessation: Results from a 5-year Longitudinal Study

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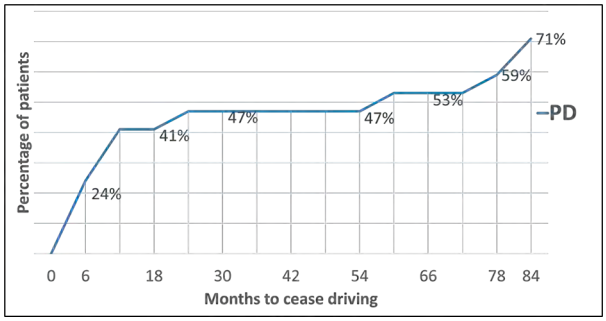
Background and aims: Motor and cognitive impairment of PD patients interfere with their driving ability. We sought to identify predictors of driving cessation among PD patients.
Methods: We examined 17 patients with PD (16 men, mean age 65 years old) and 24 healthy controls (13 men, mean age 64 years old). Baseline evaluation included neurological and neuropsychological assessment and a driving simulator test. Re-evaluation after a mean period of 60 months included a structured interview with patients and caregivers. Primary endpoints were driving cessation and death. When the primary endpoints were not met, we performed a final evaluation after a mean period of 84 months.
Results: 5 patients died during follow up (29%, p<0.001 / mean time to death: 63 months), while 12/17 ceased driving (71%, p<0.001 / mean time to cease: 30 months). Main reason to cease driving was patients' will (58%). 41% of patients had at least one dangerous driving event during follow-up (p<0.01). Performance on Hopkins Verbal Learning Test (HVLT) and Judgement of Line Orientation Test (JLO) at baseline evaluation had a strong negative correlation with driving cessation probability (r=-0.7, p<0.01). No statistically significant correlations were found between simulator measurements and primary endpoints, despite the tendency observed.



Percentage of patients with PD who ceased driving during Follow-up.

Conclusion: PD patients cease driving earlier than their healthy counterparts and have a higher accident risk. HVLT and JLO are promising predictors of driving cessation. Only few prospective studies on the subject "PD and Driving" exist. Larger prospective studies are needed to confirm our findings and establish correlations between simulator measurements and primary endpoints.
Disclosure: This review is part of Dr Stamatelos' PhD project with title " Evaluation of driving behavior of patients with MCI, Dementia or Parkinson's Disease: Diagnostic and Prognostic Markers", funded and supported by Onassis Foundation.

EPR-286

Predictors of spread in oromandibular dystonia: description of data from the Italian Dystonia Registry

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Background and aims: Oromandibular dystonia (OMD) can interest just the OM region (isolated) or other body parts (combined). The aim of our study was to identify main clinical and demographic features of OMD in the Italian population.
Methods: Data were obtained from the Italian Dystonia Registry (IDR). We analyzed the main features of those patients who presented an OM dystonia, which could be isolated or combined: age, age at the onset, etiologies, site of onset, sensory trick.
Results: 313 patients with OMD were found. Age at the onset was 66.8±31.6 y.o. (Mean±SD). The most common etiology was idiopathic (84.6%). 53 patients (17%) presented an OMD onset; 109 (34.8%) a combined onset (OM plus another site); 151 (48.2%) manifested the onset of dystonia in a non-OM site. Spread occurred in 26.4% of patients with onset at the OM site and in 8.2% of patients with combined onset. Spread of dystonia was significantly lower in the group of combined onsets when compared with other two groups and spread resulted significantly higher in patients with sensory trick.
Conclusion: Data from IDR show that OM dystonia is prevalently idiopathic and combined. Moreover, when the onset of dystonia is combined, later occurrence of dystonia in other body regions has a very low prevalence. Finally, sensory trick may predict a higher probability of dystonia spread to different body sites.
Disclosure: Nothing to disclose.

Neurocritical care

EPR-287

Spectrum of Neurologic Complications after Living Donor Liver Transplantation

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Background and aims: Liver transplant is the last resort in many acute and chronic liver diseases and inherited disorders. Neurologic complications in the immediate and extended post-operative period can cause significant mortality, morbidity, and prolonged hospital stay. This study aimed at the detection of predictive factors in the peri-operative clinical profile that could aid a timely detection of these complications.
Methods: Retrospective analysis of adult living donor liver transplantation (LDLT) recipients at our centre revealed 64 cases of post-operative neurologic complications from 2009 to 2022. Compared to 2,853 controls of the same population, their pre-operative parameters, comorbidities and aetiologic factors were analysed from day 1 to 180 of post-operative period.
Results: The incidence of neurologic complications was 2.19% (n=64). The mortality rate in the study group was 31.3% (compared to 16% in controls, n=2,853). Encephalopathy, seizures, and stroke were the most encountered complications. Patients with advanced age, diabetes, hypertension, alcoholism, pre-operative abnormal total leukocyte count, hepatic encephalopathy, pneumonia, and renal dysfunction were more likely to suffer from these complications. After multivariate analysis, those with advanced age, higher MELD score, and pre-existing minimal hepatic encephalopathy fared worse for neurologic outcome (p=0.013, 0.007 and <0.0001 respectively).

Table: Univariate Logistic Regression for Predictors of Study Group

Study Parameters	Odds Ratio (O.R.)	95% C.I. for O.R.		p-value
		Lower	Upper	
Age (>50 years)	1.935	1.15	3.26	0.013*
DM	2.064	1.24	3.44	0.005*
Hypertension	2.251	1.26	4.01	0.006*
CKD	11.306	1.25	102.59	0.031*
Abnormal TLC	3.015	1.18	7.72	0.021*
Minimal HE	3.576	2.13	5.99	<0.0001*
HRS	1.916	1.06	3.45	0.030*
ALD	1.915	1.17	3.15	0.010*
Pre op Creatinine (<2.5)	1.063	0.14	7.87	0.952
Calculated MELD	1.052	1.01	1.09	0.007*

*p<0.05; statistically significant

DM- Diabetes Mellitus, CKD- Chronic Kidney Disease, TLC- Total Leukocyte Count, HE- Hepatic Encephalopathy, HRS- Hepatorenal Syndrome, ALD- Alcoholic Liver Disease, MELD- Model for End-stage Liver Disease score

Multivariate Logistic Regression for Predictors of Post-Operative Neurologic Complications

Conclusion: Modifiable risk factors such as pre-operative pneumonia, renal dysfunction, and deranged total leukocyte count can be corrected to reduce incidence of neurologic complications after liver transplantation. Keeping a watchful eye over those with advanced age, a higher MELD score and pre-existing hepatic encephalopathy can alert the transplant physician in time to diagnose and treat adverse neurologic outcomes.
Disclosure: No financial or other disclosures are needed for any of the authors.

EPR-288

Sepsis in Neurology Intensive Care Unit – Incidence and Outcome

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Background and aims: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection.
Methods: The aim of our study was to determine the incidence, risk factors associated with higher mortality and the survival rate of patients with sepsis in the Neurological Intensive Care Unit (NICU). This retrospective, observational, study included 65 patients who were diagnosed with sepsis and treated in the NICU during a 2-year period. Sepsis-3 definition was used for diagnosing sepsis. We have statistically analyzed demographic and clinical characteristics of our patients and evaluated their impact on the outcome of sepsis. The outcome has been divided into 2 categories: survival and adverse outcome.
Results: Overall mortality rate of sepsis was 67.69%. Our study shows that GCS≤8 and higher SOFA score in the time of diagnosing sepsis, need for intubation and mechanical ventilation (MV) are highly significant predictors of adverse outcome in sepsis in NICU (p=0.001; p<0.001; p<0.001; p=0.001). Also, disseminated intravascular coagulopathy (DIC), total number of sepsis complications and Staphylococcus spp, were factors statistically associated with higher mortality in our patents (p=0.021; p=0.013; p=0.013). Staphylococcus spp. is also the most frequently isolated pathogen in hemocultures. Age, gender, all analyzed comorbidities and all the other clinical and microbiological characteristics were not significantly associated with higher mortality (p>0.05).
Conclusion: Our study shows that GCS≤8 and higher SOFA score in the time of diagnosing sepsis, DIC, total number of sepsis complications, the need for intubation, MV and Staphylococcus spp. are predictors of mortality in patients with sepsis in NICU.
Disclosure: Nothing to disclose.

EPR-289

Thalamo-cortial dysfunction in patients with hypoxic-ischemic encephalopathy

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Background and aims: The thalamic gray-white matter ratios (GWRs) on CT and quantitative suppression ratios (SRs) of background activities on EEG could reflect damages in the thalamus and cerebral hemispheres in patients with hypoxic-ischemic encephalopathy (HIE).
Methods: The poor outcome was defined as the cerebral performance category (CPC) of 3 to 5 scores. The thalamic GWRs were semi-quantitatively measured by using the region of interest (ROI). The size (30 mm^2) and location of ROI were standardized within the splenium of corpus callosum (CC) and thalamus. The GWR was calculated using the Hounsfield unit (HU) at the thalamus and CC: Thalamic GWR=HU at the thalamus/HU at the CC. The SR was calculated as an average percentage of background EEG activities below a user-specified amplitude threshold: epoch duration=10s; flat duration threshold=0.5s; flat duration amplitude=3μV; and running average duration=60s.
Results: A total of 175 patients were included, and the thalamic GWRs of 168 patients were successfully measured. The poor outcome group showed higher SRs and lower thalamic GWRs. The diagnostic accuracy of the thalamic GWRs and SRs for predicting poor outcome was satisfactory; although the sensitivity and the negative predictive value (NPV) were moderate, the specificity and positive predictive value (PPV) of the thalamic GWRs and SRs were extremely high (>90%).
Conclusion: The thalamic GWRs and SRs could reflect the damage in the thalamus and cerebral hemispheres in patients with HIE. The damage in thalamo-cortical circuit or the thalamus/cortical hemispheres could be responsible for poor outcome.
Disclosure: Nothing to disclose.

EPR-290

Abstract withdrawn

EPR-291

Multimodal prediction of 3- and 12-month outcomes in ICU-patients with acute disorders of consciousness

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Background and aims: In intensive care unit (ICU) patients with disorders-of-consciousness (DoC), functional outcome prediction is key to decision-making about level-of-care, neurorehabilitation, and management of family expectations. Current concepts are largely based on chronic DoC, while multimodal data from acute DoC-patients are scarce.

Methods: ICU DoC-patients were assessed with EEG and resting state fMRI. We assessed 3- and 12-month functional outcomes with modified Rankin Scale, Cerebral Performance Category, and Glasgow Outcome Scale-Extended. Machine-learning was applied to EEG- and fMRI-features to predict outcomes, and results were expressed as accuracies or area under the curve (AUC) of receiver-operating curves. We used Cox proportional hazards regression with in-hospital death as competing risk to identify independent predictors of time to favourable outcome.

Results: We enrolled 123 patients (mean age 51 years, 42% women) between 04/2016–07/2021. 41 (33%) died in the ICU. Of the 82 survivors, 3- and 12-month outcomes were available for 79 (96%) and 77 (94%), respectively. EEG-features predicted both 3-month (AUC 0.79 [0.77–0.82] and 12-month (0.74 [0.71–0.77]) outcomes, whereas fMRI-features only predicted 3-month outcome (accuracies 0.69–0.78). Independent predictors of time to favourable outcome were younger age (Hazards Ratio 1.04 [95% CI 1.02–1.06]), TBI (1.94 [1.04–3.61]), command-following abilities at admission (2.70 [1.40–5.23]), initial brain-imaging without severe pathology (2.42 [1.12–5.22]), improving consciousness in the ICU (5.76 [2.41-15.51]), and favourable EEG visual grading (2.47 [1.46-4.19]).

Conclusion: EEG-features predicted 3- and 12-month outcomes of acute DoC-patients in the ICU, while fMRI-features only predicted 3-month outcome. Furthermore, certain clinical features and EEG visual grading independently predicted time to favourable outcome.

Disclosure: Nothing to disclose.

EPR-292

Early prognosis of metabolic encephalopathy: the role of EEG

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Background and aims: Metabolic encephalopathy (ME) represents a syndrome of diffuse, potentially reversible brain dysfunction. The aim of our study was to determine if the electroencephalography (EEG) findings could be predictors of early prognosis in patients with (ME).

Methods: The study included 129 patients diagnosed with ME in our center over the seven- year period. All patients underwent EEG recording at the admission, when alteration of consciousness was observed and at the end of hospitalization.

Results: Intrahospital mortality of ME patients in our study was 25.6%. At the admission, delta (42.5%) and theta (33.8%) waves were most common EEG pattern in patients who survived, whereas triphasic (TW) (40.8%) and delta waves (34.7%) were most frequent in deceased ($p<0.01$). Alteration of consciousness was followed by theta waves (50%) or a normal EEG (23.8%) in those who survived, while TW (38.8%) and predominant delta activity (28.6%) with suppression of regular activity (16.3%) were noted in deceased ($p<0.0001$). EEG was normal in 58.8% of survivors at discharge, however 27.5% of them had predominant theta activity. TW (38.8%) and suppression of regular activity (16.8%) were observed at the end of hospitalization in deceased group ($p<0.0001$). There was no difference in frequency and type of epileptic and mixed patterns in studied groups.

Conclusion: Our study showed that delta activity, TW and suppression of regular activity observed on EEG could be early predictors of unfavorable prognosis in patients with ME:

Disclosure: Nothing to disclose.

EPR-293

Identification of large vessel occlusion using mobile brain perfusion ultrasound and prehospital stroke scales

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Background and aims: Identification of stroke due to large vessel occlusion (LVO) is critical for the optimal selection of the target hospital, especially for mechanical thrombectomy (MT). Application of prehospital stroke scales alone appears insufficient and i. e. may suggest LVO in patients with hemorrhage and stroke mimics, and miss LVO diagnosis in other patients. In a phase II study we successfully investigated a novel mobile brain ultrasound perfusion (BPU) device specifically designed for LVO detection and analyzed whether a complementation of BPU with prehospital stroke scales can improve LVO detection.
Methods: 20 patients suffering from acute ischemic stroke were included. The prehospital stroke scale CG-FAST was calculated for each patient in addition to the result of BPU. The positive and negative predictive values as well as sensitivity and specificity were calculated retrospectively for both methods.
Results: CG-FAST and BPU showed comparable performances taken for themselves, but still misdiagnosed patients. The combination of both methods allowed a reliable classification into three groups: A) "highly probably LVO", B) "highly probable non-LVO" and C) "not assessable" (including all patients misdiagnosed by one method alone).
Conclusion: A complementation with BPU might allow for prehospital triage of acute stroke patients and enable highly efficient, site specific transfer of patients classified A) to mTE centres, B) to the nearest stroke unit and C) transfer depending on local circumstances. However, these findings must be reproduced in larger and more heterogenous prehospital cohorts.
Disclosure: BURL® was sponsor of the SONAS™ trial performed in our hospital.

EPR-294

Correlation of Various Laboratory Parameters with Vasospasm and Outcome in Acute Non-traumatic Subarachnoid Hemorrhage

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Background and aims: Among patients with acute subarachnoid hemorrhage (SAH) lower hemoglobin (Hgb) levels and elevated white blood cell (WBC) count and C-reactive protein (CRP) levels are common. We aimed to investigate these parameters as possible early indicators of vasospasm (VS) and outcome.
Methods: Subgroup analysis of our previous prospective study was performed. In total, 116 acute, non-traumatic SAH patients with daily transcranial color Doppler (TCCD) reports were enrolled in our analysis. VS was defined as >120 cm/s mean blood flow velocity in the medial cerebral artery. The following data were also processed: SAH severity scores (Modified Fisher, Hunt-Hess, WFNS), laboratory parameters on the first week after SAH (WBC, CRP, Hgb), and 1 and 6-month outcome scores (Glasgow Outcome Scale, Barthel Scale).
Results: VS was detected in 31% of the cases. Patients with VS have significantly lower Hgb level (p=0.008) and higher WBC count (p=0.002) compared to patients without VS. There was no significant difference in CRP levels (p=0.201). Extended SAH and severe neurological damage were connected to higher CRP and WBC peaks and lower Hgb levels. On 1 and 6-month follow-up anemia, higher CRP and WBC count were related to worse outcome.
Conclusion: Based on our results, there is a correlation between lower Hgb level, higher WBC count and VS. WBC count, CRP and Hgb levels may serve as early indicators of outcome.
Disclosure: Nothing to disclose.

EPR-295

Neurovascular coupling as a biomarker for cognitive function in critical illness survivors: a case-control study

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Background and aims: Critical illness can leave a lasting impact on cognitive function, even after the underlying conditions has been treated. Despite the prevalence of these sequelae, knowledge about clinical risk factors is scarce, making it difficult to predict the cognitive trajectories of individual patients. Investigating the relationship between neuronal activation, as measured by EEG, and regional cerebral blood flow, as measured by functional near-infrared spectroscopy (fNIRS), may provide insight into biomarkers for cognitive sequelae following critical illness.

Methods: In this case-control study, 25 critical illness survivors admitted to one of four ICUs (neurological/neurosurgical, cardiologic, cardiothoracic, and general) of a tertiary care hospital for a minimum of 72 hours, and 25 age-, sex-, and education-matched healthy controls are included. Participants undergo fNIRS-EEG measurements to evaluate neurovascular coupling in the fronto-parietal and primary tongue motor cortices, both at rest and during cognitive challenges. The cognitive challenges include a novel tongue motor imagery task, as a measure of mental flexibility, and the n-back test, as a measure of working memory. Follow-up measurements, including fNIRS-EEG and a comprehensive neuropsychological battery, are conducted 3 months post-discharge from the ICU.

Results: Data collection is ongoing and will be presented at EAN.

Conclusion: We hypothesize that neurovascular coupling is impaired in survivors of critical illness who perform poorly during cognitive testing at ICU discharge but improves in those who perform normally or near-normally during cognitive testing at 3-month follow-up. We also hypothesize that the degree of neurovascular coupling at ICU discharge predicts cognitive performance at 3 months.

Disclosure: Nothing to disclose.

MS and related disorders 3

EPR-296

CSF-in gradient of thalamic and cortical damage in multiple

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Background and aims: CSF-in gradients in cortical and thalamic damage have been suggested in multiple sclerosis (MS), possibly due to CSF-mediated pathology. However, damage pattern has not been explored in vivo and concurrently in both structures yet.
Methods: Brain 3T-MRI sequences were acquired from 52 MS patients (33 relapsing-remitting [RR], 19 progressive [P]) and 56 healthy controls (HC). From 3DT1-weighted sequences, cortical layers sampled at 25%-50%-75% depths from white matter (WM)-cortical interface (Freesurfer) and thalamic concentric bands at 1-2-3-voxels from ventricular-thalamus interface (in-house implemented method) were derived. Between-group comparisons of magnetization transfer ratio (MTR) values in cortical and thalamic layers and their correlations with clinical and structural measures were evaluated using linear mixed models and Spearman correlations.
Results: Compared with HC, RRMS and PMS patients showed significantly lower MTR values in the most superficial cortical layer (RRMS=-1.23%, p=0.006, PMS=-1.70%, p=0.002), without between-group differences (Fig1). Compared to HC, RRMS and PMS patients showed significantly lower MTR values in the ventricle-closest band (RRMS=-1.63%, p=0.015, PMS=-3.62%, p<0.001) (Fig2). PMS showed also a significantly lower MTR in ventricle-closest band compared to RRMS (p=0.022) and in the second band compared to HC (-1.07%, p=0.048). Lower MTR values of CSF-closest cortical and thalamic layers significantly correlated with longer disease duration, higher Expanded Disability Status Scale (EDSS) score, higher WM lesion volume (r=-0.45–-0.35, p≤0.011) with lower normalized brain, thalamic and cortical volumes (r=0.42–0.56, p≤0.002).

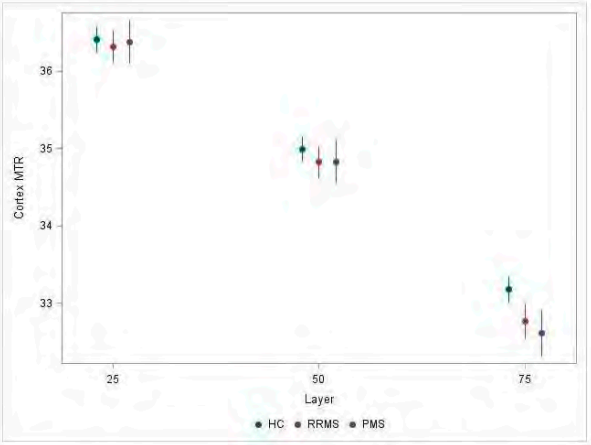

Fig 1. Cortical MTR values at 25%-50%-75% depth from WM, corresponding to 75%-50%-25% distance to CSF-cortical interface, evaluated in the 3 groups (green: HC, red: RRMS, blue: PMS) and age-corrected.

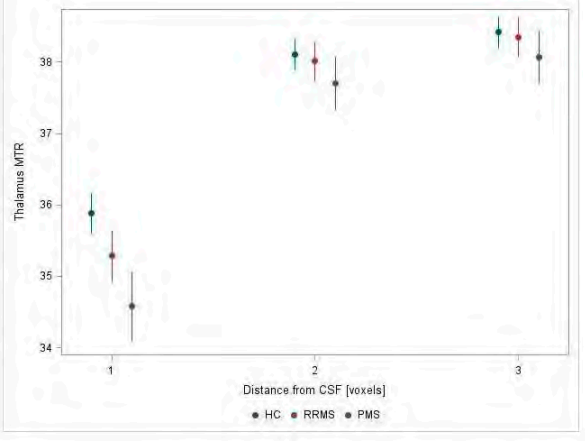

Fig 2. Thalamic MTR values at 1-2-3-voxel distance to CSF-thalamic interface, evaluated in the 3 groups (green: HC, red: RRMS, blue: PMS) and age-corrected.

Conclusion: In MS, a clinically-relevant CSF-in damage gradient is present in cortex and thalamus, more substantial in thalamus and in PMS.
Disclosure: Nothing to disclose.

EPR-297

Uncovering subtle gait deterioration in PwMS in the early phase of the disease: a 2-year multicenter longitudinal study

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Background and aims: Limited studies were conducted on gait progression overtime in non-disabled People with Multiple Sclerosis (PwMS). A deeper understanding of gait changes during disease progression is essential. The study aim to describe changes in gait quality in non-disabled PwMS, and to verify whether they are associated with changes in gait perception.

Methods: Fifty-six subjects were assessed at baseline (age:38.2±10.7 years, EDSS:1.5±0.7, disease duration:2.2±1.8 years) and 2-year follow-up (FU). Participants performed the 6MWT wearing three inertial sensors on ankles and pelvis. Velocity and quality of gait (regularity, symmetry, instability) were extracted from sensors. EDSS and MSWS-12 were administered.

Results: Twenty-four subjects (43%) out of 56 increased at least 0.5 EDSS point over the 2-year period. No differences on 6MWT and MSWS-12 between baseline and FU were found, while a significant correlation between increased EDSS and increased gait instability in the antero-posterior (AP) plane (r=0.35, p=0.01) was found. A multivariate analysis on PwMS that worsened at the EDSS (n=24) showed that changes in medio-lateral (ML) and AP gait instability and in ML gait symmetry were associated with EDSS (F=9.30 (3,19), p=0.0005, with a residual standard error of 0.45 points, R2=0.59, adj R2=0.53) and with decrease in PwMS perception on dynamic gait.

Conclusion: Although EDSS can reveal a change at the impairment level, instrumented assessment of dynamic balance can detect subtle gait disorders not revealed during routinely assessment in the early phase of the disease. Changes in gait quality (symmetry and instability) impact on perception of gait during ADL.

Disclosure: Nothing to disclose.

EPR-298

Prevalence, incidence, and mortality of myasthenia gravis: a population-based study in Denmark, Finland, and Sweden

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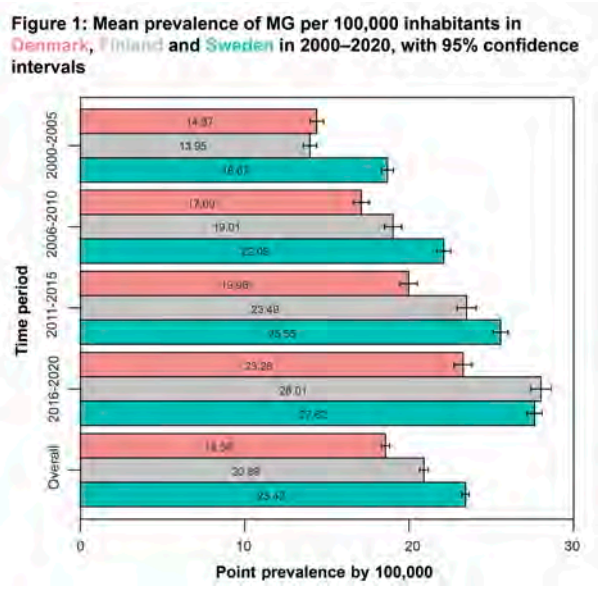
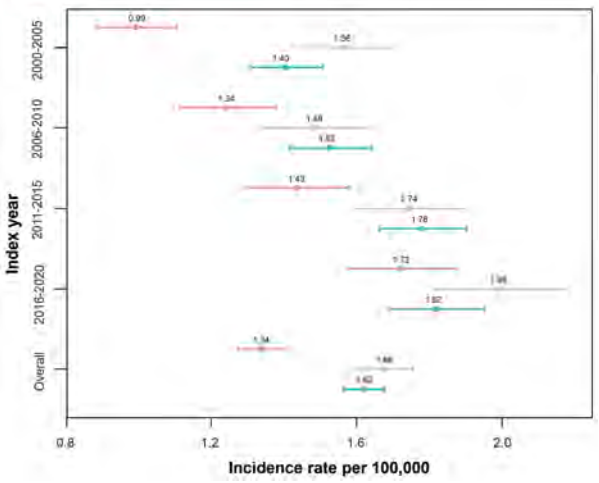
Background and aims: Myasthenia gravis (MG) is a rare, chronic, autoimmune neuromuscular disease with varying muscle weakness. The aim of this population-based, observational study was to evaluate the epidemiology of MG in Denmark (DK), Finland (FI), and Sweden (SE).

Methods: Data were collected from health registers with almost complete population coverage. Prevalent and incident patients during 2000–2020 were included. Prevalent patients had ≥2 MG diagnoses (ICD-10: G70.0*, ICD-9: 358.0*, ICD-8: 73,309, ICD-7: 74,400) in specialty care during the registries' history (starting: 1977, 1969, 1964 in DK, FI, and SE). Prevalence analyses included patients who were alive on December 31st of the calendar year. Incident patients had ≥2 first-ever MG diagnoses (ICD-10: G70.0*) during 2000–2020. Index date was the date of the first diagnosis.

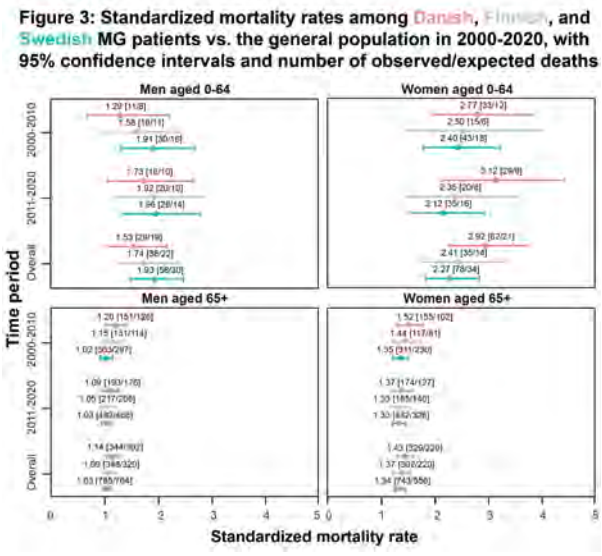
Results: During 2000–2020, mean prevalence was 18.6, 20.9, and 23.4 per 100,000 inhabitants in DK, FI, and SE, respectively (avg. increase: 48% [SE] to 100% [FI]) (Figure 1), while mean incidence rate was 1.34, 1.68, and 1.62 per 100,000 inhabitants in DK, FI, and SE, respectively (avg. increase: 28% [FI] to 74% [DK]) (Figure 2). Mortality in MG patients was numerically higher than the age- and sex-matched general population, especially in women ≤64 years (Figure 3).



Mean prevalence of MG per 100,000 inhabitants in Denmark, Finland, and Sweden in 2000-2020, with 95% confidence intervals.



Mean incidence of MG per 100,000 inhabitants in Denmark, Finland, and Sweden in 2000-2020, with 95% confidence intervals.



Standardized mortality rates among Danish, Finnish, and Swedish MG patients vs. the general population in 2000–2020, with 95% confidence intervals and number of observed/expected deaths.

Conclusion: A marked increase in prevalence and incidence of MG was observed in the Nordics over the last two decades. Factors likely contributing to these findings may include increased MG awareness, improved diagnostic tools, and an aging population, but further studies are needed to clarify underlying causes in relevant sub-populations. An excess mortality represents a concern.

Disclosure: Funded by UCB Pharma. John Vissing is a consultant on advisory boards for Roche, Sanofi Genzyme, Sarepta Therapeutics, Novartis Pharma AG, Fulcrum Therapeutics, Biogen, Lupin, Amicus, Regeneron, Argenx BVBA,UCB Biopharma SPRL, Arvinas, ML Biopharma, Atamyo, Horizon Therapeutics, Dyne Therapeutics Research, travel support, and/or speaker honoraria from Sanofi Genzyme, Alexion Pharmaceuticals, Edgewise Therapeutics, Fulcrum Therapeutics, and UCB Biopharma SPRL. Principal investigator in clinical trials for Sanofi Genzyme, Roche, Horizon Therapeutics, Argenx BVBA, Novartis Pharma AG, Alexion Pharmaceuticals, UCB Biopharma SPRL, Genethon, ML Biopharma, Reneo Pharma,Pharnext, Janssen Pharmaceutical, Khondrion, Regeneron, and Dynacure SAS, Janssen Sari Atula travels with pharmacompany: Merck, Speaker in educational sessions by pharma companies: Merck, Roche, Biogen, Novartis, Advisory boards: Biogen, Merck, Roche, Novartis, UCB Pharma Mari Savolainen, employed at UCB Pharma, Espoo, Finland Juha Mehtälä, employed at MedEngine Oy, Finland Laila Mehkri, employed at MedEngine DK ApS, Denmark Tero Ylisaukko-oja, the owner of MedEngine Oy and MedEngine DK ApS Ingrid Lindberg, employed at UCB Pharma, Stockholm, Sweden Fredrik Berggren is an employee and stockholder of UCB Pharma, Copenhagen, Denmark Fredrik Piehl has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

EPR-299

Safety patterns with ozanimod in phase 3 and open-label extension trials in patients with relapsing multiple sclerosis

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Background and aims: Ozanimod is a sphingosine 1-phosphate receptor 1 and 5 modulator approved in multiple countries for treatment of adults with relapsing forms of multiple sclerosis (RMS) or moderately to severely active ulcerative colitis.
Methods: Adults with RMS were randomised to ozanimod 0.46 or 0.92 mg/d or interferon β-1a 30 μg/wk for ≥12 months (SUNBEAM–NCT02294058) or 24 months (RADIANCE–NCT02047734). Completers could enrol in the ongoing open-label extension (OLE) trial (DAYBREAK–NCT02576717; ozanimod 0.92 mg/d). Incidence rates (IRs) and 95% confidence intervals (CI)/1000 person-years were calculated for treatment-emergent adverse events (TEAEs) up to 1 Feb 2022.
Results: At data cutoff, 2,256 participants had 10,540 person-years of ozanimod exposure during DAYBREAK. In patients treated with continuous ozanimod 0.92 mg (n=882), IRs decreased over time for overall TEAEs, infections, opportunistic infections, cardiac, hepatic, and pulmonary disorders (Table 1). In these patients, the most common opportunistic infections in phase 3 trials and OLE were oral herpes and herpes zoster (including varicella zoster virus); there were no serious opportunistic infections. IRs remained stable for serious TEAEs, malignancies, and macular oedema. The IR for serious infections remained stable until OLE >36 months, at which time the IR slightly increased (partially due to the COVID-19 pandemic). The most common serious infections (n/N) were appendicitis (3/882) (phase 3), and COVID-19 pneumonia (10/762), COVID-19 infection (5/762), and pneumonia (5/762) (OLE).
Conclusion: IRs of TEAEs in patients with RMS treated with continuous ozanimod 0.92 mg in phase 3 and OLE trials declined or remained stable over up to 6 years of observation time.

Table 1. TEAE incidence rates per 1000 PY over time with continuous 0.92 mg ozanimod treatment

TEAE IRs (95% CI)[a]	Phase 3	OLE > 48 Months
Overall TEAEs	896.1 (826.8, 971.3)	200.4 (126.3, 318.1)
Serious TEAEs	31.2 (23.0, 42.4)	33.5 (22.3, 50.4)
Infections	300.5 (268.9, 335.9)	151.2 (113.3, 201.9)
Opportunistic infections	12.0 (7.4, 19.6)	6.7 (2.8, 16.2)
Serious infections	6.7 (3.5, 12.9)	17.3 (10.0, 29.8)
Cardiac disorders	22.8 (16.0, 32.7)	7.9 (3.6, 17.6)
Hepatic disorders	77.0 (63.1, 94.0)	13.0 (6.8, 25.0)
Pulmonary disorders	11.3 (6.8, 18.7)	0.0 (0.0, 9.2)
Malignancies[b]	372.2 (120.8, 868.5)	258.5 (31.3, 933.8)
Confirmed macular oedema	0.7 (0.1, 5.3)	0.0 (0.0, 9.1)

[a]IR per 1000 patient-years is calculated as number of persons/patient-years x 1000 for each specific category and time interval. Patient-years for each category: for a patient in a particular TEAE category, the time on study is calculated based on the date the patient first has an event within the category and time interval (date of first event – first dose date of study drug/beginning of the time interval + 1)/365.25; for patients who do not have an event in the category and within the time interval, the time on study during the interval is the study duration (last date on study/last date of the time interval – first dose date of study drug/ first date of the time interval +1)/365.25. The 95% confidence intervals are calculated based on the Poisson distribution.
[b]Per 100,000 PY; excludes pre-existing malignancies.
CI, confidence interval; IR, incidence rate; OLE, open-label extension; PY, person-years; TEAE, treatment-emergent adverse event.

Disclosure: KWS: consulting for Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, and Teva. All author disclosures will be included in the presentation. This study was supported by Bristol Myers Squibb.

EPR-300

Update on Hepatic Safety of Ozanimod in Relapsing Multiple Sclerosis in the DAYBREAK Open-Label Extension Trial

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Background and aims: Hepatic enzyme increases were reported in studies of ozanimod and other sphingosine 1-phosphate receptor modulators used to treat relapsing multiple sclerosis (RMS). We report long-term hepatic safety of ozanimod in an ongoing open-label extension study (DAYBREAK).

Methods: Participants with RMS who completed a phase 1–3 ozanimod trial were eligible for DAYBREAK (NCT02576717), where they received ozanimod 0.92 mg/d and had liver enzymes measured every 3 months for 3 years, then every 6 months. Hepatic safety was analyzed through 1 Feb 2022.

Results: The 2,494 participants had a mean (SD) 56.4 (15.9) months (range 0.03–74.7 months; 11,732 person-years) of ozanimod exposure during DAYBREAK. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels ≥3 × upper limit of normal (ULN) or bilirubin >2 × ULN were infrequent (<4% each; Table 1); there were no cases of severe drug-induced liver injury (DILI). ALT elevations were uncommonly confirmed: 21 (0.8%) participants had consecutive ALT elevations ≥3 × ULN and 6 (0.2%) had consecutive ALT ≥5 × ULN. Hepatobiliary treatment-emergent adverse events (TEAEs) occurred in 100 (4.0%) participants (Table 2) and led to treatment discontinuation in 2 (0.1%) overall; 9 (0.4%) discontinued due to hepatic enzyme elevation-related TEAEs. Thirteen (0.5%) participants had serious hepatobiliary TEAEs (Table 3).

Conclusion: With up to 6 years of exposure to ozanimod 0.92 mg in DAYBREAK, ALT and AST elevations ≥3 × ULN remained infrequent. ALT elevations were uncommonly confirmed with subsequent testing. Rates of serious hepatic TEAEs and hepatic TEAEs leading to discontinuation were low. No severe DILI occurred.

Disclosure: KWS: Consulting for Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, and Teva. All author disclosures will be included in the presentation. This study was supported by Bristol Myers Squibb.

Table 1. TEAE incidence rates per 1000 PY over time with continuous 0.92 mg ozanimod treatment

TEAE IRs (95% CI)[a]	Phase 3	OLE > 48 Months
Overall TEAEs	896.1 (826.8, 971.3)	200.4 (126.3, 318.1)
Serious TEAEs	31.2 (23.0, 42.4)	33.5 (22.3, 50.4)
Infections	300.5 (268.9, 335.9)	151.2 (113.3, 201.9)
Opportunistic infections	12.0 (7.4, 19.6)	6.7 (2.8, 16.2)
Serious infections	6.7 (3.5, 12.9)	17.3 (10.0, 29.8)
Cardiac disorders	22.8 (16.0, 32.7)	7.9 (3.6, 17.6)
Hepatic disorders	77.0 (63.1, 94.0)	13.0 (6.8, 25.0)
Pulmonary disorders	11.3 (6.8, 18.7)	0.0 (0.0, 9.2)
Malignancies[b]	372.2 (120.8, 868.5)	258.5 (31.3, 933.8)
Confirmed macular oedema	0.7 (0.1, 5.3)	0.0 (0.0, 9.1)

[a]IR per 1000 patient-years is calculated as number of persons/patient-years x 1000 for each specific category and time interval. Patient-years for each category: for a patient in a particular TEAE category, the time on study is calculated based on the date the patient first has an event within the category and time interval (date of first event – first dose date of study drug/beginning of the time interval + 1)/365.25; for patients who do not have an event in the category and within the time interval, the time on study during the interval is the study duration (last date on study/last date of the time interval – first dose date of study drug/ first date of the time interval +1)/365.25. The 95% confidence intervals are calculated based on the Poisson distribution.
[b]Per 100,000 PY; excludes pre-existing malignancies.
CI, confidence interval; IR, incidence rate; OLE, open-label extension; PY, person-years; TEAE, treatment-emergent adverse event.

Table 1

Table 2. Hepatobiliary TEAEs During DAYBREAK

	DAYBREAK Participants (N=2494)	
	n (%)	IR/1000 PY[a] (95% CI)
Any hepatobiliary TEAE	100 (4.0)	8.7 (7.1–10.6)
Hepatobiliary TEAEs that occurred in ≥2 participants in the overall DAYBREAK population[b]		
Hyperbilirubinemia	27 (1.1)	2.3 (1.6–3.4)
Cholelithiasis	13 (0.5)	1.1 (0.6–1.9)
Cholecystitis chronic	12 (0.5)	1.0 (0.6–1.8)
Hepatic cyst	6 (0.2)	0.5 (0.2–1.1)
Hepatic steatosis	5 (0.2)	0.4 (0.2–1.0)
Biliary dyskinesia	4 (0.2)	0.3 (0.1–0.9)
Chronic hepatitis	4 (0.2)	0.3 (0.1–0.9)
Hepatitis	4 (0.2)	0.3 (0.1–0.9)
Gallbladder polyp	3 (0.1)	0.3 (0.1–0.8)
Hypertransaminasemia	3 (0.1)	0.3 (0.1–0.8)
Sphincter of Oddi dysfunction	3 (0.1)	0.3 (0.1–0.8)
Steatohepatitis	3 (0.1)	0.3 (0.1–0.8)
Cholecystitis	2 (0.1)	0.2 (0.0–0.7)
Cholecystitis acute	2 (0.1)	0.2 (0.0–0.7)
Hepatic cytolysis	2 (0.1)	0.2 (0.0–0.7)
Hepatic lesion	2 (0.1)	0.2 (0.0–0.7)
Hepatitis toxic	2 (0.1)	0.2 (0.0–0.7)
Hepatomegaly	2 (0.1)	0.2 (0.0–0.7)
Nonalcoholic steatohepatitis	2 (0.1)	0.2 (0.0–0.7)

[a]IR per 1000 person-years is calculated as number of persons/person-years × 1000 for specific system organ class category or preferred term subcategory. Person-years for each category/subcategory: for a person in a particular category/subcategory, the time on study is calculated based on the date the person first has a TEAE within the category/subcategory (date of first TEAE - first dose date of study drug + 1)/365.25; for persons who do not have a TEAE in the category/subcategory, the time on study is the study duration (last date on study - first dose date of study drug +1)/365.25.
[b]Additional hepatobiliary TEAEs that occurred in a single participant each (0.04%) in the total DAYBREAK population included biliary colic, biliary polyp, biliary tract disorder, cholangitis, cholestasis, drug-induced liver injury, gallbladder disorder, hepatic function abnormal, hepatitis acute, hepatitis chronic active, hepatotoxicity, liver disorder, and liver tenderness.
CI, confidence interval; IR, incidence rate; PY, person-years; TEAE, treatment-emergent adverse event.

Table 2

Table 3. Serious Hepatobiliary TEAEs

	DAYBREAK Participants (N=2494), n (%)
Any serious hepatobiliary disorder	13 (0.5)
Cholelithiasis	4 (0.2)
Cholecystitis chronic	3 (0.1)
Cholecystitis acute	2 (0.1)
Biliary polyp	1 (0.04)
Cholecystitis	1 (0.04)
Cholestasis	1 (0.04)
Chronic hepatitis	1 (0.04)

TEAEs, treatment-emergent adverse events.

Table 3

EPR-301

PANGAEA 2.0 EVOLUTION: Clinical and non-clinical parameters in the early assessment of SPMS patients in clinical routine

C. Lassek[1], C. Weiss[2], T. Ziemssen[3]
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Background and aims: Due to a lack of established reliable diagnostic criteria and standardized assessments, identification of the transition from RRMS to SPMS remains challenging. Essential characteristics of this transitional phase can be determined by comparing clinical parameters and patient reported outcomes of RRMS patients at high risk for SPMS with SPMS patients which was the aim of the PANGAEA 2.0 EVOLUTION study.
Methods: Following 609 patients with SPMS or at high risk for SPMS for up to 2 years regardless of treatment, this prospective non-interventional study assessed patient characteristics and disease management in clinical routine settings. Data collected in routine clinical measurements and quality of life and socioeconomic parameters were documented in 6-month intervals.
Results: The data set consists of 187 SPMS patients and 422 RRMS patients at high risk for SPMS. Most patients (82.9%) did not change their therapy during the study. At baseline, RRMS patients at high risk for SPMS presented with a lower overall EDSS score (4.2±1.1 vs. 5.1±1.1) compared to SPMS patients. Patients at high risk for SPMS also showed a lower FSMC total score than SPMS patients at baseline (63.8±19.0 vs. 68.5±15.8). However, while SPMS patients remained stable over 2 years (67.8±16.8), the total FSMC score of patients at high risk for SPMS increased to 69.3±17.6 with was motor fatigue being the strongest contributor. The FSMC subscale on cognitive fatigue indicated a similar impairment of both cohorts at baseline and after 2 years.
Conclusion: Combining clinical and non-clinical parameters in individual patient profiles supports the early diagnosis of SPMS.
Disclosure: C. Lassek is a neurologist at Neurologische Gemeinschaftspraxis, Kassel, Germany. C. Weiss is an employee of Novartis Pharma GmbH. T. Ziemssen has received personal compensation for participating on advisory boards, trial steering committees and data and safety monitoring committees, as well as for scientific talks and project support from: Almirall, Bayer, BAT, Biogen, Celgene, Sanofi Genzyme, Merck, Novartis, Roche, Vitaccess, and Teva.

EPR-302

Effect of Longer-term Ofatumumab Treatment on Disability Progression and Brain Volume Change

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Background and aims: In the ASCLEPIOS I/II core studies, ofatumumab delayed disability accrual compared with teriflunomide. Progression independent of relapse activity (PIRA) was the main contributor to overall 3-/6-month confirmed disability worsening (3/6mCDW). We assessed CDW, PIRA, relapse-associated worsening (RAW), and brain volume change (BVC) in relapsing multiple sclerosis patients receiving ofatumumab for up to 5 years.

Methods: Results are presented in this abstract for up to 4 years (ASCLEPIOS + ALITHIOS open-label extension) in patients on continuous ofatumumab and those switched from teriflunomide in the extension (full analysis set); 5-year data will be available at congress. CDW, PIRA (CDW events without prior confirmed relapses), RAW (event onset <90 days from a relapse), percent BVC (PBVC) and annualized rates of BVC (ABVC) were assessed.

Results: Of 1882 patients randomised in ASCLEPIOS I/II, 1367 entered ALITHIOS (Figure 1). Most patients were free from 3/6mCDW events. Up to 4 years (cut off:25-Sep-2021) 12.6% and 15.9% patients had 6mCDW in the continuous and switch groups, respectively. In the continuous group, the 6mPIRA Kaplan-Meier cumulative event rate (KM-CER) remained low (11.0%) and 6mPIRA accounted for 72.3% patients with 6mCDW; 6mRAW (KM-CER: 3.5%) accounted for only 25.2% patients (Table 1). At week 240, overall mean PBVC remained low (continuous/switch: –1.42%/–1.62%). ABVC for continuous ofatumumab also remained low(core:–0.34%/year; extension:–0.28%/year). In the switch group, ABVC was –0.42%/year(core) and –0.29%/year(extension).

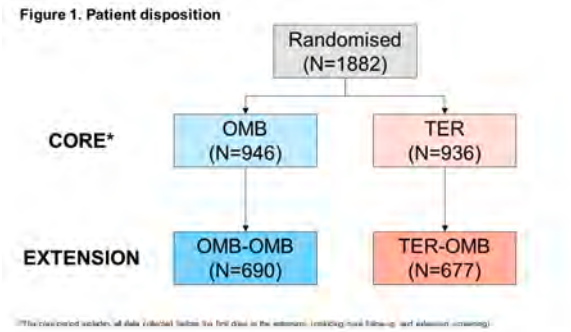

Figure 1. Patient disposition

Table 1. Contribution of PIRA and RAW to 6mCDW events

Treatment arm	Phase	OMB-OMB	TER-OMB
6mCDW events, n/N (%)	Core	91/944 (9.6)	116/932 (12.4)
	Extension	28/617 (4.5)	32/595 (5.4)
	Overall	119/944 (12.6)	148/932 (15.9)
6mPIRA, n/M (%)	Core	60/91 (65.9)	73/116 (62.9)
	Extension	26/28 (92.9)	23/32 (71.9)
	Overall	86/119 (72.3)	96/148 (64.9)
6mRAW, n/M (%)	Core	28/91 (30.8)	32/116 (27.6)
	Extension	2/28 (7.1)	4/32 (12.5)
	Overall	30/119 (25.2)	36/148 (24.3)

n= number of patients with the specified event; N= total number of patients in the treatment group in FAS with CDW variable defined; M= number of 6mCDW events

Table 1. Contribution of PIRA and RAW to 6mCDW events

Conclusion: With longer-term ofatumumab treatment, disability worsening was predominantly PIRA, the annual rate of BVC remained low, and most patients remained free from disease progression. Outcomes favoured early initiation with ofatumumab.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be provided in the subsequent presentation.

EPR-303

Outcomes of COVID-19 in Ofatumumab-treated RMS Patients: Data from the ALITHIOS open label extension study

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Background and aims: COVID-19 has created challenges in the management of patients with multiple sclerosis (MS). Data collected since the start of the pandemic to 25-Sep-2021 on COVID-19 outcomes in ofatumumab-treated relapsing MS (RMS) patients were previously reported. Here we present updated cumulative COVID-19 outcomes from the ongoing ALITHIOS study up to cut-off: 25-Sep-2022.

Methods: Incidence, seriousness, severity, and outcomes of COVID-19, including cases after initial and booster vaccinations, were analyzed in ofatumumab-treated patients from the ALITHIOS study. Risk factors associated with serious COVID-19 were also evaluated.

Results: Of 1703 patients entered ALITHIOS (mean age at baseline: 39.2 years; females, 69.6%; BMI ≥30 kg/m^2, 18%), 648 (38.1%) reported COVID-19 (confirmed, 603; suspected, 45). Most cases were non-serious (598; 92.3%). The majority of cases were mild-to-moderate in severity (94.0%); most patients recovered (96.1%), recovering (0.6%) or recovered with sequelae (1.9%). Five patients had fatal outcome (unvaccinated, 3; fully vaccinated, 2). Post-vaccination COVID-19 cases mainly occurred during the SARS-CoV-2 Omicron wave. Seriousness and severity of COVID-19 decreased in patients following booster vaccination (Table). After adjusting for age, race, vaccination status, EDSS, number of underlying conditions, and time since first dose of ofatumumab, association with higher risk of serious COVID-19 was found in BMI ≥30 kg/m^2 vs <30 kg/m^2 (HR 1.99) and male vs female (HR 1.86) (Figure).

Characteristics	COVID-19 cases		
	Overall ALITHIOS N=648/1703	After primary vaccine series and before booster N=167/704	After 1 booster dose N=109/329
COVID-19 seriousness, n (%)			
Non-serious	598 (92.3)	153 (91.6)	106 (97.2)
Serious	50 (7.7)	14 (8.4)	3 (2.8)
COVID-19 maximum severity[a], n (%)			
Mild	303 (46.8)	75 (44.9)	68 (62.4)
Moderate	306 (47.2)	84 (50.3)	39 (35.8)
Severe	33 (5.1)	5 (3.0)	2 (1.8)
Life-threatening	6 (0.9)	3 (1.8)	0
COVID-19 outcome, n (%)			
Recovered/recovered with sequalae/ recovering	639 (98.6)	163 (97.6)	109 (100)
Condition unchanged/not recovered	4 (0.6)	2 (1.2)	0
Fatal	5 (0.8)	2 (1.2)[b]	0

[a]Grading by CTCAE v5.0 [b]The two ALITHIOS female patients with fatal outcomes were fully vaccinated and had underlying comorbidities of diabetes, obesity (BMI of 43.7 kg/m^2) and hypertension in one patient (age, 51) and breast disorder, chronic tonsilitis, kidney cysts, non-serious respiratory infections in another patient (age, 46).

Table: Summary of COVID-19 cases from the ALITHIOS study (Cut-off date: 25-Sep-2022)

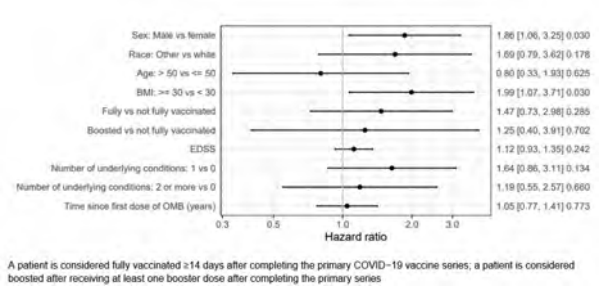

Figure: Hazard ratios from Cox model analysis of risk factors of serious COVID−19: Subset of patients who entered ALITHIOS and who were at risk till at least 01−Jan−2020

Conclusion: Most COVID-19 cases in RMS patients receiving ofatumumab in ALITHIOS were non-serious, mild-to-moderate in severity, and most patients recovered. Except for known risk factors for serious COVID-19, such as sex and BMI, no other risk factors have been identified.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-304

ILLUMINATE: A Real-World, Study Assessing Usability and Value of Integrated Digital Tools for MS care

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Background and aims: Early initiation of effective disease-modifying therapies is crucial to prevent long-term disease progression in people with multiple sclerosis (pwMS), with close clinical and radiographic observation providing best outcomes. Currently, clinical and subclinical disease activity assessments may be performed suboptimally. Therefore, potential exists to implement technology-supported care platforms facilitating detection of disease worsening and improve patient and healthcare professional (HCP) interaction. This study aims to evaluate the usability and value of a multiple sclerosis (MS) care management platform in routine medical care of pwMS.
Methods: ILLUMINATE is a real-world study, designed to enroll ~500 patients with relapsing MS at 10 sites across 5 countries. The MS care management platform consists of two certified medical devices: icompanion MS patient app, which tracks health and medications and prepares patients for consultations; and icobrain MS, an artificial intelligence solution enabling standardized quantitative analysis of brain MRI data. One-year retrospective and two-year prospective data will be collected to evaluate medical practice, treatment, clinical and MRI data and patient-reported outcomes. The primary objective is to assess usability of the MS care management platform via the System Usability Score (HCP reported), and the mHealth App Usability Questionnaire (patient reported). Change in perception of disease worsening, as facilitated by the care management platform, will be assessed by semi-structured interviews.
Results: Starting early 2023, ILLUMINATE will investigate usability and value of a digital MS platform for the care of pwMS.
Conclusion: ILLUMINATE will deliver insights into MS care delivery and the impact of integrated digital tools for detecting disease worsening.
Disclosure: T Ziemssen reports personal fees for lecturing and consulting from Biogen, BMS, F. Hoffmann-La Roche Ltd, Merck, Novartis, Sanofi, Teva and Almirall; and grants or research support from Biogen, F. Hoffmann-La Roche Ltd, Teva, Sanofi and Novartis V Zingler is an employee of F. Hoffmann-La Roche Ltd. P Dirks is an employee of F. Hoffmann-La Roche Ltd. B Addow is an employee of F. Hoffmann-La Roche Ltd. J Praet is an employee of Icometrix NV A Ribbens is an employee and shareholder of Icometrix NV D Smeets is an employee and shareholder of Icometrix NV S Krieger reports consulting or advisory work with Biogen, Cycle, EMD Serono, Genentech, Novartis, Octave, Genzyme/Sanofi, and TG Therapeutics, and non-promotional speaking with Biogen, EMD Serono, and Genentech. Grant and research support from Biogen, BMS, Novartis and Sanofi. Study supported by F. Hoffmann-La Roche Ltd and Icometrix N.V.; Writing and editorial assistance was provided by Articulate Science, UK.

ePosters

Saturday, July 01 2023
Ageing and dementia 1

EPO-001

Epilepsy in Alzheimer's disease associated with Down syndrome. Experience in real-life clinical practice.

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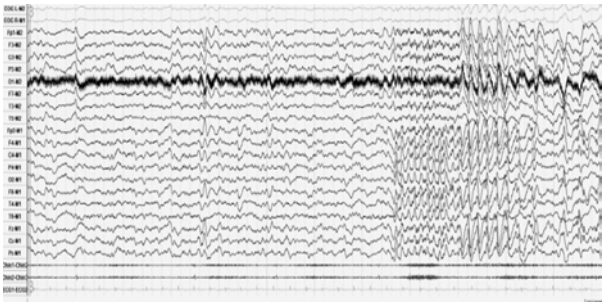
Background and aims: Down syndrome(DS) is a genetically determined form of Alzheimer's Disease(AD). AD is a risk factor for epilepsy, mainly genetic forms of AD, including DS (DSAD). Our objective is to present real-life data on clinical and electrophysiological characterization of DSAD-associated epilepsy.
Methods: A multicentric cross-sectional study in adults with DS (January 2015-January 2023). All participants were assessed by neurologists and neuropsychologists and classified into asymptomatic-aDS-, prodromal-pAD- and dementia AD-dAD- in a consensus meeting based on objective criteria. Personal history of epilepsy for all and for a subgroup routine EEG and/or 21 channel video-polysomnography(v-PSG) were performed.
Results: We recruited 966 adults with DS, 45.9% women, mean age 44.3y(+/-11.6). Of these 36.3% were symptomatic for DSAD. Frequency of untriggered seizures increased in AD continuum (7.6% aDS, 19.4% pAD, 54.7% dAD). The most frequent were bilateral tonic-clonic(BTCS) and the coexistence with myoclonic seizures was especially frequent in dAD (57.1%). The prevalence of both interictal epileptiform (short paroxysms of generalized polyspike-waves) and non-epileptiform abnormalities (slowing of background activity) increased significantly in the AD continuum and in relation to epilepsy. Most frequently used ASM was levetiracetam (61.5%), removed in 1/5 of the cases due to behavioral adverse effects and 48% of them tolerated brivaracetam. Seizures freedom for ≥1year was achieved in 65.9% of DSAD patients, with better response for BTCS.



Slow wave sleep recording (Phase N3) in DSAD patient with critical and interictal epileptiform activity.

Conclusion: The development of symptomatic AD is strongly associated with epileptic seizures in adults with Down syndrome. The good tolerance to ASMs and their good ability to control BTCs supports their use after the first untriggered seizure.
Disclosure: The authors have no relevant financial or non-financial interests to disclose.

EPO-002

Dysautonomia in the differential diagnosis of Dementia with Lewy Bodies and Alzheimer's Disease

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Background and aims: Dementia with Lewy bodies (DLB) is the second most common degenerative dementia in the elderly. Despite their differences in clinical presentation, DLB misdiagnosis as Alzheimer's disease (AD) remains frequent. Autonomic dysfunction is a known supportive clinical feature of DLB but is often overlooked in dementia evaluation. The aim of this work is to evaluate the role of dysautonomia in the differential diagnosis between DLB and AD.
Methods: We selected a convenience sample of 40 patients divided into 2 equal groups, matched for sociodemographic data and neuropsychological scores. Dysautonomia was assessed with Scales for Outcomes in Parkinson's Disease-Autonomic Questionnaire (P-SCOPA-AUT). Core clinical features were assessed with motor score of Unified Parkinson's Disease Rating Scale (mUPDRS), Rapid Eye Movement Sleep Behaviour Disorder Screening Questionnaire (RBD-SQ), Clinician Assessment of Fluctuation (CAF) and hallucination score of Neuropsychiatry Inventory (hNPI).

Results: We enrolled 40 patients, 21 women, with a mean age of 77.9±5.0 years. P-SCOPA-AUT scores correlated with mUPDRS (r=0.632; p<0.001), RBD-SQ (r=0.613; p<0.001), CAF (r=0.49; p=0.001) and hNPI (r=0.397; p=0.012). DLB patients presented higher P-SCOPA-AUT scores compared to AD patients (p<0.001). P-SCOPA-AUT showed a high diagnostic accuracy in differentiating DLB from AD (AUC = 0.845; p<0.001).
Conclusion: Dysautonomia seems to be associated with all four core clinical features of DLB and may help differentiate between DLB and AD. P-SCOPA-AUT may be a reliable tool to define patients for a detailed investigation of DLB symptoms.
Disclosure: Nothing to disclose.

EPO-003

Abstract withdrawn

EPO-004

Using a PET atlas to probe neurotransmitter-disease associations in Mild Cognitive Impairment and Alzheimer's disease

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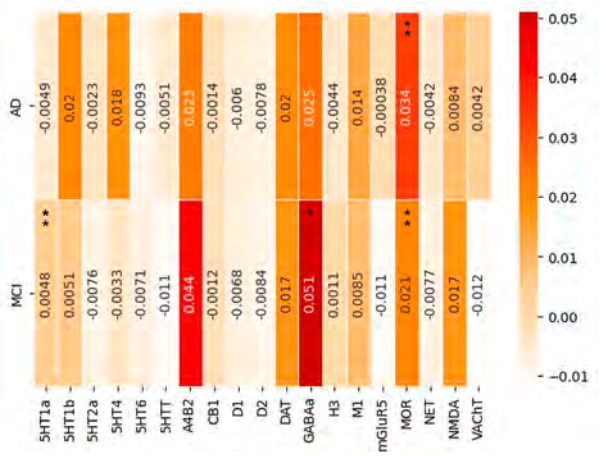
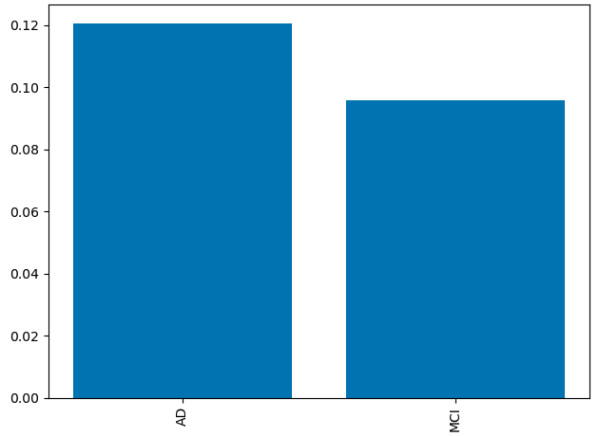
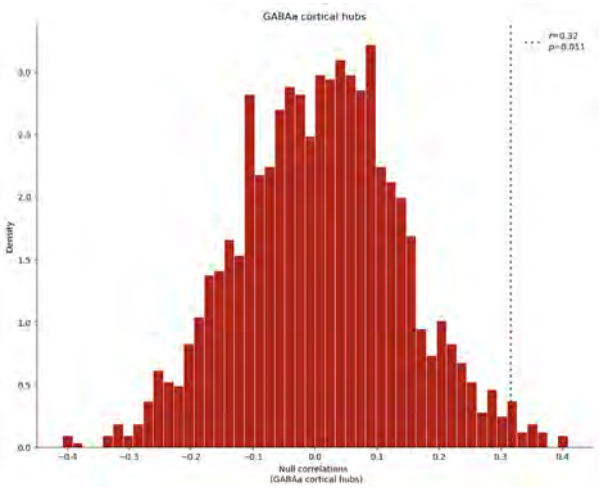
Background and aims: Disease-neurotransmitter associations may identify druggable pathways in Mild cognitive impairment (MCI) and Alzheimer's disease (AD). Current symptomatic treatments target receptor systems. Disease PET can measure neurotransmitter activity but is difficult to scale to multiple systems. Hansen et al (2022) have created an atlas of 19 neurotransmitter systems in healthy subjects. We examined associations between disease cortical atrophy with PET. The MCI-AD biological gradient enables testing of methodological validity.
Methods: We used MRI data from ADNI (457 AD, 713 MCI, 881 controls). Cortical thickness values were derived with FreeSurfer v7.1.1. These were processed in R to generate Cohen's d values, and then with the ENIGMA toolbox. PET maps were averaged from 1200 healthy subjects. Associations were analysed with dominance analysis (contribution to regression model fit). Output was a heatmap of relative dominance (Figure). Spin test generated p-values adjusting for spatial autocorrelation.
Results: For MCI, GABAa (p=0.011) and MOR receptors (p = 0.021) showed significant association, with 5HT1A (p=0.066), approaching significance. In AD, MOR receptor was significant (p=0.045). AD total dominance (0.12) was greater than MCI (0.095). There was progression in receptor dominance values from MCI to AD.



Heat map of dominance analysis. Contribution of each variable can be assessed and compared to other input variables normalised by the total fit. ** means p value <=0.05 * means discussed in abstract for ease of reference.



Total dominance from AD greater than MCI: a validation of biological gradient. Total dominance is average of the relative increase in R^2 when adding a single input variable of interest to a submodel, across all 2p − 1 submodels.



Example output of spin test to determine statistical significance of cortical atrophy – GABAa neurotransmitter receptor/transporter system distribution on PET map. Associations are made to maps created through map rotation.

Conclusion: We did not demonstrate differences in the cholinergic system or the NMDA receptor system. There are multiple possible explanations. The GABAa receptor is perturbed in AD imaging studies. The opioid system has known associations with amyloid beta. Further target research is warranted. The increase in total dominance values from MCI to AD suggests a biological gradient.
Disclosure: No competing interests.

EPO-005

Meta-analysis of cerebrospinal fluid immune markers in frontotemporal dementia patients compared to healthy controls

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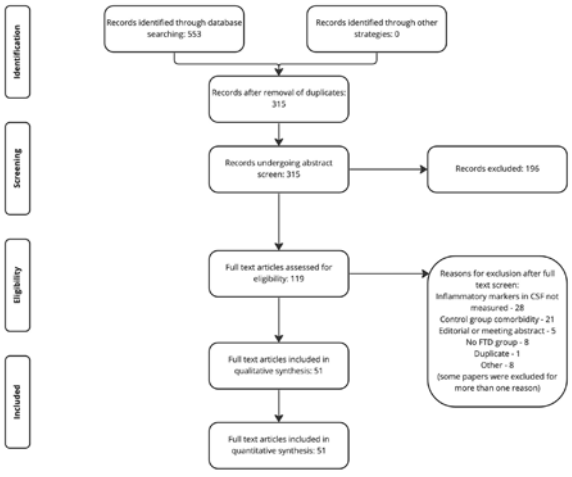
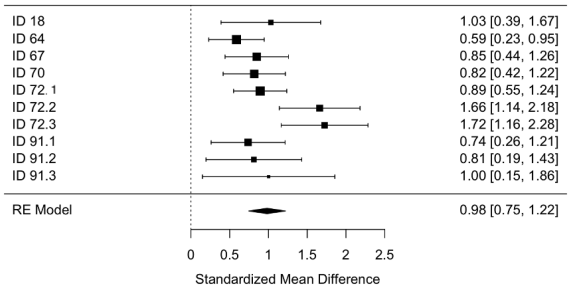
Background and aims: There is pleiotropy between frontotemporal dementia (FTD) and immune related conditions, within the Chromosome 6 HLA region, related to microglial function. PET studies with a marker of activated microglia demonstrate increased binding in frontotemporal regions across FTD pathologic and genetic subtypes. We aimed to identify perturbations in cerebrospinal fluid cytokines and chemokines in FTD versus healthy controls.
Methods: See also Prospero Protocol (ID: 212528). Databases searched were MEDLINE, Web of Science, and EMBASE. For immune markers where two or more papers were identified, a random effects model was used to calculated standardized mean difference (Hedge's g) between FTD and controls. Heterogeneity was assessed by funnel plot, Cochran Q-test and I^2 statistic. Data analysis was in R using Estmeansd and Metafor packages.

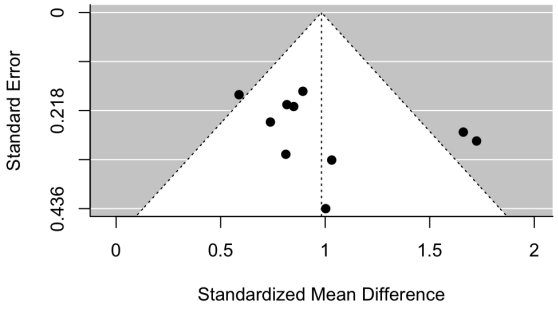


PRISMA flowchart of study selection. Abstract and full text screen and data extraction were carried out by two researchers (SB and YA) independently.

Results: The following immune markers were raised in FTD versus controls: Neurofilament light chain (NfL), standard mean difference (SMD) of 1.46 (1.26-1.66); CHI3L1, SMD of 0.98 (0.75-1.22); CHIT1, SMD of 0.50 (0.26-0.73). There was significant heterogeneity in NfL values (I^2 93%). The following immune markers were decreased in FTD versus controls: progranulin, SMD of -0.59 (-1.06– -0.12). Results from the following immune markers were obtained from two of more papers, without statistically significant differences found: CCL2, IL-6, MCP1, MIP1-alpha, TGF-beta, TNF-alpha.



Example forest plot of studies measuring CHI3L1 (YKL-40)



Example funnel plot of studies measuring CHI3L1 (YKL-40), enabling visual inspection of heterogeneity. I^2 for CHI3L1 was 54%

Conclusion: The perturbations detected in FTD replicate findings from the literature in plasma immune markers, and studies of brain transcriptomics. Findings suggest macrophage and microglial activation. Therapies targeting progranulin are in development. These findings may serve to identify additional targets.
Disclosure: No conflicts of interest to disclose.

EPO-006

Repetitive Transcranial Magnetic Stimulation of Dorsolateral Prefrontal Cortex in MCI

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Background and aims: Repetitive transcranial magnetic stimulation (rTMS), a non-invasive neuromodulation technique rTMS has been shown to modify cognitive performances and brain functional connectivity (FC) in neurological and psychiatric diseases. In this preliminary study, we evaluated the possible effects of rTMS of the bilateral dorsolateral prefrontal cortex (DLPFC) in patients with mild cognitive impairment (MCI).
Methods: 27 MCI patients were randomly assigned to two groups: one received high-frequency (10 Hz) rTMS for four weeks (MCI-TMS, n=11), and the other received sham stimulation (MCI-C, n=16). Cognitive and psycho-behavioral scores, brain FC analyzed by resting state functional MRI (RS-fMRI) networks, and regional atrophy measures, were evaluated at baseline (T0), after five weeks (T1), and six months after rTMS stimulation (T2). Neuropsychological and MRI measures were compared with 15 healthy controls (HC).
Results: MCI-TMS scored higher than MCI-C on semantic fluency and visuo-spatial subtests, in T1. Longitudinal analysis of brain FC in MCI-TMS showed increased FC within the salience network (SLN), in the left superior temporal gyrus and in the left parahippocampal gyrus at T1 and within the left fronto-parietal network (L-FPN), in the supramarginal gyrus, prefrontal cortex, and middle frontal gyrus, at T2. No FC differences were observed in MCI-C. Conversely, regional atrophy measures did not show significant longitudinal changes between the two groups across six months.
Conclusion: Our findings suggest that targeting DLPFC by rTMS application may lead to a long-term increase in FC in MCI patients in RS network associated with executive functions. This process might counteract the progressive cortical dysfunction affecting this domain.
Disclosure: I have no disclosure.

EPO-007

EEG correlates in the three variants of Primary Progressive Aphasia

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Background and aims: The analysis of EEG cortical sources is promising for the investigation of neurodegenerative disorders. The aim of this study is to explore its value in the characterization of the three clinical presentations of primary progressive aphasia (PPA).
Methods: A resting-state 19-channel EEG was obtained in 48 patients diagnosed with PPA (21 nonfluent/agrammatic variant PPA [nfv-PPA], 18 logopenic variant PPA [lv-PPA], 9 semantic variant PPA [sv-PPA]) and in 21 matched healthy controls. Using eLORETA, EEG current source density (CSD) values were estimated at voxel-level and compared among groups of patients and controls.
Results: Patients showed a low-to-moderate cognitive impairment. Lv-PPA cases showed a higher delta density over the left frontal and temporal regions when compared to sv-PPA subjects, and in left precuneus and posterior cingulate when compared to nfv-PPA patients. They also displayed a higher delta density in left frontal, parietal and temporal regions than healthy subjects, and lower alpha1 density in left occipital regions compared with other patient groups. Lv-PPA patients also showed reduced alpha2, beta1 and beta2 density over the left occipital regions when compared to healthy subjects. No significant differences were found in terms of CSD among sv-PPA, nfv-PPA and healthy subjects.
Conclusion: Consistently with our previous studies, findings in PPA patients suggest that Alzheimer's disease (AD), but not fronto-temporal degeneration (FTD), might induce a characteristic disruption of the cortical electrical activity, detectable by EEG. EEG might thus help in the differential diagnosis between AD-related and FTD-related PPA variants.
Disclosure: The authors have nothing to disclose.

EPO-008

A Systematic Review of Pharmacological Treatments for Neuropsychiatric Symptoms in Creutzfeldt Jakob Disease (CJD)

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[1]University of Edinburgh, National CJD Research and Surveillance Unit, Edinburgh, UK, [2]Oxford University Hospital NHS Foundation Trust, Palliative Medicine, Oxford, Unitingdom, [3]Newcastle Hospitals NHS Trust, Palliative Med Kedicine, Newcastle, UK, [4]Cambridge University Hospitals, Pallaitve Medicine, Cambridge, UK, [5]University of Edinburgh, Centre for Dementia Prevention, Edinburgh, UK

Background and aims: Creutzfeldt-Jakob Disease (CJD) is a rare but important cause of rapidly progressive dementia with challenging symptomatology and significant public health implications. Whilst neuropsychiatric symptoms form a large burden of care, evidence-based approaches to pharmacological treatments are lacking. We aimed to investigate the evidence base for pharmacological management of neuropsychiatric symptoms in CJD using a rigorous, systematic, and unbiased approach to identify treatment approaches that can be recommended in clinical practice. We also aimed to evaluate administration routes and reported side effects.
Methods: We completed a systematic review of the literature using MeSH terms derived from the Neuropsychiatric Inventory (NPI) and classes of commonly prescribed medications, interrogating Embase, Medline, Pubmed, and Web of Science. There were no language or date restrictions (searches completed 1st September 2022). Inclusion-criteria applied using COVIDENCE software.
Results: 47 studies including over 300 participants were included, detailing medications for the 12 NPI domains. Atypical antipsychotics were reported to have benefit in management of agitation, and cholinesterase inhibitors for hallucinations. Antidepressants were reported to lack efficacy for mood disturbance. Benzodiazepines have utility for multiple symptoms. Quality of evidence is hampered by small study size, variability in dosing and administration routes, and separating side effects from disease progression. Evidence available ranges from class 3 to 4.
Conclusion: Studies dedicated to evaluation of symptomatic control of neuropsychiatric symptoms in CJD are limited and have methodological flaws. However, atypical antipsychotics seem to be of benefit for agitation and cholinesterase inhibitors for hallucinations. There is need for larger prospective longitudinal studies for these challenging symptoms.
Disclosure: Nothing to disclose.

EPO-009

Longitudinal Quantification of Hippocampal Amyloid-Beta Burden from the AppNL-G-F Mouse Model of Alzheimer's Disease

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Background and aims: Amyloid-beta (Aβ) pathology is suggested to precede the onset of clinical Alzheimer's disease symptoms by up to two decades. The humanised AppNL-G-F knock-in model of amyloidopathy has accelerated pathogenesis and is used here to quantify the temporal and spatial characteristics of Aβ accumulation as it first appears in the hippocampus.
Methods: AppNL-G-F and wild-type mice are transfused and sliced for immunohistochemistry analysis, incubated with neuronal marker (NeuN), anti-Aβ antibody (6E10), and DAPI. Fiji was used to quantify Aβ plaques in regions of interest, representative of sub-hippocampal regions (CA1, CA3, DG), in left/right hemispheres, and ventral/dorsal segments.
Results: We found age to be a significant factor on determining area density, with hippocampal deposition observed by 3 months. Bin analysis showed a near-exponential reduction in plaque number with increasing plaque size, increasing with age. Regionally, there was an increase in plaque density in CA3, with non-linear regression analysis indicating area density for CA3 is most strongly correlated with age. Within the CA1 region, the densest plaque formation was in the pyramidal cell layer. The aged 9-month time point suggested a differential pathology across the axial plane and hemispheric lateralisation.
Conclusion: This data provides further evidence for the protracted timeline to which AppNL-G-F mice recapitulate AD neuropathologies including insoluble amyloidosis beginning before 3 months in the hippocampus. It also indicates potentially novel differential sub-regional Aβ accumulation patterns, axial variations, and hemispheric asymmetries, offering mechanistic insights for plaque localisation and differential susceptibility to Aβ. This could aid advancement of Aβ-targeting therapies.
Disclosure: Nothing to disclose.

EPO-010

Orexin-A determination in different biological fluids in neurodegenerative dementias

R. Cremascoli[1], F. Verde[2], S. Cattaldo[1], E. Prina[1], I. Milone[2], A. Ratti[2], L. Priano[1], L. Pradotto[1], A. Mitkova[1], F. Solca[2], B. Poletti[2], D. Soranna[3], A. Zambon [3], V. Silani[2], A. Mauro[1]

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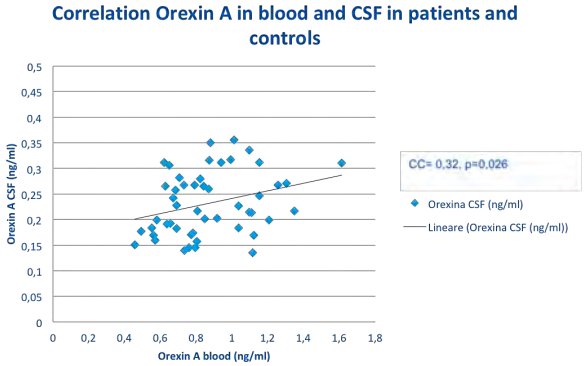
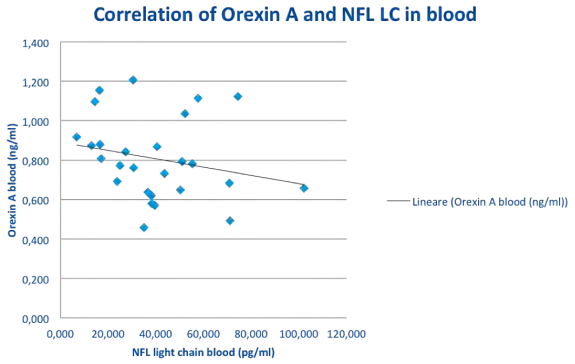
Background and aims: The main aim of this study is to evaluate correlations of Orexin-A (OXA) in different biological fluids, such as blood and CSF, in patients affected by several neurodegenerative dementias (ND). The secondary aim is to evaluate OXA concentration compared to other neurodegeneration associated peptides.

Methods: ND considered were the following: Alzheimer disease and its logopenic variant patients (AD/ADlv), non-logopenic primary progressive aphasia and behavioural variant of Fronto-Temporal Dementia (PPA/bvFTD). A group of patients with no evidence of ND served as controls. Both patients and controls underwent OXA determination in CSF and blood (ELISA). Other neurodegeneration associated peptides measured were: serum neurofilament light chain (NFL, SIMOA), CSF total-tau (t-tau, ELISA), CSF phospho-tau (p-tau, ELISA), CSF Amyloid beta 1-40 (Abeta 1-40) and Amyloid beta 1-42 (Abeta 1-42, ELISA).

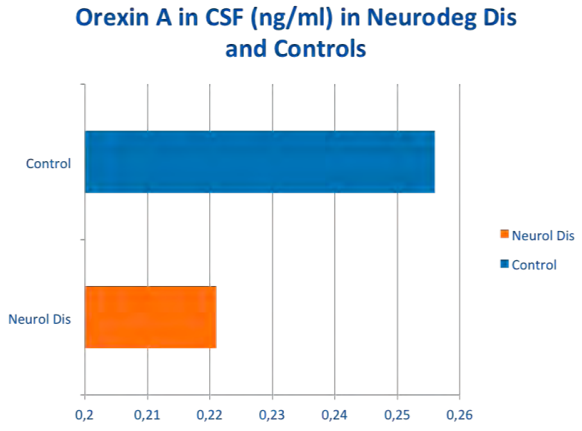
Results: Sample size was the following: 10 AD/ADlv patients (pts), 19 PPA/bvFTD pts, 21 controls. Gender and age did not statistically differ between groups (p=0.6067; p=0.147). We found a positive correlation between OXA levels in CSF and blood in the whole group of subjects (CC= 0,32, p=0,026) with a stronger correlation in controls (CC= 0,74) than in ND (CC= 0,29). Mean OXA concentration in CSF was significantly reduced in ND than controls (p=0,04). We also found an inverse correlation between OXA and NFL in ND group (CC= -0,37, p=0,04).



Correlation of Orexin A in blood and CSF in patients and controls.



Correlation between Orexin A and NFL LC in blood



Orexin A levels in CSF in patients and controls.

Conclusion: Despite the small sample size, our results suggest that OXA level in different biological fluids may represent a biomarker of degeneration in ND, especially when correlated to NFL.

Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work.

EPO-011

Abstract withdrawn

EPO-012

Dementia care in Italy in the era of anti-amyloid agents for AD: an Expert Opinion and practical guideline

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Background and aims: Current evidence from clinical trials testing anti-beta amyloid (Aβ) monoclonal antibodies (mAbs) in patients with early Alzheimer's disease (AD) suggests a likely authorization in Europe in the next years, requiring a huge change of dementia care in all countries.
Methods: A group of prominent AD clinical experts in Italy met to discuss patients' selection for immunotherapies and management strategies. The current diagnostic-therapeutical standards in Italy were taken as the starting-point.
Results: Immunotherapies' prescription must follow a biological diagnosis of AD, defined through the assessment of both amyloidopathy and tauopathy biomarkers. Their high risk/benefit ratio, moreover, needs a highly specialized diagnostic assessment, which should be dispensed by a neurologist. The Expert Panel suggests a reorganization of dementia and cognitive decline centers (CDCD) for the diagnosis of AD in Italy into 3 levels of increasing complexity, with specific tasks and requirements/resources: 1) community centers, with at least 1 neurologist / geriatrician / psychiatrist, with global screening purposes; 2) first-level centers, deputed to biological diagnosis; and 3) second-level centers, requiring the presence of on-site facilities for the biological diagnosis and of at least one neurologist with expertise also in rarer neurodegenerative syndromes. Finally, specific characteristics of a center deputed to prescribe anti-Aβ mAbs were discussed, highlighting the need for clinical and neuroradiological management protocols.
Conclusion: The number of potentially treatable patients in Italy will be tens of thousands. To successfully face such a breakthrough, a quick reorganization of Italian CDCDs will be required, together with the allocation of the necessary resources.
Disclosure: Funding: Unrestricted grants from Biogen.

EPO-013

Differentiation between frontotemporal dementia and primary psychiatric disorder using visual rating scales of atrophy

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Background and aims: Frontotemporal dementia (FTD) and primary psychiatric disorders (PPD) may overlap in terms of clinical presentations with behavioral change and altered executive functioning, however the role of brain atrophy in differentiating the two conditions has not been thoroughly investigated. The aim of the study is to identify the discriminative pattern of brain atrophy between FTD and PPD.
Methods: Among the patients followed in Neurology and Psychiatry departments of Ospedale Maggiore Policlinico of Milan, we retrospectively selected subjects with frontal lobe symptoms with an age at onset between 40 and 75 and with mild severity at the time of MRI. All the subjects underwent extensive neuropsycological testing, neurological and psychiatric examination. Two rater, blind for all the clinical infomations, applied a protocol of 6 visual rating scales of atrophy and 2 of white matter hyperintensities.
Results: A total of 52 subjects were recruited for the study: 15 FTD, 22 PPD and 15 controls. Compared to PPD, FTD cases showed higher degree of atrophy in left orbitofrontal, anterior cingulate and fronto insula, bilateral anterior and medial temporal and parietal areas. ROC curve analysis showed that left orbitofrontal scale was the most useful in the differentiation between FTD and PPD (AUC 0.88) while left anterior temporal better discriminated between FTD and controls (AUC 0.873). No differences between PPD and controls was found.
Conclusion: Visual rating scales can be useful to discriminate FTD and PPD and the left orbitofrontal showed the highest accuracy.
Disclosure: Nothing to disclose.

EPO-014

Differences and Similarities in Empathy Deficit and Its Neural Basis between Logopenic and Amnesic Alzheimer's Disease

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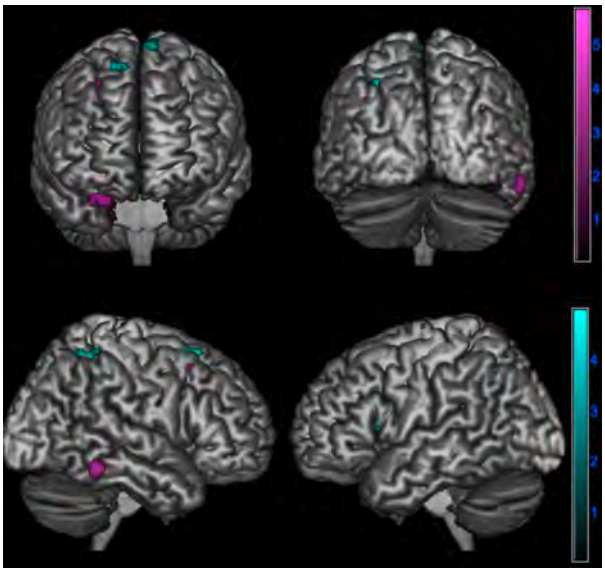
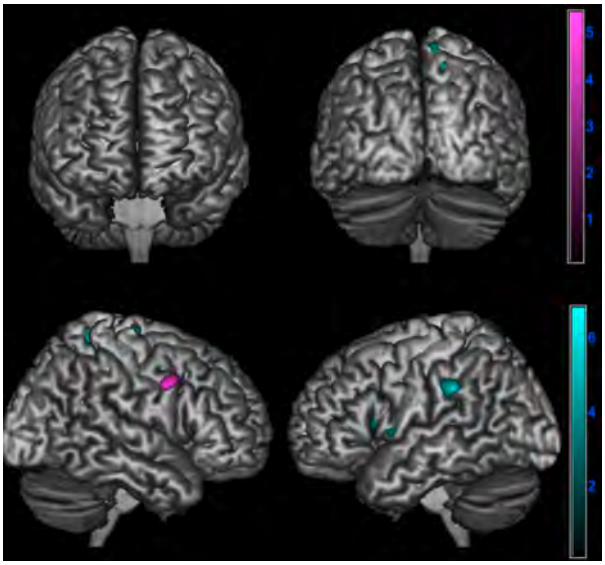
Background and aims: Empathy represents the ability to both feel and comprehend what others feel. The aims of the study were to assess empathy deficit and its neuronal correlates in logopenic primary progressive aphasia (lv-PPA) and amnesic Alzheimer's disease (a-AD).
Methods: Empathy was assessed in eighteen lv-PPA and thirty-eight a-AD patients by Informer-rated Interpersonal Reactivity Index (perspective taking, PT, and fantasy, FT, for cognitive domain; empathic concern, EC, and personal distress, PD, for affective domain) before (T0) and after (T1) cognitive symptoms' onset. Neural correlates of empathy were explored using cerebral FDG-PET.
Results: From T0 to T1, PT decreased, and PD increased in both lv-PPA (PT $z = -3.43$, $p = 0.001$; PD $z = -3.62$, $p < 0.001$) and a-AD (PT $z = -4.57$, $p < 0.001$; PD $z = -5.20$, $p < 0.001$). Delta PT (T0–T1) negatively correlated with metabolic disfunction of the right superior temporal gyrus, fusiform gyrus, and middle frontal gyrus (MFG) in a-AD and of the left inferior parietal lobule (IPL), insula, MFG, and bilateral superior frontal gyrus (SFG) in lv-PPA ($p < 0.005$). Delta PD (T0-T1) positively correlated with metabolic disfunction of the right inferior frontal gyrus in a-AD ($p < 0.001$) and of the left IPL, insula, and bilateral SFG in lv-PPA ($p < 0.005$).



Negative correlation between changes in ΔPT (PT-T0 - PT-T1) and brain metabolism in lv-PPA and a-AD patients at 18F-FDG-PET SPM analysis. Color grading: cyan, lv-PPA; violet, amnesic AD.



Positive correlation between changes in ΔPD (PD-T0 - PD-T1) and brain metabolism in lv-PPA and a-AD patients at 18F-FDG-PET SPM analysis. Color grading: cyan, lv-PPA; violet, amnesic AD.

Conclusion: Lv-PPA and a-AD share the same empathic changes, with damage of cognitive empathy and heightening of personal distress over time. The corresponding metabolic disfunctions' differences might be due to a different vulnerability of specific brain regions in the two AD clinical presentations.
Disclosure: The authors have nothing to disclose.

EPO-015

Novel pathogenic variants in frontotemporal dementia: whole exome sequencing monocentric cohort study.

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Background and aims: Frontotemporal dementia (FTD) etiology has an important genetic component, the three most frequently involved genes (MAPT, GRN and C9orf72) are implicated in about 5-10% of cases. In recent years, other causative genes were discovered opening new ethyologic and therapeutic perspectives. The present study aims to identify gene variations by WES (whole exome sequencing) in a cohort of FTD patients.
Methods: 78 patients (38 female, 40 male) were involved. They received a diagnosis included in FTD spectrum. The most frequent genetic variants known at the time of the diagnosis (MAPT, GRN and C9orf72) resulted negative. Investigation was then expanded using WES focused on unknown variants in already evaluated genes and on sixteen genes responsible for rare forms of familial FTD.
Results: Seven novel variants classified as pathogenic (ACMG guidelines) were detected: six frameshift mutations (two in GRN, two in CHMP2B, one in UBQLN2 and one in FUS) and one splice site variant of TBK1. Other three variants were classified as likely pathogenic: one in FUS and two in UBQLN2. There were also thirty one variants of uncertain significance (VUS), affecting MAPT, C9orf72, SQSTM1, VCP, OPTN, TARDBP, CHCHD10, CCNF, TIA1, DCTN1.
Conclusion: Investigating genes responsible for rare forms could have a significant diagnostic impact in FTD. In this study, 15% of cases are carriers of mutations classified as pathogenic or likely pathogenic. VUS emerged in one third of cases. Finally, WES will allow to search for variants in new candidate genes or for genetic risk factors for FTD.
Disclosure: No disclosures to declare.

	Total variants	Variants of interest	VUS	Pathogenic + likely pathogenic
MAPT	163	3	3	-
GRN	33	7	4	3
C9orf72	33	4	4	-
SQSTM1	25	3	3	-
TBK1	43	3	2	1
CHMP2B	25	2	-	2
VCP	35	1	1	-
OPTN	41	2	2	-
TARDBP	29	1	1	-
CHCHD10	9	1	1	-
UBQLN2	6	3	-	1 + 2
FUS	22	2	-	1 + 1
TUBA4A	14	-	-	-
CCNF	32	2	2	-
TIA1	36	3	3	-
DCTN1	53	5	5	-
Total	**599**	**42**	**31**	**11**

Synopsis of identified variants.

Autonomic nervous system diseases; Peripheral nerve disorders

EPO-016

Clinical and genetic features of congenital myasthenic syndrome in adult patients from Serbia

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Background and aims: Congenital myasthenic syndrome (CMS) is a group of inherited disorders of the neuromuscular junction (NMJ). The study aimed to characterize the clinical and genetic features of Serbian patients with CMS from the largest national neuromuscular center.
Methods: We retrospectively evaluated nine patients diagnosed with CMS at the Neurology Clinic, University Clinical Center of Serbia in the last ten years. Clinical symptoms and signs, electrophysiological findings, and genetic analysis were evaluated.
Results: We found mutations in four genes in our cohort. RAPSN gene mutation was the most prevalent discovered in 4 patients. These patients presented with facial and limb muscle weakness and fatigability and skeletal abnormalities, usually with head drop. Homozygous c.1327delG mutation in CHRNE gene was found in two patients of Roma origin with ptosis, facial and proximal limb muscle weakness and fatigability. One patient had p.Thr265Ser mutation in CHRNB1 gene presenting as a slow channel disease responding flunirine. DOK7 gene mutations were identified in one patient with ptosis, limb muscle weakness, and fatigue. COLQ gene mutations c.1228C>T and c.109del were identified in one patient. She had more proximal limb muscle weakness and fatigability with hyperelastic skin and joints. All patients had a decremental response to repetitive nerve stimulation (RNS).
Conclusion: Our findings contribute to the clinical and genetic spectrum of congenital myasthenic syndrome in Serbia. Neurologists should consider this rare disorder in the differential diagnosis of myasthenia gravis, congenital myopathies, and even limb-girdle muscular dystrophies.
Disclosure: Nothing to disclose.

EPO-017

Multidisciplinary care approach in familial dysautonomia – a single centre experience

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Background and aims: Familial dysautonomia is a rare, multi-systemic genetic syndrome caused by the impaired development of sensory and afferent autonomic nerves. We aimed to describe the phenotype of the FD cohort in the UK, its multidisciplinary approach, and treatment.
Methods: Data regarding autonomic function, ophthalmological, cardiovascular, respiratory, gastrointestinal, renal, behavioural, psychological, and orthopaedic involvement were collected retrospectively, as well as the number of specialists involved, and the medication regimen. All results are presented as average ± SD.
Results: Our cohort included 11 FD patients (5 females), aged 34 ± 11 years old (range 19-50). 2 patients died at 26 and 48 years of age. AFT was available for 8 patients, showing evidence of baroreflex failure. Autonomic crises were daily in 2, frequent in 2, and rare in 5 patients respectively. 2 patients had a diagnosis of epilepsy, 4 had evidence of optic atrophy, 6 had pulmonary involvement (bronchiectasis), 3 were on nocturnal NIV for SDB. Echocardiograms were available and normal in 5 patients. 6 patients had a PEG, 1 had an NGT, 2 had previous fundoplication. Average weight was 48.8 ± 9.64 kg. 1 patient had CKD and underwent transplantation and haemodialysis. Spinal surgery for scoliosis was performed in 4 patients, mostly wheelchair bound. 12 specialists were involved in the care of FD patients, who used an average of 15 ± 9 (range 4-29) medications daily.
Conclusion: Patients with FD require a multidisciplinary management including several specialists and carers. Yearly monitoring is recommended to increase life expectancy and quality of life.
Disclosure: Nothing to disclose.

EPO-018

An induced pluripotent stem cell-based model to study neurodegeneration in RFC1 disease

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Background and aims: Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) is a late-onset ataxia associated with biallelic AAGGG expansions in RFC1. The disease mechanisms of this disorder remain elusive and previous studies on patients' cell lines (i.e., fibroblasts, lymphoblasts) did not show a reduction of RFC1 RNA or protein. Induced pluripotent stem cells (iPSCs) have been proposed as a powerful experimental model for several diseases, as they allow to generate patient-specific cell lines from different sources. As sensory system is constantly involved in RFC1 disease, we generated IPSC-derived sensory neurons to investigate the pathomechanisms of this disorder.
Methods: We used Chamber's modified protocol to differentiate sensory neurons from IPSC lines derived from patients' and controls' fibroblasts. We assessed morphological parameters such as neurite outgrowth and number of branching points. We compared the transcriptome profile of CANVAS and control lines by RNAseq. Finally, we quantified markers of DNA and axonal damage in basal conditions and after pharmacological stress.
Results: We generated mature colonies of sensory neurons derived from IPSCs lines (3 CANVAS and 3 controls). No significant difference in neurite outgrowth and branching points was observed between patients and controls. Transcriptomic analyses revealed unchanged RFC1 transcription and splicing. Quantification of DNA and axonal damage markers is ongoing.
Conclusion: The study confirmed no overt reduction of RFC1 transcript or abnormal splicing in a disease relevant model as IPSCs-sensory neurons. Future studies on long-term cultures of IPSCs-derived neurons will provide a better insight into the mechanisms underlying neurodegeneration in this disorder.
Disclosure: Nothing to disclose.

EPO-019

Will all Axonal forms of Guillain-Barré syndrome have poor prognosis? A serial nerve conduction study can help to answer

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Background and aims: Electrodiagnostic (EDx) studies play a crucial role in subtypes classification of Guillain-Barré syndrome (GBS). It provides diagnostic and prognostic information. However, initial EDx findings may change because of the reversible conduction failure (RCF).
Methods: In a prospective study, we included all patients admitted with a diagnosis of GBS in two general referral hospitals in Tehran in 2021. We performed two serial NCSs in admission time and after 2-4 weeks. The Uncini criteria were applied to the NCSs, and subtype classification and changes on serial NCS were determined.
Results: This study included fifty-four patients. The mean age of the patients was 45.9±20.39 years, and 67 percent of patients were male. The patients were treated with intravenous immunoglobulin (IVIg) or plasma exchange (PLEX). The serial NCSs were performed on 26 patients. In seven patients (26.9%), variant changes were seen. In four of these patients, initial AMAN variants changed to AIDP due to distal RCF, And in three patients, the initial AIDP variant changed to Axonal variants due to Length-dependent conduction failure. Response to treatment in distal RCF was good similar to AIDP variants.
Conclusion: For the dynamic pathophysiology of GBS, only serial studies allow an accurate diagnosis of subtypes. The pathophysiology in axonal GBS differs from functional axonal involvement manifesting as RCF to axonal degeneration appearing as distal CMAP reduction or as a length-dependent conduction failure pattern.
Disclosure: Nothing to disclose.

EPO-020

Abstracts withdrawn

EPO-021

NERVE ULTRASOUND AND MRI FINDINGS IN NODO-PARANODOPATHIES: CORRELATION WITH CLINICAL AND NEUROPHYSIOLOGICAL EXAMINATIONS

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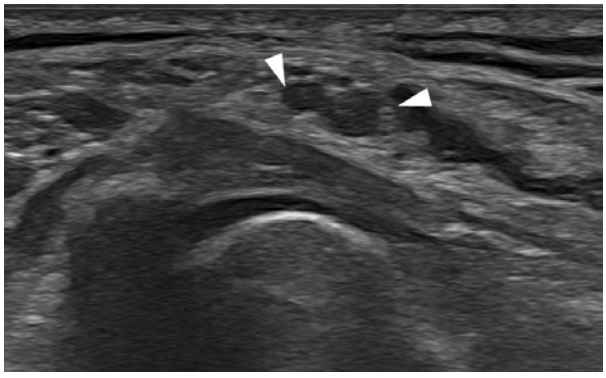
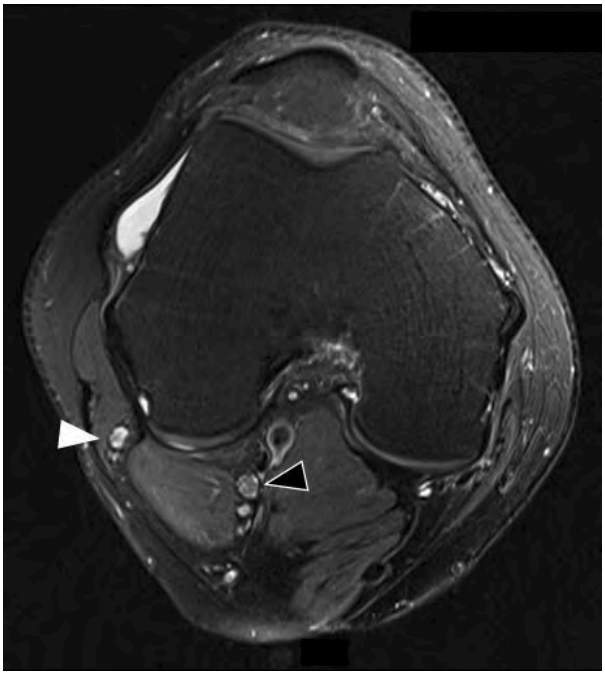
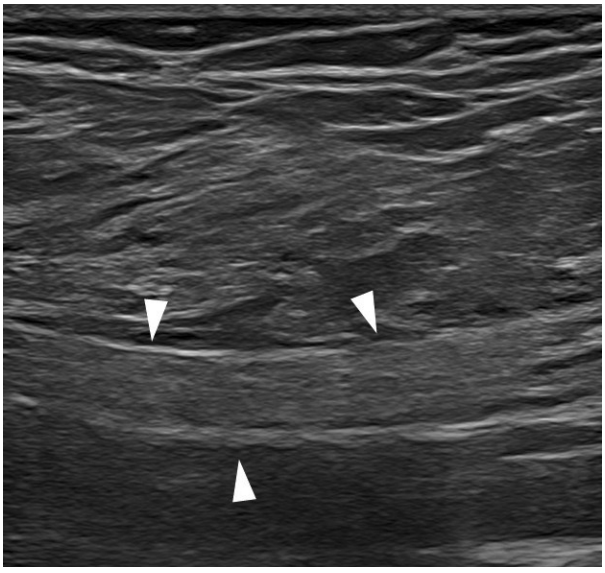
Background and aims: Immune-mediated neuropathies with anti-nodal/paranodal antibodies are rare polyneuropathies that have been increasingly identified within the last decade. Six patients with inflammatory nodo-paranodopathies were evaluated by use of nerve ultrasound and nerve 3T-MRI, comparing imaging with clinical and neurophysiological examinations.
Methods: Five patients tested positive for anti contactin-1 and one positive for anti-NF155 were included in the series. Clinical evaluation, motor/sensory nerve conduction study and nerve ultrasound of the four limbs were performed. The nerve cross sectional area (CSA) and the nerve echotexture were analyzed with qualitative (according to a modified Padua et.al. classification) and quantitative methods (using an automatic software). A 3-Tesla-system MRI was performed in the most affected limb on nerve conduction study.
Results: In the patients with a short duration of disease or worsening of symptoms we observed heterogeneous enlarged hypo and hyperechoic fascicles with different distributions: moderate/diffuse or multifocal. The MRI confirmed ultrasound abnormalities with a particular pattern: only part of the nerve fascicles was hyperintense and swollen with a multifocal distribution. Curiously, despite the presence of an altered sural nerve conduction study in most patients, no sural nerve ultrasound abnormalities were seen in all patients except one.



Nerve ultrasound: Linear probe 18-5 MHz, Short-axis section of common peroneal nerve (arrow head) with enlarged fascicles.



Nerve MRI: T2-weighted sequences with fat signal saturation technique. Common peroneal nerve (white arrow head) hyperintense with some fascicles enlarged Tibial nerve (black arrow head) with some hyperintense fascicles



Nerve ultrasound: Linear probe 18-5 MHz, Long-axis section of hyperechoic sciatic nerve (arrowheads) with loss of fascicular structure.

Conclusion: These data suggest that nerve ultrasound and MRI abnormalities could reflect an active phase of disease and can be used for diagnosis/evaluation/prognosis even in patients affected by nodo-paranodopathies. A larger sample of patients is needed to provide information about the ultrasound pattern in nodo-paranodopathies and the absence of sural nerve ultrasound alterations.
Disclosure: Nothing to disclose.

EPO-022

Polyneuropathy: the role of peripheral nerve biopsy in the clinical decision

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Background and aims: Peripheral nerve biopsy (PNB) is a complementary mean of diagnosis used in the investigation of patients with peripheral neuropathy of undetermined aetiology. The increasing use of non-invasive/minimally invasive complementary means, such as neurophysiological studies and imaging studies by ultrasound and MRI, may impose new challenges to its diagnostic relevance. This study aims to evaluate the results of PNB in the diagnostic definition and therapeutic decision in patients with peripheral neuropathy of undetermined etiology.
Methods: Retrospective study including adult patients who underwent a peripheral nerve biopsy at the Centro Hospitalar e Universitário de Coimbra (CHUC) since 2010. Clinical, laboratory, neurophysiological and histopathological information was obtained. The presence of neurophysiological criteria of polyneuropathy, associated with clinical and laboratory manifestations concordant with a diagnosis of peripheral neuropathy, was defined as a probable etiological diagnosis.
Results: From a total of 46 peripheral nerve biopsies, we obtained complete information from 40 patients (60% female). The mean age at the time of the biopsy was 56.9 years. In 26.7% of patients, a probable etiological diagnosis was obtained with the information provided by PNB (p=0.435).
Conclusion: PNB continues to be an important complementary diagnostic tool in the etiological clarification of peripheral neuropathy, and strict criteria should be followed in patient selection to optimize its results.
Disclosure: Nothing to disclose.

EPO-023

Case series of pyridoxine-induced neuropathy

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Background and aims: Vitamin B6 in the form of pyridoxine is commonly used by the general population. The use of pyridoxine-containing supplements had gained lots of attention over the past years as they have been related to the development of peripheral neuropathy. In the light of this, the number of reported cases of adverse health effects due to the use of vitamin B6 have increased.
Methods: We described eight cases of peripheral neuropathy associated with pyridoxine supplements.
Results: Nerve conduction study revealed axonal sensorimotor polyneuropathy in 6 patients and demyelinating sensorimotor polyneuropathy in 2 patients. Extensive diagnostic work-up was without any etiological clue. Measurement of blood levels of vitamin B6 (normal range; 15-73 nmol/L) showed increased levels (mean; 397.3 nmol/L, range 163.8 – 623.5). We advised the patients to immediately stop vitamin B6 administration.
Conclusion: Based on the current limited data, it can be concluded that very low doses of daily pyridoxine are required to prevent peripheral neuropathy. There is inadequate evidence to support routine pyridoxine supplementation in patients with disorders of peripheral nervous system. Supplementation with pyridoxine at doses greater than 50 mg/d for extended duration may be harmful and should be discouraged.
Disclosure: Nothing to disclose.

EPO-024

Changes of neurophysiological and nerve ultrasound characteristics in CIDP over time: follow-up period more than 5 years

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Background and aims: Diagnosis of Chronic inflammatory demyelinating polyneuropathy (CIDP) is made by demonstrating peripheral nerve demyelination, commonly by electrophysiological testing. It remains unclear whether the neurophysiological and ultrasound signs characteristic of demyelination in the long-term clinical remission and absence of motor deficits. We evaluate changes of neurophysiological and nerve ultrasound characteristics in CIDP over time: follow-up period ≥ 5 years.
Methods: We included 45 adult patients that fulfilled EAN/PNS diagnostic criteria for CIDP 2021 at onset and have follow-up period ≥ 5 years. Disease activity status (CDAS, Gorson 2010), electrophysiological examination (4 motor and 4 sensory nerves), needle EMG of tibialis anterior muscle and nerve ultrasound (UPPS, Grimm 2015) were performed.
Results: Median follow-up period was 10 [7; 14], average age 47.6±13.6 years. There were 33 (73,3%) typical CIDP patients and 12 (26,7%) multifocal CIDP. 34% had CDAS 1 (≥5 years off treatment), 13,3% - CDAS 5 (unstable active disease). 82,2% of patients had neurophysiological signs of demyelination, fulfilled criteria of EAN/PNS 2021 and 50% had nerve enlargement in proximal ulnar and median nerves segments and brachial plexus. 42% had electrophysiological signs of axonal degeneration.
Conclusion: In the long-term follow-up of CIDP (≥5 years) in spite of treatment neurophysiological and ultrasound signs of peripheral nerve damage are persistent and do not completely regress, there is clinical and neurophysiological dissociation.
Disclosure: The authors have nothing to disclose.

EPO-025

Axonal Guillain-Barre Syndrome variants: analysis of clinical features and prognosis of patients in a tertiary hospital

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Background and aims: Axonal variants of Guillain-Barré syndrome (GBS) mainly include acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN). Our aim was to describe the epidemiological, clinical presentation and outcomes of axonal variant of Guillain-Barré syndrome in a tertiary university hospital in Córdoba, Spain.
Methods: An observational, retrospective and descriptive study was performed. We obtained 81 patients with the diagnosis of GBS from the Neurology department between 2015 and 2022. Finally, we included 21 cases of axonal variant of GBS: 8 cases of AMAN and 13 of AMSAN. Clinical presentation, electrophysiological pattern, cerebrospinal fluid (CSF) findings, as well as final clinical outcomes were collected using the modified Hughes Functional Grading Scale.
Results: In our series, 12 patients (57.1%) were male. Mean age at presentation was 62.9 years (range 39-80). Most cases (61.9%) debuted in winter and spring. 15 patients (71.4%) had gastroenteritis before onset. 16 patients (76%) had an abnormal CSF biochemical pattern (hyperproteinorrachia in the first 24h). 6 patients suffered from respiratory failure (RF) and 5 of them were admitted to the Intensive Care Unit. All of them were treated with IVIG and 8 required plasmapheresis in addition. The mean number of days of hospitalization was 31.4. 66.6% were confined to a wheelchair at discharge and all of them had residual impairment after 6 months (85.7%: Hughes 2-3).
Conclusion: We observed clinical features and outcomes similar to those described in the current literature, including RF and residual disability.
Disclosure: Nothing to disclose.

EPO-026

Phenotypical and Genotypical Variability of Patients with Charcot-Marie-Tooth Disease at Charité Berlin, Germany

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Background and aims: Charcot-Marie-Tooth disease (CMT) is the most frequent hereditary peripheral neuropathy. Symptoms often start in early childhood and progress over time, leading to disability and loss of self-sufficiency. There are over 100 known mutations known but no causal therapy available up to now. The characterization of phenotypical variability and natural disease history is essential for present and future therapy development and clinical trial preparation.
Methods: At Charité Berlin, we used an extensive battery of clinical scores, laboratory examinations, and electrophysiological examinations to characterize patients with CMT during 2022. Furthermore, we established a biobank for skin biopsies as well as fibroblast cultures for future genomic, proteomic, and morphological analyses.
Results: We collected over 40 patients with clinical diagnosis of CMT, out of which about 70% received a genetic diagnosis. Variants of 11 causal genes were identified, including 6 variants of unknown significance. The average age of onset was 19 years with a range from 0 to 55 years, and clinical severity as well as phenotypes varied greatly even within single mutations.
Conclusion: CMT is a genetically and phenotypically diverse disorder. There is an urgent need to better understand this variability in order to predict disease course, identify possible modifiers of disease severity, and prepare for clinical studies.
Disclosure: This project was supported by financial reimbursement/travel support by Alnylam Pharmaceuticals Inc, research funding by Alnylam Pharmaceuticals Inc., and Pfizer Pharmaceuticals, and research funding by Deutsche Gesellschaft für Muskelkranke (DGM)

Cerebrovascular diseases 1

EPO-027

The relationship between vascular risk factors and white matter hyperintensities in patients with lacunar stroke.

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Background and aims: The purpose of the study was to determine association between the severity of WMH and vascular risk factors in lacunar ischemic stroke.
Methods: 62 patients with lacunar IS were enrolled in this study. Brain MRI and CT scans were performed within 7 days after stroke onset. Periventricular WMH(P-WMH) and deep WMH(D-WMH) were assessed independently by Fazekas scale. Patients were divided into two groups according to Fazekas scores: Group I participants with a P-WMH/ D-WMH Fazekas score of 0–1 and Group II patients with a P-WMH/ D-WMH Fazekas score of 2 and 3.
Results: The severe P-WMH group had higher age (p=0.028) and higher proportion of hypertension (p=0.038) compared to mild P-WMH group, while percent of smoking was higher in P-WMH group. The results of binary logistic regression analyses(BLRA) showed that there were a significant association between higher age (OR=1.048, 95% CI, 1.032-1.086, p=0.001) and the recurrent stroke (OR=4.892, 95%CI, 2.456-9.216 p<0.001) with severe degree of P-WMH after adjusting for sex and vascular risk factors. The severe D-WMH group also had higher age (p<0.001), and higher proportion of hyperlipidemia (p=0.008) and stroke (p<0.001) in comparison with mild D-WMH group. BLRA demonstrated that there were a significant relationship between higher age and the recurrent stroke with the severity of D-WMH after adjusting for sex and vascular risk factors.
Conclusion: The results of our study showed that there are relationship between age and recurrent stroke with the severity of P-WMH and D-WMH in patients with lacunar IS.
Disclosure: Nothing to disclose.

EPO-028

Outcomes of intravenous (IV) thrombolysis in acute ischemic stroke in Albania

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Background and aims: Stroke is a leading cause of disability worldwide. IV thrombolysis represents a mainstay therapy that can improve neurological deficits in patients with acute ischemic stroke. However, there are some factors that influence the outcome in those who receive alteplase.
Methods: We included data of the patients hospitalized in the Neurovascular Service of "Mother Teresa" University Hospital during the year 2022, who met the criteria for thrombolytic treatment. Demographic data, stroke risk factors, time window of alteplase administration, National Institutes of Health Stroke Scale (NIHSS) before thrombolysis and in the discharge from hospital were analyzed.
Results: IV alteplase was administered in 87 patients aged from 46 to 95 years. 35 were male sex with a mean age of 69.6 and 52 were female with a mean age of 71.12. 90.8% of patients had hypertension, 19.5% diabetes mellitus, 30% hypercholesterolemia and 40.2% had atrial fibrillation, of which 6.9% were under treatment with anticoagulants. 19 patients (21.8%) had intracranial hemorrhage. 37 patients had good outcome, defined as Modified Rankin Scale (mRS) score at discharge of 0-2 and NIHSS of 0-5 points. There was no significant difference in the outcome between male and female sex (p<0.594) in terms of mRS. We found a statistically significant correlation between NIHSS before treatment and outcome (p<0.001), hemorrhagic transformation and advanced age and poor outcome [mRS score of 5-6 points] (p<0.001).
Conclusion: The best predictor of outcome after thrombolysis is the NIHSS before treatment. Hemorrhagic transformation and advanced age are predictors for poor outcome.
Disclosure: Nothing to disclose.

EPO-029

The opacification time of ascending aorta during CT angiography as a predictor of heart failure.

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Background and aims: Heart failure (HF) represent the second most frequent cause of cardioembolic (CE) stroke. Brain CT angiography is routinely performed in the suspect of a large vessel occlusion. Placing a region of interest (ROI) at the level of the ascending aorta, the opacification of the vessel is monitored until a threshold value of Hounsfield Unit (HU) is reached, starting images acquisition. The opacification time of the ascending aorta may be affected by heart ejection fraction (EF). We evaluated the existence of a correlation between these parameters and tried to identify a cut-off value able to predict a diagnosis of heart failure.
Methods: We screened all patients discharged from the Fondazione Policlinico Gemelli in Rome between December 2019 and June 2021, with a CT angiography of cerebral vessel and an echocardiographic evaluation of the

EF. The opacification time of the ascending aorta was calculated as the time needed to reach a threshold of 40 Hounsfield Unit (T40HU) in the ROI.
Results: We enrolled 366 patients and found an inverse correlation between the EF and the T40HU, indicating longer time for aorta opalization as the EF decreases. Through a receiver operating characteristic (ROC) curve analysis we identified a cut-off value of 16,8 seconds for the T40HU as able to predict with good sensitivity (81%) and specificity (61%) a diagnosis of heart failure with EF <40%.
Conclusion: The T40HU is a reliable indicator of HF with reduced EF, allowing to esteem heart function already in the emergency department even in the setting of an acute stroke.
Disclosure: The authors declare no conflict of interest.

EPO-030

Early plasma YKL40 level predicts 3-month functional outcome after ischemic stroke treated with endovascular therapy

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Background and aims: More than 40% or large vessel occlusion ischemic stroke patients remain disabled at 3 months despite successful reperfusion therapies including intravenous thrombolysis and endovascular therapy (EVT). This neurological disability is mainly due to sensori-motor sequelae and post-stroke cognitive impairment (PSCI). Glycoprotein YKL40 is a biomarker of microglial activation. It is elevated in plasma in numerous neurodegenerative disorders but also in acute ischemic stroke. We hypothesized that acute microglial inflammation plays a key role in PSCI and that plasma levels of YKL40 could be a predictive biomarker of future cognitive and functional outcomes.
Methods: Monocentric prospective study included patients treated with EVT, for whom 3 blood samples (before, within 1h, 24h post-EVT) were drawn to measure plasma YKL40 concentration as a marker of microglial activation. Excellent outcome was defined as a modified Rankin scale (mRS) 0 or 1 at 3 months.
Results: We included 120 patients between 2016 and 2020. Median NIHSS was 17 and median ASPECT score was 7. Repercussion was achieved at mean delay of 5h44. After 3 months, median mRS was 3 and 25% of patients with pre-stroke mRS< 2 had excellent outcome. Excellent clinical outcome was significantly associated with lower plasma YKL40 levels (p= 0,001) after adjustment on age, NIHSS and delay since onset.
Conclusion: Plasma YKL40 levels is a candidate predictor of functional outcome at 3 months in ischemic stroke treated by EVT. This novel biomarker of stroke could allow optimizing rehabilitation strategies and give new insight on pathophysiology of PSCI.
Disclosure: INSERM U1144 INSERM U1148

EPO-031

Glycemic variability after mechanical thrombectomy for acute ischemic stroke is associated with increased mortality

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Background and aims: Acute ischemic stroke (AIS) is a leading cause of death and disability. Mechanical thrombectomy (MT) is standard of care for patients with large vessel occlusion. Even with effective recanalization morbidity remains high. Therefore, it is important to recognize modifiable risk factors for adverse outcomes after MT. Glycemic variability (GV) has been related to poor outcomes in critically ill patients, but conflicting data exist on whether it affects prognosis after MT for AIS. Thus, we aimed to clarify how GV after MT impacts functional outcome and survival of AIS patients.
Methods: This was a single-center retrospective study. We included AIS patients who received MT for anterior circulation vessel occlusion between January 2015 and December 2019 at our stroke center. Demographic, clinical and paraclinical data were recorded. We used standard deviation (SD) of the mean blood glucose for the first 24 hours post MT as a measure of GV. Outcomes were modified Rankin Scale (mRS) score and mortality at 3 months follow-up. Univariate and multivariate analyses were performed.
Results: We included 657 patients (43.5% males; median age 77 years). In univariate analysis, patients with unfavorable functional outcome (mRS score 3-6; 42.5%) and patients that died (14.8%) had significantly higher SD. When adjusting for confounders, SD remained statistically significant for mortality (adjusted OR for unfavorable functional outcome: 1.007 [95% CI 0.990-1.025]; adjusted OR for mortality: 1.020 [95% CI 1.001-1.040]).
Conclusion: Our results suggest GV as a relevant and targetable risk factor for mortality in AIS stroke patients treated with MT.
Disclosure: The authors have nothing to declare.

EPO-032

Juvenile arterial ischemic stroke due to focal cerebral arteriopathy: a case-based approach

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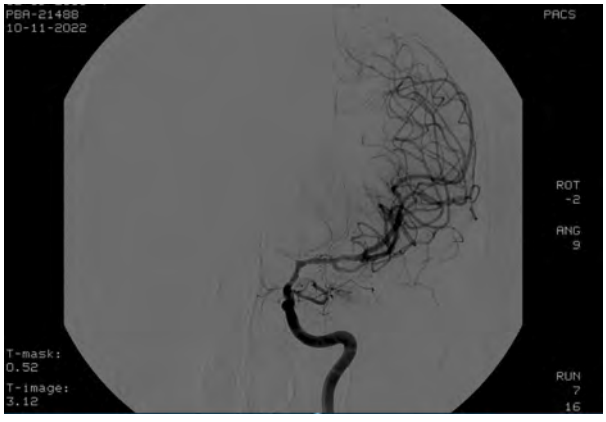
Background and aims: Focal cerebral arteriopathy (FCA) is one of the most common causes and strongest risk factor of recurrence of childhood arterial ischemic stroke (AIS), involving large vessels of the anterior cerebral circulation.
Methods: Diagnostic work-up included brain MRI and DSA, ECG monitoring, transesophageal echocardiography for PFO, TCCD, CSF and serological evaluation for infections, autoimmunity, coagulopathy.
Results: A 17-year-old woman with unremarkable medical history except for obesity was admitted to emergency department for aphasia and right hemiplegia due to left M2 dominant branch occlusion(NIHSS 21). She was treated with intravenous rt-PA only, with early neurological improvement(NIHSS 1). TCCD highlighted moderate stenosis of the proximal segment of left carotid syphon, while cerebral DSA showed banded appearance of left M1 segment suggestive for FCA (FCA Severity Score –FCASS 6). CSF analysis excluded infective and autoimmune vasculitis. Other tests were unremarkable. The patient received aspirin 100 mg daily and high dose of intravenous methylprednisolone(ivMP), followed by tapering at discharge. Three weeks later, the patient experienced right leg paresis due to left A1 occlusion. TCCD revealed early A1 recanalization but progressing M1 stenosis involving proximal M2 segment. IvMP and DAPT for 21 days was administrated with neurological improvement(NIHSS 1). Monthly follow-up demonstrated TCCD stability.



Cerebral DSA showed banded appearance of left M1 segment suggestive for focal cerebral arteriopathy.

Conclusion: FCA ranges from stabilization to improvement or resolution although arteriopathy caused a 5-fold increase of recurrence compared to idiopathic AIS. Predictive markers of recurrence and outcome, such as FCASS, are on-going validation. Use of steroid with or without antiviral therapy (hypothetical post-infectious pathophysiology) are commonly used although lack of interventional trial results.
Disclosure: All the authors have no disclosure.

EPO-033

The presence of pre-diabetes predicts the early neurologic deterioration in acute ischemic stroke using IV thrombolysis

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Background and aims: Pre-diabetes is an intermediate state between normal glucose metabolism and diabetes. However, there has been debated whether pre-diabetes might influence on short and long-term outcomes after AIS. In this study, we investigated the association between the presence of pre-diabetes and the early neurologic deterioration (END) in AIS using IV thrombolysis.
Methods: We recruited patients with AIS using IV thrombolysis prospectively registered CRCS-K database in Dong-A university stroke center from 2016 into 2020. According to their HbA1C levels, patients were divided into three groups: normal, pre-diabetes, and diabetes. We assessed the occurrence of END after using IV thrombolysis in AIS.
Results: Total 661 AIS patients using IV thrombolysis enrolled in this study. Among those subjects, pre-diabetes was diagnosed in 197 patients (29.8%) and diabetes in 210 patients (31.8%). In multiple logistic regression analysis, pre-diabetes was an independent predictor of END (OR, 1.79; 95% CI, 1.01 to 3.22; $p<0.05$) and of in-hospital death (OR, 3.31; 95% CI, 1.12 to 9.80; $p=0.03$).
Conclusion: Pre-diabetes influences on the occurrence of END in AIS with IV thrombolysis.
Disclosure: Nothing to disclose.

EPO-034

Outcome Determinants in Patients with Acute Mild Ischemic Stroke

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Background and aims: This study was conducted to clarify the risk factors of unfavorable early outcomes (UEO) in acute mild ischemic stroke (AMIS).
Methods: Patients with AMIS, defined as a National Institute of Health Stroke Score (NIHSS) <4 and admission within 48 hours after symptoms onset, were prospectively registered. A favorable outcome was defined as a modified Rankin Scale (mRS) or 1 or lower. Risk factors of UEO were analyzed.

Results: Among the 832 patients with AMIS, 174 patients had unfavorable outcomes (modified Rankin Score 2-6) at 3 months. Older age and higher initial NIHSS score are more common among those with poor outcome. On the contrary, antithrombotics given within 48 hours after stroke onset, and dual antiplatelet use among patients indicated, are associated with better outcome.

	Total (n=832)	Initial MRS 0-1 (n=610)	Initial MRS ≥ 1 (n=222)	P value
Age (years)	67.0 (57-76)	65.0 (55-74)	72.0 (62-82)	<0.001
Male, n (%)	572 (68.8%)	422 (69.2%)	150 (67.6%)	0.719
Body mass index (kg/m²)(n=787)	25.0 (22.8-27.5)	24.9 (22.9-27.4)	25.2 (22.7-27.6)	0.852
Hypertension, n (%)	612 (73.6%)	433 (71.0%)	179 (80.6%)	0.007
Diabetes, n (%)	341 (41.0%)	238 (39.0%)	103 (46.4%)	0.067
Atrial fibrillation, n (%)	131 (15.7%)	86 (14.1%)	45 (20.3%)	0.040
Heart failure, n (%)	29 (3.5%)	22 (3.6%)	7 (3.2%)	0.919
Ischemic heart disease, n (%)	83 (10.0%)	54 (8.9%)	29 (13.1%)	0.097
Total cholesterol, mg/dL (n=809)	174.0 (148-205)	174.0 (147-204)	176.0 (149-206)	0.601
Triglyceride, mg/dL (n=807)	111.0 (82-165)	112.0 (83-165)	105.0 (80-164)	0.264
HDL cholesterol, mg/dL (n=807)	44.0 (37-52)	44.0 (37-52)	43.0 (35.8-52)	0.163
LDL cholesterol, mg/dL (n=827)	108.0 (85-134)	106.0 (85-133)	111.0 (85-136)	0.431
Stroke subtype (TOAST), n (%) (n=693)				0.119
Large-artery atherosclerotic type	142 (20.5%)	87 (18.9%)	55 (26.1%)	
Cardioembolic type	190 (27.4%)	139 (28.8%)	51 (24.2%)	
Lacunar type	152 (21.9%)	103 (21.4%)	49 (23.2%)	
Undetermined type	14 (2.0%)	10 (2.1%)	4 (1.9%)	
Other determined type	195 (28.1%)	143 (29.7%)	52 (24.6%)	
Antithrombotics within 48 hours after stroke onset, n (%)	802 (96.4%)	584 (97.4%)	208 (93.7%)	0.021
Antithrombotics at discharge, n (%)	811 (97.5%)	601 (98.5%)	210 (94.6%)	0.003
No antithrombotic, n (%)	21 (2.5%)	9 (1.5%)	12 (5.4%)	0.093
Monotherapy, n (%)	361 (43.4%)	254 (41.6%)	107 (48.2%)	0.108
Dual antiplatelets, n (%)	402 (48.3%)	310 (50.8%)	92 (41.4%)	0.021
Anticoagulant, n (%)	94 (11.3%)	66 (10.8%)	28 (12.6%)	0.549
Statin use, n (%)	683 (82.1%)	504 (82.6%)	179 (80.6%)	0.575
Initial NIHSS score	2.0 (1-2)	1.0 (0-2)	2.0 (1.8-3)	<0.001

Data are expressed as median (interquartile range) for continuous variables and frequency (%) for categorical variables.
HDL, high density lipoprotein; LDL, low density lipoprotein; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institute of Health Stroke Score.

Table 1. Characteristics of patients with acute minor ischemic stroke

	Favorable early outcome (n=678)	Unfavorable early outcome (n=154)	P value
Age (years)	65.0 (56-74)	74.0 (63.8-84)	<0.001
Male, n (%)	474 (69.9%)	96 (62.3%)	0.156
Body mass index (kg/m²) (n=787)	25.0 (22.9-27.5)	25.0 (22.8-27.5)	0.241
Hypertension, n (%)	487 (71.8%)	125 (81.2%)	0.023
Diabetes, n (%)	272 (40.1%)	69 (44.8%)	0.328
Atrial fibrillation, n (%)	96 (14.5%)	33 (21.4%)	0.043
Heart failure, n (%)	21 (3.1%)	8 (5.2%)	0.299
Ischemic heart disease, n (%)	62 (9.1%)	21 (13.6%)	0.126
Total cholesterol, mg/dL (n=806)	177.0 (149.5-207)	169.5 (144.5-198)	0.089
Triglyceride, mg/dL (n=807)	113.0 (83-169)	100.0 (73.8-142)	0.012
HDL cholesterol, mg/dL (n=807)	45.5 (37-52)	44.0 (35-53)	0.577
LDL cholesterol, mg/dL (n=827)	108.0 (85-135)	107.5 (83-129)	0.239
Stroke subtype (TOAST), n (%) (n=693)			0.239
Large-artery atherosclerotic type	107 (19.4%)	55 (24.8%)	
Cardioembolic type	158 (28.6%)	32 (22.7%)	
Lacunar type	124 (22.5%)	28 (19.9%)	
Undetermined type	9 (1.6%)	5 (3.5%)	
Other determined type	154 (27.9%)	41 (29.1%)	
Antithrombotics within 48 hours after stroke onset, n (%)	662 (97.6%)	140 (90.9%)	<0.001
Antithrombotics at discharge, n (%)[a]	666 (98.2%)	145 (94.2%)	0.008
No antithrombotic, n (%)[a]	12 (1.8%)	9 (5.8%)	0.008
Monotherapy, n (%)	281 (41.4%)	80 (51.9%)	0.022
Dual antiplatelets, n (%)	346 (51.0%)	56 (36.4%)	0.001
Anticoagulant, n (%)	71 (10.5%)	23 (14.9%)	0.150
Statin use, n (%)	564 (83.6%)	113 (74.7%)	0.011
Initial NIHSS score	2.0 (0-2)	2.0 (2-3)	<0.001

Data are expressed as median (interquartile range) for continuous variables and frequency (%) for categorical variables.
[a]Chi-square test. [b]Fisher's Exact test.
HDL, high density lipoprotein; LDL, low density lipoprotein; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institute of Health Stroke Score.

Table 2. MRS at 3rd month

	Simple model			Multiple model		
	OR	95% CI	p value	OR	95% CI	p value
Age (years)	1.05	(1.04-1.06)	<0.001	1.04	(1.03-1.06)	<0.001
Male	0.75	(0.52-1.09)	0.130			
Body mass index (kg/m²)	0.97	(0.92-1.02)	0.170			
Hypertension	1.69	(1.09-2.62)	0.019	1.62	(0.94-2.78)	0.083
Diabetes	1.21	(0.85-1.72)	0.286			
Atrial fibrillation	1.61	(1.04-2.51)	0.033			
Total cholesterol, mg/dL	1.00	(0.99-1.00)	0.049			
Triglyceride, mg/dL	1.00	(0.99-1.00)	0.024			
HDL cholesterol, mg/dL	1.00	(1.00-1.00)	0.641			
LDL cholesterol, mg/dL	1.00	(0.99-1.00)	1.093			
Stroke subtype (TOAST)						
Large-artery atherosclerotic type	Ref					
Cardioembolic type	0.62	(0.36-1.06)	0.081			
Lacunar type	0.69	(0.39-1.21)	0.195			
Undetermined type	1.70	(0.55-5.41)	0.370			
Other determined type	0.81	(0.49-1.36)	0.432			
Antithrombotics within 48 hours after stroke onset	0.24	(0.12-0.51)	<0.001	0.22	(0.08-0.60)	0.003
Antithrombotics at discharge	0.29	(0.12-0.70)	0.006			
No antithrombotic	5.44	(1.42-8.33)	0.006			
Monotherapy	1.58	(1.08-2.17)	0.018			
Dual antiplatelets	0.55	(0.38-0.79)	0.001	0.64	(0.41-1.00)	0.049
Anticoagulant	1.50	(0.90-2.49)	0.116			
Statin use	0.57	(0.38-0.87)	0.008			
Initial NIHSS score	1.82	(1.53-2.17)	<0.001	1.91	(1.53-2.39)	<0.001

HDL, high density lipoprotein; LDL, low density lipoprotein; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institute of Health Stroke Score.

Table 3. Logistic regression model of unfavorable outcome at 3rd month

Conclusion: Older age, presence of hypertension, and higher initial NIHSS score were associated with unfavorable early outcome. Whereas antithrombotics within 48 hours and dual antiplatelet use seemed to have protective effect.
Disclosure: Nothing to disclose.

EPO-035

Clinical profile and outcome of cerebral venous thrombosis at Oran University Hospital

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Background and aims: Cerebral venous thrombosis (CVT) is a rare but serious disease whose clinical and etiological aspects are diverse. Unlike arterial ischemic strokes, epidemiological studies are limited. This study aims to describe clinical, etiological and outcome particularities of CVT in the Algerian population.
Methods: This is a retrospective observational study conducted at the neurology department of Oran University Hospital from January 2021 to December 2022. In a clinical context suggestive of CVT, the diagnosis was provided by cerebral MRI. All subjects underwent a complete etiological assessment. Anticoagulant treatment was based on low molecular weight heparin with relay by vitamin K antagonists.
Results: 45 patients participated in the study. The mean age was 36.94 ± 9.81 years, the sex ratio F/M was 4.6 (37/8). The onset was subacute in 55% of cases. The main initial signs were headaches (88.8%), visual disturbances (50%), epileptic seizures (44.4%) and motor deficit (44.4%). Thrombosis predominated in the superior sagittal sinus and the lateral sinuses; parenchymal lesions were associated in 2/3 of the cases. Obstetrical causes were by far the most frequent. The evolution was favorable in 83.3% of cases.
Conclusion: The characteristics of CVT in the Algerian population are distinguished by a high frequency of obstetrical causes. Awareness campaigns for women of childbearing age are proving useful.
Disclosure: Nothing to disclose.

EPO-036

Clinical profile and etiology of ischemic stroke in young adults : a study from Oran, Algeria

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Background and aims: Ischemic stroke in young adults is a real diagnostic and therapeutic challenge. it differs from stroke occurring in the elderly by etiology. Despite an exhaustive assessment, a high proportion remains of unknown causes. This study aims to describe the clinical

profile and to gain further insight into the etiology of ischemic stroke in young adults in Oran.
Methods: This observational prospective study was carried out at the stroke unit of Oran University Hospital between January 1st 2021 to June 30th 2022. We included all acute ischemic stroke patients aged 18 to 44 years.
Results: Twenty one first-ever ischemic stroke patients were identified during the study period. The mean age was 36.7% and sex-ratio M/F 0.97. NIHSS at admission was 12±4.3. According to the modified TOAST criteria, spontaneous cervical arterial dissection was the leading probable etiology (19.05%). Patent foramen ovale or atrial septal aneurysm was a possible cause of stroke in 9.52% of cases, IgG anticardiolipin antibodies (4.76%), oral contraceptive use (14.3%), and migraine (4.76%). Mortality rate was 4.7% and the one year mRs 1.26.
Conclusion: The results of this study confirm the need for preventive strategies, by detecting risk factors of ischemic stroke in young adults, and early medical care of these patients in a neurovascular unit to enable the confirmation of the etiological diagnosis.
Disclosure: Nothing to disclose.

EPO-037

Predictors of good outcome after Unsuccessful Mechanical Thrombectomy in patients with hyperacute ischemic stroke

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Background and aims: The endovascular thrombectomy (EVT) has become the standard treatment for major acute anterior circulation ischemic stroke (AIS), but not all EVT guarantee successful recanalization. The predictors of good clinical outcome in patients who have experienced unsuccessful recanalization are not unknown. The study objective was to identify the predictors associated with clinical improvement after unsuccessful EVT in patients with AIS.
Methods: In this retrospective study, a total 1046 consecutive patients with AIS who underwent EVT from January 2012 to December 2021 in a single tertiary center were included. Among them, 181 patients (17.3%) had unsuccessful recanalization (modified Thrombolysis In Cerebral Infarction (mTICI) ≤2a) after EVT. Those patients with good outcomes (modified Rankin Scale [mRS], ≤2) were evaluated with clinical and procedural parameters.
Results: The 41 patients (22.7%) had good outcomes. The initial median NIHSS was 12.2 ± 5.4 and Alberta Stroke Program Early CT 7 (4-8). In multivariate analysis, predictors of good outcomes after unsuccessful EVT were age (OR, 0.937; 95% CI, 0.886-0.985, p=0.013), pre-stroke statin medication (OR, 3.145; 95% CI, 1.003-9.933, p=0.048), and total procedural time (OR, 0.973; 95% CI, 0.951–0.992, p=0.012).
Conclusion: Despite the unsuccessful recanalization after EVT, ~>20% patients with AIS showed clinical improvement. Younger age, shorter procedural time and pre-stroke statin medication were associated with good outcome after unsuccessful EVT.
Disclosure: Nothing to disclose.

EPO-038

Assessment of histological characteristics of thrombi after acute ischemic stroke

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Background and aims: Mechanical thrombectomy (MT) allows the study of acute ischemic stroke thrombi material. The aim of this study is to correlate thrombi composition and stroke aetiology, imaging, and revascularization outcomes.
Methods: Patients whose thrombus removed by TM were sent to the Neuropathology Laboratory were included. Retrospective analysis of clinical and radiological variables was performed. Three groups: 1-rich in erythrocytes (≥60% erythrocytes), 2-mixed (erythrocytes=fibrin/collagen) and 3-rich in fibrin/collagen (≥60% fibrin/collagen); presence or absence of leukocytes. Statistical analyses were performed using Fisher's exact test.
Results: 16 patients were included, 68.8% (n=11) male, median age 74 years old. 81.3% (n=13) with hypertension, 50% (n=8) with dyslipidaemia, 37.5% (n=6) with diabetes, 31.3% (n=5) were smokers, 31.3% (n=5) with atrial fibrillation/flutter, and 6.3% (n=1) with overweight/obesity. 33.3% (n=5) under antiplatelet therapy and 6.7% (n=1) under anticoagulant therapy. Median NIHSS 14.5. Median ASPECTS 8.5. 93.8% (n=15) had anterior circulation occlusion. Half had spontaneous hyperdense vessel sign on brain CT. Half underwent thrombolysis. 76.9% (n=10) underwent MT with aspiration system (global median of 2 passes). 80% (n=12) had mTICI3/2c. 43.8% (n=7) presented thrombi rich in erythrocytes and the entire sample presented leukocytes. 66.7% (n=10) had cardioembolic aetiology. There was an association between the presence of thrombi rich in erythrocytes and mRS≤3 (p=0.031).
Conclusion: Patients with less disability had thrombi rich in erythrocytes. It may be related to a higher rate of recanalization after TM in this group, previously described. Larger sample size will allow to corroborate this clinicopathological correlation.
Disclosure: Nothing to disclose.

EPO-039

Previous statins use and the risk for haemorrhagic transformation in acute ischemic stroke patients

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Background and aims: According metanalysis studies, long term statin use can slightly increase the risk for intracerebral haemorrhage, including haemorrhagic transformation (HT) of ischemic stroke. The aim of our study was to evaluate the risk for HT in acute ischemic stroke (AIS) patients with previous statin use and the correlation with the patients' outcome and recovery.
Methods: In a prospective, consecutive way, we've included patients with AIS admitted to a tertiary neurological hospital from 2018 to 2022, to evaluate possible risk factors for HT and its' impact on discharge and 3 months follow-up status by the modified Rankin Scale (mRS). The patients were grouped, based on the HT presence, into 2 cohorts: active group (with HT) and control group (without HT).
Results: From 150 patients, 55 patients presented HT during the hospitalization. The mean LDL-cholesterol level was 3.3±0.07 mmol with similar values in the compared groups (p=0.99). Up to 50% of the analysed patients presented very high cardiovascular risk prior stroke. Only 8.7% (13/150 patients) were taking high dosage statins with slightly more patients in the active cohort (11% vs 7.4%, p=0.55). The correlation analysis revealed that previous statin use didn't significantly increase the rate of HT (OR=1.62, 95% CI: 0.43-6.13, p=0.46), didn't influence the discharge mRS score (OR=0.37, 95% CI: 0.08-2.67, p=0.25), and the follow-up mRS: OR=0.46, 95% CI: 0.1-2.41, p=0.32.
Conclusion: In our study the previous statin use didn't increase the risk for HT, neither influenced the discharge or follow-up neurological functional status.
Disclosure: Nothing to disclose.

EPO-040

Stroke due to infective endocarditis treated with mechanical thrombectomy: Case Report and Literature Review.

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Background and aims: Acute ischemic stroke (AIS) due to large vessel occlusion (LVO) is a common complication of infective endocarditis. Intravenous thrombolysis is contraindicated in these patients due to risk of hemorrhagic complications. However, mechanical thrombectomy (MT) may be an effective treatment in these patients, but there is limited data on it's safety in infective endocarditis.
Methods: A case of AIS patient from infective endocarditis treated with MT was reported and literature review was performed.
Results: A 41- year-old man with infective endocarditis who developed AIS due to RICA occlusion was admitted to the comprehensive stroke center. MT was performed with successful recanalization (TICI 2B). Control CT performed after 24h revealed no hemorrhagic transformation. After 6 days from onset neurological deterioration was observed. Control CT with angiography revealed intracranial hemorrhage due to raptured mycotic aneurysm of MCA (aneurysm was not observed on the baseline cerebral arteriography). Patient underwent successful endovascular embolization. Although the patient received immediate treatment he died. 47 similar cases were identified from 16 articles. 11 patients developed hemorrhagic complications (23%). Depending on different studies functional independence (mRS 0-2) after stroke occur in 50-57% of patients.
Conclusion: MT appears to be safe and effective treatment option in patients with infective endocarditis-related AIS due to LVO, but further validation of this finding in large cohort studies is warranted.
Disclosure: The authors declare no conflict of interest.

EPO-041

Uncovering the Hallmarks of Infective Endocarditis in Retrieved Cerebral Thrombi from Acute Ischemic Stroke Patients

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Background and aims: Infective endocarditis (IE) is a major cause of ischemic stroke, and early diagnosis is crucial. The analysis of cerebral thrombi retrieved during endovascular thrombectomy in patients with large vessel occlusion acute ischemic stroke (LVO-AIS) and suspected IE may provide a diagnostic tool. The aim of this study was to identify hallmarks in the thrombus composition that could diagnose IE.
Methods: The study analyzed cerebral thrombi from patients with LVO-AIS and definite IE (n=8), cardioembolic stroke patients with concomitant acute infections (n=9), and cardioembolic stroke patients without infections (n=18). Thrombus culture, PCR, and histology were used to assess microorganisms and structural and immune components.
Results: Thrombus culture was positive in 1/2 IE thrombi, PCR and sequencing detected bacteria in 4/4 IE thrombi, and bacteria were found in 7/8 IE thrombi on histology. One IE sample displayed fungal hyphae, but no microorganisms were found in the controls. IE thrombi had lower red blood cell counts (4.8% vs. 55.5%) and macrophage counts (45.5 vs. 208.7 cells/mm2) compared to controls. No differences were found in fibrin, platelets, T- and B-lymphocytes, or neutrophils. However, IE thrombi had higher prevalence of neutrophil extracellular traps with cell-filopodia-dominant morphology.
Conclusion: The analysis of cerebral thrombi represents a useful adjunctive tool in diagnosing stroke with suspected IE.
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 1

EPO-042

Treatments, Healthcare Utilization and Costs in Newly Diagnosed and Pre-existing Myasthenia Gravis Patients in Sweden

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disorder characterized by muscle weakness and fatigue. This study aims to evaluate treatment use, healthcare resource utilization and costs in patients with newly diagnosed (ND) vs pre-existing (PE) MG in Sweden.
Methods: Data were linked from four Swedish nationwide population-based registries. Adults with ≥ 2 primary diagnosis of MG (ICD-10-SE: G70.0) in inpatient or outpatient specialist visits (≥ 12 months apart within 24 months, ≥ 1 MG diagnosis recorded by a neurologist) during 1/1/2010-12/31/2017; had a pharmacological treatment for MG were selected. Index date was date of first primary MG diagnosis. Patients were categorized into ND vs PE groups based on whether they had a MG diagnosis before index date (back until 2001).
Results: A total of 1,275 patients were included, of which 554 patients were ND MG. Mean (±SD) age was 61.3 (±17.4) years; 52.3% were female. During 12-month post-index period, 5.6% of patients had thymectomy and 0.7% used intubation/mechanical ventilation; ND MG had higher all-cause (70.9% vs 35.8%, p<0.01) and MG-related (62.5% vs 18.4%, p<0.01) hospitalization rates; experienced 11 more hospitalization days (p<0.01); incurred €7302 (p<0.01) higher total all-cause costs, with an incremental difference of €6275 derived from inpatient costs; incurred €6188 (p<0.01) higher total MG-related costs, of which 84% was attributable to inpatient costs.
Conclusion: MG patients incurred substantially higher economic burden in the first year compared to later years. Future research should aim to better understand potential factors (e.g., delayed diagnosis and/or treatment) associated with the increased burden.
Disclosure: Alberto E. Batista, Qian Cai, Peter Kunovszki, Qiaoyi Zhang, and Kristin Heerlein are employees of Janssen Pharmaceuticals and may hold stock in Johnson & Johnson. Jakob Börsum and Gabriel Isheden are employees of SDS Life Science.

EPO-043

Immune-mediated necrotizing myopathies: clinical-serological features of a large Italian cohort of patients

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Background and aims: Immune-mediated necrotizing myopathies (IMNMs) represent a heterogeneous group of muscle disorders recently identified within the spectrum of idiopathic inflammatory myopathies (IIMs) by distinctive clinical, pathological, serological, and therapeutic features. Currently, three different IMNM entities have been defined: 1) anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) myopathy; 2) anti-signal recognition particle (SRP) myopathy; 3) antibody negative IMNM. An accurate diagnosis of IMNMs is relevant for prognostic purposes and to provide the best chance of treatment for patient subtypes and prevent long-term disability. We aimed to investigate clinical and histological features of different serological subgroups within an Italian cohort of IMNM patients.
Methods: We included 116 patients diagnosed with IMNM in 12 neuromuscular referral centers in Italy, relying on the 2017 European Neuromuscular Centre criteria.
Results: The study population was composed by 51 males and 65 females, with an overlapping median age at disease onset equal to 65 years old for men and 64 for women. Thirty-nine patients (33,6%) were positive for HMGCR autoantibodies (Abs), of whom 26 had a history of statin exposure (11 males, 15 females). Among anti-HMGCR Ab–positive IMNM patients naïve to statin therapy, females were more represented (61,5%). Furthermore, 33 patients (28,4%) had anti-signal recognition particle (SRP) Abs, 24 patients (20,7%) resulted seronegative, and 20 patients (17,2%) did not have a complete Ab assessment. Muscle weakness distribution at onset, myopathological features, clinical outcome after therapy, and therapeutic regimen data together with extramuscular manifestations according to serological phenotype have been reported.

Conclusion: This study provides new insights about IMNM characteristics in a large Italian cohort.
Disclosure: SB received honoraria for advisory board activities, and compensation for travel and congress participation from Sanofi Genzyme, Biogen and Roche.

EPO-044

Anxiety and depression in generalised myasthenia gravis in Europe, Middle East and Africa: A systematic review

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune disease characterised by muscle weakness and fatigue. Progression of these symptoms has a negative impact on quality of life. A systematic literature review was conducted to determine the extent of anxiety and depression in patients with generalised MG (gMG).
Methods: Electronic database searches (conducted March 2022), supplemented by interrogation of grey literature were conducted to identify studies reporting depression and/or anxiety patient reported outcomes in patients with gMG in Europe, Middle East and Africa.
Results: Of the 13 eligible studies, eight reported comparative data for anxiety using five scales and 12 reported depression using seven scales (Table 1). Where reported, data indicate that anxiety (n=3 studies) and depression (n=5) was statistically significantly worse in patients with gMG versus controls. However, while anxiety was significantly worse in gMG versus ocular MG (oMG) (n=2), no consistent difference was reported for depression (n=4). Two further studies reported a higher proportion of clinically relevant anxiety and depression in patients with gMG versus oMG; a benefit of pharmacological remission in MG was also observed (Figure 1). Finally, in patients with gMG, stage of disease (n=2) and Patient Acceptable Symptom State status (n=1) were associated with the severity of anxiety and depression whilst antibody status was not.
Conclusion: Although statistically significant differences in the extent of anxiety and depression are reported in patients with gMG compared with relevant populations and subgroups, these findings need to be confirmed in large cohorts administering consistent, validated questionnaires.

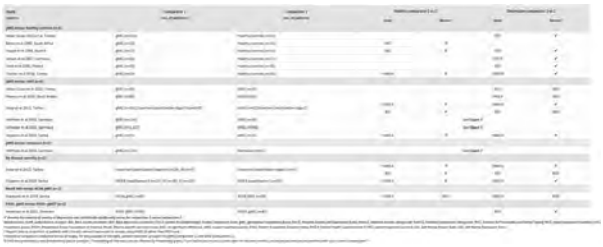

Table 1: Studies reporting anxiety and depression patient reported outcome data in patients with gMG against relevant comparators or within gMG subgroups

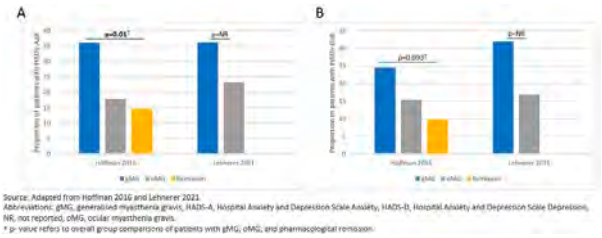

Figure 1: Proportion of patients with clinically relevant anxiety (Panel A) and depression (Panel B) by disease stage

Disclosure: This study was funded by Janssen-Cilag EMEA.

EPO-045

Matrin-3 autosomal dominant distal myopathy in Portuguese patients

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Background and aims: The nuclear matrix protein matrin-3 (MATR3) autosomal dominant distal myopathy, most commonly caused by a Ser85Cys (S85C) missense mutation, determines a heterogenous phenotype.
Methods: We present three Portuguese patients diagnosed with p.Ser85Cys MATR3-related myopathy, diagnosed by genetic assessment, using a specific gene panel dedicated to "distal myopathies".
Results: Patient no. 1 is a 57-year-old male presenting with lower leg weakness, followed by upper limb distal force loss for fine motricity gestures. Neurological examination revealed important muscle atrophy of the distal limbs and symmetrical motor deficit. The second patient, the brother of the aforementioned subject, is a 54-year-old male with similar symptoms, associated with dysphagia and dysphonia. Patient no 3 is a 58-year-old female, unrelated to previous patients, presenting with distal weakness in the upper limbs and severe Achillean contractures. All the subjects were investigated by needle electromyography and

whole-body MRI, which revealed a fatty infiltration pattern, predominantly affecting the gastrocnemius, soleus, and tibialis anterior muscles. Muscle biopsy was performed solely for patient no 1 and revealed rimmed vacuoles, consistent with previous reports. The gene analysis found the same mutation in all three cases: c.254C>G, p.Ser85Cys in the MATR3 gene.

Conclusion: Despite being a rare myopathy, with only few families reported, MATR3 gene mutations should be considered in patients with distal myopathy and rimmed vacuoles on muscle biopsy. To our knowledge, this is the first report of this phenotype in the Portuguese population.

Disclosure: Nothing to disclose.

EPO-046

Higher Need for Medical Resources in Moderate-To-Severe MG Patients: A Comparison With The General Population

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Background and aims: Myasthenia Gravis (MG) patients suffer from muscular fatigue affecting their vision, swallowing, speech, mobility, dexterity and breathing. This analysis compared the medical resource utilization (MRU) of moderate-to-severe MG (msMG) patients with the general population.

Methods: MyRealWorld-MG is an observational study conducted in the US, UK, Canada, France, Italy, Germany, Spain, and Japan among adult MG patients. Patients entered personal and disease characteristics via a smartphone application, and provided data on MRU. All patients with a self-assessed MG-Activities of Daily Living (MG-ADL) score >6 were considered as msMG. POPUP is an observational study collecting comparable data among members of the general public and was conducted in similar countries. National samples were representative of age, gender, education and region.

Results: Four times more msMG patients (N=431) took sick leave during the past month compared to POPUP (N=9000) (43.5% versus 10.2%); but the duration of sick leave did not differ (Table 1). The hospitalization rate was eighteen times higher among msMG patients (rate=0.158/month versus 0.009/month in POPUP) with three times longer length-of-stays (10.0 versus 3.4 days). Furthermore, an eleven-fold increase in ER visits (0.151 vs. 0.013/month) and a four-fold increase in specialist visits (0.811 vs. 0.184/month) were observed for msMG compared to POPUP. msMG patients had double the number of GP and physiotherapy visits per month (0.392 and 0.172 for msMG versus 0.211 and 0.092 in POPUP).

	General Population	Moderate & Severe MG patients	Relative Rate
Sick leave			
% Did take time off work / studies in the past month	**10.9%**	**43.5%**	**4.0**
Average number of days (std, range):	12.4, 11.5 (0 - 31)	14.8, 12 (1 - 31)	1.2
Use of health care services in the past month			
Had a hospitalization	0.009	0.158	18.0
Length of stay	3.4	10.0	3.0
Number of ER visits	0.013	0.151	11.6
Number of Hospital outpatient visit	0.064	0.192	3.0
Number of specialist visit	0.184	0.811	4.4
Number of GP visits	0.211	0.392	1.9
Number of Physiotherapist visit or visit to a rehabilitation cent	0.092	0.172	1.9
Number of nurse / healthcare worker visit	0.132	0.131	1.0

Table 1. Medical Resource Utilization of moderate-to-severe MG patients compared to the general population

Conclusion: Suffering from msMG was associated with a considerable impact on MRU compared to the general population, likely resulting in substantially higher health care costs.

Disclosure: EC has received public speaking honoraria and compensation for advisory boards and/or consultations fees from Argenx, UCB, Alexion and Janssen. RM has received speaking honoraria from Biomarin, Alexion and UCB, served on advisory boards for Alexion, argenx BV and UCB and received support for congress participation from Merck, Teva and Biogen FS has received public speaking honoraria from Almirall, Biogen, Mylan, Novartis, Roche, Sanofi and Teva; and served on advisory boards for Almirall, argenx BV, Avexis, Biogen, Forward Pharma, Lexeo, Merk, Novartis, Novatek, Pomona, Roche, Sanofi, and Takeda. SP is an employee of argenx BV, the sponsor of the study SD, NT and MFJ have been commissioned by argenx BV and received honoraria to design the study, analyze data and write the abstract.

EPO-047

Fatigue among generalised myasthenia gravis: real-world data from physicians and patients across 5 European countries

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Background and aims: Generalised myasthenia gravis (gMG) is a rare, chronic condition causing generalised fatigue and muscular weakness. Generalised fatigue is hard to manage, often manifesting with other symptoms. There are no objective ways to measure generalised fatigue, making the patient perspective important in understanding fatigue-related disease burden.

Methods: Data were drawn from an Adelphi Disease Specific Programme™, a point-in-time survey of physicians and MG patients in France, Germany, Italy, Spain, and the UK, between March-September 2020. Physicians reported patient demographics and symptoms from a pre-selected list. Patients separately reported their current symptoms.

Descriptive analyses were run alongside bivariate comparisons.
Results: Overall, 128 physicians reported on 554 patients with gMG. Mean age was 53.8 (Standard Deviation; SD±15.42) and 51.4% were female. Physicians reported generalised fatigue for 65.3% of patients, significantly more were female than male (55.0%, p<0.05). A higher overall number of gMG symptoms were reported in fatigued patients (mean: 7.2, SD±3.83, p<0.05) than those non-fatigued (mean: 4.2, SD±2.70). A larger proportion of fatigued patients were reported in Myasthenia Gravis Foundation of America classifications III and IV (38.1%, p<0.05) than non-fatigued patients (27.1%). Of 181 self-reporting patients, 139 (76.8%) reported fatigue. Of these 139 patients, 15.1% were not reported with fatigue, and 2.2% were reported asymptomatic, by their physicians.
Conclusion: Fatigue in gMG patients was reported in a significant number of patients, often correlated with markers of greater disease severity. Lower physician-reported, than patient-reported, fatigue may indicate a higher level of attention to fatigue is needed to understand the burden of fatigue on gMG patients.
Disclosure: This project has been funded by Janssen-Cilag EMEA.

EPO-048

Early-onset generalised myasthenia gravis in women aged 18-50: results from a real-world study in 5 European countries

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Background and aims: Generalised myasthenia gravis (gMG) is a rare, chronic condition that can present in women aged 18-50. There is a need to understand the clinical profile of early onset female (EOF) gMG patients to ensure optimal treatment outcomes.
Methods: Data were drawn from the Adelphi Myasthenia Gravis Disease Specific Programme™, a survey of gMG-treating physicians conducted in France, Germany, Italy, Spain and the United Kingdom, from March-September 2020. Physicians reported patient demographics, clinical characteristics, and treatment history including surgery. EOF was defined as females aged 18-50 at survey. Descriptive analyses were run alongside bivariate comparisons.
Results: 128 Physicians provided data for 554 gMG patients. Patients had a mean [standard deviation] age of 53.8[15.4], 51.4% were female and had been diagnosed for 48.2[63.6] months on average. Of those, 147 (26.5%) were EOF patients. EOF patients were diagnosed significantly more recently than non-EOF patients (mean [SD], 35.9[42.4] vs 52.7[69.3] months, p<0.05). 29.9% of EOF and 35.9% of non-EOF patients were in Myasthenia Gravis Foundation of America classification III or IV (p=0.22). Among EOF patients, 27.2% underwent thymectomy versus 22.9% of non-EOF patients (p=0.05). EOF patients had a mean [SD] of 1.1[0.7] myasthenic crises and 0.8[0.8] hospitalizations in the last 12 months compared to 0.9[0.7], p=0.23 and 0.6[0.7], p=0.13 in non-EOF patients, respectively.
Conclusion: The study shows that although EOF patients are earlier in their disease journey, the number of thymectomies, myasthenic crises and hospitalizations trend higher in EOF patients than in the general gMG population, potentially indicating that the unmet treatment needs of EOF patients.
Disclosure: This project has been funded by Janssen-Cilag EMEA.

EPO-049

Myotonic dystrophy type II unmasked by immune checkpoint inhibitor

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Background and aims: Although cancer immunotherapy with immune checkpoint inhibitors (ICIs) has been a milestone in cancer treatment, their increasing use has resulted in a growing number of neuromuscular adverse events, most of them immune-related (irAEs).
Methods: A 63-year-old woman, with colorectal cancer treated with pembrolizumab, presented with a 9-month history of progressive proximal lower limb weakness and minor camptocormia. Symptoms appeared 1 month after initiation of immunotherapy and progressed gradually leading to a significant motor impairment. She had marked difficulty climbing stairs and rising from sitting position. She also reported a chronic minor difficulty rising from low chairs, a symptom that was also reported by the patient's sister and father.
Results: Nerve conduction studies and 3Hz repetitive nerve stimulation were normal while electromyography revealed diffuse waning myotonic discharges and a chronic myopathic pattern. Genetic testing demonstrated a pathogenic mutation in the CNPB gene, confirming the diagnosis of type 2 myotonic dystrophy.
Conclusion: Neuromuscular toxicity induced by ICIs treatment is rare but potentially underreported. The most commonly reported irAEs are myositis, myasthenia gravis and neuropathy with several cases resulting in a fatal outcome. Due to the susceptibility of the skeletal muscle,

myotoxic drugs may unmask a primary asymptomatic or oligosymptomatic hereditary myopathy. To the best of our knowledge there are three other reported cases of hereditary neuromuscular diseases unmasked during treatment with ICIs. Patients under treatment with ICIs should be carefully evaluated for neuromuscular side-effects and the possibility of a concomitant hereditary myopathy, should also be considered.

Disclosure: I have no financial interests or relationships to disclose.

EPO-050

IgG and anti-AChR Antibody Reduction Explain Nipocalimab Effect on MG-ADL Score Improvement in Patients with gMG

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Background and aims: Nipocalimab is an anti-FcRn monoclonal antibody that lowers IgG, including anti-AChR antibodies (Ab). This analysis was conducted to quantify the relationship between IgG, anti-AChR Ab and the clinical efficacy endpoint (MG-ADL) to understand if IgG or anti-AChR Ab reduction could account for nipocalimab effect on MG-ADL.

Methods: Data from 68 patients with gMG from a Ph2 study (NCT03772587) were utilized for statistical and population modeling and simulation analyses to quantify the relationship between IgG, anti-AChR Ab and MG-ADL reduction

Results: IgG and anti-AChR Ab reduction expressed as percent change from baseline were highly correlated (R2=0.75), and correlated similarly to MG-ADL improvement. IgG was selected to quantify the relationship to MG-ADL to allow inclusion of all patients (AChR+ and AChR-). Placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL) was proportional to IgG reduction. A 50% IgG reduction was estimated to lead to a median ΔΔMG-ADL reduction of 1.07 points. Subjects with higher individual baseline MG-ADL exhibited higher ΔΔMG-ADL reductions (eg a 2-fold baseline increase resulted in a 1.9-fold higher reduction). Simulations showed a that a large proportion (>80%) of the Nipocalimab-induced MG-ADL improvement could be explained by IgG reduction.

Conclusion: Serum IgG reduction explains most of the ΔΔMG-ADL change following nipocalimab treatment. Thus, IgG reduction may qualify as a biomarker for efficacy if confirmed by data from the ongoing Ph3 study. The quantitative relationship between IgG, anti-AChR Ab and MG-ADL is critical for model-informed decisions on nipocalimab development.

Disclosure: WSD is an employee of Human Predictions, LLC and a consultant for Johnson & Johnson. Other authors are employees or contractors of Janssen Pharmaceuticals any may own stock or stock options in Johnson & Johnson.

EPO-051

Cancer frequency in muscle-specific tyrosine kinase (MuSK) myasthenia gravis

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Background and aims: Cancer frequency in myasthenia gravis with anti-MuSK antibodies (MuSK-MG) has not yet been explored. The link between neurological autoimmunity and cancer is bidirectional: autoimmune diseases may increase cancer risk through long-term immunosuppression, conversely antitumor immune response may result in autoimmunity development.

Methods: In this retrospective study, we reviewed records of patients with confirmed diagnosis of MuSK-MG who had been followed for at least 1 year from disease onset in our Center. We recorded associated cancers and timing of oncological diagnosis in relation to MG onset, type and duration of immunosuppressive therapy.

Results: 94 patients were recruited, 21 males and 73 females. The median age at MG onset was 51 years [19-75]. Immunosuppressive therapy was performed in 90/94 (95.7%) cases with corticosteroids and/or immunosuppressants; 16 patients were treated with Rituximab. Fifteen cancers occurred in 13/94 patients (13.8%). Median age at cancer onset was 60 years [18-79]. Tumor detection preceded MG onset (median: 11 years, [3-17]) in 5 patients, it was concomitant in 2 and it followed MG diagnosis in 8 cases (median time from MG onset: 11.5 years, [1-32]). Six patients were on long-term immunosuppression at cancer diagnosis. Blood malignancies were the most common (N=5), all detected before MG onset. In addition, we found cancer in breast (N=3), womb (N=2), digestive organs (N=2), lung (N=1), vocal cords (N=1), skin (N=1).

Conclusion: Onco-hematological diseases, particularly mediastinal lymphoma (N=3/5, 60%), were the most common malignancy detected in MuSK-MG patients. We did not find a higher frequency of cancer occurrence in patients on long-term immunosuppression.

Disclosure: The authors declare no conflicts of interest.

EPO-052

Thymectomy in Thymomatous and Nonthymomatous Myasthenia Gravis: a 10-year follow-up cohort

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Background and aims: Thymectomy remains a mainstay of treatment in Thymomatous (T) and Nonthymomatous (nT) Myasthenia Gravis (MG). However, there is little research regarding long-term follow-up. We aim to assess the impact of surgery on the long-term outcome of patients with MG at our centre.
Methods: Retrospective analysis of MG patients submitted to thymectomy between 2007 and 2017 at the thoracic surgery department of our tertiary centre. Clinical assessment was performed according to the MG Foundation of America (MGFA) Clinical Classification (cMGFA). The follow-up was categorized according to the MGFA Post-intervention Status (MGFA-PIS) and cMGFA.
Results: Thirty-seven patients underwent extended thymectomy. Median age at diagnosis was 46.7±19.2 years. Most patients (83.8%) had anti-acetylcholine receptor antibodies and 81.1% had generalized forms of MG. Many patients (67.6%) had surgery less than 12 months after the clinical diagnosis. TMG was present in 19 (51.4%) patients. Compared to nTMG, these patients were older (54.1±17.9 vs 40.2±19.4 years) and most were men (52.9% vs 16.7%). We obtained a good outcome in most patients in the first (81.1%), second (83.3%), fifth (84.8%) and tenth (83.3%) year of follow-up. There was a shift towards better prognosis categories in the good outcome group: 11.1% complete stable remission and 61.1% minimal manifestation status in the tenth year. A shorter time to surgery (< 12 months) correlated with better outcomes.
Conclusion: Thymectomy led to a sustained clinical improvement in our cohort, allowing for a reduced need for medication. A shorter time to surgery seems to have a positive influence on long-term prognosis.
Disclosure: The authors report no disclosures relevant to this presentation.

EPO-053

Emery-Dreifuss Muscular Dystrophy type 1 (EDMD1): a phenotype characterization from a large Italian pedigree

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Background and aims: Emerin-related Emery-Dreifuss Muscular Dystrophy type 1 (EDMD1) represents an X-linked form of symmetrical humeroperoneal myopathy with almost invariable cardiac arrhythmias.
Methods: A cross-sectional evaluation of past medical history, and motor, cardiac and ventilatory assessments in 9 related individuals (5 males and 4 females) with genetically confirmed emerinopathy (exon 2 c.104_106del – p. Lys36del) was performed.
Results: Age of patients at last clinical evaluation ranged 19-82 years (57.4 + 20.1). Out of 5 males, muscular symptoms generally manifested within adolescence with scapular + axial weakness (asymmetrical winged blades, rigid spine, scoliosis – 2/9) and contractures (neck extensors, brachial biceps, finger flexors 3/9). Gardner-Medwin-Walton (GMW) graded 1 in 4/5, confirming overall favourable motor performances. From a cardiac angle, symptoms presented at 50.3 + 10.8 years in the whole cohort, with grade 1-2 atrioventricular block in 3/9, atrial fibrillation in 1/9 and ventricular extrasystoles in 2/9; 4/9 necessitated a pacemaker/implantable cardioverter. A non-ST elevation myocardial infarction (NSTEMI) occurred in one male patient at 78. Last echocardiography detected a mean ejection fraction of 58.7 + 8.1%. Spirometry, when available, revealed a mean forced vital capacity (FVC) of 101.5 + 10.6% and forced expiratory volume in the first second (FEV1) of 107 + 17%; 2/9 used nocturnal non-invasive ventilation from the 6th decade onwards.
Conclusion: Besides common neuromuscular impairment and arrhythmias, our pedigree emphasizes further and less typical complications in EDMD1, such as cardiac ischemia and sleep hypoventilation, suggesting the need for a multidisciplinary monitoring to eventually broaden the clinical spectrum.
Disclosure: Nothing to disclose.

EPO-054

Efgartigimod Demonstrates Consistent Magnitude of Response Across Subgroups of Patients With gMG

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Background and aims: Treatment with efgartigimod, a human IgG1 antibody Fc-fragment that blocks neonatal Fc receptor, resulted in clinically meaningful improvements in patients with generalised myasthenia gravis (gMG) in the ADAPT study. Efgartigimod was well tolerated and common adverse events (mostly mild or moderate) were headache, nasopharyngitis, nausea, diarrhoea, and upper respiratory/urinary tract infection. Here we assess efgartigimod efficacy in subgroups of patients with gMG.

Methods: Intravenous efgartigimod 10 mg/kg or placebo was administered in cycles of 4 weekly infusions, with subsequent cycles initiated based on clinical evaluation. Efficacy was assessed using MG-ADL and QMG scores. Here we report mean change from baseline and responder status (defined as ≥2-point [MG-ADL] and ≥3-point [QMG] improvement for ≥4 consecutive weeks, with first improvement ≤1 week after last infusion) for cycle 1 in AChR-Ab+ patients grouped according to clinical characteristics, including time since diagnosis and concomitant medications.

Results: A greater proportion of efgartigimod-treated patients were MG-ADL responders compared with those receiving placebo regardless of duration of disease (Figure 1A). Likewise, when stratified by concomitant medication use, a greater proportion of efgartigimod-treated patients were MG-ADL responders compared with those taking placebo (Figure 2A). Proportion of QMG responders was similar and consistent across subgroups (Figures 1B and 2B). Mean improvements in MG-ADL/QMG scores were also greater with efgartigimod across all subgroups (Table 1).

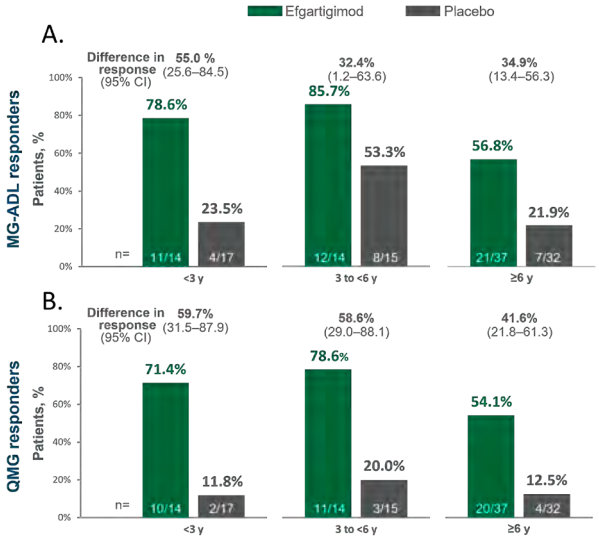

Figure 1: Proportion of MG-ADL (A) and QMG (B) responders by disease duration in AChR-Ab+ patients in cycle 1.

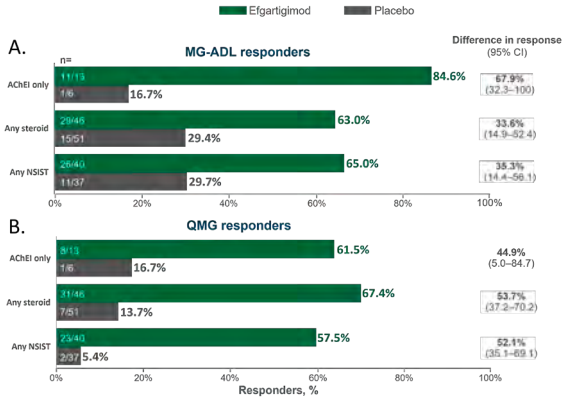

Figure 2: Proportion of MG-ADL (A) and QMG (B) responders by concomitant therapies in AChR-Ab+ patients in cycle 1.

Subgroup	Efgartigimod		Placebo	
Time since diagnosis	n	mean (SD)	n	mean (SD)
MG-ADL				
<3 y	13	-5.1 (2.63)	14	-2.0 (1.84)
≥6 y	36	-4.4 (3.47)	31	-1.4 (2.13)
QMG				
<3 y	13	-7.5 (5.41)	13	-0.6 (3.69)
≥6 y	36	-6.0 (5.39)	30	-0.9 (2.47)
Concomitant medications				
MG-ADL				
AChEI only	12	-7.4 (4.48)	5	-2.0 (1.41)
Any steroid	44	-6.3 (5.41)	47	-0.8 (3.01)
Any NSIST	39	-5.8 (5.39)	33	-0.4 (2.81)
QMG				
AChEI only	13	-5.5 (3.04)	5	-2.2 (2.17)
Any steroid	44	-4.5 (3.29)	48	-1.6 (2.28)
Any NSIST	39	-4.4 (3.11)	36	-1.5 (2.41)

Table 1: Change from baseline in MG-ADL and QMG scores by subgroup in AChR-Ab+ patients (cycle 1, week 4).

Conclusion: The proportion of responders and magnitude of response for patients treated with efgartigimod was consistent regardless of above defined subgroups, providing support for efgartigimod efficacy across a broad population of patients with gMG.
Disclosure: Multiple relationships financial and non-financial nature for authors SH, AM, SA, JLdB, JV, RK, EB, KU, NG, YL, SP, JFH Jr. and FS stated at point of presentation.

EPO-055

Gender-specific analysis of efgartigimod efficacy in patients with gMG: Subanalysis of the randomised phase3 ADAPT trial

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Background and aims: Generalised myasthenia gravis (gMG) is a rare, chronic autoimmune disease leading to potentially life-threatening muscular weakness. Efgartigimod is a human IgG1 antibody Fc-fragment that blocks the neonatal Fc receptor, leading to reduced IgG autoantibody levels. The ADAPT trial demonstrated that efgartigimod treatment resulted in clinically meaningful improvement (CMI) in gMG-specific outcome measures in the overall study population. Considering the Sex and Gender Equity in Research (SAGER) guidelines, this analysis aimed to identify potential gender-specific differences in outcomes between efgartigimod and placebo.
Methods: ADAPT (NCT03669588), a randomised, phase 3 trial included gMG patients (MG-ADL >=5: >=50% non-ocular symptoms) regardless of autoantibody-status. Efgartigimod (10 mg/kg) or matching placebo was administered as four infusions per cycle (one infusion per week), repeated as needed depending on clinical response. The primary endpoint was percentage of AChR-Ab+ patients who were MG-ADL responders (>=2 points improvement sustained for >=4 weeks) in the first treatment cycle. Secondary endpoints included Quantitative Myasthenia Gravis (QMG) responders (>=3 point QMG improvement for >=4 consecutive weeks). In this analysis, only AChR-Ab+ patients receiving a stable dose of >=1 gMG treatment were included. The outcomes were analysed by Zelen's Exact test for homogeneous odds ratio between sex subgroups.
Results: Overall, 129 patients were analysed, 86 (66.7%) were female. Differences are noted between females and males in age, disease duration, BMI and thymectomy (Table 1). There were no gender-specific treatment differences across gMG-specific outcome measures (Table 2).

Baseline characteristic	Female (n=86)	Male (n=43)
Mean age, years (SD)	42.9 (14.27)	54.8 (14.52)
Mean no. of years since diagnosis (SD)	9.95 (8.40)	8.02 (7.74)
Mean BMI, kg/m^2 (SD)	26.28 (6.13)	31.77 (7.57)
Thymectomy performed for gMG, n (%)	56 (65.1)	19 (44.2)
MGFA class at screening, n (%)		
2-2A	20 (23.3)	8 (18.6)
2-2B	15 (17.4)	10 (23.3)
3-3A	24 (27.9)	10 (23.3)
3-3B	25 (29.1)	12 (27.9)
4-4A	2 (2.3)	2 (4.7)
4-4B	0	1 (2.3)
Mean MG-ADL score at baseline (SD)	8.8 (2.19)	8.8 (2.80)
Mean QMG score at baseline (SD)	16.3 (4.83)	14.3 (4.44)

Table 1. Demographics and baseline disease characteristics in the AChR-Ab+ population, by gender

	Overall AChR-Ab+ population			Female (n=86)		Male (n=43)		
Endpoint, n (%)	Efgartigimod (n=65)	Placebo (n=64)	Between-treatment analysis; OR (95% CI)*a	Efgartigimod (n=46)	Placebo (n=40)	Efgartigimod (n=19)	Placebo (n=24)	Between-sex subgroup analysis*b
MG-ADL responders	44 (67.7)	19 (29.7)	4.99 (2.21–11.53); p<0.0001	31 (67.4)	13 (32.5)	13 (68.4)	6 (25.0)	p=0.7014
QMG responders	41 (63.1)	9 (14.1)	10.84 (4.18–31.20) p<0.0001	28 (56.5)	7 (17.5)	13 (76.9)	2 (8.3)	p=0.1995

a. Treatment effect was tested using exact conditional logistic regression.
b. Homogeneous odds ratios were tested using Zelen's Exact test.

Table 2. MG-ADL and QMG responders during the first cycle, in the AChR-Ab+, modified intent-to-treat population and by gender

Conclusion: These analyses suggest efgartigimod results in consistent improvement across gMG-specific measures, regardless of patient gender.
Disclosure: S Hoffmann has received speaker´s honoraria from Alexion, argenx and UCB and honoraria for attendance at advisory boards from Alexion and argenx; S Zhao, F Callewaert and S Schoppe are employees of argenx, the study sponsor.

EPO-056

Retrospective Study of Select Adverse Events of Special Interest Associated With Corticosteroid Use in Myasthenia Gravis

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Background and aims: Myasthenia gravis (MG) is an autoantibody-driven disease. Oral corticosteroids (OCS) remain the initial medication for patients requiring immunotherapy despite known toxicities. The objective of the study was to assess the risk of select adverse events of special interest (AESIs) during real-world OCS use in MG patients.
Methods: US adults with newly diagnosed MG between 01/2015 and 06/2022 were identified from the Optum Clinformatics database. Periods of OCS exposure and non-exposure were defined for each patient. AESIs were identified based on the Glucocorticoid Toxicity Index using ICD codes. Frailty models were fitted to assess risks of recurrent AESIs during OCS-exposed periods compared to non-exposed periods as hazard ratios (HR). OCS dose and concomitant medications were included as time-variating covariates along with time-fixed baseline characteristics.

Results: Among the 3,839 newly diagnosed MG patients identified, 1,781 (46%) were treated with OCS after diagnosis (Table1). The patients had median 1 episode (IQR 1-3) of OCS exposure with median duration of 45 days (IQR 14-142). The crude incidence rate of any AESI was 1.57 (95%CI: 1.5-1.65) per patient-year during OCS exposure and 0.57 (0.56-0.59) during non-exposure (Table2). Adjusted frailty models identified significantly increased hazard of any AESI during OCS exposure for all OCS dosages, low: 2.45 (2.24-2.67), medium: 2.24 (2.03-2.46), high: 2.56 (2.32-2.82). Increased hazards were also observed for each of the AESIs evaluated including cardiac and bone events (Figure1).

Table 1. Myasthenia gravis patient demographic and clinical characteristics. Baseline comorbidities reported in the 1 year prior to index date. Baseline OCS patients were defined as patients who started OCS within 90 days of index date, and non-OCS patients were defined as patients not receiving OCS OR starting OCS after 90 days.

Characteristic	Overall MG N = 3,839	Baseline OCS Use* N = 1,083	No Baseline OCS Use* N = 2,756
Patient Demographics			
Age at Diagnosis (Mean, SD)	68.08 (14.62)	68.27 (13.96)	68.01 (14.87)
Female Sex (n, %)	1,922 (50%)	495 (46%)	1,427 (52%)
Follow-up Time (Years, Mean, SD)	2.06 (1.68)	2.09 (1.67)	2.05 (1.68)
Health Insurance Type (n, %)			
Commercial	1,129 (29%)	308 (28%)	821 (30%)
Medicare	2,710 (71%)	775 (72%)	1,935 (70%)
US Region (n, %)			
Midwest	749 (20%)	223 (21%)	526 (19%)
North	544 (14%)	134 (12%)	410 (15%)
South	1,956 (51%)	527 (49%)	1,429 (52%)
West	590 (15%)	197 (18%)	383 (14%)
Race (n, %)			
Asian	124 (3.4%)	33 (3.2%)	91 (3.4%)
Black	355 (9.7%)	106 (10%)	249 (9.4%)
Hispanic	396 (11%)	114 (11%)	282 (11%)
White	2,802 (76%)	779 (75%)	2,023 (76%)
Comorbidities			
Charlson Comorbidity Score (Mean, SD)	1.73 (2.24)	1.84 (2.33)	1.69 (2.20)

*OCS use includes patients who started OCS within 90 days of index date, and 'No OCS Use' includes patients not receiving OCS OR starting OCS after 90 days.

Table 2. Crude Incidence Rates and Ratios of Adverse Events of Interest. Incident rates reported as event/person-years.

Event	Incidence Rate (No OCS-exposure, 95%CI)	Incidence Rate (OCS-exposure, 95% CI)	IRR (95% CI)
Any Adverse Event	0.57 (0.56 - 0.59)	1.57 (1.50 - 1.65)	2.74 (2.59 - 2.9)
Congestive Heart Failure	0.13 (0.12 - 0.13)	0.33 (0.30 - 0.37)	2.64 (2.33 - 2.98)
Hypertension	0.02 (0.01 - 0.02)	0.02 (0.02 - 0.04)	1.57 (1.01 - 2.37)
Endocrine	0.01 (0.01 - 0.01)	0.05 (0.04 - 0.06)	4.07 (2.86 - 5.75)
Bone	0.05 (0.05 - 0.06)	0.12 (0.10 - 0.14)	2.20 (1.80 - 2.68)
Muscle and Tendon	0.06 (0.05 - 0.06)	0.09 (0.08 - 0.11)	1.70 (1.36 - 2.10)
Eye	0.22 (0.21 - 0.24)	0.45 (0.41 - 0.49)	2.01 (1.82 - 2.23)
Glucose Tolerance	0.24 (0.22 - 0.25)	0.7 (0.66 - 0.76)	2.98 (2.73 - 3.25)
Gastrointestinal	0.02 (0.02 - 0.02)	0.04 (0.03 - 0.05)	1.94 (1.34 - 2.73)
Skin	0.19 (0.18 - 0.20)	0.35 (0.31 - 0.38)	1.87 (1.66 - 2.09)
Neuropsychiatric	0.25 (0.24 - 0.27)	0.55 (0.51 - 0.59)	2.15 (1.96 - 2.36)
Infection	0.11 (0.10 - 0.12)	0.28 (0.25 - 0.31)	2.52 (2.20 - 2.88)
Other	0.12 (0.11 - 0.13)	0.26 (0.24 - 0.3)	2.17 (1.90 - 2.48)

OCS: oral corticosteroid, IRR: incidence rate ratio, CI: confidence interval.

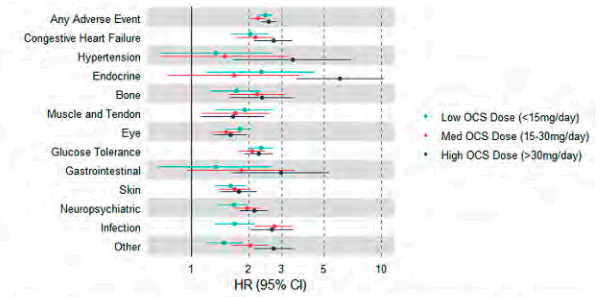

Figure 1. Adjusted frailty model results for hazard ratios of adverse events with OCS-exposure.

Reference group: Non-OCS exposed period.
OCS: oral corticosteroid.
Frailty models adjusted for time-varying OCS exposure (by prednisone equivalent daily dose) and concomitant medication (IVIg, IST, and PLEX) use as well as other fixed covariates (age, sex, race, region, payer, Charlson Comorbidity Index, and OCS use in the 1 year prior to MG diagnosis).

Conclusion: OCS exposure was associated with significantly increased hazard of AESIs in MG patients. Steroid-sparing immunotherapies for the underlying disease are needed in this population.

Disclosure: Sicong Huang, Sindhu Ramchandren, Kristin Heerlein, Hemanth Kanamedala are or were employees of Janssen Pharmaceuticals and may own stock in Johnson & Johnson. Lauren Wilson, Xin Zhao, Amanda Howarth, Carlos Flores are or were employees of Genesis Research.

Cognitive neurology/neuropsychology

EPO-057

Frequency of depressive and anxious symptoms in patients with Subjective Cognitive Complaints

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Background and aims: Subjective Cognitive Complaints (SCC) are frequent in Neurology. They may be defined as the self-perception of cognitive decline without objective deficits in neuropsychological tests. SCC have been associated with a poorer cognitive performance, a higher risk of developing Cognitive Impairment or Dementia as well as with neuropsychiatric symptoms such as depression and anxiety. Depression and anxiety are frequent mental health issues, with a remarkable impact in cognitive function. An increase in prevalence in both of them is estimated during COVID-19 pandemic. The objective is to report the frequency of depression, anxiety symptoms in a population with SCC.
Methods: We selected patients with cognitive complaints and normal neuropsychological tests. Demographic data, depressive and anxious symptoms were collected. Anxious symptoms were assessed with the Beck Anxiety Inventory-(BAI) and depressive symptoms with the Beck Depression Inventory-(BDI-II) and the Geriatric Depression Scale-(GDS-15).
Results: 166 patients were included. Mean Age was 63.13 (SD 12.2) years, Mean Education was 11.25 (SD 3.62) years. The frequency of anxiety symptoms was 44.57% (n=74). Depression symptoms were detected in 33.13% (n=55) of the patients.
Conclusion: Our study showed a significant frequency of anxiety and depression symptoms in patients with SCC. This reminds us how valuable it is to assess these symptoms in standard Neuropsychological Testing, in order to take a comprehensive approach of the patients. Future studies will help to determine dementia-developing predictors.
Disclosure: Nothing to disclose.

EPO-058

Experience and needs on social cognition measures in Italian memory clinics: a joint effort of the signature consortium

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Background and aims: Harmonisation of evidence-based neuropsychological protocols among different countries has become a priority for the benefit of researchers, clinicians and most importantly patients. The international SIGNATURE consortium has been recently established to evaluate the use of socio-cognitive measures in memory clinics and define priorities for their implementation in clinical settings.
Methods: An ad-hoc developed survey was launched through the SIGNATURE mailing list (122 members, 90 institutions, 18 countries) to evaluate state-of-the-art, experience and needs in memory clinics. Italian responses were compared to the international scenario.
Results: 406 (104 Italian) responses were collected. Italian respondents were balanced by professional background and geographic distribution. Both in Italy and abroad, all main cognitive domains are routinely assessed in the standard cognitive battery only in a quote of NCD patients. Comparably to the overall scenario, two thirds of Italian respondents use socio-cognitive measures only in selected cases both for major and minor NCDs. Insufficient time for testing is a major obstacle in Italy, while limited availability of standardised measures emerged overall. Experience and needs did not significantly differ in Northern vs Central-Southern Italy, but we found a trend to assess socio-cognitive abilities more in the North.
Conclusion: In memory clinics, social cognition assessment is usually considered in selected cases and it is expendable in case of lack of time. Despite the geographical inhomogeneity in terms of resources, there is an overall strong need for greater knowledge and availability of socio-cognitive harmonised clinical protocols in clinics.
Disclosure: Nothing to disclose.

EPO-059

Atypical onset of an atypical parkinsonism

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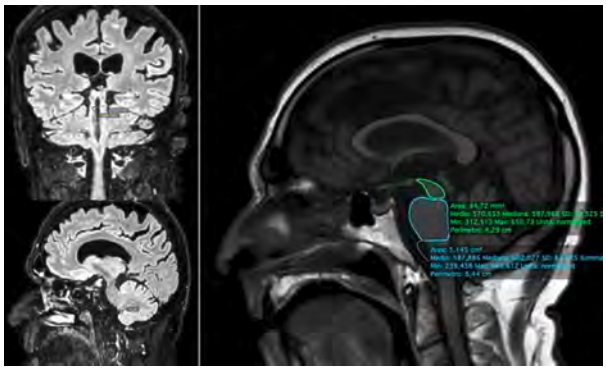
Background and aims: Progressive non-fluent aphasia is a language disorder commonly considered as a form of frontotemporal dementia, but it may also be associated with corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP). A proper differential diagnosis is important to guide treatment strategies and define a correct prognosis. In this setting, neuroimaging can help clinicians to make a more accurate diagnosis. Herein we report a case of a patient with a primary progressive motor speech disorder finally diagnosed as PSP.
Methods: A 63-year-old man with a 10-month history of gradually progressive language disturbance.
Results: Neuropsychological evaluation showed halting speech with sound errors and distortions, alteration of sentence comprehension, normal single-word comprehension and object knowledge. In addition, letter fluency and executive function were impaired, while category fluency was normal. Furthermore, memory deficit and ideomotor apraxia were absent. Neurological examination revealed hypokinetic and spastic dysarthria, up and down gaze palsy, diffuse bradykinesia with reduced right arm swing during walking and upper right limb dystonia. Brain MRI showed mild cortical atrophy and severe midbrain atrophy. Midbrain-to-pons ratio (M/P) was 0,18; Magnetic Resonance Parkinsonism Index (MRPI) was 13,81. Transcranial-ultrasound (TCS) showed absence of substantia nigra hyperechogenicity and third ventricular enlargement.



Brain MRI showed mild cortical atrophy and severe midbrain atrophy. Midbrain-to-pons ratio (M/P) was 0,18 (Cut-off <=0,215); Magnetic Resonance Parkinsonism Index (MRPI) was 13,81 (Cut-off>=13,55).

Transcranial-ultrasound showed absence of substantia nigra hyperechogenicity and third ventricular enlargement (10,5 mm).

Conclusion: Our patient met clinical criteria for diagnosis of "Possible-CBD" but also for "Probable-PSP with predominant frontal presentation" and "Possible-PSP with predominant speech/language disorder". In this case, TCS and quantitative MR planimetric measurements, like M/P ratio and MRPI, lead to a diagnosis of PSP. This case highlighted the essential role of neuroimaging in the differential diagnosis of atypical parkinsonism.
Disclosure: Nothing to disclose.

EPO-060

Accelerated hippocampal atrophy in elderly onset multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) with elderly onset (EO) has been increasingly recognized. Assessing disease-related cognitive and MRI features in elderly patients is extremely challenging, as it is necessary to consider changes due to aging. We aim to identify the distribution of recently defined cognitive phenotype in MS patients with EO and its MRI substrates.
Methods: We enrolled 159 MS patients and 80 healthy controls (HC). All patients underwent neuropsychological evaluation including Rao's brief repeatable battery and Stroop Color Word Test and were classified in cognitive phenotypes (as defined in our previous study: "preserved-cognition", "mild verbal memory/semantic fluency", "mild-multi-domain", "severe-attention/executive", and "severe-multi-domain"). Patients and HC also underwent a 3T MRI examination. Fifty-three MS patients were classified as EO, and remaining ones were equally split in disease duration-(DMS) and age-(AMS) matched groups. We compared prevalence and distribution of cognitive phenotypes across the three groups as well as their MRI features.

Results: Compared to DMS, EOMS patients showed higher frequency of "mild verbal-memory/semantic-fluency" (p=0.02) and lower frequency of "preserved-cognition" (p=0.04). Although not reaching statistical significance a similar trend was also observed when comparing EOMS with AMS patients. Compared to DMS, EOMS patients showed accelerated atrophy of the hippocampus (p=0.05), while no significant differences were observed between AMS and EOMS.
Conclusion: The distribution of cognitive phenotypes showed that EOMS had a prominent involvement of memory and linguistic abilities. These results are in line with the MRI findings of accelerated hippocampal atrophy, thus suggesting that EOMS is likely to affect more severely brain regions susceptible to aging processes.
Disclosure: The Authors report no conflict of interests related to the present manuscript.

EPO-061

Neuropsychiatric symptoms in Idiopathic Brain Calcification

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Background and aims: Idiopathic basal ganglia calcification (IBGC) is a rare neurological disease characterized by the deposition of calcium in the brain, without calcium metabolism abnormalities. Neuropsychiatric symptoms in IBGC are currently poorly defined in literature. The aim of this study is to deepen the knowledge on psychiatric disorders associated with IBGC, providing an accurate description of eleven cases and summarizing information from the review of literature.
Methods: From our clinical database, we selected patients meeting the diagnostic criteria for IBGC and collected demographic, clinical, genetic, and neuroradiological data. We also searched the PubMed database for papers dealing with psychiatric features in IBGC, and the related treatments.
Results: Eight of the eleven patients included in the study reported at least one psychiatric symptom during the course of the disease. The assessment through the HAM-D and HAM-A scale confirmed the presence of mild depression and anxiety as the main psychiatric disturbs associated with IBGC. Data from literature confirmed a significant psychiatric involvement in IBGC. Available case reports mainly concern atypical presentations of IBGC with abrupt onset psychotic symptoms. An in-depth analysis of psychiatric features associated with IBGC is lacking.

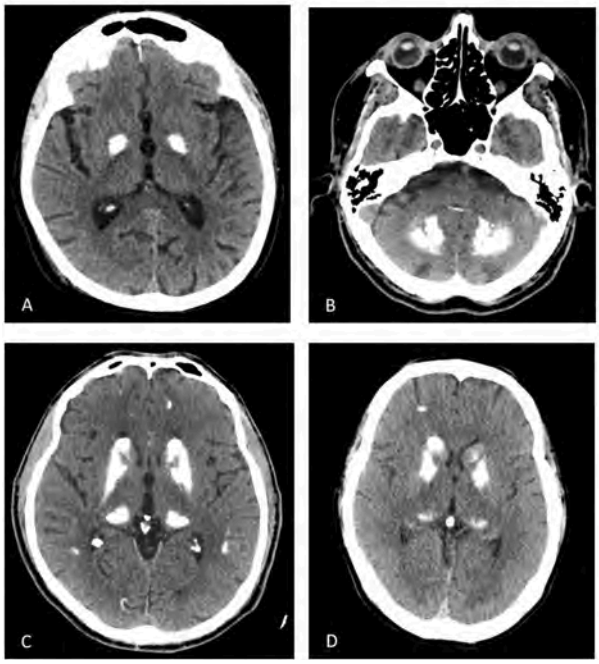

Figure 1. Brain computed tomography scan (CT scan) of PT7 (A), PT8 (B, C), and PT5 (D) showing bilateral symmetrical calcifications in the basal ganglia (A, C, D) and in the cerebellum (B).

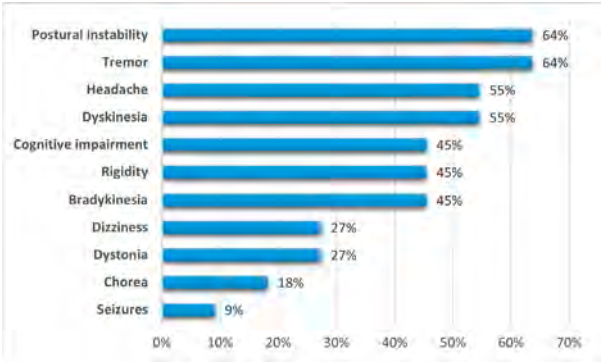

Figure 2. Histogram showing frequency of neurological clinical symptoms by percentage.

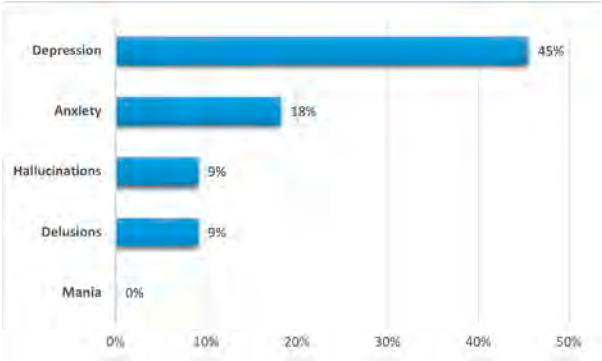

Figure 3. Histogram showing frequency of psychiatric disorders by percentage.

Conclusion: Neuropsychiatric involvement is frequent in IBGC. A neuropsychiatric evaluation is highly recommended in patients with evidence of brain calcifications. Conversely, IBGC should be considered in patients presenting with psychiatric symptoms, especially if movement disorders and neurocognitive impairment are co-existing features.
Disclosure: No conflicts of interest.

EPO-062

Testing the acute cognitive effects of tadalafil: neuropsychological outcomes from the PASTIS trial

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Background and aims: Cerebral small vessel disease (CSVD) is a major cause of cognitive impairment in older people. In a phase-2 randomised clinical trial, we tested the acute effects of a widely-used PDE5 inhibitor, tadalafil, on cognitive performance in older people with CSVD.
Methods: In a double-blinded, placebo-controlled, cross-over trial, participants received tadalafil (20mg) and placebo on two visits ≥7 days apart (randomised to order of treatment). The Montreal Cognitive Assessment (MOCA) was administered at baseline, alongside a measure to estimate optimal intellectual ability, and a battery of neuropsychological tests assessing aspects of attention, information processing speed, working memory and executive function was administered before and after treatment.
Results: Sixty-five participants were recruited and 55 completed the protocol (N=55, age: 66.8 (8.6) years, range 52-87; 15/40 female/male). Median MOCA score at baseline was 26 (IQR: 23, 27], range 15-30. No significant treatment effects were seen in any of the neuropsychological tests. However, there was a trend towards improved performance on forward digit span, a measure of immediate verbal recall considered to index attentional efficiency (treatment effect 0.37, C.I. 0.15, 0.63; P=0.052).
Conclusion: There was no significant acute treatment effect of single dose tadalafil on neuropsychological performance in older people with CSVD. The trend observed on forward digit span indicates that performance on this measure of attentional efficiency may be more malleable than previously thought and provides effect sizes useful for further research.
Disclosure: Dr Isaacs has received a speaker's fee from Biogen and consultancy fees from Roche and Nestle Health Science, all paid to his institution and unrelated to the current work. He has received conference registration and expenses from Roche. Dr Kruuse has received funding from NovoNordisk, Bayer and Bristol-Myers-Squibb, none relevant to the present trial. Dr Hainsworth has received honoraria from Eli Lilly.

EPO-063

Sensitivity of the TMA-93 for diagnosis of early Alzheimer's disease according to age and cognitive reserve

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Background and aims: TMA-93 examines relational binding by images. New norms based on age and cognitive reserve have recently been developed for the test. The aim was to analyze the sensitivity of these new norms for diagnosing early AD.
Methods: Retrospective analysis of a Biobank database associated to the Outpatient Memory Clinic of a tertiary hospital in Southern Spain. Patients' records initially consulted for memory complaints, scored MMSE≥22, and had the TMA-93 and the Cognitive Reserve Questionnarie (CRC) administered, and AD biomarker determination (Amyloid-PET or CSF) done, either positive or negative, were selected. As cutoffs, TMA-93 total scores for the 10-percentile (P10) according to the new norms were considered. Crosstabs were made up for sensitivity analysis: rows, TMA-93 positive (≤ P10) vs. negative (>P10) results; columns, positive vs. negative AD biomarkers.
Results: 188 patients were included [median age 70.5±6.4 years (range 52-84); 47.9% female; 135 (71.8%) positive AD biomarkers, 53 (28.2%) negative AD biomarkers. Tests total scores (median/interquartile range/range) were: MMSE (25/23-27/22-29), CRC (10/7-13/1-23), TMA-93: (21/14-25/0-30). The sensitivity for P10/TMA-93 was

74.1%. False negatives (25.9%) were more frequent if MMSE >24, CRC<10, age>72 and/or total TMA-93 score ≥21.
Conclusion: Sensitivity of 74.1% for diagnosing early AD in a representative but heterogeneous sample of patients referred to a Memory Clinic of a tertiary hospital is a new good result for the TMA-93. False negative are mainly distributed among less cognitively impaired elderly with lower cognitive reserve.
Disclosure: Maillet is the autohor of the TMA-93 Esteve supported the work.

EPO-064

Identification of cognitive phenotypes in pediatric multiple sclerosis using unsupervised machine learning

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Background and aims: Cognitive impairment affects approximately one-third of pediatric multiple sclerosis (PedMS) patients. Despite the high variability in neuropsychological manifestations, previous research has focused on the dichotomous classification of impairment. Aim of this study was to identify cognitive phenotypes in PedMS using an unsupervised machine learning approach and to characterize their clinical and MRI features.
Methods: Seventy-three PedMS patients and 30 healthy controls underwent 3.0T MRI and clinical examination including Expanded Disability Status Scale (EDSS). MRI analysis included quantification of T2-lesion volumes and normalized brain volumes assessment. A comprehensive neuropsychological battery (Wechsler Scale, Selective Reminding Test, Spatial Recall Test, Trail Making Test, Symbol Digit Modalities Test and Semantic and Phonemic verbal fluency test) was administered to all patients. K-means cluster analysis was used on cognitive tests z-scores to identify cognitive phenotypes.
Results: A three-clusters solution was selected including a "preserved cognition" cluster (27 patients [37%]), a "mild verbal memory/semantic fluency involvement" cluster (28 patients [38%]) and a "multidomain involvement" cluster (18 patients [25%]). Across groups, there were no significant differences in age, sex and disease duration. Compared to other groups, patients with multidomain involvement had higher EDSS scores, lower IQ, higher T2-lesion volume, lower normalized brain volume, lower normalized gray matter volume, lower normalized white matter volume and lower normalized deep gray matter volume.
Conclusion: PedMS patients present with distinct cognitive phenotypes ranging from preserved cognition to multidomain involvement. Cognitive phenotypes are not associated with age, sex and disease duration but are associated with physical disability and measures of brain structural damage.
Disclosure: The authors have nothing to disclose.

EPO-065

Encephalopathy with a reversible lesion in the splenium of the corpus callosum in adults

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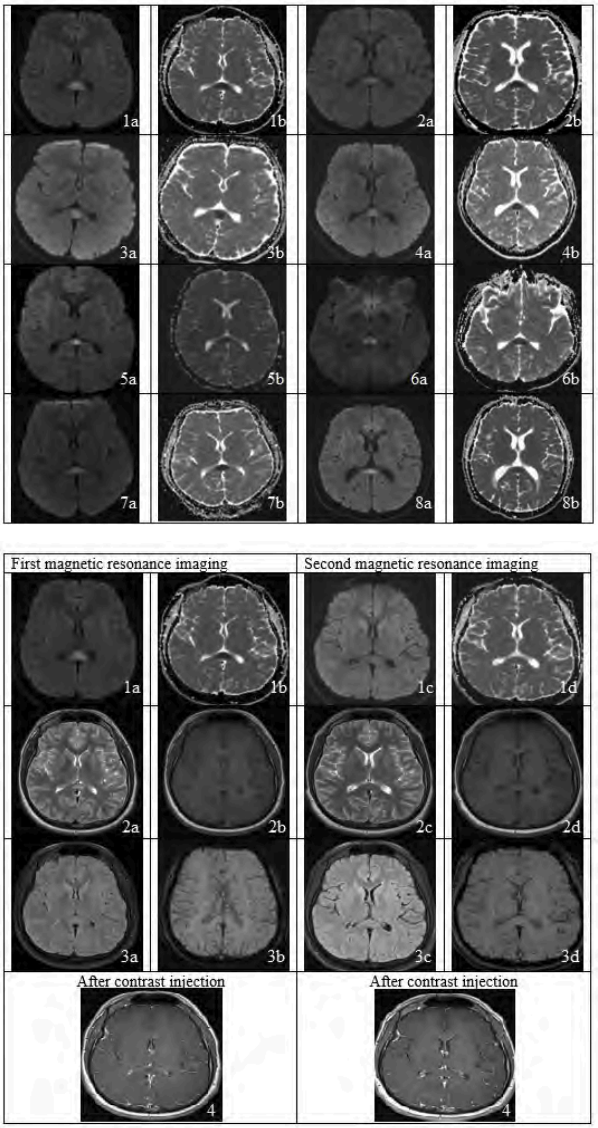
Background and aims: Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a clinico-radiological syndrome involving the splenium of the corpus callosum. This lesion is typically observed in the corpus callosum on magnetic resonance imaging (MRI) and it usually disappears in a few weeks. There are few case reports in the literature. We have reported twelve adult patients with MERS associated with infection and/or epilepsy. Also we have described the clinico-radiological features of these patients.
Methods: The patients' ages, genders, clinical and radiological features, laboratory data, treatment strategies and prognoses were demonstrated.
Results: There were seven male and five female patients in the case series. All of the patients had the fever. There was a history of upper respiratory tract infection in seven patients, visual loss episodes in three patients, epileptic seizure in two patients, arthroplasty in two patients, and cardiac arrhythmia (atrial fibrillation) in one patient.
Conclusion: Focal diffusion was restricted in the splenium of the corpus callosum on the diffusion-weighted MRI. Corpus callosum lesions resolved on diffusion MRI and clinical symptoms improved on follow-up. Thus, it is important to consider MERS as one of the differential diagnoses in adult patients with fever and cognitive changes.
Disclosure: Nothing to disclose.



EPO-066

Regression of post-stroke hemianopia with zolpidem: insights from neuropsychology, EEG, and tDCS

P. Cardone[1], L. Sanz[1], M. Vitello[1], E. Szymkowicz[1], M. Meys[1], A. Thibaut[1], C. Andris[2], V. Demoulin[3], R. Panda[1], S. Laureys[1], S. Chokron[4], J. Annen[1], C. Martial[1], O. Gosseries[1]

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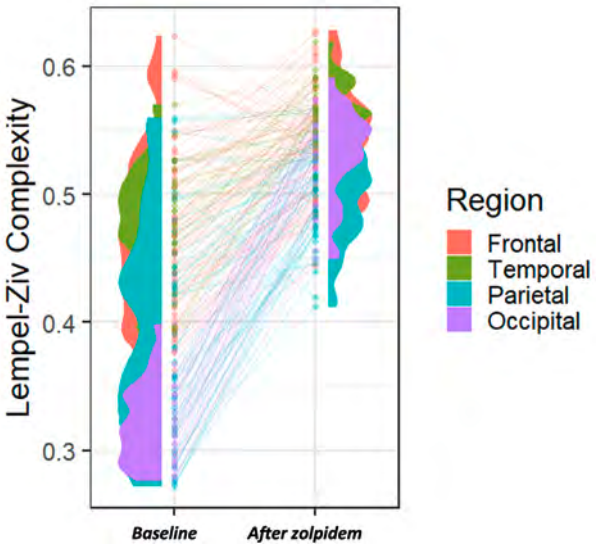
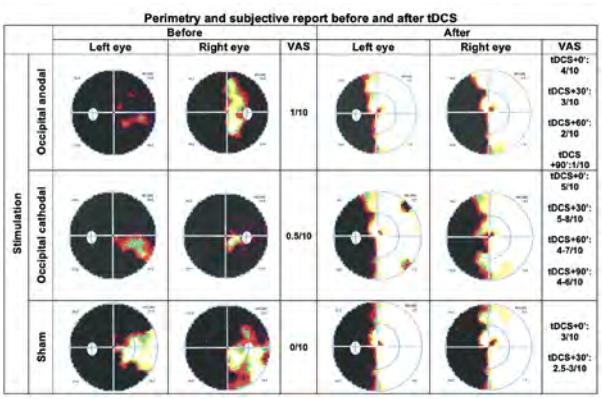
Background and aims: Humans are visual animals, and visual impairments significantly impact patients' quality of life. Here, we present the case of a patient with chronic acquired hemianopia due to occipital stroke, who demonstrates transient visual improvement after intake of zolpidem. We used neuropsychological testing, EEG, and tDCS to investigate its neural mechanisms.

Methods: We tested for neglect via a dedicated battery before and after zolpidem. High-density EEG was recorded at baseline, while taking zolpidem, when zolpidem effects were stable, and when effects started fading. We calculated regional Lempel-Ziv complexity (LZC)[1] and whole-brain alpha power. Finally, we stimulated the occipital cortex with tDCS in 3 sessions (anodal, cathodal, and sham) without zolpidem, controlling for effects with an automated static visual perimetry.

Results: The neuropsychological examination was not in favor of neglect. The post-zolpidem EEG showed decreased alpha and increased LZC compared to baseline, particularly in parietal and occipital regions. We observed a concurrent decrease of alpha while sight improved, but no effect of alpha as effects faded. The patient reported sight recovery with both anodal and cathodal occipital tDCS stimulation (strongest effects with cathodal stimulation). Nevertheless, the patient also reported visual amelioration after sham, of shorter duration.



We observed an increase of LZC all over the cortex after zolpidem compared to baseline. The effect is particularly pronounced in the occipital and the parietal cortex. LZC was calculated over time per each electrode, then averaged across trials.



Subjective effects (A) and perimetry (B) before and after the three sessions of tDCS (occipital anodal, occipital cathodal, and sham). Legend: VAS = visual analogue scale; tDCS = transcranial direct current stimulation.

Conclusion: The results suggest that zolpidem-mediated sight improvements operate on visual impairments rather than attentional deficits, in line with increased occipital metabolism previously described.[2] EEG results hinted a possible role of alpha. While tDCS partially reproduced zolpidem effects, sham stimulation demonstrated a concurrent psychological component. Future work should investigate the underlying mechanism of zolpidem-induced effects on vision.
Disclosure: The authors report no conflict of interest.

EPO-067

Altered dynamics of statistical learning due to the manipulation of rapid consolidation periods

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Background and aims: Traditionally, the time scale of hours or days has been used to study memory consolidation processes. However, the most recent advances in memory research demonstrated that memory consolidation processes could take place even within seconds, probably due to the neural replay of freshly practiced memory traces during short breaks. Here, we investigate this quick form of consolidation during statistical learning. We seek to determine (a) if general skill learning and statistical learning both benefit from this rapid consolidation and (b) whether the length of rest periods has a different impact on these two forms of learning.
Methods: Participants completed the Alternating Serial Reaction Time (ASRT) test, a commonly used statistical learning paradigm that allows us to independently measure implicit statistical and general skill acquisition. The ASRT task had rest breaks between its 25 learning blocks. In a between-subjects design, the duration of the rest periods was either set at 15 or 30 seconds, or the participants could choose their own duration.
Results: According to our findings, while the duration of rest periods does not impact the extent of statistical learning, it does alter the dynamics of learning. Shorter rest times resulted in improved learning during the learning blocks, whereas longer rest periods—possibly because of more replay—promoted learning also in the between-block rest periods. Furthermore, we found that the self-paced group learned general skills less effectively than the fixed rest period groups.
Conclusion: Our results imply that distinct learning and consolidation processes are affected differently by the length of short rest periods.
Disclosure: From a methodological perspective, our findings also demonstrate the relevance of evaluating the temporal dynamics of learning and not only giving a broad indication of the overall learning across the task.

EPO-068

High frequency multimodal training for improving motor and cognitive function in people with Parkinson's disease

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Background and aims: Cognitive decline is an important and common complication in patients with Parkinson's disease (PD) since it significantly reduces the quality of life. A breakthrough in the prevention of cognitive decline in PD remains to be achieved. This study aimed to evaluate the effectiveness of a high-frequency multimodal training in improving motor and cognitive function.
Methods: 28 patients diagnosed with idiopathic PD completed a comprehensive neuropsychological test battery and were neurologically examined. The patients of the intervention group (n=15, including 26.6% women; mean (SD) age = 63y (59y-75y)) underwent two weekly sessions of Tai Chi therapy over 4 weeks and carried out an individually tailored training program consisting of two modules: smartphone-based speech and cognitive training A matched control group consisted of n=13 patients with PD who received computer-assisted cognitive training. The data were analyzed with repeated-measures ANOVA.
Results: Four weeks of high-frequency training showed significant effects within the intervention group on verbal episodic memory: 〖ηp〗^2=.25; p=0.01 [95% CI-1.35; -0.24] and visual-spatial function: 〖ηp〗^2=0.38;p=0.00 [95% CI-0.78;-0.26]. The significant improvement was also shown in the Tinetti mobility test: r=0.85; p=0.00; [95% CI 9; 14.5]. The significant effects in verbal episodic memory, visual-spatial function and Tinetti mobility test remained after 6 months follow-up. Compared to the control group, the cognitive performance of the intervention group improved significantly in visual-spatial function: 〖ηp〗^2=0.15; p=0.04 [95% CI-0.47;1.38].
Conclusion: In patients with PD, a multimodal training program not only improves gait and stability but may also contribute to improvement of cognition.
Disclosure: Nothing to disclose

EPO-069

Musical Perception in Neurodegenerative Disorders, a Pilot Study

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Background and aims: According to recent studies, patients with Alzheimer's Disease (ADD) indicate attenuated melody processing and a reduced ability to perceive changes in amplitude and rhythm, while patients with Parkinson's Disease (PD), seem to have difficulties in rhythm perception and production. This study aimed to investigate whether patients with ADD and PD have deficits in the perception of melody, rhythm, and musical excerpt recognition as measured by the Montreal Battery of Evaluation of Amusia test (MBEA). Another objective was to explore the possible correlation of musical perception with other cognitive functions.
Methods: Musical perception was assessed to 10 patients with ADD, 10 patients with PD, and 10 healthy older adults. In addition, a neuropsychological assessment was performed including Addenbrooke's Cognitive Examination, Digit Span forward & backward, and Hopkin's Verbal Learning test – revised (HVLT-R).
Results: Patients with ADD performed worse than patients with PD and healthy individuals in the perception of melody and musical excerpt recognition but outperformed patients with PD in rhythm perception. The control group indicated higher scores in all musical perception scores than patients with ADD and PD. A strong positive correlation was found between the musical excerpt recognition and the total score of the verbal episodic memory test (HVLT-R) [rho (28) =.619], the short-term verbal memory (Digit Span Forward) [rho (28) =.481], and the verbal working memory test (Digit Span Backward) [rho (28) =.643].
Conclusion: Musical perception is affected differently in ADD and PD. Musical recognition is also strongly related to verbal episodic, short-term verbal, and verbal working memory tests.
Disclosure: Nothing to disclose.

EPO-070

Higher degree of cognitive impairment in late-onset compared to adult-onset MS patients with similar disease duration

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Background and aims: Cognitive impairment affects more than 70% of patients with multiple sclerosis (MS). This study aimed to investigate whether late-onset MS patients (LOMS, age at MS diagnosis >= 45 years) experience more cognitive impairment compared to adult-onset MS (AOMS) patients.
Methods: Participants were recruited from two Italian MS centers. Disease duration was capped at six years from MS diagnosis. All participants underwent an extensive neuropsychological test battery including the Symbol Digit Modalities Test (SDMT), Selective Reminding Test (SRT), Paced Auditory Serial Addition Test (PASAT), and Spatial Recall Test (SPART). Participants filled out questionnaires on fatigue (FSS) and depression (MADRS). To perform between-group comparisons, we used pairwise Wilcoxon tests with Holm-Bonferroni corrections. Patients with more than two abnormal tests were considered cognitively impaired.
Results: We included 139 AOMS, 39 LOMS and 169 healthy controls (HC). 20.5% of LOMS and 11.5% of AOMS were cognitively impaired (impairment in >= 2 cognitive domains). LOMS showed higher degree of cognitive impairment on the SDMT, SRT recall and SPART ($p < 0.01$ for all) compared to AOMS and HC ($p<0.01$ for all). No differences between AOMS and LOMS were found on the PASAT ($p>0.05$). Depression and fatigue did not differ between LOMS and AOMS ($p>0.05$ for all), but when compared to HCs ($p<0.01$).
Conclusion: LOMS were more frequently impaired on information processing speed, visuospatial memory and verbal learning and memory compared to AOMS with similar disease duration. Early cognitive intervention and rehabilitation are crucial in LOMS to prevent further cognitive decline.
Disclosure: AW received an ECTRIMS-MAGNIMS fellowship to pursue this research. All other authors report no conflicting interest regarding this abstract.

Headache 1

EPO-071

Relation of post-stroke headache to cerebrovascular pathology and hemodynamics

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Background and aims: Despite the high prevalence of cerebrovascular stroke, headache attributed to ischemic strokes is often undertreated and overlooked. The aim is to detect the relation of a post-stroke headache to cerebrovascular pathology and changes in hemodynamics through a high-resolution duplex ultrasound examination.

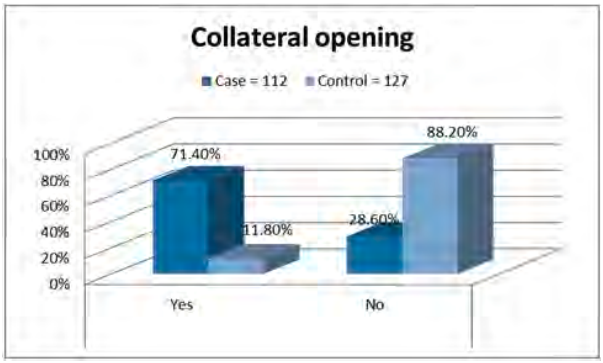
Methods: This is a case-control study that was conducted from January 2021 to August 2021.The study was conducted on 239 patients who presented with an acute ischemic stroke. Patients were subdivided into two groups; Group I included 112 patients with headache attributed to ischemic stroke (cases) and Group II included 127 headache-free stroke patients (controls). History included headache characteristics and risk factors. Clinical and radiological examination were preformed to detect the type of stroke. Ultrasound duplex examination of the extracranial and intracranial cerebrovascular system was carried for both groups.

Results: Post-stroke headache was more frequent in patients with posterior circulation infarction (58%). Post-stroke headache was reported within 7 days post-stroke in (61.6%) of patients. Pre-stroke headache was an independent predictor for post-stroke headache occurrence (OR=28.187, 95%CI; 6.612-120.158, P<0.001). Collateral opening and various degrees of intracranial vascular stenosis were strong predictors of headache occurrence (OR=25.071, 95% CI; 6.498-96.722, P<0.001).

Conclusion: Post-stroke-headache is a common phenomenon especially in patients with pre-stroke headache, history of old stroke, posterior circulation infarction, and large artery disease. The intracranial cerebrovascular pathological changes including opening of the collateral channels and variable degrees of stenosis of cerebrovascular systems were implicated in the production of that headache.

Disclosure: The authors declare that there was no conflict of interest.

Character, n (%)	Headache patients (n=112)
Pulsatile	30 (26.8%)
Stabbing	4 (3.6%)
Tighting	78 (69.6%)
Intensity, n (%)	
Moderate	82 (73.2%)
Severe	30 (26.8%)
Location, n (%)	
Anterior	57 (50.9%)
Posterior	35 (31.3%)
Diffuse	20 (17.9%)
Side, n (%)	
Ipsilateral to Infarction	65 (58%)
Contralateral to Infarction	15 (13.4%)
Unilateral alternating	7 (6.3%)
Bilateral	25 (22.3%)
Association, n (%)	
Nausea and Vomiting	46 (41.1%)
Photophobia	30 (26.8%)
Phonophobia	12 (10.7%)



Multivariate logistic regression to detect independent predictors of post-stroke headache				
Predictor variables	**OR**	**95% C.I.**		**P value**
		Lower	**Upper**	
Pre-stroke Headache	28.187	6.612	120.158	< 0.001
PCA stenosis <50%	84.657	10.418	687.947	< 0.001
VA4 stenosis <50%	842.472	50.262	14121.06	< 0.001
Intracranial cerebrovascular system pathological changes	25.071	6.498	96.722	< 0.001
Collateral opening	60.826	13.003	284.541	< 0.001
PCA, posterior cerebral artery; VA4, vertebral artery segment 4. $p<0.05$ was considered statistically significant.				

EPO-072

Neurophysiological and neuroimaging characteristics in migraine with visual aura

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Background and aims: Activation of the trigeminovascular system with trigeminal nuclei sensitization play a significant role in the migraine pathophysiology. The cortical spreading depression (CSD) underlying migraine aura may cause structural changes in the brain. We investigated the differences in the neurophysiological and MRI data between migraine patients with and without aura.

Methods: 48 migraine patients were examined during headache-free periods: 21 with visual aura (1st group) and 27 -without aura (2nd group). We used blink reflex (BR), sympathetic skin response (SSR) and MRI voxel-based morphometry (MRIvm).

Results: There were no differences between groups in male to female ratio, age and disease duration. However, in the 1st group, migraine attacks were observed more often, and they were shorter than in 2nd group. No differences were found between 1st and 2nd groups when comparing the all BR parameters. But compared to controls, migraine patients revealed an amplitude increase in the both BR components. Using SSR, sympathetic activity predominance was observed more often in the1st group(80,9%) compared to 2nd(62,9%) and control(50%). MRIvm demonstrated grey matter reduce in the pain processing areas in the both groups. Additionally, a volume increase in the structures responsible for visual information processing was observed in the 1st group (table).

Conclusion: The migraine patients have a sympathetic activity predominance, a supraspinal descending control deficiency on the brainstem and reduction in the structures volume involved in pain processing. Repetitive CSD with regional cortical hyperexcitability have long-term effects on the areas involved in the visual aura formation and leads to an increase in their volume.

Disclosure: Nothing to disclose.

Parameters	Control group n = 20	1st group (migraine patients with visual aura) n = 22	2nd group (migraine patients without visual aura) n = 26
	Median (IQR)		
Age, years	34 (20 – 44)	34 (21 – 43)	36 (21 – 44)
male to female ratio (M/F)	8/12	8 / 14	9/17
Disease duration, years		15 (7 - 19)	17 (8 – 20)
Migraine attacks duration, min		4 (2 – 7)	7 (4 – 11)*
Migraine attacks frequency, per month		2 (1 – 2)	1 (0,5 – 1,5)*
Headache intensity, visual analog scale		6 (5 – 8)	7 (5 – 8)
Values of the BR amplitudes			
A R1 ipsilat., mV	0,2 (0,1 – 0,3)	0,3 (0,2 – 0,4) Δ	0,4 (0,2 – 0,5)
A R2 ipsilat., mV	0,3 (0,2 – 0,4)	0,5 (0,3 – 0,8) Δ	0,6 (0,4 – 0,8)
A R2 contralat., mV	0,3 (0,2 – 0,4)	0,5 (0,3 – 0,7) Δ	0,5 (0,3 – 0,8)
Brain MRI measurements (mm3)			
Left amygdala	1485 (1358 - 1588)	1254 (1184 – 1368) Δ	1286 (1193 – 1373)
Right amygdala	1450 (1285 - 1583)	1307 (1174 – 1395) Δ	1275 (1188 – 1380)
Left postcentral gyrus	8378 (7591- 9737)	7579 (7253 – 85630) Δ	7680 (7174 - 8674)
Right postcentral gyrus	8300 (7633 - 9026)	7499 (7296 – 8648) Δ	7365 (6942 - 8894)
Left superior parietal lobule	13203 (10974 – 14958)	14210 (11274 -16649)	12868 (12065-13547) *
Right superior parietal lobule	13195 (10854 – 14839)	14306 (12857 - 16835)	13135 (11974-14783)
Left cuneus	3024 (2847-3212)	3514 (3368 – 3696)	3117 (2754 – 3372) *
Right cuneus	3118 (2893-3249)	3537 (3402 – 3692)	3164 (2929 -3243) *
Left lingual gyrus	6297 (5738 – 6398)	6997 (6237 – 7174)	6198 (5665 – 6468) *
Right lingual gyrus	6292 (5847 – 6458)	7097 (6347 – 7258)	6371 (5772 – 6542) *

IQR - interquartile range
* - Statistically significant difference ($p < 0.05$) between 1st and 2nd groups (Mann–Whitney test);
Δ - Statistically significant difference ($p < 0.05$) between control, 1st groups and 2nd groups (Kruskal–Wallis test)

Table. Comparative assessment of the patients with migraine and healthy controls

EPO-073

Frequency and impact of headache in transgender women patients: a pilot study.

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Background and aims: There are still uncertain data in the literature about the prevalence of headache in the transgender women population, as well as the impact of hormone replacement therapy. The objective of our study is to compare the prevalence, intensity, and impact of headaches in the transgender women population in comparison to cisgender women.

Methods: This study was a case-control observational pilot study. It was conducted at an outpatient endocrinology clinic, a reference in transgender patient care, in a tertiary university hospital in the northeast of Brazil. Samples were age-matched. Inclusion criteria were transgender with estrogen replacement. Exclusion criteria were cisgender pregnant women and cisgender women with amenorrhea. Headache impact was measured by the Headache Impact Test (HIT-6) scale and depression and anxiety were measured by The hospital Anxiety and Depression Scale (HADS).

Results: We analyzed 50 patients, 25 transgender women patients, and 25 cisgender women in the control group. The median age was 35 for each group. The intensity median in the transgender women group was 7,0(P25:7,0 -P75:9,0) and in the cisgender group was 6,0(P25:5,5 -P75:8,0). We found higher frequency rates of headache impact(52%vs40% - Pvalue:0,002), anxiety(52%vs36%- Pvalue:0,260), and depression (24%vs12%- Pvalue:0,274) in the transgender women sample.

Characteristics		Transgender women (n= 25)	Cisgender women (n= 25)	P value	OR (CI 95%)
Age (years)	Mean (P_{25}; P_{75})	35 (25; 39)	35 (28; 45)	0,155	
Headache in the last 12 months n (%)	Yes No	22 (88%) 3 (12%)	25 (100%) 0 (0%)	0,076	Undefined (0,60-undefined)
Episodes headache number (days/3 months)	Mean (P25; P75)	5 (2; 12)	8 (2,5; 12)	0,762	
Headache intensity (EVN[1])	Mean (P25; P75)	7 (7; 9)	6 (5,5; 8)	0,011	
Migraine n (%)	Yes No	11 (44%) 14 (56%)	14 (56%) 11 (44%)	0,400	1,60(0,51-5,06)
Tension type headache n (%)	Yes No	9 (36%) 16 (53%)	11 (44%) 14 (56%)	0,567	1,38 (0,43-4,46)
Headache impact (HIT-6[2]) n (%)	Impact	13(52%)	10 (40%)	0,002	0,62(0,195-1,92)
Ansiety (HAD-A[3]) n (%)	Yes No	13 (52%) 12 (48%)	9 (36%) 16 (64%)	0,260	0,52 (0,16-1,64)
Depression (HAD-D[3]) n (%)	Yes No	6 (24%) 19 (76%)	3(12%) 22 (88%)	0,274	0,43(0,08-2,01)

Table 1 - Characterization of the sample

Conclusion: We observed a higher rate of impact of headache and intensity in the transgender women group, and a higher rate of anxiety and depression in the transgender women group, without statistical significance difference. We conduced a pilot study and type II error is a possibility.
Disclosure: We do not have conflicts of interest to declare.

EPO-074

Primary headache in transgender men: a pilot study.

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Background and aims: The prevalence of headaches in transgender individuals on crossed hormone replacement therapy is not well established in the literature. The study's main objective is to analyze the prevalence and impact of headaches among transgender men on gender-affirming hormone therapy.
Methods: This study was a case-control observational pilot study. It was conducted at a reference outpatient endocrinology clinic in a tertiary university hospital. The sample was age-matched. Inclusion criteria were composed of transgender men patients on gender-affirming hormone therapy. Exclusion criteria were individuals with previous use of anabolic steroids and pregnant transgender men. The intensity was measured by the Visual Analogue Scale(VAS). Headache Impact Test(HIT-6) was used to estimate the headache impact. The hospital Anxiety and Depression Scale(HADS) was used to diagnose anxiety and depression.
Results: The total number of study participants was 50 men, and 25 of them were transgender. The median age of the sample was 30 years old(P25=25;P75=36) among transgender men and 32 years old(P25=26;P75=40) among cisgender men. We found a statistical difference of intensity between the two groups, with a median intensity in transgender men group of 7(P25=5;P75=8,5) and the median of cisgender men group was 5(P25=4;P75=6) Pvalue:0,005. Transgender men had a significantly higher rate of headache impact 52,0%vs12,0%(CI0.22-0.53;pvalue:0,002) and a higher frequency of anxiety 56,0%vs25,0%(CI=0.07-0.85–pvalue:0,028) and depression 36,0%vs 00,0% (CI=0.00-0.29 – p value:0,001).

Characteristics		Trangender women (n= 25)	Cisgender women (n= 25)	P value	OR (CI 95%)
Age (years)	Mean (P_{25}; P_{75})	30 (25; 36)	32 (25; 40)	0,491	
Headache in the last 12 months n (%)	Yes No	22 (88%) 3 (12%)	24 (96%) 1 (4%)	0,302	3,20 (0,32-89,49)
Episodes headache number (days/3 months)	Mean (P25; P75)	6 (1; 27)	3 (1; 6)	0,158	
Headache intensity (VAS[1])	Mean (P25; P75)	7 (5; 8,5)	5 (4; 6)	0,005	
Migraine n (%)	Yes No	14 (56%) 11 (44%)	8 (32%) 17 (68%)	0,091	0,37 (0,11-1,20)
Tension type headache n (%)	Yes No	8 (32%) 17 (68%)	16 (64%) 9 (36%)	0,025	3,67 (1,14-12,53)
Headache impact (HIT-6[2]) n (%)	Impact	13 (52%)	3 (12%)	0,002	0,13 (0,02-0,53)
Ansiety (HAD-A[3]) n (%)	Yes No	14 (56%) 11 (44%)	6 (25%) 19 (75%)	0,021	0,25 (0,07-0,85)
Depression (HAD-D[3]) n (%)	Yes No	9 (36%) 16 (64%)	0 25 (100%)	< 0,001	0,00 (0,00-0,29)

Table 1 - Characterization of the sample.

Conclusion: We found a higher prevalence of TTH among cisgender men and a higher rate of impact of headache among transgender men, as well as higher rates of anxiety and depression.
Disclosure: We do not have conflicts of interest to declare.

EPO-075

Real-world effectiveness of switching to fremanezumab from other CGRP pathway targeting mAbs: PEARL 3rd interim analysis

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Background and aims: Patients who do not benefit from or tolerate preventive migraine treatment with a monoclonal antibody (mAb) targeting the calcitonin gene-related peptide (CGRP) pathway may benefit from switching to another; however, effectiveness data on this are limited and granular.

Methods: PEARL (EUPAS35111) is an observational, prospective, Phase IV study, evaluating the effectiveness of fremanezumab for migraine prevention in adults with episodic or chronic migraine (EM, CM). Patient data are recorded through daily headache diaries, including information on past-preventive treatment. This third interim analysis was conducted when all enrolled patients had completed >=6 months of treatment, and this sub-analysis explored the proportion of switch patients (previously treated with another mAb targeting the CGRP pathway) achieving >=50% (EM and CM) and >=30% (CM only) reduction in monthly migraine days (MMD) during the 6 months post-fremanezumab initiation.

Results: Of 732 patients with available data, 62 were switch patients (Table 1). One patient had been previously treated with galcanezumab, 59 with erenumab and two with galcanezumab and erenumab on separate occasions. During the first 6 months of fremanezumab treatment, 20 switch patients (32.3%) achieved >=50% MMD reduction, with similar proportions for EM and CM patients (Figure 1). Notably, 28 patients (60.9%) with CM achieved >=30% MMD reduction (Figure 2).

	Total patients (N=62)	EM patients (n=16)	CM patients (n=46)
Switch due to lack of efficacy, n (%)	26 (41.9)	6 (37.5)	20 (43.5)
Switch due to reasons other than 'lack of efficacy', n (%)	36 (58.1)	10 (62.5)	26 (56.5)

CGRP, calcitonin gene-related peptide; CM, chronic migraine; EM, episodic migraine; mAb, monoclonal antibody.

Table 1: Reasons for switching to fremanezumab from another mAb targeting the CGRP pathway according to patients at baseline visit, by migraine type.

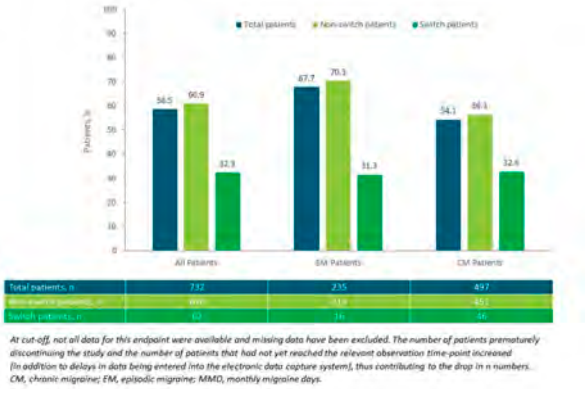

Figure 1: Proportion of Total, Non-switch and Switch patients with >=50% reduction in MMD during the 6 months after fremanezumab initiation, by migraine type.

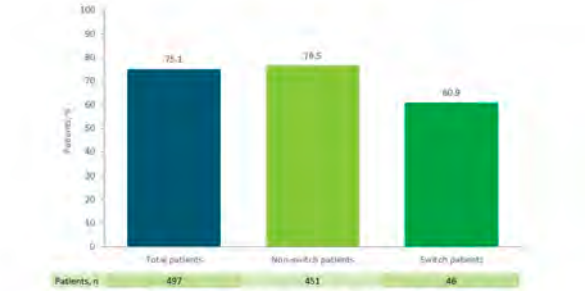

Figure 2: Proportion of Total, Non-switch and Switch patients with CM with >=30% reduction in MMD during the 6 months after fremanezumab initiation.

Conclusion: This analysis provides real-world evidence of fremanezumab effectiveness in over 30% of patients with EM and CM who had previously failed or not tolerated another mAb targeting the CGRP pathway. Switching to fremanezumab should be considered for these patients as it may offer a beneficial treatment option.
Disclosure: Funded by Teva Pharmaceuticals.

EPO-076

Long-term effectiveness of eptinezumab in patients with prior preventive migraine treatment failures

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Background and aims: DELIVER (NCT04418765) evaluated the efficacy and safety of eptinezumab for migraine prevention in patients with migraine and prior preventive treatment failures. Here, we report results of the 48-week dose-blinded extension period.
Methods: Eptinezumab 100mg and 300mg were evaluated vs placebo (infusions every 12 weeks) in adults with migraine and 2-4 documented preventive treatment failures. Patients randomized to placebo during the initial treatment period received eptinezumab 100mg or 300mg in the extension period; patients initially receiving eptinezumab continued their assigned dose. Efficacy measures included change from baseline in number of monthly migraine days (MMDs), >=50% and >=75% reduction from baseline in MMDs (ie, migraine responder rates [MRRs]), change from baseline in the 6-item Headache Impact Test (HIT-6), migraine severity, and acute headache medication use.
Results: 782/865 patients (90.4%) completed the extension period. Patients switching from placebo experienced an initial significant decrease in MMDs (Figure), migraine severity, acute headache medication use, and HIT-6 scores after the first eptinezumab dose (weeks 25¬-36); similar to what was initially observed (weeks 1-12). All treatment arms had sustained MMD reductions, with >=50% and >=75% MRRs of >60% and >30%, respectively, during weeks 61-72. No new safety or tolerability concerns were identified.

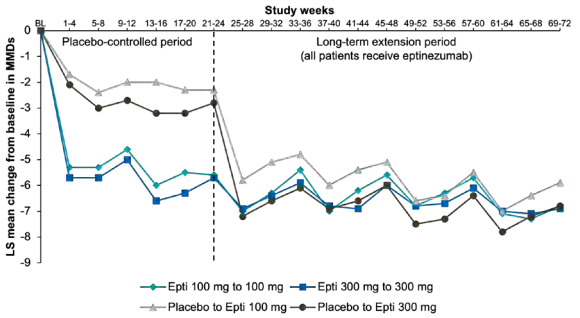

Figure. Change in MMDs with up to 18 months of eptinezumab treatment. Abbreviations: BL, baseline; Epti, eptinezumab; LS, least squares; MMDs, monthly migraine days.

Conclusion: The long-term effectiveness of eptinezumab is highlighted by the >90% completion rate of the DELIVER extension period. Marked and sustained reductions in MMDs, increases in MRRs, and reductions in migraine severity and burden experienced by those switching from placebo to active treatment indicate long-term effectiveness of eptinezumab for up to 18 months.
Disclosure: MA-Fees: AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, Teva. ST-Grants: Allergan/AbbVie, Amgen, Eli Lilly, Lundbeck, Neurolief, Novartis, Satsuma, Zosano. Fees: Aeon, Allergan/AbbVie, Alphasights, Amgen, Aruene, Axsome Thera, Becker Pharm. Consulting: BSI, Biohaven, CVHP, ClickThera, CoolTech, CRG, Decision Resource, Defined Health, DRG, Eli Lilly, ExpertConnect, FCB Health, Fenix, GLG, Guidepoint Global, Health Advances, HSC, HMP Comm, Impel, Initiator Pharma, InteractiveForums, Keyquest, Krog and Partners, Lundbeck, M3 Global Research, Magnolia Innovation, MJH Holdings, Miravo Healthcare, Neurofront Thera, Neurolief, Novartis, P Value Comm, Pain Insights Inc, Palion Medical, Pulmatrix, Putnam Associates, Rehaler, SAI Medical Partners, Satsuma, Slingshot Insights, SGI, Strategy Inc, SMC, System Analytic, Taylor and Francis, Teva, Theranica, Tremeau, Trinity Partners, Unity HA, Vial, XOC, Zosano. CME: AAN, AHS, ACHS, CME, DHC, Forefront Collaborative, HME, HMP Global, MAI, MMC, NACE, NAC for CME, OSU, PER, PlatformQ Education, Primed, VME, WebMD/Medscape. AG-Fees: Abbvie/Allergan, Amgen, Ärztekammer Nordrhein, Ärztekammer Westfalen Lippe, DGS, Esanum perfood, Grünenthal, Hexal, Hormosan, Lilly, Lundbeck, Medscape, Mundipharma, Novartis, Stada, Streamed Up, Teva. BJ, AE, MKJ-Employees of Lundbeck LLC. AJS-Fees: AbbVie, Allergan, Amgen, Axsome Therapeutics, Eli Lilly, Everyday Health, Impel, Lundbeck, Med-IQ, Medscape, Neurolief, Novartis, Satsuma, Teva, Theranica.

EPO-077

Patient-perceived improvements in migraine and most bothersome symptom among patients treated with eptinezumab

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Background and aims: This post hoc analysis of 24-week data from DELIVER (NCT04418765) evaluated the improvement in patient-identified most bothersome symptom (PI-MBS) and explored the relationship between PI-MBS and Patient Global Impression of Change (PGIC) among patients treated with eptinezumab.
Methods: Patients identified the PI-MBS at baseline and rated its change at week 12 and 24; patients also completed the PGIC assessment using an identical scale. The impact and maintenance of PI-MBS improvement between weeks 12 and 24 among eptinezumab-treated patients (i.e., pooling 100mg and 300mg in those who completed PI-MBS at both timepoints; N=563) was evaluated through a frequency table. The relationship between PI-MBS and PGIC was assessed in all patients (eptinezumab and placebo) who reported on both scales at both weeks (N=865) using Spearman's rank correlation test and a frequency table.
Results: At week 12, 52.4% eptinezumab-treated (versus 19.5% placebo; p<0.001) had much or very much improved PI-MBS. Of the 52.4%, 79.3% maintained or further improved PI-MBS by week 24. There was a strong relationship between improvement in PI-MBS and PGIC (r=0.85, p<0.001). The overlap of PGIC and PI-MBS scores was 68.2% (95%CI: 66.0, 70.4). 87.9% of patients with improved PGIC also improved in PI-MBS. 96.0% of patients had an PI-MBS change within +/-1 level of the PGIC score.
Conclusion: Patients treated with eptinezumab experienced sustained improvement in PI-MBS over 24 weeks. The strong relationship between PI-MBS and PGIC suggests that they are both important contributors to patients' perception and assessment tools for overall improvement in migraine.
Disclosure: SA-Employee of Lundbeck A/S AR-Employee of Lundbeck A/S XL-Employee of Lundbeck A/S LB-Employee of Lundbeck A/S SR-Employee of Lundbeck A/S. Stock/Options: Novartis AB

EPO-078

Responders and super-responders to anti-CGRP mAbs: the large, prospective, multicenter, real-life, I-NEED study

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Background and aims: In randomized clinical trials (RCTs), responders (>50% response) to monoclonal antibodies (mAbs) targeting calcitonin gene-related peptide (CGRP) range from 30% to 49%, while super-responder (>75% response) from 12% to 19%. We prospectively explored response and super-response to anti-CGRP mAbs in high-frequency episodic migraine (HFEM: 8-14 days/month) and chronic migraine (CM) in a large, real-life population.
Methods: Multicenter (n=29), prospective, cohort, real-life study, across 10 Italian regions. We enrolled all consecutive patients with HFEM or CM receiving >1 anti-CGRP mAbs dose from 01/02/2019 to 28/12/2022. All subjects had failed >3 preventive medications classes. Primary endpoint: responders at week 12. Secondary endpoints: super-responders at week 12, and responder and super-responder at weeks 4, 24 and 48.
Results: 1582 patients received >1 dose of mAbs (erenumab/fremanezumab/galcanezumab: 912/463/207). Responders/super-responders were monitored at weeks 12, 24 and 48 in all centers, conforming to Italian Medicines Agency regulations. Eight centers monitored treatment effects monthly, according to their routine practice. The table summarize results.

Table

		HFEM (n=473)		CM (n=1109)	
Week	Patients (n)	Responders	Super-responders	Responders	Super-responders
4	1582	48.9%	17.7%	49.5%	19.6%
12	1124	**58.3%**	**23.8%**	**63.4%**	**32.2%**
24	880	55.6%	25.8%	69.0%	37.2%
48	507	59.4%	30.0%	71.7%	44.2%

(Primary endpoint in **BOLD**)

Conclusion: Proportions of responders and super-responders to anti-CGRP mAbs in real-life are greater than in RCTs. Response and super-response occur very early (week 4), increase progressively (especially in CM patients) and are sustained over time (48 weeks).

Disclosure: P. Barbanti received grants and honoraria from Alder, Allergan, Angelini, Assosalute, Bayer, ElectroCore, Eli-Lilly, GSK, Lundbeck, Lusofarmaco, 1MED, MSD, New Penta, Noema Pharma, Novartis, Stx-Med, Teva, Visufarma, Zambon C. Aurilia received grants from FB-Health, Lusofarmaco, Almirall, Eli-Lilly Novartis and Teva G. Egeo received grants from Eli-Lilly, Novartis, New Penta and Ecupharma P. Torelli received grants and honoraria from Allergan, Teva, Eli-Lilly and Novartis C. Finocchi received grants and honoraria from Novartis, Eli Lilly, TEVA, AIM group F. d'Onofrio received grant and honoraria from Novartis, Teva, Neopharmed Gentili, Qbgroupsrl, K link srl and Eli-Lilly S. Messina has no disclosures to declare B. Colombohas received congress fee from Teva and Novartis. A. Carnevalehas no disclosures to declare M. Aguggia received grants from Novartis and Lilly M. Tasillo has no disclosures to declare M. Filippi is Editor-in-Chief of the Journal of Neurology; received compensation from Bayer, Biogen Idec, Merck-Serono, Novartis, Roche, Sanofi Genzyme, Takeda, Teva Pharmaceutical Industries; research support from Biogen Idec, Merck-Serono, Novartis, Roche, Teva Pharmaceutical Industries, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA G. Fiorentini has no disclosures to declare. B. Orlando has no disclosures to declare. S. Proietti has no disclosures to declare. S. Bonassi has no disclosures to declare.

EPO-079

Anti-CGRP monoclonal antibodies normalize peripheral sensitization in migraineurs

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Background and aims: Peripheral sensitization is abnormal in migraineurs as documented by Pressure Pain Threshold (PPT) which investigates nociceptive afferent fibres differently from laser or electrical stimulus. This study investigates changes of PPT as a neurophysiological effect of anti-CGRP monoclonal antibodies (mAbs) in migraineurs.
Methods: According to the Andersen's standardized guidelines, five muscles of the trigemino-cervical-complex and one far from this area were tested. PPT values of all above-mentioned muscles were measured at baseline (t0) and after 3 (t1) and 4 (t2) months after the first injection of an anti-CGRP mAb. Data were compared with PPT in healthy controls.
Results: 11 migraineurs and 11 healthy controls (mean age 43±15; F=63.6%) were enrolled. Patients were diagnosed as high-frequency episodic migraine (45.5%) or chronic migraine (54.5%) and treated with Erenumab (63.6%), Fremanezumab (27.3%) or Galcanezumab (9.1%). Migraine outcomes improved at t1 and t2 (migraine days/month: 18.2±6.9 t0 vs 8±4.7 t1 vs 6.1±3.8 t2; severe hours/month: 28.1±40.7 t0 vs 1.6±2.9 t1 vs 3.7±5.6 t2; MIDAS: 100±25 t0 vs 21±15.4 t1). At t0, migraineurs showed a significant lower PPT respect to controls in all muscles, except in the left temporalis and procerus. PPT increased in all migraineurs' muscles at t1 and t2 without significant differences between migraineurs and healthy controls.
Conclusion: PPT detects an abnormal peripheral sensitization in high-frequency episodic migraine and chronic migraine. Treatment with anti-CGRP mAb in migraineurs reduces the peripheral hypersensitivity detected by PPT, correlating with the improvement of the headache.
Disclosure: The authors have no conflicts of interest to declare.

EPO-080

Anti-CGRP antibodies effects on migraine psychiatric comorbidities

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Background and aims: We evaluated the effects of the treatment with monoclonal antibodies (mAbs) acting on the calcitonin gene-related peptide (CGRP) or its receptor (anti-CGRP/R mAbs) on depression, anxiety, and fatigue in migraine patients resistant to traditional prophylaxis.
Methods: 77 patients (77% females, median age 47 years old) with chronic resistant migraine, studied in an open-label longitudinal study, underwent anti-CGRP mAbs (57%) or its receptor treatment (43%). Clinical parameters including allodynia and psychiatric comorbid symptoms were evaluated with specific questionnaire and scales at baseline and at 3-month follow-up. Responders were defined as subjects with at least 50% reduction of headache frequency after three months treatment.
Results: Twenty-ninesubjects (38%) were non-responders and 48 subjects (62%) were responders. Comorbid psychiatric scoring and migraine burden did not differed between groups at baseline. In responders the reduction of disease severity in terms of frequency (median days/month 22 vs 4 $p < 0.001$) and allodynia (6.00 vs 1.50 $p < 0.001$) was associated with a significant decrease of migraine-related disability, fatigue and psychiatric comorbidities. Also in non-responders a significant reduction of the headache frequency (median 30.0 vs 20.0 $p=0.003$), was reported as well as reduced migraine-related disability, but no significant improvement was observed for psychiatric

symptoms.
Conclusion: Anti-CGRP/R mAbs treatment improves psychiatric symptoms as expressed by both depression and anxiety score values only in responder subjects indicating that they are likely related to chronic pain condition. Further studies comparing anti-CHRP/R with other prophylaxis may help understand its potential specific role in psychiatric comorbidities.
Disclosure: Nothing to disclose.

EPO-081

Migraine and COVID-19: Migraine headache developement after COVID-19 and SARS-CoV-2 vaccination in migraine patients

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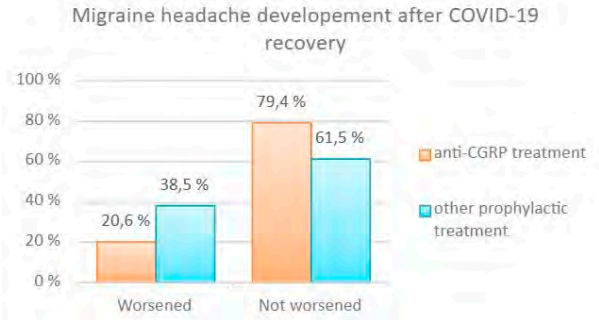
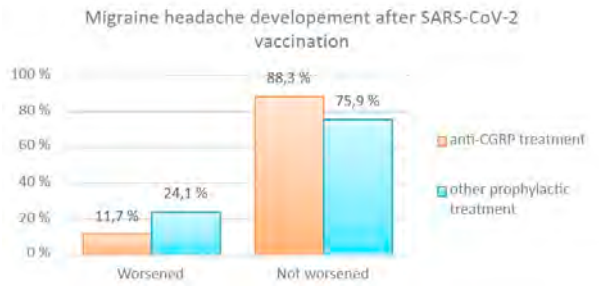
Background and aims: Migraine is a common primary headache with great impact on quality of life and socioeconomic status. It was demonstrated that COVID-19 infection can lead to headache in healthy population as well as in migraine patients. Our objective was to assess how migraine headache developed during one month following COVID-19 depending on prophylactic treatment in migraine patients. Furthermore, we analyzed the impact of SARS-CoV-2 vaccination on migraine headache as well.
Methods: We conducted an in-person survey with 388 patients diagnosed with migraine in 6 Headache Centers in Czech Rebublic. We recorded demographic data, migraine history, prophylactic treatment, COVID-19 history, SARS-CoV-2 vaccination history, subjective worsening of migraine headache during one month after COVID-19 recovery and worsening of headache after vaccination. Comparisons between groups of patients with and without anti-CGRP treatment were performed using Chi-square test. $P<0.05$ was considered statistically significant.
Results: 300 of our subjects had COVID-19 infection. There was no difference in frequence of headache during the infection between patients treated with and without anti-CGRP. However, patients with anti-CGRP treatment reported less frequently (20.6%) worsening of migraine headache in the following month after recovery from COVID-19 compared to patients with other prophylactis medication (38.5%). Similarly, worsening of migraine headache after vaccination was less frequent in group with anti-CGRP treatment (11.7%) in comparison to group with other prophylactics (24.1%).



Migraine headache developement after COVID-19 recovery



Migraine headache developement after SARS-CoV-2 vaccination

Conclusion: Our results showed that patients treated with anti-CGRP were less likely to experience worsening of their migraine after recovery from COVID-19 as well as after vaccination in comparison to patients with other prophylactic treatment.
Disclosure: Nothing to disclose.

EPO-082

Long-term effectiveness of eptinezumab in treatment of patients with chronic migraine and medication-overuse headache

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Background and aims: PREVAIL demonstrated long-term safety, tolerability, and meaningful reductions in migraine-related burden with repeated eptinezumab doses in patients with chronic migraine (CM). Medication-overuse headache (MOH), a secondary headache disorder caused by overuse of acute medication, exacerbates CM. This analysis evaluated eptinezumab in patients with CM and MOH.

Methods: PREVAIL (NCT02985398) was a single-arm, open-label trial in which adults with CM received eptinezumab 300mg every 12 weeks (wks) for up to 8 doses. MOH diagnosis at screening was based on International Classification of Headache Disorders criteria. Long-term effectiveness endpoints included: Migraine Disability Assessment (MIDAS), 6-item Headache Impact Test (HIT-6), patient-identified most bothersome symptom (PI-MBS), Patient Global Impression of Change (PGIC), EQ-5D-5L visual analog scale (VAS), and 36-item Short-Form Health Survey (SF-36).
Results: 49/128 (38.3%) patients with CM had a secondary MOH diagnosis. All patient-reported outcomes showed marked improvements at the first post-baseline assessments (Wk4 or Wk12) that was maintained or improved throughout the study. MIDAS total score decreased from 60.0 (baseline) to 8.6 (Wk84). MIDAS-derived headache days decreased from 47.5 (baseline) to 11.8 (Wk84). HIT-6 total score decreased from 65.2 (baseline) to 53.3 (Wk84). At Wk48, 67.4% and 76.1% of patients reported "much" or "very much" improved PI-MBS and PGIC, respectively. Mean EQ-5D-5L VAS total score improved from 79.9 (baseline) to 83.3 (Wk48). Patients reported improved health-related quality of life per the SF-36. No new safety signals were identified in patients with CM and MOH.
Conclusion: In patients with CM and MOH, long-term treatment with eptinezumab was associated with improvements in multiple patient-reported outcomes.
Disclosure: AB: Consulting fees-Alder, Allergan, Amgen, Biohaven, electroCore, Lilly, Lundbeck, Novartis, Promius, Supernus, Teva, and Theranica. DK: Personal compensation for serving on a Scientific Advisory or Data Safety Monitoring board for: Amgen, Novartis, Biohaven, Eli Lilly, Lundbeck. Speakers Bureau fees for: Amgen, Eli Lilly, Teva, Allergan, Lundbeck, Biohaven. RC-Employee at Lundbeck at time of study. PM: personal fees and research support: AbbVie, Amgen/Novartis, Biohaven, Eli Lilly, Lundbeck, and Teva; consulting fees: Aeon; Speakers Bureau fees: Lilly, Teva, AbbVie, Biohaven, Lundbeck and has received stock or an ownership interest from Precept. LB-Employee of Lundbeck. JH: personal fees and research support-Lundbeck. Consulting fees-Lundbeck, Impel NeuroPharma

EPO-083

Anti-CGRP Monoclonal Antibodies for the Treatment of Migraine with Aura: a prospective observational cohort study

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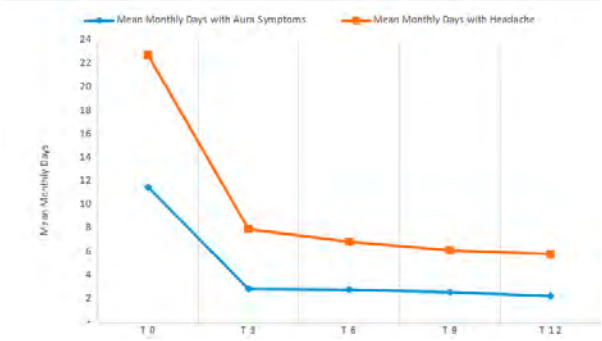
Background and aims: About 25% of migraineurs experience aura symptoms. Aura is a reversible focal neurological phenomenon involving visual, sensory, speech, and motor symptoms that usually precede migraine pain. Monoclonal antibodies against calcitonin-related peptide (anti-CGRP mAbs) are effective in preventing chronic and episodic migraine, but little is known about their effectiveness in specifically preventing migraine with aura. This study aims at evaluating the effectiveness of anti-CGRP mAbs in migraine with aura, and aura symptoms.
Methods: This is a prospective observational cohort study, aiming at evaluating the efficacy of Erenumab, Fremanezumab and Galcanezumab for the treatment of 14 patients suffering from migraine with aura. Duration of follow-up was 12 months. We assesed mean monthly days with aura symptoms, with or without subsequent headache, as well as mean monthly days with headache, by reviewing standardized headache diaries every three months.
Results: We observed a mean reduction of mean monthly days with aura symptoms of - 8.17 (- 5.76, - 10.57; CI 95%) and a mean reduction of mean monthly days with headache of - 15.92 (- 11.09, - 20.75; CI 95%). No significant differences were found bewteen mAbs.



Mean Monthly Days Reduction of Headaches and Aura Symptoms

Conclusion: Our findings show that anti-CGRP mAbs are highly effective in migraine with aura, both in reducing mean monthly headache days and mean monthly days with aura symptoms.
Disclosure: Simone Braca, Angelo Miele, Antornio Stornaiuolo and Mattia Sansone declare that there is no conflict of interest. Cinzia Valeria Russo received personal compensation from Sanofi Genzyme and Merck Serono. Roberto De Simone received personal compensation from Lilly for oral presentations (2020 – 2021).

EPO-084

Diagnosis and misdiagnosis of resistant and refractory migraine – Data from the REFINE study

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Background and aims: : Resistant and refractory migraine are burdensome conditions. Some patients may receive inaccurate diagnoses, leading to unnecessary diagnostic tests and treatments. We evaluated the history of misdiagnosis and use of neuroimaging in patients with resistant (RES) and refractory (REF) migraine compared to non-resistant, non-refractory (NRNR) patients.

Methods: The REFINE study is an observational, multicenter, international study including patients with migraine stratified as REF, RES, or NRNR. In this analysis we assessed patients' baseline characteristics.

Results: We included 612 patients: 340 (55.6%) with NRNR migraine, 228 (37.3%) with RES and 44 (7.2%) with REF. Overall, a misdiagnosis was made in the medical history of 184 (30.1%) cases, with a lower number of misdiagnoses in the REF group (15% vs. 33% of RES and vs. 30% of NRNR, p=0.020). The most frequent misdiagnoses included sinusitis (57, 31.0%), cervical spine disorders (68, 37.0%), hormonal headache (29, 15.7%), and temporomandibular disturbances (21, 11.4%). REF patients had also higher prevalence of accesses to the Emergency Department (27% vs. 16% of RES vs. 13.5% of NRNR, p=0.017). REF (88% and 43%) and RES (97% and 45%) patients underwent, at least once, brain and/or cervical magnetic resonance imaging (MRI) in higher proportion, compared to NRNR (74% and 29%, p<0.001 and p=0.005). Moreover REFs underwent brain MRI and computed tomography scan more frequently.

Conclusion: REF patients had lower rates of misdiagnosis, probably due to their difficult condition, resulting in higher use of neuroradiological exams and access to urgent medical care to exclude secondary diagnoses.

Disclosure: Nothing to declare.

EPO-085

COMPLICATION OF LUMBAR PUNCTURE: RETROSPECTIVE ANALYSIS OF A MONOCENTRIC SERIES.

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Background and aims: Describe the incidence and characteristics of the complications of the lumbar puncture (LP), analyzing possible risk factors in a monocentric series.

Methods: Retrospective study of the medical records of patients undergoing LP in the neurology department, in a period of fifteen years (January 2006-December 2020). The clinical characteristics of the patients are specifically collected (gender, age, weight, height, body mass index [BMI], history of headache, antiplatelet or anticoagulant treatment), and the indication (diagnostic, cerebrospinal fluid removal, [CSF] intrathecal treatment) of LP, and the characteristics of the registered complications.

Results: In the study period, 1,950 patients (950 women/1,000 men), with a mean age of 56.2 years (SD= 18) underwent a total of 2,331 LPs. The procedure was repeated at least 2 times in 218 (11.2%) patients. Indications were diagnostic, CSF drainage and therapeutic in 73.7%, 11.8% and 14.5%, respectively. Complications were recorded in 167 of the LPs (7.2%): headache (103 [4.4%]), low back pain (57 [2.5%]), chemical arachnoiditis (7 [0.3%]); vasovagal symptoms (5 [0.21%]), transient lumbar monoradiculopathy (7 [0.3%]), bacterial meningitis (1 [0.04%]), and spinal epidural hematoma (1 [0.04%]). A history of headache, female gender, a lower BMI, and younger age were significantly associated with a higher risk of post-puncture headache.

Conclusion: In our series, complications have been reported in 7.2% of LPs. The most common was headache (4.4%). A history of headache, female gender, low BMI, and young age are the factors that are associated with a higher risk of this last complication.

Disclosure: With respect to this communication, there are no relationships that could be perceived as potential conflicts of interest. The communication that I present has not been financed, in whole or in part, by any company with economic interests in the products, equipment or similar mentioned in it.

Neuroimmunology 1

EPO-086

Influence of FCGR3A-V158F polymorphism on the therapeutic response to Ocrelizumab in patients with Multiple Sclerosis

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Background and aims: Recent evidence demonstrated that the fragment c gamma receptor 3A (FCGR3A) 158F genotype is an independent predictor of peripheral B-cell depletion and clinical response to rituximab in patients with neuromyelitis optica, as it reduces the affinity of the receptor for human IgG. To evaluate the influence of FCGR3A genotypes on B cell kinetics and disease activity in Relapsing Multiple Sclerosis (RMS) patients on ocrelizumab.
Methods: Ocrelizumab-treated RMS patients were consecutively enrolled at the time of drug initiation and were prospectively followed-up for eighteen months. We collected clinical (EDSS and number of relapses) and immunological (B cell count) data every six months. Radiological data (presence of gadolinium lesion/s) were collected at six and eighteen months of follow-up. At enrollment, patients were genotyped for the FCGR3A-V158F polymorphisms. To explore the Influence of FCGR3A-V158F polymorphisms on the therapeutic response to Ocrelizumab we applied logistic and Poisson regression models, as appropriate.
Results: We enrolled 45 RMS patients. There was no statistically significant association of FCGR3A gene polymorphism (either according to recessive or dominant pattern) with the presence of disease activity or early B cell repopulation (at six-, twelve- and eighteen-month follow-ups). However, all the patients that experienced early B cell reappearance at 6 months (9 on 45) carried at least one F allele (p=0,153).
Conclusion: These results suggest further investigation of the possible relationship between B lymphocyte kinetics under ocrelizumab treatment and the FCGR3A polymorphism.
Disclosure: The authors declare no competing interests for this work.

EPO-087

Prevalence of HLA DQ2 and DQ8 in seronegative neuromyelitis optica spectrum disorders

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Background and aims: Neuromyelitis optica spectrum disorders is an entity not well understood whose pathophysiological substrate is unknown yet. Despite the discovery of the AQP-4 and MOG antibodies, there are still a high number of patients diagnosed with NMOSD who remaining seronegative. HLA-DQ2 and HLA-DQ8 are gene alleles that predispose to celiac disease, nevertheless their association to other autoimmune disorders is unclear so far.
Methods: We evaluate patients diagnosed with seronegative NMOSD at the unit of neuroimmunology and multiple sclerosis of Girona - University Hospital Dr. Josep of Girona, Spain, compared with seropositive NMOSD patients from February 2019 to December 2022. All patients met criteria to be diagnosed with NMOSD. All patients who were positive for AQP-4 and MOG were considered as seropositive. No patient had history of celiac disease.
Results: We collected a total of 18 patients who met NMOSD criteria, seropositive as well as seronegative. Of 18 patients, 12 were seronegative NMOSD (66.66%) Of 12 seronegative NMOSD patients, 75% were positive for either HLA-DQ2 or HLA-DQ8 92% patients had marked improvement after reduction of gluten consumption measured by EDSS. The prevalence of HLA-DQ2/DQ8 in seropositive NMOSD patients was 33.33% HLA-DQ2 was the allele more frequently associated to NMOSD seronegative as well seropositive.
Conclusion: Despite there are still lacking further studies which evaluate the pathogenic role HLA-DQ2/DQ8 in non-celiac patients, the positivity for these alleles could be a useful diagnostic biomarker for seronegative forms of NMOSD. In addition, this finding may bring therapeutic implications as the reduced gluten consumption could favor better outcomes in patients with NMOSD.
Disclosure: Nothing to disclose.

EPO-088

Estensive spinal hypertrophic pachymeningitis in IgG4-related disease.

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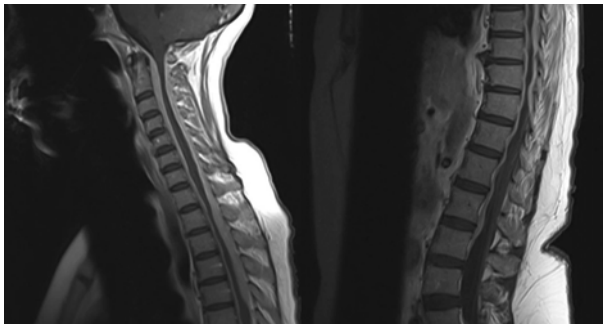
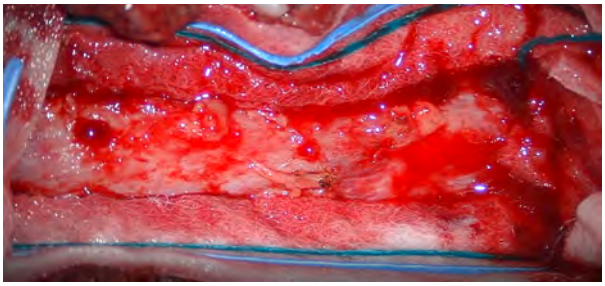
Background and aims: We describe a 66-year-old woman with a two-month history of neck stiffness, limbs dysesthesias and progressive weakness to inability to walk, diagnosed as an isolated extensive spinal hypertrophic pachymeningitis (HP) due to IgG4-related disease (IgG4-RD).
Methods: HP diagnosis due to IgG4-RD could be challenging because clinical features are non-specific. Medical assessment should include comprehensive evaluation to exclude differential diagnosis and histopathological exam represents the diagnostic gold standard.
Results: Cervicothoracic-MRI disclosed almost complete obliteration of cerebrospinal fluid signal in the entire spinal tract, with marked contrast enhancement of the meningeal envelopes, and with signal alteration in the cervical-thoracic spinal cord due to compressive myelopathy. A complete workup was performed, disclosing high serum concentration of IgG4, and total body CT scan and FDG-PET also showed signs of subclinical aortitis. Meningeal biopsy revealed lymphoplasmacytic infiltrate, with high-level-per-field plasma-cells and an IgG4+/IgG+ ratio >40%, confirming HP due to IgG4-RD diagnosis. Patient was treated with high-doses steroids, followed by rituximab (two-1g infusions 15 days apart), with clinical improvement.



Intraoperative tissue observation of spinal meningeal revealed pearly-colored dura mater, increased consistency, and tendency to hemorrhage. Two focal mamelon-like extroversions are also present.



Spinal MRI (T1-weighted post-contrast sequence) showing almost complete obliteration of cerebrospinal fluid (CSF) signal in the entire spinal tract, with meningeal Gadolinium enhancement around the entire spinal cord.

Conclusion: Despite IgG4-RD HP mainly affects brain meninges, clinicians should be aware that isolated cases of spinal HP could also occur. Such involvement might also warrant for an aggressive immunotherapy due to the risk of long-term neurological disability.
Disclosure: Nothing to disclose.

EPO-089

Determination of which factors are more effective on work difficulties in persons with multiple sclerosis

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Background and aims: Employment is known to significantly contribute to the quality of life in persons with MS (pwMS), and any workplace difficulties that arise directly from MS can play an important role in work life. This study aims to utilize magnetic resonance imaging (MRI) to calculate subcortical gray matter (scGM) volumes to examine the neurological underpinnings of work difficulties in pwMS. The secondary aim is to determine which factors are more effective on work difficulties.
Methods: Twenty-three pwMS employees were included. Physical disability was assessed with Expanded Disability Status Score (EDSS), Timed-25-Foot-Walk (T25FW) test, and Nine-Hole Peg test. Brief International Cognitive Assessment in MS (BICAMS) was used to evaluate cognitive functions. Facial Emotion Identification (FEI), Reading the Mind in the Eyes Test (RMET), and Empathy Quotient (EQ) was used to assess social cognition. ScGM volume calculated with freesurfer from 3T MRI.
Results: According to the linear regression model, cognition and physical disability were not effective factors in work difficulties ($p<0.05$). However, it was found that the decrease in the EQ score, scGM Volume, Total Gray Matter Volume, Left Thalamus, Left Putamen, Left Hippocampus, Right Thalamus, Right Caudate, and Right Hippocampus increased the severity of work difficulties ($p<0.05$).

Risk factors (physical disability) on severity of work difficulties

Risk Factors	Beta Coefficient	95% CI	P value
EDSS	0.228	-3.586; 9.475	0.465
Timed 25 Foot Walk Test	0.009	-1.912; 1.981	0.557
Nine-Hole Peg Test	0.443	-0.002; 5.200	0.228

Risk factors (social cognition and brain volumes) on severity of work difficulties

Risk Factors	Beta Coefficient	95% CI	P value
Reading the Mind in the Eyes Test	-0.411	-5.041; 0.203	0.068
Facial Emotion Identification	-0.192	-2.881; 1.068	0.346
Empathy Quotient	-0.530	-1.527; -0.148	**0.020**

Risk factors (cognition) on severity of work difficulties

Risk Factors	Beta Coefficient	95% CI	P value
Symbol Digit Modalities Test	-0.300	-1.126; 0.338	0.273
California Verbal Learning Test	0.071	-2.097; 2.675	0.398
Brief Visuospatial Memory Test-Revised	-0.266	-1.664; 0.691	0.803

Risk factors (scGM) on severity of work difficulties

Risk Factors	Beta Coefficient	95% CI	P value
Subcortical Gray Matter Volume	-0.057		**0.011**
Total Gray Matter Volume	-0.001		**0.008**
Left Thalamus	-0.084		**0.007**
Left Caudate	-0.004		0.936
Left Putamen	-0.069		**0.041**
Left Hippocampus	-1.141		**0.017**
Left Amygdala	0.035		0.249
Right Thalamus	-0.067		**0.024**
Right Caudate	-0.120		**0.027**
Right Putamen	-0.043		0.244
Right Hippocampus	-0.080		**0.020**
Right Amygdala	-0.038		0.238

Results

Conclusion: This study shows which factor could be more effective on work difficulties in pwMS. There is a highly complex relationship between ScGM, work difficulties, and social cognitive impairment. It is still debatable how the thalamus, hippocampus, putamen, and caudate volumes affect work difficulties and needs to be studied with other employment-related factors in larger groups.
Disclosure: Nothing to disclose

EPO-090

Predictive and diagnostic significance of markers in the progression of HIV encephalopathy in children

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Background and aims: The study included 260 children 153 boys and 107 girls, 59% and 41%, respectively, diagnostic markers in the development of HIV encephalopathy with varying severity were assessed. Diagnostic markers were interpreted by the concentration of IL-6, IL-10, TNF-alpha, C-reactive protein and C3, C4 complement components.
Methods: PCR study, Student's t-test.
Results: The study of indicators in children with HIV found that the concentration of TNF-alpha and IL-6 were increased compared to the reference values (12.67±0.25pg/ml and 23.04±0.64pg/ml, respectively, at the reference, values less than 8.1pg/ml and 7pg/ml, respectively), and the concentration of IL-10 is reduced (5.93±0.10pg/ml with a reference value of more than 9.1pg/ml). The concentration of complement components 3 and 4 as a whole in the entire cohort of children included in the study remained within the normal range and amounted to 1.07 ± 0.05 g/l for C3 and 0.38 ± 0.04 g/l for C4 (reference values are 0.9-2.07g/l and 0.174-0.522g/l, respectively).
Conclusion: An increase in the concentration of IL-6 above 19.6pg/ml is associated with an increase in the risk of developing symptomatic HIVE by 9.14 times, an increase in the concentration of TNF-alpha above 12.5pg/ml – 4.07 times ($P<0.001$ for both factors).
Disclosure: A comparative analysis of the concentration of markers in patients with AND was carried out in comparison with the group of MAD + HAD, and the frequency of occurrence of symptomatic HIVE was determined depending on the diagnostic concentration of markers.

EPO-091

Neural organoids to model neuroinflammation: a systematic review focused on microglia's integration

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Background and aims: Neural organoids are in vitro models, made from human pluripotent stem cells, grown in three-dimensional conditions, which can complement and accelerate neurological research. Neuroinflammation is a common condition to several neurological diseases, in which inflammatory pathways involving nervous system cells lead to neuronal loss and disability. Microglia is thought to play a main role in cell's interaction. Therefore, microglia's integration into neural organoids is crucial to the study of neuroinflammation.

Methods: A comprehensive search was conducted using Embase and PubMed to identify relevant studies. The inclusion criteria were original studies using neural organoids to study neuroinflammation pathways and/or microglia integration. After duplicates and reports excluded (figure 1), 31 articles were included in the review. PRISMA recommendations were followed.

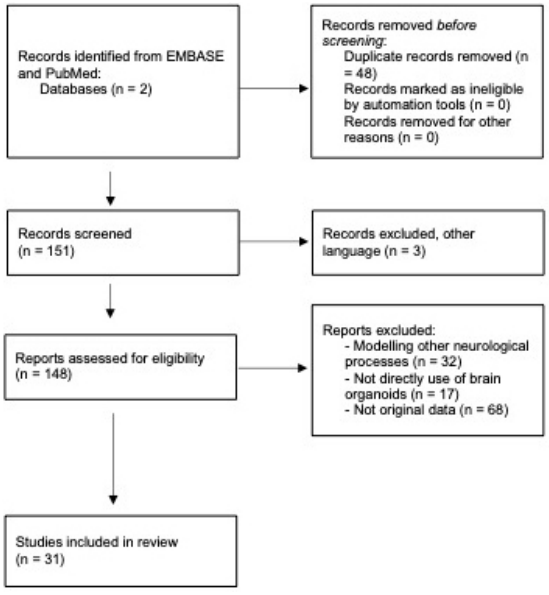

Figure 1. Flow diagram of study selection

Results: Microglia's integration into neural organoids is a bioengineering challenge. This has been achieved through various experimental models that have studied neuroinflammation's pathways in models of different neurological diseases (table 1). The use of cocultures, grafting of organoids into mice and the use of on-a-chip technologies have enabled this integration (figure 2). Different molecular techniques have been used to test the identity and functionality of microglia. There are important limitations regarding the use of neural organoid technology for the study of neurological diseases, notably the lack of standardisation.

Reference	Microglia's integration	Disease	Triggering factor	Main findings
Ormel *et al* (2018), Sun *et al* (2022), Bodnar *et al* (2021)	Innately developed	-	-	Microglia innately develops in neural organoids and assembloids. It mimics the transcriptome and inflammatory response.
Samudyata *et al* (2021)	Innately developed	COVID-19	SARS-CoV-2	Innately developed microglia causes extensive cell death and loss of synapses
Kim *et al* (2022)	Innately developed	AD	SARS-CoV-2	SARS-CoV-2 infection facilitates AD pathology
Winkler *et al* (2019)	Innately developed	La Crosse encephalitis	LACV	Neural maturation increases the susceptibility of neurons to LACV. IFN signaling is protective.
Speicher *et al* (2022), Sabate-Soler *et al* (2022), Popova *et al* (2022), Fagerlund *et al* (2022), Song *et al* (2019), Bejoy *et al* (2019), Gao *et al* (2022), Carroll *et al* (2021)[a], Abreu *et al* (2018), Schwartz *et al* (2015), Berry *et al* (2017)	Coculture at different times into guided and unguided neural organoids.	-	Different inflammatory triggers	Integrated microglia demonstrate in vivo-like phenotype
Mansour *et al* (2018)	Grafting	-	-	Grafted organoids showed integration of microglia and growth of axons of the host brain
Zhang *et al* (2020)	Exposition to activated microglia	Glioblastoma	LPS	dPGS-treated microglia reduce invasion of the tumor in a neural organoid
Cakir *et al* (2022)	Coculture with overexpression of transcription factor and grafting	AD	Aβ protein	Integrated microglia demonstrate in vivo-like phenotype and protects against Aβ
Wenzel *et al* (2022)	Coculture	AD	Aβ protein	Aβ augments the release of cardiolipin from microglia into the extracellular space, where it can enhance the astrocytes and microglia's endocytosis of Aβ
Marotta *et al* (2022)	Coculture of patient-specific cells	PPMS and PD	Microgravity	Dysregulation of cell division, DNA repair, packaging and post-translational modifications.
Xu *et al* (2021)	Coculture	Zika disease	Zika	Integrated microglia demonstrate in vivo-like phenotype and respond to Zika virus infection
Muffat *et al* (2018)	Coculture of infected and uninfected microglia	Zika and Dengue	Zika and Dengue viruses	Microglia may act as a viral reservoir of Zika virus. Zika and Dengue viruses affect the integrity of BBB allowing infection of the brain.
Jin *et al* (2022)	Coculture of patient-specific cells	DS and AD	Tau protein	DS microglia undergo senescence and exhibit elevated type-I-interferon signaling
Dos Reis *et al* (2020), Gumbs *et al.* (2022)	Coculture of infected and uninfected microglia	HAND	HIV infection	Infected organoids exhibited increased inflammatory response
Nzou *et al* (2020)	Coculture	BBB dysfunction	Hypoxia	Anti-inflammatory agents in neural organoids showed reduced damage to hypoxic condition
Ao *et al* (2021)	On-a-chip	Substance use disorder	Opioid receptor agonist	Microglia responds after exposure to opioid receptor agonist

Table 1. Approaches of microglia's integration into neural organoids and different neuroinflammatory pathways and diseases studied.
Abbreviations: AD: Alzheimer's disease, Aβ: Amyloid-beta, BBB: blood-brain-barrier, dPGS: dendritic polyglycerol sulfate, DNA: deoxyribonucleic acid, DS: Down's syndrome, HAND: HIV-associated neurocognitive disorder, HIV: human immunodeficiency virus, IFN: interferon, LACV: La Crosse virus, LPS: lipopolysaccharide, PD: Parkinson's disease, PPMS: primary progressive multiple sclerosis. [a]Murine cells.

Table 1. Approaches of microglia's integration into neural organoids and different neuroinflammatory pathways and diseases studied.

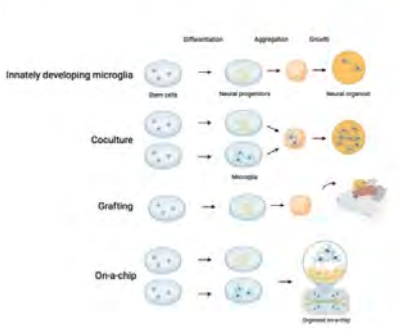

Figure 2. Microglia's integration into neural organoids

Conclusion: The use of neural organoids with integrated microglia is a novel and promising tool for the study of neuroinflammation. It can be used as disease models for the study of neurological disease's pathophysiology, the discovery of new therapeutic targets and the development of new treatments.

Disclosure: The authors present no disclosures or conflict of interest.

EPO-092

Prognostic value of quantitative and longitudinal CASPR2/LGI1 antibody testing in patients with autoimmune encephalitis

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Background and aims: Autoantibodies against Leucine-rich glioma-inactivated 1 (LGI1) and anti-contactin-associated protein-like 2 (CASPR2) are diagnostic and pathogenic markers of of autoimmune encephalitis (AE). We aimed to study the relevance of longitudinal anti-LGI1/CASPR2 titres.
Methods: Retrospective cohort study including patients with anti-LGI1/CASPR2 definite AE, and at least one available longitudinal sample > 60 days from onset. Titers were measured with endpoint dilution using a live cell-based assay. Sixteen/99 samples (16%) were classified as from "acute phase", 15 (15%) as "postacute" and 68 (69%) as "remission". Outcome was measured with modified Rankin Scale (mRS) and with Clinical Assessment Scale in Autoimmune Encephalitis (CASE).
Results: We enrolled 18 patients (anti-CASPR2=7; LGI1=11). Median age at diagnosis was 63 (range:46-83), and 7 were females. Manifestations at onset included seizures (18/18), psychiatric symptoms (10/18) and cognitive dysfunction (9/18). Median follow-up was 31 months (range 3-57). Seven/18 patients had relapses. Acute phase samples had higher median titres (1:10400, range 400-102400) compared to post-acute (1:3200) and remission (1:200) samples ($p<0.001$), even analyzing separately anti-LGI1 ($p<0.001$) and CASPR2 ($p=0,0197$) sera. Titres did not correlate with disease severity at onset/follow-up. Relapses always occurred with a positive sample (n=7), and in 3 patients with pre-relapse samples available titres increased at relapse. Seven patients became seronegative (2 with anti-CASPR2, 4 after rituximab) after a median time from diagnosis of 12 months (range 5–58), and none experienced post-seroconversion relapses.
Conclusion: Anti-CASPR2/LGI1 titres correlate with disease phase. Seroconversion-to-negative might associate with treatment and relapse risk. warranting further studied on antibody-titres as a biomarker in AE.
Disclosure: Nothing to disclose.

EPO-093

A case of treatment-refractory anti nuclear-rim necrotizing autoimmune myositis

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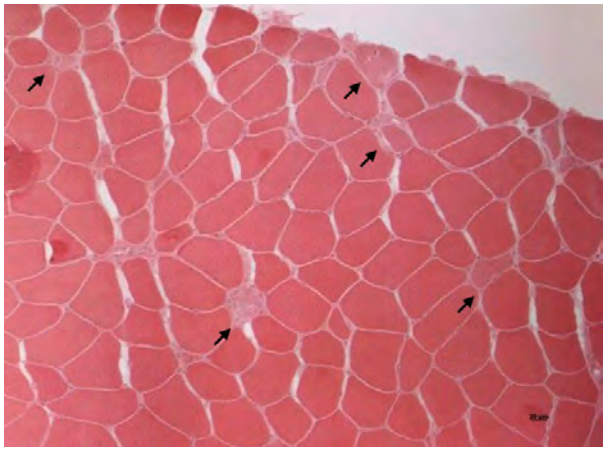
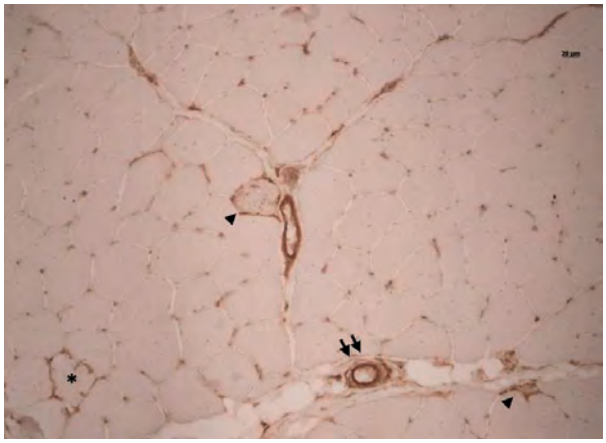
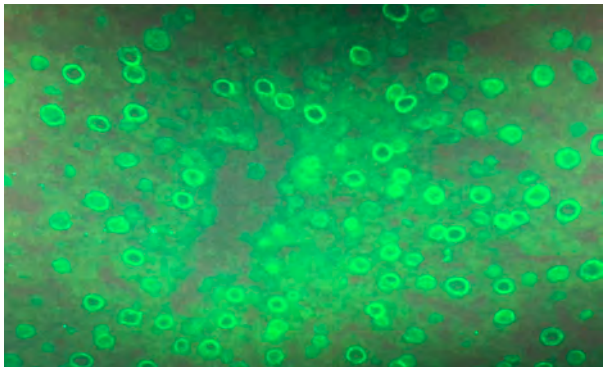
Background and aims: We describe the case of a 30-year-old patient affected by necrotizing autoimmune myositis with predominantly bulbar symptoms and positivity for anti-nuclear-rim antibodies.
Methods: We report this case detailing medical and clinical history together with histological, genetic and autoimmune tests.
Results: A 30-year-old male was referred to our department due to onset of dysphagia and dysarthria. High CPK levels and electromyographic test were consistent with acute autoimmune myositis. Despite the presence of an anti-nuclear-rim pattern of antinuclear antibodies, myositis-specific autoantibodies panel tested negative. Muscular biopsy was then performed and showed a necrotizing autoimmune myositis. Patient was then treated with high-dose steroids, with a rapid, but incomplete, response. Due to persistent clinical and biochemical abnormalities, intravenous immunoglobulins (2g/kg over 5 days) and cyclophosphamide (1 g/m^2) were administered. Due to a clinical and biochemical relapse patient was re-treated with high-dose steroids followed by rituximab (two 1 g infusions 15-day apart). A complete and long-lasting response was then achieved. Genetic analysis tested positive for HLA DQA1 (02:01, 03:01) and DQB1 (02:01, 03:02) haplotypes, described in some cases of autoimmune myositis associated with antibodies anti-nuclear pore complex.
Conclusion: In this report we show a case of anti-nuclear-rim autoimmune myositis showing that, albeit rare, this autoimmune pattern reflects the presence of a necrotizing myositis that could be refractory to conventional treatment and might need rituximab administration to induce a long-lasting remission.



Haematoxylin-Eosin staining (magnification 20x). Several necrotic or degenerating fibres are evident (arrows).



Immunoperoxidase with antibody against MHC class 1 (magnification 20x). The reaction is focal in some fibres both at the sarcolemma (asterisk) or at the sarcoplasm level (arrow heads). Vessels are also positive (double arrows).



Anti-nuclear-rim pattern of antinuclear antibodies.

Disclosure: Conflict of Interest Disclosures: None reported.

EPO-094

Carpe protocol: chronic ambulatory treatment with rituximab and plasma exchangefor immune-mediated neurologic disorders

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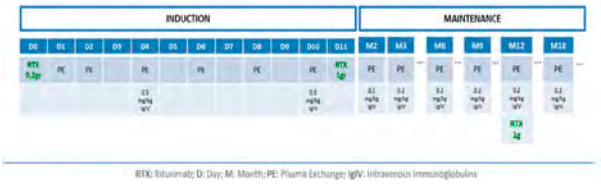
Background and aims: In acute or subacute immune-mediated disorders such as autoimmune encephalitis, treatment with steroids, plasma exchange (PE), or intravenous immunoglobulins (IVIg), and rituximab or cyclophosphamide is widely used. In contrast, for chronic presentations the long-term use of PE has not been explored, and therapeutic options are very limited.
Methods: CARPE protocol (Fig.1) comprises: 1) an induction phase (days 0 to 11), with rituximab combined with 6 PE and 2 IVIg sessions; and 2) a maintenance phase (monthly sessions), in which one PE is followed by IVIg on the same day.



Carpe Protocol Schedule

Results: Nine patients (5 males); median age 45 years (range 31-72) were included. Four had polyneuropathy (2 chronic idiopathic demyelinating polyneuropathy, 1 with anti-disialosyl IgM antibodies, and 1 anti-Hu); 3 drug-resistant epilepsy (2 with anti-GAD65, and 1 anti-Ma2); and 2 other anti-GAD65 associated syndromes (1 stiff-person syndrome; 1 cerebellar ataxia). Seven patients previously received diverse therapies (5 IVIg, 4 rituximab, 3 steroids, 2 azathioprine or mycophenolate, 1 cyclophosphamide, 1 hematopoietic stem-cell transplantation), and 2 patients received CARPE as initial therapy. After a median follow-up of 8 months (range 6-31), including a median of 7 maintenance PE (range 5-18), all patients remained in the protocol. We observed clinical stability or mild improvement in all. Anti-GAD65 titers decreased in 3 of 4 patients. Adverse events were mild: headache (7 patients), presyncope (2), hypoglycemia (1) and compressive radial nerve neurapraxia (1)
Conclusion: CARPE is a safe and well tolerated therapeutic option for patients with established immune-mediated neurologic disorders.
Disclosure: Nothing to disclose.

EPO-095

Neuropsychiatric symptoms and sleep disorders in autoimmune encephalitis: from the acute stage to the long term

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Background and aims: Autoimmune encephalitis (AE) involves neuropsychiatric changes during the acute stage, which vary from mild mood disorders to overt psychosis. Sleep disruption is also increasingly identified, being a prominent feature of certain types of AE. However, how both these issues evolve in the long-term is not well defined. We aim to characterize sleep and mood disorders in this setting.
Methods: Observational cross-sectional study, including ≥18-yo patients diagnosed with AE followed at a Portuguese tertiary centre (January 2007-December 2021). Sociodemographic and clinical data were obtained from electronic records. Questionnaires to evaluate sleep quality and anxiety and mood disorders were applied (Satisfaction, Alertness, Timing, Efficiency and Duration Questionnaire for Sleep Health Measurement [SATED-RU]; Pittsburgh Sleep Quality Index [PSQI-PT], Hospital Anxiety and Depression Scale [HADS]).
Results: We enrolled thirteen patients (median follow-up 62 months [29-97.5]). The median age on evaluation was 44-yo; 5(38.5%) were female. Five patients (38.5%) had anti-NMDAR, 3(23.1%) anti-LGI1, 1(7.7%) anti-neurexin, 1(7.7%) anti-Gluk2, 1(7.7%) anti-Yo, and 2(15.4%) had seronegative AE. During the acute stage most patients had neuropsychiatric and behavioral changes (n=11, 85.4%); sleep was inconsistently recorded, but insomnia was reported in 7 (53.8%). During follow-up 3 subjects presented mild depression (23.1%); anxiety frequency was 38.5%. No patient experienced mania or psychosis. Five patients (38.5%) reported bad sleep quality, scoring higher with greater admission delay (r=0.574, p=0.040).
Conclusion: We found subtle but frequent disturbances in mood, anxiety and sleep quality in this sample. If not systematically evaluated, these changes might go unrecognized and if left untreated can significantly impair patients' quality of life.
Disclosure: The authors have nothing to declare.

EPO-096

Clinical characteristics and predictors of relapse in anti-LGI1 encephalitis

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Background and aims: Autoimmune encephalitis (AE) with antibodies against leucine-rich glioma-inactivated 1 (LGI1) is usually monophasic, but approximately 15% of patients experience a relapse. Herein, we aim to clinically characterize the relapses and identify factors predicting their appearance.
Methods: Retrospective chart review of patients with isolated LGI1-antibody positivity in serum and/or cerebrospinal fluid (CSF). Relapse was defined as a worsening of previous symptoms or appearance of new symptoms after clinical stabilization.
Results: Among 216 patients with enough clinical data, we identified 30 (14%) that experienced a total of 33 relapses (table 1, figure 1). The median time to first relapse was 23.9 months (range 4.9-110.1). During relapses, clinical manifestations included memory impairment (70%), psychiatric/behavioral symptoms, facio-brachial dystonic and temporal lobe seizures (30% each). Brain imaging was abnormal in 16/26 (62%), while CSF was inflammatory in 13/25 (52%). LGI1-antibody testing was positive in 16/23 in serum (70%) and in 9/21 (43%) in CSF. At last follow-up 14 patients (47%) had a poor outcome. Patients that relapsed did not differ in their initial clinical and paraclinical features from a group of 85 patients that did not relapse and had similar length of follow-up (table 2). However, residual cognitive dysfunction after the initial episode was significantly associated with an increased risk of relapse (hazard ratio = 9.5, 95% confidence interval 1.7-182.0, p=0.038).

Table 1: Summary of main clinical and paraclinical features during the relapses.

	Relapses (n=33)
Median age at relapse, years (range, IQR)	68 (30-90; 14)
Median delay onset-first relapse, months (range, IQR)	23.9 (4.9-110.1, 17.8)
Median delay stabilization-relapse, months (range, IQR)	10.2 (2.5-85; 11.2)
Relapse occurring under immunotherapy	8 (24)
Median follow-up after relapse, months (range, IQR)	15.7 (0.3-65.6, 20.8)
Relapse onset	
Acute	6 (18)
Subacute	27 (82)
Clinical features	
Memory impairment	23 (70)
FBDS	10 (30)
TLS	10 (30)
Other seizures	8 (24)
Psychiatric	10 (30)
Other symptoms[a]	11 (33)
Hyponatremia	4/28 (14)
mRS score	3 (2-5; 1)
CASE score	3 (0-8; 2)
Paraclinical findings	
T2/FLAIR hyperintensity of limbic structures on brain MRI[b]	14/26 (54)
EEG documenting ictal activity	3/25 (12)
Inflammatory CSF	13/25 (52)
Mean CSF protein content (n=20)	0.58 ± 0.48
Mean CSF leukocyte count (n=20)	14.9 ± 48.2
Oligoclonal bands	0/16 (0)
LGI1-Ab positivity in serum	16/23 (70)
LGI1-Ab positivity in CSF	9/21 (43)
Altered metabolism in brain FDG-PET	2/5 (40)
Treatment	
IVIG	9 (27)
CS	15 (45)
RTX	19 (58)
Cyclophosphamide	10 (30)
Outcome (n=30 patients)	
Median mRS (range, IQR) after encephalitis and relapse	2 (0-6, 2)
Poor outcome (mRS ≥3)	14 (47)
Cognitive dysfunction	23 (77)

[a] sleep disturbances, 4; repeated falls and gait instability, 2; mood disorders, 2; abnormal limb movements, 1; buccal dyskinesia, 1; aphasia, 1.

[b] 2/26 patients developed T2/FLAIR hyperintensity of other areas (1 basal ganglia, 1 cerebellar peduncles and mesencephalon).

Abbreviations: IQR, interquartile range; FBDS, faciobrachial dystonic seizures; TLS, temporal lobe seizures; mRS, modified Rankin Scale; CASE, Clinical Assessment Scale in Autoimmune Encephalitis; MRI, magnetic resonance imaging; EEG, eletroencephalogram; CSF, cerebrospinal fluid; LGI1, leuchine-rich glioma-inactivated protein 1; Ab, antibody; FDG-PET,

Table 2: Characteristics of the initial encephalitis episode in relapsing patients compared to the control group.

	Relapsing patients (n=30)	Control group (n=85)	p
Median age at onset, years (range, IQR)	66 (29-86, 17)	64 (21-83, 14)	0.30
Male sex	23 (77)	51 (60)	0.10
Median diagnostic delay, days (range, IQR)	73 (18-3339, 130)	136 (2-1530, 161.5)	0.09
Median follow-up, months (range, IQR)[a]	23.9 (4.9-110.1, 17.8)	36.2 (24.4-156.7, 26)	< 0.001
Clinical features			
FBDS	14 (47)	45 (53)	0.55
TLS	14 (47)	48 (56)	0.35
SE	2 (7)	7 (8)	1
Other seizures	21 (70)	54 (64)	0.52
Psychiatric/behavioural	26 (87)	62 (73)	0.13
Memory impairment	29 (97)	83 (98)	1
Maximal mRS	3 (2-5, 1)	3 (1-5, 1)	0.13
Paraclinical findings			
Inflammatory CSF	20 (67)	40/82 (49)	0.09
Pleocytosis (>=5 cells/mm^3)	4/29 (14)	15/84 (18)	0.78
LGI1-Ab positivity in CSF	24 (80)	62/79 (78)	0.86
ICU admission	4 (13)	10/80 (13)	0.91
Hyperintensity of limbic structures on MRI	20/29 (69)	62/84 (74)	0.61
First-line treatment			
IVIG only	4 (12)	15 (18)	0.78
CS only	2 (7)	8 (9)	1
Combination IVIG+CS	23 (77)	59 (69)	0.45
Median delay onset-start of any first-line therapy, days (range, IQR)	81 (17-360, 118)	145 (6-750, 156.5)	0.013
Second-line treatment	18 (60)	48 (56)	0.74
RTX only	6 (20)	15 (18)	0.77
Cyclophosphamide only	3 (10)	8 (9)	1
RTX + cyclophosphamide	9 (30)	26 (31)	0.95
Median delay onset-start of any second-line therapy, days (range, IQR)	167.5 (43-960, 105)	230 (55-1516, 214.5)	0.09
Chronic oral immunosuppression	5 (17)	16 (19)	0.79
Outcome			
Median mRS (range, IQR)[b]	1 (0-4; 1)	1 (0-5, 2)	0.75
Poor outcome (mRS ≥3)	6 (20)	14 (16)	0.66
Cognitive dysfunction	23 (77)	51 (60)	0.1

[a] time to relapse in the relapsing group

[b] after encephalitis resolution and clinical stabilization in the relapsing group, and at last follow-up in the control group

Abbreviations: IQR, interquartile range; FBDS, faciobrachial dystonic seizures; TLS, temporal lobe seizures; SE, status epilepticus; mRS, modified Rankin Scale; CSF, cerebrospinal fluid; LGI1, leuchine-rich glioma-inactivated protein 1; Ab, antibody; ICU, intensive care unit; MRI, magnetic resonance imaging; IVIG, intravenous immunoglobulins; CS, corticosteroids; RTX, rituximab.

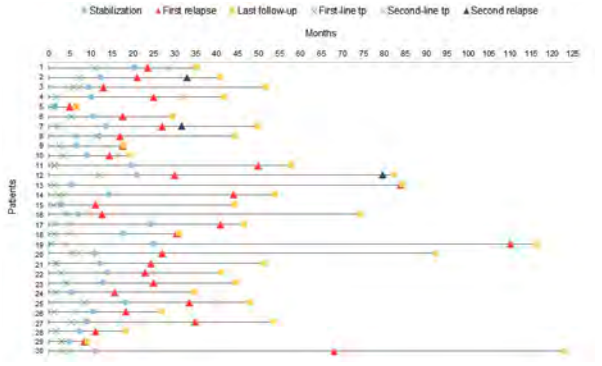

Figure 1: Swimmer plot illustrating the disease course and treatment of the relapsing patients.

Conclusion: Relapses can occur years after the initial episode of LGI11-encephalitis and should be suspected even without paraclinical signs of inflammation. Residual cognitive dysfunction after initial encephalitis increases the risk of future relapses.

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EPO-097

Fixed cell-based assay vs live cell-based assay for MOGAD diagnosis: a comparative study

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Background and aims: Myelin Oligodendrocytes Glycoprotein-Antibodies (MOG-Abs)-associated disease (MOGAD) is an inflammatory disorder in which the diagnosis relies on MOG-Abs presence in patients with a compatible phenotype. The gold-standard for MOG-Abs

detection is live cell-based assay (LCBA), but commercial fixed cell-based assays (FCBA) are often used. Previous studies comparing LCBA vs FCBA reported a lower specificity in FCBA and similar sensitivity. Aim of the study was to characterize patients tested negative on LCBA but positive on FCBA in a prospective French cohort.
Methods: Serum samples referred for MOG-Abs testing were analyzed using both techniques (Euroimmun FCBA, in-house LCBA). Clinical information were collected by the referring physicians. Two neurologists reviewed the clinical records and classified the cases into 3 groups: MOGAD, Multiple Sclerosis (MS), other neurological disorders (OND).
Results: Overall, 222/1166 prospective samples tested positive for MOG-Abs, 151/222 were positive with both techniques, 11 were positive only on LCBA, 71 were positive only on FCBA. Clinical information was available for 40/71 patients. Of these 40 patients, median age at onset was 36.5 [IQR 24.5-49.4], 60% were female. Clinical presentation at onset were optic neuritis (37.5%), myelitis (37.5%), brainstem syndrome (20%), cerebral focal syndrome (10%), cortical syndrome (7.5%) and ADEM (2.5%). Final diagnosis was MOGAD in 17/40 (42.5%), MS in 14/40 (35%), OND in 9/40 (22.5%). Two patients fulfilled diagnostic criteria both for MOGAD and NMOSD.
Conclusion: Though FCBA is associated to a risk of false positive results, testing with both LCBA and FCBA could increase diagnostic accuracy for MOGAD.
Disclosure: Nothing to disclose.

EPO-098

A non-invasive approach to demonstrate the underlying neuroinflammatory responses to severe TBI

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Background and aims: Neuroinflammation is a secondary injury mechanism that contributes to significant mortality and morbidity with severe traumatic brain injury (sTBI). Therefore, the application of non-invasive methods for detecting the neuroinflammatory response is of great interest. This study assessed the temporal profile of ionised calcium-binding adaptor molecule 1 (Iba1) and transmembrane Protein 119 (TMEM119) microglia marker proteins in the urine of sTBI patients for 7 days post-injury as a method of conceptualising the underlying neuroinflammatory response.
Methods: Urine samples were acquired from fifteen patients with sTBI upon hospital admission and the subsequent 7 days post-injury. Western blot analysis was used to quantify the urinary levels of Iba-1 and TMEM119 expression in each sample. The patients were stratified by functional outcomes (group 1, death- vegetative state; group 2, moderate-to- severe disability; group 3, good outcomes).
Results: Iba1 was detected in all (100%) whilst TMEM119 was detected in 65% of urine samples. The mean total normalised Iba1 expression increased for group 2 whilst the opposite response was observed for groups 1 and 3. The mean total normalised TMEM119 expression decreased for group 3 whilst the opposite response was observed for groups 1 and 2. However, these findings were not statistically significant. No significant differences were found in Iba1 or TMEM119 expression between favourable and unfavourable outcome groups.
Conclusion: Overall, this study cannot associate urinary Iba1 or TMEM119 expression with functional outcomes. However, the presence and temporal patterns of the urinary microglia markers suggest it may be reflective of the underlying neuroinflammatory process and merits further studies.
Disclosure: Nothing to disclose.

EPO-099

Autoimmune encephalitis during pregnancy: a diagnostic and therapeutic challenge

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Background and aims: Autoimmune encephalitis (AE) is one of the most common causes of noninfectious encephalitis in youth. In this systematic review, we summarize and analyze the available data on the diagnostic and therapeutic approach to AE during pregnancy, highlighting the associated maternal and fetal clinical outcomes.
Methods: A systematic search of the literature to identify the diagnostic and therapeutic management of AE during pregnancy and the associated maternal and fetal clinical outcomes was performed.

Results: Data from 49 patients were extrapolated. AE onset was mainly observed during the first trimester of pregnancy. Psychiatric manifestations and seizures were the first clinical symptoms. Cerebrospinal fluid (CSF) analysis was reported in 39 cases. Cellular pleocytosis was found in 30 and AE-specific autoantibody positivity in 33 patients. The most frequent autoantibodies detected were against the anti-NMDA receptor. EEG was performed in all patients, with 21 showing normal findings. Thirteen patients presented hyperintense signal changes on T2-FLAIR sequences, mostly in the temporal region. Tumor screening was reported in 45 cases, with positive findings in 14. Forty-four patients were treated with single or combination first-line immunosuppressants. Most of the women had an excellent early outcome after delivery. In long-term follow-up, 22 women showed persistent neurological deficits. Twelve cases of fetal death were reported. Newborn outcome was normal in 33 cases.
Conclusion: The diagnosis and treatment of AE during pregnancy are challenging. Caution should be paid to the potential teratogenic effects of several medical and diagnostic interventions. Maternal and fetal outcomes are mostly positive, although mothers may show long-term neurological deficits.
Disclosure: Nothing to disclose.

EPO-100

Proximal myopathy as a prominent feature of anti-IgLON5 disease

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Background and aims: Anti-IgLON5 disease is a novel entity, and recognizing all clinical symptoms and clues for diagnosis is therefore important. We specifically investigate the neuromuscular symptoms, and provide a link between IgLON5 and biopsy-proven myopathy. Moreover, response to immunotherapy is assessed.
Methods: All patients diagnosed in the Netherlands between 2016 and 2021 were included. National coverage was ascertained.
Results: Fifteen patients with anti-IgLON5 disease were included. Seven patients (47%) were male, the median age at symptom onset was 62 years (range 45-85). The median time from symptom onset to diagnosis was six years (range 0.6-23). Most striking were the neuromuscular symptoms, present in 7/15 patients (47%), including proximal muscle weakness (n=7), atrophy (n=5), and fasciculations (n=3). Muscle biopsy in six of them confirmed myopathy, with myopathic alterations in all, neurogenic lesion in one and immune cell infiltration in another patient. Other symptoms were sleep disorders (n=12), gait abnormalities (n=13), movement disorders (n=12), bulbar symptoms (n=10), dysautonomic symptoms (8/14), behavioural changes (n=8) and cognitive disorders (n=6). The median follow-up time since symptom onset was 90 months (range 12-297). Eleven patients (73%) were treated with first-line immunotherapy, showing a partial or temporary response in ten of them (91%). Eight of them were treated with second-line therapy (rituximab), showing some response in 4/7 patients and stabilization in 1/7 of the patients in which the effect could be assessed.
Conclusion: We found proximal myopathy as a new clinical feature in anti-IgLON5 disease. This finding extends the clinical phenotype and can be an important clue for diagnosis.
Disclosure: Nothing to disclose.

COVID-19; Infectious diseases 1

EPO-101

MRI findings in viral meningo-encephalitis – a study of 129 patients

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Background and aims: In workup of acute encephalitis (E) and meningoencephalitis (ME) brain magnetic resonance imaging (MRI) is essential to confirm and rule out alternative diagnoses, but is not an established prognostic tool. We aimed to 1) systematically describe MRI findings in patients (p) with viral E/ME 2) identify eventual MR related factors predicting clinical outcomes.
Methods: We conducted a retrospective analysis of p with E who underwent MRI scan and were treated in Inselspital 2016 - 2018.
Results: From a total of 258 p included in the original study (1), 129 made part of our analysis. Of 129 p, 28 were classified as E and 101 as ME. Most frequent causes were tick borne encephalitis in 54 (TBE, 42%), varicella zoster virus in 9 (VZV, 7%) and herpes simplex virus I in 7 (HSVI, 5%). In 52 (40%) p, disease cause remained unclear. First MRI were performed 7 days (median, IQR: 10) after symptom onset. Overall, abnormal diffusion-weighted imaging (DWI) and/or fluid attenuated inversion recovery (FLAIR) was found in 17 and 30%. All HSVE p had abnormal FLAIR and DWI scans, 27% of TBE and 31% of unknown E cases had abnormal MRI findings, most importantly FLAIR sequences showed signal abnormalities.
Conclusion: Rates and localization of MRI changes in different infectious causes of E vary significantly. Most important MRI changes are found in FLAIR sequences. Whether localization and lesion load correlates with clinical outcome is currently analysed. Results will be presented at the congress.
Disclosure: Nothing to disclose.

EPO-102

The return of spread of meningitis?: The drop in child vaccinations after the COVID-19 pandemic

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Background and aims: In Brazil, that drop of vaccination in children made the meningitis rate increase from 2021 to 2022, approximately 1000 cases were registered in some states, and this alarmed WHO and other world institutions. The principals risk factors of meningitis are extremes of age, undervaccination, exposures and chronic medical disorders. Among these risk factors, the current drop in vaccination has been prevalent in the world after the COVID-19 pandemic period. Related to the low demand for health services and the concentration of efforts on caring for patients affected by coronavirus, there was a large wave of anti-vaccination. Furthermore, international studies showed that the global vaccination coverage continued to decline in 2021.
Methods: Ecological study, based on interrupted time series, carried out with data collected through the European Health for All database (HFA-DB).
Results: According to the HFA-DB, the WHO European region has a vaccination rate of Tdap vaccine from 95,8% in 2013 to 94,3% in 2020, Measles 95,1% in 2013 to 94,2% in 2020, HBV in 2018 94,1% to 93% in 2020 and Hib in 2013 with 93,1% to 94% in 2019 to drop to 93,3% in 2020.
Conclusion: The covid-19 pandemic has fueled an ongoing backlash in vaccinations, which has been achieved through decades of advertising and studies. Mainly, in European countries, it is necessary to observe and disseminate more news and research that influence the immunization of children from birth. Thus, reversing the decline in vaccination and increasing prevention against meningitis.
Disclosure: No potential conflict of interest was reported by the author.

EPO-103

Immune Response Following COVID-19 Vaccination (mRNA or Non-mRNA) in Evobrutinib-treated Patients with RMS: An Update

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Background and aims: Evobrutinib is a highly selective, CNS-penetrant, covalent Bruton's tyrosine kinase inhibitor currently under clinical investigation for the treatment of relapsing multiple sclerosis (RMS). Building on our previous findings, we investigated the humoral response of evobrutinib-treated patients with RMS (PwRMS) to mRNA and non-mRNA COVID-19 vaccination during the open-label extension (OLE) of a Phase II clinical trial (NCT02975349).

Methods: A post hoc analysis was performed among PwRMS who received both evobrutinib 75mg twice-daily and COVID-19 vaccines during the OLE period (n=45; mRNA n=37, non-mRNA n=8; booster n=14). Immunoglobulin G (lgG) anti-S1/S2 (SARS CoV-2 spike protein domains) specific COVID-19-antibodies were measured using an indirect chemiluminescence immunoassay (DiaSorin Molecular LLC, USA; lower limit of quantification, 3.8AU/ml; seronegative<15.0 AU/ml, seropositive≥15.0 AU/ml).
Results: Baseline mean(±SD) age of patients was 46.0±9.6 years, 68.9% were female and mean/minimum evobrutinib exposure pre-vaccination was 105.2/88.7 weeks. Of 45 evobrutinib-treated patients, 43 developed or increased S1/S2 lgG antibody levels post-vaccination (Table1). Patients who were either S1/S2 lgG seronegative or seropositive pre-vaccination demonstrated an antibody response post-vaccination. Most patients (n=36/45), whether seronegative or seropositive, demonstrated a 10–100-fold increase of S1/S2 lgG antibody levels from pre- to post-vaccination (Table2). S1/S2 lgG levels post-booster were higher versus post-vaccination.

	mRNA Covid vaccinated patients n=37	Non-mRNA Covid vaccinated patients n=8
Pre-vaccination	8.5±4.3	12.1±3.2
Post-vaccination	247.7±4.5	197.1±6.2

Data are represented as geometric mean ± SD, AU/mL

Table 1: S1/S2 lgG antibody levels at pre- and post-vaccination time-points (by vaccine type)

S1/S2 lgG antibody levels	Seronegative patients n=32	Seropositive patients n=13	All patients N=45
Pre-vaccination	4.3 ± 1.3	55.5 ± 4.0	9.0 ± 4.0
Post-Vaccination	133.6 ± 3.7	984.4 ± 2.9	237.8 ± 4.7
Fold change from pre- to post-vaccination	31.0 ± 3.4	17.7 ± 3.3	26.4 ± 3.4

Data are represented as geometric mean ± SD, AU/mL
Fold change are ratio between the post-dose and pre-dose IgG antibody levels

Table 2: S1/S2 lgG antibody levels at pre- and post-vaccination time-points (by serostatus at pre-vaccination)

Conclusion: This analysis supports our prior data showing that evobrutinib-treated PwRMS can mount an antibody response to mRNA COVID-19 vaccination. These results provide additional evidence that evobrutinib-treated PwRMS can mount a humoral response to COVID-19 vaccinations and that, with boosters, antibody levels increase further than after the first vaccination cycle.
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EPO-104

Does serum and CSF cytokine dosage differ between post- and para-infectious SARS-CoV-2-related Guillain-Barré Syndrome?

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Background and aims: Guillain–Barré syndrome (GBS) is a postinfectious immune-mediated polyneuropathy, which pathogenic hypothesis comprises virus-related neuropathogenic mechanisms and hyperacute immune response. We explored the hypothesis of a hyperacute immune response by dosing cytokines on CSF and serum of patients with SARS-CoV-2-related GBS.
Methods: Twenty-six patients with SARS-CoV-2-related GBS were divided in two groups: 1) "classic onset", 2) "parainfectious onset, according to whether they developed GBS after 7 days or before 7 days from COVID-19 onset. We dosed cytokines (IL-1b, IL-6, IL-8, TNF-alpha) on CSF and serum, compared the dosages in both groups and correlated the dosage of each cytokine with the severity of both infection and GBS, both at onset and at last follow-up.
Results: Fifteen patients were listed in the "classic onset" group (F = 6, mean age 62) and 11 in the "parainfectious onset" group (F = 4, mean age 62). Sixteen patients developed COVID-19 pneumonia, 9 developed upper respiratory tract infection and 1 developed gastrointestinal symptoms; 7 were admitted in ICU, 8 were not hospitalized. The mean GBS disability scale (GBS-DS) was 4 at onset and 2 at follow-up. We found no difference in the total amount of cytokines in serum and CSF between the two groups. No correlation was found between the dosage of each cytokine and severity of COVID-19 and GBS-DS both at onset and follow-up.
Conclusion: Since our observations showed no differences in the amount of cytokines between the two groups, we can conclude that the cause of a parainfectious onset must be other than hyperacute immune response.
Disclosure: The authors declare that they have no competing financial interests.

EPO-105

FATIGUE IN POST-COVID SYNDROME: A POSSIBLE CENTRAL ETIOLOGY?

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Background and aims: Post-COVID syndrome consists in symptoms persistence for more than 12 weeks after acute infection begins. Fatigue is a frequent and long-lasting symptom, its pathophysiology is still unclear. We assessed fatigue presence with a validated questionnaire (short modified fatigue impact scales sMFIS5) and investigated possible correlations between perceived fatigue and brain metabolism in patients with post-COVID syndrome.
Methods: We considered two patients populations visited in our clinic for post-COVID syndrome: P1 (69 subjects affected by neurological symptoms other than fatigue; 35 females; mean age: 59 +/- 12 years) and P2 (260 subjects not affected by any neurological symptom; 97 females; mean age: 64 +/- 11 years). 18 P1 pts (P3; mean age: 67 +/- 8 years; 10 females) performed brain FDG-PET at least six months after COVID resolution. PET images were processed using SPM12 to assess correlation between sMFIS scores and regional metabolism, considering inter-individual sex and age differences. P value of 0.001 uncorrected at voxel level and of 0.05 FWE corrected at voxel level were considered significant.
Results: Fatigue (sMFIS greater than or equal to 5) was prevalent in P1 (76%) than in P2 (47%). In P3 sMFIS scores were 9.1 +/- 3.2. Voxel-wise correlation of sMFIS scores with brain metabolism revealed a left temporal pole significant cluster, with lower relative metabolism linked to higher levels of perceived fatigue.
Conclusion: Our data suggest a possible fatigue central etiology since observed fatigue higher levels in P1 and an association between long-term fatigue and temporal dysfunction after Sars-Cov2 infection.
Disclosure: Nothing to disclose.

EPO-106

Not myopathic, but autonomic changes in patients with Long-COVID Syndrome (PASC).

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Background and aims: Neurological sequelae following SARS-CoV-2 infection still represent a serious concern both for neurologists and neuroscientists. In our paper, we investigated myalgia and fatigue as symptoms in Long-COVID patients with an electrophysiological approach, comprising the evaluation of sympathetic skin responses (SSRs) and quantitative Electromyography (qEMG).
Methods: 12 patients were enrolled, referred to our attention because of myalgia, pain or muscle cramps, which persisted about six months after the diagnosis of SARS-CoV-2 infection. They underwent conventional Electroneurography (ENG), needle electromyography (EMG) and SSRs; moreover, qEMG was performed by sampling at least 20 Motor Unit Potentials (20-30 MUPs), during weak voluntary contraction, in deltoid and tibialis anterior muscles. The mean duration, amplitude, and percentage of polyphasic potentials were assessed and compared with healthy and age-matched volunteers.
Results: ENG did not disclose significant changes compared to healthy subjects; qEMG showed MUPs similar to those recorded in healthy volunteers, in terms of polyphasia (deltoid: p=0.24; TA: p=0.35), MUP area (deltoid: p=0.45; TA: p=0.44), mean duration (deltoid: p=0.06; TA: p=0.45) and amplitude (deltoid: p=0.27; TA: p=0.63). SSRs were not recordable from lower limbs in seven patients (58%), and from the upper ones in three of them (25%). In remaining cases, SSR latencies are significantly longer compared to healthy volunteers when recorded from lower limbs (p=0.0019).

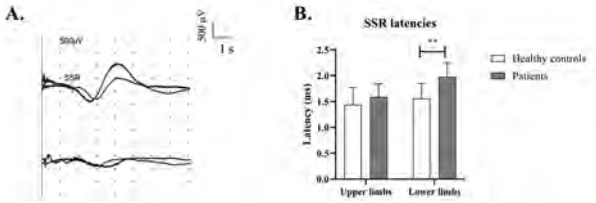

Figure 1 – Neurophysiological evidence of a small-fibers neuropathy (SFN).

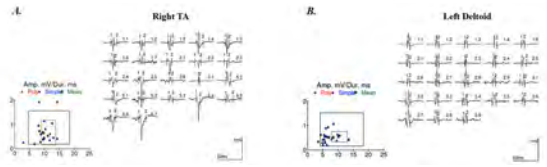

Figure 2 – Quantitative EMG in a representative long-COVID patient.

Conclusion: Our data suggest an involvement of the autonomic system, with a focus on cholinergic efferent sympathetic activity, without any evidence of myopathic changes.
Disclosure: Nothing to disclose.

EPO-107

DNA of herpesviridae is not detectable in cerebrospinal fluid of patients with neurological symptoms in Post-COVID-19

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Background and aims: Underlying pathophysiological mechanisms of Post-COVID-19 syndrome (PCS) are yet to be determined, but one of the possible mechanisms contributing to PCS is the reactivation of latent herpesviruses. In this study, we analyzed cerebrospinal fluid (CSF) and blood for viral DNA via PCR in PCS patients with neurological symptoms.
Methods: Patients fulfilling WHO PCS criteria and with a positive SARS-CoV-2 PCR result at least three months before presentation were included. Preexisting neurological and psychiatric diseases led to exclusion. DNAs of HSV1, HSV2, VZV, CMV, EBV and HHV6 were analyzed in CSF and blood via PCR.
Results: Sixty patients were included. No DNAs of HSV1, VZV, EBV, CMV and HHV6 were detectable in patients' CSF. One patient had a borderline positive result of HSV2 DNA in CSF with no signs of HSV-2 encephalitis in standard CSF analysis. There was one borderline positive PCR result for HSV1 and HHV6 in blood analysis. For EBV, four patients had a borderline positive PCR result in blood with a detection of less than 1000 copies per milliliter in quantitative analysis.
Conclusion: We found no evidence of replication of herpesviridae in the central nervous system of PCS patients with neurological manifestations. We detected a small number of borderline positive EBV results in blood of patients, so further investigation of the role of EBV including serological studies and analysis of EBV-specific T-cells in PCS patients is needed.
Disclosure: This study was partially funded by the Deutsche Forschungsgesellschaft (DFG; grant number FR 4479/1-1 | PR 1274/8-1 | WA 4101/2-1).

EPO-108

Presenting the Post-Corona-Virus Immune Treatment trial (PoCoVIT) – a study outline

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Background and aims: The Post COVID-19 syndrome (PCS) is a severely debilitating condition in which cognitive impairment is reported frequently. Recent research underlines the relevance of (auto-) immunological hyperreactivity in the central nervous system. However, there is little evidence for treatment strategies. Here, we present the Post-Corona-Virus Immune Treatment trial (PoCoVIT), a randomized controlled trial starting in 2023 that will investigate the effects of immunosuppression on cognitive deficits in PCS.
Methods: Patients ≥18y, matching the WHO criteria of PCS and reporting cognitive impairment as leading deficit are eligible. 418 participants will be allocated 1:1 to 4 weeks of 1mg/kg bodyweight oral methylprednisolone (followed by 14d tapering) or placebo. After a washout period, all participants will receive unblinded methylprednisolone over 6 weeks. All participants will undergo structural MRI at baseline. Participants found to have anti-neuronal autoantibodies in cerebrospinal fluid will be subjected to functional MRI. Primary outcome is an increase ≥ 15 points in the memory satisfaction subdomain on the Multifactorial Memory Questionnaire (MMQ) that will be assessed at baseline, follow-up 1 (two weeks after blinded treatment phase) and 2 (two weeks after unblinded treatment).
Results: The primary study aim is to investigate the effects of methylprednisolone versus placebo on cognitive deficits in PCS. Among others, secondary study objectives include the changes in neuropsychological functions and quality of life.
Conclusion: These findings will provide information on treatment strategies for PCS and potentially enable greater insights into the underlying pathophysiological mechanisms of the syndrome.
Disclosure: This study will be conducted within the Nationale Klinische Studiengruppe (NKSG) for the investigation of PCS and ME/CFS and has been supported by a Bundesministerium für Bildung und Forschung (BMBF) grant.

EPO-109

Comparison of the HFNC and NIMV Usage on COVID-19 Severity Scales With Neuroinflammatory and Neurocognitive Aspects

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Background and aims: Coronavirus disease (COVID-19) is a fatal disease that affects all systems, especially the pulmonary system and can affect pulmonary-cerebral interaction. This study compares the effects of High-Flow Nasal Cannula Oxygen (HFNC) and Non-Invasive Mechanical Ventilator (NIMV) use on COVID-19 severity scales and neuroinflammatory parameters determine its relevance on the cognitive system.
Methods: We conducted this study on 50 patients using HFNC (n:25) or NIMV (n:25), who were followed up with COVID-19 pneumonia in the Neurology Intensive Care Unit (ICU). Demographic data, COVID-19 severity scales (Brescia-COVID Respiratory Severity Scale (BCRSS), Rapid COVID-19 Severity Index (QCSI), H-Index), serum neuroinflammatory parameters, Coronavirus Anxiety Scale (CAS) and Montreal Cognitive Assessment Scale were evaluated and compared on the first and seventh days in both groups. In addition, thorax computed tomography (CT) findings, Total Lung Severity Score (TLSS) were determined.
Results: Both groups were homogeneous in terms of age, gender, and education level. Each participant had at least one RT-PCR test of positivity. At the end of the 7th day, QCSI and H-Index were higher in the NIMV group; MOCA was lower in the NIMV group(Table-1); CAS scores were higher in the NIMV group(Table-2); ESR, NLO, pro-calcitonin and troponin values from neuroinflammatory parameters were higher in the NIMV group($p<0.05$).

	HFNC(means±2)	NIMV(means±2)	p
MONTREAL COGNITIVE ASSESSMENT (MOCA) (1. Day Measurement)	19,2	18,84	0,117[¶]
MONTREAL COGNITIVE ASSESSMENT (MOCA) (7. Day Measurement)	19,48	15,84	**0,044**[¶]

[¶]p<0,05 n: Number; [¶]p<0,05 %: Percentage; ¶ Mann Whitney-U test ¶ Student's t test

Table-1. Comparison of MoCA (Day 1-7) in NIMV and HFNC group

				Groups		Critical Value	p
				HFNC	NIMV		
Coronavirus Anxiety Scale (CAS)	1.Day Measurement	Negative	n	3	1	1,087	0,297
			%	75,0%	25,0%		
		Positive	n	22	24		
			%	47,8%	52,2%		
	7. Day Measurement	Negative	n	13	1	**14,286**	**0,001****
			%	92,9%	7,1%		
		Positive	n	12	24		
			%	33,3%	66,7%		

[¶]p<0,05 n: Number; [¶]p<0,05 %: Percentage; ¶ Chi-Square Test

Table-2. Comparison of CAS (Day 1-7) in NIMV and HFNC group

Conclusion: We concluded that the noninvasive oxygen module to be selected for patients to be monitored in intensive care conditions may affect COVID-19 severity, neuroinflammatory levels, and neurological, cognitive processes. In this aspect, the use of HFNC should be given priority in patients considered for noninvasive ventilation.
Disclosure: No affiliations with or involvement in any organization or entity with any financial interest exist.

EPO-110

Small fibre neuropathy in long-COVID-19 syndrome: a prospective case series.

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Background and aims: Peripheral nervous system disorders are part of the spectrum of neurological complications that may follow the SARS-CoV-2 infection, known as "long COVID-19" syndrome. Recent evidence suggest that small fibre neuropathy (SFN) could be responsible of some long-COVID-19 manifestations, such as acral paraesthesia and pain, but the role of small fibre damage in this population and its clinical impact remains unclear. In this prospective observational study, we aimed to assess small fibre damage in patients complaining of new-onset sensory symptoms and pain after SARS-CoV-2 infection.
Methods: We collected clinical data, standardized questionnaires assessing pain severity and autonomic symptoms, and investigated quantitative sensory testing (QST) and skin biopsy in 26 prospectively enrolled patients with new-onset paraesthesia and pain after SARS-Cov-2 infection. Inclusion criteria were age > 18 years, symptoms persisting from at least six months, and normal nerve conduction study.
Results: All patients developed new- onset paraesthesia, burning or electric shock-like pain, and autonomic symptoms within 2 months following infection, with acute onset in 9 patients. Skin biopsy confirmed intraepidermal nerve fibre reduction at calf in 6 patients, while 9 had thermal detection abnormalities at QST. Overall, 11 patients met diagnostic criteria for SFN. Of the remaining 15 patients, with diffuse pain and paraesthesia, 9 met diagnostic criteria for fibromyalgia.
Conclusion: Our study suggests that Sars-Cov-2 infection can trigger SFN, manifesting both acutely or short after COVID-19 with a variety of painful and autonomic symptoms. Fibromyalgia can underlie painful and autonomic symptoms in a considerable proportion of patients who don't fulfil SFN criteria.
Disclosure: Nothing to disclose.

EPO-111

Central Nervous System Tuberculosis: Clinical Manifestations And Neuroradiological Features

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Background and aims: Tuberculosis is a global health problem and remains the first cause of death by infectious disease in the world. Central nervous system tuberculosis (CNST) represents a severe presentation of the disease and is known for its clinical and radiological polymorphism. We aim to describe the clinical and radiological characteristics of CNST in a Tunisian cohort.
Methods: We conducted a retrospective study of 25 patients with CNST from the neurology department between 2004 and 2022. All patients underwent a cerebral +/- spinal MRI and a bacteriological study of cerebrospinal fluid (CSF).
Results: In this cohort, sex ratio was 1.08 and the mean age at onset was 47.7 years (20-83 years). At onset, patients' complaints were motor deficit (23.5%); headaches (17.6%); behavioral problems (11.7%); and altered consciousness (11.7%). On examination, clinical symptoms were: cerebellar ataxia (25%); hemiparesis (25%); paraparesis (16.7%); posterior cord syndrome (12.5%); confusion (12.5%) and cranial nerve impairment (8.3%). Among them, 29.2% had meningoencephalitis; 12.5% had radiculo-myelitis and 4.7% had meningo-encephalo-radiculo-myelitis. CSF analysis showed predominantly lymphocytic meningitis with hypoglycorrhachia in 37.5%, while CSF BK research was positive in only 4.7%. On neuroimaging, cerebral tuberculomas (66.7%); myelitis (16.7%); pachymeningitis (12.5%) and hydrocephalus (8.3%) were the most common features. At follow-up, 62.5% had a favorable disease course, while 16.6% had complications and 8.3% died.
Conclusion: CSNT is a serious health problem. However, clinical polymorphism and diagnostic difficulties should not delay therapeutic management.
Disclosure: Nothing to disclose.

EPO-112

Neuroimmune disorders after SARS-CoV2 vaccination

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Background and aims: Several neuroimmune syndromes have been reported after exposure to SARS-CoV2 vaccine. The aim of this study was to know the frequency and characteristics of these syndromes.
Methods: Observational retrospective cohort study, including patients who were hospitalized in the Neurology department of La Paz University Hospital from January 2021 to May 2022 with a probable neuroimmune disorder. Demographic, clinical and outcome data were collected, comparing recently exposed to SARS-CoV2 vaccine cases to those who weren't.
Results: From a total of 108 patients, 30 were excluded because of a final diagnosis other than immune mediated. Thirty-six patients (46.2%) had received one dose of COVID-19 vaccine in the 3 months prior (21.8% during the previous month). 63.9% were women and the median age was 51.2 years (SD 22.6), without significative difference with the non-recently vaccinated (Mann-Whitney U p=0.256). The Biontech-Pfizer vaccine was the most frequent (63.9%). The neurological syndromes found (vaccinated/total) were: polyradiculoneuropathy (8/16), encephalitis (5/11), multiple sclerosis relapse (5/16), optic neuritis (1/4), myelitis (3/6), cranial nerve neuropathy (6/10), aseptic meningitis (1/3) and others (7/11). 22.2% of the recently vaccinated patients had suffered a previous SARS-CoV2 infection (vs 21.4% of non-recently vaccinated). 61.1% of the recently vaccinated cases received acute immunomodulatory treatment and 47.2% presented complete clinical improvement, without significant differences with non-recently vaccinated cases (Chi-squared p=0.643; p=0.570).
Conclusion: The most frequent neuroimmune disorders after the recent vaccination against SARS-CoV2 were polyradiculoneuropathies and cranial neuropathies. The neuroimmune syndromes that appear after the administration of the Covid-19 vaccine don't seem to present specific differences.
Disclosure: Nothing to disclose.

Movement disorders 1

EPO-113

Cervical Vestibular-Evoked Myogenic Potentials in Patients with Parkinson's disease

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Background and aims: The role of vestibular otolith function and its central connections is still obscure and overlooked. We aimed to investigate brain stem function and to understand the abnormalities of cVEMPs and their differential clinical correlations with symptoms related to brainstem involvement in Parkinson's disease (PD) patients using a validated, comprehensive, neurophysiologic tool; Cervical vestibular-evoked myogenic potentials (cVEMPs).
Methods: This study is an observational prospective case-control study that was conducted from January 2022 to November 2022. The study was conducted on 62 subjects, and they were equally subdivided into two groups; Group I (Cases) included patients diagnosed with idiopathic PD and Group II (Controls) included age and gender healthy matched subjects. Cervical Vestibular-Evoked Myogenic Potentials (cVEMP) testing was carried out for all subjects to assess the saccular function and inferior branch of the vestibular nerve.
Results: However, the prolonged latencies of P13 and N23 were positively correlated with UPDRS-III and H&Y Scale; the P13-N23 amplitude didn't show significant correlation. Having the identification of cVEMP, the response was present in about two-third of the case group with a statistically significant difference between the two groups (P<0.001). Among the case group, the mean P13 latency and N23 latency was significantly prolonged, while the mean P13-N23 amplitude was significantly reduced with a statistically significant difference between the two groups (P<0.001).
Conclusion: We demonstrated the pathophysiological dynamics of saccular part of otolith and its central connection involvement in patients with PD using a cVEMP can be considered an electrophysiological marker to explore brainstem dysfunction.
Disclosure: The authors declare that there was no conflict of interest.

Table 1. Clinical characteristics among the case group.

Variable	Case group (n=31)
Age (years)*	63.10 ± 9.44
Gender (males), n (%)	19 (61.3%)
Disease duration (years)*	7.10 ± 4.02
Most affected side, n (%)	
Right side of the body	12 (38.7%)
Left side of the body	19 (61.3%)
History of falls, n (%)	
None	20 (64.5%)
Rare falling	6 (19.4%)
Occasionally falls	3 (9.7%)
Falls on average once daily	2 (6.5%)
Falls more than once daily	0 (0%)
The Pull test, n (%)	
Normal	25 (80.6%)
Retropulsion but recovers unaided	3 (9.7%)
Absence of postural response	2 (6.5%)
Very unstable, *tends to lose balance spontaneously*	1 (3.2%)
Unable to stand without assistance	0 (0%)
H&Y Scale*	1.77 ± 0.62
UPDRS-III*	14.10 ± 8.42

*Data presented as mean ± standard deviation (SD).
UPDRS-III; Unified Parkinson's Disease Rating Scale section III, **H&Y Scale;** Hoehn and Yahr scale

Table 2. Characteristics of cVEMP in patients with Parkinson's disease.

	Case group (n=31)
Present VEMP Response, n (%)	22 (70.9%)
Gender (males)	13 (59.1%)
History of fall	4 (18.2%)
Postural instability	2 (9.1%)
Absent VEMP Response, n (%)	9 (29%)
Gender (males)	6 (66.7%)
History of fall	7 (77.8%)
Postural instability	3 (33.3%)
cVEMP Response (P13 latency), r*	
UPDRS-III	0.391
H&Y Scale	0.552
cVEMP Response (N23 latency), r*	
UPDRS-III	0.566
H&Y Scale	0.623
cVEMP Response (P13-N23 Amplitude), r*	
UPDRS-III	- 0.266
H&Y Scale	- 0.277

*The Pearson correlation coefficient **(r)** was used to describe the degree of relationship between two variables. The sign of correlation coefficient (+ , −) defines the direction of the relationship, either positive or negative
UPDRS-III; Unified Parkinson's Disease Rating Scale section III, **H&Y Scale**; Hoehn and Yahr scale, **cVEMP;** Cervical vestibular-evoked myogenic potential.

Table 3. Identification of cVEMP among the included subjects.

Variable	Case group (n=31)	Control group (n=31)	P value^{x}
cVEMP, n (%)			
Present response	22 (70.9%)	31 (100%)	< 0.001
Absent response	9 (29%)	0 (0%)	< 0.001
P13 latency (ms)	15.57 ± 2.82	12.23 ± 2.02	0.001
N23 latency (ms)	24.68 ± 2.78	21.13 ± 1.98	0.001
P13-N23 Amplitude (μv)	37.85 ± 4.35	49.31 ± 2.77	0.001

*Data presented as mean ± standard deviation (SD)
^{x}***P*<0.05** was considered statistically significant
cVEMP; Cervical vestibular-evoked myogenic potential

EPO-114

A new variant for autosomal recessive complicated hereditary spastic paraplegia (SPG26) - a case report

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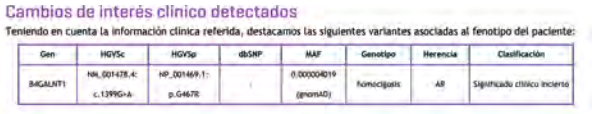
Background and aims: The term hereditary spastic paraplegia (HSP) describes a group of inherited heterogeneous disorders characterized by progressive spasticity and weakness of the lower limbs. One of the less common variants is spastic paraplegia-26 (SPG26), an autosomal recessive form that begins in the first 2 decades of life with gait disturbance. Some patients have upper limb involvement and additional features such as intellectual disability, peripheral neuropathy, dysarthria and cerebellar signs. The SPG26 is caused by mutation in the B4GALNT1 gene on chromosome 12q13.
Methods: We present a clinical case compatible with SPG-26.
Results: A 55-year-old woman consulted for progressive gait impairment since she was 6 years old and intellectual disability. Family history shows similar clinical features in paternal cousins and brothers. All of them made their clinical debut in their childhood. The neurological examination revealed scanned dysarthria, hypometric saccades, skew deviation, mild spastic tetraparesis, cerebellar dysmetria, hyperreflexia, extensor plantar responses and pes equinovarus. The genetic study identified our patient as a homozygous carrier of the change of uncertain significance c.1399G>A (p.G467R) in the B4GALNT1 gene. Biallelic variants in this gene are responsible for an autosomal recessive form of complicated spastic paraparesis. Other disease-related missense variants affecting the same domain have been described. Family segregation is in progress.


Cambios de interés clínico detectados

Teniendo en cuenta la información clínica referida, destacamos las siguientes variantes asociadas al fenotipo del paciente:

Gen	HGVSc	HGVSp	dbSNP	MAF	Genotipo	Herencia	Clasificación
B4GALNT1	NM_001478.4: c.1399G>A	NP_001469.1: p.G467R		0.000004019 (gnomAD)	homocigosis	AR	Significado clínico incierto

Conclusion: We present an undescribed variant of the B4GALNT1 gene and a family history compatible with SPG-26. The descriptions of new variants by new genetic advances are important as they provide information for research and genetic advice.
Disclosure: The authors do not have conflicts of interest.

EPO-115

Bilateral and bi-hemispheric deep brain stimulation (DBS) in Lesch-Nyhan Disease: shifting the treatment paradigm

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Background and aims: Lesch-Nyhan Disease (LND) is a rare debilitating genetic x-linked disorder caused by a mutation affecting the HPRTI gene, encoding the purine salvage enzyme. When the enzymatic activity is under 2% patients present with severe intellectual disability, behavioral and extrapyramidal symptoms, classically characterized by self-injury behavior (SIB), dystonia and opisthotonus, and currently there is no specific and effective medical treatment for these deficits. Very few cases of LND have been submitted to DBS, in different cerebral targets with variable results.
Methods: A 5-year-old male diagnosed with LND at 11 months, Xq26.3 deletion, presented with severe generalized dystonia, opisthotonus, and SIB with severe bite injuries. DBS was done with the implantation of 4 electrodes, targeting nucleus accubens (NA) and motor internal globus pallidus (GPi) bilaterally.
Results: In the immediate post-surgical assessment, the patient was globally calmer, revealed less SIB and improvement in dyskinetic movements. Fourteen days after surgery, according to the parents, he was calmer and there were no self-mutilating behaviors during this period, and additionally presented with less dystonia and without opisthotonus.
Conclusion: DBS may present as a promising treatment of refractory SIB and dystonia in LND. There are still many open questions, particularly concerning ideal time frame for surgery, with some reports pointing towards the benefit of early treatment of SIB during critical windows of development; and optimal targets, with growing evidence supporting the benefits of GPi and NA bilateral and bi-hemispheric stimulation. Additional studies and longer follow up is needed to better inform the effectiveness and safety of DBS in LND.
Disclosure: Nothing to disclose.

EPO-116

Asymmetry and side concordance of rest tremor and bradykinesia in patients with essential tremor

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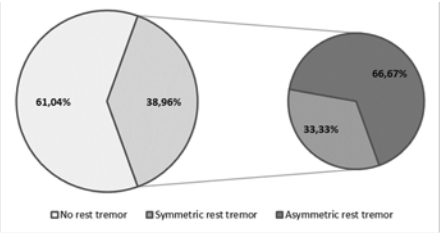
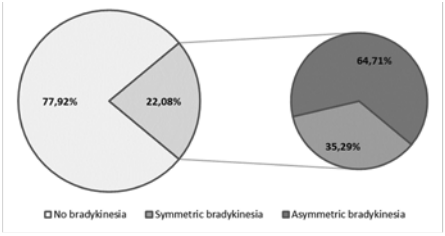
Background and aims: Subtle parkinsonian signs, i.e., rest tremor and bradykinesia, can occur in patients with essential tremor (ET) and can be considered soft signs for the definition of ET-plus. In the present study, we aimed to investigate the clinical and kinematic features of rest tremor and bradykinesia in ET, with a focus on body distribution and side concordance.
Methods: Standardized clinical scales and a kinematic system for movement analysis were used to assess tremor and movement velocity during repetitive finger movements in a sample of 77 ET patients. We then investigated tremor asymmetry, side concordance and possible correlations between motor symptoms in our sample.
Results: Rest tremor and bradykinesia were clinically detectable in 30 (38.96%) and 17 (22.08%) out of 77 patients, and clearly asymmetric in 66.67% and 64.71% of cases, respectively. In patients with asymmetric rest tremor, asymmetry of the movement velocity was observed in 15 cases (75%). However, in the majority of patients (9 out of 15, 60%), there was no side concordance between rest tremor and bradykinesia. Conversely, we observed a side concordance between asymmetric postural tremor and bradykinesia in a high percentage of cases (13 out of 17 patients, 76.47%: p=0.02). No correlation was observed between action tremor amplitude and movement velocity.



	ET patients with rest tremor	ET patients without rest tremor	p
Sex	14F/16M (46.67%/53.33%)	17F/30M(36.17%/63.83%)	0.36
Age (years)	71.93 ± 7.73	66.47 ± 14.74	0.06
Age of onset (years)	53.03 ± 19.51	54.46 ± 18.25	0.75
Tremor duration (years)	18.9 ± 16.34	12.01 ± 11.64	**0.03**
Family history	14Y/16N (46.67%/53.33%)	27Y/20N(57.45%/42.55%)	0.36
FTM-TRS total score	31.47 ± 13.69	16.38 ± 11.20	**<0.01**

Characteristics of ET patients with and without rest tremor. The pie charts show the prevalence of rest tremor in our sample and the percentage of patients in which it is asymmetrical. Significant p-values are in bold.



	ET patients with bradykinesia	ET patients without bradykinesia	p
Sex	7F/10M (41.18%/58.82%)	24F/36M(40%/60%)	0.93
Age (years)	70.76 ± 12.43	67.98 ± 12.83	0.43
Age of onset (years)	54.53 ± 18.9	53.73 ± 18.72	0.88
Tremor duration (years)	16.24 ± 11.23	14.26 ± 14.71	0.61
Family history	30Y/30N (50%/50%)	11Y/6N(64.71%/35.29%)	**0.02**
FTM-TRS total score	27.71 ± 13.49	20.72 ± 14.15	0.07

Characteristics of ET patients with and without bradykinesia. Pie charts show the prevalence of clinically detectable bradykinesia in our sample and the percentage of patients in whom it is asymmetric. Significant p-values are in bold.

	N° of patients with both soft signs asymmetric	Concordant	Discordant	p
Rest tremor - Bradykinesia	15	6 (40%)	9 (60%)	0.4
Rest tremor - Action tremor	12	7 (58.3%)	5 (41.7%)	0.41
Bradykinesia - Action tremor	17	13 (76.47%)	4 (23.53%)	**0.02**

Data regarding the side concordance of the different motor symptoms in ET patients. Significant p-values are in bold in the table and marked with an asterisk in the graphs.

Conclusion: Rest tremor and bradykinesia are relatively frequent in ET and often asymmetric. Our findings suggest that these parkinsonian soft signs in ET possibly reflect different pathophysiological mechanisms. In contrast, postural tremor and bradykinesia may share a common pathophysiological basis, possibly reflecting the prominent cerebellar involvement in ET.
Disclosure: Nothing to disclose.

EPO-117

Wilson's disease and dangerous of copper deficiency phenomenon – the systematic review

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Background and aims: Wilson's disease (WD) is a genetic disorder with copper accumulation in tissues leading to clinical symptoms (mainly hepatic, neuropsychiatric). The

copper metabolism results in WD patients show increased serum "free copper" with its normalization during WD treatment. As WD treatment is lifelong, the possibility of copper deficiency (CD) during WD long treatment may occur. Aim of our study was to systematically assess data according to CD in WD, its frequency, association with anti-copper drug as its clinical symptoms and outcome.
Methods: This systematic literature review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were identified by searching the PubMed database (up to 23 December 2022).
Results: Among the 19 articles, 21 cases of CD were described, most commonly in patients treated with zinc salts(16/21; 76%). The symptoms of CD occur insidiously during long WD treatment, including: sideroblastic anemia, neutropenia, axonal-sensory-neuropathy, posterior cord myelopathy or increased ratio of epileptic seizures(or epilepsy). The diagnosis of CD is based on clinical symptoms and severe decrease of urinary copper excretion(<20 μg/24 hours in patients treated with zinc or<100 μg/24 hours on chelators) with low serum copper and ceruloplasmin in WD patients.
Conclusion: Physicians should be aware of CD possibility during WD treatment. The transient discontinuation of anti-copper treatment usually reverses the CD in the serum, as well as pancytopenia, however the clinical symptoms, mainly neuropathy and myelopathy caused by CD, may persist. The regular control of copper metabolism during WD treatment is needed to avoid CD.
Disclosure: The authors have no potential conflict of interest to report.

EPO-118

Is there horizontal transmission of Creutzfeldt-Jakob disease?

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Background and aims: Sporadic Creutzfeldt-Jakob disease (s-CJD) is a rare, fatal neurodegenerative disorder. Familial cases of Creutzfeldt-Jakob disease (f-CJD) due to mutations in the PRNP gene are even rarer around the world; however, in Israel there is a focus of f-CJD patients carrying the E200K mutation. As the number of CJD E200K carriers in Israel is high and increasing, transmission of CJD to normal people was suspected. If such transmission occurs, the incidence of s-CJD would be expected to increase.
Methods: Using data from the national CJD registry and official statistics on the Israeli population, we studied incidence rates of f-CJD and s-CJD for the period from 1985 to 2018 applying the SEER statistical packet developed in the US National Cancer Institute.
Results: In total, 621 CJD patients (405 f-CJD and 216 s-CJD) cases are included in the registry. In the cohort of f-CJD patients the mean age-adjusted annual incidence rate over the above-mentioned period was 1.88±0.09 (95% CI: 1.7–2.08) per 1,000,000. In the cohort of s-CJD patents, the mean age-adjusted incidence rate over the same period was 0.93±0.06 (95% CI: 0.81–1.06) per 1,000,000 people. No significant time trends were found over the observation period in either s-CJD or f-CJD.
Conclusion: Israel has a high predominance of f-CJD compared to s-CJD. Between 1985 and 2018, the annual age adjusted incidence rates for both forms of CJD remained stable. Thus, there is no evidence that CJD is transmitted from affected individuals to others.
Disclosure: Nothing to disclose.

EPO-119

Action myoclonus (Lance-Adams syndrome). 3 different causes of 3 unique cases

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Background and aims: Lance-Adams syndrome (LAS) is a disease that may appear after a period of cerebral hypoxia usually after cardio-respiratory arrest of different etiology.
Methods: Diagnosis is clinical. LAS has no correlation with EEG or neuroimaging abnormalities.
Results: Case 1. Cardiac arrest caused by poisoning with belladonna tincture. The patient had been resuscitated, consciousness was recovered with the consequent onset of myoclonic hyperkinesis, provoked by ideation of movement or any movement itself, aggravated by unexpected sounds and disappeared in rest and sleep. Cerebellar gait ataxia affected independent standing. Case 2. The patient was admitted with acutely onset myoclonic jerks. Patient's history is specific for severe heart failure (LVEF 40%), respiratory insufficiency, severe obesity (BMI 35,8). Most of the time patient takes sitting position (with head droop forward on chest), because of severe dyspnea. Case 3. A 71 years old man was admitted to the hospital on the 12th-day of COVID-19 with severe cerebellar ataxia, myoclonus and cognitive impairment. The day before admission generalized tonic-clonic seizures occured and repeated on the day of admission.

Case 1. Action myoclonus (Lance-Adams syndrome) as a consequence of cardiorespiratory arrest caused by accidental poisoning with belladonna tincture.

Case 2. Action myoclonus (Lance-Adams syndrome) as a consequence of chronic brain hypoperfusion.

Case 3. Action myoclonus (Lance-Adams syndrome) secondary to generalized tonic-clonic seizures during COVID-19.

Conclusion: Lance-Adams syndrome, as a manifestation of posthypoxic encephalopathy after cardiorespiratory arrest and successful resuscitation with restoration of consciousness, intellectual-mnestic functions, but with preservation of subcortical myoclonus, grievously violating self-service. In the abstract we are describing 3 different causes of the same symptom, occurred in 3 different patients: as a consequence of cardiorespiratory arrest caused by poisoning with belladonna tincture, as a consequence of chronic brain hypoperfusion and secondary to generalized tonic-clonic seizures during COVID-19.

Disclosure: Prof., MD, T. Slobodin., Department of Neurology No l. Shupyk National Healthcare University of Ukraine. Kyiv Ukraine - management of the patients, descriptive part of the abstract. PhD Student, MD, S. Bandrivska - Department of Neurology No l. Shupyk National Healthcare University of Ukraine. Kyiv Ukraine - assistance in management of the patients, video recording of patients.

EPO-120

Pantothenate kinase-associated neurodegeneration: clinical, radiological and genetic study of six Tunisian families

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Background and aims: Pantothenate kinase-associated neurodegeneration (PKAN) is a rare neurodegenerative disorder caused by mutations in the PANK2 gene. It is characterized by progressive extrapyramidal dysfunction due to excessive iron deposition in the basal ganglia. Herein, we describe the genetic, clinical, radiological and therapeutical aspects of PANK2 mutations in pediatric patients.
Methods: We conducted a retrospective study over a 15-year-period including children diagnosed with PKAN. Genetic confirmation was performed by Sanger sequencing of the coding regions of the PKAN2 gene (NM_153638.3). Epidemiological, clinical, radiological and therapeutical aspects were analyzed.
Results: Four girls and two boys have been included. The mean age of onset was 4.4 years [1,13]. Sex-ratio(F/M) was 2/1. Four children had developmental delay. Oromandibular dystonia was the main clinical feature found in all patients. Other symptoms were dysarthria(n=1), parkinsonism(n=3) and behavioral changes(n=1). In all cases, Brain MRI showed the "eye-of-the-tiger" sign. CT scan showed calcifications in the basal ganglia in two cases. Genomic studies revealed five different PANK2 mutations. Molecular analysis showed the mutation in a homozygous state in five patients.
Conclusion: Study of this pediatric series highlights the particularity of the classical forms of PKAN compared to the late-onset forms. Dystonia is the major sign in the classical forms. The evolution is rapidly unfavorable. No curative treatment has proven to be effective. Genetic counselling is therefore essential in affected families.
Disclosure: I declare that there are no conflicts of interests.

EPO-121

Differential diagnostic and therapeutic challenges in atypical Parkinsonian disorders

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Background and aims: Heterogenous clinical presentation of atypical Parkinsonian disorders pose major challenges to accurately diagnose patients suffering from these conditions. In past decades, significant advancements in genomic technologies have provided us with increasing insight into the molecular pathogenesis of disorders, fueling new hopes to incorporate molecular knowledge into diagnostic and therapeutic approaches towards managing these conditions.
Methods: To facilitate the diagnostic succes of patients with atypical Parkinsonian disorders, we performed whole exome sequencing to better understand the genetic background and optimize therapy.
Results: WES identified the genetic background of atypical Parkinsonian symptoms in three pateints. Patient #1 presented with right sided rigidity, severe bradykinesia, followed by dystonia, atypical tremor and complex psychiatric symptoms, including anxiety, mood swings, panic attacks. WES detected a rare, heterozygous variant of unidentified significance (VUS) (c.1991G>A) in PDE10A gene, associated with striatal degenaration, limb and orofacial dyskinesia. DATSCAN supported the diagnosis. #2 patient's symptoms started after physical trauma. Acute left arm dystonia occured, followed by ipsilateral rigidity, bradykinesia and mental confusion. Atypical symtoms improved spontaneously after several weeks. WES revealed pathogenic mutation (c.18877C>T) in ATP1A3 gene, linked to rapid-onset dystonia-parkinsonism. His father had milder, but similar symptoms. Patient #3 showed symptoms of ataxia and muscle weakness, later parkinsonism, tetrapyramidal signs and severe orthostasis appeared. WES discovered a rare CHCHD2 gene VUS (c.179C>T), which was prevoiusly associated with Parkinson's disease and MSA.
Conclusion: In conclusion, genetic testing is an important differential diagnostic tool in rare neurodegenerative disorders. Understanding the molecular background may help choose the right therapeutic approaches in atypical Parkinsonian disorders.
Disclosure: Nothing to disclose.

EPO-122

CLINICAL AND IMAGING CHARACTERIZATION OF A COHORT OF SEVENTY-ONE MULTIPLE SYSTEM ATROPHY PATIENTS

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Background and aims: MSA is a rare neurodegenerative disease, classified into two subtypes, MSA-P and MSA-C. Beyond the core symptoms, many non-motor features can be part of the clinical picture. The diagnosis in the early stages can be challenging. This study aimed to review the characteristics of large cohort of MSA patients diagnosis in our center.
Methods: We examined a cohort of 71 patients with probable MSA, according to the Gilman criteria [1], assessed at the Movement Disorders clinic of Ospedale Maggiore Policlinico in Milan between 2012 and 2022.

Results: All patients are European. 37 patients had MSA-P and 34 MSA-C. The two sexes were equally distributed. Age at onset was slightly lower in MSA-C (58 years) than in MSA-P (62 years). In MSA-P the symptoms at onset were equally distributed among motor (54%) and non-motor (46%), whereas in MSA-C there was a prevalence in the motor onset (80%). All patients experienced autonomic dysfunction, with 90% of MSA-P and 80% of MSA-C presenting orthostatic hypotension, and all patients having genitourinary disturbances; constipation was more common in MSA-C (96%) than in MSA-P (73%). A small subset of patients presented hyposmia. The most common MRI findings were: atrophy of putamen (P 28%, C 9%), middle cerebellar peduncle (P 4%, C 21%), pons (P 4%, C 24%), cerebellum (P 16%, C 65%), and hot cross bun sign (P 8%, C 35%). Study outcomes confirmed previous clinical and imaging data from the literature [2].
Conclusion: MSA is still insidious, but some clinical and imaging features can help the diagnostic process.
Disclosure: Nothing to disclose.

EPO-123

Neurophysiological changes of primary motor cortex in patients with essential tremor-plus

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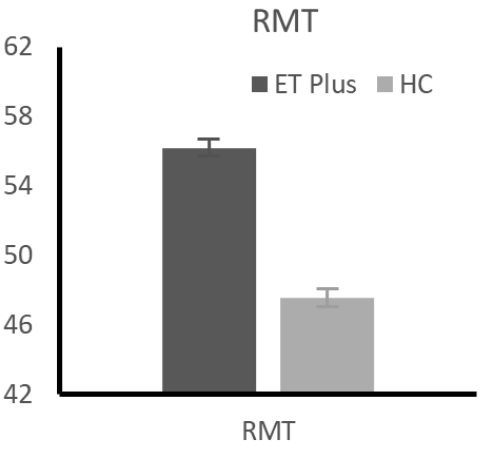
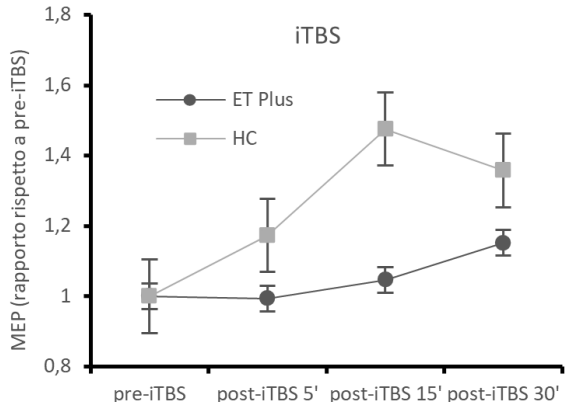
Background and aims: Essential tremor-plus (ET-plus) represents a recently introduced entity indicating ET patients with additional neurological signs of uncertain significance. The aims of our study was to investigate possible neurophysiological changes of the primary motor cortex (M1) and their relationship with soft signs in patients with ET-plus.
Methods: Thirteen ET-plus patients were enrolled (5 females, 70±7.97 years). Most patients had rest tremor, subtle bradykinesia, MCI and only 3 of them had impaired tandem gait. Patients were evaluated by standardized clinical scales. Objective measurements of rest tremor and bradykinesia were obtained by kinematic analysis. M1 excitability was assessed by the recordings of resting motor thresholds (RMTs), input/output curve of the motor-evoked potentials (MEPs), short-interval intracortical inhibition (SICI) and short-latency afferent inhibition (SAI). Plasticity-like mechanisms were indexed according to MEPs amplitude changes after intermittent theta-burst stimulation (iTBS). Data were compared to those from 16 healthy controls (HCs).

Distribution of the different soft sign in patients with Essential tremor plus (ET-Plus)

Results: Compared to HCs, ET-plus patients had higher RMTs (P=0.019), indicating a lower corticospinal excitability and a lower MEPs facilitation after iTBS (P=0.032), reflecting a lower cortical plasticity. ET patients were slower than HCs during finger tapping (P=0.03). No correlations were found between neurophysiological, clinical and kinematic data, nor relationships between neurophysiological changes of M1 and the type or severity of soft signs in ET plus patients.



Motor evoked potential (MEP) amplitude of the resting motor threshold (RMT) in the 2 groups. Essential tremor plus (ET-Plus) (black indicator) and healthy controls (HC) (grey indicator)



Motor evoked potential (MEP) amplitude changes (Y-axis) induced by the intermittent theta burst stimulation (iTBS) protocol in the 2 groups. Essential tremor plus (ET-Plus) (black indicator) and healthy controls (HC) (grey indicator)

Conclusion: We here provided novel information on excitability and plasticity abnormalities of M1 in patients with ET-plus. Our results suggest that neurophysiological changes of M1 underline common pathophysiological mechanisms in the different forms of ET plus patients
Disclosure: No conflict of interest.

EPO-124

Novel insights into the origin of subthalamic (STN) beta oscillations in Parkinson's Disease

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Background and aims: Neuronal subthalamic (STN) activity in Parkinson's Disease (PD) is characterized by an excessive rhythm in beta band frequency range (12-35 Hz), which is normalized by levodopa. The aim of our study was to explore the origin of beta oscillations, by assessing possible changes of subthalamic LFPs in different moments during Deep Brain Stimulation (DBS) surgery. That is of key importance because the beta rhythm is now considered the most reliable electrophysiological marker for guiding novel adaptive DBS approaches.
Methods: STN signals were recorded in four patients in three different moments during DBS implantation: before sedation, during Propofol alone and under the effect of both Propofol and Rocuronium. LFPs were analyzed in terms of both linear and non-linear analyses (e.g. power spectral density, sample entropy and multi-scale entropy), as well as burst analysis.
Results: Although other analyses, either linear or non-linear, did not disclose any statistical difference among the three experimental conditions, burst analysis revealed significant changes in terms of mean amplitude and beta burst duration during curarization when compared to other experimental conditions.
Conclusion: Whether there is an involvement of the peripheral system, or gamma-motoneurons, in the modulation of the hyper-synchronized β power is still a matter of debate, our work could highlight novel insights into the origin of the beta rhythm, possibly suggesting that these oscillations arise away from the basal ganglia network.
Disclosure: I have no conflicts of interest to declare.

EPO-125

Phase-amplitude coupling between beta power and high frequency oscillations as a biomarker for deep brain stimulation.

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Background and aims: The aim of this work was to study the potential clinical usefulness of the beta power phase-amplitude coupling (PAC) with high frequency oscillations (HFO´s). Beta hypersynchrony has been introduced into clinical practice recently in Parkinson´s disease (PD) to identify the best stimulation contact and for adaptive deep brain stimulation (aDBS) sensing. However, many other oscillopathies accompany the disease and beta power sensing is not optimal for all patients.
Methods: Subthalamic nucleus (STN) local field potentials (LFP´s) from externalized DBS electrodes were recorded and analyzed in PD patients (n=19). Beta power and HFO´s were evaluated in resting state condition, then the phase-amplitude coupling (PAC) was studied and correlated with the electrode contact positions and structural connectivity.
Results: Beta- HFO´s PAC (mainly in 200-400Hz range) was observed in all subjects. PAC was significantly stronger during high beta power episodes and in more affected sides. Moreover, this PAC was detectable also in contacts located within the STN, where beta power was non-conclusive.
Conclusion: Coupling between beta power and HFO´s increases with the beta power synchronization, which is known to be a correlate of PD off state. Beta- HFO´s PAC seems to be more sensitive than beta power fluctuations itself and could be more helpful in the best stimulation contact clinical selection and probably also as potential future input signal for aDBS.
Disclosure: This research has been financially supported by Czech science foundation GAČR 21-25953S

EPO-126

GPi-DBS in a patient with pathology-confirmed Corticobasal Degeneration

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Background and aims: Deep brain stimulation (DBS) may be very effective for focal dystonia1. There have been no case reports of DBS for corticobasal syndrome (CBS), except one patient initially diagnosed with Parkinson's disease and referred to as a 'DBS failure'2.
Methods: We describe a male patient presenting at 70 years old with weakness in the left hand which progressed to dystonic hand posturing. Superimposed, there were painful, action-induced spasms. CBS was suspected but the very focal presentation and absence of cortical involvement (both clinically as on MRI brain) was atypical. EMG ruled out neuromuscular disorders and CSF was negative for paraneoplastic disorders (including stiff person syndrome).
Results: Multiple pharmacological agents were tried to address the dystonia and spasms including levodopa, baclofen, trihexyphenidyl, levetiracetam, valproic acid without success. Clonazepam initially provided some benefit. Botulinum toxin injections only had a partial and transient effect. Right GPi-DBS was undertaken four years after symptom onset. Despite multiple programming attempts the patient obtained only modest alleviation of symptoms. Six years after symptom onset, the patient underwent medical-assistance in dying. Prior to death, dystonic features were also present in the other limbs and graphesthesia had become apparent as well as some cognitive decline. Autopsy revealed pathognomonic features of the 4R tauopathy, corticobasal degeneration. Tau pathology predominated in motor and parietal cortices but affected basal ganglia and brainstem as well.
Conclusion: Lack of benefit of DBS highlights the complex pathophysiology of dystonic posturing in CBS that might be influenced by severe upper motor neuron involvement as exemplified in this case.
Disclosure: • Dr. Boogers – nothing relevant to this abstract • Dr. Candeias da Silva – nothing relevant to this abrasct • Dr. Marras – nothing relevant to this abstract • Dr. Kovacs - nothing relevant to this abstract • Dr. Lang – nothing relevant to this abstract • Dr. Fasano – nothing relevant to this abstract References 1. Vidailhet M, Jutras MF, Grabli D, Roze E. Deep brain stimulation for dystonia. J Neurol Neurosurg Psychiatry. 2013;84(9):1029-1042. doi:10.1136/jnnp-2011-301714 2. Okun MS, Tagliati M, Pourfar M, et al. Management of Referred Deep Brain Stimulation Failures. Arch Neurol. 2005;62(8):1250. doi:10.1001/archneur.62.8.noc40425

EPO-127

A simple machine learning algorithm to classifying atypical parkinsonian syndromes

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Background and aims: In the big data era, artificial intelligence techniques have been proposed to treat classification problems especially among neurodegenerative diseases. Aim of this study is to develop a machine learning (ML) algorithm based on clinical variables in order to correctly classify atypical parkinsonian syndromes (APS), such as Multiple system atrophy (MSA), Progressive supranuclear palsy (PSP) and Corticobasal syndrome (CBS).
Methods: This is a cross- sectional study of 22MSA-C, 13MCA-P, 15PSP and 10CBS patients. We used predictors such as clinico-demographics (age, gender, education, disease duration, MDS-UPDRSIII, LEDD, UMSARScore, PSPScore, Hoyen&Yahr, Schwab&England, SCOPA-AUT) five neuropsychological tests (MOCA, FAB, Goldenberg Scale, Digit Span total, Geriatric depression Scale). The "Pearson product moment correlation coefficient" (PPMCC) was obtained by the ratio of the covariance of two variables, normalized to the square root of their variances. Then, the values were normalized between 0-100%(100 the most important variable). Afterwards, the data was inserted into a KNN classifier model with feature scaling and k=4.
Results: SCOPA, MDS-UPDRS III, MOCA and FAB scores were the variables that mostly influence the APS type (100%, 78%, 72%, 66% respectively). Regarding the KNN classifier model, the accuracy was 71.11%, the precision values 66.67%, 52%, 66.67% ,100% for each class, the recall values 85.71%, 66.67%, 43.33% and 50% for each class, and 75%, 50%, 44.44% and 66.67% for each class MSA-C, MCA-P, PSP and CBS respectively.
Conclusion: Despite the small sample, the data was adequate to fit in a KNN-ML model and determine in a quite satisfying degree from which APS does a patient suffer.
Disclosure: Nothing to disclose.

Epilepsy 1

EPO-128

Neuroimaging findings after a first seizure – interim report from the Swiss First study

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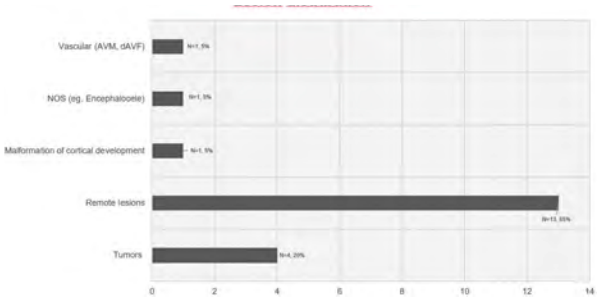
Background and aims: MRI can depict potentially structural epileptogenic lesions as well as incidental, potentially non-epileptogenic lesions after a first seizure. The SWISS FIRST study was closed in December 2022. Here, we report the interim results about incidence of structural and peri-ictal image abnormalities in first seizure patients.
Methods: All patients underwent MRI with a dedicated epilepsy imaging protocol (incl. SWI, DWI and perfusion imaging). Diagnostic criteria for established epilepsy follow the ILAE practical guidelines and were determined after 2 years of follow-up. MRI lesions were classified as either structural epileptogenic lesions (SEL), potentially nonepiletogenic lesions (pNEL) or normal MRI.
Results: Overall, 615 patients were investigated with MRI after a first suspected epileptic seizure. Up to now, 83 received a final diagnosis. Fifty-nine were diagnosed with established epilepsy based (71%, mean age 51.0 ± 19.2, M: 34, F: 25). In patients with established epilepsy, SEL were present in 34% and pNEL in 49%. Main findings were remote lesions (65%), brain tumors (20%), vascular lesions (5%) and malformations of cortical development (5%) (Image). Transient peri-ictal MR signal abnormalities (TPMA) were present in 15% of patient with SEL, 10% in patients with pNEL and none in nonlesional MRI (χ^2-test; n.s.).



Lesion distribution in the structural epileptogenic group cohort.

Conclusion: Both SEL and pNEL are common findings in patients who undergo immediate imaging after a first seizure, with similar distribution of WML in both cohorts. TPMA are rarely observed after a first seizure in comparison to established epilepsy or status epilepticus and do not differ significantly between SEL and pNEL patients.
Disclosure: The authors report these preliminary results on behalf of the SWISS FIRST investigators. The study was funded by the SWISS National Foundation (SINERGIA) project 180365: The SWISS FIRST Study

EPO-129

Investigation of Prognostic Characteristics of Medically-Refractory Epilepsy Based on Invasive Monitorization

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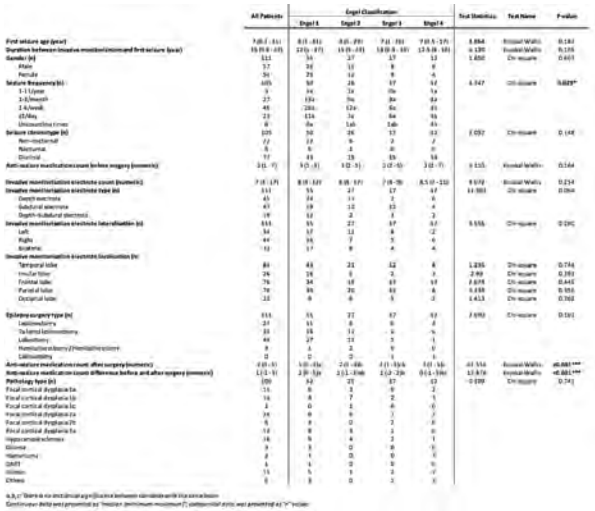
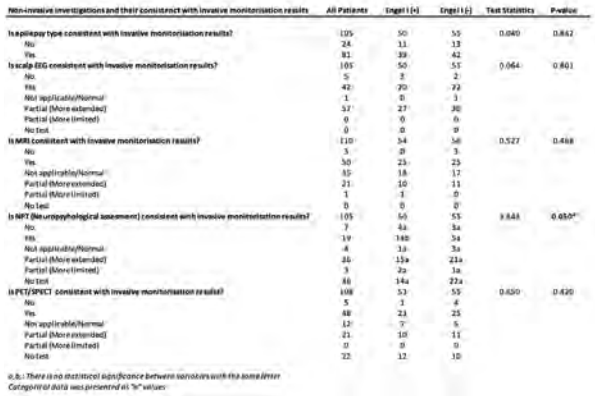
Background and aims: : In selected cases of medically-refractory epilepsy, pre-surgical invasive monitorization is critical for the precise lateralization and localization of the epileptogenic zone. This study was designed to determine the parameters which affect the post-surgical prognosis.
Methods: Patients who underwent epilepsy surgery between 2002-2022, with prior invasive monitorization were retrospectively analyzed. Clinical, electroencephalographical, neuropsychological and structural/functional neuroimaging findings and prognostic features of all patients were evaluated.
Results: Of 162 patients who met inclusion criteria, 111 with complete records were included (female/male: 54/57). The mean age at seizure onset was 9.26±7.74, at epilepsy surgery was 24.95±11.72, and the mean duration between the first seizure and surgery was 15.42±9.27 years. 45 patients were applied with the stereotactic-electroencephalography, 47 with subdural and 17 with subdural+depth electrodes. Fifty-three were temporal lobe and the others were extra-temporal epilepsy; thirty-five were with normal MRI. The most common pathologies in patients who underwent surgery were focal cortical dysplasia (n=67), hippocampal sclerosis (n=16) and gliosis (n=11). The statistical analysis demonstrated that high pre-surgical seizure frequency and high number of anti-seizure medications used, as well as the inability to discontinue anti-seizure medications post-surgically were associated with poor prognosis (Fig-1). The presence of neuropsychological findings compatible with the invasively-detected epileptogenic zone was found to be significantly correlated with Engel-1 outcome (Fig-2).





Conclusion: The extent to which the data obtained from the non-invasive assessment can predict the invasively-detected epileptogenic zone is critical, and this study has shown that clinical and neuropsychological findings were prominent in this regard.

Disclosure: The authors have no conflict of interest to declare.

EPO-130

Physical activity and sedentary behaviour in people with epilepsy

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Background and aims: There is accumulating evidence that physical activity (PA) is essential to promote health and well-being in people with epilepsy (PWE). However, detailed information on PA and sedentary behaviour in PWE is currently unclear. We aimed to contrast the activity behaviour between PWE and healthy controls.

Methods: The SenseWear activity monitor was used to measure PA behaviour in daily life. It was attached to the dominant upper side of participant for 7 consecutive days. Mental, emotional, and psychological health status were assessed with the Montreal Cognitive Assessment (MoCA, cognitive function), Generalized Anxiety Disorders scale 7-item (GAD-7, anxiety symptoms), Beck Depression Inventory (BDI, depression symptoms), Fatigue Severity Scale (the severity and impact of fatigue), Pittsburg Sleep Quality Index (self-perceived sleep quality). Health-related physical fitness was evaluated with the Activities-spesific Balance Confidence scale (balance confidence), Biodex Balance System- Fall Risk Index, 30-second Chair Stand test (lower-limb strength), Timed Up and Go test (functional mobility), Six-minute Walk test (functional exercise capacity).

Results: Sixty-three PWE and 65 healthy controls participated. PWE took on average less steps per day and engaged on average in less sleep duration and spent more time in sedentary compared with healthy individuals. The MoCA, GAD-7, BDI and physical fitness outcome measures of PWE were worse than healthy individuals ($p<0.05$, Table 1).

Table 1. Comparison of activity behaviour, mental, emotional, and psychological health status, and health-related physical fitness between the groups

	People with epilepsy group Median (IQR) (n=63)	Healthy controls group Median (IQR) (n=65)	p
SenseWear activity monitoring			
Daily steps (*steps/day*)	7765.2 (5090.2)	9764.7 (4126.7)	0.007*
Sedentary behaviour (*min/day*)	530.4 (133.1)	453.5 (99.7)	<0.001*
Sleep duration (*min/day*)	445.2 (118.5)	376.8 (91.1)	<0.001*
Mental, emotional, and psychological health status			
Montreal Cognitive Assessment (*0-30*)	24.0 (6.0)	28.0 (3.0)	<0.001*
Generalized Anxiety Disorders scale 7-item (*0-21*)	7.0 (9.0)	4.0 (7.0)	0.019*
Beck Depression Inventory (*0-63*)	12.0 (17.0)	5.0 (8.5)	<0.001*
Fatigue Severity Scale (*7-63*)	33.0 (19.0)	30.0 (22.5)	0.087
Pittsburg Sleep Quality Index *(0-21*)	4.5 (4.0)	4.0 (3.0)	0.481
Health-related physical fitness			
Activities-spesific Balance Confidence scale (*0-100*)	84.0 (16.3)	96.2 (6.8)	<0.001*
Biodex Balance System- Fall Risk Index	1.0 (0.6)	0.8 (0.4)	0.003*
30-second Chair Stand test (*times/30sec*)	18.0 (5.0)	20.0 (5.0)	0.001*
Timed Up and Go test (*sec*)	6.1 (0.9)	5.7 (0.7)	<0.001*
Six-minute Walk test (*meter*)	543.9 (71.7)	612.9 (59.7)	<0.001*

*p<0.05, Mann-Whitney U test.
IQR: Interquartile range.

Comparison of activity behaviour, mental, emotional, and psychological health status, and health-related physical fitness between the groups

Conclusion: PWE were engaged in excessive sedentary time compared to healthy individuals and suffered from mental, emotional, and psychological comorbid conditions and impairment in physical fitness. Future intervention strategies should include behaviour change techniques to promote PA participation in PWE.

Disclosure: The authors report there are no competing interests to declare. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

EPO-131

An iEEG investigation of sex-specific differences in seizure duration

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Background and aims: Male patients with epilepsy are at higher risk for bilateral tonic-clonic seizures (BTCS) as well as sudden death compared to female patients. Despite its tremendous clinical and personal implications, little is still known about sex specific differences in seizure propagation and termination. Aims: To investigate the seizure duration in male versus female epilepsy patients.
Methods: Adult patients with unifocal epilepsy and available intracranial EEG (iEEG) recordings (09/2006-03/2022) were identified retrospectively. Up to 20 clinical seizures were analyzed per patient, excluding patients with status epilepticus or periodic lateralized discharges. The seizure duration was determined based on the iEEG recordings. In case of a focal to BTCS (FBTCS), the duration of the focal and the generalized seizure phase were determined via EEG and seizure semiology. A multiple linear regression model was used for the sex-specific evaluation of the seizure duration, including age, epileptic hemispheric, frontal onset, lateralizing signs, onset during sleep, and aura as independent variables.
Results: A total of 100 patients (m/f=50/50; age: 33.6±12.2 years) and 758 seizures (120 FBTCS) was analyzed. While women had significantly longer focal seizures (p=0.021) than men, male patients revealed significantly longer FBTCS (p=0.001), including longer focal seizure phases (p=0.003). No significant difference was observed for the BTCS phase.
Conclusion: For the first time, sex-differences in seizure duration were described. Our findings may contribute to a better pathophysiological understanding of the sex-specific differences in seizure manifestation and associated risks and underline the yet unmet need of a sex-specific approach in epilepsy research and patient management.
Disclosure: Nothing to disclose.

EPO-132

Sustained ≥90% response and seizure freedom in patients with focal-onset seizures treated with cenobamate

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Background and aims: The maintenance of clinical response over time is a main concern in patients with epilepsy, thus, sustained seizure freedom is the ultimate goal of epilepsy treatment. Unfortunately, many studies failed to show sustained seizure freedom. Here, we analyze sustained seizure control in patients treated with cenobamate.
Methods: Adults with focal seizures despite treatment with 1-3 concomitant ASMs completed the double-blind treatment and entered the open label extension (OLE). 354 were included in the C017 OLE modified intent-to-treat population (mITT), 265 originally randomized to CNB, 90 to placebo. All patients underwent a 2-week double-blind conversion to a target dose of cenobamate 300 mg/d. This post-hoc analysis examined sustained seizure response >= 90% and sustained seizure freedom.
Results: During the OLE, >= 90% sustained response for at least one year was achieved by an estimated 38.5% of the patients, and an estimated 23.6% showed sustained seizure freedom. Among these patients, half of them achieved >= 90% sustained response from day 1 and time to achieved sustained seizure freedom,12 months. An estimated 28.4% of the patients achieved >= 90% sustained response for at least 2 years, and 14.3% of being seizure free. Sustained >= 90% response for at least 3-years was achieved by an estimated 23.9% of the patients and 7.5% were seizure-free.
Conclusion: These results suggest that adjunctive cenobamate is a promising drug and may be a suitable long-term treatment for patients with focal-onset seizures to achieve and maintain a high-level of clinical response, including seizure freedom.
Disclosure: The original study (NCT01866111) was supported by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini S.p.a. (Rome, Italy).

EPO-133

Association of seizure frequency and suicidal tendencies in adults with epilepsy

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Background and aims: Adults with epilepsy (AWE) sometimes present suicidal tendencies (ST). In this study we aimed to understand whether seizure frequency was associated with ST in AWE.
Methods: AWE were assessed in epilepsy center: clinical interview covered the duration, seizure frequency during last month and last year, current medication. ST were assessed based on the respective Hamilton Depression Rating Scale (HAMD) item. Mann-Whitney U and Chi-square tests were used.
Results: Overall, 168 AE were divided into two groups: ST group (SG, n=24, mean age - 37±12.6, females – 41.7%) and no ST group (NSG, n=144, mean age – 34.5±13.6, females – 47.2%). AWE with ST were more in focal epilepsy, however not statistically significant (SG/NSG – 91.7%/74.3%, p=0.06). Epilepsy duration was similar

between groups (11.8 vs 10.8 yrs, p>0.05). Seizure frequency during the past year was significantly higher in SG (SG/NSG – 57.4/33.3, p<0.05). A similar tendency was seen for seizure frequency during the last month albeit not statistically significant (SG/NSG – 4.3/3.8, p>0.05). Interestingly, there was no difference between SG and NSG groups in regard to the presence of generalized tonic-clonic seizures (87.5% vs 89.5%, p>0.05).

Conclusion: Our results show that seizure frequency during the last year is higher in adults with epilepsy who have suicidal tendencies. This was not seen for seizure numbers in the preceding month. We found that patients with epilepsy are more likely to have suicidal tendencies. The presence of generalized tonic-clonic seizures and the duration of epilepsy were not associated with suicidal tendencies.

Disclosure: Nothing to disclose.

EPO-134

Cenobamate as treatment of "super-refractory" focal epilepsy: Results from a cohort of the Spanish expanded access

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Background and aims: Objective: To assess the effectiveness and tolerability of cenobamate (CNB) in patients with uncontrolled focal-onset seizures despite treatment with at least two anti-seizures medication (ASM) through a name-patient program (NPP) in Spain.

Methods: We performed an unicenter, retrospective, observational study aimed to determine the efficacy and safety of CNB in patients with a 3-month minimum follow-up. Inclusion criteria were 1) >=18 years; 2) focal seizures; 3) NPP-expanded access authorization. Data were obtained from medical records at baseline, 3- and 6-month visits.

Results: 39 patients with a mean(SD) age of 42,6(13,6) years and median(IQR) number of trialed ASM of 9(5-13) were included. At 3 months, the mean(SD) and median dose were 153,3mg(68,5) and 200mg, respectively. 50% and 90% seizure frequency reduction occurred in 64,8% and 16,2% of patients, respectively. 12% of patients become seizure-free. At 6 months, 72,7% of patients had 50% seizure reduction, 4,7% had 90% reduction and 4,7% become seizure-free with a mean and median dose of 213,6mg(53,8) and 200mg, respectively. 75,6% and 36,3% of patients reported adverse effects (AEs) at 3 and 6 months, including somnolence, dizziness, cognitive, fatigue, ataxia and diplopia. The number of concomitant ASM was reduced from a mean of 3,1 to 2,8 and 2,4 at 3- and 6-month visits, respectively. One patient discontinued treatment because of inefficacy and three due to AEs.

Conclusion: CNB is effective in "super-refractory" focal epilepsy and allowed for reducing drug load. Also, is a well-tolerated ASM with mild-moderate AEs that can be resolved by adjusting concomitant ASMs without leading to discontinuation.

Disclosure: P C-G and PJ S-C received (speaking) fees from Angellini.

EPO-135

Intraoperative electrocorticography in epilepsy surgery: data from the Epilepsy Center of Modena

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Background and aims: Intraoperative electrocorticography (ECoG) is used in epilepsy surgery to identify the presence of epileptiform activity related to the epileptogenic lesion. We present data regarding ECoG recordings collected from 2019 to 2022 at the Epilepsy Center of Modena.

Methods: All patients addressed to epilepsy surgery underwent serial iECoG recordings with 1 x 4 strip with platinum-iridium electrodes placed over and along the lesional cortex before resection and along the surgical neocortical margin of the resection. Bipolar and referential electrode montages were reviewed to identify epileptiform abnormalities. ECoG patterns were subdivided according to Palmini et al. classification.

Results: 49 patients underwent to surgical procedure. In 37 patients (26M, 11F, mean age 37.2Â±14.1) we could obtain at least one ECoG recording. Among the 35 pre-resection recordings, the following patterns were found: A (13/35), A+B (3/35), A+B+C (2/35), A+C (2/35), A+C+D (1/35), B (2/35), B+C (1/35) B+D (1/35), C (1/35), absence of epileptiform abnormalities (6/35). In 5/35 patients with tumoral lesions (3) and focal cortical dysplasia (FCD) (2/25), intraoperative electrographic seizures were recorded (D pattern). Abnormal ECoG patterns were found in 9/11 patients with FCD (type Ia, IIb, IIIa), in 7/11 patients with a tumoral lesion, 3/3 with hippocampal sclerosis, in 6/6 with gliosis and in 4/5 with a cavernoma.

Results of the frequency of Palmini classification Pattern, the IED related to different disease pathology and the Number of intra operative seizures

Conclusion: These findings demonstrated that there is a good concordance between the histopathological data and the ECoG patterns. ECoG could be a valuable operative instrument to identify epileptiform abnormalities during the surgical procedure with the potential to help in guiding the surgical resection extent.
Disclosure: Nothing to disclose.

EPO-136

Chemogenetic activation of the locus coeruleus increases noradrenaline levels and modulates hippocampal excitability

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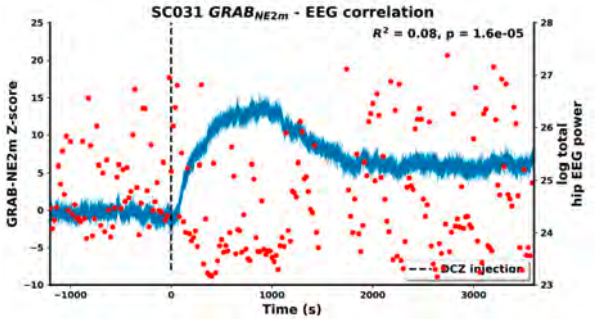
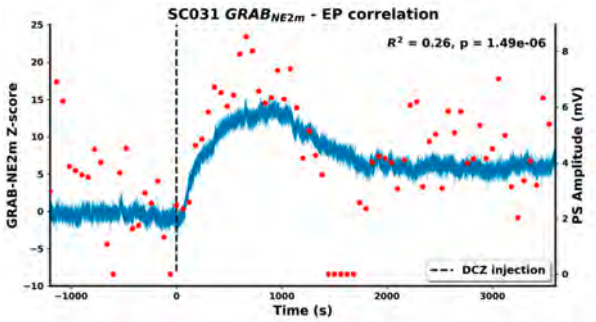
Background and aims: The brainstem locus coeruleus (LC) is the sole source of noradrenaline in the neocortex, hippocampus and cerebellum. Noradrenaline is a neuromodulator involved in the regulation of excitability of brain networks. Recent development of tools for precision modulation of the LC, including Designer Receptors Exclusively Activated by Designer Drugs, allow the study of LC physiology with unprecedented detail. In this study, we assessed the influence of activating the LC on noradrenergic signaling and excitability in the hippocampus.
Methods: Male Sprague Dawley rats (n=5) were injected with the viral vectors CAV2-PRSx8-hM3Dq-HA hSyn-mCherry in the LC and AAV9-hSyn-NE2m-mRuby3 in the hippocampus to induce expression of hM3Dq in LC neurons and the GRABNE2m biosensor in the hippocampus. All rats were implanted with a stimulation electrode in the perforant path and a recording optrode in the dentate gyrus. Rats were injected with deschloroclozapine (DCZ) to activate the LC and to assess the effects on noradrenaline signaling and dentate gyrus electrophysiology.
Results: Injection of DCZ resulted in an increase in GRABNE2m fluorescence, a decrease in EEG power and an increase in the amplitude of the population spike of the dentate gyrus evoked potential. Changes in population spike amplitude and EEG power were significantly correlated to the observed changes in GRABNE2m fluorescence.



Injection of DCZ, activating the LC, results in a pronounced increase in GRABne fluorescence, which is significantly correlated to a decrease in EEG power.



Injection of DCZ, activating the LC, leads to an increase in the amplitude of the population spike of the dentate gyrus evoked potential. This change is significantly correlated to changes in GRABne fluorescence.

Conclusion: This study is the first to assess the effect of chemogenetic activation of the LC on noradrenaline signaling in the hippocampus with GRAB-sensor technology, providing unprecedented temporal resolution. This research is able to confirm previous findings of pharmacological studies with superior precision and specificity.
Disclosure: Nothing to disclose.

EPO-137

Antiseizure medication monitoring: patient-self-collected versus nurse-collected volumetric absorptive microsampling

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Background and aims: Volumetric absorptive microsampling (VAMS - Mitra®, Neoteryx) is increasingly proposed as a clinically reliable sampling methodology for therapeutic drug monitoring (TDM). The study's aim was to establish the feasibility of patient self-collected VAMS as a practical tool for TDM of antiseizure medications (ASM).

Patient self-collected and nurse-collected-VAMS were compared. Plasma ASMs concentrations from venous blood were used as a reference standard to compare blood concentrations found in VAMS.
Methods: Persons with epilepsy (PWE) were enrolled in this study. Morning venous and capillary blood by VAMS were collected by nurses. Afterward, patients performed VAMS collection by themselves. Blood and plasma analyses were analyzed by ultra-high liquid chromatography-mass spectrometry. ASMs blood concentrations from nurse-collected-VAMS were compared to plasma concentrations. A cross-validation study was performed comparing ASMs concentrations obtained by nurse-collected versus patient-self-collected VAMS samples.
Results: 301 PWE (173 females, mean age: 44.33±16.10 years) were enrolled providing a total of 456 ASMs concentration measurements. Linear correlation analyses between ASMs plasma and blood nurse-collected-VAMS concentrations showed heterogeneous results depending on the analyte (R2 ranging from 0.4 to 0.9; $p<0.001$). Cross-validation analysis between nurse-collected vs patient self-collected VAMS showed a bias within ±20% for more than 78% of intrasubject ASMs determinations.
Conclusion: To our knowledge, this is the first study considering the real-world application of patient self-collected VAMS for ASMs-TDM. Furthermore, concentration from self-collected-VAMS has proved comparable with those from nurse-collected, demonstrating that patients' self-sampling can be feasible after minimal training. Results give a promising basis for at-home VAMS applications.
Disclosure: All authors declare no conflicts of interest.

EPO-138

Imaging neuronal currents for the delineation of the seizure onset zone in epilepsy: initial clinical experiences

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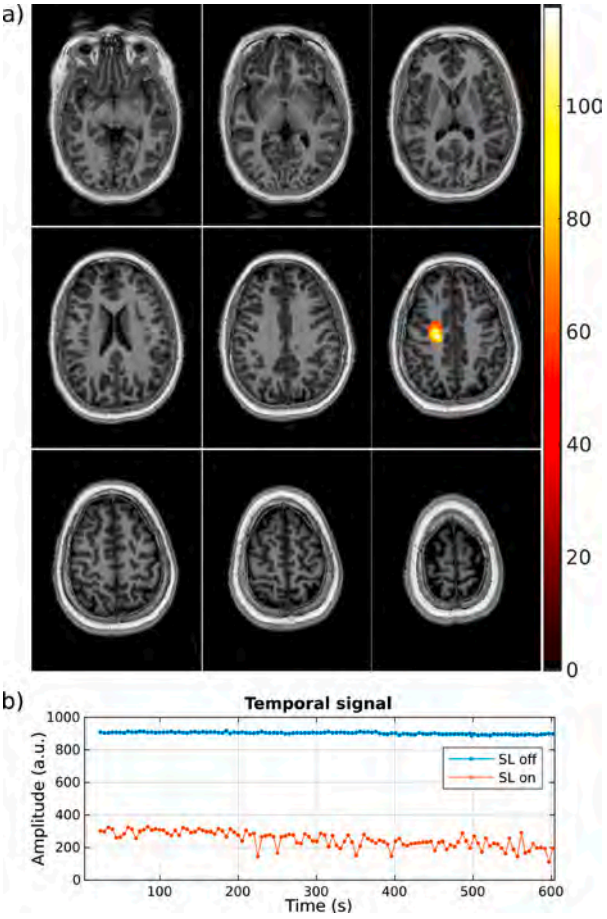
Background and aims: Non-invasive delineation of the seizure onset zone (SOZ) remains challenging for neurophysiological methods such as EEG or MEG, due to spatial accuracy. Neuronal current imaging (NCI) with magnetic resonance imaging is a novel functional neuroimaging method that simultaneously encodes functional and spatial information. As this method is frequency selective, we targeted high-frequency oscillations (~120Hz) as SOZ markers. In this work, we report on the initial experience in epilepsy patients, challenges and limitations of the method.
Methods: Eleven epilepsy patients (with negative MRI) and 24 healthy volunteers were imaged with NCI at pre adjusted spin-lock frequencies to target high-frequency oscillations. In the patients, results were compared with interictal EEG. A post-processing pipeline is presented and used to identify key features of the contrast.
Results: We used mean signal contrast and standard deviation to compare NCI signal intensity of epilepsy patients vs. healthy volunteers. Using the data from healthy volunteers, we determined the significant NCI threshold levels. Activations above threshold were identified in 8 out of 11 patients with negative MRI. Hemispheric concordance with the presumed seizure onset zone was depicted in 7 and lobar concordance in 4 patients. False-positive results were observed in 1 and false-negative results in 5 patients.



a) Exemplary case of NCI activation hemispheric concordant with EEG finding.

b) Signal temporal response of ROI within detected area for baseline and NCI contrast acquisition.

Conclusion: NCI is a novel imaging contrast that highlighted activated areas in 8 out of 11 patients with negative MRI. The method is currently under prospective evaluation in the SWISS FIRST study in first seizure patients.
Disclosure: This study was funded by the Swiss National Science Foundation via the SINERGIA project 180365: The SWISS FIRST study

EPO-139

Effects of hormonal replacement therapy on seizures' frequency of postmenopausal women with epilepsy:A systematic review

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Background and aims: Hormonal replacement therapy (HRT) is used for symptomatic treatment of menopause. Some evidence suggests a proconvulsant effect of estrogen and an anti-convulsant role of progesterone. Thus, the use of exogenous sex steroid hormones might influence the course of epilepsy in peri- and postmenopausal women with epilepsy (WWE). We conducted a systematic review on the impact of HRT on the frequency of seizures in WWE.
Methods: PubMed and Scopus were searched for articles published from inception until August 2022. Abstracts from the last five years from the European Academy of Neurology and European Epilepsy Congresses were also reviewed. Article reference lists were screened, and relevant articles were retrieved for consultation. Interventional and observational studies on WWE and mice models of estrogen deficiency were included. Critical appraisal was performed using the Revised Cochrane risk-of-bias tool for randomized trials (ROB2) and ROBINS-E tools.
Results: Of 497 manuscripts screened, twelve studies were included, including three human studies. One cross-sectional study showed a decrease in seizures' frequency in WWE using combined HRT (estrogen and progesterone), a case-control study showed an increase in comparison with controls and a randomized clinical trial found a dose-dependent increase in seizures' frequency in women with focal epilepsy taking combined HRT. Nine studies addressing the impact of HRT in rat models were also included, which showed conflicting results.
Conclusion: There is scarce evidence of the impact of HRT in WWE. Further studies should evaluate the harmful potential and prospective registries are needed for monitoring in this population
Disclosure: The authors do not have any conflict of interest to declare in relation to this project.

EPO-140

STEPPER (Status Epilepticus in Emilia Romagna): therapeutic interventions and quality of care in Emilia-Romagna Region

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Background and aims: SE (status epilepticus) is one of the primary neurological emergencies. Several studies conducted in Emilia Romagna Region (ERR), in the previous two decades have shown that mortality is still high and variable in different areas. STEPPER (STatus EPilePticus in ER) aimed at studying clinical characteristics, management and prognostic factors of SE in the adult population of ERR, focusing on refractory SE (RSE) and non-convulsive SE (NCSE).
Methods: We conducted a multicenter prospective observational study on SE in 17 neurological and intensive care units in ERR between 2019 and 2021. Follow-up was performed thirty days after SE onset.
Results: 610 cases were recruited: 56% female; mean age 70 years; 54% with prominent motor symptoms; 43% had in-hospital onset, 30% were NCSE in coma. Etiology was known in 87% of SE (acute 49%, remote 27%, progressive 20%, definite epileptic syndrome 3%). The mean pre-SE Rankin score was 2; mean STESS and EMSE were 3 and 71. 34% of cases were RSE. Benzodiazepines were used well beyond the first line of treatment, while only 47% of RSE cases received a third-line therapy with anesthetic drugs. Thirty-day mortality was 24% in the whole population, 24% in NCSE, and 38% in RSE. The mean Rankin score at follow-up was 3.
Conclusion: We confirmed high 30-day mortality of SE and worsening of functional outcome in survivors. High EMSE scores are in line with a poor prognosis in our cohort. Poor adherence to SE treatment guidelines might have influenced the prognosis in some cases
Disclosure: This study was funded by the Italian Ministry of Health (RF-2016- 02361365)

EPO-141

EEG Reactivity Predicts Individual Response to Vagal Nerve Stimulation (VNS) in Children with Drug-resistant Epilepsy

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Background and aims: Vagal nerve stimulation (VNS) represents a therapeutic option in patients with drug-resistant epilepsy. This type of treatment leads to significant seizure reduction in 50-60% patients (VNS responders). The resting 50 % patients do not profit from VNS therapy (VNS non-responders). We developed a statistic classifier - Pre-X-Stim - predicting VNS efficacy based on analysis of pre-implantation EEG (Brazdil et al., 2019). This classifier was developed in adult population (> 18 years). In this project, we tried to extrapolate our results on children population (< 18 years).
Methods: We retrospectively identified a group of children treated with VNS. In each child, EEG with photic stimulation and hyperventilation was found. EEG was filtered into four common frequency bands and segmented into 8 time-intervals based on their relation to photic stimulation and hyperventilation. Relative mean power was calculated for each time-interval in each frequency band. Then after, existing classifier post-processed relative mean powers in every child to determine the predicted response (predicted responder vs. predicted non-responder). As the last step, we compared the predicted and the real-life response to determine accuracy, sensitivity, and specificity.
Results: There were 6 children (median age 9 years, minimum 8 years, maximum 18 years). Two (33 %) children non-responders, the resting four (67 %) were responders to VNS therapy. We were able to predict correctly the response to VNS in 5 out of 6 children (accuracy 0,83, sensitivity 0,75, specificity 1).
Conclusion: Our statistic classifier – Pre-X-Stim – can predict VNS efficacy in both adult and children population.
Disclosure: This project is supported by the Ministry of Health of the Czech Republic, gran nr. NV19-04-00343.

EPO-142

Angiotensin receptor blocker (ARBs) drugs in post-stroke epilepsy (PSE) prevention: a retrospective observational study

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Background and aims: Among the risk factors for epilepsy and stroke, hypertension is a prominent one. Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blocker (ARBs) seem to promote a protective effect in the development of seizures in the general population. However, no data are available about their possible preventive role in post-stroke epilepsy (PSE). In this study, we evaluate the effectiveness of anti-hypertensive treatment in preventing PSE.
Methods: In this retrospective, observational study, patients with hypertension and diagnosis of ischemic stroke confirmed by clinical and neuroimaging evaluation were retrospectively selected between January 2016 and December 2022. Diagnosis of PSE was made according to ILAE criteria. The details of the anti-hypertensive treatment as well as demographics, and clinical and neuroradiological data were reviewed.
Results: 361 patients (mean age 70.2 ± 13.5 , 200 men, 58%) were enrolled. Twenty-seven (7.5%) patients developed PSE. Large vessel occlusion (p=0.031), atrial fibrillation (p=0.033), and cortico-sottocortical lesions (p=0.003) were related to a higher risk of PSE development. A lower risk of PSE was observed in patients treated with ARBs (p=0.027). No differences were observed according to ACEi, Calcium Channel Blocker, and Beta-blockers.
Conclusion: ARBs show a potential protective role in epilepsy development in patients with hypertension and stroke. If confirmed by larger studies, these findings suggest ARBs could be used as a novel approach for preventing epilepsy in patients with stroke.
Disclosure: Nothing to disclose.

MS and related disorders 1

EPO-143

Factors associated with decision to switch SPMS patients to siponimod versus staying on fingolimod

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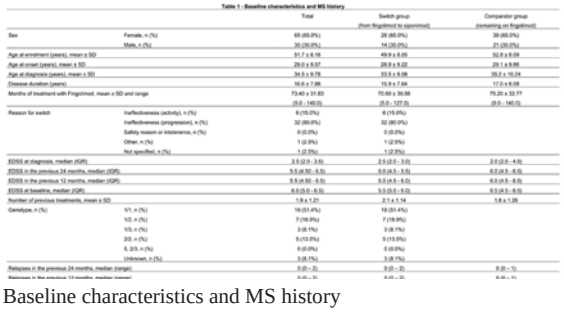
Background and aims: To explore factors associated with switching to siponimod versus staying on fingolimod in SPMS patients treated with fingolimod.
Methods: Multicentric cross-sectional study. SPMS patients treated with fingolimod and switching from fingolimod to siponimod were enrolled. Patients in both groups were treated with fingolimod for at least 2 years until the time of enrollment. We collected demographics (age and sex) and clinical data (age at onset, treatment duration with fingolimod until the enrollment, EDSS at the time of enrollment, number of previous DMTs, relapses in the previous 12 months). Univariable and multivariable models were applied to explore factors associated with switching to siponimod versus staying on fingolimod.
Results: 100 SPMS patients were enrolled (demographics and clinicals are displayed in table 1). 40% of SPMS patients treated with fingolimod switched to siponimod. The multivariate regression analysis showed EDSS at baseline and number of previous DMTs as the only independent variables associated with the outcome (respectively OR: 0.60; 95%CI: 0.41 – 0.89; p = 0.011 and OR: 1.53; 95%CI: 1.02 – 2.31; p = 0.042; table 2). Furthermore, although not statistically significant, higher number of relapses in the previous year occurred in switched patients compared to patients on fingolimod (OR: 2.92; 95%CI: 0.67 – 12.78; p = 0.16; table 2).



Baseline characteristics and MS history

Table 2 - Factors associated with the change from Fingolimod to Siponimod

	UNIVARIATE OR (95%CI); p value	MULTIVARIATE OR (95%CI); p value
Sex, males vs females	1.00 (0.43 – 2.31); 0.99	-
Age at enrolment (years)	0.96 (0.91 – 1.01); **0.09**	0.96 (0.91 - 1.02); 0.21
Age at onset (years)	1.00 (0.96 – 1.04); 0.90	-
Disease duration (years)	0.98 (0.93 – 1.03); 0.49	
EDSS at baseline	0.69 (0.50 – 0.97); **0.031**	0.62 (0.43 – 0.91); **0.014**
Number of previous DMTs	1.26 (0.90 – 1.76); 0.19	1.53 (1.02 – 2.31); **0.042**
Relapses in the previous 12 months	2.72 (0.70 – 10.59); 0.15	2.92 (0.67 – 12.78); 0.16
Months of treatment with Fingolimod	1.00 (0.98 – 1.01); 0.48	

Factors associated with the change from Fingolimod to Siponimod

Conclusion: Only 40% of SPMS patients treated with fingolimod were switched to siponimod. Lower EDSS and higher number of previous DMTs were associated with the decision to switch to siponimod.
Disclosure: The authors declare no competing interests for this work.

EPO-144

Safety and tolerability of Zadiva® (NanoAlvand Co. brand-generic product of dimethyl fumarate) in Iranian MS population

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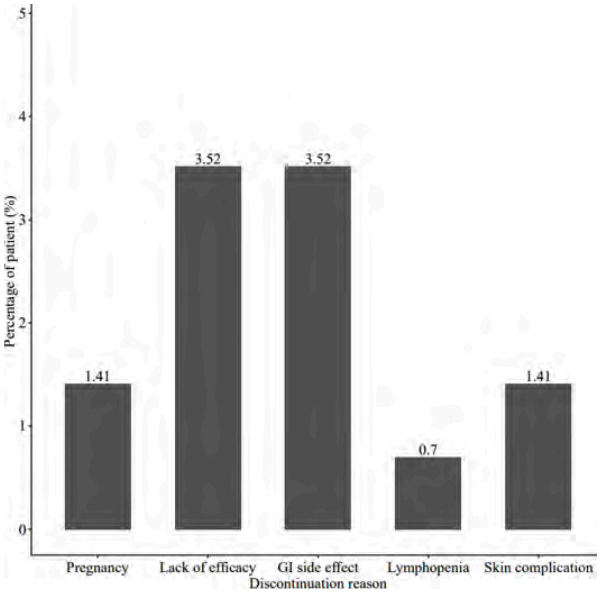
Background and aims: Dimethyl fumarate (DMF) was approved in 2013 to reduce disease activity in relapsing remitting multiple sclerosis (RRMS) patients. Although randomized controlled trials' evidences are high-level, they cannot reflect the clinical context in which drugs are used in reality.
Methods: The study is an observational, retrospective and real-world assessment of the safety and tolerability of Zadiva® in Iranian RRMS patients. Individuals' data in the neurology clinics of a referral university hospital following receiving informed consent were collected. The main objectives of the study were to assess the safety and discontinuation rate of the drug during the follow-up period and the reasons for the discontinuation. Other objectives were the number of patients who experienced a relapse and their EDSS score.
Results: A total of 142 patients with mean age of 33.90 ± 7.76 years were enrolled in the study. During the evaluation, only 15 patients (10.56%) discontinued treatment with the drug. The leading causes for discontinuation were adverse events, lack of efficacy, and pregnancy respectively. Besides, the most common adverse events were flushing (N=34, 23.94%), though no serious adverse event were

reported. The data also demonstrated a significant reduction in the number of patients with relapse, and 90.85% (N=129) of patients were relapse-free at the end of the study. The mean EDSS score changed from 1.64 ± 0.44 to 1.68 ± 0.50 before and after one-year treatment.

Age (yr) Mean ± SD	33.90 ± 7.76
Gender, Female N (%)	126 (88.73)
EDSS score Mean ± SD	1.64 ± 0.44
Duration of disease (yr)* Mean ± SD	4.55 ± 3.82
Previous medication history N (%)	
Interferon beta-1a, IM	50 (35.21)
Interferon beta-1a, SC	21 (14.79)
Interferon beta-1b, SC	9 (6.34)
Glatiramer Acetate	36 (25.35)
Fingolimod	2 (1.41)
Teriflunomide	1 (0.70)
Naive	11 (7.75)
Unknown	12 (8.45)

*Calculated for 139 patients

Demographics and baseline characteristics



Reasons of discontinuation

System Organ Class	Preferred Term Name	No. of Patients (N=142)
Vascular disorders	At least one event	34 (23.94)
	Flushing	34 (23.94)
Gastrointestinal disorders	At least one event	27 (19.01)
	Abdominal pain	23 (16.2)
	Diarrhoea	13 (9.15)
	Dyspepsia	11 (7.75)
	Nausea	9 (6.34)
	Vomiting	2 (1.41)
Skin and subcutaneous tissue disorders	At least one event	17 (11.97)
	Erythema	10 (7.04)
	Rash	4 (2.82)
	Pruritus	4 (2.82)
	Lichenoid keratosis	1 (0.7)
Investigations	At least one event	16 (11.27)
	Transaminases increased	16 (11.27)
Blood and lymphatic system disorders	At least one event	7 (4.93)
	Lymphopenia	6 (4.23)
	Eosinophilia	1 (0.7)
Infections and infestations	At least one event	3 (2.11)
	Varicella zoster virus infection	2 (1.41)
	Tinea versicolour	1 (0.7)
Nervous system disorders	At least one event	2 (1.41)
	Headache	2 (1.41)
Immune system disorders	At least one event	1 (0.7)
	Urticaria	1 (0.7)

Incidence of adverse events classified based on the Medical Dictionary for Regulatory Activities (MedDRA) as the preferred term (PT) and system organ class (SOC)

Conclusion: The results of this study confirmed the acceptable safety and tolerability of Zadiva® in a real-world setting for RRMS patients in addition to its efficacy.
Disclosure: All authors declared there is no relationships, activities and interests related to the manuscript.

EPO-145

Erectile dysfunction in men with multiple sclerosis

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Background and aims: To evaluate the prevalence and predictors of erectile dysfunction in men with multiple sclerosis (mwMS).
Methods: 179 consecutive mwMS (age 37.25±9.48 years, disease duration 7.64±5.54 years) and 32 (33.72±8.53 years) healthy controls (HC) were enrolled. mwMS completed The sexual health inventory for men (IIEF-5), Modified Fatigue Impact Scale (MFIS) (cognitive, physical, and psychosocial subdomain), Beck depression inventory (BDI-2), and The 5-level EQ-5D questionnaire (your health

today question, range from 0-100). HC completed the IIEF-5. We performed a linear regression analysis and statistically significant predictors from the univariable analysis were included in the multivariable regression analysis.
Results: mwMS scored less on IIEF-5 compared to HC (23, range 6-25 vs 24, range 14-25, p=0.017). Erectile dysfunction (defined as IIEF-5 score ≤21) was present in 37.9% of mwMS and 25.8% of HC, p=0.227. In the univariable linear regression analysis age, multifunctional initial presentation of MS, MRI lesions in the brainstem, EDSS, physical, cognitive, and psychosocial domains of MFIS were negative and your health today question of the EQ-5D was a positive predictor of the IIEF-5 score. In a multivariable linear regression analysis age (B=-0.155, 95% CI -0.275- -0.035), the multifunctional initial presentation of MS (B=-7.857, 95% CI -15.625 - -0.089) and cognitive part of MFIS (B=-0.212, 95% CI -0.410 - -0.014) were negative predictors of the IIEF-5 score.
Conclusion: Erectile dysfunction is very frequent in mwMS. Increased age and presentation with multifunctional symptoms at disease onset and cognitive fatigue are negative predictors of the IIEF-5 score.
Disclosure: IA: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals. TG: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals. MKS: received consultation and/or speaker fees from: Sanofi Genzyme, Roche. MH: Participated as a clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Bayer, Novartis, Pliva/Teva, Roche, Alvogen, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals.

EPO-146

Remibrutinib: A Novel BTKi in Development for MS With a Favorable Safety Profile in Various Autoimmune Disorders

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Background and aims: Remibrutinib is a novel, potent, highly selective, covalent, oral Bruton's tyrosine kinase inhibitor (BTKi) currently investigated in Phase 3 trials for treatment of multiple sclerosis (MS; NCT05147220/NCT05156281). This analysis presents an overview of the safety of remibrutinib from Phase 2 clinical trials in various autoimmune disorders.
Methods: Data were collected from final analyses of trials in chronic spontaneous urticaria (CSU), Sjögren syndrome (SjS), and asthma, and interim analysis of open-label extension (OLE) in CSU. Safety assessments comprised of AEs, including serious and AEs of special interest (AESI), vital signs, ECGs, and laboratory parameters.
Results: Overall, 363 patients (267 CSU; 49 SjS; 47 asthma) who received various doses (10–100 mg q.d./b.i.d.) of remibrutinib for 12–52 weeks were included. Among CSU patients, the safety of remibrutinib 100 mg b.i.d. in the 52-week OLE study was comparable to doses in the core study (Table 1). Overall, most frequently reported grouped AEs (≥10%) were infections and infestations, skin, subcutaneous, gastrointestinal, and nervous system disorders. AEs were similar to placebo in core studies except for skin disorders, where post-treatment CSU flares caused an imbalance. There were no increases in infection rates. Other AESI, including bleeding (all minor) and cytopenia were not altered during long-term treatment. No safety concerns were noted in laboratory analyses, ECGs, or vital signs.

Patients, n (%)	Core study		Extension study
	Remibrutinib any dose (n=267)	Placebo (n=42)	Remibrutinib 100 mg b.i.d. (N=183*)
Duration of exposure, weeks, median (IQR)	12 (12.0–12.3)	12 (12.1–12.7)	35 (14.4–52.0)
Patients with ≥1 AE	155 (58.1)	18 (42.9)	105 (57.4)
Discontinued study treatment due to AE(s)	7 (2.6)	0 (0.0)	6 (3.3)
Patients with SAE(s)	5 (1.9)	0 (0.0)	4 (2.2)
Death	0 (0.0)	0 (0.0)	0 (0.0)

*At the time of interim analysis (July 2021).
AE, adverse event; b.i.d., twice a day; CSU; chronic spontaneous urticaria; IQR, interquartile range; N, total number of patients; n, number of patients in each arm; SAE, serious adverse event.

Table 1. Safety and Tolerability of Remibrutinib (10–100 mg q.d./b.i.d.) in the 12-week Core and 52-week Extension Phase 2b Studies in CSU patients

Conclusion: Remibrutinib demonstrated a favorable safety profile and was well tolerated at all doses studied in Phase 2 trials and the 52-week OLE (up to 100 mg b.i.d.), supporting its development in Phase 3 clinical trials in MS.
Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPO-147

ACE and ACE-2 as potential biomarkers in multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune neurodegenerative disease characterized by demyelination in the central nervous system (CNS). It is heterogeneous in terms of clinical expression, histopathological and radiological changes, and response to therapy. Renin-Angiotensin System (RAS) plays a pivotal role in autoimmune inflammation in the CNS. Angiotensin-converting enzyme (ACE) and its homolog ACE-2 are considered two of the major enzymes in the RAS system. The aims of this study were to measure protein levels of ACE and ACE2 in the serum obtained from MS patients and healthy controls, and to find significant associations with demographics and clinical characteristics of patients.
Methods: This was a case-control study that included 87 MS patients and 87 age and sex matched healthy controls. Serum levels of the target markers was measured using human enzyme-linked immunosorbent assay (ELISA) technique.
Results: Median serum ACE and ACE-2 levels were significantly higher in MS patients (220.60 pg/ml and 1867.68 pg/ml, respectively) compared to healthy controls (159.28 pg/ml and 1059.72 pg/ml, respectively) (p-value<0.001). Cut-off values of 188.66 pg/ml for ACE and 1459.03 pg/ml for ACE2 were found to discriminate MS patients from healthy controls (sensitivity = 66.7% and 78.2%, and specificity = 62.1% and 75.9%, respectively). Significant correlations were revealed between serum ACE level and BMI (p-value=0.012) and MS disease duration (p-value=0.002), also between ACE2 level and gender (p-value=0.027).
Conclusion: Serum ACE and ACE-2 can be potential diagnostic biomarkers for MS. However, future prospective studies should focus on investigating their role in predicting response to therapy in MS patients.
Disclosure: The authors declare that there are no conflicts of interest.

EPO-148

Cognitive assessment in a large Argentinian cohort of patient with Multiple Sclerosis

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Background and aims: Cognitive impairment (CI) is a common symptom of multiple sclerosis, with a negative effect on patients' daily lives. **Objectives:** 1-To describe the prevalence of CI and cognitive profile of the PwMS cohort. 2-To compare the cognitive performance of PwMS in relation to Expanded Disability Status Scale (EDSS) and MS duration.
Methods: Cross-sectional study. Measuring instruments: Clinical and cognitive variables were assessed (EDSS, Fatigue severity scale, Beck Depression Inventory, BICAMS battery, PASAT, verbal fluency, 7/24 test). CI was defined as impairment in ≥2 cognitive domains. Parametric and non-parametric statistics were used, $p<0.05$ was considered significant.
Results: 323 PwMS were recruited. Mean age: 40.71±12.89 years; mean education: 13.43±4.2 years; mean EDSS: 2.05±1.94 (median 2.5 IQR8) and stratified EDSS was 0-3:61.7%; 3.5-8:38.3%; mean MS duration: 8.51±8.29 years; female 62.8%; relapsing-remitting MS (RRMS) 91.6%. Objectives:1)The prevalence of CI at inclusion study was 47.5%. The most affected cognitive domains were: attention and processing speed followed by verbal memory, verbal fluency and visual memory. 2)Patients with EDSS between 3.5-8 presented worse cognitive performance ($p<0.05$). The PwMS duration >20 years presented worse cognitive performance compared to those of ≤5 years ($p<0.05$). The group of >20 years presented worse performance than those of 6-10 years ($p<0.05$). In a multivariable logistic regression model, EDSS was an independent risk factor to reach CI when adjusted for potential confounders (adjusted Odds Ratio(OR) 1.43, 95% confidence interval(CI) 1.09-1.87, p=0.01).
Conclusion: The prevalence of IC in our cohort was similar to previous reports. Disability (EDSS) was an independent predictor of CI.
Disclosure: Nothing to disclose.

EPO-149

Comorbidities among myasthenia gravis patients: a population-based observational study in Denmark, Finland, and Sweden

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Background and aims: Myasthenia gravis (MG) is a rare autoimmune neuromuscular disease. Comorbidities complicate medical management and can be a consequence of MG or its treatment. Here, we assessed the evolution of MG comorbidity burden in Denmark (DK), Finland (FI), and Sweden (SE).

Methods: Data were collected from healthcare registers with almost complete population coverage. Incident MG patients were identified based on ≥2 MG diagnostic codes (ICD-10; G70.0*) in specialty care during 2000–2020, defining first (incident) MG diagnosis as the index date. The presence of comorbidities was assessed based on hospital discharge diagnoses five years before and up to 20 years after the index date. Comorbidities reaching 10% cumulative incidence at 20 years are presented. Cumulative incidences were estimated from the index date onwards regardless of the pre-existence of comorbidity, treating death as a competing risk.

Results: Among 6415 patients, 76% had ≥1 of 41 comorbidities. Difference (%-points) in comorbidities five years prior and five years after the index date was highest for hypertension in FI (+10.9%) and SE (+12%), and osteoporosis in DK (+8.7%) (Figure 1). Across countries, age and sex, highest cumulative comorbidity incidence at 10 and 20 years after index date was observed for hypertension (Figure 2). Similarly, the highest cumulative incidences over 20 years were hypertension followed by malignancies (excluding thymoma) and cataract (Figure 3).

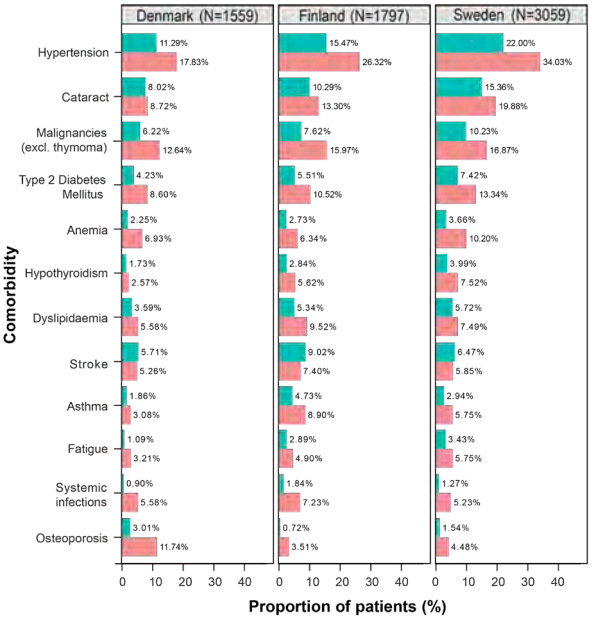

Figure 1: Comorbidities five years prior and five years after the incident myasthenia gravis diagnosis in Denmark, Finland, and Sweden.

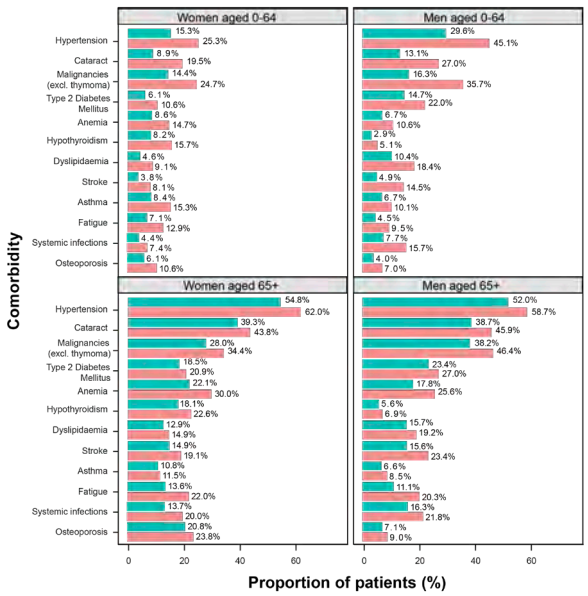

Figure 2: The cumulative incidence of comorbidities at 10 and 20 years on or after the incident myasthenia gravis diagnosis (index date) in Denmark, Finland, and Sweden, by age and sex.

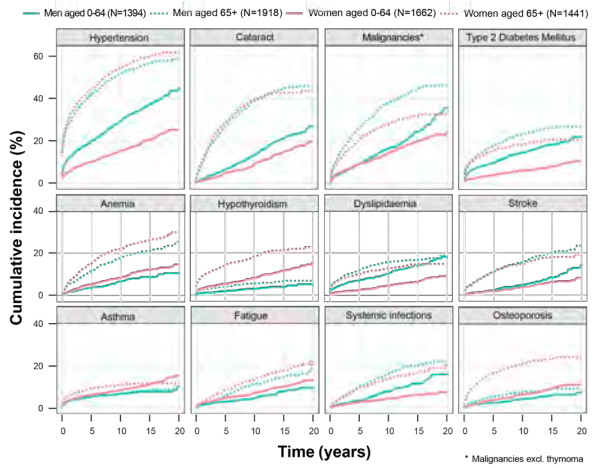

Figure 3: The cumulative incidence of comorbidities during the 20 years on or after the incident myasthenia gravis diagnosis (index date) in Denmark, Finland, and Sweden.

Conclusion: MG is associated with a wide range of comorbidities in a substantial proportion of patients. This highlights the complex management needs of MG patients, to limit comorbidity burden and exacerbation of existing conditions.

Disclosure: Funded by UCB Pharma. John Vissing is Consultant on advisory boards for Roche, Sanofi Genzyme, Sarepta Therapeutics, Novartis Pharma AG,Fulcrum Therapeutics, Biogen, Lupin, Amicus, Regeneron, Argenx BVBA,UCB Biopharma SPRL, Arvinas, ML Biopharma, Atamyo, Horizon Therapeutics, Dyne Therapeutics Research, travel support, and/or speaker honoraria from Sanofi Genzyme, Alexion Pharmaceuticals, Edgewise Therapeutics, Fulcrum Therapeutics, and UCB Biopharma SPRL. Principal investigator in clinical trials for Sanofi Genzyme, Roche, Horizon Therapeutics,Argenx BVBA, Novartis Pharma AG,Alexion Pharmaceuticals, UCB Biopharma SPRL, Genethon, ML Biopharma, Reneo Pharma, Pharnext, Janssen Pharmaceutical, Khondrion, Regeneron, and Dynacure SAS, Janssen Sari Atula travels with pharmacompany: Merck, Speaker in educational sessions by pharma companies: Merck, Roche, Biogen, Novartis, Advisory boards: Biogen, Merck, Roche, Novartis, UCB Pharma Mari Savolainen, employed at UCB Pharma, Espoo, Finland Juha Mehtälä, employee of MedEngine Oy, Finland Laila Mehkri, employee of MedEngine DK ApS, Denmark Tero Ylisaukko-oja, owner of MedEngine Oy and MedEngine DK ApS Didier Pitsi, employed at UCB Pharma, Brussels, Belgium Fredrik Berggren is an employee and stockholder of UCB Pharma, Copenhagen, Denmark Fredrik Piehl has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

EPO-150

The Relationship Between Neurofilament Light Chain and B Lymphocyte Chemoattractant and Cognition in Multiple Sclerosis

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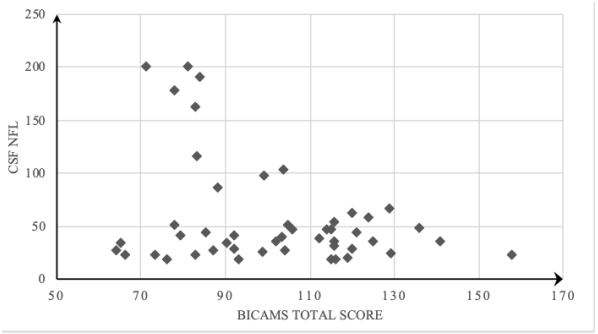
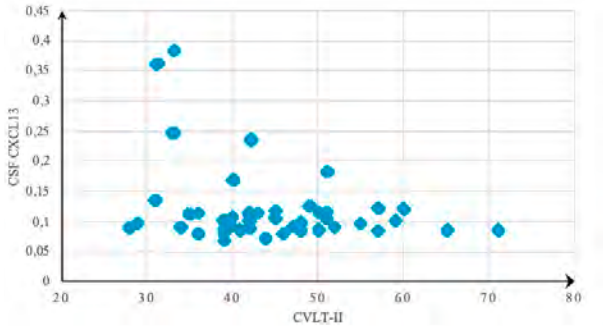
Background and aims: Multiple sclerosis (MS) is a chronic inflammatory, autoimmune, demyelinating disease of the central nervous system. Cognitive impairment can be seen in all stages of MS. This study aims to investigate the relationship between neurofilament light chain (NfL) and B Lymphocyte Chemoattractant (CXCL13) potential biomarkers and cognitive impairment in MS.

Methods: This study included 57 patients diagnosed with Radiologically Isolated Syndrome (RIS), Clinically Isolated Syndrome (CIS), Relapsing-remitting MS (RRMS) and 70 healthy controls. NfL and CXCL13 were studied by The Enzyme-Linked Immunosorbent Assay Method (ELISA) in the patient's cerebrospinal fluid (CSF) and serum samples. These biomarkers were studied just in serum samples in the control group. The Brief International Cognitive Assessment for MS (BICAMS) test was applied to all participants. Serum biomarker levels and cognition tests were compared between the control and patient groups.

Results: A significant negative correlation was found between CSF NfL and BICAMS (p=0.030), and CSF CXCL13 and California Verbal Learning Test-II (p=0.034). Serum NfL and CXCL13 values in the patient group were significantly higher (p=0.043; p<0.001, respectively). A significant positive correlation was found between CSF NfL and CSF CXCL13 (p=0.004). There is a strong relationship between serum and CSF NfL (p=0.002). BICAMS were found to be significantly lower in the patient group (p<0.001).



The correlation between BICAMS and CSF NfL in the patient group



The correlation between CVLT-II and CSF CXCL13 in the patient group

Conclusion: NfL and CXCL13 potential biomarkers are associated with cognitive impairment in MS patients. For this reason, it has been seen that there are promising biomarkers in cognition follow-up and predicting prognosis.
Disclosure: The authors have no conflict of interest. No funds was received.

EPO-151

ASSESSMENT OF SLEEP DISORDERS IN NEUROMYELITIS OPTICA

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Background and aims: Although sleep disorders are frequently reported by neuromyelitis optica (NMO) patients, they are often overlooked. This study aimed to characterize factors that contribute to fatigue and excessive daytime sleepiness in NMO patients.
Methods: Fifty patients with a confirmed diagnosis of NMO and 52 sex and age matched healthy control group were admitted to the sleep laboratory for 2 days to perform 1 night of polysomnography (PSG) and a 5-nap multiple sleep latency test (MSLT) the following day. The results were evaluated with regards to the clinical scales.
Results: Excessive daytime sleepiness was found in 43.1%, and sleep quality was poor in 72.2% of NMO patients. According to the PSG-MSLT, a sleep disorder was found in 92.4% of NMO patients. A diagnosis of hypersomnolence was made in 51.1% of patients, and 5.1% of them were categorized as type 2. Compared to healthy control group, patients with NMO had a lower quality of sleep and higher sleep disorders.
Conclusion: Understanding the mechanism of NMO-associated-sleep disorders is necesary to improve the patient's quality of life. Correction of sleep disorders by effective treatments could be important for reducing fatigue symptoms and improving general state of NMO patients.
Disclosure: Nothing to disclose.

EPO-152

Progression independent of relapse activity drives permanent disability accrual in relapsing multiple sclerosis

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Background and aims: Progression independent of relapse activity (PIRA) occurs frequently in relapsing multiple sclerosis (MS) and is recognized as the most frequent driver of confirmed
Methods: Relapsing-onset MS patients with follow-up >/= 5 years (n=16,130) were extracted from the Italian MS Registry. CDA was defined by an increase in Expanded Disability Status Scale (EDSS) score confirmed at 6 months, and classified per temporal association with

relapses. Sustained disability accumulation (SDA) was a CDA with no EDSS improvement in subsequent visits. Predictors of SDA were assessed using logistic multivariable regression analyses.
Results: Over a follow-up of 11.8+/-5.4 years, 16,731 CDA events occurred in 8,998 (55.8%) patients. Overall, PIRA (n=12,175) accounted for 72.3% of CDA events. SDA occurred in 73.2% of PIRA and 56.7% of RAW (p<0.001). 56.8% of patients transitioned to secondary progressive MS at first PIRA; this proportion progressively increased to 87.5% of transition at fourth PIRA. In the multivariable analysis risk of SDA was associated with PIRA (OR=1.64;95%CI 1.49-1.80,p<0.001), male sex (OR=1.26;95%CI 1.14-1.38,p<0.001), higher EDSS (OR=1.17;95%CI 1.13-1.21,p<0.001) and older age at baseline (OR=1.02;95%CI 1.01-1.03,p<0.001), and shorter exposure to disease modifying therapies (OR=0.43;95%CI 0.38-0.50,p<0.001).
Conclusion: In our population PIRA represents the main driver of disability accumulation in relapsing MS. Compared with RAW it was associated with increasing risk of evolution to secondary progressive MS and permanent disability accrual. Identification of early clinical, radiological and laboratory predictors of PIRA is key to guide personalized treatment decisions.
Disclosure: E.P. received funding from Biogen, Merck, Sanofi, Novartis. L.P. received funding from Novartis, Biogen. L.R. received funding from Novartis. R.T. received funding from Bayer, Biogen, Merck, Novartis, Sanofi, Roche. D.S. received funding by Bayer, Novartis and Sanofi, Biogen, Teva and Merck. A.L. served as a Biogen, Merck, Mylan, Novartis, Roche, Sanofi and Teva Advisory Board Member. E.C. received funding from Almirall, Bayer, Biogen, Merck, Novartis, Sanofi, Teva and Roche. F.P. received funding from Bayer, Biogen, Merck, Novartis, Roche, Sanofi and Teva. P.C. received funding from Merck, Biogen, Novartis and Roche. G.T.M. received funding from Serono, Biogen, Novartis, Roche and Teva. V.B.M. received grants from Biogen, Merck, Novartis, Roche, Sanofi and Teva. G.S. received grants from Biogen, Merck-Serono, Novartis, Roche, Sanofi and Teva. F.G. received grants from Biogen, Merck-Serono, Novartis, Roche, Sanofi and Teva. R.B. received research support from Almirall, Bayer, Biogen, Merck, Novartis and Sanofi. U.A. received grants from Biogen, Merck-Serono, Novartis, Roche, Sanofi and Teva. P.I. received grants from Biogen, Merck, Novartis, Roche, Sanofi and Teva.M.F. received compensation from Bayer, Biogen Idec, Merck Serono, Novartis, Roche, Sanofi, Takeda, and Teva. M.T. received funding from Sanofi, Biogen Idec, Teva, Merck, Serono and Novartis. M.P.A received funding from Biogen Idec, Merck Serono, Bayer Schering and Sanofi. M.B, E.D.M, report no disclosures.

EPO-153

Microchimerism and multiple sclerosis: the impact of sex of offspring on maternal clinical and ophthalmological features

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Background and aims: Multiple sclerosis (MS) is a chronic autoimmune disorder characterised by inflammation and neurodegeneration. Several pregnancy-related changes have been accounted for the protective role of gravidity in MS. XX and XY fetal microchimeric cells (fMCs) migrate to maternal blood during pregnancy and survive for decades. However, their biological significance is still unknown. The aim of this study was to investigate the role of the sex of offspring, an indirect marker of fMCs, in clinical and ophthalmological MS features.
Methods: We enrolled 43 female MS patients, including 18 nulliparous (NPp), 19 patients with at least a male son (XYp), and 6 patients with only daughters (XXp). Each patients underwent clinical assessment and optical coherence tomography (OCT) scan. Data for retinal nerve fibre layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) thickness were extracted.
Results: The risk of MS onset in post-partum was higher in XYp than XXp (OR=4.43, p=0.043). XXp had higher annual relapse rate (0.45±0.30 vs 0.89±0.71, p=0.009), while XYp reached lower scores at Paced Auditory Serial Addition Test (50.26±28.39 vs 65.56±19.11, p=0.039). In the optic nerve, RNFL was higher in XYp than NPp (89.88±18.26 μm vs 97.22±13.65 μm, p=0.049), while no difference was detected between XXp and NPp (p>0.050). Similar trends were found in GCIPL, but they did not reach statistical significance.
Conclusion: Our findings showed different trends between patients with male and female offspring. Being other pregnancy-related changes similar in male and female pregnancies, we hypothesised that XX and XY fMCs could play a role on the biological processes underlying MS.
Disclosure: A Bianchi received Research Grant from the Italian Society of Neurology (Società Italiana di Neurologia, SIN). G Salemi received grants for speaking or consultancies from: Almirall, Biogen, Merck, Novartis, Roche, Sanofi Genzyme. P Ragonese received grants for speaking or consultancies from: Biogen, Bristoll-Myers-Squibb, Merck, Novartis, Roche, Sanofi Genzyme. M Aprile, S Viscomi, G Schirò, R Di Blasio, S Iacono, M Andolina, M Marrale, G La Tona, M Midiri, C Gagliardo, M Vadalà, and VME Bonfiglio do not report any disclosure for the project. authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-154

SF36 in the domain of physical activity predicts confirmed disability progression in people with multiple sclerosis

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Background and aims: To assess whether the Patient reported outcome measure (PROM) scores may predict disease progression in relapsing remitting multiple sclerosis (RRMS) patients within three years of follow-up, and investigate which of PROMs single components is most closely associated with the outcome (progression within three years of follow-up).

Methods: Observational prospective multicenter study. Stable RRMS patients were enrolled consecutively. At the time of enrollment, we assessed EDSS, and all patients completed the following PROMs: Beck Depression Inventory- II (BDI-II), The Treatment Satisfaction Questionnaire for Medications (TSQM), Medical Outcomes Study Short Form 36- Item (SF36), Fatigue Severity Scale (FSS). EDSS was re-assessed three years later for all patients. The outcome measure was defined as the occurrence of confirmed disability progression (CDP) over three years of follow-up. Univariable logistic regression models were performed to study the association between the final score of each test and the outcome. Subsequently, a multivariable model was performed including variables with p-value<0.10 in the univariable analysis.

Results: Demographics and clinicals are reported in Table 1. At the multivariable regression model, SF36-Physical Functioning (SF36-PF) was the only independent variable associated with the outcome. (Table 2) The ROC curve analysis determined a score of 77.5 at SF36-PF sub-scale as the cut-off point resulting in the best combination of sensitivity and specificity (Se=0.65; Sp=0.64) for the occurrence of CDP within three years of follow-up [AUC: 0.66 (0.56-0.75)].

	Overall N=200	Not worsened N=158(79%)	Worsened N=42(21%)	p-value
Age, mean (SD)	39.67(10.29)	39.00(9.95)	42.28(11.27)	0.068
Female, N (%)	123(62%)	95(60%)	28(67%)	0.439
Education, mean (SD)	13.46 (3.22)	13.64(3.25)	12.76(3.05)	0.130
Presence of comorbidities, N (%)	39(20%)	32(20%)	7(17%)	0.602
Disease duration, mean (SD)	10.81(7.89)	10.60(7.71)	11.61(8.61)	0.464
Number of previous relapses, median (IQR)	2(1; 3)	2(1; 3)	2(1; 3)	0.368
Number of therapies, median (IQR)	1(1;2)	1(1;2)	1(1;2)	0.396
Therapy, N (%)				
Dimethyl fumarate	45(23%)	35(22%)	10(24%)	0.881
Glatiramer acetate	25(13%)	18(11%)	7(17%)	
Interferon	111(56%)	92(58%)	19(45%)	
Teriflunomide	19(10%)	13(8%)	6(14%)	

Table 1. Characteristics of the patients, overall and based on the outcome. P-values refer to T-test or Mann-Whitney for continuous variables and to Chi-squared test for the categorical ones.

Characteristics of the patients, overall and based on the outcome. P-values refer to T-test or Mann-Whitney for continuous variables and to Chi-squared test for the categorical ones.

Table 2. The association between the final score of each test and the outcome

	N	Median (IQR)	Univariate analysis		Multivariate analysis	
			OR (95%CI)	p-value	OR (95%CI)	p-value
BDI (10-unit increase)	197	6(2; 11)	1.48(0.98; 2.26)	0.062	1.09(0.59; 2.01)	0.778
TSQM (10-unit increase)	199	52(46; 61)	0.84(0.68; 1.13)	0.252	—	—
FSS (10-unit increase)	196	28(15; 45)	1.26(1.03; 1.54)	**0.027**	1.10(0.80; 1.51)	0.574
SF36 PF (10-unit increase)	185	90(60; 95)	0.83(0.71; 0.94)	**0.002**	0.82(0.67; 1.00)	**0.046**
SF36 RP (10-unit increase)	185	100(25; 100)	0.94(0.86; 1.02)	0.155	—	—
SF36 BD (10-unit increase)	183	74(51; 100)	0.89(0.75; 0.98)	**0.023**	0.95(0.79; 1.14)	0.572
SF36 GH (10-unit increase)	183	56(42; 72)	0.85(0.71; 1.01)	0.061	0.94(0.74; 1.20)	0.635
SF36 VT (10-unit increase)	185	55(45; 70)	0.85(0.71; 1.03)	0.099	1.19(0.88; 1.62)	0.268
SF36 SF (10-unit increase)	185	75(50; 100)	0.92(0.81; 1.05)	0.245	—	—
SF36 MH (10-unit increase)	185	60(32; 100)	0.99(0.90; 1.09)	0.848	—	—
SF36 RE (10-unit increase)	185	64(52; 89)	0.90(0.74; 1.09)	0.267	—	—

Legend. Beck Depression Inventory- II (BDI-II); The Treatment Satisfaction Questionnaire for Medications (TSQM); Fatigue Severity Scale (FSS); Medical Outcomes Study Short Form 36- Item (SF36): Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Mental Health (MH), Role Emotional (RE).

The association between the final score of each test and the outcome.

Conclusion: RRMS patients scoring higher at SF36-PF subscale present a higher likelihood to experience CDP within the next 3 years.

Disclosure: Nothing to disclose.

EPO-155

A clinical diffusion MRI protocol to simultaneously dissect brain grey and white matter microstructure

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Background and aims: Chronic inflammatory process in MS involves both white matter (WM) and grey matter (GM). Diffusion MRI (dMRI), thanks to advanced signal modelling like the Soma And Neurite Density Image (SANDI) can probe microstructural information from both GM and WM. We propose a 10 minute acquisition protocol that enables to acquire such images on a clinical 3T scanner in both healthy subjects (HS) and MS patients.

Methods: We enrolled 5 HS and 5 relapsing remitting (RR) patients. MPRAGE, FLAIR and multishell dMRI images were acquired on a 3T Siemens Prisma scanner. We compared microstructural maps from diffusion tensor imaging (DTI) and neurites orientation dispersion and density image (NODDI) with neurite, soma and extracellular densities (f-neurite, f-soma, f-extra), apparent soma radius

and intra ed extra neurites diffusivities from SANDI. Mean values of all the metrics in HS WM, MS NAWM, MS WM lesions, HS GM, MS NAGM and MS GM lesions were evaluated.
Results: Repeatability and reproducibility of SANDI was comparable with those of DTI and NODDI (intraclass correlation coefficient, ICC>0.7 and coefficient of determination, R^2>0.7). SANDI showed increase of f-extra in almost all WM lesions, but different f-soma behaviors within lesions and in comparison to NAWM. SANDI allowed an accurate separation in mean values between HS WM/GM and MS patients NAWM/NAGM as well as NAWM, WM lesions and NAGM and GM lesions within MS patients.
Conclusion: Our result suggest that SANDI is a repeatable, reproducible, feasible and a practical method to characterize WM and GM tissues in both HS and MS patients.
Disclosure: M.I. received research grants from NIH, DOD, NMSS, FISM and Roche; and received consulting fees from Novartis, Roche, Merck, SanofiGenzyme, Janssen and Admirall.

EPO-156

Autologous hematopoietic stem cell transplantation in multiple sclerosis: updating outcomes in the Valencian cohort.

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Background and aims: Autologous hematopoietic stem cell transplantation(aHSCT) has been recognized as a therapeutic option for very aggressive multiple sclerosis(MS) patients, although it is not a commonly used technique. The current aHSCT indications are highly activeMS, short duration of disease (≤ 5-10 years) and a suboptimal response to high-efficacy treatments.
Methods: A prospective cohort of 46 consecutive MSpatients undergoing aHSCT between 1999-2022 was included in the analysis. The main indication for transplantation was clinical relapse despite active targeted treatment for at least one year. Efficacy was assessed in patients followed for at least 2 years and toxicity was assessed during the entire follow-up.
Results: The baseline characteristics of the patients were, mean age 36.53 years(SD 9.2), 31 women and 15 men, baseline EDSS of 5(SD 4–6), 33 recurrent MS -11 secondary progressive MS -2 primary progressive MS. 24 patients had gadolinium enhancing lesions(GEL) at baseline. The median time to follow-up was 8 years (2,5-13). 28 patients had lost NEDA3 status at last visit, 8 patients progressed de novo, and 20 required re-initiation of specific treatment. Median EDSS post-aHSCT was 4(SD 3–6.5), we found a median overall EDSS improvement of 0.5(SD -1.5– 1). Malignancies and autoimmune events were infrequent (3 for each group).
Conclusion: aHSCT as an alternative therapy to manage aggressive MS patients is a relatively safe and effective procedure. It is necessary to propose comparative studies with adverse effects and effectiveness between immunomodulatory treatments and aHSCT.
Disclosure: Boix Lago, A. No potential conflict of interest. Gil-Perotín, S. Speaker: Biogen, Merck, Sanofi-Genzyme, Bial; Consultant and advisor: Merck; Research grants: Almirall. Ramió-Torrentà Ll: has received compensation for consulting services and speaking fees from Biogen, Novartis, Bayer, Merck, Sanofi, Genzyme, Roche, Bristol-Myers-Squibb, TEVA, Almirall. Casanova Estruch, B. has received compensation for consulting services and speaking fees from Genzime, Roche, BMS, Jensen, Almirall, Merck-serono.

EPO-157

Thalamus volume as a convenient marker of degenerative-atrophic changes in the brain of multiple sclerosis patients

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Background and aims: In recent years, it has become clear that MS is a disease characterized not only by a demyelinating inflammatory process but also by a neurodegenerative. However, methods for monitoring the progression of neurodegeneration in MS are still in their infancy. The development of easy-to-use methods for assessing neurodegenerative processes in MS would significantly improve diagnostic and prognostic possibilities.
Methods: Randomly selected 17 multiple sclerosis patients and a control group of 20 healthy individuals corresponding to the studied group regarding age and gender were examined in the MS centre of Lviv Regional Clinical Hospital. They underwent an MRI of the brain, followed by a volume analysis of brain structures using the Vol2Brain pipeline with further correction regarding the intracranial cavity volume.
Results: We found that thalamus volume in patients with MS was significantly smaller than in healthy individuals (p=0.002). The most pronounced decrease in thalamus volume in MS patients was associated with an increase in the total number of MS relapses (r=0.633, p=0.006). The decrease in the thalamus volume did not have a statistically significant relationship with the age and duration of the disease. At the same time, thalamus volume in MS patients was closely related to the volume of brain white matter (r=0.752, p<0.001) and other brain structures.
Conclusion: Thalamus volume could be a convenient marker to evaluate general degenerative-atrophic changes associated with MS relapses in the brain of MS patients. Assessing its volume in dynamics can be a good option for monitoring the course of MS.
Disclosure: Nothing to disclose.

MS and related disorders 2

EPO-158

Matching-Adjusted Indirect Comparisons of Diroximel Fumarate, Ozanimod, and Interferon beta-1a for Relapsing MS

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Background and aims: Diroximel fumarate (DRF), ozanimod (OZA), and interferon beta-1a (IFN) are disease-modifying therapies for relapsing multiple sclerosis. No randomised trials have directly compared DRF vs OZA or IFN. We report matching-adjusted indirect comparisons (MAIC) of efficacy for DRF vs OZA and DRF vs IFN.
Methods: Analyses were based on individual patient data from the 2-year, open-label, single-arm, phase 3 EVOLVE-MS-1 study (NCT02634307) of DRF (462mg BID; n=1057), and aggregated data from the 2-year, double-blind, active-comparator, phase 3 RADIANCE study (NCT02047734) of OZA (1mg QD; n=433) and IFN (30µg weekly; n=441). EVOLVE-MS-1 data were restricted (per RADIANCE inclusion/exclusion criteria) and weighted to match baseline characteristics in RADIANCE. Outcomes were compared for annualised relapse rate (ARR), 12-week confirmed disability progression (CDP), 24-week CDP, absence of gadolinium-enhancing (Gd+) T1 lesions, and absence of new/newly enlarging T2 lesions.
Results: After weighting, baseline variables were balanced across groups. ARR outcomes were similar for DRF and OZA but favoured DRF vs IFN. Outcomes for 12- and 24-week CDP favoured DRF vs OZA; 12-week CDP favoured DRF vs IFN, but there was not strong evidence favouring DRF over IFN for 24-week CDP. Compared with OZA and IFN, DRF had higher proportions of patients without Gd+ T1 lesions and patients without new/newly enlarging T2 lesions.
Conclusion: Disability progression and radiological outcomes favoured DRF vs OZA. All clinical and radiological outcomes favoured DRF vs IFN, except for 24-week CDP. Limitations include potential residual confounding due to different study designs and the application of unanchored MAIC since there was no cross-trial common comparator.
Disclosure: Supported by Biogen.

EPO-159

Effectiveness of Dimethyl Fumarate After Switching From Non-Specific Immunosuppressants

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Background and aims: Non-specific immunosuppressants (NSIS) have been used as off-label therapy for the treatment of multiple sclerosis (MS) but most lack controlled phase 3 clinical trials. This study investigated patient outcomes on dimethyl fumarate (DMF), an oral disease modifying therapy with demonstrated clinical effectiveness in treating MS, after switching from NSIS in a real-world setting.
Methods: This retrospective, single arm, observational analysis of patients in the MSBase registry database assessed 18−65 year old relapsing-remitting MS patients with EDSS score 0−6.0 on NSIS treatment, who switched to DMF between 2014 to 2022. NSIS included azathioprine, cyclosporine, cyclophosphamide, methotrexate, mitoxantrone, and mycophenolate mofetil. Annualized relapse rate (ARR), proportion relapse free, time to first relapse (TTFR), 6-month confirmed disability progression (CDP) and improvement (CDI), and DMF discontinuation were assessed prior to switching, and during DMF treatment.
Results: Of 127 patients that switched from NSIS to DMF (Table 1), ARR (95% CI) was 0.17 (0.10, 0.27) during last 12 months on NSIS and 0.12 (0.07,0.19) on DMF; proportion relapse-free was 89% (48/54) and 100% (26/26) at 12 and 24 months of DMF, respectively. DMF discontinuation rate was 18.66/100 person-years (12.49, 26.79) (Table 2); TTFR (95% CI) was 9.01/100 person-years (4.92, 15.11; see Figure); 6-months CDP was 2.57/100 person-years (0.70,6.59); and 6-months CDI was 5.27/100 person-years (1.71, 12.31).

Table 1: Patient characteristics at time of switch from NSIS to DMF

Characteristics at time of switch to DMF	Category	n=127
Age (years), mean (SD)		41.2 (10.0)
Sex, n (%)	Female	106 (83.5)
	Male	21 (16.5)
Disease duration (years), mean (SD)		12.8 (7.8)
Baseline EDSS, median (IQR)		1.5 (1, 2.5)
Country, n (%)	Iran	77 (60.6)
	Turkey	17 (13.4)
	Italy	16 (2.4)
	Czechia	6 (4.7)
	Spain	3 (2.4)
	Lebanon	3 (2.4)
	Australia	2 (1.6)
	Canada	2 (1.6)
	Belgium	1 (0.8)
Duration of pre-switch IS (years)	Mean (SD)	3.9 (3.7)
	Median (IQR)	2.6 (0.9, 6.2)
Treatment gap between NSIS and DMF (months)	Mean (SD)	27.5 (43.0)
	Median (IQR)	6.5 (0.0, 39.1)

EDSS, expanded disability severity score

Table 1: Patient characteristics at time of switch from NSIS to DMF

Table 2: Outcomes in patients who switched from NSIS to DMF

OUTCOME	
ARR (95% CI)	
On DMF	0.12 (0.07, 0.19)
Last 12 months on NSIS	0.17 (0.10, 0.27)
Proportion relapse free, % (n)	
1 year on DMF	88.9% (48/54)
2 years on DMF	100.0% (26/26)
3 years on DMF	100% (15/15)
TTFR[1], (95% CI)	9.01 (4.92, 15.11)
6-month CDP[1], (95% CI)	2.57 (0.70, 6.59)
6-month CDI[1], (95% CI)	5.27 (1.71, 12.31)
DMF discontinuation[1], (95% CI)	18.66 (12.49, 26.79)

[1]Rate per 100 person-years
ARR, annualized relapse rate; CDI, confirmed disability improvement; CDP, confirmed disability progression; DMF, dimethyl fumarate; NSIS, non-specific immunosuppressants;

Table 2: Outcomes in patients who switched from NSIS to DMF

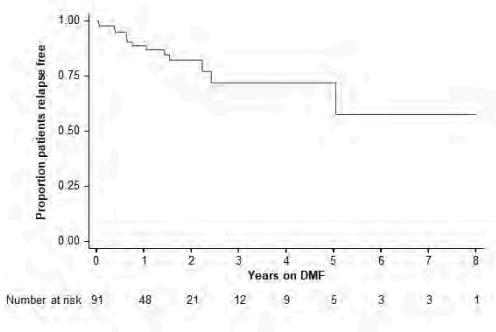

Figure. Kaplan-Meier Curve for Time-to-First-Relapse

Conclusion: These data represent the first analysis of efficacy on DMF after switching from NSIS, and suggest good treatment response to DMF after switching from immunosuppressant medication, although our dataset size is relatively small.

Disclosure: Supported by Biogen.

EPO-160

Safety and Efficacy of Diroximel Fumarate in Older Patients with Multiple Sclerosis from the Phase 3 EVOLVE-MS-1 Study

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Background and aims: Oral diroximel fumarate (DRF) has similar efficacy/safety to dimethyl fumarate in relapsing-remitting multiple sclerosis (RRMS), but improved GI tolerability. Safety/efficacy of DRF was assessed in patients with RRMS aged >=55 years from EVOLVE-MS-1.

Methods: EVOLVE-MS-1 (NCT02634307) was a phase 3, open-label, 96-week study of DRF in adults with RRMS. Safety/efficacy outcomes were compared in older (aged >=55 years) vs younger patients (aged <55 years).

Results: Of 1057 patients, 158 (14.9%) were classified as older (mean [SD], 58.8 [2.9] years) and 899 (85.1%) as younger (mean [SD], 39.6 [9.0] years) (Table 1). Adverse events (AEs) occurred in 139 (88.0%) older and 799 (88.9%) younger patients. AEs led to discontinuation in 16 (10.1%) of older and 69 (7.7%) of younger patients (Table 2), including lymphopenia, GI disorders, MS relapse, and lymphocyte count decrease. Annualized relapse rate reduction from 12 months prior to study to Week 96 of DRF treatment was 89.3% (95% CI: 81.7-93.7) in older and 80.4% (76.9-83.4) in younger patients. Proportions with no evidence of disease activity (NEDA-3), estimated from Kaplan-Meier, were 65.8% (older) and 36.9% (younger). At Week 96, mean (SD) EDSS score change from baseline was 0.09 (0.82; older) and 0.03 (0.66; younger); mean (SD) number of Gd+ lesions decreased 0.1 (0.78; older) and 0.8 (4.05; younger).

Characteristic	< 55 years n=899	≥55 years n=158
Mean (SD) Age	39.6 (9.0)	58.8 (2.9)
Female, n (%)	648 (72.1)	114 (72.2)
Region, n (%)		
Non-US	531 (59.1)	73 (46.2)
US	368 (40.9)	85 (53.8)
BMI (kg/m^2), mean (SD)	26.6 (6.3)	27.1 (4.8)
No. of Gd+ lesions, mean (SD)	1.3 (3.8)	0.2 (1.0)
T2 lesion volume (cc), mean (SD)	12.9 (14.1)	16.5 (14.9)
EDSS score, mean (SD)	2.57 (1.4)	3.39 (1.5)
No. of relapses in previous year, mean (SD)	0.7 (0.8)	0.6 (0.7)
No. of prior DMTs, mean (SD)	1.2 (1.2)	1.5 (1.2)
Time since MS diagnosis (yr), mean (SD)	6.8 (6.6)	12.2 (9.6)

BMI, body mass index; DMT, disease-modifying therapy; EDSS, expanded disability status score; GD, gadolinium endhancing; MS, multiple sclerosis; SD, standard deviation

Table 1. Patient characteristics at enrollment

Classification	< 55 years n=899, n (%)	≥55 years[2] n=158, n (%)
Any TEAE	69 (7.7)	16 (10.1)
Investigations	14 (1.6)	4 (2.5)
Lymphocyte count decreased	6 (0.7)	1 (0.6)
Glomerular filtration rate decreased	0 (0.0)	2 (1.3)
Blood pressure abnormal	0 (0.0)	1 (0.6)
Blood/lymphatic system disorders	10 (1.1)	5 (3.2)
Lymphopenia	9 (1.0)	5 (3.2)
Nervous system disorders	14 (1.6)	1 (0.6)
Multiple sclerosis relapse	11 (1.2)	0 (0.0)
Hemiparesis	0 (0.0)	1 (0.6)
Gastrointestinal disorders	5 (0.6)	2 (1.3)
Anal incontinence	0 (0.0)	1 (0.6)
Irritable bowel syndrome	0 (0.0)	1 (0.6)
Skin and subcutaneous tissue disorders	4 (0.4)	1 (0.6)
Pruritis generalized	0 (0.0)	1 (0.6)
Vascular disorders	5 (0.6)	0 (0.0)
Flushing	5 (0.6)	0 (0.0)
Cardiac disorders	2 (0.2)	1 (0.6)
Hypertensive heart disease	0 (0.0)	1 (0.6)
General disorders and administration site conditions	1 (0.1)	1 (0.6)
Fatigue	0 (0.0)	1 (0.6)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	1 (0.6)
Dyspnoea	0 (0.0)	1 (0.6)

TEAE, treatment-emergent adverse events
[1]Included TEAEs leading to discontinuation in >= 0.5% patients
[2]No infections or neoplasms were found in patients >= 55 years old

Table 2. Summary of adverse events leading to discontinuation

Conclusion: After 96 weeks of DRF treatment, overall benefit/risk ratio was similar in older and younger patients. At baseline, older patients had fewer Gd+ lesions than younger patients and higher EDSS scores. More older patients achieved NEDA-3 versus younger patients.
Disclosure: Supported by Biogen.

EPO-161

Google Maps Timeline: an open-access digital tool to evaluate gait impairment in people with multiple sclerosis

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Background and aims: Gait impairment is common in multiple sclerosis (MS), but difficult to evaluate in clinical practice. We have used Google Maps Timeline (GMT) data to provide direct measurements of the overall walking abilities in MS and validated towards conventional clinical measures.
Methods: This is a proof-of-concept observational study. We collected Expanded Disability Status Scale (EDSS), Time-25 Foot Walking Test (T25FWT), Multiple Sclerosis Walking Scale (MSWS), Fatigue Severity Scale (FSS), European Quality of Life questionnaire (EuroQoL). We used open-access GMT to record the total number of days with walking activity, walking distance, walking time, and walking speed. Each GMT variable was included in a different stepwise linear regression model to select best clinical correlates.
Results: We included 9 pwMS (age 43.1±6.6 years; females 55.6%; disease duration 12.7±3.1 years). Percent of days with recorded walking was associated with lower FSS (Coeff=-1.14; 95%CI=-1.95, -0.33; p=0.01), and higher MSWS (Coeff=0.73; 95%CI=0.01, 1.46; p=0.04). Average daily walking distance was associated with shorter T25FWT (Coeff=-150.58; 95%CI=-278.00, -23.15; p=0.02), lower EDSS (Coeff=-171.91; 95%CI=-296.65, -47.18; p=0.01), and higher EuroQoL (Coeff=10.20; 95%CI=0.40, 20.00; p=0.04). Average daily walking time was associated with shorter T25FWT (Coeff=-0.06; 95%CI=-0.11, -0.01; p=0.03). Higher walking speed was associated with lower FSS (Coeff=-0.02; 95%CI=-0.04, -0.01; p=0.04).
Conclusion: GMT parameters were associated with conventional clinical measures, providing actual estimates of daily walking activities in MS. Extension to a larger sample, validation towards other clinical/MRI measures, and longitudinal evaluation are warranted.
Disclosure: The authors declare no competing interests.

EPO-162

Multiple Sclerosis and SARS-CoV2 pandemic: a population based study.

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Background and aims: Environmental factors, in particular infections, are risk factors for Multiple Sclerosis disease activity. Aim of the study was to evaluate the impact of the SARS-COV2 pandemic on disease activity in the MS population from the Italian MS Registry (RISM).
Methods: We compare the incidence of clinical/radiological disease activity occurring during the pandemic phase (Jan 2020-Jul 2021) and the pre-pandemic period (Jan 2018-Jul 2019) in the MS population followed during boths periods, according to different regions of residence. We investigated potential differences in the neurological functional system affected.
Results: 18669 out of 72959 patients had visits registered in the pre-pandemic and pandemic periods and were analysed. 4312 relapses were registered in 3306 patients (17.7%, relapse rate (RR)=0.23) in the pre-pandemic period, while 1206 relapses were reported for 1054 patients (5.6%, RR=0.06) in the pandemic period (chi-square test, p<0.0001). The exploration of potential differences in functional system involved was limited by the different number of missing data between the two preiods. A total of 38182 MR data were reported for 14382 patients in the pre-pandemic period while 20329 MR data were reported for 9849 patients in the pandemic: 2194 (5.7%) and 912 (4.5%) gadolinium-positive scans were respectively recorded in the 2 period (chi-square, p<0.0001).

Conclusion: A reduced disease activity was observed during the pandemic period compared to the pre-pandemic: this may be ascribed to an overall decrease in the risk of infections as results of lockdown, social distancing, isolation strategies and hygiene measures, supporting the role of viral infections as triggers of inflammation in MS.
Disclosure: Nothing to disclose.

EPO-163

Testing the Padova Emotional Dataset of Facial Expressions in Multiple Sclerosis: a neuropsychological-MRI study

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Background and aims: Social cognition can be altered in multiple sclerosis-patients (MS), even from the early stages of the disease[1]. We aimed to study in a group of recently-diagnosed relapsing-MS and controls the Padova Emotional Dataset of Facial Expressions (PEDFE), a new facial emotion recognition (FER) test in which patients are asked to recognize the type and genuineness of different genuine or posed emotions[2].
Methods: PEDFE was acquired in 32 relapsing-MS (<2 years from diagnosis) and 32 controls, by calculating the emotion-type (ET) and emotion-genuineness (EG) scores. Patients also underwent clinical, neuropsychological evaluation and MRI. Brain segmentation of regional grey matter (GM) atrophy and white matter (WM) lesion probability map were obtained and Spearman correlations with FER scores were evaluated, setting $p<0.05$.
Results: Recently-diagnosed MS and controls did not show significant differences at PEDFE scores, but ET and EG scoring displayed different patterns in MS. ET correlated with executive performances at PASAT-3/PASAT-2 ($p=0.01$) and SRT ($p=0.01$) and with GM thickness in many cortical frontal, parietal and temporal regions (Fig.1). Conversely, EG correlated with WLG ($p=0.01$) and with GM thickness in cingulum isthmus and different subcortical areas (Fig.2). Macroscopic WM-lesion load did not affect our results (Fig.3).

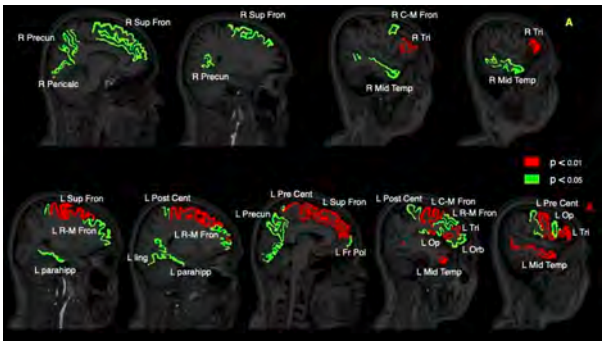

Fig.1: Spearman correlations between ET scores and cortical GM thicknesses [A: anterior]

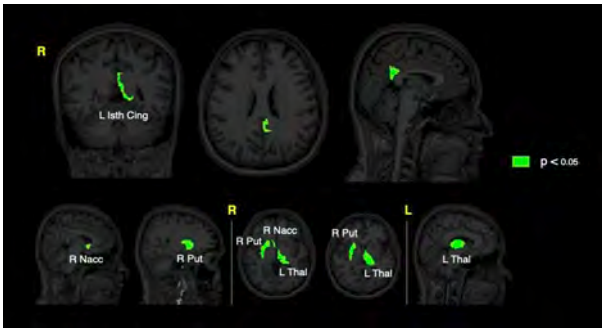

Fig.2: Spearman correlations between EG scores and cortical GM thicknesses and subcortical volumes [R: right; L: left]

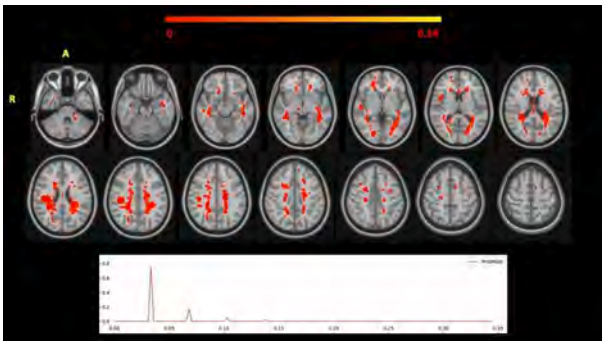

Fig.3: WM macroscopic lesions probability map; data are expressed as percentages from 0 up to 34% [A: anterior; R: right]

Conclusion: PEDFE may represent a valid tool to assess FER in MS and to detect early alterations in social cognition. As an adding value, the PEDFE possibly distinguishes different anatomical structures involved in FER, with ET scores that are mostly linked to executive and memory functions, while EG scores that are more related to the limbic system functioning.
Disclosure: All authors declare no disclosures.

EPO-164

Validation of the RoAD score in an Italian cohort of people with Relapsing Multiple Sclerosis

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Background and aims: Scoring the risk of future disability in Multiple Sclerosis(MS) is a big challenge of today's clinical practice. Recently, the Risk of Ambulatory Disability(RoAD) Score was proposed as an useful tool to predict individual prognosis and optimize treatment strategy for MS patients. The score includes both baseline factors and one-year outcomes on platform treatment with a score of ≥4 as the best cut-off score for the risk of reaching EDSS score≥6. In this study, we evaluated the performance of RoAD score in our cohort of long-term RMS patients.
Methods: We analysed a dataset of RMS patient from our MS centre who started platform injectable disease modifying therapies (DMTs) with at least 10 years of follow-up.
Results: 255 patients met all inclusion criteria and were included in the analysis. Median RoAD score was 2 with 61(24%) patients having a RoAD score≥4. At 10-year follow-up, 42(16.5%) patients reached a confirmed EDSS score≥6. The best RoAD score cut-off for estimating the risk of EDSS score≥6 was 4 with an AUC of 0.77 (IC 0.70-0.85, p<0.01).
Conclusion: In our study we confirmed a RoAD score≥4 as the best cut-off score for discriminating patients at higher risk of reaching the disability milestone of EDSS score≥6. This study confirmed that RoAD score could represent a valuable tool to help the clinician in the assessment of long-term prognosis in patients treated with platform injectable DMTs as first-line treatment.
Disclosure: Nothing to disclose.

EPO-165

MSCopilot® Real Life Data Show Influence of Multiple Sclerosis Phenotypes and Disability Levels on Functional Parameters

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Background and aims: We describe the evolution and potential influences of phenotypes (relapsing-remitting or progressive) and the Expanded Disability System Status Scale (EDSS) score on four main functional parameters, walking, dexterity, cognition and low-contrast visual acuity, in patients with multiple sclerosis (PwMS), assessed in real life using MSCopilot®, a clinically validated software medical device.
Methods: MSCopilot® database was analysed from 2017-Oct to 2022-Apr and 1047 females/473 males (mean age 41.3±12), having consented, were included. Patients were split by phenotypes and EDSS levels (<3.5 or ≥3.5). PwMS performed the four unsupervised digital assessments following embedded tutorials.
Results: A significant group effect was found in MS phenotypes resulting in a decreased performance in walking, dexterity and cognition (p<0.05). These parameters were also significantly impaired in PwMS with an EDSS≥3.5 (p<0.05). No specific interaction was found between low-contrast visual acuity and phenotypes or EDSS. Compared to baseline and over three time points, 26.4% and 23.1% of patients had a sustained worsening (<10%) of their dexterity and walking capacity respectively.
Conclusion: In PwMS, impairment of three functional parameters, measured in real-life via MSCopilot®, relate to a more severe course and degree of disability. Visual acuity was not influential, which could be explained by an optic neuritis history or a lesser influence over the EDSS. This novel insight opens new avenues for phenotype discrimination and disability progression prediction, two unmet needs in the PwMS care pathway.
Disclosure: L. Carment, L. Diouf, L. Ahamada, A. Plaud, L. Klaeyle, S. Zinai, S. Bieuvelet are employees of Ad Scientiam, A. Tourbah is a member of its scientific committee and received honoraria for lectures, travel grants and research support from Biocara, Hikma, Novartis, Roche.

EPO-166

Plasma exchanges in acute relapses of inflammatory demyelinating diseases: a multicenter study

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Background and aims: Plasma exchange (PE) can improve recovery of patients with severe relapses of CNS demyelinating diseases (CNS-DD). We aimed to 1)assess the effectiveness and 2)identify predictors of improvement to PE.

Methods: Retrospective, non-interventional study, including patients receiving PE at 3 Spanish hospitals between 2012-2021 who met: 1)severe relapse of CNS-DD unresponsive to methylprednisolone; 2)≤3 months until PE administration; 3)5-10 exchanges administered. Improvement at 6 months after PE was defined as: return to pre-relapse Expanded Disability Status Scale (EDSS) score; or decrease ≥1 or 1.5 points for patients with EDSS nadir ≤7.5 or ≥8, respectively; or improvement in ≥2 lines on the visual acuity chart for patients with optic neuritis (ON). Uni and multivariate logistic regression models were used to determine factors associated with improvement.
Results: Ninety patients were included (66% female, median (IQR) age: 42(32-51.8) years, EDSS 5.0(4.0-7.0) at PE initiation). Most frequent diagnosis were multiple sclerosis (49%), idiopathic CNS-DD (28%) and AQ4-positive NMOSD (16%). Relapses phenotype were myelitis (36%), ON (23%), multifocal/disseminated forms (22%), brainstem/cerebellum (10%) and pseudotumoral (8.9%). In one center, 32 patients received 200 mg of rituximab pre- and post-PE. Median time between MTP-PE was 18(7-34) days. A median of 7(6-7) exchanges were administered. Improvement was achieved by 77% of patients. Younger age (p=0.04) and lower pre-relapse EDSS (p=0.01) were independently associated with improvement, while etiology, relapse phenotype, number of exchanges or rituximab were not.
Conclusion: PE produced a marked improvement in a large proportion of patients with severe CNS-DD relapses, particularly younger patients, and those with lower baseline disability.
Disclosure: The authors report compensation for consulting services and speaker honoraria: JLCG from Bayer, Sanofi, Biogen and Bial. JM from Sanofi. FRJ from Sanofi and Bial. SSM from Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, Sanofi, and Teva. EM from Biogen, Merck,Novartis, Roche, Almirall, and Sanofi-Genzyme. MS from Roche and Biogen. EMH from Biogen-Idec. LCF rBiogen, Bristol Myers Squibb, Janssen, Merck-Serono, Novartis, Sanofi, Roche and Teva. JEML from Biogen, Bristol-Myers-Squibb, Merck, Novartis, Roche and Sanofi. YB from Merck-Serono, Biogen-Idec, Sanofi, Brystol-Myers and Roche. AS from Merck-Serono, Biogen-Idec, Sanofi, Novartis, Roche, Janssen, and Alexion. SL from Biogen Idec, Novartis, TEVA, Genzyme, Sanofi and Merck. ES received travel reimbursement from Sanofi. ELS received travel reimbursement from Sanofi and ECTRIMS. EF received funding for an ECTRIMS Clinical Training Fellowship Programme. The remaining authors have no conflict of interest to declare.

EPO-167

Relationship of disease severity and the diffusion along the perivascular space in multiple sclerosis

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Background and aims: The glymphatic system in multiple sclerosis has not been thoroughly explored yet. Recently it was suggested that this 'waste clearance' system can be examined by measuring the diffusion along the perivascular space index.
Methods: DTI parameters of 107 MS patients were calculated with FSL's DTIFIT, followed by registration to the common space without creating the skeleton. ALPS index was calculated using two ROIs along the periventricular white matter (Taoka et al. 2017). Using linear regression model the EDSS score was correlated with the ALPS index with different nuisance regressors and tested on a test and training set. Based on EDSS (>=1.5 and <1.5) two groups were created to compare the ALPS indices.
Results: EDSS and DTI-ALPS showed weak correlation (rho=-0.19, $p<0.0478$). The linear regression model revealed that DTI-ALPS index did not contribute significantly to the patients' EDSS (beta: -0.33, p=0.73), however, disease duration was the only significant contributor to EDSS (beta: 0.083, $p<0.001$). Testing the model on the unseen dataset it achieved an R2=0.239. The DTI-ALPS index of the patients with higher EDSS was significantly lower ($p=0.011$, $\alpha=0.05$).
Conclusion: According to our results there is only a weak relationship between the DTI-ALPS index and the clinical disability due (i) scanner reference-based diffusion directions should probably be replaced by fibre-based reference frame; (ii) registration issues should be resolved by TBSS approach, using the voxels only in a skeleton; (iii), thus the connection between the DTI-ALPS index and the glymphatic system should be further investigated.
Disclosure: Image processing, statistical analysis.

EPO-168

The analysis of miRNAs in CSF identifies upregulation of miR-146a in patients with early diagnosed multiple sclerosis

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Background and aims: Recently microRNAs (miRs) have been proposed as possible disease biomarkers in Multiple Sclerosis (MS) field. Few studies have focused on cerebrospinal fluid (CSF) miRs, although these might be more relevant to understanding disease regulation.
Methods: This is a case-control study performed at the Department of Medical and Surgical Sciences, University of Foggia, Italy. Patients have not been yet exposed to disease modifying therapies (DMTs) and had received a confirmed diagnosis of relapsing remitting MS (RRMS). We analyzed the CSF expression of 6 miRs by using Quantitative Real-Time PCR, comparing RRMS to HCs, with a 2:1 ratio. Subsequently, the differentially expressed miRNAs, were further tested with receiving operator curves (ROC). We aimed to explore possible role of CSF miRs as disease biomarker at the time of diagnosis.
Results: A total of 32 patients were enroled, 67.7% female, mean age 32±12.5. MiR-146a had higher levels in RRMS patients when compared to HCs (p<.01). The ROC curve indicated that both miR-146a could be considered as biomarkers with an area under the curve of 0.772 (p=.003; 95% CI: 0.610–0.935).
Conclusion: Our study suggested CSF miR-146a as possible disease biomarkers in early diagnosed RRMS patients, not yet exposed to DMTs.
Disclosure: The authors have nothing to disclose related to this poster.

EPO-169

A registry study of highly active disease modifying therapies in relapsing remitting MS motor and psychiatric outcomes

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Background and aims: The United Kingdom MS Register (UKMSR) is an online registry recording patient-reported outcomes (PROs) from >15,000 people with MS (pwMS) and clinical data from 46 NHS centers nationwide with 12 years of follow-up. This study examined the real-world efficacy of highly and normally active DMTs versus no treatment.
Methods: Psychiatric and motor symptoms were assessed using MSIS-29 questionnaires, answered <6 months after the previous and >2 weeks from the last questionnaire. Patients were separated into a highly active (HA), normally active (NA) and no treatment (NT). Patients were propensity matched on a 1 to 1 ratio for age, gender, time since disease diagnosis and treatment length. Kaplan Meier cumulative time to event analysis was performed on the time to a clinically significant event defined as a 6-point change in MSIS-29 score
Results: In total, 800 patients with Relapse Remitting MS (RRMS) met the inclusion criteria. Over four-years of follow up from baseline patients on HA-DMTs showed a statistically significant improvement in motor ($p < 0.0008$) and psychiatric symptoms ($p = 0.047$). There was no difference found in worsening of motor ($p = 0.27$) or psychiatric symptoms ($p = 0.96$). There was no significant difference in worsening or improvement when NA-DMTs were compared to NT.
Conclusion: These investigations demonstrated that RRMS patients on HA-DMTs had a statistically significant improvement in psychiatric and motor symptoms compared to NT. These results suggest that HA-DMTs have beneficial effects in improving psychiatric symptoms beyond their established efficacy in improving motor symptoms.
Disclosure: This project was supported by the United Kingdom MS Register, Imperial College London and The University of Swansea.

EPO-170

Journey of MS Patients in Turkey; a questionnaire based survey

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Background and aims: MS is a chronic neurodegenerative disease that is one of the most important causes of disability in young adults. In this study, it is aimed to highlight all the obstacles in the MS journey of the patients and to collect information for solution suggestions.
Methods: The online survey, in which a total of 2176 MS patients participated between November 11, 2022 and December 16, 2022, was evaluated by making analysis and statistics according to the questions.
Results: 57% patients have numbness and/or weakness in an arm or leg before being diagnosed. Physicians perform additional examinations and tests for 71% of patients

receiving MS treatment, and It takes an average of 6.4 weeks. 29% of the patients who received MS treatment did not have an attack requiring cortisone, but of the remaining 71%, 18% had a single attack requiring cortisone and 17% had more than 4 attacks requiring cortisone. 53% patients were hospitalized during the attack and they stated that they stayed in the hospital for an average of 9 days. Since 57% (n=2097) of the patients who continued the treatment showed high disease activity, their treatment was changed with the decision of the physician. In 72% of them, it was stated that the reason was ineffectiveness against the treatment they used, while the problems of compliance with the treatment they used in 23%.

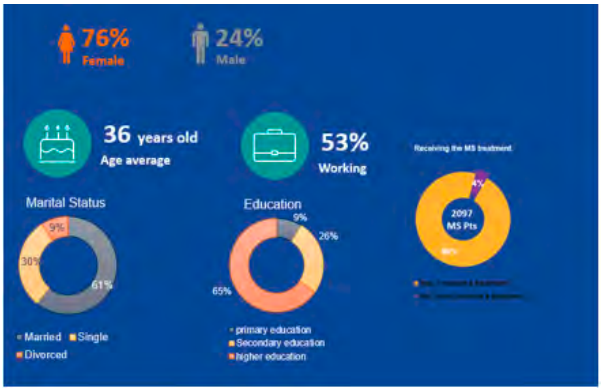
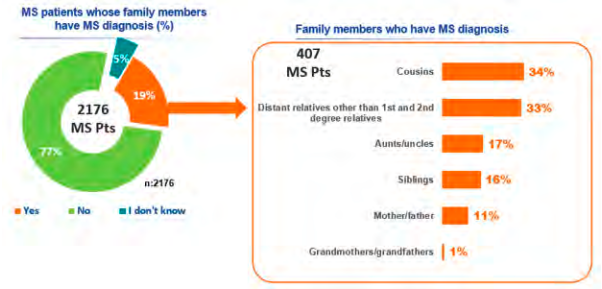


Figure 1: A total of 2176 patients participated in our study. The female-male ratio in the patients participating in the study was 76% and 24%, respectively. and the average age is 36 years. 65% of the patients who participated in the survey are graduates



Patients have MS diagnosis for averagely 8 years. (between 1984 and 2022). 1 of 5 MS patients' family members have MS diagnosis.1/3 of them are cousins and 1/3 of them are distant relatives who are other than 1st and 2nd degree relatives.

While ¼ of the MS patients receiving treatment went to the follow-up examination every 6 months, 27% of them stated that they went to the follow-up examination every 2 years. 85% of patients can make an appointment with their neurologist within 1 month.

Conclusion: Discussion: This Questionnaire gave an idea about how physicians can support MS patients living in Turkey with their problems detected during their journey.
Disclo.ure: This study was funded by Novartis Pharma Turkey

EPO-171

Journey of MS Patients in Turkey; a questionnaire based survey- Nurse Support Evaluation

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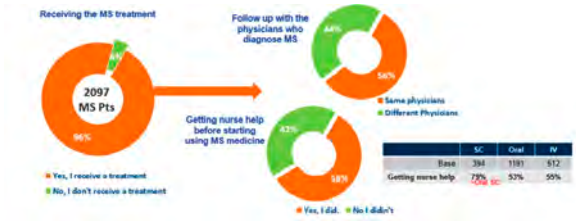
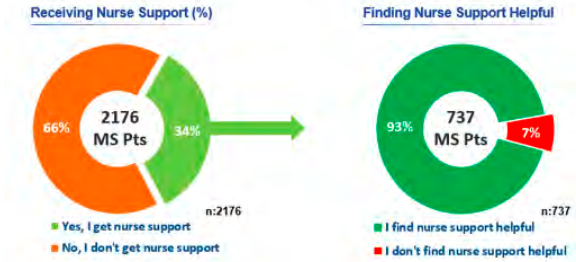
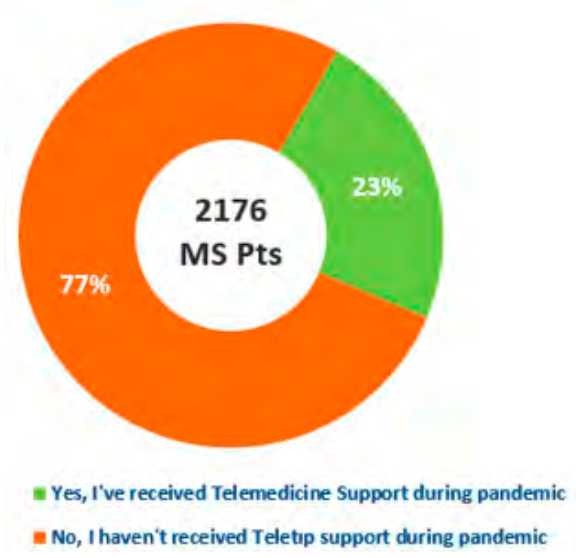
Background and aims: In this study, it was aimed to evaluate the frequency and satisfaction of the nurse support that MS patients received during their MS treatment and the telemedicine support they received during the pandemic period, according to the treatment groups.
Methods: It is an online survey study conducted by the MS Association of Turkish in which a total of 2176 MS patients participated between 11 November 2022 and 16 December 2022
Results: Almost ¼ of MS patients have received telemedicine service during Covid19 pandemic.Ratio of MS patients received Telemedicine Support during Covid19 pandemic is higher among IV and oral patients compared to SC patients. Female-male ratio was similar in patients receiving telemedicine service (22%, 23% retrospectevely) it was found to be unrelated to the educational status of the patients.



A total of 2176 patients participated in our study. 96% of MS patients receive MS treatment. 56% of patients who receive MS treatment continue follow up with the physicians who diagnose 58% of patients got nurse support before starting using MS



34% of all patients receive clinical nurse support (IV patients receive nurse support more than SC patients.) and 93% of these patients find this support helpful. This result did not differ between sc, oral, iv treatments (90%, 92%, 95%, retrosp



Those who have received telemedicine Suport during Pandemic

Conclusion: Studies have shown that telemedicine offers a supportive alternative to face-to-face visits. here has been a huge increase in the use of telemedicine during the COVID-19 pandemic . Nurses play an important role in coordinating the care of patients with multiple sclerosis (MS) throughout their disease course in a complex treatment setting. This information may support the role of nurses in the multidisciplinary management of MS, facilitating shared decision making.

Disclosure: This study was sponsored by Novartis Pharma Turkey

EPO-172

Effect of disease-modifying treatment on coronavirus disease 2019 vaccination in patients with multiple sclerosis

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Background and aims: Coronavirus disease 2019 (COVID-19) vaccination while receiving disease-modifying-treatment (DMT) with B-cell depleting agents or sphingosine-1-phosphate receptor modulators (S1PRMs) has repeatedly been associated with a dampended humoral and/or cellular immune response in patients with multiple sclerosis (MS),[1] but it remains unknown whether this translates into a decreased clinical protection against severe forms of the infection.

Methods: Since March 2020, demographics and infectious outcome of patients with MS who developed COVID-19 have been collected at the Belgian National MS Center in Melsbroek. Patients were considered to be 'protected by vaccination' if they were (a) fully vaccinated and (b) tested positive for COVID-19 in the period ranging from 14 days to 6 months after the last administered vaccine dose.[2]

Results: On December 19, 2022, we have identified 450 cases of COVID-19 in 436 individual patients (Table 1). Hospitalisation and mortality rates resulting from the infection were 10.0% and 2.2%, respectively. Being 'unprotected by vaccination' was associated with a worse COVID-19 outcome (i.e., hospitalisation and/or death) in the total cohort (OR 3.93, 95% CI 2.03-7.97, P < 0.001) and after exclusion of patients on B-cell depleting agents or S1PRMs (324 infections, OR 7.74, 95% CI 3.37-19.86, P < 0.001) but not in those on B-cell depleting agents (Table 2). The S1PRMs subgroup was considered too small (23 infections) for a meaningful analysis.

Table 1: Characteristics of the total cohort of COVID-19 infections

Infections, *N* (individual patients)	450 (436)
Mean age, years (SD)	54 (13)
Sex, *N* females (%)	304 (67.6)
Mean MS disease duration, years (SD)	23 (12)
Clinical MS subtype, *N* with progressive disease (%)	239 (53.1)
DMT, *N* (%)	264 (58.7)
Fully vaccinated, N (%)	345 (76.7)
Protected by vaccination at time of COVID-19, *N* (%)	271 (60.2)

Table 2: Variables used in the multivariate logistic regression models

Dependent variable (outcome)
- COVID-19 outcome (hospitalisation and/or death versus ambulatory care)
Independent variables (predictors)
- Age (years)
- Sex (male versus female)
- Clinical MS subtype (progressive versus relapsing)
- Disability (Expanded Disability Status Scale scores)

References

1. Reder T, Stuve O, Tankou S, Leist T.T cell repsonse to COVID-19 infection and vaccination in patients with multiple sclerosis receiving disease-modifying treatment. Mult Scler. 2022 Nov 28;1 3524585221134216. doi: 10.1177/13524585221134216.

2. Fiolet T, Kherabi Y, MacDonald CJ, Ghosn J, Peiffer-Smadja N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. Clin Microbiol Infect. 2022;28(2):202-221; doi: 10.1016/j.cmi.2021.10.005.

Conclusion: Overall, COVID-19 vaccination protects against a worse infectious outcome in patients with MS but we were not able to confirm this effect in those on DMT with B-cell depleting agents.

Disclosure: The authors have no conflicts of interest relevant to this study.

ePosters

Sunday, July 02 2023
Ageing and dementia 2

EPO-173

Identification of pre-frailty in the elderly through serum metabolomics and its impact on Parkinson's disease phenotype

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Background and aims: Pre-frailty is a potentially reversible condition increasingly common with aging. However, whether it represents a continuum between healthy and frail status or a well-defined clinical entity is still unclear. Here, we attempted to better characterize pre-frailty using serum metabolomics in a large cohort of elderly subjects without neurodegenerative diseases. Next, we sought to investigate the impact of concurrent pre-frailty on elderly subjects with Parkinson's disease (PD).
Methods: We recruited 96 elderly non-PD subjects and classified them as non-frail, pre-frail, and frail based on Fried criteria. Untargeted metabolomics was carried out using Nuclear Magnetic Resonance (1H-NMR) on serum samples. Partial least-squares discriminant analysis and Pathway enrichment analysis were used to identify metabolites and biochemical pathways discriminating the three groups. Next, 83 mild-stage PD patients underwent Fried classification and assessment of motor and non-motor domains, ADL and QoL.
Results: Serum metabolomics identified three distinct clusters for non-frail (n=39), pre-frail (n=20), and frail (n=37) non-PD, with pre-frails showing the most evident separation from other groups. Multivariate analyses revealed L-Serine, Betaine, and Histidine as the most discriminating molecules. Pathway analysis pointed to dysregulation of amino acid metabolism, first of all, Serine-Glycine ($p<0.001$). In PD, pre-frail (n=25) patients showed intermediate levels of motor, ADL, QoL, and psychiatric impairment compared to both non-frail (n=45) and frail (n=13) subgroups (all FWER-adjusted $p<0.05$).

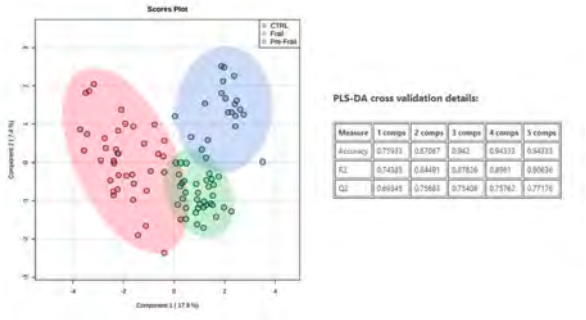

Fig. 1. Partial least squares-discriminant analysis (PLS-DA) score plot and cross validation results showing a clear clusterization of pre-frail serum metabolomics profile compared to non-frail and frail subgroups. CTRL = non-frail controls.

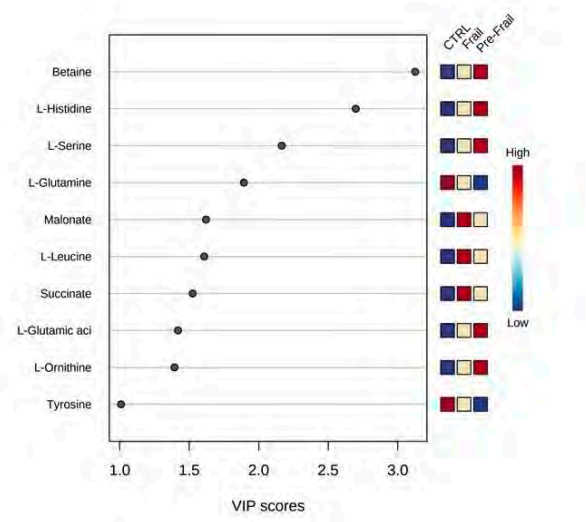

Fig. 2. Variable Importance in the Projection (VIP) score generated from PLS-DA showing Betaine, L-Histidine and L-Serine as the best discriminating molecules (VIP score > 2) between pre-frail, frail and non-frail subjects.

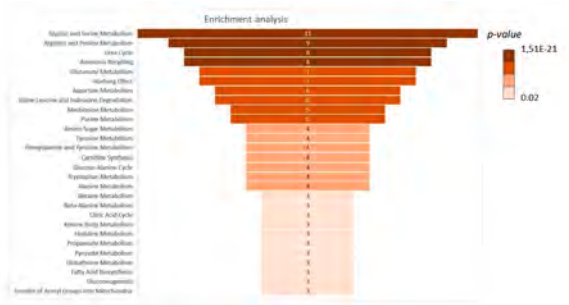

Fig. 3. Pathway enrichment analysis showing dysregulation of several amino acid pathways in frail and pre-frail subgroups, firstly Serine-Glycine metabolism. Further dysmetabolism is related to energy and reactive oxygen species pathways.

Conclusion: We identify L-Serine pathway dysregulation as a distinctive signature of pre-frailty in the elderly. In PD, pre-frailty status significantly affects both clinical phenotype and QoL, representing a potentially modifiable factor to be targeted with specific interventions.

Disclosure: This study was financially supported by Fondazione Cariplo (Call 2017 – Scientific Research "Biomedical research on aging-related diseases", grant no. 2017-0575).

EPO-174

Abstract withdrawn

EPO-175

The role of sleep structure analysis in the recognition of cognitive decline

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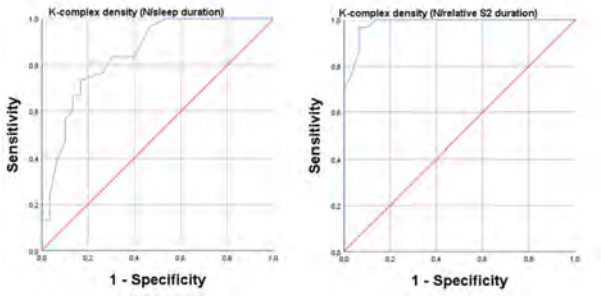
Background and aims: Alzheimer's disease (AD) effective treatment is absent due to difficulties in early differential diagnosis. Sleep-wake disturbances are common in AD, even at early stages. Our aim is to study the potential role of micro- and macrostructural sleep changes as early differencial diagnostic tools.

Methods: We involved 30 individuals with AD, and 30 controls. Sleep structure was examined with 24-hour Holter electroencephalograph (EEG), followed by visual evaluation. For microstructural analysis K-complex detection was used. Brain magnetic resonance imaging (MRI) and neuropsychological tests were also performed. 32 patients with mild cognitive impairment (MCI) and 46 healthy controls were also involved. Spearmann correlation and ANCOVA analyses were used for statistical evaluation.

Results: A rearrangement of sleep stages was observed in AD. Significant decrease was found both in K-complex densities avaraged for total sleep (F: 0.216; $p<0.001$) and for S2 sleep (F: 0.386; $p<0.001$). Based on the MRI examination, significant positive correlation was found between right caudal anterior gyrus cingulate thickness and both type of K-complex densities (total sleep: $r=0.458$; $p=0.042$; S2 sleep: $r=0.472$; $p=0.036$). In the MCI patient group, there was a significant reduction in right caudal anterior gyrus cingulate thickness (2.53±0.2 mm vs. 2.42±0.3 mm; $p=0.004$; Cohen's d: 0.353), showing the potential of K-complex analysis in early recognition.



ROC curve was used for testing the diagnostic abilities of K-complex densities. AUC=0.85 for K-complex density averaged for whole sleep duration and AUC=0.98 for K-complex density averaged for S2 sleep duration. AUC: area under the curve

Conclusion: Macro- and microstructural sleep changes were

significantly observed in AD which may be good markers of neurocognitive status. K-complex density is significantly decreased in AD, which raises the possibility that it may have a great impact in the preclinical detection of AD.
Disclosure: Nothing to disclose.

EPO-176

Genetic association between ADAM17 gene polymorphisms and risk of Alzheimer's disease: a case-control association study

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Background and aims: ADAM17 (a disintegrin and metalloproteinase 17) is a sheddase that participates in the proteolysis of several substrates playing a key role in Alzheimer's disease (AD), like amyloid precursor protein and Nerve Growth Factor Receptor (NGFR/p75NTR). The general aim of this study is to characterize the association between ADAM17 gene Single Nucleotide Polymorphisms (SNPs) and AD risk.
Methods: This case-control association study was conducted in a Southern Italian cohort consisting of 147 AD patients and 114 age- and sex-matched controls. Seven tag-SNPs were selected and genotyped with TaqMan SNP genotyping assays. The associations between these tag-SNPs and AD risk were assessed by logistic regression models.
Results: The variability of rs12692385 and rs11690078 polymorphisms was related to the AD onset. Subjects who were homozygous for the T allele of the rs12692385 polymorphism had 2.15 higher probability to develop AD than subjects carrying a single copy of the C allele (p=0.011). A significant effect was also detected for the rs11690078 polymorphism for which carriers of the T allele showed a significant reduced risk to develop AD with respect to those who were homozygous for the C allele (OR=0.24, p=0.011). A borderline effect was also detected for rs12464398 polymorphism for which carriers of the C allele showed a reduced risk to develop AD with respect to those who were homozygous for the T allele (OR=0.58, p=0.065).
Conclusion: Our results reveal a new role of ADAM17 gene in AD from a genetic perspective. ADAM17 gene tag-SNPs analysis should be considered for the genetic screening of AD.
Disclosure: Nothing to disclose.

EPO-177

Genetic variants in the NGFR/p75NTR gene predict cognitive impairment and functional decline in Alzheimer's disease

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Background and aims: Alzheimer's Disease (AD) is the most widespread neurodegenerative disorder. AD is commonly categorized as either early onset (EOAD) or late onset (LOAD) based on an age cutoff, typically 65 years. Previously, we have shown that Single Nucleotide Polymorphisms (SNPs) of the Nerve Growth Factor Receptor (NGFR/p75NTR) gene could represent risk factors both for EOAD and LOAD. The principal aim of this study is to better characterize the association between NGFR/p75NTR gene SNPs with AD, considering cognitive impairment and functional decline.
Methods: This study was conducted on 295 AD patients (109 EOAD and 186 LOAD) recruited at the Regional Neurogenetic Centre (CRN) – ASPCZ of Lamezia Terme (CZ, Italy). Nineteen tag-SNPs were selected within the entire NGFR/p75NTR gene and genotyped using TaqMan SNP genotyping assays on DNA extracts prepared from blood samples. The associations between these tag-SNPs, cognitive impairment (MMSE scores) and functional decline (ADL and IADL scores) were assessed by linear and logistic regression models after adjustment for gender, APOE genotype and level of education.
Results: The variability of two investigated polymorphisms was correlated with MMSE score only in LOAD patients. The variability of other polymorphisms was significantly associated with ADL and IADL scores in both EOAD and LOAD patients.
Conclusion: Our results reveal a new role of NGFR/p75NTR gene in the cognitive impairment and functional autonomy of both EOAD and LOAD patients. NGFR/p75NTR gene tag-SNPs analysis should be considered for the genetic screening of AD.
Disclosure: This work was supported by funds granted by the Italian Ministry of Health Ricerca Finalizzata 2018:SG-2018-12366233.

EPO-178

Apathy and unawareness of apathy differ in neural pathways in prodromal Alzheimer's disease: an FDG-PET study

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Background and aims: The discrepancy in apathy ratings between patients with amnestic MCI and their informants predicts transition to Alzheimer's disease(AD) dementia as a measure of disease awareness. We investigated whether the metabolic changes linked to discrepant estimations differ topographically from those in the frontal-subcortical circuits typically connected to apathy.
Methods: 29 individuals with amnestic MCI and an intermediate-to-high likelihood of AD progressing to dementia over an average of two years were retrospectively chosen (21 F;age 76.2±4.9 years;education 8.7±4.0; MMSE score 25.9.2±1.5). All participants completed at baseline an extended neuropsychological assessment including the Apathy Evaluation Scale (AES) to measure apathy, either patients' self-(AES-S) or informant-reported(AES-I), and [18F]-FDG-PET analysis. Patients' self-ratings were subtracted from caregivers' estimations to produce a "Discrepancy" score. We identified the various regions of correlation of AES-S, AES-I, and "Discrepancy" with brain metabolism using voxel-based analysis of [18F]-FDG-PET images(multiple regression analysis, nuisances:age, MMSE score).
Results: The "Discrepancy" in the bilateral hippocampal gyri and thalami, right posterior cingulate cortex, and putamen, and the AES-S score in the left cingulate, precentral, superior frontal cortices, and right medial frontal area were found to correlate with metabolic levels negatively. The two subgroups of patients split according to the degree of the "Discrepancy" (median score=6) showed no differences in cognitive functioning.
Conclusion: Our findings are consistent with the relationship between frontal network activity and the degree of apathy in MCI-AD patients. In contrast, regardless of the amount of cognitive impairment, the "Discrepancy" between patients' self- and informant-estimated apathy is linked to limbic areas typically involved in memory functioning.
Disclosure: Nothing to disclose.

EPO-179

Language and biomarker profile of data-driven subtypes of mixed semantic-logopenic primary progressive aphasia

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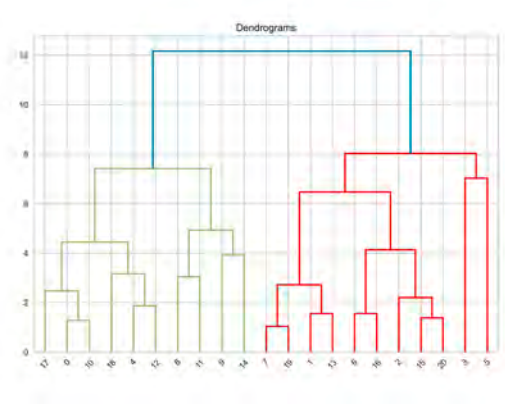
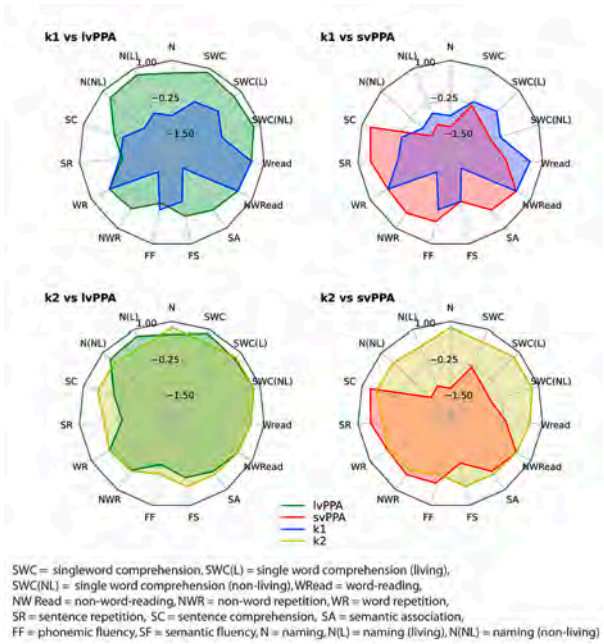
Background and aims: A variable amount (6–41%) of primary progressive aphasia (PPA) cases did not fulfill criteria for prototypical variants and are defined as mixed PPA (mPPA). Patients with mPPA are poorly characterized. We aimed to detail linguistic and biomarker profiles of patients with mixed semantic-logopenic PPA (s/lv-PPA).
Methods: We considered 56 patients with diagnosis of PPA: 12 semantic variant (svPPA), 23 logopenic variant (lvPPA) and 21 s/lvPPA. All patients underwent neuropsychological and language evaluation, CSF concentration of Aβ42, Aβ42/Aβ40, phosphorylated tau and total tau measurement. Reduction of dimensionality was performed by principal component analysis (PCA). We used Agglomerative Hierarchical Clustering (HCA) as unsupervised learning algorithms.
Results: Five principal components were defined based on language tests and were used to run an HCA identifying two clusters: k1 (n=10) and k2 (n=11) (Fig. 1). k1 group had lower Aβ42/Aβ40 ratio ($p=0.018$, $\eta2=0.40$) and higher t-tau ($p=0.012$, $\eta2=0.35$) and p-tau ($p=0.023$, $\eta2=0.34$) concentrations than k2. Moreover, k1 group had lower scores in test assessing for semantic fluency ($p=0.021$, $\eta2=0.27$), naming ($p=0.003$, $\eta2=0.42$), single word comprehension ($p<0.001$, $\eta2=0.59$) and semantic association ($p=0.001$, $\eta2=0.58$) than k2 group. Linguistic profile of k1 was more similar to svPPA and the one of k2 was more similar to lvPPA (fig.2).



Dendrogram from Agglomerative Hierarchical Clustering



SWC = singleword comprehension, SWC(L) = single word comprehension (living), SWC(NL) = single word comprehension (non-living), WRead = word-reading, NW Read = non-word-reading, NWR = non-word repetition, WR = word repetition, SR = sentence repetition, SC = sentence comprehension, SA = semantic association, FF = phonemic fluency, SF = semantic fluency, N = naming, N(L) = naming (living), N(NL) = naming (non-living)

Comparison between clusters and prototypical PPA variants

Conclusion: Based on language features, we identified two s/lvPPA subtypes showing different AD biomarkers profile. Interesting the subtypes with a CSF biomarker profile showed a linguistic profile more consistent with svPPA. This result might suggest the existence of a linguistic spectrum influenced by AD pathology across mPPA.
Disclosure: The authors declare no commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-180

Blood-CSF barrier impairment and regional brain atrophy in prodromal and overt AD and DLB

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Background and aims: Alzheimer's disease (ADdem) and Lewy body dementia (DLB) are characterized by cholinergic impairment and regional brain atrophy. In DLB, overlapping AD associates with greater atrophy). However, other factors may play role in atrophy and clinical impairment. Choroid plexus (CP), part of blood-CSF barrier, regulates inflammation and monitors CSF synthesis, composition, and circulation. Association between blood-CSF barrier impairment and regional atrophy, and effect of AD biomarkers, is unknown in prodromal and overt AD and DLB.
Methods: 108 participants (n=30 prodromal AD, n=24 ADdem, n=10 prodromal DLB, n=20 overt DLB, n=24 unimpaired controls, CN) had clinical, MRI and CSF tests. FreeSurfer algorithm and cholinergic basal forebrain ROIs measured CP and nucleus basalis of Meynert (NBM) volumes and regional cortical thickness. From CSF, AD biomarkers and albumin quotient (QAlb), proxy of blood-CSF barrier impairment, were derived. MANOVA adjusted for age, sex assessed the associations between atrophy and blood-CSF barrier; mediation analysis assessed how the CSF AD biomarkers mediated this relationship.
Results: CP volume was larger and NBM volume was smaller in both DLB and AD compared to CN, and CP increased from prodromal to overt dementia. Larger CP was associated with smaller NBM in AD and DLB. Larger CP was associated with abnormal QAlb, and with abnormal AD biomarker levels. Abnormal AD biomarker levels mediated association between larger CP, abnormal AlbQ and regional atrophy.
Conclusion: Impaired blood-CSF barrier is associated with greater regional atrophy including cholinergic regions in prodromal and overt AD and DLB.Investigation into blood-CSF barrier as additional potential treatment target may be beneficial.
Disclosure: Supported by grants: Charles University (PRIMUS 22/MED/011) and EXCELES Project No. LX22NPO5107.

EPO-181

Abstract withdrawn

EPO-182

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EPO-183

A comparison of cerebral amyloid angiopathy in the cerebellum and occipital lobe from routine autopsies

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Background and aims: The occipital lobe is most frequently and severely affected by cerebral amyloid angiopathy (CAA). CAA can also occur in the cerebellum, although less frequently than in the cerebral lobes. Until recently, there have been limited studies assessing cerebellar CAA. In the present study, we semiquantitatively compared the frequency and severity of CAA in the cerebellum and occipital lobe.
Methods: We reexamined the senile changes in approximately 440 autopsied brains in our institute. We selected 60 subjects in whom the CAA were observed in the occipital lobe. Five-micrometer-thick paraffin-embedded brain sections were immunostained with monoclonal anti-amyloid-β (Aβ) peptides 17–24 (4G8) and monoclonal anti-phosphorylated tau (AT8) antibodies.
Results: In the 60 subjects with CAA-positive occipital lobe, cerebellar CAA was observed in 29 subjects (48.3%), and the severity of cerebellar CAA was relatively mild compared with occipital lobe CAA. Capillary CAA was observed in the occipital lobe of 12 subjects and the cerebellum of three subjects. CAA-related vasculopathies were observed in the occipital lobe of 15 subjects and the cerebellum of two subjects–the severity of CAA-related vasculopathy was mild in both of these subjects. Aβ plaques were observed in the occipital lobe of 54 subjects (90%) and the cerebellum of 16 subjects (26.7%)–the severity of Aβ plaques in the cerebellum was mild compared with the occipital lobe.
Conclusion: We confirmed that cerebellar CAA is frequently observed in the cerebellum, but with a lower severity than CAA in the occipital lobe. Clinicians should pay more attention to cerebellar CAA.
Disclosure: The authors declare no conflicts of interest for this study.

EPO-184

Dependency as a result of AD across disease stages measured by activities of daily living

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Background and aims: Alzheimer's disease (AD) is a progressive disease causing cognitive dysfunction, reduced ability to perform activities of daily living (ADLs), and behavioural changes. The study objective is, to describe neuropsychiatric symptoms and ability to conduct ADLs among cognitively unimpaired participants and AD.
Methods: Data from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set were used for this study. The NACC collects annual follow-up data from participants seen at participating Research Centers. Participants with unimpaired cognition, clinically diagnosed MCI or dementia due to AD were included. ADLs were assessed at each visit using the NACC-Functional Assessment Scale (FAS) and neuropsychiatric symptoms using the Neuropsychiatric Inventory Questionnaire (NPI-Q).
Results: The study included participants with unimpaired cognition (13,692 [48.5%]); MCI due to AD (7,075 [25.1%]); and dementia due to AD (7,453 [26.4%]). Participants responses to individual NACC-FAS questions demonstrate that impact on ADLs may emerge as early as the MCI stage. For example, 0.4% of cognitively unimpaired participants were dependent on others when traveling out of the neighbourhood, driving, or arranging to take public transportation compared to 8.0%, 47.4%, 85.5% and 94.9% of participants with MCI due to AD, mild, moderate, and severe AD dementia, respectively. Similarly, 0.3% of cognitively unimpaired participants reported severe anxiety compared with 1.5%, 3.5%, 7.6% and 7.5% of participants with MCI due to AD, mild, moderate and severe AD dementia, respectively.
Conclusion: These data demonstrate that deterioration of ADLs and emergence of psychiatric symptoms are apparent as early as the MCI stage in AD continuum and increase with disease progression.
Disclosure: Nothing to disclose.

EPO-185

Cortical morphological dissimilarities as potential biomarkers of Alzheimer disease and late mild cognitive impairment

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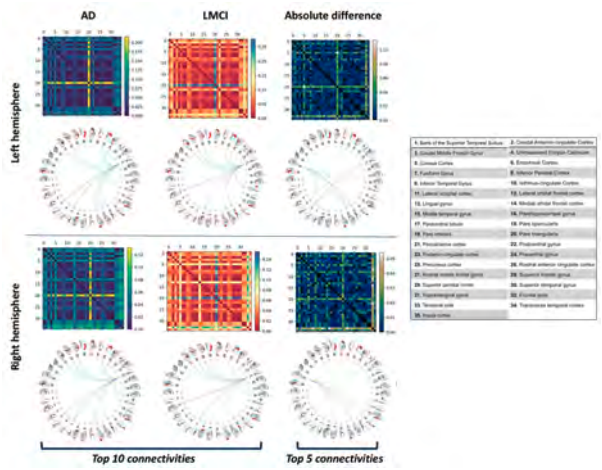
Background and aims: Deep learning methodologies have achieved great progress regarding classification of neurological disorders and yet, failed to learn efficiently from connectomic brain graph data. Graph neural networks(GNNs) have provided learning by considering the connectivity of regions of interests (ROIs) which extracts a deeper interpretation of the brain networks. In this study, we implemented a GNN model to extract the biomarkers distinguishing Alzheimer's disease(AD) from late mild cognitive impairment(LMCI).

Methods: We used a dataset with 70 subjects(35 AD,35 LMCI) from the Alzheimer's Disease Neuroimaging Initiative(ADNI) database GO public dataset. The networks are derived from maximum principal curvature, mean cortical thickness, mean sulcal depth, average curvature measurements and cortical surface area. The cortical surface is reconstructed from T1-weighted MRI using the FreeSurfer and each view is defined with 35 ROIs by Desikan-Killiany atlas. The weight of the entry denotes the strength of connectivity between given ROIs.

Results: The top 10 connectivities within the right hemisphere pinpoints that Pericalcarine cortex(PrC) and precuneus connectivity is specific to AD patients and could be considered as a discriminative biomarker of AD(Figure1), a fact that has been established using functional MRI. Dissimilarities of the connections of the the PrC with the inferior parietal cortex(IPC) and with the caudal middle frontal gyrus(CMFG) represent fingerprints of LMCI.

Conclusion: Dissimilar morphological connectivity and functional connectivity are intertwined. The concept of cortical morphological connectivity exceeded the morphology-cortical-region-based approach providing accurate biomarkers: The PrC with precuneus as a distinctive connectivity in AD and PrC with the IPC and with the CMFG in LMCI.

Disclosure: Arwa Rekik and Oben Özgür are first authors.



Representation of the top 10 most discriminative connectivities within the left and the right hemispheres seperately, in AD and LMCI along with the absolute difference matrices between AD and LMCI illustrated with the top 5 connectivities.

EPO-186

Different CSF tau measures and their association with traditional CSF and PET biomarkers in a memory clinic population

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Background and aims: Alzheimer's Disease (AD) is characterized by abnormal deposition of amyloid (A) and tau (T) proteins in the brain. A and T can be measured by using PET, cerebrospinal fluid (CSF) and blood. Several CSF pTau epitopes have been described and could be more specific for the different stages of the disease. The present study aims to assess the association between several pTau epitopes and Tau368, the traditional CSF and PET biomarkers and global cognition.

Methods: The following CSF biomarkers were quantified using single molecular arrays developed at the University of Gothenburg from 112 subjects (49 cognitively-unimpaired,55 MCI,8 demented) of the Geneva Memory Center: pTau181, pTau212, pTau231, pTau217, Tau368 (analyzed as Tau368/tTau). Subsets of: n=84 underwent an amyloid PET; n=48 a tau PET; n=63 a lumbar puncture (traditional biomarkers: Aβ42, pTau181, tTau); n=109 a MMSE. A Kruskal-Wallis test was used to assess the differences in levels of CSF tau measures among diagnostic

groups; Pearson correlation to assess the association between CSF tau measures and traditional CSF and PET biomarkers and cognition.
Results: pTau181, pTau212, pTau231, pTau217 but no Tau368/tTau were able to differentiate disease stages ($p<0.005$). All CSF pTau epitopes and Tau368/tTau strongly correlate with traditional CSF biomarkers ($R>0.5;p<0.001$) and PET biomarkers ($R>0.6;p<0.05$). All CSF pTau epitopes and Tau368/tTau can differentiate A+/A- and T+/T- assessed through PET and they all correlate with MMSE ($R>0.3;p<0.005$).
Conclusion: Further analyses are needed to investigate the prognostic value of different CSF pTau epitopes across disease stages. However, they seem to identify AD patients and they strongly correlate with traditional AD biomarkers.
Disclosure: HZ has served at scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, Alzinova, ALZPath, Annexon, Apellis, Artery Therapeutics, AZTherapies, CogRx, Denali, Eisai, Nervgen, Novo Nordisk, Optoceutics, Passage Bio, Pinteon Therapeutics, Prothena, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures in symposia sponsored by Cellectricon, Fujirebio, Alzecure, Biogen, and Roche, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program (outside submitted work). KB has served as a consultant, at advisory boards, or at data monitoring committees for Abcam, Axon, BioArctic, Biogen, JOMDD/Shimadzu. Julius Clinical, Lilly, MagQu, Novartis, Ono Pharma, Pharmatrophix, Prothena, Roche Diagnostics, and Siemens Healthineers, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program, outside the work presented in this abstract. FR, AJM, AL, VG, GBF declare that they have no competing interests.

EPO-187

Attitudes toward seeking professional help among patients with early Alzheimer´s disease

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Background and aims: Limited information is available on the active process of seeking professional help when patients with Alzheimer's disease (AD) perceive cognitive impairment in the early stages. The aim of this study was to assess the phenomenon of help-seeking in early AD and to identify associated factors.
Methods: A multicenter, non-interventional study was conducted including patients of 50–90 years of age with prodromal or mild AD, a Mini-mental State Examination (MMSE) score ≥22, and a Clinical Dementia Rating-Global score (CDR-GS) of 0.5-1.0. A battery of self-report instruments was used to evaluate different patients´ psychological and behavioral domains. A multivariable logistic regression analysis was conducted.
Results: A total of 149 patients were included. Mean age (SD) was 72.3 (7.0) years and 50.3% were female. Mean disease duration was 1.4 (1.8) years. Ninety-four (63.1%) patients sought help when they realized their symptoms, mostly from neurologists (71.3%). Patients with help-seeking attitudes were mostly female (60.6%) with a CDR-GS score of 0.5 (91.5%) and had a greater awareness of diagnosis, poorer quality of life, more depressive symptoms, and more severe perception of their condition than their

counterparts. Lack of help-seeking attitudes was associated with male gender (OR=0.33 [95%CI 0.15, 0.69], p=0.003), a low awareness of diagnosis (OR=0.96 [95%CI 0.92, 0.99], p=0.015), and the perception of non-threatening illness (OR=0.32 [95%CI 0.15, 0.71], p=0.005) in the multivariable analysis after adjustment for confounders.

Conclusion: These findings should be considered when developing strategies to promote positive attitudes towards professional help-seeking in patients with cognitive impairment at earlier stages.

Disclosure: This study was funded by Roche Farma SA, Spain (Medical Department) Alberto Villarejo-Galindo discloses honoraria from a consulting/advisory role with KRKA, Kern Pharma, Exeltis, Esteve, Roche, AbbVie, Schwabe, Neuraxpharm, Nutricia, and Alter. Antonio del Olmo-Rodríguez discloses honoraria from a consulting/advisory role with Alter, Biocross, Biogen, KRKA, Esteve, Schwabe, Nutricia, and Lilly. Emilio Franco-Macías discloses honoraria from a consulting/advisory role with Kern Pharma, Esteve, Roche, and Neuraxpharm. Mercè Boada discloses honoraria from a consulting/advisory role with Grifols, Araclon Biotech, Roche, Lilly, Merck, Biogen, Zambon, Novo-Nordisk, Bioiberica, Biogen, Eisai, Servier, and Schwabe Pharma; funding sources with Life Molecular Imaging, Bioiberica, and Schwabe; and grants from CIBERNED, EU/EFPIA, Instituto de Salud Carlos III (ISCIII), Fundación La Caixa, and Grífols. Albert Lleó discloses honoraria from a consulting/advisory role with Grifols, Fujirebio-Europe, Novartis, Roche, Otsuka, Nutricia, Zambón, Biogen, Lilly, and KRKA. Co-author of a patent on markers of synaptopathy in neurodegenerative diseases (EP18382175.0, PCT/EP2019/056535). Elena García-Arcelay and Jorge Maurino are employees of Roche Farma SA Spain. The rest of authors declare no potential conflict of interest.

Motor neurone diseases

EPO-188

A longitudinal evaluation of early sleep and respiratory impairment in ALS patients

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Background and aims: ALS is a neurodegenerative disease characterised by motor neuron death. 30% present a bulbar onset, while 70% a spinal one. Extra-motor systems involved in ALS include circuits regulating sleep; the early identification of sleep impairment and his better definition could improve patient's quality of life (QoL). One of the most important prognostic factors in ALS is respiratory impairment. It's early recognition and an early starting of non-invasive ventilation (NIV) allow a prolongation of survival.
Methods: Between August 2021 and July 2022 we enrolled 45 ALS patients and 45 healthy controls (HC). At baseline and at month six, patients underwent neurological examination, polysomnography (PSG), arterial blood gases (ABG), spirometry and filled sleep and respiratory questionnaire (RLSRS, STOP-BANG, ISI, ESS, PSQI, PIRS, MEQ, STAI, BDI). SPSS software was used for data analysis.
Results: At baseline, ALS patients without respiratory symptoms showed an increase of AHI-index and of ODI-index compared to HC (respectively, p=0.001 and p=0.04). Contrarily, spirometry and ABG were not so altered. Longitudinally we observed a significant worsening of PSG parameters (p<0.05). Patients who started nocturnal-NIV (15 out of 45) showed a significant improvement of PSG parameters. At baseline we also observed an excess of periodic limb movement in ALS vs HC (p=0.01). Direct correlation between progression rate of disease and both AHI and ODI (r=0.546 and r=0.442 p<0.05).

Sex (M/F)	ALSFRS (± SD)	FVC (± SD)	FEV1 (± SD)	AHI (± SD)	ODI (± SD)	PLMS (± SD)
25/20	39,2 ± 4,6	92 ± 21	93 ± 23	18,5 ± 15,5	13,3 ± 11,0	22,5 ± 31,6

Demographic and clinical data of ALS patients

Conclusion: This preliminary study showed the presence of respiratory and sleep impairments in ALS patients since the beginning of the disease. Their identification is fundamental for an early treatment and for an improvement of QoL.
Disclosure: I have nothing to disclose.

EPO-189

Role of TDP-43 in the diagnosis and phenotypic characterization of ALS: comparison between CSF and plasma data.

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Background and aims: Background: the diagnostic work-up for Amyotrophic Lateral Sclerosis (ALS) diagnosis is complex and often associated with diagnostic delay. Scientific research focused on the neurodegeneration biomarkers that can anticipate the diagnosis and phenotypically characterize patients is necessary. Among these, TDP-43, which accumulates in the neuronal cytoplasm in most ALS patients, is one of the most promising. This study aimed to compare the data obtained from the cerebrospinal fluid (CSF) and blood TDP-43 dosage and to correlate the results obtained from the assays with clinical and laboratory data.
Methods: Methods: 14 patients were recruited, and CSF and serum TDP-43 were determined by the ELISA method. Clinical-phenotypic and functional data (ALSFRS-R, BMI, FVC%), blood chemistry, and genetic data were also collected.
Results: Results: a strong negative correlation (r=-0.70; p=0.03) was observed between CSF and serum levels. There was also a significant positive correlation (r=0.67; p=0.03) between CSF and Creatine phosphokinase (CPK) and a negative correlation (r=-0.90; p≤0.01) between serum TDP-43 and CPK values. Patients with the bulbar phenotype appear to show lower levels of CSF TDP-43 compared to spinals (p=0.04); moreover, there was a positive correlation between CSF TDP-43 and the bulbar subscore of the ALSFRS-R (r=0.67; p=0.03). Correlating with the genetic data, the patient carries the lowest absolute CSF TDP-43 concentration within the cohort characterizes a SOD1 mutation.
Conclusion: Conclusions: data from this study support the utility of TDP-43 as a biomarker in ALS, both at CSF and plasma levels, also showing significant correlation with clinical and genetic data.
Disclosure: Nothing to disclose.

EPO-190

Upper motor neuron involvement in ALS: a correlation between neurophysiological and metabolic brain pattern.

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Background and aims: In Amyotrophic Lateral Sclerosis (ALS) diagnostic work-up, the involvement of lower motor neurons (LMNs) is easily demonstrated by electromyography; on the contrary, finding markers of upper motor neuron (UMN) suffering is harder. Transcranial magnetic stimulation (TMS)-induced motor-evoked potentials (MEPs) are one of the proposed markers of (sub)clinical UMN damage. Our study aimed to verify a possible correlation between the metabolism brain pattern and the MEPs findings for highlighting the UMN damage.

Methods: A total of 20 ALS patients who underwent FDG-PET and TMS-MEPs at diagnosis were retrospectively enrolled in the study. Patients were enrolled between 2018 and 2022 at the ALS Tertiary Center, Novara, Italy. For each patient, we collected clinical-phenotypical variables. We measured the motor latency, amplitude, and central motor conduction time (CMCT) for TMS-MEPs from the upper and lower limbs. For FDG-PET, following a validated voxel-based Statistical Parametric Mapping procedure, we obtained hypometabolism maps at the single-subject level, correlating the regional hypometabolism with clinical and neurophysiological values.

Results: Of enrolled patients, the mean age was 57.2±12.63 years (30% bulbar, 70% spinal onset). 14/20 patients (70%) had abnormal MEPs in at least one limb: 8/20 (40%) had unreliable MEPs, and 12/20 (60%) had delayed CMCT. We observed a direct correlation between lower limbs CMCT and precentral, frontal superior, and supplementary motor areas (r=0.65,p=0.05;r=0.76,p=0.02;r=0.72,p=0.03). For the upper limbs, the correlation is limited with the supplementary motor area (r=0.78,p=0.02).

Conclusion: Our data suggest an essential single and additive role of TMS-MEPs and FDG-PET in highlighting the UMN suffering in ALS patients at diagnosis.

Disclosure: Nothing to disclose.

EPO-191

Electrodiagnostic Findings in Facial Onset Sensory and Motor Neuronopathy (FOSMN)

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Background and aims: FOSMN is a rare clinical syndrome initially described in a seminal case series of five patients who presented with facial sensory deficits, followed by motor deficits, evolving rostro-caudally. Clinical, genetic and neuropathological data strongly suggest that FOSMN is a rare phenotype of amyotrophic lateral sclerosis (ALS). Herein, we review the published electrodiagnostic data for FOSMN and report detailed electrophysiological data from two cohorts (n=10) with this syndrome, proposing a specific approach to electrodiagnostic testing in patients who present with facial sensory symptoms.

Methods: Blink Reflexes, Electromyography, Nerve Conduction Studies, Somatosensory Evoked Potentials, Threshold Tracking Transcranial Magnetic Stimulation.

Results: Findings on standard electrophysiological assessment were in broad agreement with those published: blink reflexes were abnormal in all but one patient (Figure 1); SNAPs were reduced but CMAPs preserved; mixed acute and chronic neurogenic change was identified on needle EMG in bulbar and cervicothoracic muscles in approximately 50% of patients. In addition, upper limb SEP central conduction times were increased (n=4) and progressed on repeat testing (n=3) (Figure 2), and upper motor neuron dysfunction was revealed by several measures [ipsilateral MEPs (n=1); reduced short interval intra-cortical inhibition on threshold-tracking TMS (n=2); absent beta-band intermuscular coherence (n=3)].

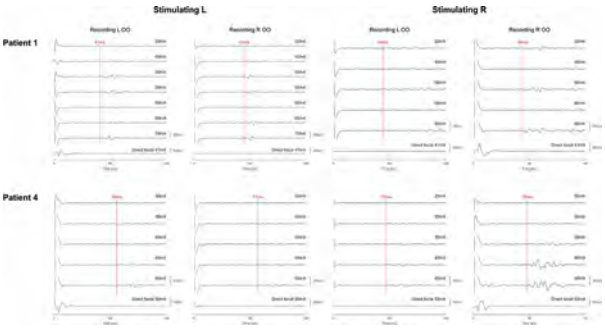

Figure 1: Illustrative examples of blink reflex responses acquired from 2 patients.

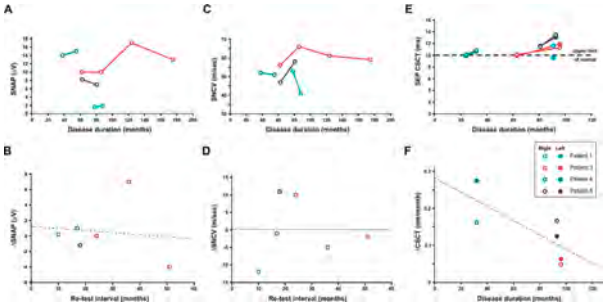

Figure 2. Changes in sensory nerve action potential (SNAP) amplitudes, sensory nerve conduction velocities (SNCVs) and upper limb somatosensory evoked potentials (SEPs).

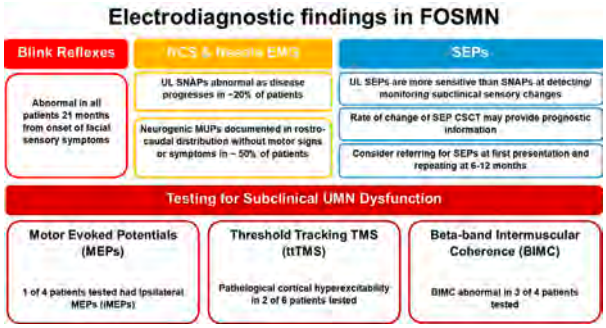

Figure 3. Summary of electrodiagnostic findings in facial onset sensory and motor neuronopathy (FOSMN).

Conclusion: Electrodiagnostic investigation of FOSMN should include blink reflex testing, SEPs and tests of upper motor neuron function (Figure 3). The combination of progressive lower motor neuron disease and upper motor neuron disease on neurophysiological investigation provides further support for the contention that FOSMN is a rare phenotypic variant of ALS.

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EPO-192

Transcriptome signature in Amiotrophic Lateral Sclerosis (ALS) phenotypes

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Background and aims: Unmet needs for ALS patients includes both the identification of criteria for clinical stratification, and the discovery of reproducible biomarkers. We aim to identify a transcriptome signature in homogenous MND sub-groups obtained using specific phenotype classification.

Methods: We have stratified n=48 newly-diagnosed sporadic ALS patients by Chiò et al (JNNP, 2011) criteria, and enrolled n=19 age-matched healthy controls. We have isolated PBMCs, performed RNA sequencing, and compared the transcriptome profiles for all the subjects compared to healthy controls.

Results: We have collected the following phenotypes: n=12 classic, n=10 bulbar, n=7 flail arm, n=10 flail leg, n=9 pyramidal. We have observed a different gene expression between patients and controls ($p<0.05$), particularly for the flail leg subgroup (fig. 1). Moreover, bulbar phenotype has been characterized by a great number of altered genes ($p>0.05$). Finally, we have noticed a single gene altered in all the phenotypes (Y-RNA, a component of the Ro60 ribonucleoprotein involved in cellular response to interferon-alpha and in regulation of gene expression) while the other genes seem to be phenotype-specific (fig. 2), and many of them are involved in inflammatory pathways.

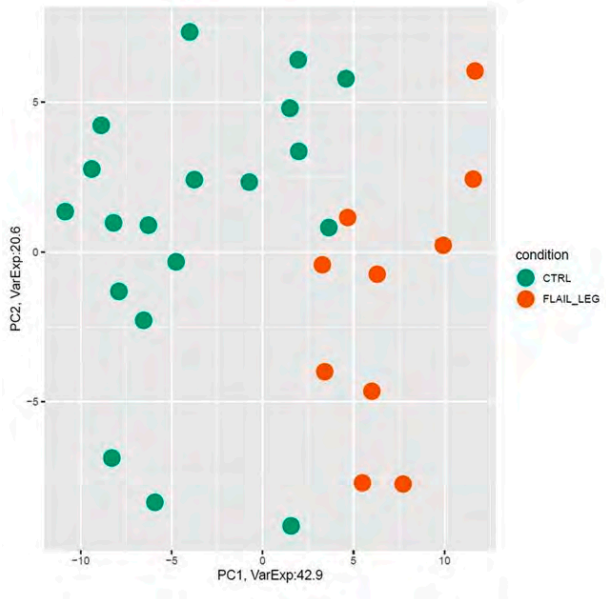

Figure 1. Principal Component Analysis of sALS patients' RNA-sequencing (flail leg phenotype)

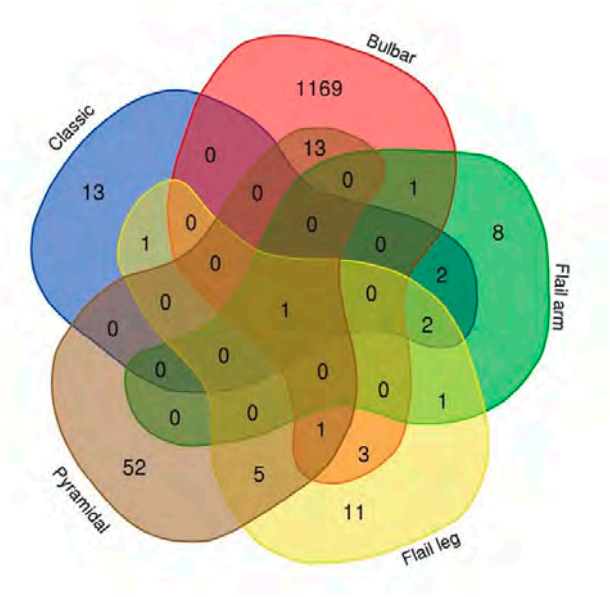

Figure 2. Venn diagram showing common deregulated genes among phenotypic groups.

Conclusion: The identification of phenotype-specific pathogenic mechanisms could be pivotal for the study of progression biomarkers. Future development of this work will regard the longitudinal evaluation of transcriptomic patterns.

Disclosure: The authors declare no competing interests. this work was supported by grants of the Italian Ministry of Health to Luca Diamanti (2021-2022).

EPO-193

Hidden hints from routine blood analyses in patients with amyotrophic lateral sclerosis

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Background and aims: There is an unmet need in amyotrophic lateral sclerosis (ALS) to provide specific biomarkers for the disease. Due to their easiness and reproducibility, we aimed to investigate whether routine blood parameters may provide useful clues for phenotypic classification and prognosis.

Methods: We analysed a large inpatient cohort of 836 ALS patients who underwent deep phenotyping in terms of clinical upper (UMN) and lower (LMN) motor neuron scores and active and chronic denervation scores. Disability and disease progression rate were measured through the revised ALS functional rating scale (ALSFRS-R) and its changes during time. Cox regression analysis with relative hazard ratios (HR) was performed to assess potential survival associations.

Results: Creatinine showed significant correlations with LMN damage (r=0.38), active (r=0.18) and chronic (r=0.24) denervation and baseline ALSFRS-R (r=0.33). CPK, ALT, and AST correlated with ongoing (r=0.35, 0.27, 0.24) and chronic (r=0.37, 0.20, 0.19) denervation, respectively while albumin and CRP significantly correlated only with LMN score (r=0.20 and 0.17). Disease progression rate showed correlations only with chloride (r= -0.19) and potassium (r= -0.16). After adjustment for known prognostic factors, creatinine (HR 0.86, 0.81–0.92), AST (HR 1.02, 1.01–1.02), total proteins (HR 0.70, 0.57–0.86), LDH (HR 0.998, 0.997–0.999) and chloride (HR 0.95, 0.92–0.99) were independently associated with survival in ALS.

Conclusion: creatinine is a reliable biomarker for ALS, associated with clinical features, disability and survival. Markers of muscle damage and inflammation correlate with neurophysiological and clinical scores, respectively. Chloride and potassium were significantly associated with progression rate and survival.

Disclosure: Nothing to disclose.

EPO-194

Association between retinal vascularization and disease severity in Amyotrophic Lateral Sclerosis

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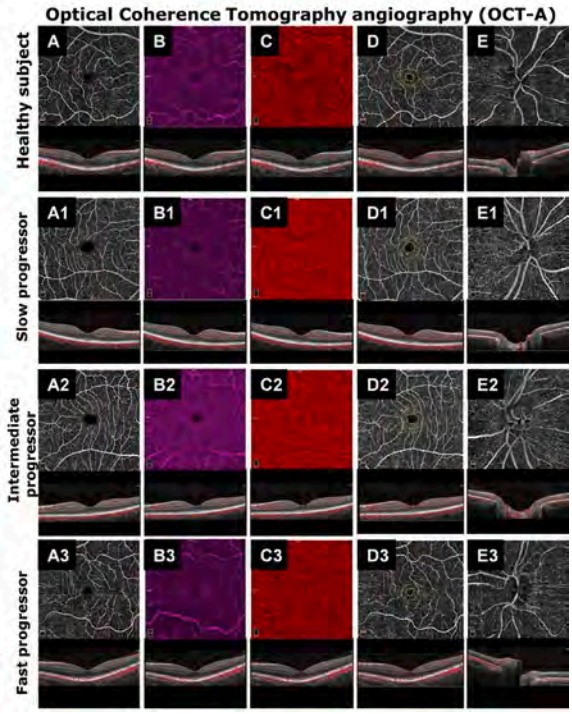
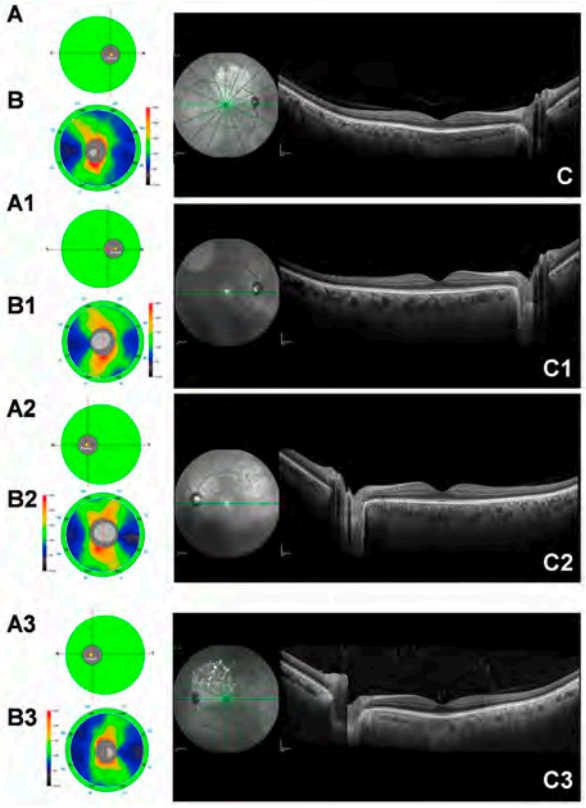
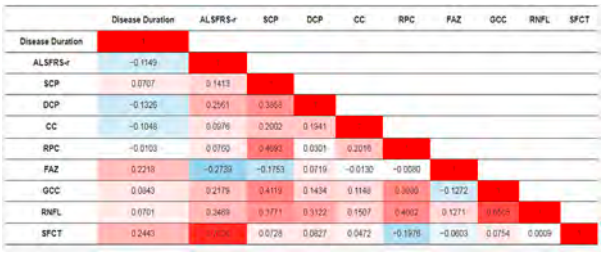
Background and aims: Alterations in retinal vascularization and neural density have been found in many neurodegenerative diseases, however conflicting results are described in Amyotrophic Lateral Sclerosis (ALS). The aim of the present study was to analyse retinal layers and vascularization using structural and Optical Coherence Tomography angiography (OCT-A) in ALS patients classified according to disease severity.
Methods: We enrolled 48 ALS patients, classified into three groups: slow progressors (n=10), intermediate progressors (n=24) and fast progressors (n=14) according to the disease progression rate, and 45 healthy controls. For structural-OCT we evaluated the Subfoveal Choroidal Thickness (SFCT), Ganglion Cell Complex (GCC), Retinal Nerve Fiber Layer (RNFL). Regarding the OCT-A we assessed the vessel density (VD) in Superficial and Deep Capillary Plexuses, Radial Peripapillary Capillary Plexus, Choriocapillary and the Foveal Avascular Zone (FAZ) area.
Results: Structural-OCT did not show any significant differences in GCC and RNFL thicknesses between patients and controls, and among the three ALS groups. The SFCT was significantly greater in patients compared with controls, interestingly the SFCT was thicker in patients with slow and intermediate disease progression than in those with fast disease progression. OCT-A did not reveal any significant results. Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) and disease duration did not correlate with any of OCT parameters, except for SFCT with ALSFRS-R.



OCT-A exam did not show any significant differences in GCC and RNFL thicknesses between patients and controls, and among the three ALS groups



The SFCT was statistically greater in patients compared with controls. The SFCT was thicker in patients with slow and intermediate disease progression than in those with fast disease progression (Figure 2a, 2b and 2c).



Pearson's correlations between OCT measures and clinical findings represented as visual matrix form with color coding based on strength and sign of correlations. Note the positive significant relationship between ALSFRS-r and SFCT.

Conclusion: This study demonstrated the possible association between higher SFCT and disease activity in SLA, likely due to inflammatory vascular phenomena. OCT could be a useful biomarker in management of this neurodegenerative disease.
Disclosure: Nothing to disclose.

EPO-195

Study of non-neuronal cell populations in an experimental model of Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a rare neuromuscular disorder caused by survival motor neuron (SMN) protein insufficiency. The SMNΔ7 is a widely used rodent model exhibiting SMA type II disease.
Methods: Triple transgenic FVB.Cg Grm7Tg (SMN2)89Ahmb Smn1tm1Msd Tg(SMN2*delta7) 4299Ahmb/J mice were euthanized on postnatal day 13 after clinical and neuromuscular evaluation. Spinal cord (L1-L5) was harvested and paraffin sections were used for immunohistochemistry and immunofluorescence of microglia (Iba1, iNOS). Frozen tissue was used for western blot for SMN protein.
Results: Smn1-/-SMN2+/+SMNΔ7+/+(SMNΔ7) mice exhibited increased activation of Iba1+ cells in contrast to Smn1+/+SMN2+/+SMNΔ7+/+(healthy control / HC) mice (87.5±5.43 vs. 60.1±4.17 respectively, $p<0.05$) and same trend was observed for iNOS+ cells in SMNΔ7 mice (26± 0.656) in contrast to HC mice (15.9±0.229), $p<0.0001$. SMNΔ7 mice exhibited reduced weight (4.83±0) compared to HC (2.93±0), $p<0.05$. Upon Tail suspension test SMNΔ7 mice exhibited neuromuscular impairment (1.778±0.49) in contrast to healthy controls (3.944±0.03), as well as upon hind limb suspension test (SMNΔ7 mice (2.167±0) vs. HC (4.0±0), $p<0.05$). SMNΔ7 mice exhibited decreased levels of SMN protein (0.255± 0.0347) compared to healthy siblings (1±0), $p<0.05$.
Conclusion: Preliminary data support that late stage SMNΔ7 mice, manifested with neuromuscular impairment in hind-limbs and verified by reduced presence of SMN protein, exhibit increased activation of M1 microglia.
Disclosure: The present study is funded by Biogen in the frame of Investigator Initiated Trial (IIT) [GR-SMG-11658] entitled "Non-neuronal cellular elements of the Central Nervous System and structural biomarkers in an experimental model of Spinal Muscular Atrophy".

EPO-196

Cdk5 inhibition in the SOD1G93A transgenic mouse model of ALS suppresses neurodegeneration and extends survival

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Background and aims: Deregulated cyclin-dependent kinase 5 (Cdk5) activity closely correlates with hyperphosphorylated tau, a common pathology found in neurodegenerative diseases. Previous postmortem studies had revealed increased Cdk5 immunoreactivity in amyotrophic lateral sclerosis (ALS); hence, we investigated the effects of Cdk5 inhibition on ALS model mice and neurons in this study.
Methods: In vitro study, motor neuron cell lines and primary neuronal cultures with wild-type superoxide dismutase 1 (SOD1) or SOD1G93A were compared for the expression of proteins involved in tau pathology, neuroinflammation, apoptosis, and neuritic outgrowth. In vivo study, SOD1G93A mice and non-transgenic (TG) mice were intrathecally injected with adeno-associated virus 9 (AAV9)-scramble (SCR)-short hairpin RNA (shRNA) or AAV9-Cdk5-shRNA at the age of 5 weeks. Motor function and longevity were evaluated, and the tissues were collected from 90-day-old or 120-day-old mice.
Results: Neurons with SOD1G93A showed increased phosphorylated tau, attenuated neuritic growth, mislocalization of SOD1, and enhanced apoptosis, all of which were reversed by Cdk5 inhibition. SOD1G93A mice treated with AAV9-Cdk5-shRNA showed significantly delayed disease onset ($p < 0.001$), delayed rotarod failure ($p = 0.032$), and prolonged survival ($p = 0.007$) compared with those treated with AAV9-SCR-shRNA. The brain and spinal cord of SOD1G93A mice intrathecally injected with AAV9-Cdk5-shRNA exhibited suppressed tau pathology, neuroinflammation, apoptosis, and an increased number of motor neurons compared to those of SOD1G93A mice injected with AAV9-SCR-shRNA.

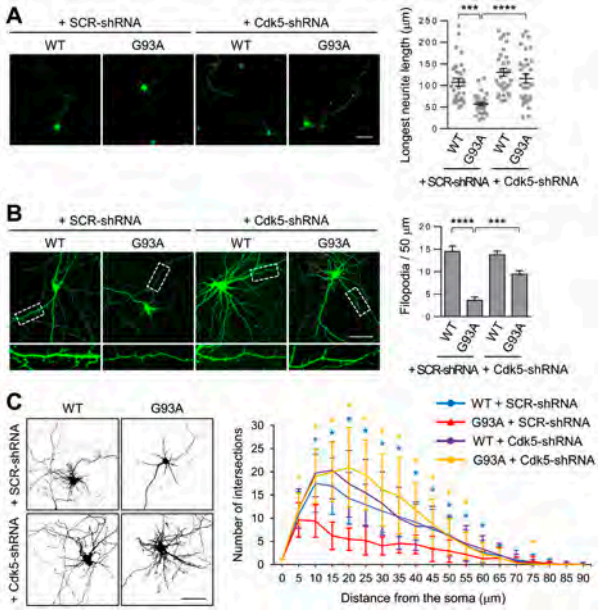

Fig. 1. Cdk5 knockdown promotes neuronal development in primary neuronal cultures with SOD1G93A.

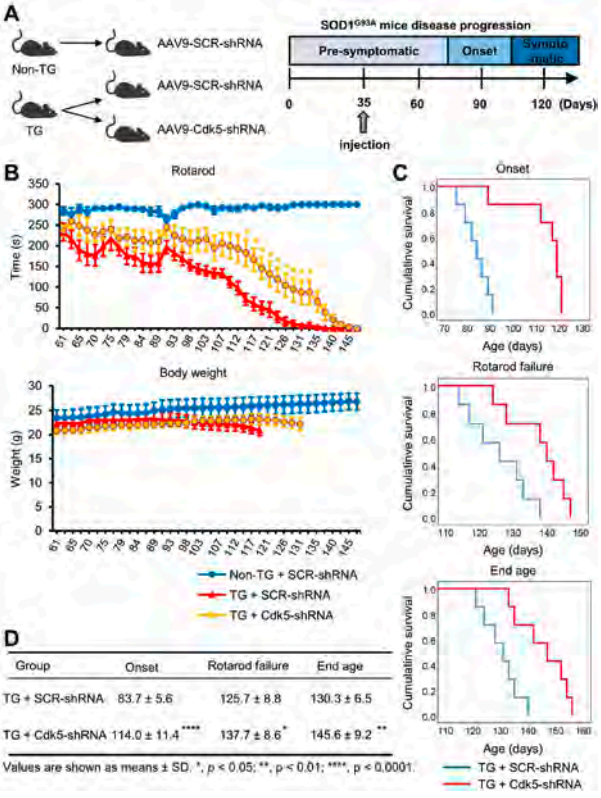

Fig. 2. In vivo study of non-transgenic (TG) and TG mice with or without Cdk5 knockdown.

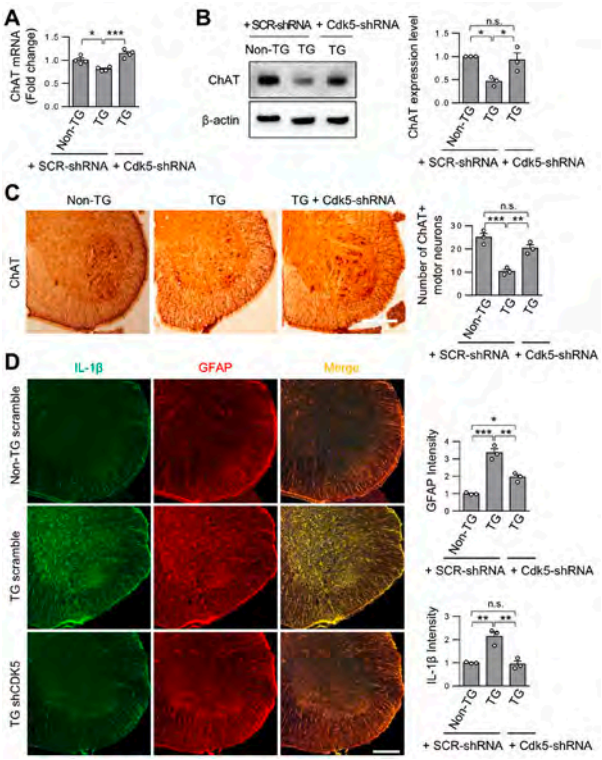

Fig. 3. AAV9-Cdk5-shRNA inhibits motor neuron degeneration and neuroinflammation in spinal cord of 120-day-old SOD1G93A transgenic mice.

Conclusion: Cdk5 inhibition could be an important mechanism in the development of a new therapeutic strategy for ALS.

Disclosure: Nothing to disclose.

EPO-197

Upper Motor Neuron Involvement Examined by Triple Stimulation in Amyotrophic Lateral Sclerosis

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Background and aims: The diagnosis of ALS requires the presence of lower (LMN) and upper (UMN) motor neuron involvement. LMN involvement is demonstrated by clinical and EMG findings whereas UMN neuron signs are dependent on the clinical examination. Even though such signs often are ambiguous, no electrophysiological methods are currently included in the diagnostic criteria for UMN involvement.
Methods: To evaluate the importance of transcranial magnetic stimulation (TMS) including the triple stimulation technique (TST) to detect upper motor neuron (UMN) involvement in ALS we examined 144 consecutive ALS patients at the time of diagnosis. EMG was carried out in all patients to assess LMN affection. TST was performed in both arms and conventional motor evoked potentials (MEP) in the legs to assess central motor conduction time (CMCT).
Results: The TST in the arms showed a central conduction abnormality in 63% of 142 patients (2 patients had no cortical responses), while only 15% had prolonged CMCT. In the legs, prolonged CMCT was found in 50% of patients. The overall sensitivity to detect UMN dysfunction was 77%. In pure clinical LMN involvement, the TST increased the sensitivity to detect UMN involvement by a factor of 4.7. The combined TST and conventional MEP disclosed a central abnormality in 62% of pure LMN patients.
Conclusion: TMS with TST is a sensitive method to detect corticospinal dysfunction in ALS. This TMS protocol is applicable in the clinical routine supporting the proposal that MEP abnormalities are a reliable marker of UMN damage and could be incorporated into diagnostic criteria for ALS.
Disclosure: Nothing to disclose.

EPO-198

Priorities of SMA adult patients and their HCPs toward evaluation. First results of a French qualitative study

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Background and aims: This work aims to study the assessment needs of adults with spinal muscular atrophy (SMA) and healthcare professionals (HCPs) using qualitative methods. SMA assessment is important for guiding care and objectifying the effects of treatments. However, little is known about the assessment needs of patients.
Methods: A scientific committee of SMA specialists designed a qualitative study. 18 patients and 30 HCPs were needed to reach saturation according to the purposive sampling method. Recruiting (ongoing) is carried out in 8 specialized centers. Interview guides were set around: 1) patients' role, 2) practice of HCPs, 3) changes of practice since the treatments. Semi-structured interviews are conducted by a sociologist and analyzed using grounded theory.
Results: After 3 months, 14 patients and 18 HCPs were interviewed. Patients report: 1) living an unstable disease that might evolve unpredictably. 2) trying to control their environment to achieve an acceptable life balance, which is cumbersome. 3) fear of losing meaningful gestures on

which their acceptable life balance is based. 4) asking for care oriented towards the preservation of their life balance. 5) expecting evaluations that accurately reflect their situation. HCPs report: 1) diverse assessment practices according to the patient's needs, the level of disability, the requirements of research protocols and the resources of their center. 2) tinkering with measures for patients with severe disabilities due to few validated assessments.

		N=14
SEX	female	6
	male	8
AGE	minimum	29 y.o.
	maximum	63 y.o.
	median	38,5 y.o.
	mean	43,5 y.o.
	standard deviation	11,6y.o.
SMA TYPE	Ib	2
	II	5
	III	7
INFERIOR LIMB MOTOR FUNCTION	non ambulant (electric wheelchair)	10
	non ambulant (manual wheelchair)	2
	ambulant	2
UPPER LIMB MOTOR FUNCTION	severely impaired	6
	impaired	5
	normal	3
RESPIRATORY FUNCTION	no ventilation	9
	non invasive ventilation	3
	invasive ventilation	2

Table 1. Patients' characteristics

		N=18
HEALTHCARE PRACTITIONERS FROM SMA SPECIALIZED CENTERS	Neurologists	4
	Pulmonologists	1
	Physical and Rehabilitation Medicine Specialists	3
	Occupational Therapists	2
	Physiotherapists	4
	Psychologists	1
	Nurses	1
	Adaptated Physical Activity Specialists	1
	Social Workers	1

Table 2. HCPs' characteristics

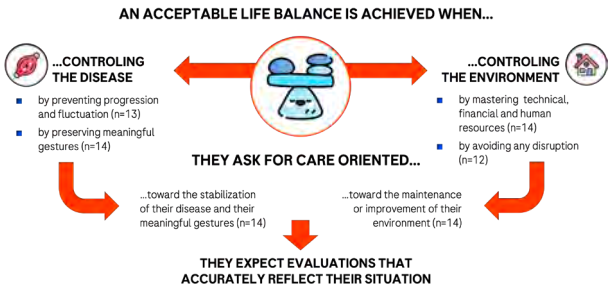

Figure 1. Patients' perspective regarding the preservation of an acceptable life balance

Conclusion: This unprecedented work highlights the preservation of meaningful gestures as an important goal for adults with SMA and the needs for reliable and feasible assessment.

Disclosure: Funding: Roche France SAS

EPO-199

The Phase 3 RESILIENT Study: Taldefgrobep Alfa in Spinal Muscular Atrophy

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Background and aims: Spinal muscular atrophy (SMA) is a progressive, debilitating, genetic condition that results from deficient survival of motor neuron (SMN) protein. Patients experience muscular atrophy and motor neuron loss. Despite the use of SMN upregulators, many patients continue to experience muscle weakness that impairs function and quality of life. Myostatin inhibitors have shown promise in increasing muscle mass and function when administered along with SMN upregulators in murine SMA models. Taldefgrobep alfa (BHV-2000) targets the myostatin pathway directly by lowering myostatin and also blocking downstream signaling. Supported by extensive nonclinical data and an established safety profile in patients with neuromuscular disease, RESILIENT (NCT05337553) will study the efficacy and safety of taldefgrobep as an adjunctive therapy along with SMN upregulators in patients with SMA.

Methods: RESILIENT is a phase 3, randomized, placebo-controlled trial with a 48-week double-blind phase and optional 48-week open-label extension. Patients with SMA (aged 4–21 yrs) will receive weight-based 35 mg or 50 mg weekly subcutaneous injections of taldefgrobep vs matching placebo. Patients must have genetically confirmed 5q autosomal recessive SMA with SMN2 copy number and plan to remain on the same SMN upregulator regimen throughout the study. Patients who have previously received treatment with a myostatin inhibitor are excluded. The primary outcome measure is change in the 32-item Motor Function Measure from baseline to Week 48.

Results: Study recruitment is in progress.

Conclusion: This phase 3 study aims to investigate the efficacy and safety of taldefgrobep as an adjunctive treatment with SMN upregulators in patients with SMA.

Disclosure: LL, IQ, CB, SD, DC, JM, and VC are employed by and hold stock/stock options in Biohaven.

EPO-200

Allelic variants at atypical parkinsonism loci influence phenotypic variability in amyotrophic lateral sclerosis

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Background and aims: Among the group of atypical parkinsonisms, progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) share common genetic, pathological, and clinical features with the frontotemporal dementia (FTD)/amyotrophic lateral sclerosis (ALS) spectrum. Here, we investigated whether genetic risk factors for PSP and CBD might influence phenotypic variability in ALS.

Methods: We extracted genotype data of 16 single nucleotide polymorphisms (SNPs) associated with PSP and CBD from a cohort of 865 ALS patients. For each SNP, demographic and clinical features were compared across genotypes by additive, dominant, and recessive genetic models.

Results: The minor alleles of the rs2011946 (CXCR4), rs12203592 (IRF4) and rs7035933 (GLDC) SNPs were associated with reduced survival. The major allele of rs1768208 (MOBP) was correlated with reduced age at onset and higher frequency of classical ALS phenotype, whereas the minor one with cognitive impairment. Bulbar onset was overrepresented among the homozygotes for the major allele of rs7571971 (EIF2AK3). More severe behavioral symptoms were found in carriers of the minor alleles of rs242557 (MAPT H1c), rs759162 (EGFR) and rs199533 (NSF), as well as the major one of rs2011946 (CXCR4). The homozygotes of the rs759162 (EGFR) minor allele showed also higher lower motor neuron involvement and an increased progression rate.

Conclusion: Overall, our study provides evidence that genetic risk factors for PSP and CBD contribute to phenotypic variability of ALS patients, thus further supporting the hypothesis of a common neurodegenerative pathway linking the FTD/ALS spectrum and 4R-tauopathies.

Disclosure: Nothing to disclose.

EPO-201

Abstract withdrawn

Cerebrovascular diseases 2

EPO-202

Gender-specific relationship between homocystein levels and carotid atherosclerosis in apparently healthy individuals

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Background and aims: Several epidemiological studies have shown that hyperhomocysteinemia is a risk factor for cardiovascular disease and stroke in both men and women, presumably by accelerating vascular atherosclerosis. However, the contribution of gender for homocysteine-driven atherosclerosis is still matter of controversy.
Methods: In this study we aimed to investigate the gender-specific effects of homocysteine serum levels on indicators of carotid atherosclerosis (i.e. intima–media thickness (IMT) and plaque characteristics) in apparently healthy individuals. For this, recruited individuals aged ≥18 years underwent comprehensive medical history collection, physical examination, blood sampling, and carotid Doppler-Duplex ultrasound.
Results: The study included 300 apparently healthy subjects with a mean age of 49.9±14.5 years, including 180 (60%) women and 120 (40%) men. High levels of homocysteine were observed in 166 (55%) subjects, with comparable women to men ratio. Seric homocysteine levels significantly correlated with IMT ($r=0.18$, $p<0.001$), number of carotid plaques ($r=0.24$, $p<0.001$), and total plaque area ($r=0.25$, $p<0.001$) in women but not in men. Subjects with elevated homocysteine displayed higher values of IMT ($t=-2.6$, $p=0.008$), higher number of carotid plaques ($Z=-2.5$, $p=0.01$), and higher total plaque area ($Z=-2.5$, $p=0.008$) compared to subjects with normal homocysteine levels. Seric levels of homocysteine yielded an AUC of 0.68 (95% CI 0.54-0.82) and 0.64 (95% CI 0.57-0.71) in discriminating women with normal/abnormal IMT and women with/without plaques, respectively.
Conclusion: Our findings suggest that only women show a specific association between seric homocysteine levels and carotid atherosclerosis, considered a subclinical marker of stroke risk.
Disclosure: Nothing to disclose.

EPO-203

Economic evaluation of direct oral anticoagulants for stroke prevention in Spain: systematic review

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Background and aims: Direct oral anticoagulants (DOAC) have proven efficacy for preventing stroke in patients with non-valvular atrial fibrillation (NVAF). Limitations in economic resources and the expense of many new treatments make it necessary to allocate health spending as effectively as possible. The aim of this study was to perform a systematic review of the cost-effectiveness analysis of DOAC in the prevention of stroke in patients NVAF in Spain.
Methods: A systematic search in Pubmed, Embase, Cochrane, Web of Science and MEDES databases was carried out from January 2010 to March 2020 to identify Spanish economic evaluations of DOAC in the prevention of stroke in patients with NVAF.
Results: Ten published economic evaluations through Markov models were identified, all of them were conducted from the National Health Service (NHS) perspective, and 6 also included the societal perspective. The most studied drug was apixaban (n=7). Incremental cost-effectiveness ratios (ICER) were within the willingness-to-pay thresholds in Spain (€25,000–€30,000) in all cases. ICER when DOAC were compared alone to VKA was €17,581 for dabigatran, €12,825 for apixaban, €11,247 for rivaroxaban, and €11,518 for edoxaban. ICER of apixaban versus aspirine was €6,289. One model compared dabigatran, apixaban and rivaroxaban to VKA (ICER of €6,397, €8,039, and €29,957 respectively) and each other (dabigatran was the dominant alternative, followed by apixaban). Four models compared apixaban to the other DOAC and showed that it is cost-effective from NHS perspective (median ICER of €4,972.76).
Conclusion: DOAC are cost-effective therapeutic alternatives for stroke prevention in patients with NVAF in Spanish economic evaluations.
Disclosure: Nothing to disclose.

EPO-204

The Burden of Stroke Mimics Among Hyperacute Stroke Unit Attendees with Special Emphasis on Migraine

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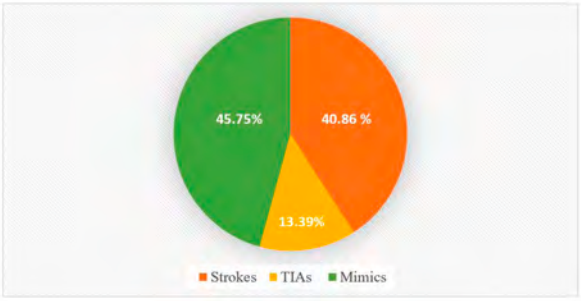
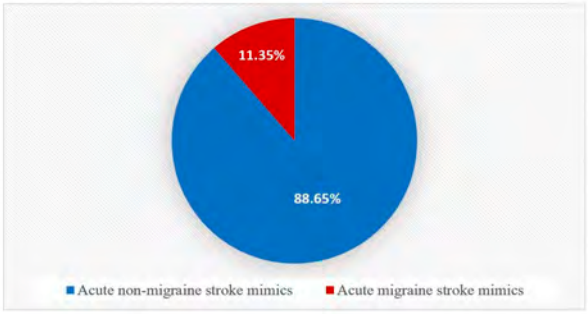
Background and aims: The hallmark of a stroke is the sudden onset of focal neurological impairment. Since many treatments for acute stroke are time dependent, it is important to find acute ischemic insults as rapid as possible. On the other hand, stroke overdiagnosis, formerly known as stroke mimics, may result from the pressure to make quick diagnostic and therapeutic judgments. The main goals of this study are to look at the prevalence of stroke mimics on the stroke pathway and how many of them are migraines.
Methods: A retrospective service evaluation was conducted at the hyperacute stroke unit of the Royal Hallamshire Hospital in the United Kingdom. The total admissions from 2013 to 2022 were collected and the number of stroke mimics was evaluated in each year. Then a one-year sample of stroke mimics was extracted to look for the types of each mimic.
Results: During the last ten years, 45.75% of the stroke pathway patients (26,573) were stroke mimics, with an increment of up to 55% in the last two years. During these ten years, migraine stroke mimics accounted for 11.35% of admissions. The three most common mimics in a one-year sample of the stroke pathway patients were migraine (14.70%), functional neurological disorders (7.17%), and peripheral neuropathies (6.66%). Seizures, syncope, and metabolic derangements were reported as a mimic in 4.17%, 3.14%, and 1.77%, respectively.



The diagnosis of all patients presented to HASU in the last 10 years



The burden of migraine stroke mimics over 10 years

Stroke Mimics Diagnosis	Frequency	Percentage
Migraine	373	14.70%
Functional neurological disorders	182	7.17%
Guillain Barre syndrome and other peripheral neuropathies	169	6.66%
Headaches excluding migraine	148	5.83%
Unknown diagnosis	144	5.67%
Spinal cord and disc lesions	135	5.32%
Facial palsy	126	4.96%
Vestibulocochlear disorders	115	4.53%
Unspecified dizziness	110	4.33%
Seizures	106	4.17%
Disorders of skin sensations	105	4.14%
Ophthalmological disorders	102	4.02%
Unspecified speech disorders	87	3.42%
Syncope and hypotension	80	3.14%
Parkinson disease and related movement disorders	60	2.36%
Systemic infections	55	2.16%
Myopathy and myasthenia gravis	52	2.05%
Anaemia and fatigue	51	2.01%
Multiple sclerosis and other demyelinating diseases	48	1.89%
Nutritional deficiencies and Metabolic derangements	45	1.77%
Brain tumours	41	1.61%
Undiagnosed brain disorders	37	1.45%
Alzheimer disease and other dementia	33	1.30%
Motor neuron disease and spinal muscular atrophy	32	1.26%
Head trauma	28	1.10%
Brain infections	24	0.94%
Cerebellar ataxia	18	0.70%
Postoperative complications	12	0.46%
Gastro-intestinal swallowing disorders	10	0.39%
Hypertensive encephalopathy	4	0.15%
Drugs side effects	4	0.15%

The type of stroke mimics in a one year sample

Conclusion: About half of hyperacute stroke unit attendees were stroke mimics rather than actual strokes and the most common mimics were migraines.
Disclosure: The authors declares that they do not have an conflicts of interests.

EPO-205

Relationships between serum Neurofilament Light Chain and blood inflammatory markers in acute ischemic stroke patients

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Background and aims: Serum neurofilament Light chain (NfL) is a reliable biomarker of axonal injury in many neurological disorders, including stroke. We aimed to study the relationship between NfL and blood inflammatory markers, comprising interleukin-6 (IL6).
Methods: In this longitudinal prospective observational study we included patients with acute ischemic stroke fulfilling these criteria: >18y, onset <24h, NIHSS >1, pre-stroke mRS=0–1, evidence of acute stroke at neuroimaging. Exclusion criteria: >80y, TIA, previous stroke/traumatic head injuries, other neurological disease, immunosuppression before stroke, eGFR<30mL/min, pregnancy. Patients were treated as standard of care, routine blood tests done upon admission. IL6 and NfL serum concentrations were determined with Ella Automated Immunoassay System on samples collected within 24h from onset (T0), after 3–5 days (T1) and 7+2 days (T2).
Results: We included 21 patients (16 males, mean age 61[±17.23]); 66.7% with minor, 23.8% moderate, 9.5% severe stroke. Median values were IL6=6.98 pg/mL (IQR 6.93), NfL=25 pg/mL (IQR 47). IL6 did not change across time-points, while NfL was higher at T2vs.T0 (p=0.006). IL6 and NfL correlated with each other at all time-points. Both biomarkers positively correlated at T0 with CRP (IL6 p<0.001; NfL p=0.002) and negatively with lymphocytes (IL6 p<0.005; NfL p=0.04). NfL retained significancy also at T1 and T2 for CRP, and at T1 for lymphocytes.
Conclusion: Increased NfL serum concentrations are associated with blood inflammatory markers in the acute setting of ischemic stroke. These preliminary results are part of a larger Study to identify a biomarker panel to better characterize the physiopathological complexity and clinical evolution of ischemic stroke patients.
Disclosure: Nothing to disclose.

EPO-206

Transient Hypertension in Transient Global Amnesia: a single center observational study

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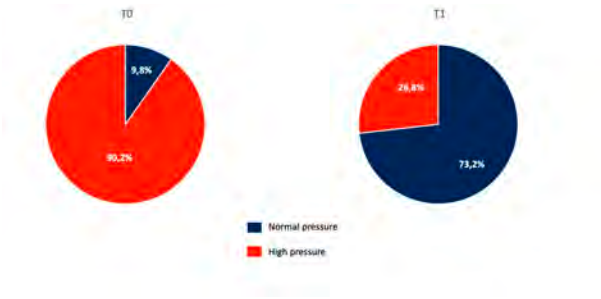
Background and aims: Transient Global Amnesia (TGA) is a syndrome with an unclear pathophysiologic mechanism. Different hypotheses and trigger factors have been proposed [1]. This study aimed to evaluate the incidence of arterial hypertension in patients with TGA to identify its causative role in support of the vascular hypothesis.
Methods: We retrospectively examined data of patients affected by TGA according to Hodges and Caplan criteria [2], who were admitted to the Neurology Unit of the University of Messina, from December 2012 to December 2020. Blood pressure (BP) was recorded on admission and at 24 hours after the TGA onset. High BP was defined as a systolic BP≥140 mmHg and/or a diastolic BP≥90 mmHg.
Results: We selected 41 patients, 22 males (53.7%). The mean age at the TGA attack was 63.3 years. A hypertension history was present in 27 patients (67.5%). On admission, 37 patients (90.2%) had a high BP, SBP was 160.85±26.05 mmHg and DBP was 88.15±14.93 mmHg. At 24 hours, 11 (26.8%) had a high BP, SBP was 124.88±15.47 mmHg and DBP was 74.17±9.54 mmHg. A significant decrease in SBP and DBP was observed comparing BP at the two different time points (p-value <0.0001).



Blood Pressure in T0 and T1

Conclusion: This study described BP trend in TGA patients. We observed an admission high BP during the TGA attack, whereas BP was normal at 24 hours. Our analysis showed a significant difference between T0 and T1, providing further evidence of transitory high BP as possible TGA trigger.
Disclosure: In the interest of transparency, I disclose all relationships/activities/interests related to this manuscript.

EPO-207

Clinical determinants of late diagnosis and recurrence in patients with stroke associated with antiphospholipid syndrome

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Background and aims: Antiphospholipid syndrome (APS) is characterized by arterial or venous thrombosis, in the presence of antiphospholipid antibodies. Stroke is one of its most common complications. Objectives: to characterize APS associated with stroke, clinical determinants of late diagnosis, treatment and recurrence, and compare them with APS with non-stroke manifestations.
Methods: Retrospective cohort study of patients diagnosed with APS between 2018–2022 with and without stroke. Descriptive and comparative analysis of different variables and comparative study using chi-square, t-tests, and non-parametric tests when applicable.
Results: 88 patients were included, 42 of which had stroke. 52.3% were women, mean age at diagnosis was 56-year-old (20-84, SD=16.9). The most frequent vascular risk factors (VRFs) were hypertension, dyslipidemia, and smoking. In 48% of the cases, stroke was the first event. The most common presentations were ischemic stroke (59.5%), TIA (19%), and cerebral venous thrombosis (16.7%). APS diagnosis was made in the first stroke episode in 54.8%. 40.5% had recurrency and it was correlated with hypertension (p=0.002) and diabetes (p=0.032). APS was more likely to manifest with stroke in men (p=0.002) and those with more VRFs, particularly smoking habits (p=0.029). Patients with stroke were less likely to be diagnosed with APS in the first event (p=0.001), start anticoagulation in the first episode (p=0.002) and have a higher number of recurrent events (p=0.001).
Conclusion: Prompt diagnosis, risk-factor control, particularly smoking cessation, and anticoagulation are crucial to prevent stroke and its recurrence in patients with APS. APS remains a challenging diagnosis and requires a high suspicion, particularly in patients with recurrent strokes.
Disclosure: Nothing to disclose.

EPO-208

5-Year survival and cognitive changes in patients with cerebral small vessel disease

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Background and aims: Cerebral small vessel disease(cSVD)is a common disease of the adults and elderly with a high contribution to disability and mortality. Research objective: to investigate the five-year survival,cognitive and MRI changes in patients with cSVD and cognitive impairment(CI).
Methods: 54 patients with cSVD,CI and the widespread white matter hyperintensity(WMH) were observed prospectively during 5 years (average age were 60.51±6.76, women – 37 (20%)). 22 patients undergo an extended examination with an interval of 5 years. Cognitive functions with the definition of the type of CI, diagnostic MRI signs, volumes of WMH,white and gray matter, cerebrospinal fluid(CSF), microstructural changes of the brain were assessed (Fig1). Relationships between cognitive and MRI indicators were clarified.
Results: Over 5 years, the mortality rate was 14% and dementia acquired in 14%. Increasing severity of CI is noted in the domain of executive functions and memory with rising of mixed type of CI.WMH and CSF volume widening, reducing the volume of white matter and axial diffusion in the corpus callosum were exposed (Table1). CSF volume was correlated with Stroop test results and delayed memory (r=0.803 and r=-0.701), white matter atrophy (r=-0.256), and the last one – with axial diffusion in the corpus callosum (r=-0. 560, Table2).

Parameter	CSVD 2016/2017 n=22 mean±SD	CSVD 2021/2022 n=22 mean±SD	p
Volume of white matter hyperintensity(sm^3)	29,80±20,40	36,57±21,83	**<0,05**
Total volume of grey matter (sm^3)	608,88±44,55	609,91±47,55	0,76
Total volume of white matter (sm^3)	493,36±41,27	460,12±45,51	**<0,05**
Volume of cerebrospinal fluid (sm^3)	343,04±74,50	374,57±83,71	**<0,05**
Axial diffusion, 10^{-3} (mm^2/sec)			
Corpus callosum	1,306±0,20	1,307±0,17	**<0,05**
Cingulate gyrus	2,191±0,25	2,017±0,20	0,217
Abbreviations: CSVD – cerebral small vessel disease.			

Table 1. MRI parameters in patients with CSVD in dynamic

	Test of «memorizing 10 words», delayed playback	Stroop test	White matter volume	Volume of CSF	Volume of white matter hyperintensity (WMH)	Axial diffusion in the corpus callosum
Test of «memorizing 10 words», delayed playback	1					
Stroop test	-,792**	1				
Volume of white matter	,315	-,138	1			
Volume of CSF	-,701**	,803**	-,256*	1		
Volume of white matter hyperintensity (WMH)	-,353	,444	-,215	,420	1	
Axial diffusion in the corpus callosum	-,393	,289	-,560*	,336	,407	1

Table 2. Correlation between cognitive tests results and MRI parameters in dynamic

Conclusion: cSVD with widespread WMH is characterized by high mortality and an increase in dementia. The general cognitive level and MRI signs have insufficient sensitivity in assessing disease progression over a 5-year period. The Stroop test, memory (delayed reproduction of the 10-word test) and the transition to a mixed type of CI reflect the progression of CI and can be used for dynamic assessment. cSVD in the advanced stage affects the deterioration of cognitive functions through atrophy and changes in CSF circulation.

Disclosure: The study was supported by Grant No.22-15-00183 of the RussianScienceFoundation; https://rscf.ru/project/22-15-00183.

EPO-209

Blood pressure control and stroke outcome at Douala General Hospital

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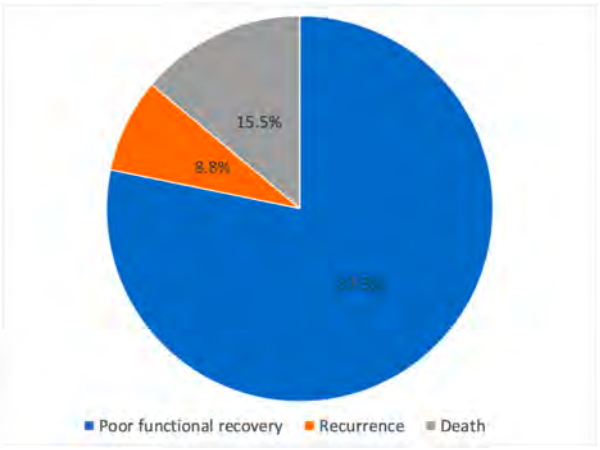
Background and aims: Hypertension (HTN) is the major risk factor for the occurrence of strokes. Uncontrolled hypertension is a predictive factor for poor outcome during the first episode and recurrence stroke.

Methods: We conducted a retrospective cohort study using stroke records from January 1, 2010 to March 1, 2019 at the HGD. We included all patients aged 21 and over who admitted for a first stroke confirmed by neuroimaging and followed up for 3 years. All patients with chronic kidney disease, sub-arachnoid hemorrhage or cerebral veinous thrombosis were excluded. We collected data (sociodemographic, clinical presentation, investigations, treatment and outcome) according to our survey sheet and analyzed using SPSS 26.0 software and a p value <0.05 was considered statistically significant.

Results: 517 patient files were included with an average age of 58.4±13.4 years (men = 58.8%). The prevalence of poor BP control was 81%. The predictive factors of poor BP control were de novo post-stroke hypertension (p<0.001) and de novo post-stroke diabetes (p=0.008). The factors associated with mortality in patients with poor BP control were: Barthel index≤60 (p<0.001), occurrence of vascular dementia (p=0.036), low level of education (p=0.017).



Outcome of stroke patients with poor blood pressure control

Conclusion: Hypertension is not controlled in more than 4 stroke patients out of five in our setting. Hypertension or diabetes discovered during the first stroke would promote poor BP control. Functional dependence, dementia and low level of education would increase the risk of death in stroke patients with poor BP control.

Disclosure: Nothing to disclose.

EPO-210

Prevention strategy of patients with concomitant atrial fibrillation and intracranial stent after acute ischemic stroke

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Background and aims: Intracranial stenosis treatment in the long-term in patients with atrial fibrillation (AF) remains unknown. There is no scientific evidence that confirms that the strategy validated in the AUGUSTUS trial (AF and acute myocardial infarction) can be applied to patients with AF and intracranial stents. We present our experience.
Methods: Retrospective study with prospective gathering of patients with ischemic stroke treated in our hospital with intracranial stent within 2017-2022. Demographic, clinical and radiological variables were gathered. We compared security and efficacy among patients with and without AF.
Results: Twenty-seven patients with intracranial stent were included (74.1% males, median age of 67.18±16.85, 59.2% with hypertension, 44.4% with dyslipidemia, 25.9% diabetic, 33.3% had AF (55.5% with recent diagnosis). Eighteen patients had permeable stent in the early control (100% of "Augustus like" AF group vs 80% of "no Augustus like" AF group vs 62.5% of AF group, p=0.032) and 6 patients died (0% of "Augustus like" AF group vs 33.3% of "no Augustus like" AF group vs 16.6% of no AF group, p 0.081). The most frequent strategy in the AF group was the combination of antiplatelet monotherapy and anticoagulation therapy. In the follow-up, 2 patients presented stent occlusion, both in no AF group (p=0.55). One patient from the "Augustus like" AF group had a major hemorrhagic complication. No patients had new ischemic events.
Conclusion: In our series, the combination of one antiplatelet and anticoagulation in secondary prevention strategy for patients with AF and intracranial stent resulted effective and safe in our experience.
Disclosure: Nothing to disclose.

EPO-211

Hemorrhagic transformation and non-CNS complications after iv. thrombolysis: a brain and body autopsy study

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Background and aims: The intravenous thrombolysis is a significant advancement in the treatment of acute ischemic stroke. Since imaging and detailed clinical examination of stroke patients is not always possible in the agony phase, only the autopsy can provide us reliable data about the frequency of complications.
Methods: Between 2007–2017, 1.426 venous lysis were performed in our department and we had access to the clinical and brain/body autopsy data of 98 (6,9 %) patients treated with iv. lysis 0.9 mg/kg rt-PA, following the international guideline, but died during the clinical period.
Results: We diagnosed 20 hemorrhagic transformation (HT) (20.4%) on the last CT before death: P1:4 P2:8 H1:1 H2:3 (in 4 cases, bleeding occurred in the non-ischemic brain area). On brain autopsy we diagnosed other 26 patients (26.5%), whose HT occured between the period of the last premortal CT and death. We compared the clinical data of patients with HT complications (46) with those, whose brain autopsy did not show HT (52). Admission INR 1.03[0.93–1.04], 1.05[0.96–1.09] P:0.043 and lower platelet count 188, 4 [150.0–227.0] 226.6 [171.0–264.0], p=0.011 increased the risk of a HT. During the autopsy, 2 malignant tumors, 4 thromboembolic complications (+3 aortic thrombus), and 10 pneumonias were detected, but not diagnosed premortal.
Conclusion: The brain and body autopsy provide more reliable data on complications of iv. thrombolysis patients with fatal outcome. The correlation between INR/platelet and increased risk of HT and/or fatal outcome is of clinical importance and need further investigations.
Disclosure: None. Supported by the grant of ELKH-DE CerebrovascularHemor Research Group.

EPO-212

Comorbid conditions in COVID-19 associated ischemic stroke

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Background and aims: To study the relationship between COVID-19 associated ischemic stroke and comorbid conditions.
Methods: We analyzed 176 cases of hemispheric IS.The patients were divided into two groups.The main group consisted of 72 patients with hemispheric IS and laboratory-confirmed coronavirus infection.The control group consisted of 104 patients with hemispheric IS who did not have a history of COVID-19.
Results: In both groups, the following comorbid diseases of the cardiovascular continuum were analyzed: arterial hypertension was the most common of them and had the same prevalence in both groups (94 and 98%,respectively). Atherosclerosis was also a common risk factor; in the group of patients who had undergone COVID-19, it was detected in 57% of cases (n=41), and in the control group it was statistically significantly more common in 82%(n=85) of cases ($p<0.002$). Diabetes mellitus as a risk factor for the development of IS significantly prevailed in the group of patients with concomitant COVID-19 (16%) compared with the control group (7%)($p<0.037$). Atrial fibrillation in both groups was detected in the same number of patients(19%). IHD (history of acute myocardial infarction or angina pectoris) in the group of patients with COVID-19 was observed in 37%(n=27) of cases, while in patients without this infection it was detected in 32%(n=33) of cases ($p<0.077$).
Conclusion: The results obtained showed that diabetes mellitus was significantly more common in patients with stroke in combination with COVID-19,which can be explained by the role of endothelial dysfunction in the pathogenesis of COVID-19 associated stroke, which most likely determines the course of IS.
Disclosure: Nothing to disclose.

EPO-213

Glycated Albumin and IL-10 are associated with Obesity in Hyperacute Ischemic Stroke

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Background and aims: There is growing interest in the use of new biomarkers such as glycated albumin (GA). In contrast to glycated hemoglobin (HbA1c), GA showed an inverse correlation with prestroke obesity status, but data are limited for ischemic stroke (IS).
Methods: We explored the association between GA and body mass index (BMI) and investigated inflammatory cytokines to support the academic background. In total, 155 patients with hyperacute IS (HIS) between 2011 and 2019 were included. To identify the association between GA and BMI, patients were divided into four groups according to BMI quartiles. Levels of inflammatory cytokines, including IL-1β, IL-10, IL-6, TNF-α, and TNF-R1, were determined by ELISA using a ProcartaPlex multiplex immunoassay.
Results: The mean age of the 155 patients was 68±12 years, and 67.1% were men. The lowest BMI group had higher GA levels (GA 2T and 3T=80%) (p-value=0.017), and these U-shaped associations were maintained only for small vessel occlusion etiology (p-value=0.004). Plasma IL-10 levels were positively correlated with BMI and showed a U-shaped pattern (p-value=0.001).
Conclusion: GA levels and BMI had U-shaped associations with HIS. IL-10, which acts as a protective cytokine for cardiovascular disease, may play a novel role in this association. Although GA is an emerging favorable clinical marker of cardiovascular outcomes, obesity status should be considered when interpreting these associations.
Disclosure: Nothing to disclose.

EPO-214

Occlusion Pattern and Clinical Outcome in Acute Large Vessel Occlusion with Intracranial Stenosis

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Background and aims: To investigate whether angiographically defined occlusion location could affect the periprocedural and clinical outcomes of the acute middle cerebral artery (MCA) occlusion associated with intracranial atherosclerotic stenosis (ICAS) and the rescue stenting response.
Methods: We reviewed consecutive patients with acute MCA occlusion associated with ICAS who underwent intracranial stenting and balloon angioplasty after initial mechanical thrombectomy. Patient demographic findings, baseline characteristics, clinical outcomes, and periprocedural complications including in-stent thrombosis and re-occlusion were compared according to the anatomical occlusion location. The occlusion location was divided according to the presence of the proximal MCA stump in enrolled ICAS patients.
Results: Of 44 patients, 30 (68.4%) were classified as having a stump group. When initial NIHSS was compared between the groups, the without stump group was more severe than the with stump group (14.0 (8.0–17.0) vs. 7.5 (6.0–13.0) p=0.044), and received intravenous thrombolysis was more prevalent in the without stump group (71.4% vs. 16.7%, p=0.001). There were no significant differences in procedure time, technique, and devices. However, the successful revascularization rate was significantly lower in the without-stump group (57.1% vs. 100%, p=0.001). Additionally, the immediate re-occlusion rate after the first endovascular reperfusion therapy was a higher tendency in the without-stump group (71.4% vs. 36.7%, p=0.068). However, no significant association was found between periprocedural complications including intracerebral hemorrhage and mortality.
Conclusion: Angiographically presented MCA occlusion without stump in patients with ICAS, predicts complicated intracranial stenting and poor clinical outcome.
Disclosure: Funding This work was supported by a research grant from Jeju National University Hospital in 2022 Competing interests The authors declare that they have no competing interests.

EPO-215

Acupuncture for Spontaneous Intracerebral Hemorrhage; A Systematic Review and Meta-analysis

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Background and aims: This is a systematic review and meta-analysis of randomized clinical trials (RCTs) to figure out the efficacy of acupuncture treatment for patients with spontaneous intracerebral hemorrhage (s-ICH).
Methods: We searched publications in MEDLINE via Pubmed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), CiNii, and several Korean databases. After eligibility assessment, 14 studies that compared acupuncture treatment added to western conventional treatment with only western conventional treatment for s-ICH were included in this systematic review and meta-analysis.

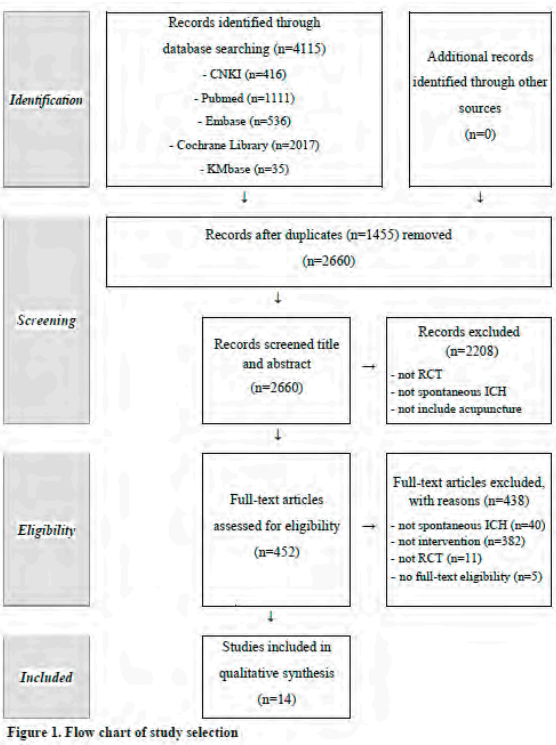

Fig 1. Flow chart of study selection

Results: The pooled meta-analysis showed the statistical significance in Chinese Stroke Scale (CSS) score [MD 3.61, 95% CI 2.82–4.40], Fugl-Meyer assessment (FMA) score of lower extremity [MD 4.30, 95% CI 3.50–5.11], Barthel Index [MD 8.58, 95% CI 5.95–11.21], and clinical efficacy rate (CER) [n=557, RR 3.51, 95% CI 2.39–5.16]. Subgroup analysis also showed the significant effect of acupuncture treatment in CSS scores of acute phase [MD 3.20, 95% CI 2.26–4.14] and subacute phase [MD: 3.89, 95% CI: 2.34–5.44] and CER of acute phase [n=144, RR: 2.59, 95% CI: 1.30–5.18] and subacute phase [n=228, RR 2.38, 95% CI 1.21–4.68]. There were similar results in hypertensive intracerebral hemorrhage, which is a subgroup of s-ICH.

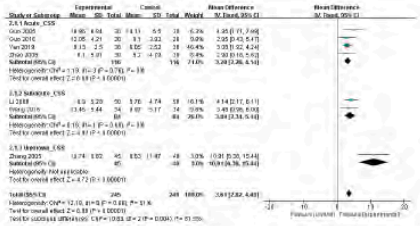

Figure 2. Forest plots of meta-analysis of CSS on acute and subacute phase. Comparison; acupuncture plus western conventional treatment vs western conventional treatment alone

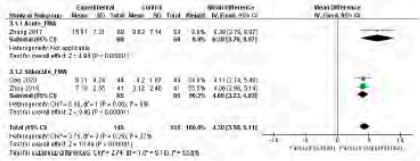

Figure 3. Forest plots of meta-analysis of FMA of lower extremity on acute and subacute phase. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

Figure 4. Forest plots of meta-analysis of BI. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone.

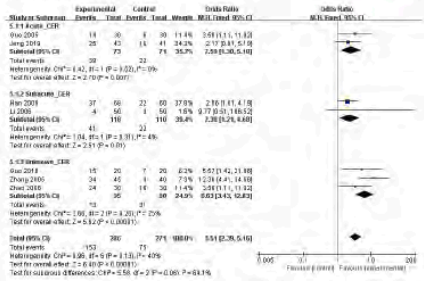

Figure 5. Forest plots of meta-analysis of modified CER on acute and subacute phase. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

Result 1; meta analysis

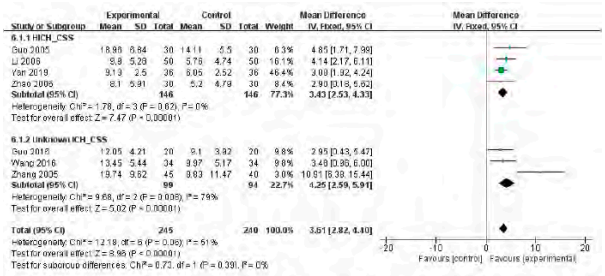

Figure 6. Forest plots of meta-analysis of CSS on ICH. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

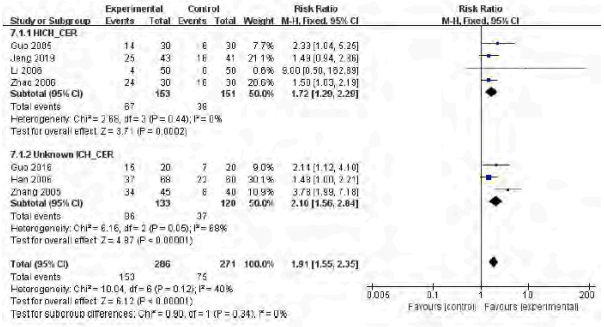

Figure 7. Forest plots of meta-analysis of modified CER on ICH. Comparison; acupuncture plus western conventional treatment versus western conventional treatment alone

Result 2; meta analysis

Conclusion: Acupuncture appeared to be effective in neurological impairment in s-ICH. Also, acupuncture helps not only recovering motor function, but also improving activities in daily living.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-216

Deficit in topographical orientation - relation to the affected cerebral hemisphere after stroke

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Background and aims: About 90% of stroke survivors have sequels and cognitive impairment is the most prevalent one. Injury to cortical and subcortical right structures may impair topographic orientation with impact on daily living activities. The aim of this study was to estimate the frequency and characterize impairments of topographic orientation in patients, in a chronic phase, after stroke.
Methods: In this observational cross-sectional case-control study, we performed a subjective (Questionnaire on Everyday Navigational Ability) and an objective assessment of topographic orientation, through topographical tests. In the stroke group, we apply others tests to evaluate the perceptual-cognitive and functional deficits and its impact.
Results: 44 stroke patients (left stroke group, n=23; right stroke group, n=21) and 44 control individuals matched for gender, age and schooling were included. There was a significative difference of subjective assessment of topographical disorientation between the stroke group and the controls. Complaints were more frequent in the right stroke group (42.9%) compared to the left stroke group (8.7%) and to controls (2.3%). Furthermore, right stroke group performance was significantly worse (21.5 points) on the topographical location test, a test of allocentric orientation, than the others. The score on topographic imagery test and topographic location test of patients with neglect was significantly worse compared to patients without neglect.
Conclusion: This indicates a higher frequency of topographic impairment in subjective complaints and objective performance in patients with right hemisphere lesions. Neglect may partially mediate these impairments. Our work reinforces the need to evaluate topographical orientation after right hemisphere stroke.
Disclosure: There isn't relation of interest related to this manuscript.

Muscle and neuromuscular junction disorder 2

EPO-217

Treatment differences between Black and non-Black patients with gMG receiving eculizumab in the United States

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Background and aims: Racial inequities have been observed in healthcare access and treatment. Myasthenia gravis (MG) is a rare autoimmune neuromuscular disease resulting in muscle weakness and functional impairment affecting 6.2% of Black patients in a US-based registry. This study explored differences in treatment and care approaches between Black and non-Black patients with generalized MG (gMG) receiving eculizumab in the USA.

Methods: This retrospective analysis of data from an observational study used physician-reported electronic medical record data from adults (≥18 years) with gMG from 14 sites in the USA. gMG status and treatment 2 years before and 2 years after eculizumab initiation were analysed for Black and non-Black patients.

Results: Black patients (n=19) were predominantly female, diagnosed at a younger age, had a longer time from diagnosis to initiation of eculizumab, and initiated eculizumab with higher disease severity compared with non-Black patients (n=100; Table 1). More Black patients were treated in academic centres and had commercial insurance compared with non-Black patients (Table 1). Prior to eculizumab initiation, prednisone, pyridostigmine and long-term intravenous immunoglobulin were prescribed less frequently, and rituximab prescribed more frequently in Black patients than non-Black patients (Figure 1). At eculizumab initiation, fewer Black patients received prednisone and non-steroidal immunosuppressive therapy than non-Black patients, but more were receiving long-term plasma exchange (Figure 2).

Characteristic	Black patients (n = 19)	Non-Black patients (n = 100)	All patients (N = 119)
Sex at birth, n (%)			
Male	3 (15.8)	45 (45.0)	48 (40.3)
Female	16 (84.2)	55 (55.0)	71 (59.7)
Age at gMG diagnosis, years, mean (SD)	33.3 (15.7)	53.8 (20.0)	50.5 (20.7)
Race, n (%)			
White	0 (0.0)	96 (96.0)	96 (80.7)
Black	19 (100.0)	0 (0.0)	19 (16.0)
Asian	0 (0.0)	2 (2.0)	2 (1.7)
American Indian/Alaskan Native	0 (0.0)	1 (1.0)	1 (0.8)
Other	0 (0.0)	1 (1.0)	1 (0.8)
AChR antibody status tested, n (%)	18 (94.7)	100 (100.0)	118 (99.2)
Seropositive	16 (84.2)	98 (98.0)	114 (96.6)
Seronegative	1 (5.3)	1 (1.0)	3 (2.5)
Unknown	1 (5.3)	1 (1.0)	1 (0.8)
Insurance status, n (%)[a]			
Medicare	6 (31.6)	56 (56.0)	62 (52.1)
Medicaid	3 (15.8)	7 (7.0)	10 (8.4)
Commercial	13 (68.4)	40 (40.0)	53 (44.5)
Military	0 (0.0)	2 (2.0)	2 (1.7)
Information not provided	0 (0.0)	1 (1.0)	1 (0.8)
Time from diagnosis to eculizumab initiation, years, mean (SD)	10.2 (10.0)	7.5 (9.8)	7.7 (9.8)
Age at initiation of eculizumab therapy, years, mean (SD)	43.2 (12.9)	61.1 (17.0)	57.7 (17.7)
MG-ADL score before eculizumab initiation, mean (SD)[b]	9.3 (4.8)	7.7 (3.6)	8.0 (3.8)
Primary setting, n (%)			
Academic medical centre	15 (78.9)	50 (50.0)	65 (54.6)
Large PCP (> 10 physicians) owned by a hospital	0 (0.0)	10 (10.0)	10 (8.4)
Large PCP (> 10 physicians)	0 (0.0)	23 (23.0)	23 (19.3)
Medium-sized PCP (6–10 physicians) owned by a hospital	2 (10.5)	13 (13.0)	15 (12.6)
Medium-sized PCP (6–10 physicians)	2 (10.5)	3 (3.0)	5 (4.2)
Solo practice	0 (0.0)	1 (1.0)	1 (0.8)
Region, n (%)			
Midwest	2 (10.5)	34 (34.0)	36 (30.3)
Northeast	0 (0.0)	2 (2.0)	2 (1.7)
South	14 (73.7)	47 (47.0)	61 (51.3)
West	3 (15.8)	17 (17.0)	20 (16.8)

Table 1. Patient characteristics at baseline and primary setting of care and region of treatment

[a]Categories not mutually exclusive. [b]Most recent score before initiation of eculizumab.

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; PCP, private community practice; SD, standard deviation.

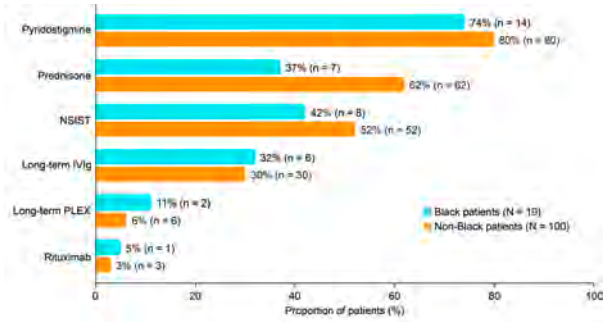

Fig. 2. Patients receiving concomitant therapies at eculizumab initiation
Note: proportions may exceed 100% because patients could have been receiving more than one treatment.
IVIg, intravenous immunoglobulin; NSIST, non-steroidal immunosuppressive therapy; PLEX, plasma exchange.

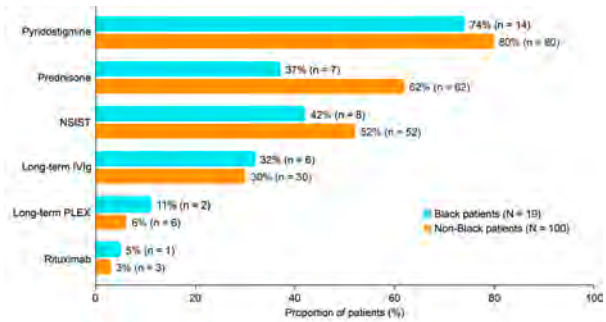

Fig. 2. Patients receiving concomitant therapies at eculizumab initiation
Note: proportions may exceed 100% because patients could have been receiving more than one treatment.
IVIg, intravenous immunoglobulin; NSIST, non-steroidal immunosuppressive therapy; PLEX, plasma exchange.

Conclusion: In clinical practice in the USA, race-based differences were observed in the care and treatment of patients with gMG receiving eculizumab; these differences may indicate health inequities and warrant further investigation.

Disclosure: AAH has received research support from Alexion, AstraZeneca Rare Disease, argenx, Cabealetta Bio, Genentech, Immunovant, Pfizer, Regeneron Pharmaceuticals, UCB Pharma, and Viela Bio (part of Horizon Therapeutics). He has also received fees from Alexion, AstraZeneca Rare Disease, argenx, Immunovant, Regeneron Pharmaceuticals, and UCB Pharma. JFH has received research support (paid to his institution) from Alexion, AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, US), the Muscular Dystrophy Association, the Myasthenia Gravis Foundation of America, the National Institutes of Health (including the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the National Institute of Neurological Disorders and Stroke), the Patient-Centered Outcomes Research Institute (PCORI), Ra Pharmaceuticals (part of UCB Pharma), and Takeda Pharmaceuticals. He has also received fees from Alexion, AstraZeneca Rare Disease, argenx, Immunovant, Ra Pharmaceuticals (part of UCB Pharma), Regeneron Pharmaceuticals, and Viela Bio (part of Horizon Therapeutics), and nonfinancial support from Alexion, AstraZeneca Rare Disease, argenx; Ra Pharmaceuticals (part of UCB Pharma), and Toleranzia AB. AK and BM are employed by, and own stocks in, Alexion, AstraZeneca Rare Disease. MM is a member of a Scientific Advisory Committee for Alexion, AstraZeneca Rare Disease.

EPO-218

Epilepsy in Dystrophinopathies: Series and review of the literature

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Background and aims: Cognitive and behavioral difficulties occur in approximately a third of patients with Duchenne muscular dystrophy. The aim of our study was to assess the prevalence of epilepsy in a cohort of 222 DMD patients.

Methods: We report the data obtained in 142 DMD patients with mutations from a tertiary neuromuscular center in Istanbul, Turkey.

Results: Epileptic seizures were found in 14 of the 222 DMD patients (6.3%). The age of onset ranged from 3 months to 16 years (mean 7.8). Seizures were more often focal epilepsy (n=6), generalized tonic–clonic seizures (n=4) or absences (n=4). They were present in 12 of the 149 boys with normal IQ (8.1%) and in two of the 73 with mental retardation (2.7%). In two cases the parents did not report any past or present history of seizures but only 'staring episodes' interpreted as a sign of 'poor attention'. In both patients EEG showed the typical pattern observed in childhood absence epilepsy.

Patient no.	Age at 2022 (yr)	Age at onsetof seizures	History of febrile seizure	Family history of epilepsy	Genetics	Seizure type	EEG	Treatment	GMFSC
1	13 yr	5 yr	no	no	del. 48-49	generalized	generalized epileptiform abnormality	LEV	1
2	9 yr	12 m	yes	no	del. 45-50	generalized	theta waves	PHB	2
3	24 yr	7 yr	no	no	del. 49-54	generalized	N	LEV	5
4	10 yr	18 m	yes	no	del. 42-43	generalized	N	-	2
5	9 yr	12 m	yes	no	del. 45-54	generalized	N	LEV	2
6	13 yr	3 yr	yes	no	del. 47-50	generalized	generalized epileptiform abnormality	LEV	2
7	15 yr	2 yr	yes	no	del 23-44	generalized	N	CBZ	1
8	8 yr	12 m	no	no	del. 45-57	generalized	N	PHB	1

Summary of patients

Conclusion: Our results suggest that the prevalence of epilepsy in our study (6.3%) is higher than in the general pediatric population (0.5–1%). The risk of epilepsy does not appear to increase in patients with mental retardation.

Disclosure: Nothing to disclose.

EPO-219

Long-term safety, efficacy & self-injection satisfaction with zilucoplan in myasthenia gravis: RAISE-XT interim analysis

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Background and aims: Long-term data from RAISE-XT (NCT04225871), a Phase 3, multicentre, open-label extension study, will enhance our understanding of the safety, efficacy, and self-injection satisfaction of zilucoplan, a C5 complement inhibitor with dual mechanism of action, in patients with generalised myasthenia gravis (gMG).

Methods: Adults (aged 18–75 years) with gMG who completed a qualifying zilucoplan study (Phase 2 NCT03315130/Phase 3 NCT04115293 [RAISE]) self-administered daily subcutaneous injections of zilucoplan 0.3 mg/kg. Primary outcome: incidence of treatment emergent adverse events (TEAEs). Secondary efficacy outcomes included change from qualifying study double-blind baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) score. The Self-Injection Assessment Questionnaire (SIAQ; domain scores 0–10; higher scores indicate more positive experience) was completed by US patients directly after self-injection and measured patient satisfaction with self-injection.

Results: At data cut-off (8 September 2022), 200 patients had enrolled in RAISE-XT. Median (range) exposure was 1.2 (0.11–4.45) years. TEAEs occurred in 188 (94.0%) patients; 64 (32.0%) patients experienced a serious TEAE (Table). Mean (standard deviation) changes from double-blind baseline in MG-ADL score continued to decrease through Extension Week 12 and were maintained through to Extension Week 48 (Week E48) for the zilucoplan and placebo-switch groups: −5.95 (4.14) and −6.85 (5.13) at Week E48, respectively (Figure 1). In the SIAQ domain of satisfaction with self-injection, median score was 8.20 (range: 3.9–10.0; n=63; Figure 2).

	All zilucoplan doses (N=200)
Any TEAE, n (%)	188 (94.0)
Serious TEAE, n (%)	64 (32.0)
TEAE resulting in permanent withdrawal from IMP, n (%)	17 (8.5)
Treatment-related TEAE, n (%)	67 (33.5)
Severe TEAE, n (%)	57 (28.5)
TEAEs leading to death, n (%)	4 (2.0)

Safety set.
IMP, investigational medicinal product.

Table: Overview of TEAEs

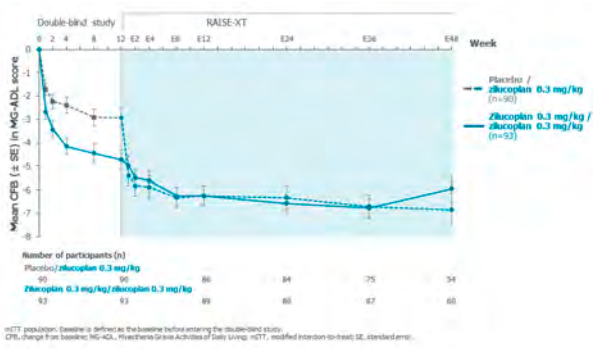
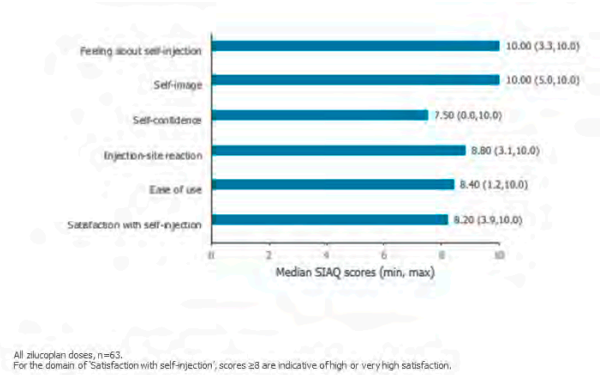


Figure 1: Mean CFB in MG-ADL score to Week E48



All zilucoplan doses, n=63.
For the domain of 'Satisfaction with self-injection', scores ≥8 are indicative of high or very high satisfaction.

Figure 2: SIAQ reported outcomes

Conclusion: In this interim analysis of RAISE-XT, zilucoplan demonstrated a favourable long-term safety profile and sustained efficacy through to Week E48. High satisfaction rates with self-injection were reported. Funding: UCB Pharma.

Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation.

EPO-220

Longitudinal MGFA-PIS evaluation in a large Italian cohort of patients with Myasthenia Gravis

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Background and aims: Myasthenia Gravis Foundation of America Post-Intervention Status (MGFA-PIS) is the most frequently used outcome measure in myasthenia gravis (MG) to define response to treatment. However, data from literature focused on the MGFA-PIS at the last follow-up, without considering modifications over the years. Aim of this study is to evaluate MGFA-PIS changes and related predictive factors during the disease course.
Methods: We included 754 ocular and generalized MG patients from 2 Italian Neuromuscular Centers, with MG onset between 2000 and 2018 and at least one year of follow-up. MGFA-PIS was determined by a database algorithm comparing INCB-MG and Mingazzini Scores at each timepoint with the previous one.
Results: Mean age at onset was 48.7±18.6 years and mean disease duration 9.1±5 years. Overall, 348 out of 754 patients had generalised AChR-MG without thymoma (46.2%), 72 MuSK-MG (9.5%), 5 LRP4-MG (0.7%), 103 seronegative MG (13.7%), 123 thymoma-MG (16.3%), 103 ocular-MG (13.7%). Complete stable remission (CSR) was reached in 77/754 (10.2%) patients, including 60 (77.9%) patients achieving and maintaining the CSR until the last follow-up and 17 (22.1%) losing CSR after its achievement, usually in first disease stages. In the latter subgroup 4 out of 17 patients then returned to CSR. Among clinical, immunological and thymus parameters, female sex was the only factor associated with the chance of losing the CSR status.
Conclusion: Chance to achieve the CSR did not vary significantly from literature, but our data showed that its modification over time may change in specific MG-subgroups.
Disclosure: LM has received honoraria for speaking, advisory boards and compensation for congress participations from Sanofi Genzyme, Roche, Alexion, Amicus Therapeutics, Lupin and Biogen, outside the submitted work.

EPO-221

The Burden MG patients Experience in Fatigue, Sleep, and Mental Health Compared to the General Population

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Background and aims: Myasthenia Gravis (MG) is a rare, IgG-driven, neuromuscular disorder marked by a variable combination of weakness of eye, bulbar, respiratory, axial and limb muscles, affecting patients' daily life. This analysis uncovers the problems MG patients experience regarding fatigue, sleep and mental health, compared to the general population.
Methods: The MyRealWorld-MG study enrolled MG patients from 9 countries and collected the following data digitally: demographics, Hospital Anxiety and Depression Survey (HADS), PROMIS-Sleep Disturbance and the FACIT-Fatigue. Comparison of the HADS was based on the POPUP digital observational study, which enrolled a representative sample of the general population in similar countries. The PROMIS-Sleep Disturbance and the FACIT-Fatigue comparisons were based on US standardized population norms.
Results: MyRealWorld-MG included 2,074 MG patients, whereas POPUP enrolled 9,000 respondents. Mean (SD) HADS-Anxiety and HADS-Depression scores for MG patients (11.5 (2.4) and 8.9 (2.0) respectively) were indicative of clinical anxiety and depression. These scores were higher than average scores in POPUP, which revealed fewer problems in depression and anxiety (6.4 (4.6), $p<0.001$ and 5.0 (4.1), $p<0.001$). MG patients had significantly higher mean (SD) PROMIS-Sleep Disturbance scores (53.7 (8.1) vs 50.0 (10.0), $p<0.0001$). Finally, the mean (SD) FACIT-Fatigue score of MG patients was markedly worse than the general population (28.9 (11.5) vs 43.5 (8.3), $p<0.0001$), signaling a large impact of MG on fatigue.

Instrument/Domain	Variable	MyRealWorld-MG	Source	P-value
N		N=324	US General Population	
FACIT Fatigue scale	Mean (std)	28.9 (11.5)	43.5 (8.3)	<.0001
		N=251	US General Population	
PROMIS: Sleep disturbance	Mean (std)	53.7 (8.1)	50 (10)	<.0001
N		N=1159	POPUP, N=9000	
HADS Anxiety	Normal	6.7%	63.6%	<.0001
	Mild	23.6%	16.1%	
	Moderate	47.7%	10.9%	
	Severe	21.9%	9.4%	
	Mean (std)	11.5 (2.4)	6.4 (4.6)	<.0001
N		N=1159	POPUP, N=9000	
HADS Depression	Normal	24.2%	84.0%	<.0001
	Mild	57.3%	9.2%	
	Moderate	16.9%	4.2%	
	Severe	1.6%	2.7%	
	Mean (std)	8.9 (2)	5 (4.1)	<.0001

Table 1. Comparison of fatigue, sleep and mental health between MG patients and the general population

Conclusion: A considerable burden in MG patients was found in this direct comparison of mental health, sleep and fatigue with the general population, using data from two international studies and published population norms.

Disclosure: RM has received speaking honoraria from Biomarin, Alexion and UCB, served on advisory boards for Alexion, argenx BV and UCB and received support for congress participation from Merck, Teva and Biogen FS has received public speaking honoraria from Almirall, Biogen, Mylan, Novartis, Roche, Sanofi and Teva; and served on advisory boards for Almirall, argenx BV, Avexis, Biogen, Forward Pharma, Lexeo, Merk, Novartis, Novatek, Pomona, Roche, Sanofi, and Takeda. SP is an employee of argenx BV, the sponsor of the study SD, NT and MFJ have been commissioned by argenx BV and received honoraria to design the study, analyze data and write the abstract.

EPO-222

Spanish Pompe Registry: New data based on the 130 patients included

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Background and aims: Pompe disease is a rare genetic myopathy with two main clinical phenotyp: Infantile Onset Pompe Disease (IOPD) and Late Onset Pompe Disease (LOPD). Epidemiological studies showed a disease prevalence about 1:40,000 but reliable data in Spain in lacking

Methods: Here we analyzed the data of the 130 patients included in the Spanish Pompe, included between 2019 and 2023. We collected information about demographics, family history, clinical features, ancillary tests, functional outcomes and response to treatments from each individual clinical report.

Results: 118 patients were classified as LOPD while 12 had an IOPD phenotype. 70 patients were males (53.85%). Mean age of our population was of 29.75 years old (SD 42.75). 44 had family history of Pompe, being most common place of birth and parent's origin Andalusia, 100 patients were symptomatic. The most frequent symptom reported was lower limb and axial weakness in 60.7%. Ninety-one patients preserved their ability to walk in their last visit. Forty patients required ventilation support (34 non-invasive). Ninety three patients had high levels of CK with a mean value of 716 UI/L (SD 457.99). The most common mutation reported was IVS1-13T>G (c.-13-32T>G) in 85 patients. 89 were treated with Enzyme Replace Therapy. According to our data the Pompe prevalence is 3/1,000,000 in our country.

Conclusion: The Spanish Pompe Registry give us valuable information about the demographics and clinical features of our population of patients with this rare disease. yielding us a lower prevalence than expected.

Disclosure: The SPR received funding from Sanofi-Genzyme.

EPO-223

Evidence-based expert consensus guidance for ongoing assessment of generalised myasthenia gravis (gMG)

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Background and aims: Regular and consistent disease assessment could provide a clearer picture of burden in gMG and improve patient outcomes; however, there is lack of standardisation on use of assessment tools in practice. This modified Delphi consensus was conducted to review current evidence on assessment tool use in gMG and propose expert-derived guidance for good practice.

Methods: A European expert panel comprising 15 experienced gMG neurologists contributed to development of this guidance, four of whom formed a lead Sub-committee. The PICO (population, intervention, control, outcomes) framework was used to define six clinical questions on gMG assessment tools and a systematic literature review was conducted. Consensus was reached when ≥70% of the experts rated agreement with a statement as ≥8 on a scale of 1–10.

Results: 18 guidance statements were developed based on evidence and expert opinion covering six themes: 1) tools for understanding gMG burden in clinical practice, clinical trials/research, and telemedicine; 2) use of depression, anxiety, and fatigue scales in patient assessment; 3) outcomes/symptoms excluded from existing gMG assessment tools; 4) thresholds for clinically important/meaningful differences; 5) assessment of treatment-related burden; 6) assessments supporting treatment decisions. Expert panel consensus was reached on 16/18 statements after one voting round (Table 1).

Statement	Evidence level and grade	Consensus, % (n)*
Optimal tools and their frequency for understanding gMG disease burden in clinical practice, clinical research and telemedicine		
Clinical practice setting		
Consistent use of the MG-ADL scale should be applied in clinical practice to understand gMG disease burden; if the MG-ADL indicates worsening gMG, the QMG scale can be used to provide greater clinical understanding and support onward decisions	1a† Grade A	93.3 (14/15)
A patient scale, such as the PASS or EQ-5D-VAS, should follow the MG-ADL in clinical practice to determine patient satisfaction with symptom state and treatment and to determine the need for further assessments	2b Grade B	66.7† (10/15)
In clinical practice, should patients be dissatisfied with their symptom state or treatment, additional outcomes should be explored, such as quality of life, psychological/emotional burden or fatigue, with appropriate assessments	5 Grade D	100 (15/15)
Timing of gMG assessments should reflect the patient's symptom state (i.e., less frequent for stable vs fluctuating symptoms) and guidance for continuing, stopping retreatment or repeating treatment, should be based on clinical evaluation	5 Grade D	100 (15/15)
Clinical trial/research setting		
The MG-ADL is recommended as the primary endpoint in clinical trials, with the QMG as a co-primary or key secondary endpoint	1a Grade A	93.3 (14/15)
PROs are recommended to be included for the assessment of patient satisfaction with symptom state and treatment in the clinical trial setting	1a Grade A	93.3 (14/15)
The MG-QOL-15r or EQ-5D-5L may be used to measure quality of life in clinical trial settings	2a Grade B	100 (15/15)
Telemedicine setting		
In telemedicine settings, MG-ADL should be used to assess disease severity, and combined with EQ-5D and MG-QOL-15r to assess QoL; the combined results can determine the need and urgency for a face-to-face consultation	2b† Grade B	93.3 (14/15)
Timing of gMG assessments should reflect the patient's symptom state (i.e., less frequent for stable vs fluctuating symptoms) and guidance for continuing, stopping retreatment or repeating treatment, should be based on clinical evaluation	5 Grade D	100 (15/15)
General principles for incorporating depression, anxiety, and fatigue scales in patient assessment for gMG		
No specific scales are validated for measuring depression, anxiety and fatigue in the context of gMG at the current time. However, fatigue and fatigability may be measured effectively using the FSS, MFI-20 or Chalder fatigue scale; and depression and anxiety may be measured effectively using the PHQ, HADS or MDI	2a Grade B	80.0 (12/15)
Comorbidity assessment should include the relevant multidisciplinary team member, such as a psychiatrist for anxiety or depression	5 Grade D	86.7 (13/15)
Patient assessment domains that are not currently included in any existing gMG patient assessment tool		
There is a need for physician- and patient-administered assessment tools to better understand the practical, psychosocial impact of gMG and its treatment on patients, their families and caregivers	5 Grade D	100 (15/15)
Although current evidence does not support the use of a specific scale over others to assess fatigability, measures such as the MFI-20 and Chalder Fatigue scales should be used more consistently to assess the burden and impact of this important symptom in patients with gMG	2b† Grade B	73.3 (11/15)
It is important to ensure full evaluation of ocular symptoms in patients with gMG with the use of ocular-specific symptom scores and scales as they may not be fully assessed by generalised assessment tools	5 Grade D	66.7† (10/15)
Thresholds for minimally important/clinically meaningful differences in assessment scores in gMG within clinical practice		
At the current time it is not possible to make recommendations on absolute thresholds for minimally important and clinically meaningful differences in gMG scores as these are heavily dependent on the patient's experience and should be considered relative to baseline assessment scores	5 Grade D	100 (15/15)
Use of a patient satisfaction scale, such as the PASS or a symptom satisfaction questionnaire, can give an indication of whether changes in symptom state as assessed by a clinician, with a scale such as the MG-ADL, corresponds to meaningful changes from the patient's perspective	2a Grade B	86.7 (13/15)
Assessment of treatment-related burden in patients with gMG in clinical practice		
There are currently no appropriate scales to measure the adverse event, psychological or practical burden associated with gMG treatment, or to differentiate treatment-related adverse events from gMG-related symptoms; however, treatment-related adverse event burden can be assessed through longitudinal measurement of objective parameters, such as frequency, and the use of toxicity indices in conjunction with MG-specific assessments of MG burden	2b† Grade B	80.0 (12/15)
Support provided by current gMG assessments on decisions around re-treatment or escalation of treatment		
Multiple disease-, patient- and treatment-related factors, including the patient's preferences, need to be considered when defining treatment goals and making therapeutic decisions in gMG; therefore, a general recommendation on how to decide upon re-treatment or treatment escalation is not appropriate	5 Grade D	86.7 (13/15)

*Consensus was reached when ≥70% of the experts rated agreement with a statement as ≥8 on a scale of 1–10; †Evidence was from patients with MG, and not gMG specifically; #Consensus not reached after first voting round; statement to be revised.
EQ-5D, EuroQol-5D; EQ-5D-5L, EuroQol-5d-5L; EQ-5D-VAS, EuroQol-5D Visual Analogue Scale; FSS, Fatigue Severity Scale; (g)MG, generalised myasthenia gravis; HADS, Hospital Anxiety and Depression Scale; MDI, Multiscale Depression Inventory; MFI-20, 20-item Multidimensional Fatigue Inventory; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QOL-15r, 15-item Myasthenia Gravis Quality of Life (revised); PASS, patient-acceptable symptom state; PHQ, Patient Health Questionnaire; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis.

Table 1. Consensus statements following the first round of voting for improving and standardising the assessment of patients with gMG

Conclusion: This process provides evidence- and expert consensus-based guidance for use of objective and subjective assessment tools across gMG care to improve outcomes for patients.

Disclosure: Financial support for this consensus was provided by argenx BV; the Sub-committee retained full control and final approval of the consensus process and outputs.

EPO-224

The ratio of blood circulating miR-206 and miR-409-3p as diagnostic biomarker for idiopathic inflammatory myopathy

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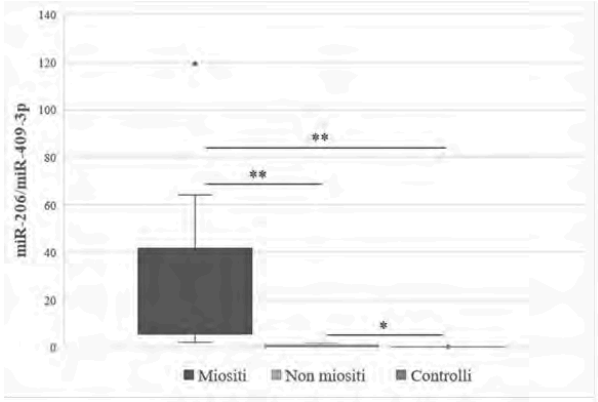
Background and aims: Idiopathic inflammatory myopathies (IIMs) are rare diseases characterised by muscle weakness and muscle inflammation. The diagnostic work-up of a suspected IIM is rather complex and expensive, and usually requires muscle biopsy. Our aim in this study was to identify new biological molecular marker as a non-invasive tool for IIMs to improve diagnostic efficiency.

Methods: We analyzed by quantitative Real Time PCR (qRT-PCR) blood microRNAs (miRs) expression levels of 15 patients with a suspected IIM. We blindly measured the ratio between plasmatic miR-206 and miR409-3p of the subjects. ROC curve analysis was used to determine specificity and sensitivity of the ratio to distinguish between IIMs patients and patients with other muscle disease.

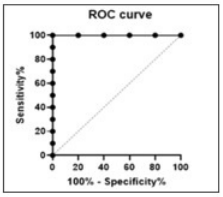
Results: Ratio values above 1.94 were identified as having 100% sensibility (95% CI: 72.25% to 100%) and 100% specificity (95% CI: 56.55–100%) in discriminating IIMs patients from the others. A value above 4.11 defines a patient as part of the IIM group, while under 0.96 identifies a non-myositic subject. Values between 0.96 and 4.11 remain in a "grey area", which warrants further tests.



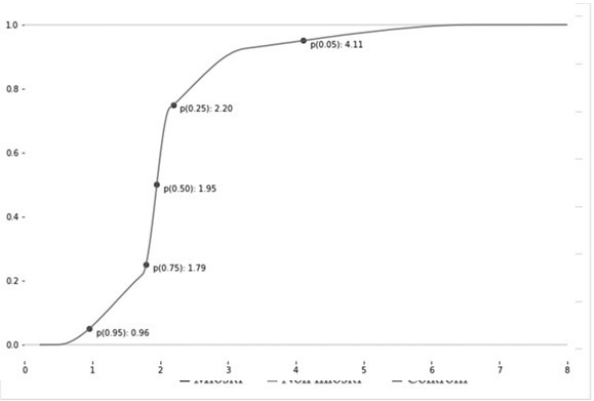
Results

Area sotto la curva ROC	
Area	1
Errore standard	0
95% intervallo di confidenza	1.000 a 1.000
P value	0,002
Dati	
Controlli (ratio non miositici)	5
Pazienti (ratio miositi)	10
Controlli mancanti	0
Pazienti mancanti	0

	Sensibilità%	95% CI	Specificità%	95% CI	rapporto di verosimiglianza
> 0.1400	100	72,25% a 100,0%	20	1,026% a 62,45%	1,25
> 0.3350	100	72,25% a 100,0%	40	7,107% a 76,93%	1,667
> 0.4850	100	72,25% a 100,0%	60	23,07% a 92,89%	2,5
> 1.120	100	72,25% a 100,0%	80	37,55% a 98,97%	5
> 1.940	100	72,25% a 100,0%	100	56,55% a 100,0%	
> 2.695	90	59,58% a 99,49%	100	56,55% a 100,0%	
> 4.875	80	49,02% a 96,45%	100	56,55% a 100,0%	
> 6.730	70	39,68% a 89,22%	100	56,55% a 100,0%	
> 7.210	60	31,27% a 83,18%	100	56,55% a 100,0%	
> 7.730	50	23,66% a 76,34%	100	56,55% a 100,0%	
> 18.93	40	16,82% a 68,73%	100	56,55% a 100,0%	
> 32.08	30	10,78% a 60,32%	100	56,55% a 100,0%	
> 49.15	20	3,554% a 50,98%	100	56,55% a 100,0%	
> 91.72	10	0,5129% a 40,42%	100	56,55% a 100,0%	



ROC and CI



Bootstrapping

Conclusion: Plasmatic miR-206/miR409-3p ratio proved to be an accurate biomarker to identify patients affected by IMM. It has the potential to become a cheap and non-invasive screening tool to guide the diagnostic and therapeutic process. Further studies are needed with higher number of patients to confirm the data and eventually find associations of the biomarker with specific IIMs subgroups.

Disclosure: Nothing to disclose.

EPO-225

Matching-adjusted indirect comparison of ravulizumab/efgartigimod in generalised myasthenia gravis: Timepoint challenges

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Background and aims: Matching-adjusted indirect comparisons (MAICs) may be used to assess the benefits of different treatments for symptom control. In this MAIC, we built on findings from previous comparisons of ravulizumab and efgartigimod and used mean changes from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) scores from the CHAMPION-MG and ADAPT trials to assess the effects of these treatments on symptom control in patients with generalised myasthenia gravis (gMG) at different timepoints.

Methods: Individual patient-level data from CHAMPION-MG were weighted to match summary baseline characteristics from the acetylcholine receptor antibody-positive subset of patients in ADAPT at the trial-arm level, and mean changes in MG-ADL scores from baseline to different timepoints were compared. Anchored comparisons were performed at Weeks 4 and 10, and at Week 8 (efgartigimod) vs Week 26 (ravulizumab).

Results: Baseline characteristics of the patients before and after matching are shown in Table 1. The timepoints chosen to assess the impact of ravulizumab and efgartigimod on MG-ADL were found to affect the results. Improvements in MG-ADL scores appeared to favour efgartigimod vs ravulizumab at Week 4, whereas at Week 10, and Week 8 (efgartigimod) vs Week 26 (ravulizumab), the results trended in favour of ravulizumab (Table 2).

	CHAMPION						ADAPT (AChR-Ab+ patients)		
	Ravulizumab (n=86)		Placebo (n=89)		Total (N=175)		Efgartigimod (n=65)	Placebo (n=64)	Total (N=129)
	Unmatched	Matched	Unmatched	Matched	Unmatched	Matched			
Mean age, years	58.0	44.7	53.3	49.2	55.6	47.0	44.7	49.2	46.9
Female, n (%)	44 (51.2)	61 (70.8)	45 (50.6)	56 (62.5)	89 (50.9)	116 (66.6)	46 (70.8)	40 (62.5)	86 (66.7)
MGFA class II, n (%)	39 (45.3)	37 (43.1)	39 (43.8)	35 (39.1)	78 (44.6)	72 (41.0)	28 (43.1)	25 (39.1)	53 (41.1)
MGFA class III, n (%)	41 (47.7)	46 (53.8)	45 (50.6)	50 (56.3)	86 (49.1)	96 (55.1)	35 (53.8)	36 (56.3)	71 (55.0)
MGFA class IV, n (%)	6 (7.0)	3 (3.1)	5 (5.6)	4 (4.7)	11 (6.3)	7 (3.9)	2 (3.1)	3 (4.7)	5 (3.9)
Mean time since diagnosis, years	9.8	9.7	10.0	8.9	9.9	9.3	9.7	8.9	9.3
Mean MG-ADL score	9.1	9.0	8.9	8.6	9.0	8.8	9.0	8.6	8.8
Steroid use at study entry, n (%)	56 (65.1)	61 (70.8)	65 (73.0)	71 (79.7)	121 (69.1)	132 (75.3)	46 (70.8)	51 (79.7)	97 (75.2)
NSIST use at study entry, n (%)	56 (65.1)	53 (61.5)	63 (70.8)	51 (57.8)	119 (68.0)	104 (59.6)	40 (61.5)	37 (57.8)	77 (59.7)

AChR-Ab+, acetylcholine receptor antibody-positive; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, non-steroidal immunosuppressant therapy.

Table 1. Baseline characteristics before and after matching

Domains **+2 new** (total: 8) *Broadest category of impacts; captures multiple impact elements*	Impact elements **+11 new** (total: 44) *More detailed category than domains; captures multiple impacts*	Impacts **+16 new** (total: 84) *Most detailed category; captures highest levels of nuance*	
		Patient examples	Caregiver examples
Occupation*	Career aspirations, freedom of occupation, unemployment or underemployment, on-the-job disruption, productivity and performance, absenteeism, and educational disruption	Being 'stuck' in a role	Passing up job opportunities
Financial*	Reduced income, financial trade-offs, financial toxicity, out-of-pocket costs, cost of daily living needs and high-cost expenses to support quality of life	Need to hire household support	Taking on dependants
Emotional health	Anger or resentment, fear or anxiety, frustration, sadness or depression, shame or embarrassment, **guilt**, **stress**, **loss of identity**, impaired cognitive function, **disproportionate sense of responsibility**	Shame or embarrassment	Guilt
Physical health†	Neglecting health needs and downstream health impacts	Downstream health impacts	Lack of focus on personal health
Sleep†	Insomnia, quality of sleep and **reliance on sleep aid**	Not sleeping comfortably	Irregular sleep schedule
Social	Strain on or change in intimate, immediate or non-immediate relationships, social isolation, reduced ability or desire to participate in activities across varying sectors, **real or perceived negative public perception and poor public understanding**	Social isolation	Difficulty forming new friendships
Planning and autonomy	Vigilance, disruptions to plans, loss of autonomy, feelings of instability about the future, personal aspirations, necessary life adaptations, illness work	Lack of independence	Altering of personal priorities
Safety	Real or perceived physical safety risks and **medical mistreatment**, and **powerlessness**	Risk of experiencing medical mistreatment	Risk and experience of injuries

Domains and impact elements in bold are newly identified.
*New domain. †Domain split from original 'Physical health and sleep'.

Table 2. Mean (95% confidence interval) MG-ADL changes from baseline to different timepoints

Conclusion: Outcomes from indirect comparisons of the effects of efgartigimod and ravulizumab on symptom control in patients with gMG can vary depending on the chosen timepoints and matching methodology. The consistency of symptom control achievable over a prolonged period should be considered, alongside efficacy and tolerability, when assessing treatment options for patients with gMG.

Disclosure: The study was sponsored by Alexion Pharmaceuticals Inc., with medical writing support provided by Hannah Wedge of OPEN Health Communications.

EPO-226

A single center experience with neuromuscular immune-related adverse events of immune checkpoint inhibitors

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Background and aims: The increasing use of immune checkpoint inhibitors (ICIs) and its immune-related neuromuscular adverse events (NM-iAE) constitutes a challenge due to the lack of guidance in the management of these neurological symptoms. We aimed to describe our experience with NM-iAE, including myositis, myasthenia gravis (MG) or overlap syndromes.
Methods: We retrospectively collected clinical data of patients presenting NM-iAE between 2015-2022 in our center.
Results: Within our 13 patients, 2 (15.4%) presented with myositis, 7 (53.8%) with MG and 4 (30.8%) with myositis-MG overlap. No neurological symptoms were reported before ICI administration. Among ICIs, 84.6% were PD1 inhibitors and 15.4% a combination of PD1+CTLA4. The median (IQR) time of onset since first ICI administration was 49 (30–225) days. The most frequent clinical presentations were bulbar and generalized (69.2% each). 69.2% presented combined symptoms. 6 patients (46.1%) were Ach-receptor antibody positive. 6 (46.1%) showed anti-striated muscle antibodies and 3 (23%) different myositis-related antibodies (Jo1, PL2 and Titin). Regarding treatment, 92.3% received pyridostigmine, 76.9% steroids and 92.3% discontinued ICI. The most severe presentations received intravenous immunoglobulins (46.2%) and plasma exchange (30.8%). 1 (7.7%) received Rituximab. 3 (23%) required mechanical ventilation but ultimately died due to acute respiratory failure (all of them with severe bulbar symptoms at onset). Remaining patients had a favorable neurological response.
Conclusion: Although ICI neurological adverse events are not very frequent, they are potentially fatal. More studies are needed to clarify the management of these complications but probably early recognition and treatment with intensive immunotherapy may be the key.
Disclosure: Nothing to disclose.

EPO-227

KY mutations are a cause of distal neuromyopathies

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[1]1. Neuromuscular Diseases Unit, Neurology Department, Hospital Universitari I Politècnic La Fe, Valencia, Spain, and Neuromuscular Reference Centre, ERN-EURO-NMD., Paris, France, [2]John Walton Muscular Dystrophy Research Centre, Translational and Clinical Research Institute, Newcastle University and Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK

Background and aims: Kyphoscoliosis peptidase gene (KY) gene mutations are rare recessive conditions related to myofibrillar myopathy-7 and hereditary spastic paraplegia.
Methods: Study of a patient with a myopathy of childhood onset, follow up in a Neuromuscular Centre, secondary to KY gene mutations, describing the phenotype and the characteristics of the ancillary test performed in order to better characterize this rare condition.
Results: A 58 years old man presented in childhood with gait disturbances and ankle retractions resembling an EDMD. He came to our clinic in adulthood due to progressive muscle weakness with difficulties walking and going up stairs. He had history of multiple fibrous dysplasia and low back pain. He showed weakness affecting mainly distal lower leg, trunk and axial muscles, and also had multiple retractions including rigid spine, scoliosis and foot deformities. CK serum levels were normal. He had a EMG neuromyopathic pattern, without spontaneous activity. Nerve conduction studies showed decreased amplitude of CMAPs in distal stimulation sites of lower legs, and normal sensory NCS . A restrictive respiratory involvement was detected in respiratory assessment. Muscle MRI showed severe involvement of axial and trunk muscles, posterior compartment of lower legs and also affected sartorius and other thigh muscles. A biopsy from tibialis anterior showed myopathic features and myofibrillar disorganization. A homozygous variant p.Arg187Cys in KY was detected in exome analysis.
Conclusion: KY gene should be included as a cause of distal neuromyopathy.
Disclosure: Nothing to disclose.

EPO-228

A comprehensive assessment of the impact of generalised myasthenia gravis (gMG): Insights from patients and caregivers

P. Narayanaswami[1], K. Gwathmey[2], S. Dos Reis[3], A. Foss[4], J. Sullivan[5], C. Thiele[6], C. Ramirez[7], A. Kielhorn[8], K. McNeil-Posey[8], A. Napoles[9], N. Betor[9]

[1]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, USA, [2]VCU Health, Richmond, USA, [3]University of Maryland, Baltimore, USA, [4]Myasthenia Gravis Association, Kansas City, USA, [5]EveryLife Foundation for Rare Diseases, Washington, USA, [6]Health Management Associates, Lansing, USA, [7]Patient, Rodgers, USA, [8]Alexion Pharmaceuticals Inc., Boston, USA, [9]Avalere Health, Washington, USA

Background and aims: The impact of rare diseases is often defined by the effect of symptoms on patients and by treatment expenses. In this study, we take a broader perspective by identifying new and assessing known impacts of gMG on the lives of patients and caregivers.

Methods: This study was performed using qualitative semi structured interviews to assess the impact of gMG on patients and caregivers. Participants included patients with acetylcholine receptor antibody-positive gMG and caregivers who provided unpaid support. The interviews were coded and qualitatively analysed to summarise the key points raised by participants. The impacts identified in interviews were categorised into impact domains and subcategorised into impact elements.

Results: 28 interviews (16 patients and 12 caregivers) were included in the analysis; participant characteristics are shown in Table 1. Of the 84 impacts of gMG identified, 16 were not previously reported in the literature. These impacts were categorised into eight domains (occupation, financial, emotional health, physical health, sleep, social, planning and autonomy, and safety), indicating effects on many aspects of patients' and caregivers' lives (Table 2). There were similarities in the reported impact elements and domains between patients and caregivers, although some of the specific impacts varied (Figure 1).

Characteristic, n (%)		Patients (n=16)	Caregivers (n=12)
Has a caregiver?	Yes	8 (50)	N/A
	No	8 (50)	
Time from diagnosis*	<5 years†	5 (31)	6 (50)
	>5 years†	11 (69)	6 (50)
Race	White	7 (44)	7 (58)
	Black	6 (38)	4 (33)
	Asian	1 (6)	0
	American Indian/ Alaskan Native	1 (6)	0
	Other	1 (6)	1 (8)
Ethnicity	Hispanic/Latinx	0	2 (17)
	Not Hispanic/Latinx	16 (100)	10 (83)
Sex	Male	3 (19)	5 (41)
	Female	13 (83)	7 (58)

*For caregivers, time from diagnosis is reported for the patient they cared for; †Diagnosis timing was noted as of September 2022. Patients diagnosed before or on 31/08/2017 were recorded as >5 years and patients diagnosed from 01/09/2017 were recorded as <5 years.
N/A, not applicable.

Table 1. Participant characteristics

Domains +2 new (total: 8) *Broadest category of impacts; captures multiple impact elements*	Impact elements +11 new (total: 44) *More detailed category than domains; captures multiple impacts*	Impacts +16 new (total: 84) *Most detailed category; captures highest levels of nuance*	
		Patient examples	Caregiver examples
Occupation*	Career aspirations, freedom of occupation, unemployment or underemployment, on-the-job disruption, productivity and performance, absenteeism, and educational disruption	Being 'stuck' in a role	Passing up job opportunities
Financial*	Reduced income, financial trade-offs, financial toxicity, out-of-pocket costs, cost of daily living needs and high-cost expenses to support quality of life	Need to hire household support	Taking on dependants
Emotional health	Anger or resentment, fear or anxiety, frustration, sadness or depression, shame or embarrassment, **guilt**, **stress**, **loss of identity**, impaired cognitive function, **disproportionate sense of responsibility**	Shame or embarrassment	Guilt
Physical health†	Neglecting health needs and downstream health impacts	Downstream health impacts	Lack of focus on personal health
Sleep†	Insomnia, quality of sleep and **reliance on sleep aid**	Not sleeping comfortably	Irregular sleep schedule
Social	Strain on or change in intimate, immediate or non-immediate relationships, social isolation, reduced ability or desire to participate in activities across varying sectors, **real or perceived negative public perception and poor public understanding**	Social isolation	Difficulty forming new friendships
Planning and autonomy	Vigilance, disruptions to plans, loss of autonomy, feelings of instability about the future, personal aspirations, necessary life adaptations, illness work	Lack of independence	Altering of personal priorities
Safety	Real or perceived physical safety risks and **medical mistreatment**, and **powerlessness**	Risk of experiencing medical mistreatment	Risk and experience of injuries

Domains and impact elements in bold are newly identified.
*New domain. †Domain split from original 'Physical health and sleep'.

Table 2. Domains, impact elements and examples of impacts from patient and caregiver interviews

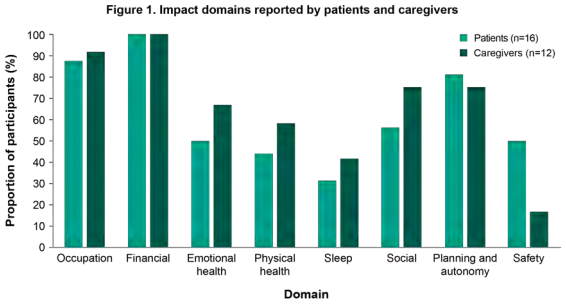

Figure 1. Impact domains reported by patients and caregivers

Conclusion: This study indicates that the impact of gMG on patients and caregivers is broader than previously reported. In the future, it is necessary to consider both patient and caregiver experiences in each of the reported domains when assessing the impact of rare diseases such as gMG.

Disclosure: The study was sponsored by Alexion Pharmaceuticals Inc., with medical writing support provided by Hannah Wedge of OPEN Health Communications.

EPO-229

Generalized myasthenia gravis (gMG) diagnostic journey and treatment: real-world physician and patient perspectives

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Background and aims: Generalized myasthenia gravis (gMG) is a rare, chronic, autoimmune disease that causes debilitating and potentially life-threatening muscle weakness. Patients may endure multiple exams and referrals before diagnosis, delaying treatment. This study characterizes and compares European and US gMG patient journeys from symptom onset to diagnosis and treatment initiation.

Methods: Data was drawn from an Adelphi Disease Specific Programme, a survey of providers and patients with gMG in France, Germany, Italy, Spain, the UK, and US, collected from March to September 2020.

Results: Overall, 557 patients with gMG were included and 36.9% were from the US. Patient demographics are presented in Table 1. The mean time from symptom onset to gMG diagnosis was 9.8 (SD: 13.7) months. Most common symptoms included ocular myasthenia (59.4%), ptosis (58.9%) and general fatigue (58.7%). Patients diagnosed earlier often had more severe gMG (Table 1). Most patients consulted primary care physicians (62.1%) and were then diagnosed by neurologists (79.9%). Providers, on average, used 8.7 (SD: 4.2) tests to aid gMG diagnosis. Among those previously misdiagnosed (26.9%), the most common misdiagnoses were chronic fatigue syndrome (34.7%) and multiple sclerosis (14.7%). Treatment initiation was, on average, 3.2 months (SD: 7.7) following diagnosis. Acetylcholinesterase inhibitors (73.8%) were the most commonly initiated, followed by steroids (42.9%) and immunosuppressive therapies (36.0%). Geographic differences between countries were noted.

Table 1: Patient Demographics by Time to Diagnosis

Time to Diagnosis*	Overall	Less than 6 Months	6 to 12 Months	Greater than 12 Months
Sample Size	557	323	113	121
Age (years)				
Mean (SD)	53.2 (15.9)	53.0 (17.0)	58.3 (15.0)	53.2 (13.8)
Sex (n (%))				
Male	277 (49.7%)	168 (52.0%)	57 (50.4%)	52 (42.9%)
Female	280 (50.3%)	155 (47.9%)	56 (49.5%)	69 (57.0%)
Ethnicity (n (%))				
White/Caucasian	466 (83.6%)	271 (83.9%)	98 (86.7%)	97 (80.1%)
African American	27 (4.8%)	15 (4.6%)	4 (86.7%)	8 (6.6%)
Hispanic/Latino	24 (4.3%)	9 (2.7%)	5 (3.5%)	10 (8.2%)
Afro-Caribbean	12 (2.2%)	9 (2.7%)	1 (0.8%)	2 (1.6%)
Mixed Race	8 (1.4%)	3 (0.9%)	1 (0.8%)	2 (1.6%)
Other	20 (3.5%)	16 (4.9%)	4 (3.5%)	2 (1.6%)
Employment (n (%))				
Full-Time	163 (29.4%)	106 (33.02%)	34 (30.0%)	23 (19.0%)
Part-Time	106 (19.1%)	50 (15.5%)	22 (19.4%)	34 (28.1%)
Retired	163 (29.4%)	100 (30.9%)	34 (30.0%)	29 (24.0%)
Other	123 (22.1%)	65 (20.2%)	23 (20.3%)	35 (28.2%)
MGFA Classification at Diagnosis (n (%))				
Class I	91 (16.3%)	44 (13.6%)	25 (22.1%)	22 (18.2%)
Class II	273 (49.0%)	149 (43.1%)	60 (53.1%)	64 (52.9%)
Class III	151 (27.1%)	94 (29.7%)	23 (20.3%)	32 (26.4%)
Class IV	38 (6.8%)	30 (9.2%)	5 (4.4%)	3 (2.5%)
Class V	4 (0.7%)	4 (1.2%)	0 (0%)	0 (0%)

*Time to diagnosis is the number of months from symptom onset to gMG diagnosis.
Abbreviations
gMG: Generalized myasthenia gravis, MGFA: Myasthenia Gravis Foundation of America, SD: Standard deviation

Table 1: Patient Demographics

Conclusion: In this international survey, patients with gMG were diagnosed 10 months following symptom onset and initiated treatment 3 months following diagnosis. Optimizing the diagnosis and treatment pathways may improve health outcomes among patients with gMG.

Disclosure: Research was sponsored by Horizon Therapeutics Jenny Park, Anthony Amatucci, Elizabeth Crane, Cornelia Fuller, Kristina Patterson, and Hari Patel are employees and stockholders of Horizon Therapeutics Gregor Gibson and Emma Chatterton are employees of Adelphi Real World

EPO-230

Clinical and therapeutic long-term follow-up in a large LOPD population: clues from a single centre experience.

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Background and aims: Pompe disease is an inherited metabolic disorder, caused by acid-a-glucosidase (GAA) enzyme deficiency. Late-onset form of Pompe disease (LOPD) presents as a limb-girdle myopathy with variable respiratory involvement. Since 2006, enzyme replacement therapy (ERT) has been available for Pompe disease. However, to date, only a few studies have been conducted on ERT long-term outcomes.
Methods: We describe a 49 LOPD patients' cohort and provide a long-term clinical and laboratory follow-up of patients under ERT, evaluating CK levels, 6MWT, GSGC score and spirometry.
Results: At onset, 43% of patients presented hyperCKemia whereas 57% presented proximal muscle weakness. Interestingly, electromyography showed a myopathic pattern in 61% of cases, of whom 85% had proximal muscle weakness at onset (Chi square=7.912; p<0.005). GAA residual activity was reduced in all 39 muscle samples (median value: 5.5 %; IQR: 7–4.8), correlating with an earlier onset (Spearman rho=0.328; p=0.039). 29/49 patients started ERT and were evaluated at baseline and T last (last evaluation). CK levels decreased after ERT (p=0.021). 6MWT showed a relevant decline at T last (p=0.001), as well as GSGC score (p=0.009). FVC presented an improving trend in the first 2 years, followed by a not statistically significant reduction at T last (p=0.011).
Conclusion: Our study confirms that LOPD is phenotypically heterogeneous. An early diagnosis is crucial to start ERT as soon as possible. Although long-term ERT follow-ups evidence variable responses, these results should be taken as a guide, even suggesting more appropriate therapeutic strategies in light of the emerging proposals.
Disclosure: Nothing to disclose.

EPO-231

Long-term follow up of generalized Myasthenia Gravis patients during 1998-2020 in a Spanish referral Unit.

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Background and aims: Myasthenia Gravis (MG) is a chronaaic, autoimmune, neuromuscular disease that leads to fluctuating muscular weakness. We describe demographic, clinical and therapeutic features of a generalized MG (gMG) patient cohort with long-term follow up.
Methods: Observational retrospective study of gMG patients treated in our referral neuromuscular disease unit in Spain from 1998 to 2020. Demographic, clinical (MGFA class, MGFA-PIS, MG-ADL, clinical exacerbations, myasthenic crisis), and therapeutic data were collected biennially over an 8-year period.
Results: A total of 220 patients newly diagnosed with gMG were included (54.5% women, 58 years of mean age at onset). Ninety percent were seropositive (84% anti-AChR, 6% anti-MusK, one patient was both positive). Overall, 99.5% of patients contributed data to the 2-year assessment and 42.73% to the 8-year assessment. Thymectomy was performed in 26.8% patients. Baseline mean MG-ADL score was 5.04 points (SD 3.23), improving to 0.7 points (SD 1.32) after 8 years follow-up. Exacerbations were more frequent in years 12 (51.1%) than in years 7–8 (20.2%). Myasthenic crisis frequency decreased from 3% in the first two years to 1% in years 7–8 of follow-up. Eighty-nine percent achieved MGFA-PIS minimal manifestations or better at 8 years, 67% of the patients being completely asymptomatic at 8 years from diagnosis. A total of 165 adverse events were reported, leading to drug withdrawal in approximately 20% of cases.
Conclusion: Some patients with gMG experience a high burden of disease despite treatment, due to persistent symptoms, exacerbations and drug side effects that can lead to treatment discontinuation.
Disclosure: This study was funded by UCB Pharma. David Reyes-Leiva, Álvaro Carbayo and Ricard Rojas-Garcia report no disclosures. Luis Querol received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, Novartis Pharma Spain, Roche, UCB and Grifols, received speaker or expert testimony honoraria from CSL Behring, Novartis, Sanofi-Genzyme, Merck, Annexon, Alnylam, Biogen, Janssen, ArgenX, UCB, LFB, Octapharma and Roche and serves at Clinical Trial Steering Committee for Sanofi Genzyme and Roche, and is Principal Investigator for UCB's CIDP01 trial. Elena Cortés-Vicente has received public speaking honoraria and compensation for advisory boards and/or consultations fees from UCB, Argenx, Janssen and Alexion and is Principal Investigator for UCB, Argenx, Janssen and Alexion.

Neurocritical care; Neuroepidemiology; Neurotraumatology

EPO-232

Prevalence study of Myasthenia Gravis in Lima – Peru

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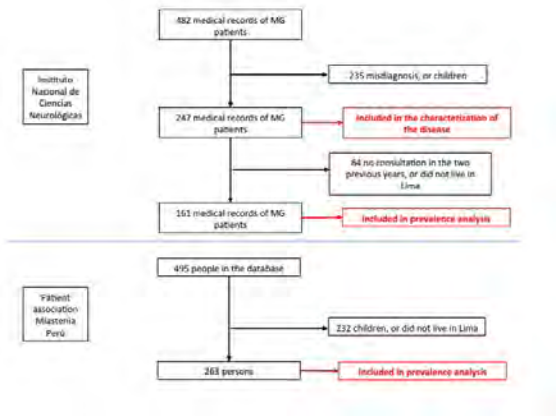
Background and aims: Myasthenia Gravis (MG) is an autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction and is the most common neuromuscular disease. The overall prevalence of MG is 150 to 250 cases per million individuals, with an estimated annual incidence of 8 to 10 cases per million person-years. There are some prevalence studies in Latin America, none of them in Peru. The objective of this study is to estimate the prevalence of MG in Lima – Peru using the capture-recapture method and to describe the clinical characteristics of the disease.
Methods: The data from MG patients were collected from two independent sources, the Instituto Nacional de Ciencias Neurológicas and the patient association Myasthenia Peru. We performed a capture-recapture analysis to estimate the prevalence of MG in Lima – Peru, in 2020. Additionally, we described the epidemiological and clinical characteristics of the patients.
Results: We identified 161 cases in the first source and 263 cases in the second source; 28 cases were common to both sources. We found a point prevalence of 17.28 cases per 100000 inhabitants (95% CI: 11.48–23.08). Early-onset MG represents 51.82% of the cases, with a female predominance (67.97%), and late-onset MG represents 48.18% of the cases, with a male predominance (63.03%).



Flow chart of the study

		Early-onset MG (n: 128)		Late-onset MG (n: 119)		P
Age at diagnosis (Median/IQR)		26	20 -35	64	58 - 69	<0.001*
Sex (n/%)	Male	41	32.03 %	75	63.03 %	<0.001**
	Female	87	67.97 %	44	36.97 %	
Phenotype (n/%)	Ocular	35	27.34 %	56	47.06 %	0.002**
	Generalized	93	72.66 %	63	52.94 %	
Time to diagnosis (months/range)		4.1	1.0 – 13.1	3	1.0 – 10.1	0.092*
Comorbidities (n/%)		33	25.78 %	52	43.7 %	0.367**

(*) Mann-Whitney U test, (**) Fisher's exact test

Clinical characteristics

Conclusion: Lima has a medium MG prevalence and is comparable to other series reported in the literature. The clinical characteristics of our patients are similar to other countries in the region.
Disclosure: Nothing to disclose.

EPO-233

Cerebrospinal fluid galectin-3 as a potential biomarker in severe traumatic brain injury

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Background and aims: There is a limited understanding of the pathophysiology underlying severe traumatic brain injury (TBI). Galectin-3 is an important alarmin in TBI mice. However, its temporal expression in the cerebrospinal fluid (CSF) of severe TBI patients has not been determined. This study measured the temporal CSF expression of galectin-3 and associated cytokines at days 1, 3, 5, and 7 post-severe TBI.
Methods: CSF from severe TBI (n = 35) and non-TBI (n=5) patients were collected. CSF galectin-3 and associated cytokines (IL-1β, IL-6, IL-10, TNF-α, CCL-2, and CCL-20) were studied using the multiplex bead array. Based on the Modified Rankin scale (mRS), patients were separated into 3 groups: mRS 6 (died), mRS 5 (severely disabled), and mRS 1–4 (mild-to-moderately disabled) at 6 months post-injury.
Results: The mRS 5 group had significantly increased galectin-3 at day 1 and 3 and IL-6 at day 3 and 5 compared to mRS 6. Furthermore, galectin-3 at day 1 and 5 post-injury, IL-6 at day 3 and 5 post-injury, IL-10 at day 5 post-injury, and CCL20 at day 1 post-injury were significantly increased in the mRS 5 group compared to patients in the mRS 1-4 group. IL-1β, TNF-α, and CCL-2 showed no significant difference between the mRS groups and time points.
Conclusion: Thus, changes in CSF levels of galectin-3 and associated cytokines correlate with functional outcomes suggesting they are potential biomarkers for diagnosis, prognosis, and a therapeutic target for severe TBI.
Disclosure: Nothing to disclose.

EPO-234

Application of Automated Pupillometry to Improve Outcomes in Patients with Traumatic Brain Injury - Systematic Review

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Background and aims: Assessing changes in pupillary light reflex (PLR) is an important aspect of routine neurological examination in Traumatic Brain Injury (TBI) patients. Research shows that automated pupillometry provides an objective, reliable, non-invasive, and quantifiable method of measuring the PLR. This systematic review aims to explore the application and utility of automated pupillometry to improve outcomes in patients with TBI.
Methods: MEDLINE, Embase, Web of Science, and Scopus databases were searched for relevant studies up to October 9, 2022. PRISMA guidelines were then applied to identify and screen relevant records. 12 observational studies were included in this systematic review.
Results: 12 observational studies met the inclusion and exclusion criteria. All studies reported on the usefulness of automated pupillometry in identifying abnormal pupillary reflexes in the acute hospital stage. 5 studies reported inverse relationship between the Neurological Pupil Index (NPi) and clinical outcomes in TBI patients. 4 studies reported correlation between NPi measured with automated pupillometry and intracranial pressure (ICP). 3 studies reported that NPi score is predictive of surgical interventions in TBI patients.
Conclusion: Automated pupillometry provides an objective, non-invasive and rapid means to assess pupillary function. Current applications of the technology demonstrated diagnostic, prognostic, and therapeutic potential in the management of TBI patients. However further evidence on the application of automated pupillometry in pre-clinical, acute hospital and rehabilitation settings is required to support wider adoption in standard clinical practice.
Disclosure: Nothing to disclose.

EPO-235

Presymptomatic geographical distribution of ALS patients: a population-based cluster analysis

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Background and aims: Environmental factors have been hypothesized to play a role in the etiology of ALS. Clusters in the spatial distributions of patients could underlie the role of environmental factors. However, the degeneration in ALS is thought to start many years before the disease onset and most geoepidemiological studies used the position of patients at the time of their diagnosis. The aim of the study was to investigate the geographical distribution of ALS patients before the disease onset.
Methods: Data from the Piemonte and Valle d'Aosta Register for ALS (PARALS) were used. Patients included were resident in Piemonte at the time of the diagnosis and received an ALS diagnosis during the 2007-2014 period. A cluster analysis was performed using the Kulldorff statistics and considering the residence address of patients at the time of onset and at 1-year intervals until 50 years before the onset. All analyses were sex- and age-adjusted.
Results: A total of 1,124 patients were included. The analysis revealed a higher-incidence cluster in the Western area of Piemonte, 2 to 9 years before the disease onset interval. Four years before the onset, in an area including circa 435,000 inhabitants, 107.99 cases were expected and 153 were observed, resulting in a relative risk (RR) of 1.48 ($p=0.046$).
Conclusion: No univocal factor able to justify our results was found. Multiple hypotheses (industrialization, soil components) have been suggested. More importantly, we showed that analyses focused on the time of diagnosis could miss previous geographical clusters of patients.
Disclosure: No relationships/activities/interests related to the manuscript.

EPO-236

Understanding brain health around the world

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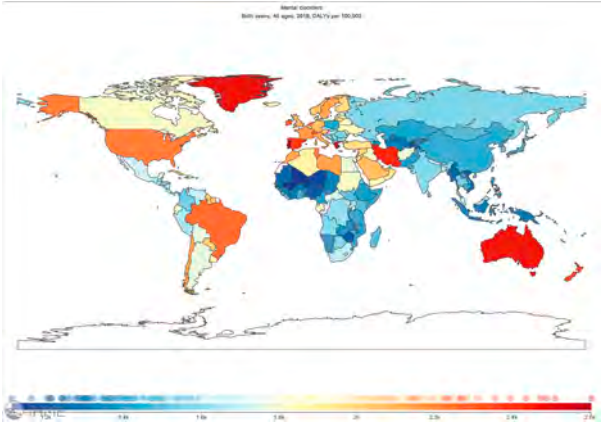
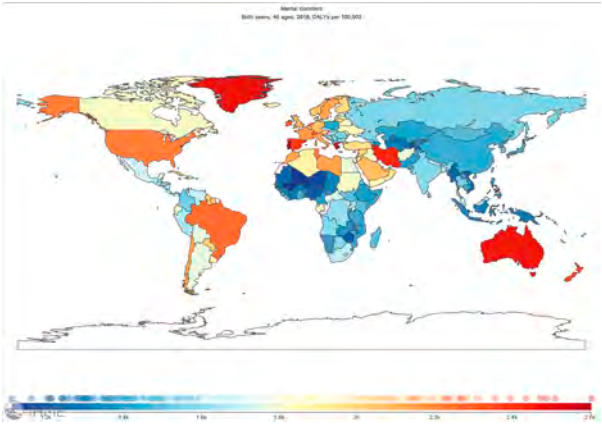
Background and aims: Brain conditions impact people of every age and in every country and have profound effects on our health and well-being.
Methods: The Global Burden of Disease (GBD) study is a systematic, scientific effort coordinated by the Institute for Health Metrics and Evaluation to quantify the magnitude of all major diseases in a highly standardized way, to allow for comparisons over time, across populations, and between health problems. In this secondary analysis of estimates from the most recent iteration of the GBD study, we describe the toll of brain conditions including neurological disorders, mental disorders, cerebrovascular disease, brain cancer, brain injuries, and select infectious conditions by location, age, and sex. We report findings in terms of prevalence, mortality, and total health loss (DALYs).
Results: Globally, more than 16% of all health loss is associated with brain conditions. In 2019, brain conditions led to as much health loss (396 million DALYs) as cardiovascular disease (393 million DALYs) and much more than cancer (251 million DALYs). Depression, among the top causes of health loss worldwide, affects 280 million people, up 64% since 1990. Alzheimer's disease cases increased by 161% since 1990, largely due to population aging, while the number of strokes increased by 95%.



The burden of neurological disorders globally



The burden of mental disorders globally

Conclusion: The burden of brain conditions will increase as populations continue to grow and age, challenging health systems, employers, and families to respond. Data such as that derived from the ongoing Global Burden of Disease study, and associated efforts, are critical to informing evidence-based planning and resource allocation.
Disclosure: Nothing to disclose.

EPO-237

Multiple Sclerosis Mortality in Poland

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Background and aims: Mortality studies in patients with multiple sclerosis (MS) are scarce. We aimed to investigate the mortality of MS in a large MS cohort from Poland compared w with the general population.
Methods: The yearly mortality data (2010–2018) for all patients with MS who died in Poland (MSD) were obtained from Statistics Poland. Mortality in MS compared with the general population was examined by standardized mortality ratio (SMR).
Results: The overall MSD during 2010–2018 was 3675. The yearly Female/Male (F/M) ratio for MSD ranged from 1.40 (in 2014) to 1.76 (in 2016) but was stable for the observation period (from 1.53 in 2010 to 1.52 in 2018) and varied between cities and the countryside from 1.70 to 1.39, respectively (p=0.0051). In the study period, the median age of death increased from 55–59 years in 2010 to 60–64 years in 2018. We found evidence of a 5-year gain in life expectancy from 2010 to 2018. However, the median life expectancy was 5 years longer in the countryside than in cities. Overall SMR was 0.95 and was decreasing over time (from 1.11 in 2013 to 0.89 in 2018) and was higher for men than women (1.16 versus 0.92).
Conclusion: A rise in survival in patients with multiple sclerosis was observed during the entire observation period. Mortality in men was higher than in women. The duration of life in patients with multiple sclerosis was lower in cities.
Disclosure: Nothing to disclose.

EPO-238

Autoimmune encephalitis and paraneoplastic neurological syndrome: Epidemiology and neuronal antibody testing in Sweden

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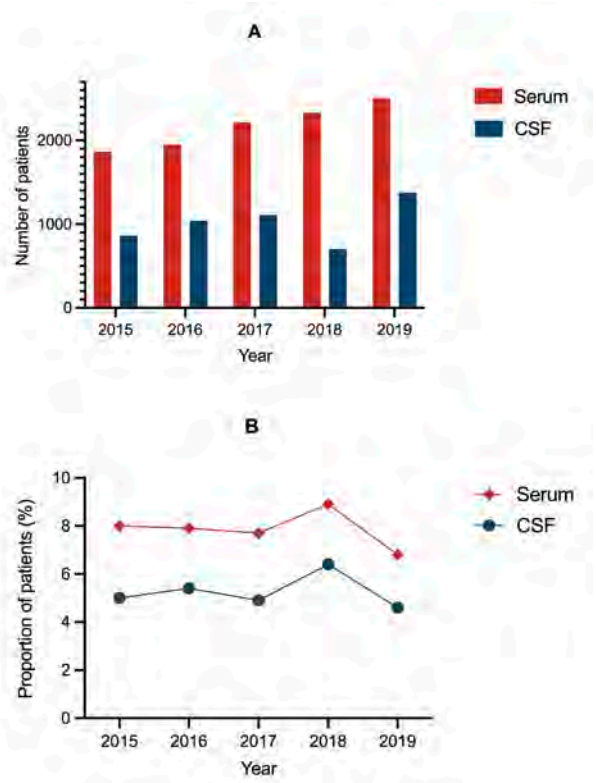
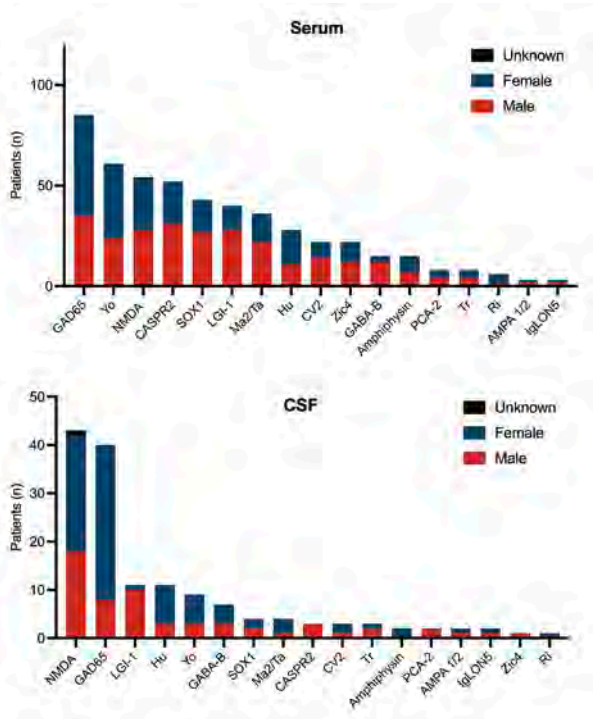
Background and aims: To estimate the 5-year incidence rate of autoimmune encephalitis (AE) and paraneoplastic neurological syndrome (PNS) in Sweden.
Methods: All patients who were tested for a neuronal antibody in Sweden between 2015 and 2019 were included. Patients in Healthcare region Mid Sweden (population 2.1 million) were invited to participate in a case ascertainment sub-study. AE and PNS cases were defined using established diagnostic criteria. Crude and age-adjusted incidence rates of AE and PNS in Healthcare region Mid Sweden were estimated.
Results: The number of tests for neuronal antibodies in Sweden increased between 2015 and 2019 from 1,867 to 2,505 (serum) and 863 to 1,376 (CSF) per annum. The frequencies of positive results were stable over the entire study period and the mean value was 6.1% for serum (CI95% 5.5–6.7), and 4.8% for CSF (CI95% 4.0–5.6). In total 125 patients tested positive for neuronal antibodies in Healthcare region Mid Sweden between 2015 and 2019. Of these, 94 were included and after case ascertainment, thirty-one cases of definite AE or PNS could be identified. The 5-year incidence rate of AE and PNS was 3.0 per million person-years (95%CI 1.9–4.1). The yearly incidence rates increased in the study period, from 1.5 per million person-years in 2015 (95%CI 0.0–3.2) to 4.3 per million person-years in 2019 (95%CI 1.5–7.1).



A) The total number of patients tested for a neuronal antibody in Sweden between 2015 and 2019 B) The proportion of patients (%) tested for a neuronal antibody that had a positive test result.



Antibody subgroups of patients who tested positive for a neuronal antibody in all of Sweden 2015–2019, serum and CSF displayed separately, sex distribution shown.

Table 1 – Crude and age-adjusted incidence rates of AE and PNS in Healthcare region Mid Sweden 2015-2019

Subgroup and time period	Crude incidence (CI95%)†	Age-adjusted incidence (CI95%)‡
AE+PNS 2015-2019	3.0 (1.9-4.1)	2.9 (1.8-3.8)
AE+PNS 2015	1.5 (0.0-3.2)	1.4 (0.0-2.9)
AE+PNS 2016	2.4 (0.30-4.6)	2.2 (0.027-4.2)
AE+PNS 2017	2.9 (0.58-5.2)	2.5 (0.30-4.6)
AE+PNS 2018	3.8 (1.2-6.5)	3.8 (1.2-6.5)
AE+PNS 2019	4.3 (1.5-7.1)	3.8 (1.3-6.3)
AE 2015-2019§	2.4 (1.5-3.4)	2.4 (1.4-3.2)
PNS 2015-2019	1.5 (0.72-2.2)	1.3 (0.66-2.0)
Anti-NMDAR encephalitis 2015-2019	0.58 (0.12-1.1)	0.58 (0.12-1.0)
Anti-LGI1 encephalitis 2015-2019	0.58 (0.12-1.1)	0.53 (0.11-0.95)

†Crude incidence rate per million person-years. ‡Age-adjusted incidence rates per million person-years standardized to the 2013 European Standard population. §AE= definite AE and definite anti-NMDA receptor encephalitis. The population of Healthcare region Mid Sweden contributed with 10 331 778 person-years between 2015–2019. AE= Autoimmune encephalitis; PNS= Paraneoplastic neurological syndrome.

Crude and age-adjusted incidence rates of AE and PNS in Healthcare region Mid Sweden 2015–2019

Conclusion: In this first epidemiological study of AE and PNS in Sweden the number of cases doubled from 2015 to 2019. This likely reflects increased availability of testing and awareness of these conditions.

Disclosure: The authors report no disclosures relevant to this abstract.

EPO-239

Correlation of disease activity and EQ-5D-3L-derived utility in myasthenia gravis patients in a Swedish national cohort

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Background and aims: Myasthenia gravis (MG) is a chronic neuromuscular disease causing motor fatiguability and weakness. The impact of MG on quality of life (QoL) is not well documented. Here, the objective was to explore correlations of either disease severity (MG-ADL) or MG QoL-ratings with the health outcome measure utility.

Methods: Patients were identified in the Swedish nationwide MG registry and included if simultaneous disease activity (MG-ADL) and QoL measures (MG-QoL and EQ-5D-3L) were available. Utility was derived from EQ-5D-3L using the UK Time Trade Off tariff.

Results: We included 121 patients (mean age 63, 45% female, 67% late-onset MG). Average utility was 0.7, compared to 0.83 in an age- and sex-adjusted reference population. Average utility was 0.85 (reference 0.83) in patients with no to minimal disease activity (MG-ADL $\leq$2) compared with 0.66 and 0.59 in patients with moderate and high disease impact (MG-ADL $\geq$3 and $\geq$6, respectively) (both reference 0.82). Negative correlations between either MG-ADL or MG-QoL, and utility were observed (ρ=-0.57 and -0.71, respectively, both $p<0.001$). In a multivariate regression model, adjusting for sex, age, and disease duration, change in utility was associated primarily with change in disease activity. Further stratifying MG-ADL into its items, change in self-care and diplopia were the strongest factors associated to change in utility.

Conclusion: In this real-life dataset of MG patients, we observed considerably impaired health status in patients with active disease. This indicates an unmet medical need, especially in those with high disease activity, in turn warranting further improvements in MG treatment and care.

Disclosure: Malin Petersson has nothing to declare. Fredrik Berggren is an employee and stockholder of UCB Pharma, Copenhagen, Denmark Ingrid Lindberg is an employee of UCB Pharma, Stockholm, Sweden Fredrik Piehl has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis. Susanna Brauner has received grants from UCB Pharma.

EPO-240

Neuro Virtual Hospital: a pilot study for a model of multidisciplinary remote management of neurological patients

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Background and aims: Some neurological diseases are difficult to diagnose and patients are often forced to move from an hospital to another, in search of a "second opinion" or a satisfactory "taking charge". This trend increases public expenditure and overload of the National Healthcare System. Alternative models are being developed to solve these problems, such as telemedicine. We carried out a pilot study to test the feasibility of the development of a virtual multicentric and multidisciplinary care system (Neuro Virtual Hospital) for patients suffering from complex neurological pathologies.

Methods: .We conducted this pilot multicentre study from April 2020 to June 2021, including six Italian centres. Seventy-three experienced specialists gathered into nine multidisciplinary teams which met virtually every month and took care of eighty patients affected by unusual clinical pictures which needed a multidisciplinary approach.

Results: The model reduced the accesses to the hospitals by 47%, resulting in a decrease of 1.78 for each case, and the time to get to a definite diagnosis or indication to treat by 66% compared to the traditional system. Most of the discussed cases were referred to Cerebrovascular Diseases Team (47.50%) and Neurooncology Team (26.25%).

Conclusion: This pilot study evaluated the first stages of the development of the virtual multidisciplinary and multi-centric model of care for neurological patients in Italy. This model will allow physicians from different medical fields and from different hospitals to meet remotely to take care of patients who require second opinion or multidisciplinary management, regardless of their possibility to access to secondary or tertiary-level centres.

Disclosure: Nothing to disclose.

EPO-241

Epidemiology of Antibody-positive Myasthenia Gravis in Sardinia, Italy

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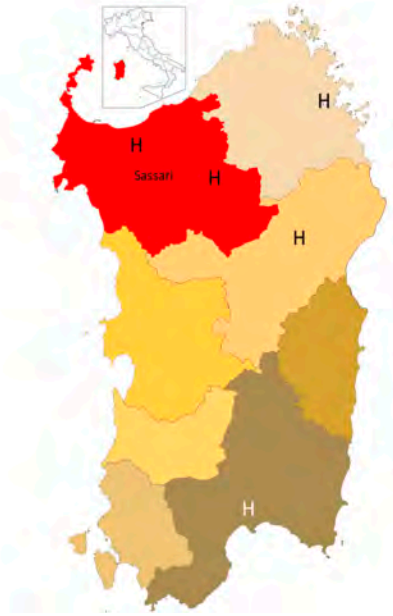
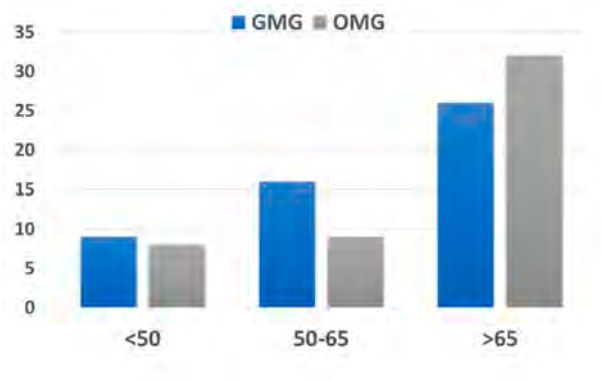
Background and aims: The global mean incidence and prevalence of myasthenia gravis (MG) have been assessed at ≈15 (range, 4-29)/million and 20 (range, 2-37)/100,000, respectively. Sardinia is a recognized area at higher risk for immuno-mediated disorders (e.g., multiple sclerosis). We assessed the incidence and prevalence of MG associated with AchR-IgG and MuSK-IgG in the district of Sassari.



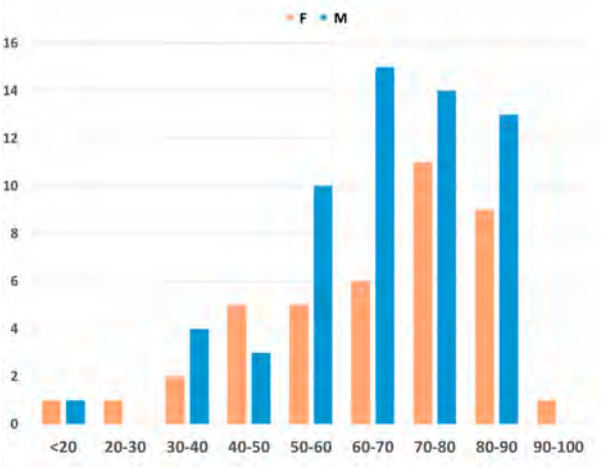
Study area: Sanitary district of Sassari; population: 325,288 (Jan 1, 2020)

Methods: From the Neurochemistry Laboratory of the University-Hospital of Sassari (reference laboratory for AchR-IgG/MuSK-IgG testing in the island since 1998) we retrospectively identified patients with: 1) AchR-IgG (titer ≥0.5 nmol/L) and/or MuSK-IgG (titer ≥100 pg/ml) positivity by radioimmunoprecipitation assay; 2) available medical records; and 3) residence within the district of Sassari. Incidence (January 2010-December 2019) and prevalence (on January 1, 2020; population 325,288) were calculated.

Results: Among 517 antibody-positive patients identified, 183 were included (incident, 97; prevalent, 165). We excluded 334 patients due to: 1) missing clinical information (n=65); 2) residency outside the Sassari district (n=168); 3) not classifiable as incident or prevalent (n=56); and 4) clinical phenotype not consistent with MG (n=45; median AchR-IgG titer, 0.7 [range, 0.5–5.5] nmol/L). The crude MG prevalence was 50.7/100,000 (95% CI, 43.4–58.9), whereas incidence was 29.8/1,000,000 person-years (95% CI, 24.3–36.2). Antibody specificities were AchR in 170 (92.9%; median titer 5.7 [range, 0.5–22]) and MuSK in 13 (7.1%; median titer 1,255 [range, 136-1–730]). Among incidence cases, age at disease onset was distributed as: <18 years (n=2; 2%); 18–50 years (n=14; 14.4%); 51-65 years (n=25; 25.8%); and >65 years (n=56; 57.7%).



Clinical phenotype distribution by age



Age and gender distribution of the patients

Conclusion: We report the highest incidence and prevalence of MG worldwide.

Disclosure: Nothing to disclose.

Headache 2

EPO-242

Persistence of Response With Eptinezumab Over 24 Weeks in Patients With Prior Migraine Preventive Treatment Failures

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Background and aims: In DELIVER, eptinezumab treatment showed greater reductions than placebo in monthly migraine days (MMDs). This analysis evaluated persistence of response to eptinezumab at the population and patient level and potential for response in initial non-responders.

Methods: DELIVER (NCT04418765) randomized adults with migraine and 2–4 prior preventive treatment failures to infusion with eptinezumab 100mg, 300mg, or placebo every 12 weeks. Migraine responder rates (MRRs [average percentage change from baseline in MMDs]) of ≥30%, ≥50%, and ≥75% over Weeks (Wks) 1–12 and 13–24, MRRs over 4-week intervals, and percentage of initial non-responders (Wks1–12) achieving response to their second infusion (Wks13–24) were calculated.

Results: Full analysis set: 890 patients (100mg, n=299; 300mg, n=293; placebo, n=298). Between Wks1–12 and Wks13–24, ≥30% MRRs increased from 65.9% to 70.4% (100mg), 71.0% to 74.5% (300mg), versus 36.9% to 43.1% (placebo; p<0. 0001 for both doses/timepoints). Four-week ≥30%, ≥50%, and ≥75% MRRs were generally maintained or increased over the 24-week period, with notable increases after the second eptinezumab infusion (Figure). Of patients with <30% response over Wks1–12, 34.7% (100mg) and 30.4% (300mg) versus 21.1% (placebo) achieved ≥30% response over Wks13-24, and 16.8% (100mg), 15.2% (300mg), vs 6.5% (placebo) achieved ≥50% response. With eptinezumab, ≥30% MRRs over Wks1–12 were maintained over Wks13–24 by >80% of patients, ≥50% MRRs by >70%, and ≥75% MRRs by >60%.

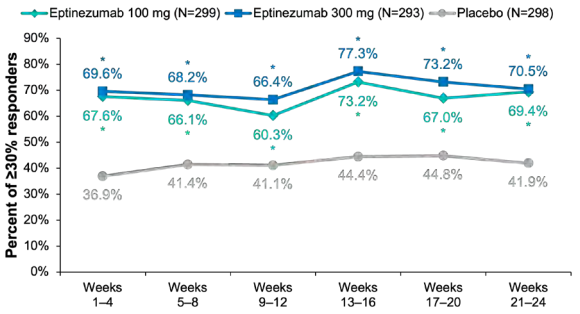

Figure. Percentage of patients achieving a ≥30% migraine response over 4-week intervals. *p<0.0001 vs placebo

Conclusion: Most patients responding to eptinezumab during Wks1-12 maintained response during Wks13-24, with MRRs further increasing with a second infusion. Approximately one-third of initial non-responders became responders after their second infusion.

Disclosure: MA: Consult and honoraria: :Lundbeck. RL-Consultant, ad board,honoraria: Lundbeck Allergan, AAN, AHSAmgen, Biohaven Pharm, BioVision, Boston Scientific, Dr. Reddy's Laboratories, electroCore Medical, Eli Lilly, eNeura Therapeutics, GSK, Merck, Pernix, Pfizer, Supernus, Teva Pharm, Trigemina, Vector, Vedanta. SStock:Biohaven Pharm, Manistee. Compensation: eNeura,Biohaven Pharm.. Research:Amgen, MRF,NHF. JA: IConsultantAlder, Amgen, Allergan, Electrocore, Eli Lilly, Promius, Teva, Impel, Satsuma, Zosano, Revance, Alpha Sites Consulting, Neurodiem, BDSI. CME: Miller Communications, Avent, Peer View, Forefront. SB: : Allergan, Amgen, Electrocore, Eli Lilly, Promius, Teva. JV-Consultant: Teva, Novartis, Lundbeck, Abbvie, Lilly. Honoraria: -Teva and Lilly. Travel support:-Teva, Abbvie. Ad Board: Teva, Novartis, Lundbeck, Abbvie, Lilly. President of BHS. SS- Grants::-Novartis, Uriach. Consultant:: Novartis, Allergan-Abbvie, Teva, Lilly, Lundbeck, Pfizer, NovoNordisk, Abbott, AstraZeneca. Honoraria: -Novartis, Allergan-Abbvie, Teva, Lilly, Lundbeck, Pfizer, NovoNordisk, Abbott, AstraZeneca. Travel support: Lilly, Novartis, Teva, Lundbeck. President ofESO. Second VPEHF DM-Consultant:: Novartis, Eli Lily, Teva, Lundbeck. Honoraria:Allergan, Eli Lily, Novartis, Lundbeck, Teva. Travel support: Allergan, Genesis, Eli Lily, Novartis, Lundbeck, Teva. President,HHS; Co-Chair, Headache Panel EAN. CLC-Employee: H Lundbeck A/S BS-Employee: H Lundbeck A/S AE-Employee: H Lundbeck A/S

EPO-243

Investigating the role of neuropeptides in migraine during anti-CGRP treatment: an exploratory study.

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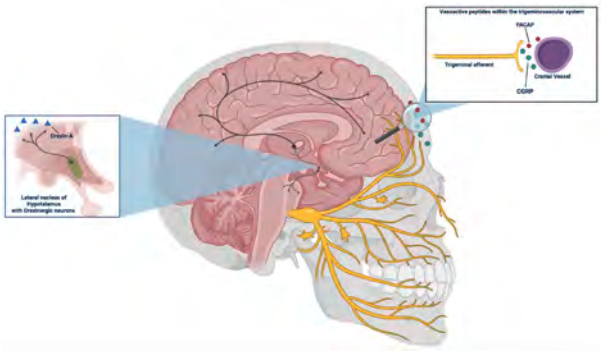
Background and aims: Migraine is a common disabling neurological condition that has been linked to the activity of specific neuropeptides. Of note, anti-Calcitonin Gene Related Peptide (CGRP) targeting therapies opened a new era in migraine prophylaxis.



Putative role of neuropeptides in migraine pathophysiology: a focus on CGRP, OxA and PACAP-38

Methods: In order to investigate the effects of such novel treatment on neuropeptides modulation, sixteen consecutive migraine patients underwent plasmatic dosage of CGRP, Orexin A (OxA) and Pituitary Adenylate Cyclase-Activating Peptide-38 (PACAP-38). Measurements were obtained at baseline (T0) and after six-month treatment (T1) along with the collection of clinical data. Plasmatic levels were then compared with non migrainous controls.
Results: In line with previous studies, results confirmed treatment efficacy. OxA and PACAP-38 levels were significantly higher in patients at baseline ($p<0.05$ and $p<0.001$ respectively) compared to control group. OxA emerged as an inverse independent predictor of clinical response ($p<0.05$). Basal CGRP levels inversely correlated with clinical outcome at T1.
Conclusion: Our pilot study suggests on one hand a possible association between OxA and clinical outcome; on the other hand it questions the role of baseline CGRP as a possible predictor of clinical response to treatment.
Disclosure: Nothing to disclose.

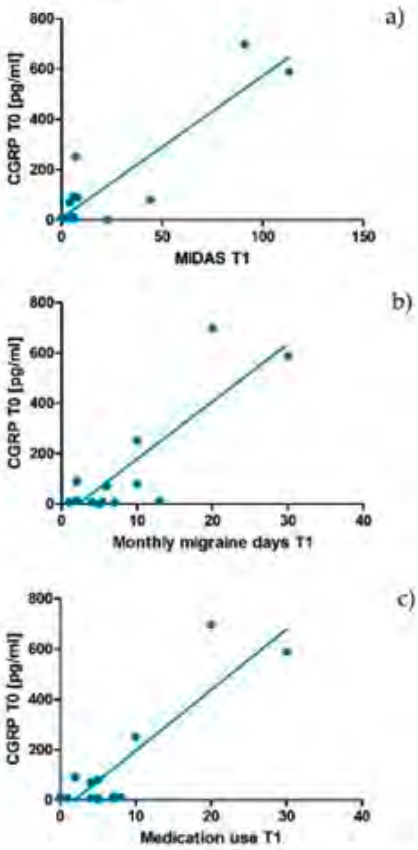
Table 1. Neuropeptides plasmatic concentration at T0. Data is expressed as mean ± standard deviation.

	Patients T0	Controls	p value
CGRP [pg/ml]	121.65 ± 214.10	30.77 ± 60.60	0.120
PACAP [pg/ml]	212.75 ± 41.68	126.83 ± 43.95	<0.001
Orexin A [ng/ml]	0.88 ± 0.24	0.73 ± 0.21	0.055

Table 2. Plasmatic neuropeptides concentration in the anti-CGRP treated patients. Data is expressed as mean ± standard deviation.

		Patients T0	Patients T6	p value
Erenumab (N=5)	**CGRP** [pg/ml]	156.6 ± 244.3	121.8 ± 210.4	0.186
	PACAP [pg/ml]	228.1 ± 50.1	219.1 ± 37.12	0.625
	Orexin A [ng/ml]	0.777 ± 0.294	0.887 ± 0.101	0.313
Fremanezumab (N=5)	**CGRP** [pg/ml]	73.47 ± 105.6	111.4 ± 173.6	0.313
	PACAP [pg/ml]	187.6 ± 14.45	203.7 ± 21.57	0.063
	Orexin A [ng/ml]	0. 934 ± 0.223	0.943 ± 0.167	1.00
Galcanezumab (N=6)	**CGRP** [pg/ml]	133.5 ± 277.9	870.3 ± 19.19	0.031
	PACAP [pg/ml]	220.9 ± 45.71	225.8 ± 61.51	1.00
	Orexin A [ng/ml]	0.927 ± 0.213	1.037 ± 0.210	0.688

Figure 2. Correlations between CGRP at T0 and clinical outcomes at T1



a) Correlation between CGRP at T0 and MIDAS at T1, Pearson correlation r = 0.897 , p<0.0001

b) Correlation between CGRP at T0 and MMD at T1, Pearson correlation r = 0.843 , p<0.0001

c) Correlation between CGRP at T0 and monthly acute medication use at T1, Pearson correlation r = 0.879 , p<0.0001

EPO-244

"Preventive oral treatment in migraine: efficacy and drop-out rates observed at a tertiary headache center."

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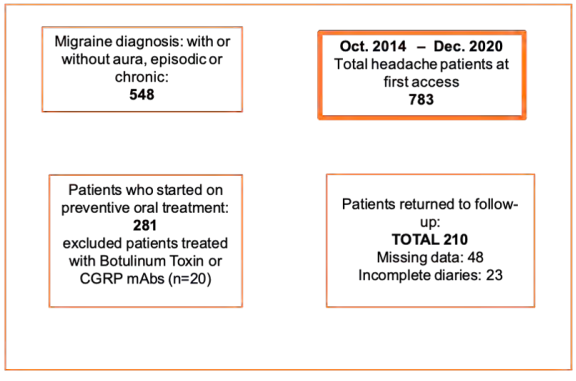
Background and aims: Migraine is a common and disabling neurological condition. Despite advances in the field, some patients remain without symptomatic pain relief. Our analysis aim to study the short and long-term effect of preventive treatment in a cohort of migraine patients, enlightening possible predictive factors for ineffectiveness and also analyzing the preventive's drop-out rates, clarifying the underlying reasons
Methods: This retrospective analysis included 210 patients who received a diagnosis of migraine without aura (MO), migraine with aura (MA) or chronic migraine (CM), according to ICHD-3 diagnostic criteria, with indication for prophylactic treatment. Three groups were defined and studied regarding the efficacy of oral preventives and drop-out rates: group A referred to patients treated with a first preventive, group B with a second and group C a third respectively.
Results: Overall efficacy of our preventive treatment was low with 40% of patients improving with their first preventive. Also, successive prophylactic attempts were associated with progressively lower rates of efficacy. Patients in whom coexisted MOH had lower rates of preventive inefficacy. The preventive's drop-out rates observed were also high (reaching 63.2% in subgroup C patients) with adverse drug reactions such as weight gain and cognitive dysfunction being the main reason for this.

The flowchart depicting patient selection is shown on fig. 1.



Conclusion: The modest effect of the oral preventive drugs as well as the high proportion of patients who dropped out due to drug side events confirm that in a significant proportion of patients, oral preventives can only delay a more focused therapeutic approach such as the new therapies with monoclonal CGRP antibodies.
Disclosure: Nothing to disclose.

EPO-245

Direct switch from onabotulinumtoxin A to erenumab in multidrug-resistant chronic migraine with medication overuse

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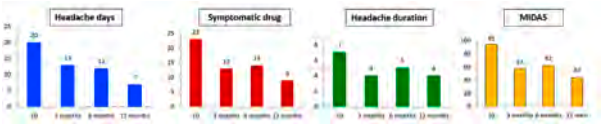
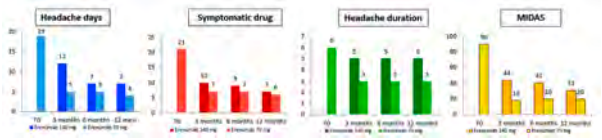
Clinical Unit of Neurology, School of Neurology, Headache Centre, Department of Medicine, Surgery and Health Sciences, University Hospital and Health Services of Trieste, ASUGI, University of Trieste, Trieste, Italy

Background and aims: Aim of this study was to evaluate the therapeutic effect of a direct switch from onabotulinumtoxin A (BoNTA) to erenumab in multidrug-resistant chronic migraine with medication overuse.
Methods: After minimum 4 different ineffective prophylaxes tried, all subjects performed 3 unsuccessful sessions of BoNTA 195 U. Three months later they received erenumab 70 mg at time 0 (T0), incrementable to 140 mg after 3 months (T1). Therefore, patients were evaluated after 6 (T2) and 12 months (T3). Subjects had not to use other prophylactic drugs. Demographic and clinical data were analyzed with SPSS 24.0.
Results: 11 patients (3 males, 8 females, mean age 44±11) were enrolled. Subjects had used 7±1 ineffective migraine prophylactic molecules. Symptomatic medications overused were triptans (63.6% of cases), analgesics combinations (18.2%), analgesics in association (9.1%), non-steroidal anti-inflammatory drugs (9.1%). 50%, 75% and 100% responders were 54.6%, 18.2% and 9% of patients respectively. All headache outcomes improved from T0 to T3 (days of headache/month: 20±5 at T0, 7±6 at T3; attacks duration [hours]: 7±1 at T0, 4±2 at T3; symptomatic drugs/month: 23±7 at T0, 9±6 at T3; MIDAS: 95±38 at T0, 44±40 at T3). Out of the six patients responders, 3 switched from erenumab 70 to 140 mg with further improvement (days of headache/month: 12±6 at T1, 7±1 at T3; symptomatic drugs/month: 10±2 at T1, 7±2 at T3; MIDAS: 44±15 at T1, 31±8 at T3).



Improvement of headache parameters in responder patients



Comparison in clinical response between patients receiving erenumab 70 and 140 mg

Conclusion: Innovatively, a direct shift from onabotulinumtoxin A to erenumab is effective in multidrug refractory chronic migraine with medication overuse.
Disclosure: No conflicts of interest to declare.

EPO-246

Clinical and therapeutic characteristics of a series of 106 patients with epicrania fugax

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Background and aims: Epicrania fugax (EF) is a headache included in the research appendix of current edition of International Classification of Headache Disorders. It is defined by brief, recurrent pain attacks, rapidly radiating forwards or backwards across the surface of one hemicranium. We aim to present characteristics of a large series of patients.
Methods: Prospective observational study of patients attended in a headache unit from March-2008 (first description of EF) to January-2023. We collected clinical and therapeutic data.
Results: We included 106 patients (79 females, 27 males). Age at onset was 46.8±17 years (16–84) with time between onset and diagnosis of 21.5±34.2 months (1–240). In 69 cases (65.1%) EF was a classic forward variant, in 34 (32.1%) a backward EF and in 3 (2.8%) paroxysms described both trajectories. In 86 (82.1%) the pain paroxysms occurred on only one side, in 14 (13.2%) on both sides and in 5 (4.7%) trajectory was sagittal. 36 (34%) patients presented an interictal pain in stemming area, generally circumscribed fulfilling diagnostic criteria of nummular headache (25 cases). Pain intensity was 7±1.8 (1–10) in verbal analogical scale (VAS). Quality was mainly electric (70 cases, 66%). In 67 patients (63.2%) it was necessary to prescribe a preventive treatment, being the most used lamotrigine (32). Lack of response requiring additional preventatives was observed in 17 cases (16%).
Conclusion: EF is not an uncommon diagnosis in a headache unit. It may be a disabling headache syndrome requiring frequently preventive therapy.
Disclosure: No potential disclosures related to this work.

EPO-247

Are PROMs passing the message?

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[1]Hospital da Luz Headache Center, Neurology Department, Hospital da Luz Lisboa, Lisbon, Portugal, [2]Pharmacy Department, Universidade Federal do Rio Grande do Norte, Natal, Brazil

Background and aims: Patient-reported outcome measures (PROMs) are of increasing importance in disease outcome monitoring in headache disorders, yet its implementation in real-life clinical practice is challenging and may influence its reliability.
Methods: We applied two identical PROMs (HALT-90 and MIDAS) simultaneously in every clinical evaluation (each 3 months) over a year to a series of patients treated with monoclonal antibodies for migraine in real life clinics. We calculated intra-individual agreement for each question in each visit, using the intraclass correlation coefficients (ICC) and analysis the missing data over the 4 visits.
Results: Our sample included 92 patients 92.4% females of 44.8 years-old on average. Missing data increased from 14% in the first to 58% in the last visit. Moderate (0.50 to 0.75) and poor (<0.50) ICC were observed all but one item of these PROM in different evaluations. No learning effect was detected.
Conclusion: We observed a reliability variability in patients motivation and responses to PROMs in repeated applications, This information serves as an alert to clinicians to the limitations of PROM use in real-life clinical practice.
Disclosure: Nothing to disclose.

EPO-248

Erenumab discontinuation in migraine patients: final results of the APOLLON study

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Background and aims: The monoclonal antibody erenumab is an anti-CGRP pathway target developed for the prevention of episodic and chronic migraine. A recent update to the EHF guideline on the use of monoclonal antibodies suggests pausing the treatment after 12 to 18 months. There is, however, only limited data on the impact of treatment discontinuation. This study aims to assess the significance of a drug holiday in patients treated with erenumab.
Methods: Patients enrolled in the 128-week open-label APOLLON study, assessing the long-term safety and tolerability of erenumab in migraine in 701 patients in Germany, were allowed to pause the treatment after 12 weeks of continuous treatment with erenumab. Impact of treatment discontinuation on monthly migraine days (MMD) was assessed 4 weeks prior to, during and 12 weeks after the medication-free epoch.
Results: This final analysis includes details on the drug holiday and its impact on the respective patients' MMD. Treatment interruption amounted to about 107 days (median). More than half the patients returned to treatment after drug holiday with the majority thereof returning to their previous dose. At drug holiday initiation, the average MMD was 4.2±2.9 days. After an increase to 7.2±5.7 MMD in the second month of treatment discontinuation, the average MMD decreased again to 4.5±2.7 MMD within the first 2 months after the drug holiday.
Conclusion: Providing insights into the patients´ response after erenumab treatment discontinuation and subsequently after the re-uptake of treatment, the results can further inform current guidelines on the treatment of migraine with the monoclonal antibody erenumab.
Disclosure: H. Göbel received honoraria for consulting and lectures from Allergan, Almirall, Astra Zeneca, Bayer Vital, Berlin-Chemie, Bionorica, Bristol-Myers-Squibb, Elli Lilly, Fujisawa, GlaxoSmithKline, Grünenthal, Hermal, Hormosan, Ipsen-Pharma, Janssen-Cilag, Johnson& Johnson, Krewel-Meuselbach, Klosterfrau, Lichtwer, Menarini Pharma, Merz Pharmaceuticals, Minster Pharmaceuticals, MSD, Novartis Pharma, Pfizer, Pharmacia, Sandoz, Schaper und Brümmer, Schwarz-Pharma, Teva, Weber&Weber, Smith Kline Beecham. M. Koch is an employee of Novartis AG. C. Weiss is an employee of Novartis Pharma GmbH.

EPO-249

Impact of preventive anti-CGRP therapies on Insomnia Severity Index scale in patients with migraine

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Headache Unit, Neurology Department, Hospital Universitario de la Princesa & Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Universidad Autónoma de Madrid, Madrid, Spain

Background and aims: Previous studies shown that insomnia is a common complaint among individuals with migraine. However, there is scarce information of the impact of anti-CGRP therapies on insomnia. We aimed to investigate possible sleep changes in patients with migraine treated with anti-CGRP preventive therapies using the validated sleep questionnaire Insomnia Severity Index(ISI).
Methods: We analyzed a cohort of patients with migraine attended at the Headache Unit of a tertiary hospital who completed one year of anti-CGRP treatment and had ISI scale scores at baseline and 12 months. We collected demographic data, headache variables and ISI scale scores during follow-up visits at 3, 6 and 12 months. The primary endpoint was the ISI scale score at 12 months after anti-CGRP preventive treatment compared to baseline.
Results: A total of 17 patients were included. Among them, 88.23%(15/17) were women, mean age 50(13.8), 94.2%(1/17) chronic migraine, mean number of preventive treatments 10(3.5). There was an improvement in the ISI scale score in 60% of patients at 3 months 60% at 6 months and 70.6% at 12 months. We found a statistically significant reduction in the mean ISI score at 12 months compared to baseline [12.12(5.9);8.12(6);p=0.023], changing from sub-threshold insomnia(8–14) to not clinically significant insomnia(0–7).
Conclusion: According to our study, 70% of patients with migraine under anti-CGRP therapies had an improvement on ISI scale score at 12 months with a statistically significant reduction and score scale change, suggesting a potential benefit of anti-CGRP therapies on sleep; further studies with larger sample size are needed.
Disclosure: Alicia González-Martinez Dr. Alicia Gonzalez-Martinez has received education funding from Lilly, Novartis, Roche, TEVA, Abbvie-Allergan, & Daichi. Dr. S. Quintas has received speaker honoraria from Lilly and Novartis. Dr. José Vivancos has served as speaker, consultant, and advisory member for or has received research funding from MSD, Pfizer, Daychii-Sankyo, Bayer, Sandoz, Bristol Myers Skibb, Lilly, Boehringer Ingelheim, Almirall, Sanofi-Aventis and Ferrer Pharma. Dr. Ana Beatriz Gago-Veiga has received honoraria from Lilly, Novartis, TEVA, Abbvie-Allergan, Exeltis & Chiesi.

EPO-250

Commonalities and differences between COVID-related headache and COVID vaccine-related headache

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Background and aims: To compare the clinical phenotype of coronavirus disease (COVID)-related headache and COVID vaccine-related headache.
Methods: Case-control study including adult patients with headache attributed to COVID (cases) and patients with COVID vaccine-related headache (controls), matched for age, sex, and prior history of headache. A standardized questionnaire was administered, assessing demographic variables, prior history of headache, headache phenotype, and associated symptoms.
Results: 238 patients were enrolled, including 143 cases and 95 controls. There were no differences regarding demographic variables and prior history, except for family history of headache. After adjusting for multiple comparisons, patients with COVID-19 related-headache exhibited a higher frequency of arthralgia, diarrhea, dyspnea, chest pain, expectoration, anosmia, myalgia, odynophagia, rhinorrhea, cough, and dysgeusia. Patients with COVID-19 related-headache had a more prolonged daily duration of headache and described the headache as the worst headache ever experienced. Patients with COVID-19 vaccine-related headache, experienced more frequently pain in the parietal region, phonophobia, and worsening of the headache by head or eye movements. Cough (Odds ratio (OR): 21.316; 95% confidence interval (CI): 4,298-105,725) and rhinorrhea (OR: 15.433; 95% CI: 3,104-76,721) were associated with COVID-19 related-headache in the multivariate analysis.
Conclusion: Headache caused by SARS-CoV-2 infection and COVID-19 vaccination related-headache present more similarities than differences, supporting a shared pathophysiology. In both cases, headache may arise from the activation of the innate immune response. The main differences between COVID-19 related-headache and COVID-19 vaccine related-headache were observed regarding frequency of associated symptoms.
Disclosure: The authors have not conflict of interest.

EPO-251

Brain derived neurotrophic factor during migraine attacks

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Background and aims: Migraine is a very common neurologic disorder. The mechanisms involved in the generation of migraine attack are probably multifactorial and are not fully understood. Brain derived neurotropic factor (BDNF) is a neurotrophin that has been implicated in the generation and modulation of pain. The present study aimed to investigate the role and importance of brain neurotrophic factor in the clinical course of migraine.
Methods: This study sponsored by International Headache Society. In our research work, the main contingent of patients were collected in the clinical hospital of Tashkent medical academy, Uzbekistan. 78 patients aged 18 to 44 years (average age 32.8±7.8) with episodic migraine were selected for the study. The control group consists of 30 healthy volunteers (average age 29.9±3.7).
Results: The increase in BDNF was 83.3% in patients with migraine attacks and 16.67% in patients without migraine attacks, while the decrease in BDNF was 16.67% in patients with attacks and 83.3% in patients without migraine attacks. In this case, x^2 was 30.9, r=0.29, the hazard ratio was 25.0. The Odds Ratio was 5.0. The Risk Difference was 66.6. Fisher-Exact index was 0.000001.
Conclusion: It was observed that the concentration of BDNF in the blood serum of patients increased during migraine attacks. This, in turn, leads to a decrease in the quality of life of patients with acute migraine, and a decrease in the effectiveness of treatment.
Disclosure: This research work founded by International headache society.

EPO-252

Post-dural puncture headache in Kuwait: A hospital-based study

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Background and aims: Lumbar puncture (LP) is a common neurological procedure that can be complicated by PDPH after both diagnostic and therapeutic procedures. We aim to identify the incidence, risk factors and clinical characterization of PDPH in the inpatient setting of the main tertiary neurology hospital in Kuwait.
Methods: We conducted a prospective observational cohort study that included patients who were admitted to neurology department at Ibn Sina hospital, Kuwait, over 2-year period, on whom LP was performed for diagnostic and/or therapeutic reasons.
Results: A total of 285 patients were included; 225 females (78.9%), mean age of 32.9±11.7 years. PDPH was reported by 84 patients (29.5%), with mean headache onset of 1.7± 0.8 days, and mean duration of 2.4 ± 2.1 days. The commonest headache type was dull aching in 49 patients (58.3%). Headache severity was mild/moderate in 64 patients (76.2%), with mean NRS of 4.1±0.9. Most PDPH (99.3%) resolved with conservative medical management. In multivariate logistic regression model, there was a statistically significant correlation between development of PDPH and young age (p=0.001), female gender (p=0 .001), low BMI (p<0 .001), pre-LP headache (p=0.001), history of previous PDPH (p=0.001), and number of LP attempts (p<0.001).
Conclusion: Our findings in the main tertiary neurology hospital in Kuwait were in line with literature findings. Younger age, female gender, lower BMI, pre-procedural headache, previous history of PDPH, and number of LP attempts were found to be independent risk factors for developing PDPH. To our knowledge, this study represents the first comprehensive description of PDPH in a population from the Arabian Gulf Region.
Disclosure: The authors report no sources of funding and no conflicts of interest.

EPO-253

Treatment with anti-CGRP monoclonal antibodies in patients with idiopathic intracranial hypertension: a pilot study

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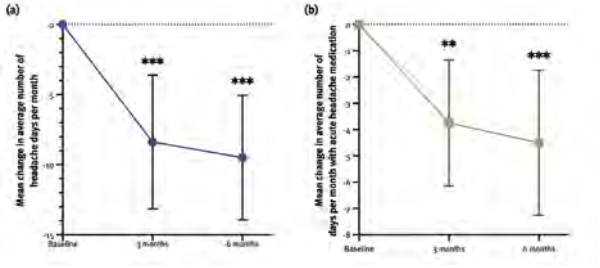
Background and aims: Idiopathic intracranial hypertension (IIH) is a disease mostly occurring in young obese women, often presenting with chronic migraine-like headache. Monoclonal antibodies (mAbs) against calcitonin gene-related peptide (CGRP) or its receptor are a novel effective preventive treatment in migraine patients.
Methods: In this pilot single-centre study, pwIIH with resolved papilledema, yet persisting migraine-like headache, were offered to receive anti-CGRP mAbs. The primary endpoint was mean change in number of headache days/month after three (M3) and six months (M6). Secondary endpoints were defined as follows: (1) reduction of acute headache medication use, (2) improvement of headache days (≥50%) or headache freedom, (3) adverse events (AE).
Results: Eight pwIIH (mean age 30.5 years [SD 10.3], 100% female, median disease duration 1.2 years [IQR 0.4–6.8]) were included (erenumab: 6, fremanezumab: 2). Mean number of headache days/month at baseline was 15.3 (5.3). The latter was reduced by 8.4 (5.7) and 9.5 (5.3) days at M3 and M6, respectively (p<0.001). Mean number of days/month with acute headache medication was reduced at M3 (–3.8 [2.9], p=0.004) and M6 (–4.5 [3.3], p<0.001). Improvement in headache days was seen at M3 (4 [50.0%]) and M6 (5 [62.5%]), whereas headache freedom was achieved in one patient at M3 but none at M6. No serious AE were observed. One patient experienced transient injection-site reaction, and no infections or elevation of liver enzymes were noted. There was no discontinuation of treatment.



Mean number of headache days per month (a) and mean number of days per month with acute headache medication (b) were significantly reduced at M3 and M6.

Conclusion: Anti-CGRP mAbs may be a safe, efficient and well-tolerated treatment option in pwIIH with migraine-like headache persisting after papilledema resolution.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-254

Isolated headache in cerebral venous sinus thrombosis due to vaccine-induced immune thrombotic thrombocytopenia

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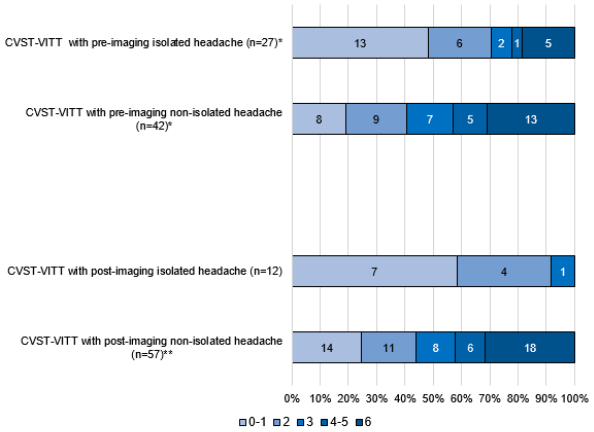
Background and aims: Cerebral venous sinus thrombosis due to vaccine-induced immune thrombotic thrombocytopenia (CVST-VITT) is a rare adverse event occurring after SARS-CoV-2 vaccination. Our aim was to analyse mortality and functional outcomes of CVST-VITT patients presenting with isolated headache.

Methods: Data originated from an international registry of patients with post–SARS-CoV-2 vaccination CVST with cases reported until 10 May 2022. We compared in-hospital mortality and functional outcomes of CVST-VITT patients presenting with isolated and non-isolated headache, assessed pre- and post-imaging. Pre-imaging isolated headache was defined as headache without other neurological signs/symptoms and post-imaging headache as pre-imaging headache without intracerebral lesions on admission neuroimaging.
Results: Of 128 CVST-VITT patients, we included 29 (23%) patients with pre-imaging isolated headache and 44 (34%) with non-isolated headache. Post-imaging, these numbers were 12 (9%) and 61 (48%), respectively. In the pre-imaging isolated headache group (21/29, 72% women and median age 35 years [IQR 25–47]) the in-hospital mortality was 5/29, 17% (vs 13/44, 30% in non-isolated, p=0.277). Post-imaging, none of the isolated headache patients died (0/12, 0%, vs 18/61, 30% in non-isolated, p=0.031). Independency at discharge among pre-imaging isolated headache patients was 19/27, 70% (vs 17/42, 40%, in non-isolated, p=0.026) and among post-imaging isolated headache patients - 11/12, 92% (vs 25/57, 44%, in non-isolated, p=0.003).

Figure 1. Discharge modified Rankin Scale scores of CVST-VITT patients with isolated and non-isolated headache pre- and post-imaging.



CVST = cerebral venous sinus thrombosis; VITT = vaccine-induced immune thrombocytopenia, as defined by Pavord et al. *two missing values; **four missing values

Figure 1. Discharge modified Rankin Scale scores of CVST-VITT patients with isolated and non-isolated headache pre- and post-imaging.

Conclusion: Despite their apparent benign presentation, CVST-VITT patients presenting with isolated headache without other neurological signs/symptoms are still at risk of poor functional outcome. Patients with isolated headache and absence of focal lesions on baseline neuroimaging had no mortality and a good functional outcome.
Disclosure: This research was funded by The Netherlands Organization for Health Research and Development (ZonMw, grant number 10430072110005) and the Dr. C.J. Vaillant Foundation. The funding organizations had no role in gathering, analysing, or interpreting the data.

EPO-255

Design of the ContemporAry ProspecTive Understanding of Migraine Real-world Evidence (CAPTURE) Study

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Background and aims: Insufficient longitudinal evidence is available describing the impact of migraine. This global study will assess how headache/migraine frequency, disability, and treatment patterns change over a 2-year period in individuals being treated for migraine.
Methods: ContemporAry ProspecTive Understanding of Migraine Real-world Evidence Study (CAPTURE) is a 2-year, global, observational, longitudinal, prospective study that will enroll individuals ≥18 years of age being treated for migraine. Participants will be stratified into 3 baseline monthly headache day (MHD) cohorts: 4–7 days; 8–14 days; ≥15 days. Eligibility criteria include men/women diagnosed with migraine for ≥1 year, ≤50 years of age at migraine onset, taking ≥1 migraine medication, and a history of ≥4 MHDs in the 3 months prior to screening, which was confirmed prospectively with headache e-diary data in the 30-day screening period. Key study design elements and endpoints are depicted in the Figure and Table.
Results: The target enrolled sample size is approximately 2000 (cohort 1: 30% [n=600]; cohorts 2–3: 35% [n=700 each]). Patients will be enrolled from approximately 135 sites in 15 countries. The target for first patient enrollment is early 2023 and the last patient completion is anticipated to be late 2025. The study will collect clinical outcomes, patient-reported outcomes, and changes in the number of patients among the migraine cohorts. Only the methodology of this study will be described.
Conclusion: CAPTURE will provide a better understanding of headache/migraine frequency, disability, and treatment patterns in individuals being treated for migraine and will be one of the first global prospective longitudinal studies of its kind.
Disclosure: Study supported by AbbVie.

EPO-256

Work impact and cost-effectiveness of anti-CGRP monoclonal antibodies in patients with migraine

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Background and aims: Migraine is one of the main causes of disability worldwide. Anti-CGRP drugs are effective preventive drugs, but their use is restricted in many countries due to the high cost. Objective: To study the efficacy and cost-effectiviness of anti-CGRP monoclonal antibodies (mAbs) in patients with migraine.
Methods: A prospective cohort study of consecutive migraine patients treated with anti-CGRP mAbs (erenumab, fremanezumab and galcanezumab) in a specialized headache clinic. Migraine characteristics and the work impact scale (WPAI) were compared between baseline (M0) and at 6 months (M6). Using WPAI and the average hourly wage in Catalonia, we calculated indirect savings attributable to the improvement in absenteeism and presenteeism. A cost-effectiveness study was performed considering the different costs and savings of treating with mAbs (Table 1).

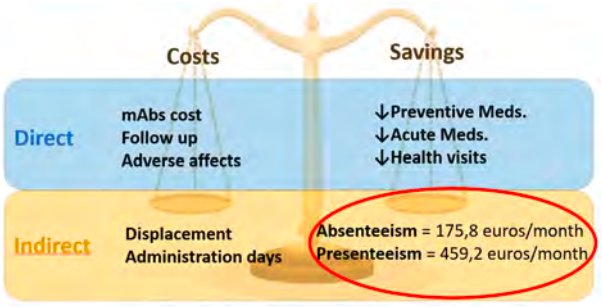

Table 1.- Variables considered in the cost-effectivity. The savings in indirect labor costs (absenteeism and presenteeism) attributable to mAbs are shown in the table.

Results: From 130 treated working age patients, 82 were employed (71 women; mean age 47.5 years, SD=8.6). 56% (46/82) were responders and 44% (36/82) were non-responders, with no significant differences in baseline characteristics. Statistically significant reductions between M0 and M6 were found for the principal clinical variables (Resp, NResp p<0.001), Absenteeism (Resp, p=0.015) and Presenteeism (Resp, NResp p<0.001) (Table 2, Figure 1). The average saving in indirect costs per patient at M6 were: absenteeism 175.8 euros/month and presenteeism 459.2 euros/month. Considering the monthly cost of anti-CGRP mAbs used, the estimated monthly savings significantly exceeded the expenses of these drugs.

	Time M0	Time M6	Difference	Resp.	No Resp.
Days of migraine/month, mean (SD) *P value*	19,2 (7,3)	9,7 (7,6)	-9,5	-14,5 **p<0,001**	-3,2 **p<0,001**
Migraine intensity, mean (SD) *P value*	1,3 (0,6)	0,6 (0,48)	-0,8	-1,04 **p<0,001**	-0,4 **p<0,001**
Acute treatment days, mean (SD) *P value*	12,8 (6,1)	6,8 (4,9)	-6	-8 **p<0,001**	-3,8 **p<0,001**
Absenteeism, hours/week (SD) *P value*	4,8 (9,9)	2,4 (6,8)	-2,4	-3,9 **p=0,015**	-0,5 P=0,66
Presenteeism, % (SD) *P value*	41,1% (31,7)	16,6% (24,9)	-24,5%	-25% **p<0,001**	-23,75% **p<0,001**

Table 2.- Results of the comparisons between M0 and M6 Absenteeism = Lost work hours due to migraine in the last week / (Number of work hours in the las week + Total of lost hours in the last week). Presenteeism = Work productivity due to migraine.

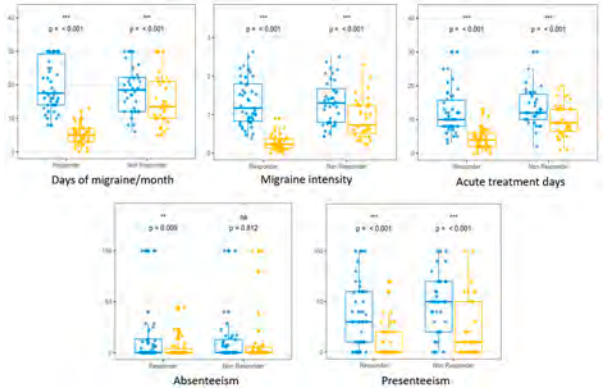

Figure 1.- Graphic representation of the main dependent variables. In blue the results at baseline (M0) and in yellow the results at 6 months (M6); for both responders (>50% reduction in headache days/month) and non-responders (<50% reduction in headache

Conclusion: The use of anti-CGRP mAbs generates a positive impact in the workforce reducing absenteeism and presenteeism. This benefit overcomes the expenses from the use of anti-CGRP mAbs in our cohort.
Disclosure: No conflicts of interest to disclose.

Neuroimmunology 2

EPO-257

Clinic and laboratory predictive factors in different types of encephalitis: the ENCOVID multicentre study

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Background and aims: Encephalitis is defined by the presence of an inflammatory process of the brain in association with clinical evidence of neurologic dysfunction. The diagnosis and treatment are still challenging and prognostic studies are currently lacking. We aimed to investigate the predictive factors associated with poor outcomes in a large spectrum of subjects with different subtypes of encephalitis.

Methods: In this observational multicenter study, 216 patients diagnosed with 4 different types of encephalitis were recruited. The four groups were compared through ANOVA and k2 test, were appropriate. Linear and logistic regression models explored predictors of mortality and worse progression of the disease.

Results: The different types of encephalitis showed several clinical and laboratory differences. Linear regression analysis confirmed lymphocytes at admission (p=0.025) and CSF cells count (p=0.035) as the strongest predictive factors of poor outcomes, independently from demographic, clinical and laboratory characteristics. Logistic regression analysis identified apathy (p=0.018) as the most significant predictor of mortality, adjusting for demographic features and neurologic/systemic symptoms.

Conclusion: In patients with encephalitis, CSF cells count and blood lymphocytes value appear to indicate worse disability at discharge. Apathy, on the other hand, is the strongest predictor of mortality, independently from the diagnosis. Further prospective studies are needed to confirm our findings, to identify patients at high risk of mortality and poor outcomes, and to develop specific strategies for prognostic improvement.

Disclosure: All the authors reported no disclosures.

EPO-258

Clinical profile, and treatment outcomes of autoimmune encephalitis: Experience from a single centre study in South Asia

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Background and aims: Autoimmune encephalitis (AE) encompasses a spectrum of non-infectious, immune mediated neurological disorders, with pathogenic antibodies targeting neuronal surface or synaptic antigens and non-pathogenic antibodies against intracellular, onconeural antigens, in addition to a seronegative group. The present study attempts to focus on clinic-radiological patterns and treatment outcomes of these two subset of AE patients.

Methods: A longitudinal follow-up study was conducted at a tertiary care neurological centre in Kolkata, India, between March 2019 and September 2020. AE was diagnosed as per Grauss et al., after exclusion of mimics. All patients were treated with immunotherapy as per institutional guidelines. Appropriate statistical tests were applied for analysis.

Results: A total of 62 AE patients were selected, of which 41 (66.13%) were sero-positive, of which anti NMDA antibodies were most common (80.45%). Majority of patients were female (59.68%). The median age of onset was significantly higher in the seronegative subset as compared to antibody positive (27 years vs 19 years., p=0.040). Behavioral abnormalities were the most common presentation (77%), followed by seizures (69%) and movement disorders (50%). Outcomes were better in the antibody positive group as compared to seronegative (78.04% vs 52.38%, p=0.02). Odds ratio of developing unfavorable clinical outcomes was more in males (22.53, p=0.036). Delay in initiation of therapy had the most significant likelihood of contributing to unfavourable patient outcomes (p=0.041).

Conclusion: Prompt initiation of immunotherapy in suspected cases AE should be emphasized. Therapeutic decision-making should be individualized, depending on antibody status, patient profile, cost-effectiveness and side-effect profile of drugs.

Disclosure: There is no conflicts of interest amongst the authors. No grants or financial aid was received. Detailed informed consent was obtained from the patients and/or their kin.

EPO-259

Abstract withdrawn

EPO-260

Clinical and real-world pharmacovigilance data of meningococcal infections in eculizumab or ravulizumab-treated patients

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Background and aims: Terminal complement inhibiting therapies (C5ITs) initially approved to treat rare haematological disorders, and more recently rare neurological disorders, are associated with increased Neisseria meningitidis (Nm) infection risk. Robust risk mitigation measures implemented worldwide include vaccination, education materials and patient safety cards. A pharmacovigilance analysis of exposure-adjusted incidence and mortality data for Nm infections in eculizumab- or ravulizumab-treated patients in clinical trial and real-world settings evaluated infection and mortality rates over time as exposure has substantially increased.

Methods: A cumulative search of the Alexion safety database was performed for eculizumab (Mar 2007–Oct 2022) and ravulizumab (Dec 2018–Jun 2022) across all indications, using the MedDRA High Level Term of Neisseria infection. Identified cases were reviewed to include only those associated with Nm.

Results: Cumulative clinical trial Nm infection rates for eculizumab- or ravulizumab-treated patients across four indications are approximately 0.30 and 0.21 cases per 100 patient-years, respectively (Table 1). Cumulative post-marketing reporting rates for Nm infections in eculizumab- or ravulizumab-treated patients are stable at approximately 0.24 and 0.08 cases per 100 patient-years, respectively (Figure and Table 2).

Table 1. *Nm* infection and mortality rates among eculizumab- and ravulizumab-treated patients in the clinical trial setting

Treatment	Cumulative exposure, PY	*Nm* infection, rate per 100 PY	*Nm* mortality, rate per 100 PY	Total *Nm* infections	Total *Nm* fatalities
Eculizumab[1]	2,331	0.30	0	7 cases per 2,331 PY	0
Ravulizumab[2]	2,870	0.21	0.03	6 cases per 2,870 PY	1

[1]Eculizumab first approvals: PNH in 2007, aHUS in 2011, gMG in 2017 and NMOSD in 2019. Data collected between March 2007–October 2022. [2]Ravulizumab first approvals: PNH in 2018, aHUS in 2019 and gMG in 2022. Data collected between Dec 2018–June 2022.
aHUS, atypical haemolytic uraemic syndrome; gMG, generalized myasthenia gravis, *Nm*, *Neisseria meningitidis*; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal haemoglobinuria; PY, patient-years

Table 1: Nm infection and mortality rates among eculizumab- and ravulizumab-treated patients in the clinical setting

Table 2. *Nm* infection and mortality rates among eculizumab- and ravulizumab-treated patients in the real-world setting

Treatment	Cumulative exposure, PY	*Nm* infection, rate per 100 PY	*Nm* mortality, rate per 100 PY	Total *Nm* infections	Total *Nm* fatalities
Eculizumab[1]	78,416	0.24	0.03	191 cases per 78,416 PY	20
Ravulizumab[2]	7,533	0.08	0.02	6 cases per 7,533 PY	1

[1]Eculizumab first approvals: PNH in 2007, aHUS in 2011, gMG in 2017 and NMOSD in 2019. Data collected between March 2007–October 2022. [2]Ravulizumab first approvals: PNH in 2018, aHUS in 2019 and gMG in 2022. Data collected between Dec 2018–June 2022
aHUS, atypical haemolytic uraemic syndrome; gMG, generalized myasthenia gravis, *Nm*, *Neisseria meningitidis*; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal haemoglobinuria; PY, patient-years

Table 2: Nm infection and mortality rates among eculizumab- and ravulizumab-treated patients in the real-world setting

Figure. Rates of *Nm* infection and associated mortality for eculizumab per 100 patient-years from 2007 to 2022 in the real-world setting

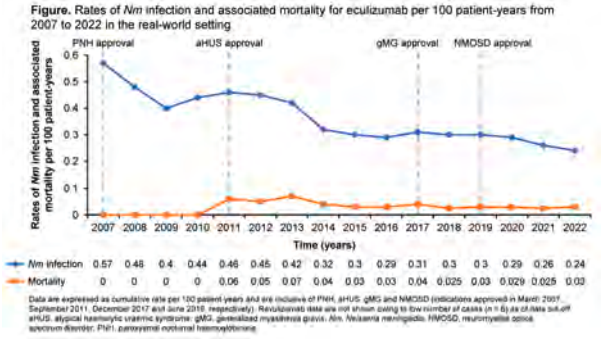

Figure: Rates of Nm infection and associated mortality for eculizumab per 100 patient-years from 2007 to 2022 in the real-world setting

Conclusion: While cumulative exposure to eculizumab has increased, including addition of rare neurological indications, Nm infection rates have steadily decreased and mortality rates have remained stable since 2007. Comparable rates were observed in patients treated with ravulizumab. Raised infection awareness, risk mitigation strategies and availability of additional vaccines effectively reduced the risk of Nm infections in C5IT-treated patients, underlining the importance of adhering to those measures.

Disclosure: All authors are employees of, and hold stock in, Alexion, AstraZeneca Rare Disease.

EPO-261

DACH1 antibodies in immune checkpoint inhibitors-related neurological syndromes

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Background and aims: Dachshund-homolog 1 (DACH1) antibodies (Ab) are recently characterized biomarkers of paraneoplastic neurological syndromes (PNS) . We report two patients with post-ICI DACH1-Ab neurological syndromes identified in the French reference centre for PNS.
Methods: DACH1-Ab were tested by a cell-based assay in 203 patients with suspected PNS for which indirect immunofluorescence assay showed a neuronal nuclear staining pattern without identification of the target antigen (March 2020-September 2022): in 7 patients the staining was selective for Purkinje cells nuclei (Figure 1), and 2 were DACH1-Ab positive.
Results: Both DACH1-Ab patients were men and developed a rapidly progressive cerebellar syndrome 10 months after the first ICI dose (atezolizumab) for small cell lung cancer (patient 1) or limbic encephalitis 3.5 months after the first ICI dose (pembrolizumab) for neuroendocrine bladder cancer (patient 2) with no evidence of cancer dissemination or infectious aetiologies. Brain MRI showed superior cerebellar peduncles T2 hyperintensity and vermian atrophy in patient 1 (Figure), while it was normal in patient 2. There were CSF-unique oligoclonal bands in patient 1 and elevated protein levels in patient 2. Both patients were severely disabled at diagnosis (modified Rankin score of 4 in patient 1, 5 in patient 2) and did not improve at last visit (9 and 4 months after onset, respectively) despite permanent ICI discontinuation and immunosuppression (intravenous steroids and immune globulins in both, cyclophosphamide in patient 2).

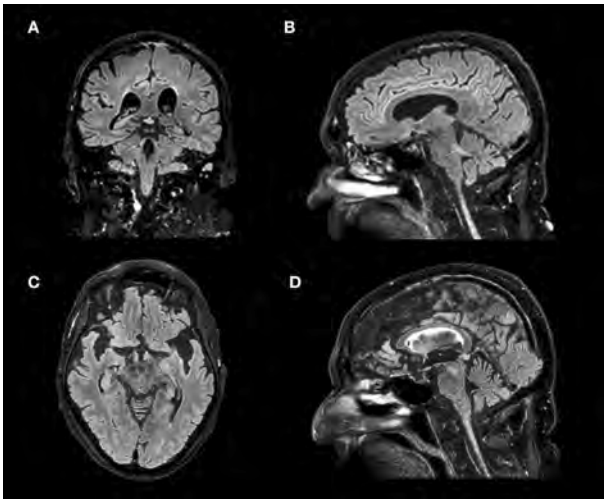

Figure. Brain MRI findings in patient 1. Superior cerebellar peduncles T2/FLAIR hyperintensity (A,B). Vermian atrophy (C,D)

Conclusion: Although exceedingly rare, DACH1-Ab may represent useful biomarkers of post-ICI neurological syndromes clinically resembling PNS.
Disclosure: Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero. Antonio Farina received a research fellowship grant from the European Academy of Neurology in 2022.

EPO-262

Switch to oral cladribine from first line DMD in MS: 2nd Interim Analysis of CLAD CROSS

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Background and aims: CLAD CROSS is a prospective, non-interventional, multicenter, Phase IV study in patients with a confirmed diagnosis of RRMS who switch from first-line disease modifying drugs to treatment with cladribine tablets in routine clinical practice. The primary objective is to evaluate the change in ARR between the 12-month pre-

baseline period and over the 12 months period before end of study follow-up (2 years). Here we report the planned one year interim analysis results.
Methods: The sample size of the study is 250 patients. The second interim analysis was planned at completion of 12-month follow-up for the initial 60% of patients. ARR was compared by the repeated measures Wilcoxon signed-rank test, between the 12-month pre-baseline and first 12 months post-switch to cladribine tablets-period. Treatment satisfaction was measured by treatment satisfaction questionnaire (TSQM) v1.4.
Results: One hundred twenty-four (124) patients were included in the efficacy analysis. ARR decreased from 1.14±0.866 to 0.12±0.451 ($p<0.0001$). Treatment satisfaction was high, with a slight increase of median TSQM score at 12 months to 82%. 60 patients had a treatment emergent adverse event (TEAE) in the total population (n=250, 24.0%), 6 had a serious TEAE (2.4%) and 5 discontinued permanently due to a TEAE (2.0%). The most common TEAEs were infections and infestations (10.4%), lymphopenia (6.4%), and headache (3.2%). No malignancy and no PML were reported.
Conclusion: In the one-year interim analysis of CLAD CROSS, cladribine tablets demonstrated high efficacy with low ARR. Treatment was generally safe and well tolerated. Patient satisfaction was high.
Disclosure: The presenter has received honoraria and travel support from Biogen Idec, Biologix, Novartis, TEVA, Bayer, Merck Serono, Genesis Pharma, Sanofi – Genzyme, ROCHE, has received consultancy fees from Biogen Idec, Novartis, TEVA, BAYER, Bayer, Merck Serono, Genesis Pharma, Sanofi – Genzyme, Cellgene , ELPEN, ROCHE, has received lecture fees from Biogen Idec, Novartis, TEVA, Bayer, Merck Serono, Genesis Pharma, Sanofi – Genzyme, ROCHE and research grants from Biogen Idec, Novartis, TEVA, Merck Serono, Genesis Pharma, Sanofi – Genzyme, ROCHE

EPO-263

Clinical characterization of patients in the post-acute stage of anti-NMDA receptor encephalitis

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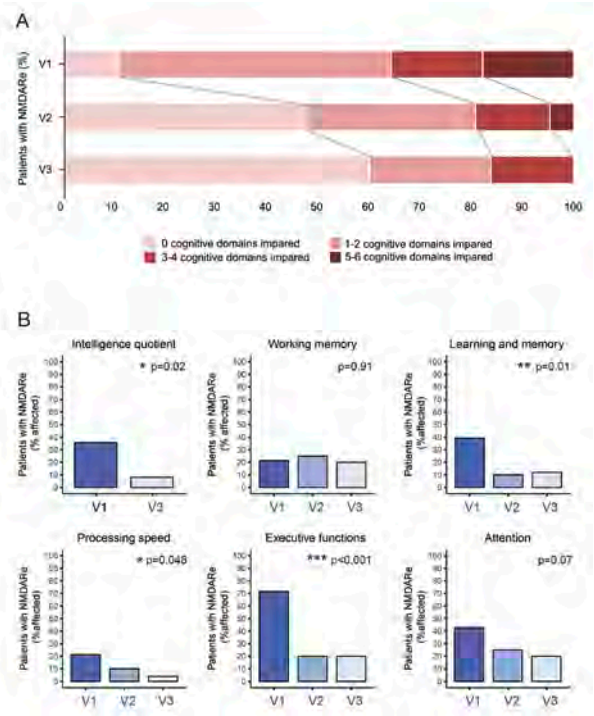
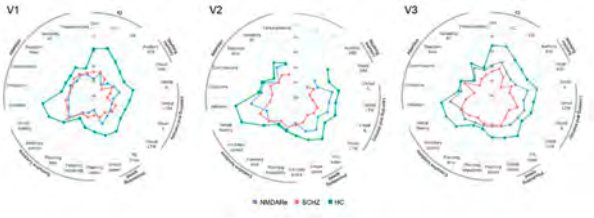
Background and aims: Anti-NMDAR encephalitis (NMDARe) associates with poorly defined protracted symptoms. We characterized the clinical features of post-acute stage NMDARe, similarities with schizophrenia spectrum disorders (SCZ), and predictors of cognitive-psychiatric outcomes.
Methods: In this prospective observational study, patients in the post-acute stage of NMDARe underwent 3 visits (V1, study entry; V2, 6 months; V3, 12 months) including comprehensive neuropsychiatric evaluations at Hospital Clínic, Barcelona. SCZ patients and healthy participants (HC) undertook similar evaluations. Linear mixed-effect models served to assess longitudinal differences.
Results: 28 NMDARe, 27 SCZ, and 27 HC were recruited. Although, by V1 (median 4 months [IQR 3–7] from disease onset), many acute-stage NMDARe symptoms had resolved (acute stage median mRS 5 [IQR 4–5] vs V1 mRS [1–2]; $p<0.0001$), 89% of patients showed deficits in ≥1 cognitive domain (CD). In NMDARe, 15/22 (68%) CD variables were impaired at V1, whereas only 8/22 (36%) were altered at V3 ($p=0.016$). In SCZ, 11/22 (50%) variables (all shared with NMDARe) were impaired at V1, without changes at V3. Two acute-stage NMDARe features (decreased consciousness; no improvement within first 4 weeks of treatment) and a visuospatial task at V1 predicted CD outcomes. At V1, all psychiatric symptom clusters were similarly altered in NMDARe and SCZ, but only NMDARe subsequently recovered ($p=0.031$). The greatest NMDARe cognitive-psychiatric improvement occurred between V1-V2.



Follow-up of cognitive domains in the post-acute stage of NMDARe



Comparison of variables of the 6 cognitive domains among study participants

Conclusion: The cognitive-psychiatric symptoms of post-acute NMDARe resembled those of stabilized schizophrenia, but only NMDARe progressively improved, predominantly during V1-V2. These findings are important for clinical trials on NMDARe and suggest the value of prompt cognitive-psychosocial rehabilitation.
Disclosure: Nothing to disclose.

EPO-264

Paraneoplastic Kelch-like protein 11 antibody-associated cerebellar syndrome caused by metastatic “burned-out” seminoma

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Background and aims: Paraneoplastic neurologic syndromes are remote immune-mediated effects of a cancer. The diagnosis is challenging, and treatment may be delayed when the suspected primary tumor shows complete spontaneous regression (i.e. “burn-out”) and masquerades as scar tissue.
Methods: Herein we present the case of a conventional neuronal antibody negative rapidly progressive cerebellar syndrome in a patient with burned out seminoma.
Results: A 45-year-old Caucasian male patient presented with progressive gait and limb ataxia, weight loss and perceptual hearing loss. Initial detailed imaging screening for malignancy as well as testing a diverse set of paraneoplastic and autoimmune neuronal antibodies in both the serum and cerebrospinal fluid (CSF) gave negative results. CSF cytology and flow cytometry, microbiology, genetic testing and serum tumor markers were negative. Serialbrain MRI showed right hippocampal transient contrast enhancing lesion and progressive cerebellar atrophy. Only repeated whole-body FDG-PET CT revealed a hard-to-detect single paraaortic lymphadenopathy – metastasis of a spontaneously regressed testicular seminoma seen as scar tissue on histology. This highly unique clinical presentation suggested, and additional serologic testing in French national reference centre confirmed anti-Kelch-like protein-11 (KLHL11) encephalitis. After 5 cycles of plasma exchange, orchiectomy, metastasis removal and adjuvant chemotherapy the patient’s symptoms only stabilized without meaningful clinical improvement: he remained essentially wheelchair-bound.
Conclusion: Our case highlights the importance of continued efforts to find an often burned-out testicular cancer (masquerading as scar tissue) in young male patients with progressive cerebellar ataxia and hearing loss that are highly characteristic of the recently described Kelch-like protein 11 (KLHL11) antibody-associated paraneoplastic encephalitis.
Disclosure: JH is funded by the BETPSY project, which is supported by a public grant overseen by the Agence

Nationale de la Recherche (ANR) as part of the second Investissements d'Avenir program (ANR-18-RHUS-0012), and by the LABEX CORTEX (ANR-11-LABX-0042) of the Université de Lyon operated by the ANR.

EPO-265

Vitamin D promotes the neuroprotective astrocyte phenotype A2 in an animal model of progressive multiple sclerosis

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Background and aims: Vitamin D (VD) is a discussed supplement for multiple sclerosis (MS) patients. Especially the VD effect on the progressive MS form still needs to be better understood. We developed an animal model with a high similarity to human progressive MS pathology. In previous studies, we could observe a positive effect of VD on cellular features of our model with an upregulation of activated astrocytes. Since neuropathology can induce two types of astrocytes that were termed A1 (C3d+; harmful) and A2 (S100A10+; neuroprotective) according to Liddelow et al., 2017; we further investigated the astrocytic phenotypes.
Methods: Male rats received 400 IE VD (Fresenius-Kabi, Graz, Austria) once weekly at age 3 weeks and underwent the standard procedure of our animal model, according to Ücal et al., 2017. Tissue was harvested on peak disease, and GFAP/A1 and GFAP/A2 immunohistochemical double-stainings were performed.
Results: Overall, male (n=10) VD-rats showed a significant upregulation of GFAP/A2+ astrocytes (90/±40 to 151/± 47A2/mm^2; $p<0.009$). An inverse pattern was observed in our preliminary results of GFAP/A1 positive astrocytes.
Conclusion: In summary, our preliminary data show an upregulation of the A2 phenotype and, at the same time, a downregulation of the A1 phenotype in VD-supplemented male rats. Since we already observed gender differences in our animal model, with females having a significant ($p=0.02$) better total antioxidative capacity and less myelin loss, in our ongoing study, we investigate whether a gender difference is detectable in astrocyte phenotypes as well.
Disclosure: This study was partially funded by Fresenius-Kabi (to Hochmeister S). MTH declares no conflict of interest. MÜ declares no conflict of interest. MN declared no conflict of interest. WW declares no conflict of interest. US declares no conflict of interest. CE declares no conflict of interest. SH declares no conflict of interest.

EPO-266

Tumefactive onset of multiple sclerosis treated with anti-CD20 therapy: a case series

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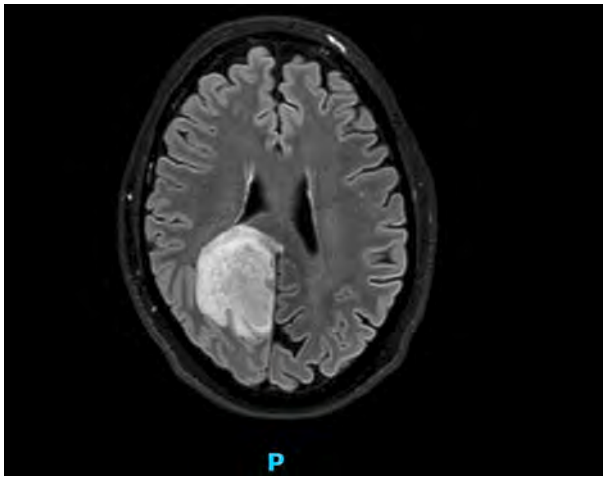
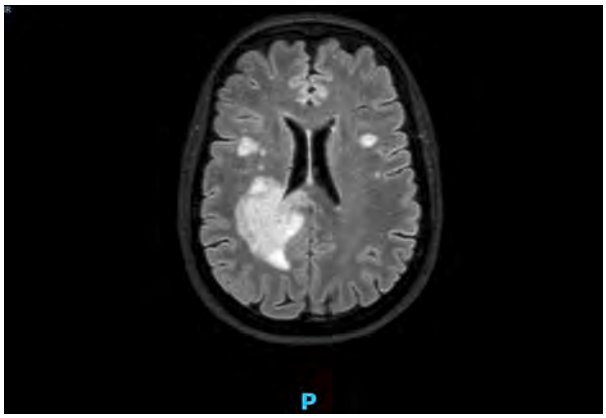
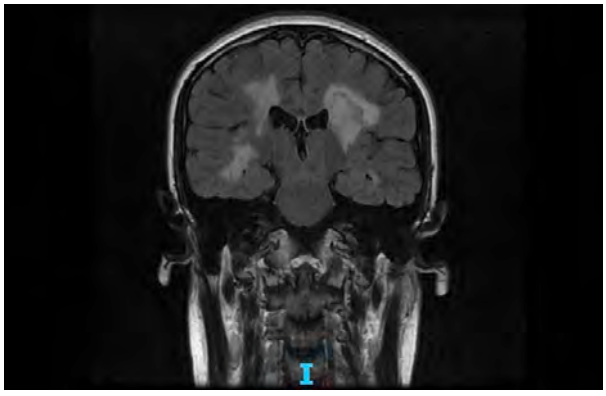
Background and aims: Tumefactive lesions are uncommon manifestations of demyelinating diseases at onset. Some clinical and radiological features may help to suspect this challenging diagnosis.
Methods: We collected three patients at our MS center (two female, mean age 39 years old). They presented differently: case 1 – cognitive impairment and seizures; case 2 – sensitive emisyndrome rapidly evolving to motor impairment and ataxia; case 3 – severe sensory-motor left deficits. Autoimmune and infective screening was negative in all of them. Only –3 had oligoclonal bands.
Results: Magnetic resonance imaging revealed: 1 – a voluminous T1-hypointense and T2/FLAIR hyperintense right parietal lesion with a peripheral enhancement; 2 – multiple hyperintense areas in FLAIR, of whom the largest enhancing in the right frontal-parietal lobe; 3 – multiple pseudotumor-like demyelinating lesions with enhancement. Spectroscopy was performed only in 1 and 3 with an increase in choline peak and a reduction in the N-acetyl-aspartate peak (suggestive for inflammation). Only case 1 underwent neurosurgical exeresis, in the suspicion of a glioma, confirming features of tumefactive demyelination. All patients were treated with high doses of corticosteroid in the acute phase, and they started anti-CD20 therapy (1 rituximab and 2–3 ocrelizumab) with no further relapses at the moment.



Case 1 before exeresis



Case 2



Case 3

Conclusion: Acute or subacute onset with rapid progression of neurological deficits with peculiar MRI/spectroscopy features are suggestive of tumefactive demylinating syndromes. We confirm an effect of B-lymphocyte-depleting agent for typical and atypical MS. Even if the first episod of tumefactive MS is more severe than an usual disease onset, mid-term prognosis could be similar if properly treated.
Disclosure: Nothing to disclose.

EPO-267

Bibliometric analysis of global literature on multiple sclerosis over eight decades (1945–2021)

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Background and aims: Bibliometric studies on the field of multiple sclerosis (MS) research are scarce. The aim of this study is to offer an overarching view of the body of knowledge about MS research over eight decades–from 1945 to 2021–by means of a bibliometric analysis.
Methods: We performed a quantitative analysis of a massive dataset based on Web of Science. The analysis included frequencies, temporal trends, collaboration networks, clusters of research themes, and an in-depth qualitative analysis.
Results: A total of 48,356 articles, with 1,766,086 citations were retrieved. Global MS research showed a steady increase with an annual growth rate of 6.4%, with more than half of the scientific production published in the last decade. Published articles came from 98 different countries by 123,569 authors in 3,267 journals, with the United States ranking first in a number of publications (12,770) and citations (610,334). A co-occurrence network analysis formed four main themes of research, covering the pathophysiological mechanisms, neuropsychological symptoms, diagnostic modalities, and treatment of MS. A noticeable increase in research on cognition, depression, and fatigue was observed, highlighting the increased attention to the quality of life of patients with MS.
Conclusion: This bibliometric analysis provided a comprehensive overview of the status of global MS research over the past eight decades. These results could provide a better understanding of this field and help identify new directions for future research.
Disclosure: The authors report no sources of funding and no conflicts of interest.

EPO-268

IgG as a biomarker of clinical efficacy in generalized myasthenia gravis: Model-based meta-analysis of FcRn inhibitors

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Background and aims: Generalized myasthenia gravis (gMG) is a rare chronic autoimmune neuromuscular disease. Therapeutic anti-FcRn antibodies are being evaluated (e.g nipocalimab) or are approved (efgartigimod) for treatment of gMG. Anti-FcRn's inhibit FcRn-mediated IgG recycling thus lower circulating serum IgG, including anti-AChR pathogenic autoantibodies. Model-based meta-analysis of clinical data from four anti-FcRn treatments were used to explore IgG as a potential biomarker for the clinical endpoint, MG-ADL score.

Methods: The proportion of treatment effect (PTE) method (Li 2001) was used. Specifically, the contribution of a biomarker (e.g IgG) to the overall treatment-related change in clinical endpoint is calculated as the ratio of an estimated surrogate-contribution (if statistically significant) versus an estimated treatment-effect. Clinical data for nipocalimab, efgartigimod, rozanolixizumab and batoclimab were combined from eight studies (Table 1). PTE was calculated using weighted regression on steady-state, aggregate values of placebo-corrected change from baseline MG-ADL (ΔΔMG-ADL) and percent change of IgG from baseline (ΔIgG) from all studies (Figure 1). Due to the limited dataset (18 datapoints) covariates or random effects were not included.

Results: The estimated IgG coefficient was statistically significant (0.03±0.005 [SE]), suggesting 10% ΔIgG translates to ΔΔMG-ADL of ~0.3. The PTE(%CV) from all aggregate-level FcRn data was 0.82(15%) indicating that a majority of the anti-FcRn effect on ΔΔMG-ADL could be explained by ΔIgG.

Compounds	Study name (NCT)	Study phase
nipocalimab	MOM-M281-004 (NCT03772587)	2
batoclimab	ASCEND-MG (NCT03863080)	2
	9161.3 (NCT04346888)	2
efgartigimod	ARGX-113-1602 (NCT02965573)	2
	ADAPT (NCT03669588)	3
	ADAPT SC (NCT04735432)	3
rozanolixizumab	MG0002 (NCT03052751)	2
	MycarinG (NCT03971422)	3

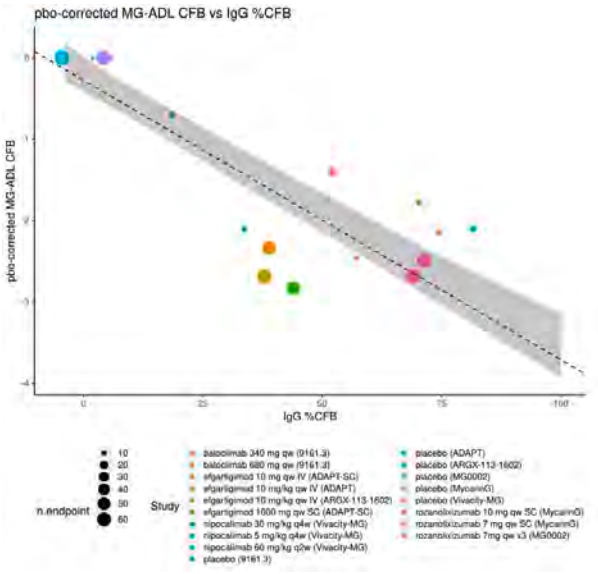

Figure 1: Weighted Linear Regression Model Correlating Placebo-corrected MG-ADL Change From Baseline to IgG Reduction at Steady-State for anti-FcRn's

Conclusion: Since ΔIgG explains a large proportion of anti-FcRn effect on ΔΔMG-ADL, IgG could be used as a potential biomarker for clinical efficacy. This would increase the efficiency of clinical trials (size and duration) to reduce burden for patients in gMG.

Disclosure: All authors except Eugène Cox are J&J employees and might hold J&J stock.

EPO-269

Efficacy of Immunotherapy and Risk Factors for Poor Outcome in LGI1 Antibody Encephalitis Patients: A Meta-analysis

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Background and aims: Anti-leucine-rich glioma inactivated 1 (LGI1) encephalitis is a group of severe antibody-mediated brain diseases presenting with mental symptoms, faciobrachial dystonic seizures, and hyponatremia, etc. Immunotherapy response rate in LGI1 encephalitis patients varied between 67%-92%. We conducted the meta-analysis to assess the efficacy and safety of immunotherapy, and considered the potential predictors of poor outcomes following immunotherapy.
Methods: We systematically searched PubMed and Embase for studies reporting immunotherapy data of LGI1 encephalitis patients. The proportion of poor functional outcome (mRS>2) and ORs with 95% CIs of predictors were pooled using fixed-effects or random-effects model.
Results: 162 articles with 1066 patients were included. The proportion of poor outcome was 14% (95% confidence interval [CI]: 10%–18%) at 12 months, 14% (95%CI: 11%–18%) at last follow-up. We did not find statistically significant association between worst mRS in the acute phase (p=0.449), delayed immunotherapy (p=0.113), second-line treatment (p=0.540), maintenance immunotherapy (p=0.872), follow-up time (p=0.878) and outcome. Adverse effects were recorded in 68 of 225 (30%) patients treated with immunotherapy. Three predictors of poor outcome were identified: elderly age (odds ratio [OR]: 1.03, 95%CI: 1.01–1.05); cognitive impairment (OR: 2.61, 95%CI: 1.15–5.93); CSF antibodies to LGI1 poitive (OR: 1.89, 95%CI: 1.08–3.31).
Conclusion: No association between worst mRS in the acute phase, delayed immunotherapy, follow-up time, second-line treatment, maintenance immunotherapy and outcome in anti-LGI1 encephalitis patients. Patients with elderly age, cognitive impairment, and the presence of CSF antibodies to LGI1 had a high risk for poor outcome. These associations may contribute to improve individualized prognostic assessment.
Disclosure: Nothing to disclose.

EPO-270

Autoimmune encephalitis with antibodies to neuronal surface antigens – the single site experience in Poland.

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Background and aims: Autoimmune encephalitis (AE) are associated with antibodies against neuronal synaptic and cell surface antigens characterized by subacute onset of memory disturbances, seizures, psychiatric changes, and particular neuroradiological findings. We present a retrospective study of cases diagnosed in the Institute of Psychiatry and Neurology in 2013–2021.
Methods: We searched the hospital database for "autoimmune encephalitis" and "limbic encephalitis" and laboratory database for the patients with positive results of antibodies (ab) to surface neuronal antigens. All the patients had their plasma and cerebrospinal fluid (CSF) tested using commercial kits with EU90 transfected cells - Autoimmune Encephalitis Mosaic 1: NMDA, GABA B, AMPA1/2, LGI1, CASPR2 (EUROIMMUN, Germany) and from 2017, AE mosaic 6 with addition of DPPX .
Results: We found 50 cases (23 males, 27 females) diagnosed as autoimmune encephalitis (43 definite and 7 probable): 22 with ab to NMDAR, 10 to LGI1, 8 to CASPR2, 2 to GABA B, 1 to AMPA-1/2 and 7 cases without antibodies but fulfilling criteria for probable AE. Through the laboratory database we found also 12 cases with the antibody presence (8 with ab to NMDA and 4 to CASPR2) without typical AE clinical features, mostly in chronic refractory epilepsy patients.
Conclusion: AE should be taken into consideration in subacute neurological and psychiatric disorders. On the other hand, we do not know clearly what is the role of autoantibodies in patients with no or only minor symptoms and what should be the management in such cases.
Disclosure: Authors have nothing to disclose concerning presented study.

EPO-271

Neuroimaging as a upfront diagnostic tool in childhood GBS

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AIIMS JODHPUR Rajasthan, Jodhpur, India

Background and aims: Guillain-Barre syndrome (GBS) is characterized as an acute, symmetric progressive, inflammatory demyelinating polyneuropathy. Enhancement of cauda equina nerve roots represents the radiological hallmark of GBS. Many clinical symptoms of GBS are non-specific, therefore contrast enhanced neuroimaging of brain and spinal cord is a important tool for diagnosis of GBS and ruling out other differentials. Neuroimaging may allow early detection in patients with inconclusive clinical examination and helps in early treatment plan.
Methods: We included a total of 33 children between 0–18 years who had a final diagnosis of GBS and followed up in pediatric neurology OPD at a tertiary care centre.
Results: The study group comprised 22 (66.6%) boys and 11 (33.3%) girls. The age ranged from 0–17 years. Clinically cranial nerve involvement was present in 17 (51%), while radiological cranial nerve involvement was seen in 14 (51.8%). 16 (48.4%) children required mechanical ventilation. Out of 27 children in whom Lumbar puncture was performed 20 (74%) children had albuminocytological dissociation. In 12 (44.4%) anterior cord involvement was seen, 9 (33.3%) had contrast enhancement or thickening of cauda equina nerve roots. 3 (11.1%) had Anterior>posterior cord involvement and 2 (7.4%) had simultaneous involvement of anterior and posterior nerve roots.
Conclusion: Contrast enhancement brain and spinal MRI is a sensitive and important diagnostic test for diagnosing GBS in children. It can be used as a supplementary diagnostic tool in resourceful settings.
Disclosure: There was no conflict of interest among authors. The project didn't required any funding.

COVID-19; Infectious diseases 2

EPO-272

The Risk of Acute Transverse Myelitis Following COVID-19 Vaccination in Korean Population-based Study

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Background and aims: Acute transverse myelitis (ATM) is a rare neurological condition, but cases of COVID-19-associated ATM have occurred during the pandemic. To address concerns about the causal relationship of reported ATM following COVID-19 vaccination, we assessed the risk of ATM after vaccination with COVID-19.
Methods: We used a large-linked database of claims data from the National Health Insurance Service and COVID-19 vaccine registry from the Korea Disease Control and Prevention Agency from January 1, 2002, to October 31, 2021. We included ATM patients who were newly diagnosed with ATM (ICD-10 code: G37.3). We performed a self-controlled case-series design within 90 days observation period after vaccination date and estimated incidence rate ratio (IRR).
Results: People received the first COVID-19 vaccination was 19,639,721. Among 52 ATM cases, risk and control intervals were 31 and 21cases, respectively. Of 21 were men (52.5%), and half of patients were over 65 (n=26, 50.0%). The risk of ATM increased following COVID-19 vaccination (IRR=2.16; 95% CI: 1.25–3.73). The ATM risk in subgroup analysis was increased for male (IRR=3.07, 95% CI: 1.35–7.00, 50-64 ages (IRR=3.54; 95% CI: 1.07-11.67), CCI score≥5 (IRR=2.82; 95% CI: 1.53–5.21), and AstraZeneca vaccinees (IRR=3.17; 95% CI: 1.50–6.70).
Conclusion: Our analysis revealed an increase in ATM following COVID-19 vaccination. Nevertheless, several concerns should be considered for a causal link between ATM and COVID-19 vaccination: 1) validity of ATM diagnosis without detailed clinical information 2) relative rarity of ATM in general population 3) small number of ATMs in this analysis. Corroborative hospital-based case review can be planned as future work.
Disclosure: There are no financial conflicts of interest to disclose.

EPO-273

Myelitis associated with COVID-19: clinical, radiological, laboratory characteristics (serum and CSF cytokines profiles)

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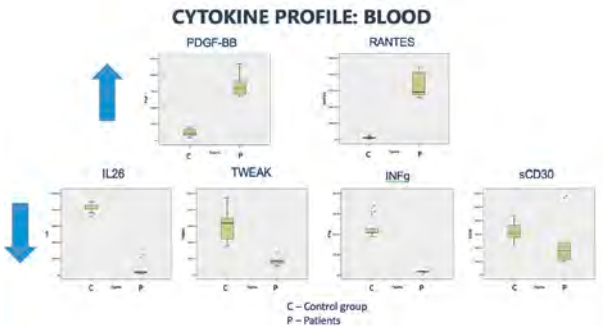
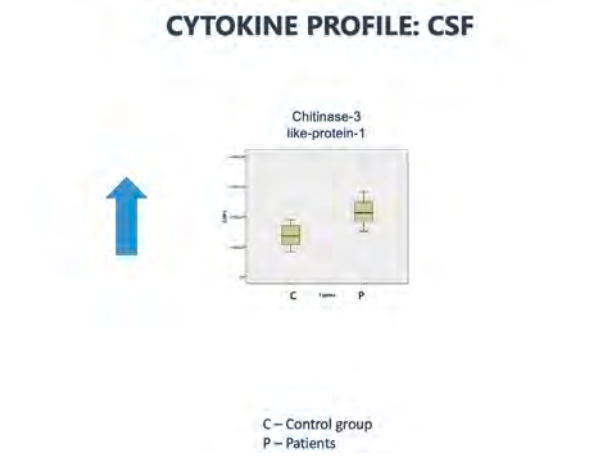
Background and aims: Spinal cord injury is a common complication of a novel coronavirus infection. Current study was aimed to analyze the various types of spinal cord pathology in COVID-19 patients, its clinical, radiological, laboratory characteristics, response to treatment as well as to study cytokine levels in patients' serum and CSF.
Methods: 27 patients with various immune-mediated spinal cord pathologies developed within 3 months after COVID-19 observed at the Research Center of Neurology in Moscow from September 2020 to December 2022 were enrolled in the study. Clinical, radiological data as well as serum and CSF findings of these patients were analyzed. Cytokine profiles were studied using both Bio-Plex Pro Human Cytokine and Bio-Plex Pro Human Inflammation Panel.
Results: Symptoms of myelitis developed in 4,3±2,6 weeks after the infection. Radiological findings were diverse: transverse myelitis (n=8), longitudinal extensive transverse myelitis (n=6), multifocal spinal cord lesions (n=6), myelitis involving dorsal and lateral columns (n=5) and myelitis without MRI abnormalities (n=2). CSF analysis revealed lymphocytic pleocytosis in 3 patients, elevated protein (>0,7 g/l) in one patient. Polyclonal IgG synthesis pattern both in serum and CSF as well as negative CSF PCR for SARS-CoV-2 were found in our group. Significantly higher levels of PDGF-BB, RANTES, lower titers of sCD30, IL26, TWEAK, INF-gamma in the serum and high level of chitinase-3-like-protein-1 in CSF were observed in myelitis patients comparing to healthy controls.



Significantly higher levels of PDGF-BB, RANTES, lower titers of sCD30, IL26, TWEAK, INF-gamma were observed in the serum of patients with myelitis comparing to controls



High level of chitinase-3-like-protein-1 in CSF were observed in CSF of patients with myelitis comparing to controls

Conclusion: This preliminary analysis confirms clinical heterogeneity of COVID-19 associated myelitis and supports the hypothesis of an important role of cytokine changes in its pathogenesis.
Disclosure: No conflict of interest.

EPO-274

Neurological complications after COVID-19 vaccines and SARS-CoV-2 infection in Lombardia (Italy)

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Background and aims: The influence of COVID-19 vaccination on the risk of different neurological diseases has been subject of intense investigation. No large scale results have been published so far in the population of around 10 million people of Lombardia in Italy.
Methods: Linkable administrative health databases from the Lombardia region were used. By using the adapted self controlled case series (SCCS) method for event dependent exposures, we estimated the relative incidence of different neurological diseases following pre-specified windows at risk after vaccination and after COVID-19 infection in the over-12 population of Lombardia. Follow-up time before vaccination (Pre-Vax period) was compared with follow-up time 0–28 days (high-risk period) from the day of vaccination as well as for COVID infection. The SCCS model was fitted using a conditional Poisson regression model to estimate the Relative Incidences (RI) and their 95% Confidence Intervals (CI).
Results: The 28-day post-vaccination period was associated with a significant increase in the occurrence of ischemic stroke, cerebral haemorrhage, TIAs and myelitis (IRR 1.44, 1.50, 1.67 and 2.65 respectively). When the risk conferred by COVID19 infection was assessed in the same cohort, significant IRR were greater in the occurrence of ischemic stroke, cerebral haemorrhage, and TIAs (IRR 5.6, 3.62, 6.83) and includes also Multiple Sclerosis, neuromyelitis, and polymyositis (5.25, 8.81, 5.67).
Conclusion: Our data suggest that the increased risk of non-inflammatory CNS disorders following COVID-19 vaccination is lower than the risk conferred by COVID-19 infection, and that COVID-19 infection increase the risk of some inflammatory neurological disorders.
Disclosure: FMB has received compensations by Roche, Biogen-Idec and Merck-Serono.

EPO-275

Altered motor cortex long intracortical inhibition and intracortical facilitation in Long COVID cognitive impairment

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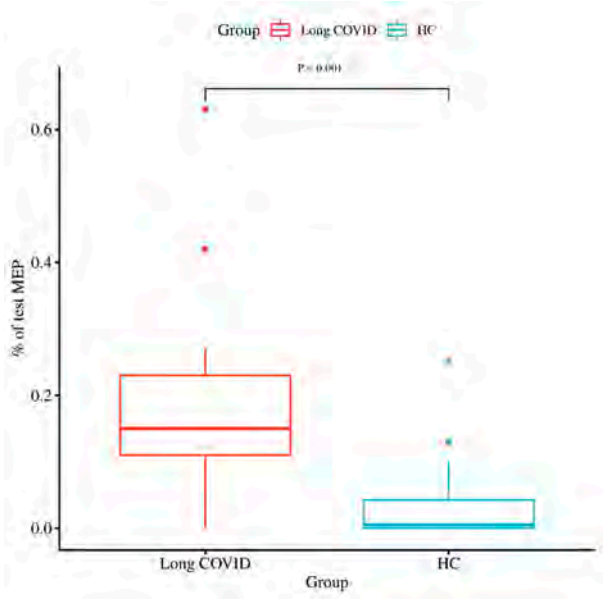
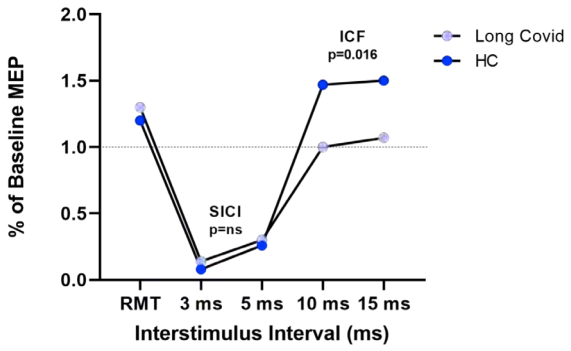
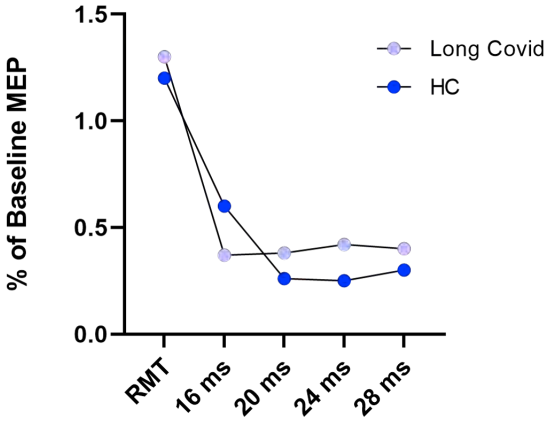
Background and aims: Attention, working memory and executive processing have been reported to be consistently impaired in Neuro-Long COVID. We investigated the functional state of inhibitory and excitatory cortical regulatory circuits by paired-pulse transcranial magnetic stimulation (ppTMS) and Short Afferent Inhibition (SAI).
Methods: We compared clinical and neurophysiological data of 18 Long COVID patients complaining of persistent cognitive impairment with 16 Healthy control (HC) subjects. Cognitive status was evaluated by means of the Montreal Cognitive Assessment (MoCA) and a neuropsychological evaluation of the executive function domain. Resting motor threshold (RMT), the amplitude of the motor evoked potential (MEP), Short Intra-cortical Inhibition (SICI), Intra-cortical Facilitation (ICF), Long Intra-cortical Inhibition (LICI) and Short-afferent inhibition (SAI) were investigated over the motor (M1) cortex.
Results: All the patients' performed sub-optimally in the neuropsychological assessment of the executive functions. RMT, MEPs, SICI and SAI were not significantly different between the two groups. On the other hand, Long COVID patients showed a reduced amount of inhibition in LICI ($p=0.003$) and a significant reduction in ICF ($p<0.001$).



LICI differences in the two groups



SICI-ICF differences in the two groups.



SAI differences in the two groups

Conclusion: Neuro-Long COVID patients performing sub-optimally in the executive functions showed a reduction of LICI related to GABAb inhibition and a reduction of ICF related to glutamatergic regulation. No alteration in cholinergic circuits was found. These findings parallel the pattern of neurophysiological alterations seen in clinical syndromes involving the frontal lobes and allow to frame cognitive deficits in Long COVID as explained by inflammatory states affecting frontal and pre-frontal executive hubs.
Disclosure: The authors declare no competing interests for this study.

EPO-276

Subacute sclerosing panencephalitis: clinical and paraclinical study of Tunisian pediatric cases

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Background and aims: Subacute sclerosing panencephalitis(SSPE) is a rare, fatal and subacute encephalitis secondary to chronic infection with Measles virus. Main signs include cognitive decline, motor disorders and vegetative signs. Our aim is to report clinical, neuroimaging and laboratory feature, treatment and outcome in recent cases with SSPE.
Methods: We conducted a retrospective and descriptive study over the period of 5 years [2019–2023] in our department of Child and Adolescent Neurology. SSPE was diagnosed according to modified Dyken's criteria.
Results: Eight children were included in the study(6 boys and 2 girls). The median age at diagnosis was 43months (38–60). The average age at the time of Measles virus infection was 6months(1-10). One patient was not vaccinated. The mean age of SSPE neurological symptoms onset was at 33months (22–48). Mean latency of 27months(15–40) was noted after primary infection. Neurological exam revealed behavioral changes (n=4), hypotonia (n=8), pyramidal signs(n=4), ataxic gait (n=8), parkinsonism (n=2), movements disorders such as myoclonus (n=7), dystonia(n=3) and swallowing difficulties (n=2). Epilepsy was noted in four patients. Brain imaging showed lesions in the pons and middle cerebellar peduncles realizing pattern of "mustache" (n=3). EEG revealed periodic activity (n=7). CSF analysis showed normal cytology, high levels of anti-measles IgG in the CSF (n=8) and oligoclonal bands (OCBs). Our patients received monthly courses of immun doglobulins(n=7) and antiviral treatment with Isoprinozine (n=7). The evolution was marked by the appearance of akinetic mutism and vegetative signs.
Conclusion: Our study highlights several important points, including the inadequate recognition of measles infection in children. This study alerts the clinicians to consider a possibility of SSPE in children with cognitive decline and myoclonus.
Disclosure: Nothing to disclose.

EPO-277

Serum markers of neuronal and glial damage after full clinical recovery from mild COVID-19 infection.

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Background and aims: Serum neurofilament light chain(sNfL)and glial fibrillar acidic protein(sGFAP)have been demonstrated to increase in patients during the acute phase of COVID-19, regardless of the presence of neurological manifestations. The aim of this study was to evaluate sNfL and sGFAP levels in COVID-19 patients with mild neurological symptoms after full clinical recovery,and compare them with age- and BMI-matched healthy controls in order to assess possible neuronal and glial damage.
Methods: We enrolled a cohort of 147 COVID-19 patients as part of the occupational health surveillance (82 females, 65 males),with an unremarkable past medical history, following a mild COVID-19,and 82 controls(52 females, 30 males). Blood samples were collected within 1 week of clinical recovery following COVID-19 infection and a negative nasopharyngeal swab for SARS-CoV2–PCR test. sNfL and sGFAP levels were assessed in each serum sample of workers and controls using the commercially available immunoassay kits for GFAP and NfL run on the ultrasensitive SR-X™Biomarker Detection System (Quanterix). Cognitive Failures Questionnaire was administered to all the patients and mild cognitive impairment was defined as a score≥43.
Results: Age and BMI-corrected sNfL and sGFAP levels were higher in COVID-19 patients(sNfL median=22.82pg/ml, range 4.18–152.74pg/ml; sGFAP median=146.32pg/ml, range19.17–570.87pg/ml)than in controls(sNfL median=7.21pg/ml, range1.85–29.26pg/ml;sGFAP median=63.53pg/ml, range 8.89–299.34pg/ml; $p<0.001$ for both). Patients with mild cognitive impairment showed higher sNfL levels (median=52.03pg/ml, range 11.41–152.74pg/ml), than those without (median=21.85pg/ml, range 4.18–84.24pg/ml; $p=0.011$),whereas no significant difference between these two groups was observed for sGFAP.
Conclusion: The results of this study show that neuronal and glial injury persists even after full clinical recovery in patients with previous COVID-19 infection.Interestingly, sNfL levels were higher in patients with mild cognitive impairment,suggesting the importance to monitor potential long-term neurological sequelae.
Disclosure: Nothing to report in relation to the study.

EPO-278

Tick-borne encephalitis clinical forms and diagnosis: retrospective study, Belarus, 2018-2021

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Background and aims: Tick-borne encephalitis (TBE) virus is the leading cause of CNS infections in Belarus. Our purpose is to describe the spectrum and characteristics of patients with TBE.
Methods: Retrospective, single-center cohort study with patients admitted due to confirmed TBE infection from 2017 through 2021 (descriptive analysis). For confirmation of TBE serology (IgM and IgG antibody detection) and polymerase chain reaction (PCR) tests of serum and cerebrospinal fluid (CSF) were used.
Results: A total of 90 adults (61.1% males) with a median age of 50.5 years were included. Abortive form was diagnosed in 10.0%, meningitis – in 72.2%, meningoencephalitis – in 15.6%, meningoencephalomyelitis – in 2.2% (2/90) of patients. 74.4% had a biphasic course. None died, but 2 patients with meningoencephalomyelitis had residual sequelae. CSF analysis showed median pleocytosis 69 WBC/uL with lymphocyte predominance (median 85%), protein level 0.52 g/L, glucose level 3.28 mmol/L and lactate level 1.75 mmol/l. TBE IgM and IgG antibodies in patients with TBE CNS invasion were detected in 100% cases but PCR of CSF was positive only in 1 patient with meningitis. RNA of TBE virus by PCR of serum was detected only in 3/8 patients with abortive form of disease.
Conclusion: Meningitis and meningoencephalitis represent the most frequent clinical forms of TBE infection in Belarus. Serology is a highly sensitive test for confirmation of TBE with CNS invasion while PCR of CSF is useless in clinical settings due to low sensitivity. PCR of serum may be useful for early diagnosis of TBE infection before CNS invasion.
Disclosure: Nothing to disclose.

EPO-279

COVID-19 outcomes and vaccination to SARS-CoV-2 in siponimod treated patients: clinical trial and real-world evidence

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Background and aims: Treatment with S1P-modulators such as siponimod may increase the risk of infection. During the SARS-CoV-2 pandemic, and once vaccines became available, the question arose whether or not patients with Multiple Sclerosis (MS) on disease-modifying therapies (DMTs) would mount a sufficient immune response. Therefore we compared infection dynamics of COVID-19 in MS patients treated with siponimod and how SARS-CoV-2 vaccination was coordinated in a clinical study as well as in real-world setting.
Methods: The two german studies, in which siponimod was prescribed as part of clinical routine were analyzed for SARS-CoV-2 vaccinations and COVID-19 infections. AMA-VACC is an open-label prospective clinical study including 41 MS patients currently treated with siponimod or a first-line DMT, analyzing serum neutralizing antibodies and SARS-CoV-2 specific T-cells after vaccination. In the ongoing non-interventional real-world study AMASIA siponimod patients are followed over 3 years.
Results: Most patients treated with siponimod received an mRNA vaccine in both studies. Final data from the AMA-VACC study indicate that patients treated with siponimod were able to mount an immune response after vaccination. The dynamics of COVID-19 breakthrough infections suggest that infections occurred predominantly during the omicron wave (n=29) after vaccination. Most cases were mild and did not require hospitalization, treatment with siponimod was continued throughout the infection.
Conclusion: COVID-19 infection dynamics in siponimod-treated patients seem similiar in the two studies, reflecting frequency and severity of the SARS-CoV-2 pandemic in the general population. This analysis will support clinicians to make an informed decision about coordinating SARS-CoV-2 mRNA vaccination and MS treatment.
Disclosure: HS received research grants and honoraria from Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva. OH served on scientific advisory boards and/or received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. TZ has received research support, consulting fee and honoraria for lectures from Alexion, Biogen, Celgene, Merck, Novartis, Roche, Sanofi, Teva. TB has received consulting fee and honoraria for lectures from Biogen, Celgene, Merck, Novartis, Pathos Therapeutics, Roche, Teva. CW and VEW are employees of Novartis. Sponsor of this study is the Novartis Pharma GmbH.

EPO-280

Long-term headache after COVID-19 infection: 2 years follow-up

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Background and aims: Headache is part of long-COVID syndrome including worsening of pre-existing or new post-COVID headache. We characterized headache in a cohort of COVID-19 patients two years after infection.
Methods: Prospective cohort of 449 COVID-19 patients consecutively diagnosed between March-June 2020. Follow-up of neurological evaluation was performed face-to-face or by phone. We applied a structured clinical questionnaire to characterize headache before and 24-months after infection.
Results: We included 449 patients with a mean age of 51.5 (s.d.=16.8) years old at COVID-19 diagnosis and 61.0% females. 60.8% (273/449) had acute symptomatic headache, of which 52.0% (142/273) reported headache at 24-months. Previous history of headache was present in 25.8% (116/449). New post-COVID headache occurred in 16.2% (54/333) patients previously headache naïve. The new headache was pressure-like in 70.4%, unilateral in 29.6%, with photophobia in 44.4%, phonophobia in 29.6%, and nausea/vomiting in 29.6%. More than a third (38.9%) had 10 or more monthly episodes, 57.4% with impact on daily life. Moreover, the new headache fulfilled migraine diagnostic criteria in 64.8% (35/54). In patients with previous headache history, 41.4% (48/116) reported changes after infection: a different type (22.9%), more frequent (15.5%), more severe (6.9%), and both (11.2%). The vaccination rate was >95% in all groups.
Conclusion: De novo long-term headache is frequent at 2 years post-COVID. Migraine was the most common type. This is an important finding with a potential impact on healthcare and quality of life, given the number of COVID-19 cases and the known burden of migraine worldwide.
Disclosure: Nothing to disclose.

EPO-281

Role of clinical, radiological and biomarkers of stress in the outcome of cerebral salt wasting syndrome in TBM.

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Background and aims: Hyponatremia and cerebral salt wasting (CSW) have been recognized as important management issues in tuberculous meningitis (TBM). The underlying pathophysiology of CSW has been attributed to stress biomarkers. We report the role of clinical MRI and biomarkers of stress in prediction of 6 months functional outcome of TBM patients with CSW.
Methods: 51 TBM patients with CSW were included. The patients with secondary causes of hyponatremia and polyuria were excluded. The demographic details, MRI finding, clinical symptoms and seizures were noted. Serum antidiuretic hormone (ADH) was measured by ELISA and vasopressin receptors and Endoplasmic stress (CHOP, ATF4, GRP 78) by reverse transcriptase polymerase chain reaction (RT-PCR) and catecholamine (adrenaline, nor-adrenaline and dopamine), Liquid chromatography Mass spectrometry (LCMS). Outcome was assessed by 6 months using modified rankin scale (0-6) and classified as death (mRS 6) or survived and good(mRS 0-2) and poor (mRS 3,4,5)
Results: 15 (34.9%) patients. 17 (39.5%) had poor and 11 (25.5%) had good outcome. On univariate analysis the predictors of death was age, gender, duration of illness, adrenaline, dopamine and V2 receptor. Multivariate analysis dopamine (OR 1.03, 95% CI 1.00–1.06; p=0.017) was independent predictors of death.The independent predictors of poor outcome were dopamine (OR 1.06; 95% CI 1.00–1.12; p=0.04) and CHOP (OR 7.37; 95% CI 1.08–1.82; p= 0.04)
Conclusion: Biomarkers of stress, especially dopamine is independent predictors of death and poor outcome in TB patients with CSW
Disclosure: Nothing to disclose.

EPO-282

The Impact of the first year of COVID-19 pandemic on stroke network performance: experience of a drip-and-ship model

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Background and aims: Regional telestroke networks have been developing recently and can offer advantages during periods of crisis. We aimed to assess the impact of the first year of COVID-19 pandemic on the performance metrics and the outcome in patients with ischemic stroke transferred for endovascular treatment (EVT).
Methods: A multicentric cohort study of a regional telestroke network was performed. We obtained clinical and imaging data from patients evaluated in teleconsultation, recorded time measures and outcome (modified Rankin scale at 3 months) for those transferred for EVT. Data from the first year of the COVID-19 pandemic (19/03/2020 to 18/03/2021) was compared the period between 01/01/2018 and 18/03/2020. Statistical analysis comprised univariate and multivariate analysis adjusted for potential confounding variables. Statistical significance was set at $p<0.05$.
Results: 3,082 Patients were evaluated in teleconsultations with a mean age of 73.3±14.0 years, 50.2% females. The number of consultations per day increased 8.2% during the pandemic (2.7 vs 2.9 consultations/day) and the number of patients transferred per day increased 12.9% (0.59 vs 0.68 patients/day). During the COVID-19 period, there was an increase of 95.8 minutes in the last-known-well-to-door interval (159.5 vs 255.3, $p<0.01$), and of 18.5 minutes in the interval between admission in the primary and the tertiary hospital (1,205.6 vs 224.1, $p=0.04$), while the time between admission in the tertiary hospital and reperfusion decreased 24.2 minutes (101.9 vs 77.7,$p<0.01$). Functional outcome was not affected by the pandemic (OR 0.66 [95%CI 0.7–1.3], $p=0.79$).
Conclusion: During the pandemic, divergent results were observed in different performance measures but without impact in patients functional outcome.
Disclosure: Nothing to disclose.

EPO-283

Impact of COVID-19 pandemic related lifestyle changes on the subjective cognitive performance of hungarian elderly

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Background and aims: Subjective cognitive decline (SCD) can be the earliest red flag of Alzheimer's disease and other dementias appearing about 10 years before diagnosis.
Methods: Our study was conducted within the framework of the World-Wide (WW) FINGERS Network. The aim of the global study was to conduct a survey to monitor the effects of the COVID-19 pandemic on the elderly regarding changes in lifestyle, behaviour and mental well-being. In this study, we analysed the data of 359 elderly Hungarians who filled out the WW-Fingers SARS-CoV2 survey.
Results: A quarter of the respondents (n:88) reported SCD affecting their memory functions that could be related to the pandemic. Participants with SCD showed special characteristics: 1) they were older; 2) they were women; 3) pre-pandemic smoking was more frequent among them; 4) they lived with higher number of chronic disorders; 5) showed more prominent impairment in physical mobility; and 6) used internet more frequently during the pandemic (all p's<0.001). To eliminate the potential interrelation across these group differences, stepwise logistic regression was applied. It highlighted that only two parameters defined the outcome of the responders, the physical mobility and independence (ability to walk 500 meters without difficulties; OR=1.186; $p<0.001$; 95%CI=1.101, 1.270) and changes in time spent with grandchildren (OR=1.04; $p=0.015$; 95%CI= 1.008, 1.073).
Conclusion: As a major finding of this model, impaired pre-pandemic physical mobility and reduced time spent with family during the pandemic were the most characteristic predictors of SCD.
Disclosure: Nothing to disclose.

Movement disorders 2

EPO-284

Social cognition in adult onset primary cervical dystonia

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Background and aims: This study aimed to evaluate the impact of adult-onset focal idiopathic cervical dystonia on general cognition and social cognition. In addition, the correlation between disease severity, duration, mood disturbances, and cognitive impairment was examined.
Methods: 36 cervical dystonia patients and 40 healthy age, gender, and education-matched control were included. Addenbrooke cognitive examination (ACE-R), trail making test (TMT) A and B, Stroop test, reading mind from eyes test, faux pas recognition test, Beck depression scale (BDI), Hamilton anxiety rating scale (HAM-A) were administered to all participants. Cervical dystonia severity was evaluated using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). Both groups were compared statistically on cognitive domains.
Results: Compared to controls, patients displayed significantly decreased performance on executive functions. All participants were shown similar results on the theory of mind test. Except when we matched 13 years or higher graduated participants, cervical dystonia patients had low scores on the faux pas recognition test, unlike controls ($r=1.25$ $p<0.001$). Disease severity and theory of mind scores were negatively correlated. It was not the case for disease severity and general cognition. Functional loss due to torticollis was most severe in patients with higher anxiety and depression scores.
Conclusion: We have found medium-high effect-sized general cognitive impairment in patients with cervical dystonia. For social cognition, education level and verbal comprehension skills were found to be determinative. Theory of mind should be evaluated with tests that have low requirements on working memory and verbal skills in neurological diseases.
Disclosure: Nothing to report.

EPO-285

Rest tremor in essential tremor patients, analysis using typing software.

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Background and aims: Patients with essential tremor (ET) have more risk of developing Parkinson´s disease (PD) compared with controls; some patients with ET can also have rest tremor. Our aim is to evaluate patients with ET and rest tremor measuring keyboard press time and time between taps using software designed for this aim.
Methods: We developed software (Teclasos) which collected data about the time between each tap (TST) and the ressing time of each key (PT). “Teclasos” was used in ET patients with and without rest tremor. We asked patients to alternate taps between “S “ and “T” keys. Data regarding gender, age, cardiovascular risk factors and non-motor features were also collected. Bradykinesia and rigidity on physical examination were exclusion criteria.
Results: Thirty-nine patients participated in this study, 16 females (41%) and 23 males (59%); the mean age was 69.18±11.4. We found differences in TST in patients with rest tremor (178.67±137.12ms; $p=0.05$) and in the PT amongst patients with non-motor features (407.24±554ms; $p=0.02$). Patients with rest tremor and non-motor features had higher TST and PT, showing statistical significance ($p=0.01$ and $p=0.08$, respectively). Although differences were also found in patients with cardiovascular risk factors, diabetes mellitus and gender, they were not significant. Patients older than 80 showed higher PT than younger patients (610.15±170ms; $p=0.01$).

AGE	75,66±10,87 years old	
HOEHN&YAHR	2,41±0,4	
LED	582,5±234mg	
		p-value
OFF time PRE	5,93±2,74	0,037
OFF time POST	4,81±2,36	
OFF PRE%	31,75±18,91	0,006
OFF POST%	21,77±12,63	
Cadence PRE	38,5±2,73	0,780
Cadence POST	38,38±2,96	
Step fluidity PRE	6,19±1,3	0,080
Step fluidity POST	6,34±1,32	
FOG PRE	2,2±4,19	0,600
FOG POST	1,88±2,42	
Step lenght PRE	1,25±1,59	0,240
Step lenght POST	1,28±1,64	
Stride speed PRE	0,5±0,07	0,150
Stride speed POST	0,51±0,09	
Acceleration PRE	0,28±0,5	0,140
Acceleration POST	0,27±0,05	

Table 1

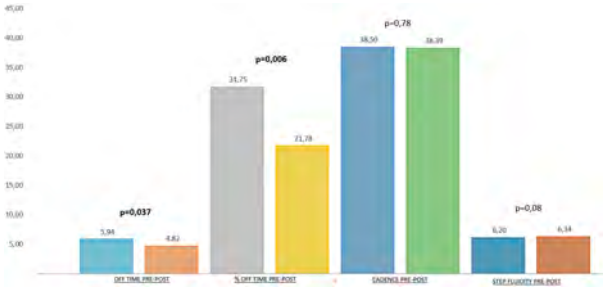

Figure 1

Figure 2

Conclusion: Patients with ET and rest tremor and non-motor features spent more time in TST and PT. These findings could indicate that the pathologic process responsible for rest tremor in ET may have spread into motor systems outside of the cerebellum-cerebellar outflow connections.

Disclosure: Nothing to disclose.

EPO-286

Safinamide improves motor and non-motor symptoms in fluctuating Parkinson's Disease patients.

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Background and aims: The occurrence of motor complications and non-motor symptoms is a crucial problem in the long-term management of Parkinsons' disease (PD). Targeting non-dopaminergic system could be a complementary approach to improve such complications. Safinamide has a unique dopaminergic and non-dopaminergic mode of action that may provide a comprehensive symptomatic relief for PD patients.

Methods: The effects of safinamide on motor and non-motor symptoms were investigated using the data from four Phase III, randomized, double-blind, placebo-controlled pivotal trials, studies 016, 018, SETTLE and XINDI.

Results: Safinamide significantly improved motor fluctuations (OFF time reduced by 1.10 hours, $p<0.0001$), motor symptoms (improvement of 5.15 points in UPDRS III, $p=0.0003$), pain (reduction of concomitant pain-killer treatments of 22%, $p=0.0478$), and mood (improvement of 0.76 points in GRID-HAMD, $p=0.0027$). These improvements were observed after only 2-weeks of treatment, showing a rapid-onset of the efficacy of the drug.

Conclusion: Safinamide, administered as add-on therapy in fluctuating PD patient, improved motor symptoms and motor complications without increasing troublesome dyskinesia, irrespective of whether other drugs were added to the baseline levodopa treatment. Moreover, safinamide improved pain and mood, two important non-motor symptoms often underestimated and undertreated. These favorable effects may be explained by its modulation of glutamatergic hyperactivity.

Disclosure: Carlo Cattaneo, and Constanza Oliveros are Zambon SpA employees; Ivan Marjanovic and Erminio Bonizzoni are Zambon SpA consultants.

EPO-287

Influence of RBD onset on the clinical characteristics of Parkinson's disease patients: a retrospective study.

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Background and aims: In Parkinson's Disease (PD), Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD) might either precede the appearance of motor symptoms, or develop during the disease course. PD patients with RBD are characterized by a higher burden of cognitive impairment and hallucinations. However, few studies have analyzed the clinical characteristics of PD patients according to the timeline of RBD onset.
Methods: PD patients have been retrospectively enrolled. Presence and onset of probable RBD (pRBD) has been evaluated using RBD Screening Questionnaire (score ≥6). Presence of Mild Cognitive Impairment (MCI) at baseline has been evaluated using the MDS criteria level II. Presence of motor complications and hallucinations has been evaluated at a 5-year follow-up.
Results: At total of 115 PD patients (65 men, 56.5%; mean age 62.5±9.7 years; mean disease duration 3.7±3.9 years) have been enrolled. Out of these, 63 fulfilled the diagnosis of pRBD (54.8%) with 21 (33.3%) reporting the RBD onset before the onset of the motor symptoms (PD-RBDpre), and 42 (66.7%) after the motor symptoms (PD-RBDpost). At enrolment presence of MCI was associated with PD-RBDpre patients (OR 5.04; 95%CI 1.33–19.05; p-value=0.02). At follow-up, a higher risk of developing hallucinations was also associated with PD-RBDpre (OR 4.82;95%CI 1.30–17.85; p=0.018).
Conclusion: PD patients with RBD occurring before the onset of motor symptoms represent a subgroup of patients with a more severe cognitive phenotype and with a higher risk of developing hallucinations along the disease course, with significant implications in terms of prognostic stratification and therapeutic approach.
Disclosure: Nothing to disclose.

EPO-288

Neurological spectra of neurofibromatosis type 1 in adults: a case series

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Background and aims: Neurofibromatosis type 1 (NF-1) is an autosomal dominant multisystem disorder, with predominant neurological involvement. Aim: To perform a clinical, imagological, and genetic analysis of a NF-1 adults' cohort.
Methods: Patients were identified from an institutional database. Files review was performed according to a structured protocol.
Results: Eleven patients (from nine non-consanguineous families) were identified, 5 females, with age 39±12 years. Ten had family history in first-degree relatives. All had disease onset in childhood, the most frequent presentation being café-au-lait (CAL) spots (9). All subjects had one or more neurological symptoms/signs: pyramidal signs (8), headache (5), learning disabilities (4), movement disorders (4), delayed milestones (2) and epilepsy (1). Two patients developed optic pathway gliomas. Cutaneous involvement was present in all: CAL spots (11), freckling (9) and cutaneous neurofibromas (7). Eight had ophtalmological manifestations, the most frequent being Lisch nodules (5). In 8 patients, brain MRI revealed T2-weighted hyperintensities, consistent with myelin vacuolization, at the cerebellum (4), hippocampus (3) and/or basal ganglia (3). All had heterozygous pathogenic variants on NF1.
Conclusion: Adults with NF-1 have a wide range of neurological phenotypes, with the most frequent being pyramidal signs, probably in relation with white matter lesions. We highlight the frequency of movement disorders in our patients, which may be underdiagnosed in previous cohorts.
Disclosure: All authors declare that they have no conflicts of interest related to the manuscript.

EPO-289

Atypical immunochemistry staining in rapidly progressive cerebellar syndrome in woman with breast cancer

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Background and aims: Rapidly progressive cerebellar syndrome (RPCS) is frequently paraneoplastic in postmenopausal women with breast and ovarian cancer, associated with so-called high-risk for cancer antibodies. The syndrome is a treatable condition but often with no full recovery.
Methods: A 67-years old woman was admitted for a ten days onset of nausea, vomit, sickness, weight loss, gait instability, dysarthria, hypophonia, diplopia, dysphagia and limb and trunk ataxia (mRS 4).
Results: The patient underwent several brain MRI scans, always negative. The lumbar puncture showed an inflammatory cerebrospinal fluid (CSF): 27 cells/mm^3, glucose 71 mg/dl, proteins 48 mg/dl; coltural, virological exams and most common anti-cerebellar antibodies were negative. PET total body and mammography detected a mammary lesion (BI-RADS 6) with axillary lymphatic metastasis. Immunochemistry and biological profile found out estrogen receptor positive breast cancer. Using indirect immunofluorescent tissue based assay exploiting lightly fixed rat brain tissue, we detected on CSF an uncharacterized nuropilar staining involving the molecular layer of the cerebellum. In the suspicion of RPCS, the patient underwent five days of intravenous immunoglobulins treatment, then replaced by steroid with slow tapering. Surgery was excluded by Breast Unit team. At 6 months follow-up, there was a little neurological improvement with persistence of dysarthria, and ataxic features (mRS 3).
Conclusion: The features of staining resemble anti-Tr/Delta/Notch-like Epidermal growth factor-related Receptor (DNER) antibodies. Our patient presented several clinical features in common with RPCS associated with these antibodies, usually lymphoma and solid tumors related, instead no breast cancer cases were still reported.
Disclosure: Nothing to disclose.

EPO-290

Reasons for exclusion from Deep Brain Stimulation (DBS) for Parkinson's Disease

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Background and aims: Understanding the reasons for exclusion from DBS for Parkinson's disease (PD) might optimize referral. Nevertheless, few studies have addressed it. We aimed to evaluate the reasons for exclusion from DBS for PD in our centre.
Methods: A retrospective observational study evaluated all patients referred to and excluded from DBS between January 2006 and May 2019. We searched our DBS database and reviewed the clinical files of patients consulted at least once for DBS, and a data extraction spreadsheet was developed.
Results: Of 320 patients consulted for DBS, 72 (22.5%) were excluded (52.4% male; average age 65.2 [±6,6] years, range 40–79 years; average disease duration 12,3 [±6.0] years). There were on average 3.3 [±2.4] consultations and 6.7 [±7.3] months until exclusion. 25.4% of patients were excluded in the first consultation. An average of 1.89 reasons were identified, although 44.4% had only one reason for exclusion. 3 patients were excluded due to atypical parkinsonism. 68.3% were referred by Movements Disorders (MD) specialists. The main reasons for exclusion were an MDS-UPDRS motor part score during Best On in items "gait", "freezing" and "postural instability" above the cutoff (23.8%); dementia (2.8%); and age >70 years (22.2%). 20.6% give up from su3rgery after an explanation of the procedure. Reasons for exclusion were similar between patients referred by MD and non-MD specialists.

Conclusion: One-fifth of the patients were excluded from DBS. Levodopa-resistant axial symptoms, dementia, and age were the main reasons, although several give up from surgery after a detailed explanation of the procedure.
Disclosure: Nothing to disclose.

EPO-291

Opicapone versus entacapone: Head-to-head comparison of HCRU in COMT-I naïve People with Parkinson's

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Background and aims: The appearance of motor fluctuations (MF) is a crucial milestone in people with Parkinson's (PwP) as they are associated with increased disability and considerable healthcare resource utilisation (HCRU). Management of MF may require add-on of enzymatic inhibitors such as Catechol-O-methyl transferase (COMT) inhibitors. To date there has been a lack of head-to-head data comparing opicapone and entacapone, the two most commonly used COMT inhibitors in real-world settings.
Methods: In this retrospective cohort study, we assessed HCRU outcomes in PwP naïve to COMT inhibition via UK electronic healthcare records (Clinical Practice Research Datalink and Hospital Episodes Statistics databases, June 2016 to December 2019). HCRU outcomes were assessed before (baseline) and after COMT inhibition at 0-6 months, 7–12 months, and 13–18 months. Opicapone treated PwP (n=173) were 1:4 algorithm-matched to entacapone-treated PwP (n=433).
Results: A significantly higher percentage of PwP in the entacapone-treated group had ≥1 neurology outpatient visits at 6-month follow-up compared to the opicapone-treated group (63% vs 44%, respectively, $p<0.001$). Head-to-head regression analyses (including age, sex, disease duration, baseline HCRU, and baseline medications as covariates) showed that PwP who received opicapone as their first line COMT inhibitor had 18.5% fewer neurology outpatient visits within 6 months of initiation compared to the entacapone-treated group.
Conclusion: This head-to-head study is the first to demonstrate using 'real-world' data that initiating COMT inhibition with opicapone is likely to decrease the need for post-treatment HCRU versus initiation of COMT inhibition with entacapone.

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EPO-292

Is fatigue in Parkinson's disease a disorder of movement preparation? A neurophysiological study

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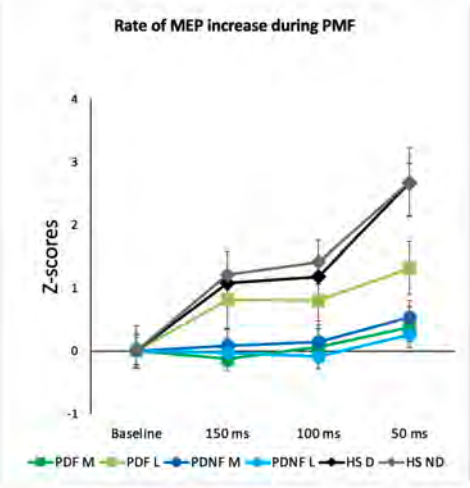
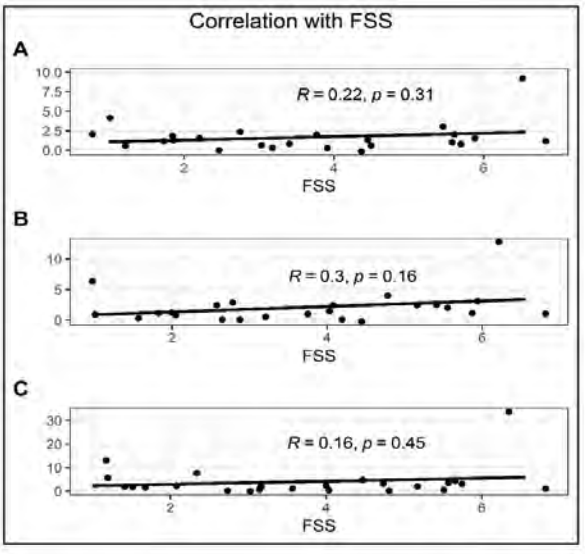
Background and aims: Fatigue is common in Parkinson's disease (PD) and it has been linked to the impairment of motor planning. In Multiple Sclerosis fatigued patients showed reduced pre-movement facilitation (PMF). We aimed at investigating whether PMF is abnormal in PD and is related to fatigue.
Methods: We enrolled 15 PD patients with fatigue (PD-F, Fatigue Severity Scale ≥4), 16 PD patients without (PD-NF) and 16 Healthy Controls (HC). We assessed PMF with transcranial magnetic stimulation (TMS) during a simple reaction time (RT) paradigm. Subjects were asked to briskly abduct their thumb after a go signal and TMS was delivered at 50 ms, 100ms and 150ms before the mean calculated movement onset. 15 PD-F patients (mean age 63.27±9.8 years).
Results: The rmANOVA corrected for age did not show significant interactions group x side x time (F= 0.26, p= 0.9) of amplitude of MEP and at three intervals during PMF (MEPPMF) compared to MEPREST. When computing the rate of MEP increase during PMF (MEPPMF/MEPREST), all groups had a significantly higher rate of PMF at 50 ms (F=4.3, p=0.014*), but HC significantly differ from patients while PD-F and PD-NF did not differ from each other (p> 0.05). No correlation was found between fatigue scores and MEP increase.



Rate of Motor evoked potentials (MEP) increase during pre-movement facilitation (PMF) in Parkinson's disease (PD) patients' most and least affected sides and in dominant and non-dominant hand of healthy controls (HC).



Analysis of correlations between Motor evoked potentials (MEP) increase during pre-movement facilitation (PMF) in Parkinson's disease (PD) patients and Fatigue Severity Scale (FSS)

Conclusion: Our results provide preliminary evidence that PMF is abnormally reduced in PD patients compared to HC and independent from fatigue. Reduced PMF could represents a hallmark of PD patients. Future works are necessary to disentangle the mechanisms of fatigue in PD.
Disclosure: The Authors have no relevant disclosure.

EPO-293

Gender differences in non-motor fluctuations in Parkinson's disease

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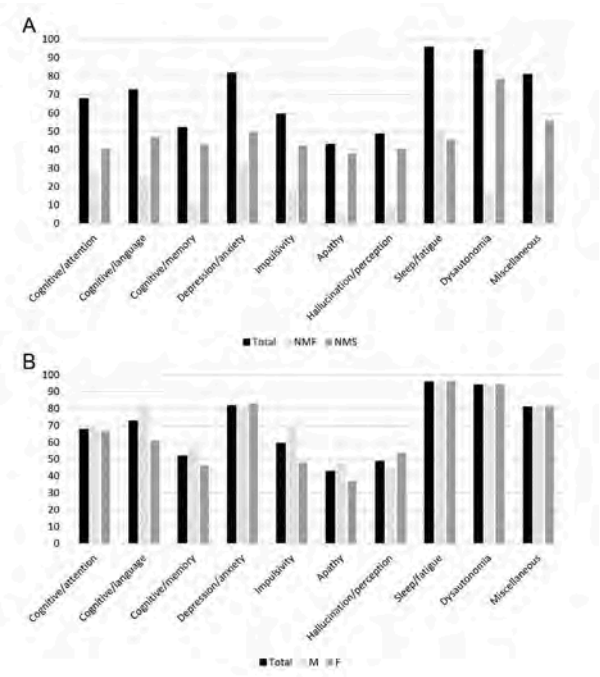
Background and aims: Non-motor symptoms (NMS) and Non-motor fluctuations (NMF) in Parkinson's Disease (PD) are common, involving several domains and affecting quality of life. Aim of the study is to estimate the burden of NMF in PD patients and to evaluate the possible gender effect.

Methods: PD patients fulfilling the MDS-PD diagnostic criteria attending the "Parkinson's Disease and Movement Disorders Centre" of the University of Catania were evaluated using the Non-Motor Fluctuations Assessment (NoMoFA) Questionnaire. NoMoFA items were also grouped into the following domains: cognitive, mood, sleep/fatigue, dysautonomia, hallucination/perception and miscellaneous domains were identified.

Results: One-hundred and twenty-one patients with PD (67 men, 55.4%; mean age 70.2±8.9 years, disease duration 8.3±4.6 years) were evaluated. All PD patients reported at least one NMS, whereas 87 (71.9%) also reported NMF. "Feel sluggish or had low energy levels" (47.2%) along with "Feel excessively sleepy during the day" (40.0%) were the most common NMF reported in the whole sample. The majority of PD patients reported presence NMF during the OFF state (79, 65.3%). At multivariate analysis, NMF were positively associated with the female gender (adjusted OR 3.41; 95%CI 1.28–9.09; p-value=0.01). Women with PD had higher NMF scores especially in depression/anxiety, sleep/fatigue and dysautonomia domains.



Frequency of reported domains in PD sample. A, differences in reported non-motor symptoms in the whole PD sample considering non-motor fluctuation and static non-motor symptoms. B, differences in reported domains between PD male and female

Conclusion: Our study reported the presence of a gender-related pattern in the frequency of NMS and NMF in PD patients, with female gender associated with a higher risk of developing NMF, highlighting the need for personalized treatment strategies when addressing NMF.

Disclosure: Authors declare no disclosures for this work.

EPO-294

Safety of safinamide in routine clinical practice in a Spanish population with Parkinson's disease

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Background and aims: Safinamide is a levodopa add-on therapy with a dual dopaminergic and non-dopaminergic mechanism of action that improves the management of Parkinson's disease (PD). This post-hoc analysis of the European SYNAPSES trial aimed to provide new evidence on the safety profile of safinamide among Spanish study participants in routine clinical practice.
Methods: Once safinamide treatment began, patients with PD were followed for 12 months. The occurrence of adverse events (AEs) was analysed overall and in preselected subgroups that included patients older than 75 or with relevant comorbidities or psychiatric conditions.
Results: Of 511 participants, 131 (25.6%) were older than 75, 373 (73.0%) had relevant comorbidities, and 249 (48.7%) had psychiatric conditions. At least one AE was reported by 280 (54.8%) patients, while 168 (32.9%) had at least one adverse drug reaction (ADR). At least one serious adverse event (SAE) was registered in 38 (7.4%) patients, and 8 (2.0%) had at least one serious ADR. The majority of AEs were mild (69.3%) or moderate (23.5%), and ultimately all resolved completely. Few AEs (2.0%) and no SAEs had a definite relationship with safinamide. No relevant differences for AE and SAE frequencies were detected in elderly patients nor in patients with psychiatric conditions, and slightly higher percentages were observed in patients with comorbidities.
Conclusion: Safinamide proved to be a safe option for different groups of PD patients in routine clinical practice.
Disclosure: The SYNAPSES trial and this post-hoc analysis were funded by Zambon S.p.A.

EPO-295

Dysphagia assessment in Parkinson's disease and risk of aspiration pneumonia

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Background and aims: Dysphagia is a complication that is common in latter stages of Parkinson's disease (PD) influencing quality of life of patients and caregivers. The prevalence of dysphagia and risk of secondary complications such as aspiration pneumonia in dysphagic PD patients is variable, being highly dependent on the methods used for the evaluation. Aim of the study: to assess the prevalence of dysphagia and aspiration pneumonia in patients with PD.
Methods: Cross-sectional study that included patients with PD evaluated in the outpatient clinic or admitted in the Department of Neurology, County Clinic Hospital Brasov. We evaluated the patients using a standardized protocol that included the Hoehn-Yahr scale, Gugging Swallowing Screen (GUSS), fibro-endoscopic evaluation of swallowing (FEES), FEDSS scale and Munich Dysphagia Test (MDT-PD).
Results: There were 35 patients included in the study (43.75% males) with a mean age of 68.2±5.7 years. The mean Hoehn-Yahr stage was 2.8. Swallowing disturbances was frequently encountered in patients with higher H-Y stage (12 patients H-Y 3-5) were 58.33% presented some degree of dysphagia in comparison with 13.04 % in stages 1–2 ($p<0.05$). Pneumonia was encountered in 16.6% of the dysphagic patients with higher H-Y stage, with no cases of pneumonia in patients with lower stages of disease. A higher MDT-PD was corelated with the risk of aspiration and corresponded with the changes observed on the FEES evaluation.
Conclusion: Dysphagia has a high impact on the quality of life of PD patients, being a risk factor for aspiration pneumonia.
Disclosure: Nothing to disclose.

EPO-296

Characterisation of OFF-Time in Levodopa-Treated Parkinson's Patients: A Post-hoc Analysis of an Exploratory Trial

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Background and aims: Optimising levodopa (LD) treatment regimens through catechol-O-methyltransferase (COMT) inhibition is an effective strategy in the management of motor fluctuations (MF) in patients with Parkinson's disease (PD). Study 203 demonstrated that adding the COMT inhibitor opicapone (OPC) to LD therapy increases LD systemic exposure and decreases OFF-time in patients with PD and MF. This post-hoc analysis evaluated the OFF/ON patterns in LD-treated patients included in Study 203 before OPC was added.

Methods: Study 203 was an exploratory, open-label, modified cross-over trial. All participants received LD/carbidopa (CD) 500/125 mg, administered as 5 daily intakes of 100/25 mg every 3 hours for 2 weeks and were then randomly (1:1) assigned to LD/CD 400/100 mg given in 4 or 5 daily intakes plus OPC 50 mg for 2 additional weeks. LD 12-hour pharmacokinetics (PK) was the primary outcome (last daily intake excluded from PK analysis); 12-hour patient ON/OFF monitoring was a key secondary outcome. This study evaluated ON/OFF patterns in patients treated with the LD/CD 500/125 mg regimen before randomisation.

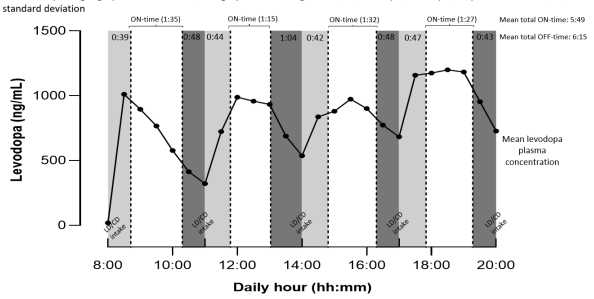
Results: Overall, 24 patients were recruited and received the LD/CD 500/125 mg regimen (Table). For all daily intakes, the mean total ON-time was 5h 49mins and the mean total OFF-time was 6h 15mins (Figure). The total OFF-time was divided into time-to-ON (2h 52mins) and 'wearing-off' (3h 23mins), which represented 45.9% and 54.1% of the total OFF-time, respectively.

Table. Baseline characteristics

	Overall N=24
Male gender, n (%)	13.0 (54.2)
Mean age, years (SD)	62.2 (7.1)
Mean weight, kg (SD)	81.9 (16.0)
Mean height, cm (SD)	167.3 (9.5)
Mean PD duration, years (SD)	6.6 (3.2)
Mean daily OFF-time, hours (SD)	7.3 (1.6)
LD/CD monotherapy or plus other PD drugs excluding DA and MAO-Bi, n (%)	10 (41.7)
Levodopa/carbidopa monotherapy (no other PD drugs), n (%)	7 (29.2)
Patients receiving DA and MAO-Bi* in addition to Levodopa/carbidopa, n (%)	
Levodopa/carbidopa plus DA only	9 (37.5)
Levodopa/carbidopa plus MAO-Bi only	4 (16.7)
Levodopa/carbidopa plus DA & MAO-Bi	1 (4.2)
PD medications given in addition to levodopa/carbidopa, n (%)	17 (70.8)
Pramipexole	6 (35.3)
Selegiline	5 (29.4)
Ropinirole	4 (23.5)
Trihexyphenidyl	3 (17.6)
Amantadine	3 (17.6)

*Some patients were receiving additional PD drugs that were not DA or MAO-Bi
CD, carbidopa; DA, dopamine agonists; LD, levodopa; MAO-Bi, monoamine oxidase inhibitors; PD, Parkinson's disease; SD, standard deviation

Figure. 12-hour ON-/OFF-time data reported on PK* days in relation to the mean LD plasma concentration versus daily hour in patients receiving the 5-intake (every 3 hours) daily oral administrations of LD/CD 500/125mg. *Last daily intake was excluded from the PK analysis. Light grey bars: time-to-ON; dark grey bars: 'wearing off'. LD/CD, levodopa/carbidopa; PK, pharmacokinetics; SD, standard deviation



Conclusion: The current analysis suggests that in LD-treated patients with 'wearing-off' MF time-to-ON following a dose of LD is responsible for nearly half of total daily OFF-time.

Disclosure: Supported by Bial.

EPO-297

Movement disorders as initial manifestation of autoimmune encephalities: A case series.

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Background and aims: Autoimmune encephalitis (AE) and paraneoplastic neurological syndromes (PNS) are a growing field in recent years. Movement disorders are one of the most consistent features of these disorders. Early diagnosis is essential since immunomodulatory treatment can considerably change the prognosis.
Methods: We describe a case series of AE in which the movement disorder was the initial manifestation (The main characteristics of the reported patients are highlighted on table-1).
Results: Patient-1, a 78-year-old man, presented acutely faciobrachial dystonic seizures of seconds of duration. LGI1 antibodies were found in serum. After starting immunotherapy, significant improvement was observed, persisting dystonia with a task-specific component. Patient-2, a 73-year-old man, presented symptoms of gait disturbance and rapidly progressive akinetic-rigid parkinsonism, with early falls, cognitive impairment and insomnia, worsening 3 months until cause serious disability. Anti-IgLON5 antibodies were found on CSF and serum. Patient-3, a 65-year-old woman, developed oral occlusion dystonia, and later on ataxia and ophtalmoplegia, with a rapid progressive course. MRI showed hyperintensity in the superior cerebellar peduncle and pons (Figure-1). Anti-Ri antibodies were detected in CSF and serum and small cell lung carcinoma was found afterwards (being the encephalitis its first symptom).
Conclusion: EAs can debut with different movement disorders. Therefore, it is important to take into account the red flags that can lead us to suspect this type of disease, highlighting acute onset, early disability and early development of other neurological symptoms, as it is a potentially curable cause of encephalitis, with a fatal course in the absence of treatment.
Disclosure: Nothing to disclose.

EPO-298

Evaluation of the effectiveness of safinamide in a Spanish population with Parkinson's disease

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Background and aims: The use of safinamide as a levodopa add-on therapy has proven efficacy in the management of Parkinson's disease (PD) in controlled trials. This post-hoc analysis of the SYNAPSES trial provides new evidence on the use of safinamide in a Spanish cohort in routine clinical practice.
Methods: Once safinamide treatment began, patients with idiopathic PD were followed for 12 months and evaluated through the Unified Parkinson's Disease Rating Scale total score (UPDRS) and UPDRS part III score during ON time.
Results: Compared with the European study population, there was a higher prevalence of psychiatric symptoms and non-compliant use of safinamide (30.9% vs. 16.9%) in the Spanish cohort. A higher percentage of the Spanish participants showed clinically relevant improvement when receiving add-on safinamide only (reduction in UPDRS total score >4.3=57.4%; reduction in UPDRS part III score >2.5=53.7%) compared to treatment with additional adjunct therapies (reduction in UPDRS total score >4.3=44.1%; reduction in UPDRS part III score >2.5=42.8%). Switching from rasagiline to safinamide showed an improvement in 55.1% of patients (UPDRS total score). Safinamide reduced the proportion of patients with motor complications independent of levodopa doses, showing a stronger effect in the absence of other adjunct therapies.
Conclusion: Despite higher off-label use of safinamide within the Spanish study population, a stronger clinical benefit was observed when using safinamide as the unique add-on therapy to levodopa, including in patients with comorbidities.
Disclosure: The SYNAPSES trial and this post-hoc analysis were funded by Zambon S.p.A.

Epilepsy 2

EPO-299

Resting-state brain connectivity differences between epileptic and non-epileptic first events

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Background and aims: Epilepsy is a brain network disorder affecting different regions across the brain. Clinical diagnosis often relies on different "markers" such as brain lesions or signs in the electroencephalography (EEG) tracing. However, in clinical routine these markers are not always clear or present at all, making it difficult to provide a certain diagnosis, especially because different pathologies can underlie the same epileptic symptoms. Here we investigated if measures of functional connectivity applied to resting-state EEG recordings differed between five patients groups (n=15 per each group): epileptic, acute symptomatic seizure (ASS), psychogenic non-epileptic seizures, syncope, and patients who suffered from a single unprovoked seizures.
Methods: We retrospectively recruited untreated first-seizure patients for whom the EEG tracing did not show interictal epileptic discharges, and who presented no epileptogenic brain lesions (besides the hemorrhagic stroke group). We calculated a weighted phase lag index as a measure of connectivity in several regions of interest (ROIs) and for different frequency bands.
Results: We found a significant interaction (p=0.034) across groups for clustering coefficient (network segregation), which was increased in epileptic and ASS patients versus controls (p<0.001 and p<0.01 respectively), specifically in delta frequency.
Conclusion: Given the often difficult diagnosis of epilepsy in the absence of clear signs on the EEG tracing, connectivity measures across patient groups could provide support for the identification of a possible underlying epileptic disorder. Future prospective studies will determine its usefulness as a biomarker for epilepsy.
Disclosure: MS has shares in Epilog.

EPO-300

Better effect of early vs delayed treatment after the first seizure: a brain connectivity study

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Background and aims: Treatment may be delayed after the first seizure in new onset epilepsy (NOE) patients, often as a result of unorganized work-up. Our own observation suggests that antiseizure medication (ASM) <48h is related to a higher rate of patients with seizure control, as compared to later treatment. In this study, we investigated EEG markers of early/late drug therapy through connectivity analysis.
Methods: 36 epileptic patients were retrospectively enrolled (mean age: 53.14; SD: 16.37; 36 females). All received an EEG while in the emergency department (ED). Follow-up EEGs were obtained 1 to 12 months after the first event. 23 patients were treated <48h and 13 were treated later. Connectivity was compared between both groups for all established frequency bands.
Results: Patient groups did not differ in age, gender, presence of a brain lesion or delay of follow-up EEG. The interaction between frequency bands and delay of ASM was significant (p<0.001). In the follow-up EEG, patients treated later showed reduced theta connectivity (p=0.006) and increased alpha connectivity (p<0.001).

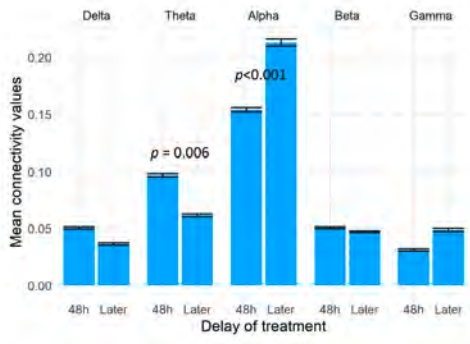

Figure: differences in brain connectivity across all brain regions per frequency band for follow-up EEG. Significant differences are noted and error bars represent standard error of mean.

Conclusion: Our results suggest that swift ASM introduction affects significantly theta and alpha frequencies, up to 1 year after the index event. Larger prospective studies are required to determine if these changes in the EEG connectivity are a useful marker for future treatment success or if it reflects a neurobiological effect of early ASM on possible excitatory and inflammatory processes at the first event.
Disclosure: MS has shares in Epilog.

EPO-301

Predicting risk of relapse by functional connectivity in patients with new onset epilepsy

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Background and aims: After a diagnosis of epilepsy, 20–30% of patients will relapse regardless of treatment. To date, markers able to predict future success in drug response are still lacking. Here, we investigated brain connectivity recorded by means of electroencephalography (EEG) between patients who respond to treatment (responders) and patients who respond poorly (non-responders), to link potential differences to treatment response.
Methods: We retrospectively recruited 65 patients with new onset epilepsy (at least 2-year follow-ups) for whom an EEG was performed before treatment directly upon arrival at the hospital, following a first epileptic seizure. We computed connectivity analyses (weighted phase-lag-index) on all brain regions for delta, theta, alpha, beta, and gamma frequencies. By performing a mixed-model analysis, we tested connectivity differences across frequency bands between responders and non-responders.
Results: After treatment, 50 patients remained seizure-free (mean age: 57; SD: 18) while 15 relapsed (23%; mean age: 54.6; SD: 18.9). No significant differences in age (p=0.11) and sex (p=0.13) were found between groups. In terms of EEG, we observed an interaction between frequency bands and groups (p<0.001). Post-hoc tests showed a delta decrease (p=0.022) and an alpha increase (p=0.022) for patients who relapsed despite treatment as compared to patients who did not. No significant differences were observed for the other frequency bands.

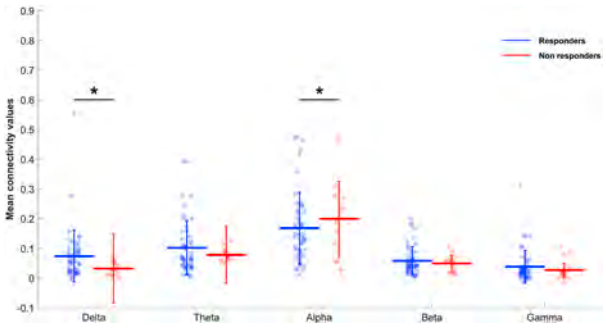

Figure: Brain connectivity values per frequency band between responders and non-responders. Differences between groups marked with a black asterisk are statistically significant (p<0.05). Error bars represent standard deviation.

Conclusion: EEG connectivity in delta and alpha frequencies after a first epileptic seizure appears to be a promising marker for future poor drug treatment response.
Disclosure: MS has shares in Epilog.

EPO-302

Serum microRNA levels can predict ketogenic diet efficacy in adult refractory epilepsy

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Background and aims: Ketogenic diet (KD), is being increasingly used in adult patients with good efficacy and tolerability. Although KD mechanisms of action are yet to be identified, microRNAs (miRs), are thought to be key players in this process. We aimed to address if epilepsy-associated miRs can predict the response to KD in adult refractory patients.
Methods: Circulating miR-146a, miR-155, miR-22, miR21, and miR-134 were quantified in 40 adult refractory epileptic patients (16 M; 33.1±11 years) before and at 3 months of Atkins modified KD regimen.
Results: Three months after treatment onset, 20 out of 40 patients presented seizure reduction, 14 patients were non-responders and 6 reported only a qualitative benefit. At baseline, miR-146a levels were higher in responder patients compared to non-responders (25.95 vs. 23.62, p=0.029). Although no significant differences were observed for the other individual miRs, we combined miR-146a – miR-155 – miR-22 – miR-21 – miR-134 and observed that this panel had a good prognostic value differentiating responders and non-responders with 77% specificity and 70% sensitivity (AUC=0.791[0.624–0.958], p=0.007). In responder patients KD induces changes in miRs levels with the upregulation of miR-134 (M0 vs. M3: 20.96 vs. 21.90, p=0020) and the downmodulation of miR-155 (M0 vs. M3: 23,99 vs. 22,73, p=0,018) and miR-22 (M0 vs. M3: 22.87 vs. 19.79, p=0.020).
Conclusion: The panel miR-146a – miR-155 – miR-22 – miR-21 – miR-134 may be a suitable biomarker for KD response, which could help select epilepsy patients that would most benefit from this treatment. Our results support an epigenetic-reprogramming action of KD, affecting namely inflammation-associated microRNAs.
Disclosure: Work funded by LPCE and CHUPorto bursaries.

EPO-303
Abstract withdrawn

EPO-304
The Long Term Prognosis of IGE: a comparison between syndromes

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Background and aims: Idiopathic Generalized Epilepsies (IGE) are usually drug responsive, but patients with a diagnosis of Juvenile Absence Epilepsy (JAE), Epilepsy with Generalized Tonic-Clonic seizure alone (GTCA) and Juvenile Myoclonic Epilepsy (JME) often require a life-lasting anti-seizure medication (ASM). We tested if syndromic diagnosis is relevant to prognosis.
Methods: Patients with JAE, GTCA or JME and a follow-up of 1) 5 or 2)15 years after the first seizure were included. By Kruskall-Wallis ANOVA , we have compared the a) total number of Generalized Tonic Clonic seizures (GTCs) occured b) the longest GTCs-free period c) time spent to reach this period d) the number of adequate ASM regimen tried to reach this period d) "drug resistant" patients considering any seizure type.
Results: We included 34 and 22 JAE, 44 and 17 JME, 23 and 10 GTCA, for the 5 and 15 years follow up , respectively. The total number of GTCs was higher for GTCA compared to JAE and JME in the 5 years follow up period ($p \leq 0.01$) and to JAE in the 15 follow up period. The longest GTCs-free period and the time spent to reach this period were not different among groups. A higher number of ASM-trials were required and drug resistance was more common in JME in the longer follow-up (1% in JAE, 27% in JME, 0% in GTCA, $p<0.01$).
Conclusion: JAE carried the more benign prognosis. JME required the highest number of adequate ASM trials and were more prone to be classified as drug resistant in the longer follow-up.
Disclosure: The authors declare no conflict of interest.

EPO-305
Social cognition in the spectrum of mesial temporal lobe epilepsy

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Background and aims: Increasing evidence suggests that social cognition is impaired in mesial temporal lobe epilepsy (MTLE). Refractory MTLE (rMTLE) has been found to affect: i) Theory of Mind (ToM), which is the ability recognize and comprehend others' mental states and ii) facial emotion recognition. Milder forms of MTLE (mMTLE), by definition characterized by response to antiseizure medication and seizure-freedom, were not evaluated. The aim of this study was to analyze social cognition in the spectrum of MTLE.
Methods: Forty-five patients with MTLE (25 mMTLE, 20 rMTLE) were compared to 25 healthy controls (HC). ToM was explored with Faux Pas Test (FP) and Reading the Mind in the Eyes Test (RMET). Facial emotion recognition was studied with Ekman Faces Test (EFT). In addition, a specific battery of tests was performed as screening for cognitive and mood disturbances.
Results: With respect to HC, both mMTLE ($p=0.017$) and rMTLE ($p<0.001$) patients had lower scores in the RMET, whereas no differences were identified between the two subgroups of patients. Moreover, only rMTLE patients had lower performances in the FP recognition when compared to HC ($p=0.004$). In EFT mMTLE had lower scores in fear and anger recognition, while rMTLE underperformed also in happiness, sadness, disgust, and surprise recognition.
Conclusion: MTLE affects circuitries of ToM and emotion recognition even in subjects with mMTLE, albeit with a more limited extension compared to rMTLE. This supports the idea that epilepsy itself, even when seizure control is achieved, could damage key areas involved in the complex neural circuits of social cognition.
Disclosure: The authors have nothing to disclose.

EPO-306

Progression of electroclinical features in Lennox-Gastaut syndrome from childhood to adulthood

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Background and aims: Lennox-Gastaut syndrome (LGS) comprises a triad of multiple, medically-refractory seizure types, cognitive impairment, and electroencephalogram (EEG) features including diffuse slow-spike-and-wave (DSSW) and background slowing during wakefulness, and diffuse fast rhythms (DFR) in sleep. However, not all of these EEG features may be present in adulthood. Our study aims to identify how EEG patterns and seizure types evolve as an LGS patient ages.
Methods: Retrospective, single-centre study, including 24 adult patients. Information was collected on types of seizures at onset and at last follow-up, and interictal and ictal findings from paediatric and adult EEG telemetry reports.
Results: Tonic seizures were the commonest in both populations; atypical absences were more common childhood, and generalised tonic-clonic in adulthood. 84.20% childhood interictal EEGs showed DSSW, 100% background slowing, and 100% had DFR in sleep. 72.73% childhood ictal EEGs showed electrodecrement (ED) with fast activity (FA) with tonic seizures, and 27.28% showed only FA. In contrast, 35% of adult interictal EEGs showed DSSW; 60% background slowing, but DFR during sleep were present all adults. DSSW was most commonly replaced by independent multifocal spike discharges (76.92%) in adults. 56.25% adulthood ictal EEGs showed only ED with tonic seizures, 31.25% ED with FA, and 12.5% only FA.
Conclusion: Our study highlights that in LGS, both interictal and ictal EEG features change significantly over the lifespan, and stresses the importance of sleep EEGs in adulthood, due to its implications for LGS diagnosis, and subsequent medical management, especially with medicinal cannabis in the UK.
Disclosure: The authors have no conflicts of interest with regards to this research study.

EPO-307

A retrospective cohort study on the management of early and established status epilepticus

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Background and aims: Status epilepticus (SE) is a time-sensitive medical emergency with high mortality and morbidity. We investigated the management of early and established status epilepticus including timing, dosing and selection of benzodiazepines and efficacy of second line treatments.
Methods: Single-centre, retrospective observational cohort study.
Results: 252 patients. Seizures terminated spontaneously in 54% cases. 46% were given benzodiazepines, of which 25% were given at least one benzodiazepine by family/carers, and 62.1% received benzodiazepines by ambulance services. Benzodiazepines terminated seizures in 71.6% cases. The commonest benzodiazepine was buccal midazolam (35.5%). Median time to first benzodiazepine was 14.5 (6–27) minutes. We found a positive correlation between time to first benzodiazepine and time to seizure cessation, progression to second- and third-line treatment, and respiratory complications ($p<0.05$). 62.9% cases received a correct benzodiazepine dose. Underdosing was commonest, and associated with longer seizure duration and progression to second-line treatment ($p<0.05$). 28.4% cases progressed to second-line treatment; mean time to treatment was 59.4 minutes (±32.3 minutes). The commonest second-line ASM was Levetiracetam (53.8%), followed by Phenytoin (43.6%). Second-line treatment terminated seizures in 57.5% cases. 12.1% cases progressed to third-line treatment; mean time to treatment was 60.6 minutes (±22.24 minutes). Anaesthetic agents included propofol and fentanyl. Respiratory complications occurred in 6.75% cases; none due to benzodiazepines. There were two deaths in refractory SE.
Conclusion: These data confirm that delays in benzodiazepine administration and incorrect dosing lead to worse outcomes. Efforts to increase awareness of SE as a time-sensitive emergency with high mortality and morbidity are needed.
Disclosure: The authors note no conflicts of interest with regards to this research.

EPO-308

Safe and effective implantation of VNS in super-refractory post-anoxic myoclonic status epilepticus in early pregnancy

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Background and aims: The management of super-refractory post-anoxic myoclonic status epilepticus (PAMSE) in pregnancy may be complicated by anti-seizure medication (ASM) polytherapy-associated teratogenicity. We aim to demonstrate the safety and efficacy of vagal nerve stimulation (VNS) in a pregnant patient presenting with super-refractory PAMSE.

Methods: This is a retrospective case-study. Information was obtained from the patient's electronic medical records at her local hospital and our centre.

Results: A 30-year old female, at 5-weeks gestation presented with drug-refractory myoclonic status epilepticus, unresponsive to anaesthetic agents, due to drug overdose. The severity of seizures did not allow extubation, and the patient remained ventilated and sedated. VNS was implanted 26 days after seizure onset. The immediate post-operative output was 0.25mA, which was rapidly titrated up to 0.5mA the next morning, and to 0.75 mA that afternoon. This was further increased to 1.0mA on 3rd day post-operation, and to 1.25mA 7 days post-op. Myoclonic jerks diminished significantly 5 days post-op, and the patient was extubated. 20 days after VNS implantation, no myoclonic jerks were observed. There was increased alertness and mobility, and ability to obey commands. An early pregnancy assessment 17 days after VNS implantation showed normal fetal heart activity, and crown-rump length. A gestational age of 12-weeks + 3-days and a normally-sited pregnancy were confirmed.

Conclusion: This is the first case-study to report the safe implantation and use of VNS during the first trimester of pregnancy for the management of PAMSE. No maternal or foetal complications occurred, and a normal pregnancy was confirmed 17 days after VNS implantation.

Disclosure: The authors note no conflicts of interest with regards to this case-report.

EPO-309

Identifying seizure onset localization using spatial activation: Applying a novel tool into practice.

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Background and aims: The precise localization of the seizure onset zone is crucial for epilepsy surgery planning. The visual analysis is the most used method for reporting seizure type, location and classification. However, in many cases, the ictal onset zone remains unclear due to fast propagation and the mixture of different frequencies. Using quantitative methods could help provide a more precise analysis.

Methods: We used a novel data-driven method, named "Brainfocus" in 10 patients evaluated with SEEG in our Epilepsy Surgery Program. This method quantifies the magnitude of seizure-related spectral changes with respect to a predefined baseline (Global activation) and the spread of these activations across recording sites. Seizures were analyzed using visual inspection and Brainfocus quantitative analysis, respectively. We compared the number of contacts involved in the first 5 seconds of seizure onset and determined the degree of spatial concordance using both methods.

Results: Patient's average age was 40,9 years and the most frequent type of epilepsy was temporal lobe epilepsy (60%). 13 was the average number of implanted electrodes. 72 representative seizures were selected for analysis. The degree of agreement between qualitative visual inspection and Brainfocus´s global activation was substantial; Lin's Concordance Correlation coefficient was 0.97. The sensitivity of Brainfocus for seizure onset localization was 0.93±0.13 (mean±std across patients).

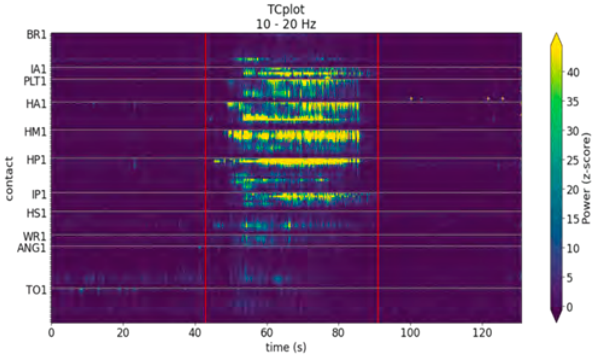
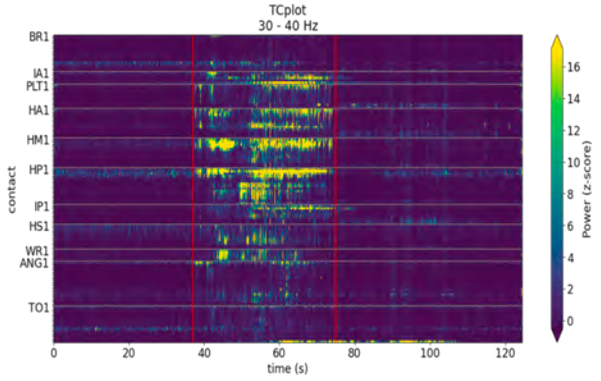


FIG1. Case1. A 37 y/o, male patient, diagnosed with refractory temporal lobe epilepsy. The seizures originated from the posterior hippocampus (HP). As we can see, in seizure (A) the maximum activation is between 10–20 Hz.



In that same case but in other seizure (B), it is between 30–40 Hz, associated with evident preictal activations

Conclusion: Brainfocus is a useful quantitative tool that helps to determine the characteristic spatio-temporal patterns at seizure onset and the visualization of the epileptic activity propagation at different frequency bands, which facilitates the precise interpretation of the SEEG results.
Disclosure: Nothing to disclose.

EPO-310

An EpiCARE survey on dissemination and implementation of guidelines for rare and complex epilepsies

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Background and aims: Clinical practice guidelines (CPGs) are systematically developed statements to standardize patient care and enhance health outcomes. The EU-funded EpiCARE network aims to develop guidelines for rare and complex epilepsies. The purpose of this study was to investigate dissemination and implementation strategies of epilepsy guidelines across EpiCARE centers and to identify main barriers influencing the implementation of guidelines.
Methods: The study was conducted in two phases: (1) the pilot-phase, conducted during the EpiCARE annual meeting among workshop participants, and (2) a network-wide survey. In the second phase, a standardized questionnaire was distributed to 56 participants (physicians and specialized epilepsy nurses) across EpiCARE network. The questionnaire consisted of three sections: demographics, dissemination and implementation, and challenges.
Results: Complete responses were received from 41 participants (71%; 34 physicians and 7 nurses). 20 participants reported previous experience in guideline development. The majority (68%) reported that guidelines were disseminated regularly at their institution. Most frequent actions taken after dissemination of new guidelines were training seminars (65%) and adaptation of guidelines (56%). Major barriers for implementation of new guidelines at a national level were lack of funding (70%); while at an institutional level time constraints (65%), were frequently cited. Moreover, 26% of participants indicated that CPGs are considered useless, because established standard of care already ensures high quality treatment.
Conclusion: Our findings provide a comprehensive overview of the dissemination and implementation strategies used for existing epilepsy CPGs. We identified several barriers to guideline implementation that may help improve application and adherence to CPGs developed by the network.
Disclosure: There are no conflicts of interst.

EPO-311

Abstract withdrawn

EPO-312

Value of neuroglial apoptosis and neuroinflammation in epileptic foci of the brain and blood in drug-resistant epilepsy

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Background and aims: The aim of this study is to evaluate neuronal and glial apoptosis in association with neuroinflammation in brain epileptic focus and inflammatory changes in blood in patients with focal drug-resistant epilepsy (DRE).
Methods: The study follows a case-control design. Biopsies of 32 patients with focal DRE (24–55 years old) were studied. Pathological changes in the temporal lobe in epilepsy (histology, transmission electron microscopy) were studied. Levels of apoptotic and neuroinflammatory proteins: active caspase-3 (immunohistochemistry), full-length form caspase-3, caspase-9, FAS, FAS-L, NF-kB, TNF-α, p53 (Western blot), and cytokine levels in blood: IL-1β, IL-2, IL-4, IL-7, TNF-α, etc. (multiplex analysis) were studied too.
Results: In the present work, ultrastructural and immunohistochemical apoptotic signs were found in neurons and oligodendrocytes in the temporal lobe of DRE patients. Levels of proinflammatory cytokines that play a role in apoptosis (TNF-α, FAS, NF-kB) were increased. The blood concentration of IL-4, IL-7, TNF-α is increased and IL-2 is reduced. Oligodendroglial apoptosis has been shown to play an important role in DRE pathogenesis and to explain demyelination.

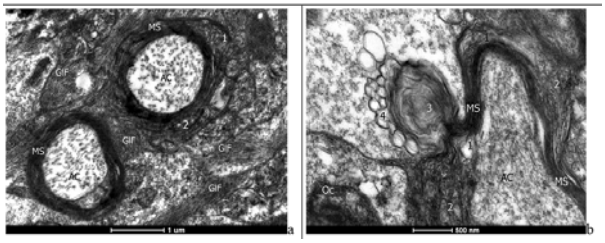

Figure: Structural changes in the epileptic focus. TEM: a - destruction of myelin sheaths; bar, 1 μm; 16500x; b - destruction of myelin sheaths; bar, 500 nm; 26500x. 1 - areas of lamella rupture, 2 – delamination of sheath, 3 – myelin dissociation

Conclusion: Thus, a comprehensive analysis of revealed changes in the blood and brain in DRE patients showed the neuroinflammation in the epileptic focus, which was combined with the development of apoptosis of glial cells and neurons. This creates conditions for the development of drug resistance and the epilepsy progression. Further study of the identified changes may contribute to the search for new methods of DRE treatment.
Disclosure: The project was implemented within the framework of the state task No. 121031000359-3 of the Almazov National Medical Research Center, St. Petersburg, Russian Federation.

EPO-313

The long-term seizure outcome patterns of epilepsy surgery in adult patients with temporal lobe epilepsy

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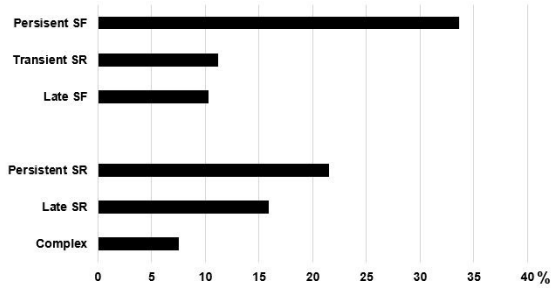
Background and aims: We investigated patterns of seizure remission and relapse after epilepsy surgery in patients with drug-resistant temporal lobe epilepsy (TLE).
Methods: We evaluated long-term (>5 years) outcome postoperatively in 107 TLE adults. Annual outcomes were determined using the ILAE outcome scale. Seizure freedom was defined as ILAE outcome class 1 and 2.
Results: The follow-up period after surgery ranged 60 to 238 months. Hippocampal sclerosis was the most common pathology (69.2%). Persistent seizure freedom was in 36 patients (33.6%), late seizure freedom after at least 1-year of initial seizure recurrence in 11 patients (10.3%), and transient seizure relapse (initial seizure-free with transient relapse, then finally remission) in 12 patients (11.2%). These patterns were grouped into 'seizure-free' (n=59; 55.1%). Persistent seizure recurrence was in 23 patients (21.5%), late seizure relapse after at least 1-year of initial seizure freedom in 17 patients (15.9%), and complex pattern of remissions and relapses in 8 patients (7.5%). These patterns were grouped into 'seizure-relapse' (n=48; 44.9%). Stepwise logistic regression showed that seizure-relapse group was more likely associated with interictal epileptiform discharges <90% concordance with the laterality of surgery (odds ratio [OR] 4.597, p=0.002) and focal to bilateral tonic-clonic seizures during presurgical monitoring (OR 2.459, p=0.047) than a seizure-free group. Older age at surgery and younger age at seizure onset were also associated with a seizure-relapse group, but they did not reach statistical significance (p values<0.1).



The percentage of seizure outcome patterns after epilepsy surgery in patients with temporal lobe epilepsy. SF, seizure freedom; SR, seizure relapse

Conclusion: Our data support the previous findings that epilepsy surgery is a good treatment option for selected patients with drug-resistant TLE.
Disclosure: Nothing to disclose.

MS and related disorders 3

EPO-314

Pediatric Multiple Sclerosis treatment: an ongoing observational study of Natalizumab and comparison with Fingolimod

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Background and aims: Natalizumab is currently prescribed off-label for Pediatric-onset Multiple Sclerosis (POMS), despite its well-known efficacy. Fingolimod is indeed the only second-line treatment approved. The aim of our study is to compare the efficacy of Natalizumab versus Fingolimod in POMS.
Methods: This is an ongoing retrospective/prospective longitudinal multicentric study. We enrolled retrospectively natalizumab (N-PMS) and prospectively N-PMS and fingolimod (F-PMS) treated PMS. We collected Annual Relapse Rate (ARR), Expanded Disability Status Scale (EDSS), and T1 gadolinium-enhancing lesions, T2 lesion load or new T2 lesions on brain MRI at baseline (T0), after 12-18 months (T1) at last observation (T2).
Results: We enrolled 37 N-PMS and 19 F-PMS. N-PMS showed baseline higher ARR vs F-PMS (2[0-5.2] vs 1[0.1–4], p=0.02). Four N-PMS switched to another DMT after a mean time of 12.4±4.2 months [1 for inefficacy (3%) and 3 for safety due to JCV positivity] vs 1 F-PMS switching after 6 months (inefficacy, 6%). Four N-PMS (11%) and 4 F-PMS (25%) experienced one relapse between T0 and T1 (p=0.18). EDSS did not change between T0 and T1. Nine out of 26 N-PMS with follow up longer than 18 months switched to another DMT (at a mean time point of 89±58 months) (1 for inefficacy and 8 for safety concerns).
Conclusion: Preliminary data suggest a comparable efficacy between natalizumab and fingolimod in POMS. However, since baseline characteristics showed higher activity in N-PMS, a comparison is difficult. Ongoing enlargement of the samples might allow to support the high efficacy of Natalizumab in highly active POMS.

Disclosure: Lanzillo R received compensations for speaking or consultancy from Biogen, Teva, Genzyme, Merck, Bristol Myer Squibb, Janssen, Novartis and Roche Carotenuto A served on advisory boards for: Merck, Novartis, Roche and Almirall Brescia Morra V received funding from Novartis, Roche, Biogen, Teva, Almirall, Sanofi-Genzyme, Merck, Bayer, Mylan, Bristol Myers Squibb. Moccia M received honoraria from Biogen, BMS Celgene, Janssen, Merck, Roche, and Sanofi-Genzyme; and serves in the Editorial Board of the Multiple Sclerosis Journal. Signoriello E received compensation from Almirall, Biogen, Genzyme, Novartis, and Teva for traveling and advisory boards. Lus G received compensation for activities with Biogen Idec, Merck Serono, Novartis, Sanofi- Aventis Pharmaceuticals, Teva neuroscience. Borriello G received fee from Almirall, Biogen, Novartis, Roche, Sanofi, Bristol, and Alexion for consultancy and advisory boards Tommasini V served on Advisory board for and received fundings from Sanofi Genzyme, Merck Serono, Novartis, Biogen. Amato MP served on advisory boards for and received honoraria from Bayer Schering Pharma, Biogen Idec, Merck Serono, Novartis, Roche and Sanofi Aventis, and serves on the editorial board of Multiple Sclerosis Journal and BMC Neurology Pozzilli C served on advisory boards, consulting and speaking fees from Almirall, Alexion, Biogen, Roche, Merck, Novartis. Other authors declar no conflict of interest.

EPO-315

Psychiatric disorder in neuro-Behçet's disease

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Background and aims: Behçet's disease (BD) is a multisystem relapsing infl ammatory disorder of unknown cause. Psychiatric disorder is one of the most serious causes of long-term morbidity and mortality in neuro-BD (NB).
Methods: A retrospective study including 150 patients followed for BD was conducted in the department of neurology and internal medicine of the Military Hospital of Tunis from 2000 to 2022. The diagnosis of psychiatric disorders was established following a specialized psychiatric consultation.
Results: We collected 35 cases of NB. Psychiatric disorders were present in 5 patients. All patients were male. The average revelling age for NB was 34. The average age of revelation of psychiatric disorders was 30 years. These were acute delirium according to DSM-IV criteria with delusions and auditory and visual hallucinations in 2 patients. These disorders were concomitant with relapse with a good evolution under corticosteroid treatment in combination with neuroleptics. Mood disorders of the hypomania state type were objectified in two cases and of the recurrent depression type in one case.
Conclusion: Psychiatric disorders in NB are various and serious this is why the importance of knowing them even in the absence of other symptoms of NB.
Disclosure: Nothing to disclose.

EPO-316

The role of treatment strategy in reducing the disability risk in multiple sclerosis

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Background and aims: The paradigm of multiple sclerosis (MS) treatment has been changing with a recent tendency to start early intensive treatment (EIT) in selected cases. We aimed to identify which treatment strategy was associated with lower disability.
Methods: A single-center retrospective study was conducted, including all patients in our MS center diagnosed as relapse remitting MS (RRMS) that started treatment between 2012 and 2022. The treatment regimen applied was analyzed - escalation or EIT, defined as starting a moderate to high efficacy treatment in the first two years after diagnosis. Reaching an Expanded Disability Scale Score (EDSS) of 3 was the primary outcome. A comparative analysis was conducted between patients with different treatment regimens through a multivariate cox regression.
Results: We included 303 patients, with a mean age at diagnosis 36.3±11.2 years and with a female predominance (67.7%). Most patients (71.0%) were treated with an escalation regimen. Fifty-four patients reached an EDSS of 3 (18.8%). In a mean follow-up of 3.6±2.7 years, there was a lower risk of reaching an EDSS of 3 in patients under EIT in the univariate analysis (HR 0.42, CI 95% 0.22-0.80 p=0.008), that remained significant adjusted to the delay in diagnosis.
Conclusion: EIT was associated with a better prognosis in MS in this analysis, with a significant reduction in the risk of reaching an EDSS of 3 in our cohort, highlighting the importance of a prompt diagnosis and reinforcing the need to consider an early start of moderate-high efficacy treatment.
Disclosure: The authors have nothing to disclose.

EPO-317

Natalizumab extended interval dosing: efficacy and safety profile analysis from a Portuguese Multiple Sclerosis Center

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Background and aims: Standard-interval-dosing (SID) (4-week interval) is the mainstay of natalizumab treatment in multiple sclerosis (MS). A 6-week extended-interval dosing (EID) proved to largely reduce the progressive multifocal leukoencephalopathy (PML) risk but its efficacy is less well studied.
Methods: Retrospective study of MS patients treated with natalizumab between 2007–2022, descriptive and comparative analysis between SID and EID.
Results: From 870 MS-patients in our center, 104 were treated with natalizumab. Time between MS-diagnosis and natalizumab treatment was 6,5 years (SD±6,5) with an average age of 34 years-old (SD±10). Fifteen were positive for JCV prior to treatment. Nine suffered moderate/severe adverse events. 39 (36,8%) were on EID regimen (34 switched from SID and 5 EID ad initio). There were no statistically significant differences between schemes regarding new T2 lesions, relapses, EDSS variation, adverse events and suspension motive. There were no cases of symptomatic and asymptomatic PML nor deaths. EID was associated with lesser suspension of treatment[OR: 0.164 (CI95%: 0.067–0.405), p<0.01]. Regarding the EID group, none exhibited new T2 lesions. Five exhibited relapses, one each. Treatment was suspended in 9 patients, after a median time of EID treatment of 26 months (SD±17) due to JCV seroconversion (n=4), suggestive course of secondary progressive MS (n=2), relapses (n=2) and possible adverse event (n=1).
Conclusion: In our MS-cohort, there were no significant differences regarding efficacy and safety under SID or EID natalizumab treatment. Interestingly, EID regimen was associated with lesser treatment suspension.
Disclosure: The authors have nothing to disclose.

EPO-318

MRI, Efficacy, and Safety of Tolebrutinib in Highly Active Disease: 2-Year Data from Phase 2b Long-term Safety Study

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Background and aims: In the phase 2b trial (NCT03889639), brain-penetrant Bruton's tyrosine kinase inhibitor tolebrutinib was well-tolerated with dose-dependent reductions in new/enlarging MRI-lesions. Here, we report MRI, efficacy, and safety outcomes at Week (W) 96 of phase 2b long-term safety (LTS) extension (NCT03996291) in participants with relapsing multiple sclerosis and highly active disease (HAD).
Methods: In double-blind LTS Part-A, participants continued receiving tolebrutinib 5/15/30/60mg daily; in open-label Part-B, all received 60mg/day. Outcomes included gadolinium-enhancing T1- and new/enlarging T2-lesions, annualized relapse rate (ARR), and Expanded Disability Status Scale (EDSS) score.
Results: 61 participants met HAD criteria at baseline; 60 continued in Part-A and 59 transitioned to Part-B. As of March 7th, 2022, 55 participants remained on study. New gadolinium-enhancing T1-lesions remained low in 60/60-mg arm through W96 and were reduced in other arms W48-W96, except for 5/60 (W96 mean±SD: 2.00±3.83, 0.56±1.04, 0.47±1.13, 0.23±0.44 in 5/60-, 15/60-, 30/60-, 60/60-mg arms, respectively). New/enlarging T2-lesions remained low for 15/60-, 30/60-, and 60/60-mg. T2-lesion volume remained unchanged for 60/60-mg. Most common treatment-emergent adverse events (TEAEs) were COVID-19 (20%), nasopharyngitis (16.7%), headache (13.3%), and upper respiratory tract infection (8.3%). There was no dose-relationship for TEAE/serious AE (Part-A) and no new safety findings upon switching to 60mg (Part-B). In participants receiving tolebrutinib 60mg/day for ≥8 weeks, ARR was 0.10 (95% CI: 0.02–0.66) and 92.9% remained relapse-free. Mean EDSS scores were stable through W96.
Conclusion: Through LTS W96, in HAD cohort, tolebrutinib 60mg demonstrated favourable safety, tolerability, and low ARR. MRI-lesion counts remained low for 60/60-mg arm. FUNDING: Sanofi.
Disclosure: Robert J. Fox: Consulting fees (AB Science, Biogen, Celgene, EMD Serono, Genentech, Greenwich Biosciences, Immunic, Janssen, Novartis, Sanofi, and TG Therapeutics) and research support (Biogen, Novartis, and Sanofi). Jiwon Oh: Consulting or speaking fees (Biogen Idec, BMS, EMD Serono, Sanofi, Novartis, and Roche) and research support (Biogen Idec, EMD Serono, and Roche).

Douglas L Arnold: Consulting fees (Biogen, Celgene, Frequency Therapeutics, Genentech, Merck, Novartis, Race to Erase MS, Roche, Sanofi, Shionogi, and Xfacto Communications), grants (Immunotec and Novartis), and equity interest (NeuroRx). Sana Syed, Zhixing Xu, and Timothy J Turner: Employees of Sanofi (may hold shares and/or stock options in the company). Anthony Traboulsee: Consulting and/or speaking fees and grant/research support (Roche and Sanofi). Daniel S Reich: Supported by the Intramural Research Program of NINDS, NIH. Additional research support (Abata, Sanofi).

EPO-319

A multidimensional self-reported evaluation of frailty in people with multiple sclerosis.

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Background and aims: Multiple Sclerosis (MS) is a neurodegenerative disease of central nervous system. People with MS have a high risk of frailty that could be measured by different tools. We aim to evaluate frailty using the Tilburg frailty indicator (TFI), a multidimensional self-reported questionnaire, and to explore its relationship with disability.
Methods: People with MS were enrolled and complete by himself TFI (frail with a TFI score ≥ 5 points). The following features were collected: disability using the Expanded Disability Status Scale (EDSS), age and gender. Data were treated through descriptive analyses and hierarchical multiple regression.
Results: A total of 208 adults with MS (mean age 44 years, SD=11; 75% of women; 89.4% relapsing-remitting) were enrolled. The mean TFI total score was 5.7 points (SD=3.0; range 0–14), with the 62.5% resulted frail. Controlling for age and gender, the EDSS influenced the total (β=0.469; R2=0.255; $p<0.001$) and the physical (β=0.571; R2=0.349; $p<0.001$) frailty score, with an explained variance of 25.5% and 34.9%, respectively. No effects on psychological and social frailty domains were detected. 91.7%, 83.3% and 66.0% of people with high EDSS ≥ 6.0, EDSS ranged from 3.5 to 5.5, and EDSS ≤ 3.0 resulted frail, respectively.
Conclusion: Our study shows a high frequency of frail patients. Frailty is more common in patients with higher disability, but it affects also those with low EDSS. Thus, in people with MS frailty could be influenced by factors different than disability.
Disclosure: The authors have not to disclose about this work.

EPO-320

Longitudinal Robustness of Emergent MS Phenotypes from Multiprotein Serum Data

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Background and aims: Novel machine learning techniques for measurement of disease activity (DA) and disease progression (DP) through serum proteomics have shown promise in multiple sclerosis (MS) management. Identifying emergent biomarker profiles (pheno-clusters) can enable proteomic-based MS subtyping and support clinical interpretability of a novel MS DA (MSDA) test, developed by Octave Bioscience. Previous research has demonstrated the feasibility and potential clinical utility of proteomic pheno-clustering in MS.
Methods: Our objective was to characterize the longitudinal stability of pheno-clusters in stable MS patients identified using unsupervised clustering of serum protein concentration data. 137 patient samples were assayed using the MSDA test. The proteomics data was balanced on medication and grouped into pheno-clusters associated with over or under-expression of 18 proteins, using k-means clustering. We applied the learned grouping to 38 longitudinal samples from an independent cohort (15 patients with ≥2 samples ≤30 days apart).
Results: We found 6 protein signatures in the training dataset. In the longitudinal dataset, 67% of patients and 87% [update] of datapoints had no cluster change. We examined protein signatures of the 5 patients who had a cluster change: Proteins with varying concentrations between samples in these patients included GFAP, CD20, CD6, and CXCLl9.
Conclusion: The stability of pheno-clusters in a high proportion of patients demonstrates the clinical relevance of this methodology. Furthermore, cluster changes in 3 patients could indicate a subclinical signal, otherwise undetectable. Neuroinflammation and progression related protein changes in the patients with changing clusters could indeed be indicative of underlying subclinical DA and DP.
Disclosure: A. Ghoreyshi and F. Qureshi are employees of Octave Bioscience. T. Hoyt has nothing to disclose. J. Foley has received research support from Biogen, Octave, and Genentech. He received speakers' honoraria from Biogen. He has participated in advisory boards for Biogen, Horizon, Sandoz, and TG Therapeutics. He has equity interest in Octave. He is the founder of InterPro Biosciences.

EPO-321

Abstract withdrawn

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Abstract withdrawn

EPO-323

Clinical features of patients with Late Onset Multiple Sclerosis in a large Centre of Central Italy

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Background and aims: Multiple Sclerosis (MS) commonly affects young people. However, people with more than 50 years old may be affected, configuring the Late Onset MS (LOMS). LOMS are supposed to have a different immunological behaviour comparing to early onset MS, with possible different responses to disease modifying therapies (DMTs). Here we describe the main features of LOMS in charge at our Centre in Pisa, Italy.
Methods: Data were achieved from our MS-patients database We included those patients who underwent at least 2 years of clinical and radiological follow-up.
Results: -38 patients (23 female, 15 male) with mean age at onset of 56.7 years -13 patients had primary progressive MS, 19 Relapsing remittent MS, and 6 secondary progressive MS -Mean temporal hiatus between disease onset and diagnosis: 20.7 months -4 patients had supratentorial lesions, 11 had supratentorial plus spinal lesions, 3 had whole-brain lesions, 20 had whole-brain plus spinal lesions -17 patients had motor impairment at disease onset -13 patients did not start any DMTs, 5 started a second line therapy and 20 started a first line treatment -11 of the 16 patients that developed new MRI lesions during follow-up were not under treatment. 5 patients had clinical relapses during follow-up. - 32 among 35 CSF exams were positive for oligoclonal bands -The mean EDSS after 2 years of follow-up remained stable
Conclusion: Since LOMS might have a different immunological behaviour, a precise categorization of this patients' category might help both in choosing a patient-tailored therapeutic approach and in avoiding possible misdiagnosing, preventing diagnostic delay.
Disclosure: The authors have no disclosures.

EPO-324

Serum neurofilament light chain levels during natalizumab treatment with every-4-week and every-6-week dosing in NOVA

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Background and aims: Results from the phase 3b NOVA trial (NCT03689972) suggest that patients with relapsing-remitting multiple sclerosis (MS) who are stable on natalizumab (TYSABRI®) every-4-week (Q4W) dosing can switch to every-6-week (Q6W) dosing without meaningful loss of efficacy. This analysis compares levels of serum neurofilament light chain (sNfL), a marker of neuronal damage in MS, between patients in Q6W and Q4W groups in NOVA.
Methods: NOVA participants who were stable on Q4W dosing for ≥1 year at baseline, had sNfL data at baseline and had ≥1 postbaseline sNfL measurement were included. sNfL levels are presented as geometric mean (GM) values by study visit. GM ratios (GMRs) were calculated using sNfL values at visit versus baseline. The Q6W GMR versus Q4W GMR ratio was determined using a mixed model for repeated measures with natural log-transformed data.
Results: sNfL GM values at baseline were 8.34 pg/mL (n=220; Q6W) and 8.13 pg/mL (n=220; Q4W) and remained stable (<9 pg/mL) through week 72 (Figure 1). GMRs for week 72 versus baseline sNfL values were 1.0 (95% confidence interval [CI], 0.97–1.11) for Q6W (n=191) and 1.0 (95% CI, 0.94–1.07) for Q4W (n=178); the ratio of Q6W to Q4W GMRs was 1.0 (95% CI, 0.96–1.11; p=0.4065).
Conclusion: sNfL levels remained stable in the Q6W and Q4W treatment groups throughout the NOVA study with no significant differences between groups at week 72. Stabilization of sNfL levels in both treatment groups suggests effective control of MS disease activity by both Q6W and Q4W dosing.

Disclosure: Study: Biogen GG: AbbVie, Aslan, Atara Bio, Biogen, BMS-Celgene, GSK, GW, Janssen/Actelion, Japanese Tobacco, Jazz, LifNano, Merck/Serono, Novartis, Roche/Genentech, Sanofi Genzyme, Teva JFF: Biogen, Genentech, Novartis, Octave GD: Biogen, BMS, Merck/Serono, Novartis, Sanofi Genzyme, Teva LZR: Biogen, Celgene, Genentech, Novartis JAC: Biogen, Convelo, EMD Serono, Gossamer Bio, Mylan, PSI; MSJ editor DLA: Biogen, Celgene, Frequency Ther, Genentech, Immunotec, Merck, NeuroRx, Novartis, Race to Erase MS, Roche, Sanofi-Aventis, Shionogi, Xfacto Comm HB: Biogen, Merck, Novartis, Oxford Health Policy Forum, Roche, UCB GC: AI Ther, Alexion, AMO, Antisense Ther, AstraZeneca, AveXis, Biogen, BioLineRx, BMS/Celgene, Brainstorm Cell Ther, Clinical Trial Solutions, CSL Behring, Galmed, Genentech, Genzyme, Green Valley, GW, Horizon, Immunic, Klein-Buendel, Mapi, Merck/Serono, Mitsubishi Tanabe, Novartis, Ntl Heart, Lung, and Blood Inst, Opko Bio, Osmotica, Perception Neuro, Protalix Bio, Prothena Bio, Pythagoras, Reata, Recursion/CereXis, Regeneron, Roche, SAB Bio, Sanofi-Aventis, UA-Birmingham, UPenn, UT-Southwestern, Visioneering Tech JK: Biogen, Genzyme, Merck/Serono, Novartis, Roche, Teva HW: AbbVie, Actelion, Alexion, argenx, Biogen, Biologix, BMS, Cognomed, EMD Serono, Evgen, Gemeinnützige Hertie-Stiftung, GSK, Idorsia, IGES, Immunic, Immunovant, Janssen, J&J, MedDay, Merck/Serono, Novartis, Roche, Sanofi Genzyme, Swiss MS Society, Teva, UCB, WebMD SS, JS, LD, MM, JS, EF, TL: Biogen

EPO-325

Monoclonal antibodies in pregnancy in patients with multiple sclerosis: an updated clinical guide

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Background and aims: The use of high-efficacy disease-modifying therapies (DMTs) early in the course of the disease has been shown to lead to improved clinical outcomes in the long term and has become a popular treatment strategy among neurologists over the past years. Therefore, monoclonal antibodies including natalizumab, ocrelizumab, ofatumumab and alemtuzumab are increasingly used for the treatment of multiple sclerosis in women of childbearing age.

Methods: A review of the published literature was conducted in January 2023 in Embase, MEDLINE and Cochrane Library.

Results: Natalizumab can be administered at approximately 34 weeks and restarted soon after birth to avoid rebound disease activity. Women who are being treated with ocrelizumab or ofatumumab should avoid infusions/injections during pregnancy, however, the last dose can be administered 3 months prior to conception. Alemtuzumab's last infusion should be given 4 months before conception.

	Natalizumab	Ocrelizumab	Ofatumumab	Alemtuzumab
Use in pregnancy	Can be used	No	No	No
Last dose	Last infusion no later than 34 weeks	Last infusion 3 months before conception.	Last injection 3 months before conception.	Last infusion no later than 4 months before conception
Risk of miscarriage	No	No	No	No
Breastfeeding	Yes	Yes	Yes	No. Wait 4 months after last infusion

Table. Monoclonal Antibodies in Pregnancy in Women with Multiple Sclerosis

Conclusion: Discussion with women of childbearing age is crucial to make the most suitable treatment option. Outcomes should be monitored in registries to provide more data.

Disclosure: Nothing to disclose.

EPO-326

Menopause in women with multiple sclerosis: clinical symptoms and possible impact on the course of the disease

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Background and aims: Menopause signals a major shift in hormonal levels in women and causes a variety of symptoms that can overlap and/or interact with those related to multiple sclerosis (MS). These symptoms can have a considerable impact on the quality of life for many women living with MS. Menopause remains a largely unexplored period for women with MS and there are only a few studies that have attempted to investigate the potential effect that menopause may have on the clinical course of MS including inflammatory activity and disability progression.
Methods: We conducted a review of the literature to investigate whether menopause affects the clinical course of the disease and disability outcomes.
Results: Two studies showed that the Expanded Disability Status Scale (EDSS) progression rate was not affected by menopause while the other two showed that EDSS progression rate might have increased after menopause. Similarly, half of the studies showed that the annualized relapse rate (ARR) remained stable after menopause while the rest showed that there was a reduction in ARR.

Study	Design	Sample Size	Results	Limitations
Ladeira et al.	Retrospective	37 women	ARR reduction No changes in EDSS progression rate	Small sample size, no control group
Otero et al.	Prospective	73 (54 after controlling for aging and disease duration)	No changes in EDSS progression rate	Small sample size
Baroncini et al.	Retrospective	108	ARR reduction, EDSS progression rate increased	Small sample size, lack of control group
Bove et al.	Prospective	124	EDSS progression rate increased	Results highly impacted by a significant worsening in one participant's EDSS

Table 1. Studies investigating the effect of menopause on the clinical course of MS

Symptoms	Behavioural/lifestyle interventions	Pharmacological treatment (non-hormonal)
Hot flushes	Air conditioning, cold drinks Avoidance of hot/spicy foods Swimming Vests or cooling collars Weight loss Smoking cessation Acupuncture Hypnosis	Antiepileptic and antidepressant drugs: gabapentin/pregabalin, citalopram, escitalopram, fluoxetine, paroxetine, sertraline, duloxetine, venlafaxine, desvenlafaxine
Affective disorders	Neuropsychotherapy Support groups Optimization of sleep and fatigue Social management of work stressors	Antidepressant drugs: fluoxetine, sertraline, escitalopram, citalopram, venlafaxine, bupropion Antimuscarinics
Urinary disorders	Bladder training: Frequent voluntary emptying (e.g. start with every 2 hours) to keep the bladder volume low. Pelvic muscle exercises (Kegel) Biofeedback. Decreased	Antimuscarinics (oxybutynin, tolterodine, fesoterodine). Antispasmodics (baclofen, tizanidine) Tricyclic antidepressants (amitriptyline). Local oestrogen, or antibiotic prophylaxis, may be required in more disabled patients.
Sexual dysfunction	Decreased sensation: vibrators and other devices may increase stimulation. Patient education and guided counselling, such as body mapping techniques or pelvic floor exercises, can increase arousal, orgasmic response, intimacy and couple communication. Vaginal dryness: lubricants Counselling focused on sexual feelings, communication and attitudes that interfere with sexual enjoyment. Couples' education/counselling: focused on mutual support, communication, stress and anger management.	Paresthesia. Antiepileptic drugs: carbamazepine, gabapentin
Cognitive impairment	Cognitive rehabilitation to develop organizational strategies (e.g. making lists, simplifying daily organization). Addressing sleep problems, fatigue, mood and pain	

Table 2. Overlapping MS and menopausal symptoms and therapeutic options

Conclusion: Menopausal symptoms can frequently overlap with MS symptoms. Clinicians should be able to recognize and address them on time before they increase the burden of disease and affect the quality of life. Limited studies with inconsistent results have been conducted to date, and most of them have important limitations, hence not allowing for safe conclusions to be drawn. Larger, longitudinal studies with improved methodology and controlling for aging and disease duration are needed to establish the link between menopause and MS.
Disclosure: Nothing to disclose.

EPO-327

Seroprevalence and seroconversion of anti-JCV antibodies in a cohort of multiple sclerosis patients

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Background and aims: The main goal was to analyse the incidence of JCVpositivity after the first test in a cohort of MS patients and the time to seroconversion during follow-up in the natalizumab-treated MS patients.
Methods: Retrospective observational cohort study including patients screened for anti-JCV antibodies using the STRATIFY JCV™test. Several variables were analyzed to find an association with the risk of seroconversion.
Results: 383 patients have been tested of JCV in the last 6 years. 66.48% were woman. 60.21% were JCV positive with a mean index .18 (0.21–4.91), 69.53% were female with a median age 43 (22–75and). JCV negative patients were 39.80 (16–64) years old. We found a significant correlation between age and JCVpositive antibodies (p=0.0003, r=0.185) and sex and JCV antibodies (p= 0.008). Positive JVC value were more persistent in males (69.5%) than in females (55.5%). However, we did not find correlation between age and index of VJC (p=0.562). 80 patients were in treatment with natalizumab. 70% are female. 24 patients were VJC positive in this cohort, of whom 12 were VJCpositive from baseline and 12 seroconverted. The mean time to seroconversion was 27.8 months (10-71). We didn't find a stadistically significant correlation between age and the time to seroconversion (p=0.176), sex (p=0.646), number of previous treatments (p=0.979) or time from diagnosis to initiation of natalizumab treatment (p=0.405)
Conclusion: We found older age and male sex is associated with the risk of JCV positive. We found no association with other variables such as number of previous treatments.
Disclosure: Nothing to disclose.

EPO-328

Phase 2b trial of NG-01-MS - Autologous bone marrow derived human mesenchymal stem cells in secondary progressive MS

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Background and aims: Over the past 15 years, there have been clinical research efforts around the possibility of bone marrow-derived MSC treatment for MS led by Karussis, et al. at the Hebrew University-Hadassah Medical Center ("Hadassah"). A recent double blind, randomized, placebo-controlled phase 2 study reported by the Hadassah team yielded data to support safety and efficacy of the approach, particularly the use of repeated intrathecal (IT) administration as proposed for this trial. NeuroGenesis Ltd. acquired the technology, now called NG-01-MS, which involves the proprietary manufacturing process of autologous MSCs derived from each patient's bone marrow.
Methods: Aim 1: To test the hypothesis that repeated IT administration of NG-01-MS at 3 months intervals has superior efficacy compared to sham administration (placebo) in SPMS assessed both clinically and by biomarkers of neuroprotection. Aim 2: To assess the safety, tolerability, and relative efficacy of 2 dose levels of intrathecal administration of NG-01 MS (either 50 million or 100 million cells per injection) versus sham administration using sterile saline medium as a placebo. Aim 3: To assess the feasibility (shipping methods, cell stability and viability, etc.) of performing a multi-center clinical trial utilizing NG-01 MS in anticipation of a future phase 3 trial.
Results: Study design considerations including the clinical and imaging endpoints and the exploratory use of neurofilament light chain (NfL) measurements as a biomarker will be discussed.
Conclusion: The proposed trial will attempt to use cell-based therapy to demonstrate neuroprotection and repair in secondary progressive multiple sclerosis (SPMS).
Disclosure: This trial is sponsored by NeuroGenesis Ltd.

EPO-688

Efficacy and Safety of Fenebrutinib, a Noncovalent, Reversible BTK inhibitor, in MS: Primary Results of a Phase 2 Trial

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Background and aims: Bruton's tyrosine kinase (BTK) is implicated in peripheral and central nervous system inflammation in multiple sclerosis (MS) and is a therapeutic target for relapsing and progressive disease. Fenebrutinib (FEN) is a potent, highly selective, noncovalent, reversible BTK inhibitor under investigation for MS.

Methods: FENopta, a randomised, double-blind, placebo-controlled, Phase 2 trial (NCT05119569), evaluated efficacy and safety of FEN in relapsing MS (RMS; Fig 1). The primary endpoint was total new gadolinium-enhancing (Gd +) T1 MRI lesions at Wks 4, 8 and 12. Key secondary endpoints were total new or enlarging T2-weighted lesions and safety. Relative reductions in lesions by visit were also analysed.

Results: At Wks 4, 8 and 12 (combined), FEN patients (pts) with evaluable postbaseline MRI data (n=70) had a 69% reduction in total new Gd+ lesions (Fig 2) and a 74% reduction in total new or enlarging T2-weighted lesions (Fig 3) vs placebo (PBO) pts (n=36). Relative reductions in Gd+ and T2 lesions were observed at Wk 8 (92% and 90%) and Wk 12 (90% and 95%, respectively). FEN pts were 4x more likely to be free from new Gd+ and T2 lesions at Wks 4, 8 and 12 vs PBO pts. Overall, 38% of FEN pts (n=73) and 33% of PBO pts (n=36) had an adverse event (AE). No serious AEs or deaths were reported.

Conclusion: These first data highlight the potential of FEN for treating RMS. The FENopta open-label extension and Phase 3 studies in RMS and primary progressive MS are ongoing.

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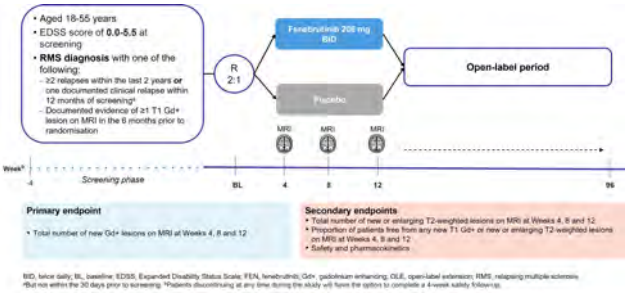

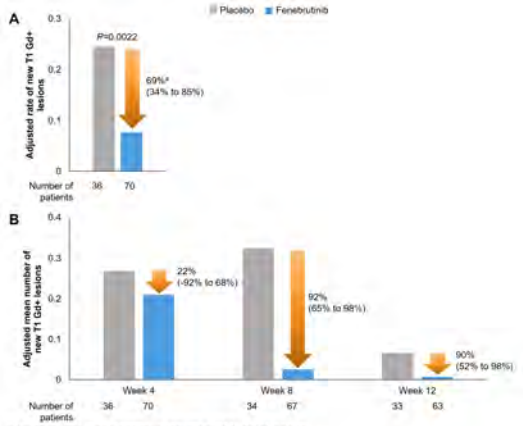

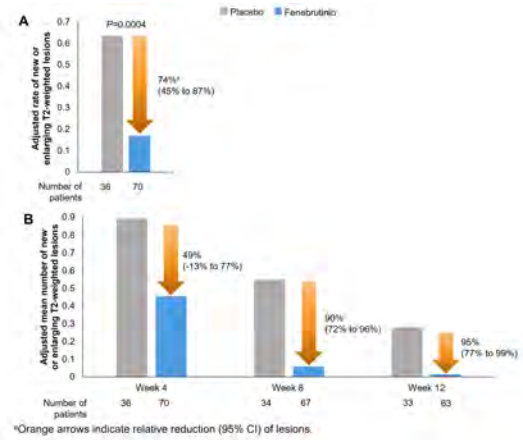

MS and related disorders 4

EPO-329

Promotor Polymorphisms in susceptibility and progression to Multiple Sclerosis

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Background and aims: The aim of this study is to investigate the synergistic effects of MMP-2 C-735T, MMP-9 C-1562T, and MMP-7 A-181G functional polymorphisms in the susceptibility to Multiple sclerosis (MS).
Methods: In this cross-sectional study, 149 patients who were diagnosed with Multiple Sclerosis between January 2017-December 2018 in the department of Neurology, Medical Faculty, Trakya University (Edirne, Turkey) and 152 healthy controls were included. Following DNA isolation from patient and control peripheral blood, allelic discrimination of MMP-7a-181G (rs11568818) polymorphisms was performed with real-time PCR using TaqMan® SNP Genotyping Assay kit for MMP-2 C-735T (rs2285053), MMP-9 C-1562T (rs3918242) and MMP-7A-181G (rs11568818).
Results: A statistically significant difference was found between CC, CT, and CC genotypes in the Expanded Disability Status Scale (EDSS) score. MMP-9 C-1562T functional polymorphism was found in MS patients in terms of transition of C to T (p=0.021). A statistically significant difference was found between men and women in terms of transition of C to T in the MMP-9 C -1562T functional polymorphism (p=0.014).
Conclusion: MMP-9 C-1562 T polymorphism is predicted to be a predictor of disability in MS and its progression, especially in male patients. MMP-2 C-735T functional polymorphism is also a value predictor of susceptibility to MS through the TT genotype and C allele. The presence of both MMP-9 C and MMP-2 C alleles has an even greater risk of MS.
Disclosure: There is no conflict of interest.

EPO-330

AMASIA: real world insight into the impact of siponimod treatment on disease progression of SPMS patients in Germany

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Background and aims: The non-interventional AMASIA study aims to investigate the long-term effectiveness and safety of siponimod for the treatment of patients suffering from active SPMS in a real-world setting and provides insight into the impact on disease progression and quality of life.
Methods: Approximately 700 siponimod-treated SPMS patients at about 120 sites in Germany are followed over 3 years. Every 6 months, disability progression and cognitive changes are evaluated by EDSS and SDMT. Questionnaires from the perspective of patients and physicians on disability progression, cognitive worsening and quality of life are documented.
Results: Extended subgroup analyses of disease progression (EDSS, SDMT) depending on patient age, time since MS diagnosis, disease progression at time of study start and last pre-treatment show the impact of 6, 12 and 18 months of siponimod treatment, by slowing down disease progression in all cases (average EDSS at study start for patients up to 50 years/older than 50 years: 5.4±1.4/5.3±1.4; after 18 months: 5.9±1.4/5.4±1.4). The analysis is an extension to previously presented preliminary data that indicated a trend towards a stable EDSS score over 12 months on siponimod treatment regardless of age or time since diagnosis. Additional data from patient and physician questionnaires will give further insights into the effectiveness of siponimod and the impact on quality of life.
Conclusion: The presented results on the effectiveness of siponimod treatment depending on patient characteristics such as age, time since diagnosis and pre-treatment underline the benefits of early treatment initiation of siponimod in patients with active SPMS.
Disclosure: O. Hoffmann served on scientific advisory boards, received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. H. Schreiber received research grants and honoraria from

Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva. L. Klotz received compensation for serving on scientific advisory boards, speaker honoraria, travel support, research support from Alexion, Janssen, Novartis, Merck Serono, Sanofi Genzyme, Roche, Biogen, TEVA. She receives research funding from the Deutsche Forschungsgemeinschaft (DFG), the German Ministry for Education and Research, the Interdisciplinary Center for Clinical Studies (IZKF) Muenster, and the Innovative Medical research Muenster. M. S. Weber received research support from the DFG (DFG; WE 3547/5-1), Novartis, TEVA, Biogen-Idec, Roche, Merck, and the ProFutura Programm of Uni Göttingen; editor for PLoS One; received travel funding and/or speaker honoraria from Biogen, Merck Serono, Novartis, Roche, TEVA, Bayer, and Genzyme. C. Weiss is an employee of Novartis Pharma GmbH, Germany. T. Ziemssen received speaking honoraria and financial support for research activities from Almirall, Biogen, Celgene, Novartis, Roche, Teva, and Sanofi. This study is financed by Novartis Pharma GmbH, Nuremberg, Germany.

EPO-331

Real world insight into the characteristics of siponimod treated SPMS patients in Germany from the AMASIA study

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Background and aims: The non-interventional AMASIA study aims to investigate the long-term effectiveness and safety of siponimod for the treatment of patients with active SPMS in a real-world setting. The study also provides insight into siponimod patient profiles and clinical routines in Germany.

Methods: Siponimod-treated SPMS patients are followed over 3 years. Every 6 months, disability progression and cognitive changes are evaluated by EDSS and SDMT. Questionnaires from the perspective of patients and physicians on disability progression, cognitive worsening and quality of life are documented.

Results: According to previous interim analyses of the AMASIA population, patients on average were 54.5 years old and had been diagnosed with MS for 17.4 years when starting siponimod treatment. The largest group of patients (more than 45%) were switched to siponimod from moderately effective therapies, while about 10% were treatment-naïve. Here, we expand these previous analyses by analyzing the complete patient population, following the end of the recruitment period in January 2023. In addition to patient characteristics, details on MS activity, FSMC, SDMT and UKNDS scores and medical history are reported. Results are compared to data from the pivotal clinical trial EXPAND to obtain further insight.

Conclusion: Data and characteristics of the AMASIA study population enable a comparison of clinical trial data to the average siponimod patient treated in routine clinical practice, thus potentially facilitating translation into real-life therapeutic strategies by underlining the importance of a timely SPMS diagnosis and treatment intervention.

Disclosure: O. Hoffmann served on scientific advisory boards, received speaker honoraria from Bayer Healthcare, Biogen, Bristol Myers Squibb/Celgene, Merck, Novartis, Roche, Sandoz, Sanofi, Teva; received financial support for research activities from Biogen, Novartis, and Sanofi. H. Schreiber received research grants and honoraria from Almirall, Bayer Healthcare, Biogen, Merck, Novartis, Roche, and Teva. L. Klotz received compensation for serving on scientific advisory boards, speaker honoraria, travel support, research support from Alexion, Janssen, Novartis, Merck Serono, Sanofi Genzyme, Roche, Biogen, TEVA. She receives research funding from the Deutsche Forschungsgemeinschaft (DFG), the German Ministry for Education and Research, the Interdisciplinary Center for Clinical Studies (IZKF) Muenster, and the Innovative Medical research Muenster. M. S. Weber received research support from the DFG (DFG; WE 3547/5-1), Novartis, TEVA, Biogen-Idec, Roche, Merck, and the ProFutura Programm of Uni Göttingen; editor for PLoS One; received travel funding and/or speaker honoraria from Biogen, Merck Serono, Novartis, Roche, TEVA, Bayer, and Genzyme. C. Weiss is an employee of Novartis Pharma GmbH, Germany. T. Ziemssen received speaking honoraria and financial support for research activities from Almirall, Biogen, Celgene, Novartis, Roche, Teva, and Sanofi. This study is financed by Novartis Pharma GmbH, Nuremberg, Germany.

EPO-332

B cell tailored ocrelizumab in relapsing multiple sclerosis: protocol of a randomized controlled trial

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Background and aims: Ocrelizumab, an anti-CD20 monoclonal antibody (mAb) resulting in B-cell depletion, is highly effective in relapsing-remitting multiple sclerosis (RRMS). Individual B-cell repopulation varies extensively (27–175 weeks), therefore a fixed infusion interval is likely suboptimal. A personalised approach based on individual biological parameters could offer various advantages: decrease of infusion visits in the majority of patients, reducing infusion relating events, and possibly reduction of infection risk and hypogammaglobulinemia. Moreover, exceeding healthcare costs in Europe demand appropriate use of costly mAbs.
Methods: This is a national multicentre randomized controlled trial with two year follow-up. A total of 300 patients will be included. Patients will be randomized 1:1 to the standard interval group or the personalized interval group in which the infusions will be extended as long as the CD19 B-cell count remains below 10 CD19 cells/μL (Figure 1). Inclusion criteria include the diagnosis of RRMS and one year ocrelizumab treatment. All patients will be subjected to visits every six months (Figure 2). All visits include a relapse and adverse event assessment, and clinical testing. An MRI-scan will be performed and blood will be drawn for neurofilament light and IgG levels yearly. By using two validated apps (MS Sherpa/Neurokeys) cognition, hand function and walking speed will be frequently monitored at home.

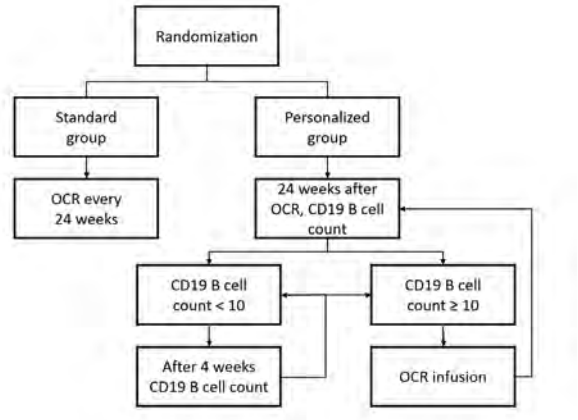

Fig. 1. Randomization procedure for the BLOOMS trial. OCR = ocrelizumab. CD19+ B cells in cells/μL.

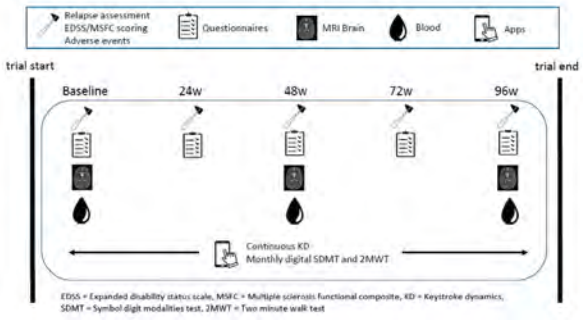

Fig. 2. Study visits BLOOMS trial.

Results: To conclude non-inferiority of personalized ocrelizumab two co-primary endpoints will be analysed: 1. percentage of relapse-free patients and 2. percentage of patients free from new/enlarging lesions on MRI.
Conclusion: Enrolment of patients started in April 2022. Results are expected in 2026. Clinicaltrials.gov Identifier:NCT05296161
Disclosure: J. Killestein report personal fees from Genzyme, Biogen Idec, Teva Pharmaceutical Industries, Merck Serono, Roche, Novartis.

EPO-333

Transcriptome analysis in the retina of mice with experimental autoimmune encephalomyelitis

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Background and aims: Visual disabilities often occur in multiple sclerosis (MS) and experimental autoimmune encephalomyelitis (EAE) an animal model of MS, but little is known about the mechanisms underlying the pathogenesis of retinitis in EAE. The aim of the study is to identify hub genes and pathways in the retina with EAE to explore its etiologies.
Methods: Differential expressed genes analysis was performed. Genes with a log 2 fold-change value >2 and false discovery rate(FDR) adjusted p-value<0.05 were considered differentially expressed genes (DEGs). Gene ontology (GO) analysis, gene set enrichment analysis (GSEA) with leading-edge analysis were conducted and constructed a protein-protein interaction (PPI) network using STRING database.
Results: 660 differentially expressed genes were identified, including 2 downregulated genes and 345 upregulated genes. GO analysis revealed that upregulated genes were associated with immune response, myofibrillar protein and extracellular matrix in the retina of mice with EAE-affected

mice. The 12 hub genes including were identified by the PPI network. Based on a curated gene set from molecular signatures database (MSigDB), GSEA showed that the upregulated genes in the retina with EAE were associated with electron transport chain and oxidative phosphorylation, and that downregulated genes are related to neuronal system and phototransduction cascade.

Conclusion: The hub genes related to immune response and phototransduction cascade pathway may be associated with the development of visual dysfunction in EAE mice. This study provided transcriptome profiles of the retinas of mice with EAE, which may help to identify new therapeutic targets.

Disclosure: There are no financial conflicts of interest to disclose.

EPO-334

Selective Vulnerability of Retinal Ganglion Cells in Multiple Sclerosis Regardless of Disease Subtypes

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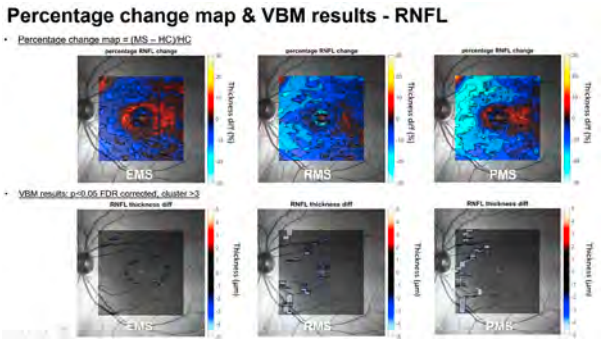
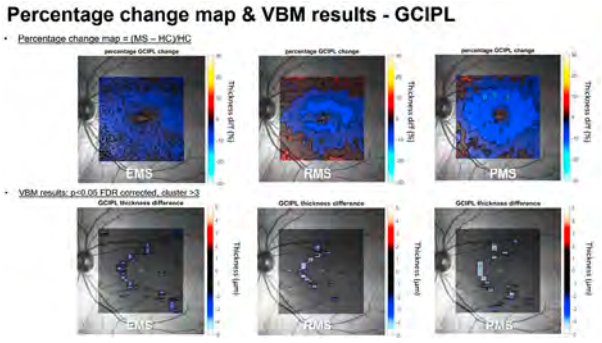
Background and aims: Neurodegeneration is the main contributor to disability accumulation in Multiple Sclerosis (MS). Studies in neuro-ophthalmology demonstrated that neurodegeneration in MS correlates with neuroretinal atrophy measured by optical coherence tomography (OCT). Thinning of retinal layers is recognized as biomarkers for axonal/neuronal loss. However, current analytical tools are unable to provide topographical information or detect focal atrophy. Here we aimed at verifying Whether applying voxel-based morphometry (VBM), a neuroimaging tool, may offer topological information on how neurodegeneration spreads among the central nervous system (CNS).

Methods: 110 people with MS (36 early, 37 relapsing-remitting, and 37 progressive MS) and 50 healthy subjects were enrolled. Only eyes with normal global peripapillary retinal nerve fiber layer (pRNFL) thickness and without histories of optic neuritis (ON) were considered. VBM was applied to macular OCT and voxel-wise ANCOVA was delivered with general linear model (GLM).

Results: Significant nasal macular ganglion cell/inner plexiform layer (GCIPL) atrophy was detected across all the MS subgroups at the same location, the thinning increases as the disease progresses. While RNFL atrophy spreads from the optic nerve head (ONH) toward the fovea as the disease moves toward the progressive phase.



VBM-OCT reults of RNFL



VBM-OCT results of GCIPL

Conclusion: Our results support primary retinal ganglion cell damage since disease onset in eyes without ON, its location implies selective vulnerability. Further, the evolution of the RNFL atrophy as the disease progresses suggests retrograde degeneration from the brain. Our data demonstrate bidirectional neurodegeneration coexists in MS and we may monitor and quantify the two mechanisms with VBM-OCT in the retina.

Disclosure: The authors have nothing to disclose.

EPO-335

Incidence and correlates of autoimmune comorbidities in multiple sclerosis: a prospective registry-based study

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Background and aims: : Multiple Sclerosis (MS) is an autoimmune disease affecting the central nervous system. Although current evidence is conflicting, people with MS (pwMS) have a higher risk to develop autoimmune comorbidities and it is reasonable that both share the same genetic susceptibility. The aims of this study are to evaluate the frequency of autoimmune comorbidities in pwMS and the impact of such comorbidities among disease activity and progression.

Methods: We included patients with relapsing remitting MS and with a follow-up period of at least 15 years. We calculated incidence of autoimmune comorbidities and the Hazard ratios (HR) for secondary progression as well as the adjusted annualized relapse ratio (ARR) in patients with and without autoimmune comorbidities.

Results: From a total of 142 pwMS (age at diagnosis: 32.8 ±9.9 years; follow up: 23.5±6.5 years), three patients (2.1%) showed preexistent autoimmune comorbidity, while n=24 developed one during follow-up period (incidence rate= 0.7/100 patients/years) without sex differences (p=0.61). The overall prevalence for autoimmunity was 19% and the more common was Hashimoto's thyroiditis (12%) followed by psoriasis (2.1%). The presence of autoimmune comorbidity was associated with a reduced risk of secondary progression (HR= 0.42 [95% CI: 0.22–0.81]; p=0.02; Fig 1) and with a higher adjusted ARR (0.29 [95% CI: 0.28–0.32] vs 0.4 [95% CI: 0.35–0.45]; p<0.0001; Fig 2).

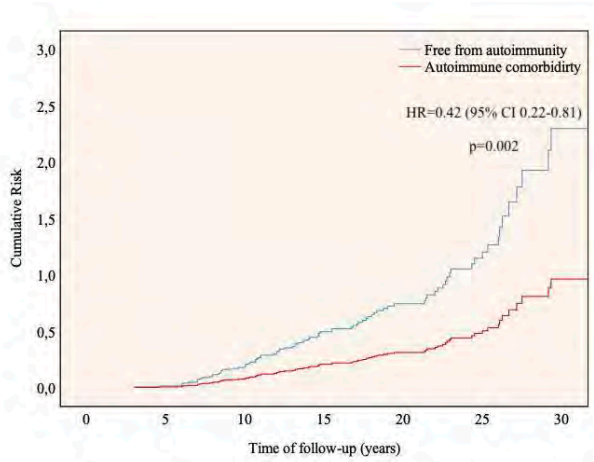

Figure 1: Cox regression analysis showing the different risk to secondary progression MS between patients with (red line) and without (blue line) autoimmune comorbidity

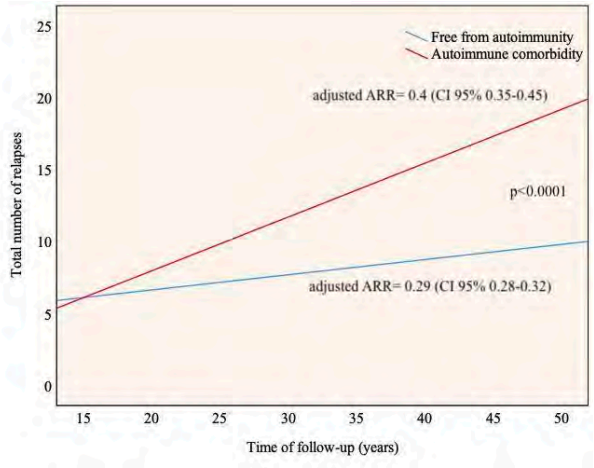

Figure 2: Scatterplot showing the different relapse rate between patients with (red line) and without (blue line) autoimmune comorbidity

Conclusion: Autoimmune comorbidities significantly affect the MS course suggesting that the accurate evaluation of these comorbidities may improve the clinical management of pwMS.

Disclosure: All authors declare that have no conflict of interests for this study.

EPO-336

Real clinical experience with alemtuzumab in patients with multiple sclerosis in Slovakia

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Background and aims: Alemtuzumab (ALEM), a monoclonal antibody targeting CD52 receptors of active lymphocytes has been monitored by several clinical studies. In our longitudinal study we evaluated efficacy of ALEM from 2014 to July 2022 in real clinical practice.
Methods: The study included patients from 10 out of 12 Multiple Sclerosis Centres in Slovakia. Neurologists from the centres provided data about their patients treated with at least 1 cycle of ALEM. Long-term efficacy was evaluated using NEDA-3 concept (absence of relapses, no new T2-hyperintense brain lesions on MRI, stabile EDSS).
Results: We obtained data about 146 MS patients. 119 patients (81.5%) received 2 ALEM cycles, 16 patients (10.9%) received 1 ALEM cycle, and 11 (7.5%) 3 cycles. Stability of NEDA-3 was 32.3 months (2–79), stability of EDSS was 28.5 months. The follow-up treatment was: ocrelizumab – 13 patients (8.9%), siponimod – 9 (6.2%), dimetyl fumarate – 3 (2.1%), cladribine – 3 (2.1%), glatiramer acetate – 2 (1.3%), and interferon beta Ia sc, cyclophospamid, aHSCT and cyclophosphamid – 1patient (0.7%) each. Four patients died after ≥2 years after the last ALEM: multiple myeloma, generalised carcinoma mammae (man), progressive multifocal leucoencephalopathy after switch to natalizumab, and sepsis after COVID-19 pneumonia. One other case of bilateral carcinoma mammae was diagnosed in a female patient after 1 cycle of ALEM. The most frequent were autoimmune thyreoidites
Conclusion: Our study adds information about real-life duration of ALEM effectivity and the need and details of further treatment.
Disclosure: The authors have nothing to disclose.

EPO-337

One year of B-cell directed therapy with ofatumumab s.c.: Results of a patient-centered real-world observational study

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Background and aims: Ofatumumab (Kesimpta™) is a subcutaneously applicable anti-CD20 antibody, which has been used for the treatment of relapsing-remitting multiple sclerosis. Home self-administration offers a high degree of independence from invasive forms of application while providing potent B-cell directed immunotherapy. In this study, we recorded the epidemiology and patient-centered experience in 99 of 127 patients. The objective was to investigate tolerability and acceptability from the patient's perspective.
Methods: Data collection was performed using physician documentation, questionnaires on tolerability and application of ofatumumab, and supplemental telephone interviews.
Results: Our cohort consists of 127 patients on ofatumumab. On average, patients received 2.8 (± SD: 1.7) prior therapies. The mean duration of ofatumumab therapy was 9.8 months (± SD: 3.5). Structured data were collected from 99 patients. 23% of the patients reported no side effects during the first application of the drug. 19% rated the side effects as "very mild" and 18% as "mild". Side effects included: 48% chills and fever, 46% headache. 19% of patients listed "other" symptoms, with fatigue being the most common here. During follow-up injections, 72% of patients reported no side effects, and 87% of patients found handling the drug "very easy." One relapse event occurred during therapy with ofatumumab.
Conclusion: Our prospective study shows that ofatumumab is well accepted and tolerated by patients. There has been one relapse event during the observation period. Side effects are mild and occur mainly during the initial application. The data suggest that ofatumumab is an effective and safe treatment option for patients with relapsing-remitting multiple sclerosis.
Disclosure: None related to this work.

EPO-338

Abstract withdrawn.

EPO-339

Probability of Cognitive Impairment Development in Patients with Multiple Sclerosis Depending on MRI Findings

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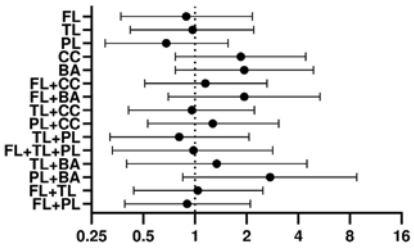
Background and aims: The aim was to assess probability of cognitive impairment (CI) development depending on location of demyelization lesions in the brain in relapsing-remitting (RR) multiple sclerosis (MS) patients.
Methods: The study enrolled 106 RR-MS patients (81 females; 25 males) from 22 to 67 years. They completed the Montreal Cognitive Assessment /MoCA (which was separated into domains: memory, language, attention, abstract thinking, visual-spatial/executive functions; Beck Depression Inventory (BDI); Hamilton Anxiety Rating Scale (HAM-A); The Pittsburgh Sleep Quality Index (PSQI); undergone MRI.
Results: During our research we discovered that perspective memory impairment was strongly associated with brain atrophy in combination with lesion of parietal lobe (OR=2.74 (0.85–8.77), p <0.0001). Probability of executive functions disorders was tied to simultaneous damage of frontal and parietal lobes (OR=3.68 (1.36–10.0), p=0.0080). Risk of anxiety onset was related to the presence of lesions in frontal and temporal lobe simultaneously (OR=2.67 (1.15–6.17), p=0.0202). Connection between MRI lesions and development of depression or sleep disorders was not found.



FL – frontal lobe, TL – temporal lobe, PL – parietal lobe, CC – corpus callosum, BA – brain atrophy

Fig. 1. Probability of development of memory decline in patients with relapsing remitting multiple sclerosis (risk assessment with 95%– OR (95%CI)).

Propability of memory decline development in RRMS patients (risk assessment with 95%-OR (95%CI))

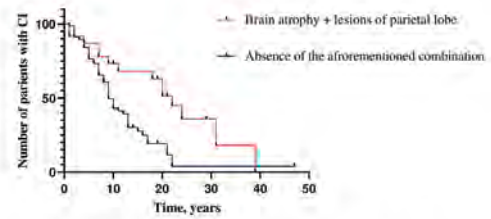
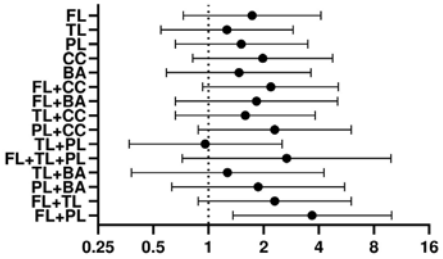


Fig. 2. Probability of development of memory decline in patients with relapsing remitting multiple sclerosis.

Propability of memory decline development in patients with RRMS



FL – frontal lobe, TL – temporal lobe, PL – parietal lobe, CC – corpus callosum, BA – brain atrophy

Fig. 3. Probability of development of executive functions disorders in patients with relapsing remitting multiple sclerosis (risk assessment with 95%– OR (95%CI)).

Propability of executive functions disoders development in RRMS patients (risk assessment with 95%-OR (95%CI))

Conclusion: Based on the location of demyelization lesions of the brain, development of CI, in particular memory and executive functions disorders, and anxiety can be predicted and potentially prevented in RRMS patients.
Disclosure: Nothing to disclose.

EPO-340

Anti GAD 65 encephalitis overlapping with multiple sclerosis : a case report

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Background and aims: Autoimmune encephalitis is a severe disorder revealed by neuropsychiatric manifestations. The concurrence with demyelinating diseases is described with NMDA-R antibodies.This overlapping is rare specifically with multiple sclerosis.
Methods: A single case presentation.
Results: A 32 year old female, is followed since 2016 for relapsing remitting multiple sclerosis and has been under Natalizumab since 2018. She was in NEDA status and the EDSS was stable at 2. In 2022 she presented a status epilepticus without any evident etiology.Sedation and Intubation were required to control the seizures. Later on, she presented visual hallucinations, memory and attentional disorders and dyskinesia. Cerebral MRI showed new lesions described as T2 and FLAIR hypersignals of the internal and medial-temporal regions in both sides without any enhancement.The CSF analysis was normal.Biological assessment, HSV and JCV PCR were negative. The immunological screening revealed positive anti-GAD65 antibodies in serum .No associated neoplasm was detected. Intravenous immunoglobulin was initiated and progressive improvement was noticed.The therapeutic protocol included the maintenance of the DMT and a monthly perfusion of IGIV during six months. The patient improved rapidly after the initiation of immunotherapy and her MS remained stable.
Conclusion: To the best of our knowledge,this is the first case describing the overlapping of relapsing remitting MS and Anti GAD65 autoimmune encephalitis.These overlap syndromes are strongly suggestive of a common dysimmune mechanism in their pathophysiology. Their Recognition is essential to avoid delay in diagnosis and treatment.
Disclosure: Nothing to disclose.

EPO-341

Effect of high-efficacy disease-modifying treatment on spinal cord lesion development in multiple sclerosis

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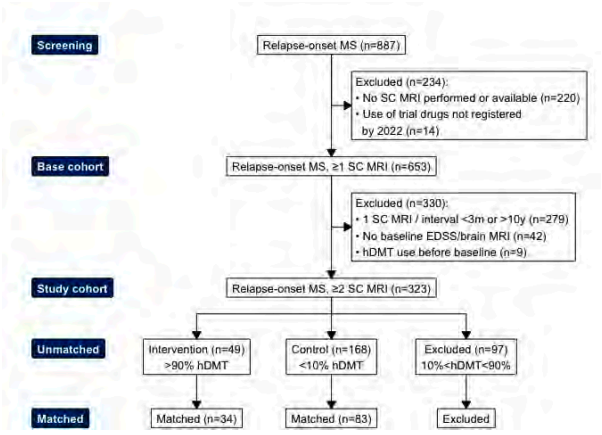
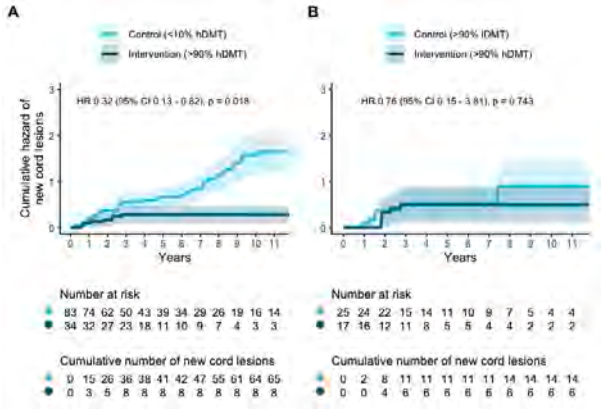
Background and aims: Spinal cord lesions in MS are an important contributor to disability. Knowledge on the effect of disease-modifying treatment (DMT) on cord lesion formation is sparse, as cord outcomes are seldom included in MS treatment trials. We aim to investigate whether high-efficacy DMTs (hDMT) can reduce spinal lesion formation, compared to low-efficacy DMTs (lDMT) and/or no treatment.

Methods: Relapse-onset MS patients with spinal cord MRI data available. were retrospectively identified. Patients with ≥2 spinal MRIs (interval >3 months and <10 years) were included. The intervention group was defined as patients that, after starting treatment, were treated with hDMTs ≥90% of spinal MRI follow-up time. Patients receiving hDMTs <10% (lDMT or no treatment ≥90%) of follow-up, served as controls. In a secondary analysis, only patients using lDMT for ≥90% of follow-up were considered controls. Patients were matched using propensity-scores. Cox proportional hazards models were used to estimate the risk of new spinal lesions.

Results: 653 patients had ≥1 spinal cord MRI and 323 an additional one with sufficient baseline data: 49 satisfied intervention and 168 control group criteria. 34 intervention group patients were matched to 83 controls. Patients in the intervention group were significantly less likely to develop new spinal cord lesions at follow-up (HR 0.32 [0.13–0.82], p=0.018). When the intervention group was matched to only controls using lDMT >90% of follow-up, the difference was not statistically significant (HR 0.76 [0.15–3.81], p=0.743).



Flowchart of screening, inclusion and matching of study population



Cumulative hazard of new spinal cord lesions. (A) Primary analysis, with patients <10% hDMT usage during follow-up as control group. (B) Secondary analysis, with patients >90% lDMT usage during follow-up as control group.

Conclusion: Treatment with hDMTs significantly reduces risk of new spinal cord lesions when compared to matched patients receiving no treatment and/or lDMTs.

Disclosure: DK, AM, RS and OG have nothing to disclose; RH received institutional research grants and fees for lectures and advisory boards from Biogen, Merck and Genzyme-Sanofi.

EPO-342

The Central Vein Sign to differentiate multiple sclerosis from migraine

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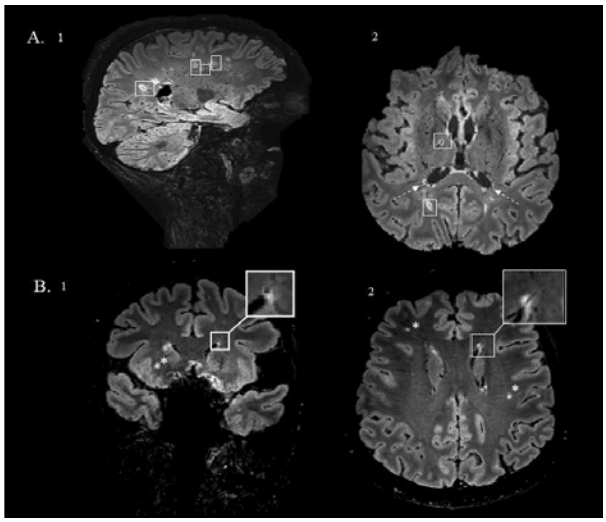
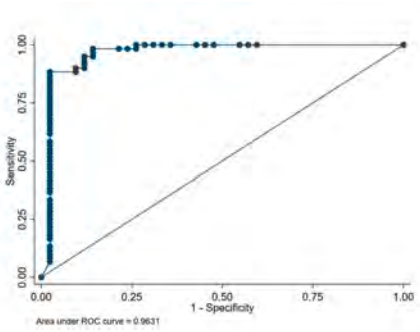
[1]IRCCS Ospedale Policlinico San Martino Genoa, Genoa, Italy, [2]University of Genoa, Genoa, Italy, [3]DISSAL, University of Genoa, Genoa, Italy, [4]DINOGMI, University of Genoa, Genoa, Italy

Background and aims: Background The Central Vein Sign (CVS) has been demonstrated its potential in differentiating multiple sclerosis (MS) from its comorbidities. Migraine represents the most common MS mimic.Aims The aims of this study were to investigate, in two cohorts including MS and migraine patients (i) the prevalence of CVS, (ii) the spatial distribution of CVS+ lesions, (iii) the best CVS threshold able to differentiate them.
Methods: 60 MS patients and 50 age and gender-matched migraine patients underwent a 3T MRI scan. A ROC-curve analysis was performed to identify the best threshold in terms of proportion of CVS+ lesions and the absolute number of CVS+ lesions able to differentiate MS from migraine.
Results: Lesion volume (LV) was different between CVS+ and CVS− lesions (median=1,273 mm³ vs 181.5 mm³ for MS cohort; median = 35.1 mm³ vs 52.2 mm³ for migraine cohort; p<0.001 for all). CVS+ LV and number were higher in MS with respect to migraine both considering whole brain and its subregions (p<0.001). The proportion of CVS+ lesions in juxtacortical and infratentorial areas was higher in MS than migraine (p=0.016 and p=0.034 respectively). The best CVS proportion-based threshold able to differentiate MS from migraine was 23% (sensitivity 90%, specificity 90.5%). The "pick 6" rule seemed to be preferable in terms of specificity with respect to the "pick 3" rule.



Example of CVS in migraine and MS patients



ROC Curve analysis to identify the best cut-off in terms of %CVS+ lesions able to differentiate MS from migraine patients

Conclusion: A CVS proportion-based threshold of 23% is capable to distinguish MS from migraine with high sensitivity and specificity. The "pick 6" algorithm may be useful in the clinical setting.
Disclosure: Authors declare no disclosures for this work.

EPO-343

Primary HIV infection as atypical cause of demyelination

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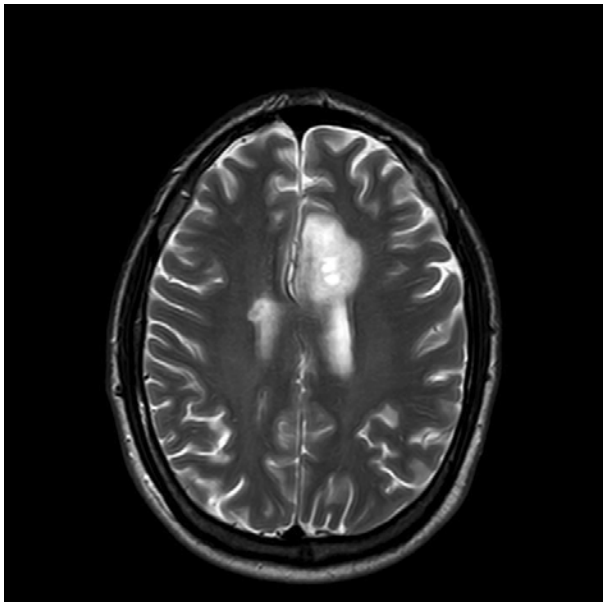
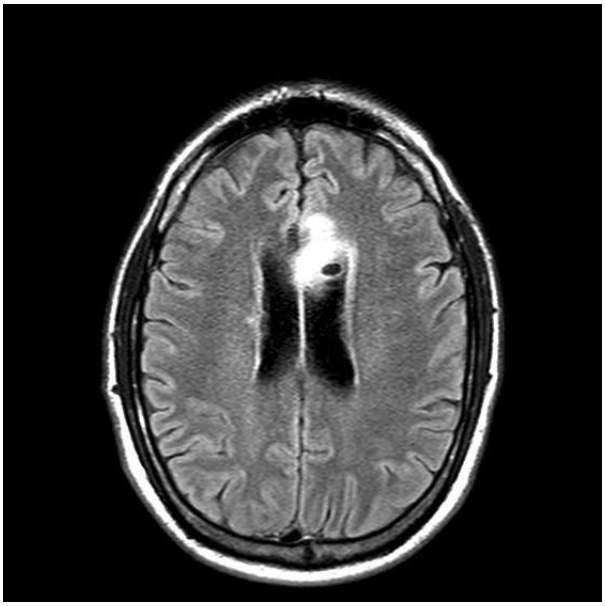
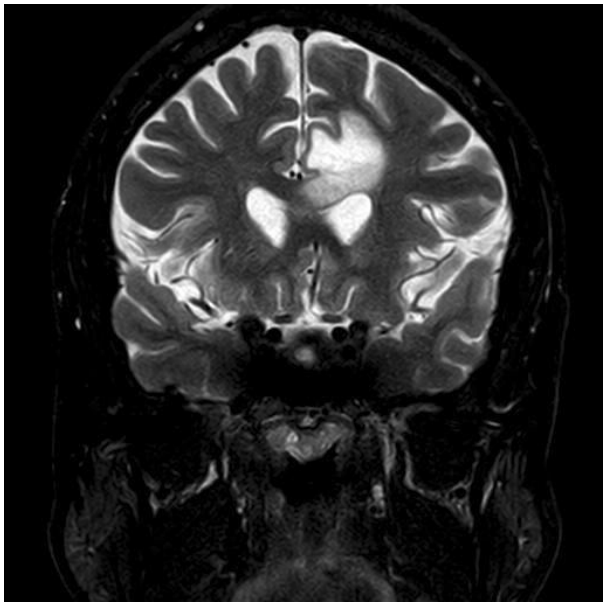
Background and aims: Demyelinating lesions secondaries to primary HIV infection are highly infrequent, with only a few case reports published in the literature. In this context, we should rule out other diagnosis, such as progressive multifocal leukoencephalopathy, primary CNS lymphoma, acute disseminated encephalomyelitis, toxoplasmosis, cytomegalovirus, cryptococcosis and multiple sclerosis. We present a case about this rare entity.
Methods: A 38-year-old male, current smoker and diagnosed with hypertension under no treatment, presented blurry vision and a hypertensive crisis. One month ago, he had experimented similar symptomatology, with completely spontaneous recovery. On physical examination he showed a right temporal hemianopsia, without delirium or another focal neurologic deficit.
Results: Brain MRI showed a lesion in the corpus callosum and left frontal lobe, hypointense on T1 and hyperintense on T2 and FLAIR, with little restriction (predominantly peripheral) in diffusion and no enhancement after gadolinium administration; stable in successive imaging tests. The brain biopsy was compatible with demyelinating disease. The results of the blood analysis were: HIV positive; serology tests for HCV, syphilis, toxoplasma and cryptococcal negative; CMV IgM negative, CMV IgG positive; CD4 428. The CSF showed a hyperproteinorraquia, IgG OCBs with a mirror pattern and negative cytology. Clinical stability had been achieved after starting antiretroviral therapy, with no new lesions.



Brain MRI: axial T2



Brain MRI: axial FLAIR



Brain MRI: coronal T2

Conclusion: An exhaustive approach in HIV patients who shows demyelinating lesions is essential for making a right diagnosis because the primary infection can be the cause.
Disclosure: Nothing to disclose.

ePosters

Monday, July 03 2023
Sleep-wake disorders

EPO-344

Confusional arousal parasomnias and the sleep factors associated with in-lab registration of episodes

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Background and aims: Non-rapid eye movement (NREM) sleep parasomnias include three subtypes: sleepwalking, sleep terrors, and confusional arousals (CA). CA are frequent but stay unnoticed in many patients, however with higher chances to be recorded during polysomnography (PSG). Our aim was to study the possible associations between CA parasomnias recorded during PSG night and sleep parameters.
Methods: We performed a retrospective review over a period of 5 years of PSGs of patients with NREM parasomnia diagnosed at a tertiary sleep center. They underwent somnological interview and a single-night PSG study preceded by a partial sleep deprivation night. PSG parameters, data on the frequency of parasomnia events, and their duration were taken into consideration. Spearman's correlation (r) and Chi-squared test were used for statistical analysis.
Results: Overall, 60 participants (mean age - 15.23±10.7 (7-89), males=86.7%, mean BMI-21.9 kg/m^2) were included, with mean CA episodes – 1.2 (0-5). The main descriptive results of the parasomnia-related parameters are presented in Table 1. Correlations with PSG parameters showed among other findings some interesting positive correlations between number of recorded episodes per PSG night and leg movement (LM) parameters (Table 2).

Parameter	Results	SD
Confusional arousals by PSG	58.3%	n/a
0 RE	41.7%	n/a
1 RE	26.7%	n/a
2 RE	15%	n/a
3 RE	8.3%	n/a
4 RE	6.7%	n/a
5 RE	1.7%	n/a
Minimum ED	32.1sec	23.98
Maximum ED	43.7sec	23.69
Average ED	37.9sec	22.26
Average difference between the longest and shortest ED	10.9sec	16.09

Table 1. Descriptive statistics of parasomnia-related data. PSG – polysomnography, RE- recorded episodes, ED- episode duration, SD- standard deviation, n/a – not applicable

PSG parameters	Spearman's *r*	P
Total sleep time	-0.204	>0.05
Wake after sleep onset	0.208	>0.05
Sleep onset	0.158	>0.05
Sleep efficiency	-0.201	>0.05
Awakenings number	**0.332**	**0.05**
Latency NREM1	0.059	>0.05
Latency NREM2	0.293	>0.05
Latency NREM3	0.299	>0.05
Latency REM	0.313	0.07
Apnea hypopnea index	0.174	>0.05
Oxygen desaturation index	0.122	>0.05
NREM1%	**0.349**	**0.04**
NREM2%	-0.018	>0.05
NREM3%	0.012	>0.05
REM%	-0.083	>0.05
Wake%	0.201	>0.05
Leg Movement Index	**0.361**	**0.03**
Periodic Leg Movement Index	0.163	>0.05
Arousal Index	0.183	>0.05

Table 2. Correlation of the number of confusional arousal episodes per recording night with PSG parameters. PSG – polysomnography

Sleep Complaints	CA by PSG	No CA by PSG	P
Insomnia	11.11%	18.18%	>0.05
Unrefreshing sleep	7.41%	9.09%	>0.05
Sleepiness	11.11%	22.73%	>0.05
Snoring	14.81%	27.27%	>0.05
Shortness of breath	7.41%	0.00%	>0.05
Restlessness in legs before sleep	7.41%	27.27%	0.06
Repetitive movements in legs in sleep	11.11%	34.78%	**0.04**
Bruxism	7.41%	18.18%	>0.05

Table 3. Association of sleep complaints with the presence of confusional arousals by PSG. CA – confusional arousal, PSG - polysomnography

Conclusion: Our results suggest the parasomnia-related parameters among patients with CA by PSG are associated with leg movements and possibly restless legs syndrome, while we found no association with sleep stage-related and respiratory variables. Probably RLS may delay sleep and worsen quality of sleep. Overall, recording CA subtype of NREM parasomnias may have added value for understanding interactions between different sleep disorders.
Disclosure: Nothing to disclose.

EPO-345

"A sleep disorder never comes alone: the association between rem sleep behaviour disorder and obstructive sleep apnoea"

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Background and aims: REM sleep behaviour disorder (RBD) is a parasomnia associated with synucleinopathies such Parkinson's disease (PD). In patients with RBD, obstructive sleep apnoea (OSA) can occurs as comorbid condition. The main goals of our study were determine the prevalence of OSA in isolated RBD (iRBD) or RBD plus synucleinopathy (RBDpS) patients and evaluate the impact of positive airway pressure therapy in RBD symptoms.
Methods: We included patients with RBD and OSA (defined as apnoea-hypopnea index(AHI)≥5/h) diagnosis followed in a tertiary sleep centre. Data on demographics, clinical characteristics, video polysomnography(VPSG) and in self-reported RBD symptoms following positive airway pressure therapy were collected. Non-parametric tests were used in statistical analyses.
Results: The prevalence of OSA in 53 RBD patients was 73.6%(n=39): 46.2% mild, 33.3% moderate and 20.5% severe. 16 patients(41.0%) with concomitant RBD and OSA, also had diagnosis of synucleinopathy, the vast majority PD(93.8%;n=15). No statistically significant differences were found between iRBD plus OSA and RBDpS plus OSA regarding male sex, age at diagnosis of RBD, BMI, AHI, total sleep time, REM-AHI and NREM-AHI. AutoCPAP, CPAP and BIPAP therapy were used by 48.7% (n=19), 7.7% (n=3) and 5.1% (n=2), respectively. These therapies improved self-reported RBD symptoms in 72.7% of the iRBD patients and in 54.5% of RBDpS patients. The main subjective improvement was the reduction in abrupt movements (87.5%-iRBD and 100.0%-RBDpS).
Conclusion: Positive airway pressure therapy may improve self-reported RBD symptoms, including in those with a coexistent synucleinopathy.
Disclosure: Nothing to disclose.

EPO-346

Suicidal tendencies and sleep disorders in epilepsy: insomnia takes the lead

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Background and aims: Suicide is more prevalent in epilepsy compared to the general population. Adults with epilepsy (AWE) report worse sleep quality. We aimed to assess subjective sleep among AWE who exhibit suicidal tendencies (ST).
Methods: AWE were assessed in a sleep and epilepsy center. AWE remained on same treatment scheme for past 3 months (or were drug-naive). Sleep complaints (SC) and their total number were addressed during structured interview (insomnia, sleep-disordered breathing, behavioral and movement disorders). Subjective sleep quality (SSQ) was measured by Pittsburgh Sleep Quality Index (PSQI). Participants were evaluated using Hamilton rating scales for depression (HAMD) and anxiety. The point on ST from HAMD was used to grade them. We divided the sample into two groups according to any suicide point positive response (SG) against none (NSG). Statistical analysis included Mann-Whitney U and Chi-squared tests.
Results: We included 168 AWE (mean age – 35.75 years, F=46.4%). Depression and anxiety rates were higher and SSQ was worse in SG. Overall, higher SC number was associated with ST (Table 1). Insomnia and its phenotypes were the most outstanding variables connected to ST. Also, abnormal behaviors in sleep, sleep paralysis and sleep bruxism were more prevalent in SG (Figure 1). No differences were obtained for sleepiness and sleep-disordered breathing, still the sleep attacks were more prevalent in SG.

Total Sample	SG	NSG
168	24	144

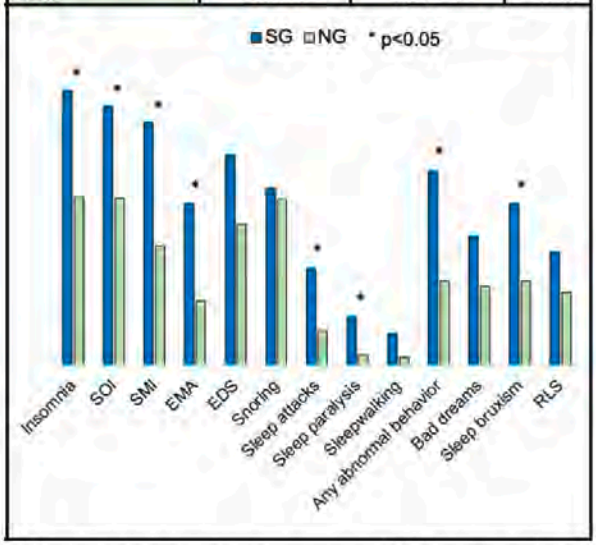
	SG	NSG	P
Age (mean, yrs)	37.0 (±12.6)	34.5 (±13.6)	>0.05
Sex (%)	58.3/41.7	52.8/47.2	>0.05
HAMD (mean)	21.1 (±7.5)	11.2 (±6.8)	<0.01*
HAMA (mean)	21.8 (±10.6)	13.4 (±9.1)	<0.01*
PSQI (mean)	10.3 (±5.4)	7.5 (±4.8)	<0.05*
SSC (num.)	5.5 (±3.8)	3.6 (±2.7)	<0.05*

Suicidal tendencies in general sample	Proportion
Suicidal tendencies total	14.3%
Feeling life is not worth living	8.3%
Thoughts of harm/possible death	4.2%
Suicidal ideas	1.2%
Suicide attempts	0.6%

SG - suicidal tendencies group, NSG – absent group, HAMD – Hamilton Depression Rating Scale, HAMA – Hamilton Anxiety Rating Scale, PSQI – Pittsburg Sleep Quality Index, SSC – Subjective Sleep Complaint.

Table 1. Descriptive data, depression, anxiety and sleep quality rates presented for two groups of epilepsy patients: with and without suicidal tendencies.

	SG	NSG	P
Insomnia	70.8%	43.4%	<0.05*
SOI	66.7%	43.1%	<0.05*
SMI	62.5%	30.6%	<0.05*
EMA	41.7%	16.7%	<0.05*
EDS	54.2%	36.4%	>0.05
Snoring	45.8%	42.7%	>0.05
Sleep attacks	25%	9.1%	<0.05*
Sleep paralysis	12.5%	2.8%	<0.05*
Sleepwalking	8.3%	2.1%	>0.05
Other behavior	50%	21%	<0.05*
Any behavior	50%	21.7%	<0.05*
Bad dreams	33.3%	20.3%	>0.05
Sleep bruxism	41.7%	21.7%	<0.05*
RLS	29.2%	18.75%	>0.05



SG - suicidal tendencies group, NSG – no suicidal tendencies group, SOI – sleep-onset insomnia, SMI – sleep-maintenance insomnia, EMA – early morning awakenings, EDS – excessive daytime sleepiness, RLS – restless legs syndrome.

Figure 1. Subjective sleep complaints are presented for both groups of adults with epilepsy with and without suicidal tendencies.

Conclusion: Sleep quality is worse and sleep complaints are more prevalent in adults with epilepsy with suicidal tendencies. Insomnia was the leading disorder for these people. Epilepsy patients with suicidal tendencies show higher burden of sleep complaints.
Disclosure: Nothing to disclose.

EPO-347

Fatigue in hypersomnolence disorders

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Background and aims: In narcolepsy and other hypersomnolence disorders besides of excessive daytime sleepiness, many patients describe rapid exhaustion, tiredness and fatigue, often associated with limitations in performance. There are only few studies on fatigue in hypersomnolence disorders.
Methods: The aim of this study was to prospectively and systematically investigate patients with different hypersomnolence disorders (narcolepsy, idiopathic hypersomnia (IH), daytime sleepiness associated with obstructive sleep apnea) for symptoms of daytime sleepiness, fatigue and affective disorders as well as the influence of therapies (medication, CPAP, others) on the symptom fatigue. Therefore, we used an online survey with multiple questionnaires like the Fatigue Scale for Motor and Cognitive Functions (FSMC), Epworth Sleepiness Scale (ESS) and others.
Results: Currently included are 176 participants (73.9% female), 72 with type 1 narcolepsy (NT1), 41 with NT2, 17 with IH, and 41 healthy controls. On average, participants were 36.6 years old (SD +/- 13.8). Participants with NT1 had a mean ESS of 16.5 (SD +/- 3.8), NT2 15.0 (SD+/- 3.8), and IH 16.5 (SD+/- 4.0). 96.9% of NT1, 97.4% of NT2 and 92.9 % of IH patients described fatigue, according to the FSMC total score (74.36; SD +/-15.9 for NT1, 77.3; SD +/-13.1 for NT2, and 75.6; SD+/- 20.0 for IH). FSMC total scores indicate a "severe" level of fatigue in all 3 disorders. Final results will be presented at the congress.
Conclusion: Preliminary results indicate that fatigue is practically always present in narcolepsy and in IH. Many patients seem to be severely affected.
Disclosure: No conflict of interest.

EPO-348

REM sleep behavior disorder in Parkinson's disease: motor and non-motor characteristics, severity and levodopa aspects

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Background and aims: REM sleep behavior disorder (RBD) is a premotor biomarker of Parkinson's disease (PD) and may accompany it during the course. Our aim was to

study the relationship of RBD, PD clinical characteristics and treatment with levodopa.
Methods: Patients with PD were diagnosed using UK PDS Brain Bank criteria and assessed by UPDRS scale and Hoehn&Yahr (H&Y). Probable RBD diagnosis (referred to as RBD) was placed based on dreams with enactment mentioned by patients and caregivers (not confirmed by polysomnography). Mann-Whitney U and Chi-squared tests were used for statistical analysis.
Results: Sample description: n=107, mean age-62.9 years (43-87), F=52.3%. UPDRS and H&Y profiles are presented in Table 1. Two groups were formed according to the RBD variable (27.4% had RBD). Mean age, sex, BMI and age of PD onset and duration were similar for both groups. Daily levodopa dose average tended to be lower in RBD ($p>0.05$), and, interestingly, the number of intakes of levodopa per day were fewer in PD patients with RBD than in patients without RBD ($p<0.05$). Table 2 encompasses comparisons for continuous and dichotomous variables in relation to RBD. PD patients with RBD had more fatigue ($p<0.05$) and vivid dreaming ($p<0.05$).

Variable	Mean	SD
UPDRS_I	2.7	2.15
UPDRS_II	11.9	5.4
UPDRS_III	30.1	14.8
UPDRS_Total	44.6	105
Hoehn&Yahr rating	2.15	0.67

Table 1. Parkinson's disease-related general descriptive data (UPDRS – Unified Parkinson Disease Rating Scale, SD – Standard Deviation).

Variables	RBD	No RBD	P value
UPDRS I	3.5	2.4	**<0.05**
UPDRS II	12.9	11.6	=0.05
UPDRS III	32.4	29.4	>0.05
UPDRS Total	48.2	43.4	>0.05
H&Y rating	2.3	2.1	**<0.05**
Restless legs syndrome %	29.6	17.2	>0.05
Fatigue %	89.7	70.15	**<0.05**
Olfactory dysfunction %	55.2	50	>0.05
Vivid dreaming %	60.9	27.1	**<0.05**
Sleep onset insomnia %	51.85	45.8	>0.05
Sleep maintenance insomnia %	66.7	52.8	>0.05
Daytime sleepiness %	58.6	50	>0.05
Levodopa in the scheme %	80.8	74.1	>0.05
Nocturnal akinesia %	66.7	62.8	>0.05
Nocturnal tremor %	50	44.2	>0.05

Table 2. Continuous and dichotomous variable distribution according to the presence or absence of RBD in patients with PD. Abbreviations: RBD – REM sleep behavior disorder, UPDRS – Unified Parkinson's Disease Rating Scale, H&Y - Hoehn&Yahr.

Conclusion: Our results show high prevalence of RBD in PD. PD patients with RBD had more fatigue and vivid dreaming. PD patients with RBD had worse results on mood, cognition, and behavior domain, while other domains were similar. Finally, the disease was more severe in the presence of RBD.
Disclosure: Nothing to disclose.

EPO-349

Sleepiness in functional motor disorders: the mismatch between self-reporting and the multiple sleep latency test.

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Background and aims: Sleep symptoms, including sleepiness, are frequently reported by patients with functional motor disorders (FMD). We aimed to identify the comorbid sleep disorders in FMD, and to investigate the relationship between subjective sleepiness and objective measures of hypersomnia.
Methods: Twenty-six patients (mean age 49.5 (SD 10.0) years) with clinically definite FMD, and 16 patients (mean age 47.9 (SD 9.6) years) with central hypersomnia (CH) were included in the study. The study protocol consisted of a medical and sleep history, neurological examination, polysomnography (PSG), multiple sleep latency test (MSLT), and questionnaires assessing sleepiness, fatigue, and depression.
Results: Fifteen FMD patients reported sleepiness as their major sleep complaint and/or scored above the cut-off for excessive daytime sleepiness. Sleep comorbidities were found in the following proportions: 11 restless legs syndrome; 13 obstructive sleep apnoea; and 2 periodic limb movements in sleep; however, their relation to sleepiness was not observed. FMD patients with sleepiness reported higher depression ($p=0.018$), and had longer sleep latencies in the MSLT ($p<0.001$) compared to the CH patients. Depression ($p=0.006$) and fatigue ($p=0.003$) positively correlated with self-reported sleepiness in FMD patients.
Conclusion: This study did not find the objective correlation of subjective sleepiness reported by patients with FMD. Although sleep abnormalities were found to be common in FMD, they were not associated with increased sleepiness. Correlations between self-reported sleepiness, depression, and fatigue support the current unified model for the development of functional symptoms. Supported by: Czech Ministry of Health Project AZV NU20-04-0332.
Disclosure: Supported by: Czech Ministry of Health Project AZV NU20-04-0332; National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107) – Funded by the European Union – Next Generation EU; Charles University: Cooperatio Program in Neuroscience; General University Hospital in Prague project MH CZ-DRO-VFN64165. The authors have no conflict of interest to disclose.

EPO-350

Sex-related differences in symptoms and impairment in patients with narcolepsy: findings from the TENAR project

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Background and aims: Recent pre-clinical findings suggest the existence of sex-related differences in narcolepsy. We aimed at comparing severity of symptoms and psychosocial impairment of female and male patients with narcolepsy.

Methods: Secondary analysis of baseline data of 106 female and 102 male patients with narcolepsy (mean age of 33.9 and 34.1 years respectively) participating in the TENAR (TElemedicine for NARcolepsy) randomized controlled trial (Italian Ministry of Health funded project RF-2016-02364742). Baseline data included: sociodemographics (educational level, sentimental, marital and occupational status), sleepiness (Epworth Sleepiness Scale, ESS), frequency and duration of cataplexy attacks, disease severity (Narcolepsy Severity Scale, NSS), depressive symptoms (Beck Depression Inventory, BDI), pharmacological treatment, and main narcolepsy-related problems.

Results: Female and male patients did not differ regarding sociodemographics, cataplexy, and pharmacological treatment. Compared with male, female patients had significantly higher ESS (11.2 vs 9.4), NSS (22.3 vs 17.1), and BDI scores (11.7 vs 6.9). With the exclusion of cataplexy and of the item "relationships with the others", compared with male, female patients reported significantly ($p<0.05$) more frequently as a problem all the narcolepsy-related problems investigated: sleepiness (71.7% vs 46.1%), sleep attacks (45.3% vs 26.5%), concentration and memory problems (65.1% vs 35.3% and 42.5% vs 27.5% respectively), and maintain the work pace and achieve goals (54.7% vs 23.5% and 40.6% vs 21.6% respectively).

Conclusion: Narcolepsy may impair differently female and male patients calling for better understanding of sex-related differences to improve management and care of narcolepsy.

Disclosure: Funding source: Italian Ministry of Health funded project RF-2016-02364742

EPO-351

Positive Effects of pregabalin and duloxetine on Sleep and Pain in Painful Diabetic Polyneuropathy (PDPN): Blossom Trial

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Background and aims: The secondary outcome of Blossom Clinical Trial was to measure effects of pregabalin (Pregabalin Krka) and duloxetine (Dulsevia®) on sleep patterns and depression in PDPN patients.

Methods: 201 PDPN patients from 5 countries were randomized to pregabalin (99) or duloxetine (102) for 12 weeks. Pain was evaluated using visual analogue scale (VAS) and Douleur Neuropathique questionnaire (DN4), insomnia with insomnia severity index (ISI), excessive daytime sleepiness with Epworth sleepiness scale (ESS) and depression with major depression inventory (MDI).

Results: After 12 weeks, worst pain intensity in last 24-hours (WPI) decreased from 69.2±16.7 to 27.7±20.6 (pregabalin) and from 67.4±16.0 to 27.4±21.0 (duloxetine). DN4 decreased from 6.9±1.6 (both arms) to 3.6±2.4 (pregabalin) and to 3.6±2.5 (duloxetine); ISI from 11.1±7.0 to 6.0±5.6 (pregabalin) and from 10.9±6.9 to 7.4±6.4 (duloxetine); ESS from 7.0±4.4 to 6.7±4.4 (pregabalin) and from 6.0±4.1 to 5.8±3.6 (duloxetine); MDI from 16.0±11.4 to 10.2±8.3 (pregabalin) and from 15.4±9.4 to 10.8±8.1 (duloxetine). On average, patients had subthreshold insomnia without excessive daytime sleepiness or depression. At the end of the treatment period, WPI, DN4, ISI and MDI scores significantly decreased ($p<0.001$) without change in daytime sleepiness.

Conclusion: According to results, pregabalin and duloxetine may have beneficial multimodal effect. The mood and sleep of PDPN patients improved after 12 weeks of treatment.

Disclosure: Krka, d.d., has financially supported this clinical trial.

EPO-352

Sociodemographic characteristics of female narcolepsy patients

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Background and aims: Narcolepsy is a rare neurological disorder, which affects men and women about equally often. Narcolepsy often results in limitations of workability and quality of life, but gender-specific data are very limited. We aimed at analyzing sociodemographic data from narcolepsy females compared to healthy female controls.
Methods: For assessment, we used an online survey. Adult female patients were invited from the outpatient clinic of a tertiary sleep and narcolepsy center. Data assessment included demographic data, use of exogenous noxae, education, work, and co-morbidities.
Results: We included 113 female narcolepsy (NC) patients and 199 healthy (HC) female controls. Mean age was 33.8 (SD 9.8) for NC and 35.4 (SD 10.1) for HC (n.s.). Mean BMI was 27.1 (SD 6.7) for NC and 25.1 (SD 3.5) in HC. In narcolepsy, the highest completed level of education reached only 29.2%, in contrast to 41.2% in HC ($p<0.05$). 19.5% of NC (vs. 12% of HC) did not complete any professional training ($p<0.05$). 81.4% of HC work full-time, but only 31.9% of NC ($p<0.01$). NC had less frequent a permanent partnership (incl. marriage): 33.6% vs. 39.7% ($p<0.05$). 32.7% of NC are smokers, whereas only 21.1% of HC ($p<0.05$). Depression was common in NC with 23% vs 9% in HC ($p<0.01$).
Conclusion: Women with narcolepsy are more often less educated and limited in their workability. Further efforts are needed to implement earlier diagnosis and treatment, as well as to pay particular attention to gender aspects in narcolepsy.
Disclosure: Nothing to disclose.

EPO-353

Involvement of sleep structure in patients with a selective stroke of the basal ganglia: An observational, cohort study.

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Background and aims: Selective basal ganglia (BG) stroke is a rare event observed after revascularization procedures. The primary endpoint of the study was the analysis of sleep structure in patients with selective ischemic BG lesions. Secondarily, we aimed to determine the prognostic role of sleep parameters in the same population.
Methods: In this observational, cohort study we included consecutive adult patients admitted to our Stroke Unit (SU) who presented a selective BG lesion consequent to a M1 occlusion treated with mechanical thrombectomy (BG group). Each BG subject was age- and sex-matched with a patient who underwent polysomnography for syncope and/or suspected sleep-related breathing disorders (CG). All BG patients underwent polysomnography during their SU stay within 10 days from stroke onset. Statistical analyses were performed through Mann-Whitney U-test and logistic regression.
Results: 45 patients were enrolled. Several sleep parameters differed between BG and CG patients in the univariate analysis. In logistic regression, BG subjects presented a lower percentage of REM sleep ($p=0.002$) and more daytime sleep ($p=0.012$) than controls. 25/39 (64%) patients presented a good outcome (3-month modified Rankin Scale (mRS)≤2). Percentage of REM sleep ($p=0.001$) and CAP rate ($p<0.001$) were higher in subjects with a good outcome than those with mRS>2.

	Patients (n=45)		Controls (n=45)		
	Mean	SD	Mean	SD	p
Macrostructure					
Total sleep time (min)	353	92	371	89	**<0.001**
Sleep efficiency index (%)	67	18	80	13	**<0.001**
Sleep latency (min)	30	39	18	22	0.364
WASO (min)	147	87	76	64	**<0.001**
REM/TST (%)	10	7	21	9	**<0.001**
N1/TST (%)	11	8	9	5	0.197
N2/TST (%)	50	14	48	12	0.329
N3/TST (%)	23	13	23	10	1.000
Awakenings > 2 min (n)	11	6	6	5	**<0.001**
All arousals (per hour)	15	14	11	15	0.333
Daytime sleep (min)	63	60	25	41	**<0.001**
Microstructure					
CAP rate (%)	34	22	47	22	**0.009**
A1 (%)	22	17	29	18	0.060
A2 (%)	32	17	23	8	**<0.001**
A3 (%)	41	24	48	18	0.147
Respiratory parameters					
central AHI (per hour)	4	10	0	1	**0.024**
obstructive AHI (per hour)	32	29	15	20	**0.003**
ODI (per hour)	26	24	14	18	**0.037**

Table 1. Results of the univariate comparison between patients with a selective basal ganglia stroke and the control group. Significant differences are reported in bold. All the statistical comparison were performed through the Mann-Whitney U-test.

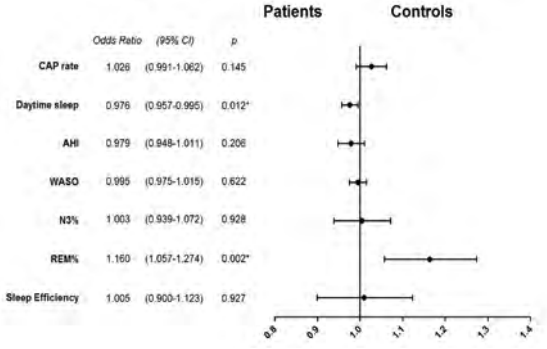

Figure 1. The Forest Plot of the logistic regression comparing patients with a selective basal ganglia stroke with the control group. Patients of the BG group presented a lower percentage of REM sleep and a higher amount of daytime sleep than controls.

	Good outcome (n=25)		Poor outcome (n=14)		
	Mean	SD	Mean	SD	p
Macrostructure					
Total sleep time (min)	533	51	529	56	0.050
Sleep efficiency index (%)	69	19	64	16	0.072
Sleep latency (min)	22	28	40	49	0.296
WASO (min)	142	83	156	94	0.481
REM/TST (%)	13	7	7	5	**0.002**
N1/TST (%)	13	8	9	6	0.174
N2/TST (%)	47	12	54	15	0.065
N3/TST (%)	24	13	21	13	0.098
Awakenings > 2 min (n)	9	3	14	9	0.518
All arousals (per hour)	12	9	20	18	0.065
Daytime sleep (min)	52	48	79	71	0.257
Microstructure					
CAP rate (%)	43	17	22	21	**<0.001**
A1 (%)	28	18	14	12	**0.002**
A2 (%)	33	11	31	23	0.545
A3 (%)	35	19	50	26	0.406
Respiratory parameters					
central AHI (per hour)	5	8	3	12	**0.033**
obstructive AHI (per hour)	35	24	28	35	0.100
ODI (per hour)	33	24	17	22	**0.033**

Table 2. A table depicting the results of the univariate comparison between the subgroups of patients with good (mRS≤2) and those with poor (mRS>2) 3-month stroke outcome. Significant differences are reported in bold.

Conclusion: A low amount of REM sleep and an increase in daytime sleep time characterize patients with selective BG stroke. A low CAP rate and a reduced proportion of REM sleep are related to poor 3-month stroke outcome. Polysomnography is a useful tool for patients with a BG stroke.
Disclosure: The authors declare no disclosures.

EPO-354

Sleep-onset REM in polysomnography is an important indicator to diagnose narcolepsy in sleep clinic patients

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Background and aims: The differential diagnosis of excessive daytime sleepiness (EDS) includes narcolepsy and sleep apnoea. In sleep medicine, the vast majority of polysomnography (PSG) is performed in order to identify sleep apnoea. In general sleep clinic patients, the frequency of sleep-onset REM (SOREM) in polysomnography is <1%. In narcolepsy, it is found in 15-44%. The aim of this study is to identify the frequency and the impact of SOREM periods in diagnostic PSG on the final sleep diagnosis.
Methods: A literature review on SOREM periods in PSG. Retrospective data analysis of consecutive sleep clinic patients on demography, clinical data, PSG and Multiple Sleep Latency Test (MSLT) data, and final diagnosis.
Results: Interim analysis includes data of 286 consecutive patients with the suspected diagnosis of sleep aponea. In 3 (1.05%) patients SOREM periods in PSG were found. SOREM occurred after 2, 8.5 and 14 minutes. Two of them were male and one was female. They were aged 34, 44 and 59 years. Epworth Sleepiness Scale (ESS) was 14, 15 and 17 points. Further diagnostic work-up showed >2x SOREM also on MSLT. Final diagnosis of the patients was narcolepsy type 1 (n=1) and type 2 (n=2).
Conclusion: PSG is an important tool for the diagnosis of sleep disorders. SOREM in PSG should be used as an important indicator for further differential diagnosis, in particular with a view to narcolepsy. This will also help to shorten the latency between symptom onset and diagnosis.
Disclosure: Nothing to disclose.

EPO-355

Sleep architecture of patients with idiopathic hypersomnia and identification of neurophysiological markers for subtypes

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Background and aims: Idiopathic hypersomnia (IH) is a rare neurologic disease characterised by excessive need of sleep including prolonged nocturnal sleep and excessive daytime sleepiness. Previously, IH has been classified into "with/without long sleep". The aim of the study is to systematically examine differences in sleep architecture, including sleep cycle features and sleep stages of patients with IH in order to identify particular neurophysiological parameters for subtypes.
Methods: In this retrospective pilot study, clinical data, and data on questionnaires, Polysomnography and Multiple Sleep Latency Tests of 60 consecutive IH patients from two major sleep centres are analysed.
Results: Interim results of 11 patients (8 female, 3 male): Mean age is 22 years. Mean score of Epworth Sleepiness Scale questionnaire is 11.0. Mean total sleep duration is 561 mins with a standard deviation (SD) of 107. Mean number of sleep cycles (MNSC) including incomplete last sleep cycle is 5.45 (SD = 1.37). Mean sleep efficiency is 93.41%. Mean sleep latency is 12 mins. Mean wake after sleep onset is 5 mins. Mean sleep cycle duration (MSCD) excluding incomplete last sleep cycle is 114 mins (SD = 20). 5 patients have a MSCD between 88 – 108 minutes (SD = 8), their MNSC is 6.0 (SD = 1.87). 6 patients have a MSCD >110 mins (SD = 18), their MNSC is 5.0 (SD = 0.63), 2 of these patients have a MSCD >140 mins. Detailed results will be presented at the congress.
Conclusion: Preliminary data indicates two subtypes of IH, one associated with long sleep cycles.
Disclosure: Nothing to disclose.

EPO-356

Sleep – wake disorders for patients with Parkinson's disease: relationship with motor and non-motor symptoms

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Background and aims: Sleep – wake disorders are among the main non-motor symptoms (NMS) that occur for the patients with Parkinson's disease (pwPD), affecting 60-90% of them [1,2,3]. Usually patients complain of insomnia, increased daily sleepiness, circadian rhythm disturbances, restless leg syndrome (RLS), REM sleep behaviour disorders (RBD) [2,3]. Recent studies show that RBD occur 10-15 years before PD specific motor symptoms evolve and is associated with increased risk of developing other neurodegenerative diseases [4].

Methods: We involved 43 patients (25 patients with PD and 18 control group patients) who underwent clinical evaluation of motor (UPDRS III scale) and non-motor symptoms (Table 1): NMS-quest, Sniffin'Sticks-12 (SS-12) test, Montreal cognitive assessment (MoCA) and sleep questionnaires (Table 2). 15 PD and 16 control group patients underwent polysomnography (PSG) and were evaluated for objective sleep disorders (Table 3).

Results: More than 75% of pwPD were diagnosed with insomnia and/or significant RLS. PSG findings suggested of longer sleep onset, reduced total sleep time, reduced sleep efficiency and more frequent arousal for pwPD compared to controls. 75% of pwPD were diagnosed with RBD, 50% - with obstructive sleep apnea syndrome (OSA) and periodic leg movement disorder (PLMD). PwPD suffering from RLS and RBD reported having significantly more NMS. PwPD having severe motor symptoms complained of insomnia more often.

Clinical characteristics	PD group (n=25)
Age, mean ± SD [min÷max]	62.8 ± 8.77 [46 ÷ 77]
Sex - Men, n (%) - Women, n (%)	 15 (60%) 10 (40%)
MoCA, mean ± SD [min÷max] - Normal, n (%) - Mild cognitive impairment, n (%) - Intermediate cognitive impairment, n (%)	22.23 ± 3.83 [13 ÷ 27] 10 (40%) 13 (52%) 2 (8%)
Brain trauma in the past, n (%)	3 (12%)
UPDRS III scale, mean ± SD [min÷max]	22.25 ± 8.6 [9 ÷ 34]
PD stage according to *Hoehn-Yahr*, mean ± SD [min÷max]	2.56 ± 0.88 [1 ÷ 4]
PD NMS questionnaire, mean ± SD [min÷max]	10.92 ± 2.97 [6 ÷ 16]
Smell test, mean ± SD [min÷max]	6.18 ± 1.99 [4 ÷ 10]
Family history of PD: - negative, n (%) - positive, n (%) - unknown, n (%)	 6 (24%) 9 (36%) 10 (40%)
Complain of sleep problems, n (%) - Cannot initiate sleep, n (%) - Arouses, n (%) - Experience nightmares, n (%)	21 (84%) 5 (20%) 20 (80%) 12 (48%)

Abbreviations: mean ± SD - mean ± standard deviation, n – number of cases, % – percentage, PD – Parkinson's disease, UPDRS – Unified Parkinson's Disease Rating Scale, NMS – non-motor symptoms

Table 1. Clinical characteristics of patients with Parkinson's disease

Indicators	PD group (n=25)	Control group (n=18)	p value
Insomnia severity index (ISI), mean ± SD [min÷max]	11.94 ± 6.86 [3 ÷ 24]	12.28 ± 5.51 [1 ÷ 20]	0,873
International Restless Leg Syndrome Scale (IRLS), mean ± SD [min÷max]	14.73 ± 11.39 [0 ÷ 32]	9.06 ± 11.73 [0 ÷ 39]	0,136
Berlin sleep apnoea scale - Low risk, n (%) - High risk, n (%)	 21 (84%) 4 (16%)	 5 (27,8%) 13 (72,2%)	**0,002**
Ullanlina Narcolepsy Scale (UNS), mean ± SD [min÷max]	7.5 ± 3.65 [2 ÷ 16]	8 ± 4.68 [2 ÷ 18]	0,723
Innsbruck RBD assessment scale, mean ± SD [min÷max]	0.25 ± 0.20 [0 ÷ 0,66]	0.22 ± 0.22 [0 ÷ 0,67]	0,606
RBD Single-Question screen (RBD1Q) - Yes, n (%)	 7 (28%)	 1 (5,6%)	**0,013**
Epworth Sleepiness Scale (ESS), mean ± SD [min÷max]	8.88 ± 4.34 [4 ÷ 19]	10.61 ± 5.88 [0 ÷ 18]	0,332

Abbreviations: PD – Parkinson's disease, RBD – REM sleep behaviour disorder, mean ± SD - mean ± standard deviation, n – number of cases

Table 2. Comparison of subjective sleep parameters using specific sleep questionnaires

Indicators	PD group (n=15)	Control group (n=16)	p value
Overall sleep time, min, mean ± SD [min÷max]	309.42 ± 86.67 [148 ÷ 465]	352.07 ± 51.21 [273,0 ÷ 432,5]	0,150
Overall sleep time, hr, mean ± SD [min÷max]	5.16 ± 1.44 [2,47 ÷ 7,75]	5.87 ± 0.85 [4,55 ÷ 7,21]	0,150
Sleep quality, %, mean ± SD [min÷max]	66.34 ± 13.24 [38,1 ÷ 83,8]	58.81 ± 12.26 [40,1 ÷ 76,1]	0,835
Sleep latency, min, mean ± SD [min÷max]	29.62 ± 44.69 [0 ÷ 147]	39.79 ± 28.01 [4,0 ÷ 96,5]	0,193
REM sleep latency, min, mean ± SD [min÷max]	188.54 ± 116.35 [23,5 ÷ 402,0]	199.10 ± 115.94 [38 ÷ 389,5]	0,945
N1 (%), mean ± SD [min÷max]	11.93 ± 10.86 [2,7 ÷ 35,2]	11.84 ± 9.16 [3,5 ÷ 37,6]	0,645
N2 (%), mean ± SD [min÷max]	48.88 ± 12.04 [21,1 ÷ 69,4]	52.81 ± 10.69 [38,6 ÷ 72,6]	0,728
N3 (%), mean ± SD [min÷max]	22.86 ± 17.85 [2,6 ÷ 72,2]	19.31 ± 9.65 [5,9 ÷ 40,8]	0,809
REM sleep (%), mean ± SD [min÷max]	16.48 ± 8.79 [2,5 ÷ 35.3]	17.12 ± 9.1 [4,1 ÷ 37,2]	0,928
AHI, e/hr, mean ± SD [min÷max]	8.33 ± 10.43 [0,4÷37,5]	34.93 ± 28.05 [3,9 ÷ 81,1]	**0,001**
AHI (on the back), e/hr, mean ± SD [min÷max]	10.8 ± 16.25 [0 ÷ 59,1]	48.95 ± 29.84 [5÷93,7]	**<0,001**
RERA, e/hr, mean ± SD [min÷max]	2.71 ± 3.63 [0,2 ÷ 13,2]	33.89 ± 31.54 [2,5 ÷ 103,5]	**<0,001**
SAI, e/hr, mean ± SD [min÷max]	18.46 ± 12.22 [2,4 ÷ 47,33]	27.19 ± 12.49 [13,9 ÷ 51,3]	**0,028**
Leg movement related arousals, e/hr, mean ± SD [min÷max]	7.29 ± 11.79 [0,3÷43,2]	2.69 ± 3.21 [0 ÷ 11,1]	0,114
Overall AI, e/hr, mean ± SD [min÷max]	30.91 ± 18.1 [9,1 ÷ 65,9]	65.43 ± 41.45 [23,1 ÷ 168,4]	**0,007**
PLMI, e/hr, mean ± SD [min÷max]	37.04 ± 32.29 [0,7 ÷ 98,5]	11.12 ± 14.89 [0 ÷ 47,4]	**0,009**
PLM-AI, e/hr, mean ± SD [min÷max]	6.24 ± 10.36 [0÷39,7]	1.64 ± 2.14 [0 ÷ 6,9]	**0,037**

Abbreviations: mean ± SD - mean ± standard deviation, n – number of cases, min – minutes, hr – hours, % – percentage, e/hr – events per hour, PD – Parkinson's disease, N1 – first sleep stage, N2 – second sleep stage, N3 – third sleep stage, REM sleep – rapid eye movement sleep stage, AHI – apnea-hypopnea index, RERA – respiratory effort related arousal, SAI – spontaneous arousal index, PLMI – periodic limb movement index, PLM-AI – periodic limb movement arousal index, AI – arousal index

Table 3. Polysomnography (PSG) results

Conclusion: Sleep – wake disorders for pwPD have a significant negative effect on other motor and NMS. Increased attention for sleep – wake disorders for pwPD may help improve management of Parkinson's disease.

Disclosure: Authors report no conflict of interest.

EPO-357

Update on SPHYNCS: the Swiss Primary Hypersomonlence and Narcolepsy Cohort Study

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Background and aims: Central disorders of hypersomnolence (CDH) comprise Narcolepsy type 1 (NT1), Narcolepsy type 2 (NT2), Idiopathic hypersomnia (IH), Insufficient sleep syndrome (ISS) and Hypersomnia associated with psychiatric disorders (NOH). Apart from NT1, further understanding of pathophysiology, diagnosis and treatment is urgently required. SPHYNCS addresses this lack of knowledge on CDH and aims at identifying new biomarkers for narcolepsy and its borderland (NBL) and thus improving diagnostic criteria and treatment.

Methods: Since 2020, 6 Swiss sleep centers have been enrolling patients with the suspected diagnosis of CDH; healthy persons are recruited as controls. Follow-up comprises 3 years. Clinical and electrophysiological data as well as blood, cerebrospinal fluid (CSF) and stool samples are collected for quantitative assessments of new biomarkers using proteomics/peptidomics, immunological, genetic, microbiome studies.

Results: 113 patients and 12 controls have been included. 92 (74%) are female and the median age is 26 (21, 34) years. The mean BMI is 23.1 (21.0, 27.1). 28 (22%) patients were diagnosed with NT1. Serum (n=125), stool (n=90) and CSF (n=81) were collected, and 110 participants agreed to wear a Fitbit device for one year. Preliminary results including Fitbit, Microbiome, CSF analyses, SART, and MINI, will be presented.

Characteristic	N	N = 125[1]
Gender (Female)	125	92 (74%)
Age	125	26 (21, 34)
BMI (calculated automatically)	119	23.1 (21.0, 27.1)
Diagnosis type	125	
Narcolepsy Type 1		28 (22%)
Other central hypersomnias		79 (63%)
Diagnosis missing		6 (4.8%)
Healthy controls		12 (9.6%)
Diagnosis certainty	107	
Definite		35 (33%)
Probable		62 (58%)

Table 1: demographics of the SPHYNCS population

Conclusion: The report shows the feasibility of the ongoing multicenter study. Hypothesis and data driven (e.g. unsupervised patient clustering) analyses are currently being explored in order to identify new CDH markers towards better patient characterization and treatment.

Disclosure: The study is supported by the Swiss National Science Foundation.

EPO-358

The Swiss Narcolepsy Network (SNaNe) and its Registry

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Background and aims: The mission of SNaNe is to foster cooperation in Switzerland among health professionals, scientists, patient organizations and the general public to promote diagnosis, treatment, psychosocial support, research and awareness of narcolepsy and central disorders of hypersomnolence (CDH). The creation of a Swiss registry for CDH is essential to collect uniform data and evaluate specified outcomes.
Methods: Sleep centers with SNaNe membership will prospectively submit patient registry information to the SNaNe REDCap database (set up at the Clinical Trials Unit (CTU) Bern). Clinical, polysomnographic and biological information are collected at baseline and follow-up visits. To be compliant with the European Narcolepsy Network (EU-NN) database, key features of the EU-NN database were adopted for the SNaNe registry. Data from the Swiss Primary Hypersomnolence and Narcolepsy Cohort Study are transferred electronically to the SNaNe database. The database regulation has been accepted by the local ethics committee.
Results: To date, we transferred data from 230 visits of 119 individuals (31 patients with narcolepsy type 1, 74 patients with other CDH or missing diagnosis and 14 controls) from the SPHYNCS to the SNaNe database.
Conclusion: The SNaNe registry aims to answer open clinical, diagnostic and therapeutic questions, support research for innovative therapeutic solutions and improve care for patients with CDH. This is needed, because Narcolepsy and other CDH are rare, debilitating and still relatively poorly understood diseases. Compatibility with the EU-NN and SPHYNCS RedCap databases enables accurate data transfer between the three databases.
Disclosure: Nothing to disclose.

Neurogenetics 1

EPO-359

Expanding the spectrum: Chorea on CANVAS.

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Background and aims: Cerebellar Ataxia, Neuropathy and Vestibular Areflexia Syndrome (CANVAS) is a recently described type of hereditary ataxia, produced by AAGGG expansions in the RFC1 gene, presenting with cerebellar, sensory and vestibular dysfunction. A multitude of other neurological symptoms have been associated with this genetic alteration, and the clinical spectrum is expanding.
Methods: We report a case of CANVAS presenting with chorea.
Results: A 60-year-old male patient, with history of chronic cough and 2 relatives affected by ataxia, started with a progressive gait disorder. The examination revealed cerebellar syndrome (dysarthria, ataxia), apalesthesia and altered Vestibulo-Ocular Reflex, suggestive of CANVAS. However, it also stands out motor impersistence, and irregular, arrhythmic and purposeless movements of the limbs, worsening with dual-task, suggestive of generalized chorea (videographic record). Complete analytical study was normal, electromyogram showed sensory neuronopathy (Figure-1), brain MRI showed cerebellar and basal ganglia atrophy (Figure-2). A CANVAS genetic study was performed with pathological results.

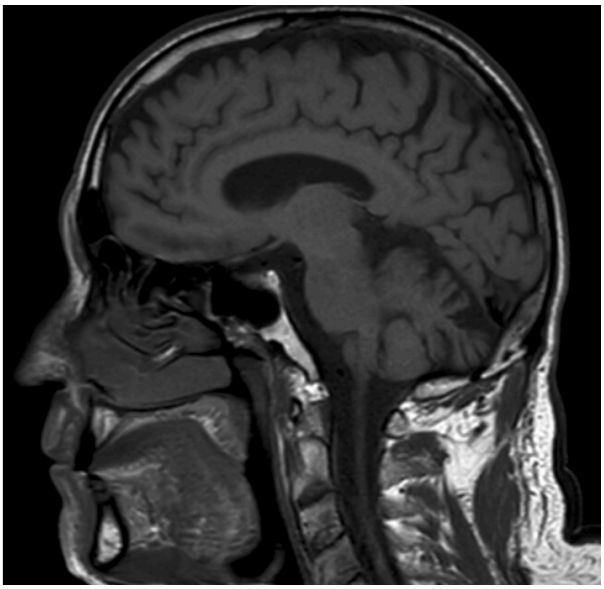
VC Sensitiva

Nervio / Lugares	Reg.	Latencia ms	Ampl µV
R Mediano - y Ulnar Dedos			
Dedo I	Muñ	NR	NR
Dedo II	Muñ	NR	NR
Dedo III	Muñ	NR	NR
Dedo V	Muñ	NR	NR
R Radial			
Ant	Tab ana.	NR	NR
R Sural - Mal Exter			
Sura	Mal Lat	NR	NR
L Sural - Mal Exter			
Sura	Mal Lat	NR	NR
R Peroneo superficial			
Pant Later	Dorso pie	NR	NR
L Peroneo superficial			
Pant Later	Dorso pie	NR	NR

VC Motora

Nervio / Lugares	Latencia ms	Ampl. mV	Dur. ms	Dist. mm	VC m/s	Reg
R Mediano - Apb						
Muñeca	4,11	8,3	4,58			APB
Codo	8,85	7,5	4,90	240	50,6	
Axila	15,26	2,6	4,74			
Erb	15,36	7,8				
R Cubital - Adm						
Muñeca	2,66	4,7	5,26			ADM
Infracodo	6,46	4,6	5,52	200	52,6	
Supracodo	8,54	4,6	5,89	110	52,8	
Axila	11,82	3,8	6,25			
EP	14,53	3,6				
R Peroneo - EDB						
Dorso Pie	3,28	4,6	5,63			EDB
Distal CP	11,46	4,3	6,77	310	38,9	
Prox CP	12,97	4,2	6,04	130	86,1	
L Peroneo - EDB						
Dorso Pie	4,48	2,5	5,68			EDB
Distal CP	12,34	2,3	6,39	320	40,7	
Prox CP	14,06	2,1		130	75,6	

Electromyogram showed sensory neuronopathy (Figure-1)



brain MRI showed cerebellar and basal ganglia atrophy (Figure-2)

Conclusion: The number of reported cases of CANVAS is increasing, progressively expanding the phenotypic spectrum, being frequent the presence of parkinsonism, sleep disorders, etc. Chorea has been described anecdotally in the past. Recently, atrophy predominantly involving cerebellum and Basal Ganglia (as in the presented case) has been described, as well as increased expression of the RFC1 gene in these locations, what could justify the presence of chorea and other dyskinesias. Although more reports are needed in this regard, chorea and other movement disorders are probably part of the clinical spectrum of CANVAS, and several authors postulate that their description will increase in the coming years.
Disclosure: the authors have no conflict of interest to report.

EPO-360

Clinical and genetic characterization of a Portuguese cohort with hereditary spastic paraparesis

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Background and aims: Hereditary spastic paraparesis (HSP) represents a heterogeneous group of neuro-degenerative disorders manifested mainly by spasticity and lower limb paresis. More than 70 genes have been identified that are associated with different clinical phenotypes and inheritance patterns. The description of case series with identified genotype may help to clarify the phenotypic spectrum associated with each genetic form.

Methods: Retrospective clinical and molecular study of HSP patients enrolled in the database of the Neurogenetics and Movement Disorders Outpatient Clinic of Hospital Santa Maria, Lisbon, since January 2021.
Results: We identified 37 patients with HSP, 59.5% female; mean age at symptom onset was 24 years. Genetic mutations were found in 70% of patients, of which 69% had a molecular diagnosis and 31% were a variant of unknown significance. SPG4 (43%), SPG3A (15%), SPG11 (14%), SPG5, SPG28, SPG76 (7% each) corresponded to the majority (78%) of HSP with molecular diagnosis and 22% formed other genetic disorders. Other neurological signs occurred in HSP, including retinal disease (SPG11), ophthalmoparesis, cerebellar ataxia and parkinsonism (SPG78), peripheral polyneuropathy (SPG11), dysautonomia (SPG4, 11, 78) and cognitive dysfunction (SPG3A). The correlation found between phenotype and genotype was consistent with the literature, except for 2 cases of SPG3A with later onset and complex forms and 1 case of SPG11 with retinopathy.
Conclusion: The clinical characterization of rare forms of HSP in the present case series and the possible association with genes whose classic phenotypes do not include spasticity and paraparesis may help to clarify the broad clinical and molecular spectrum of HSP.
Disclosure: This is an original article. We do not have conflict of interests.

EPO-361

A new heterozygous variant in the STUB1 gene linked to Spinocerebellar Ataxia type 48

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Background and aims: Spinocerebellar ataxias (SCA) are a group of clinically and genetically heterogeneous disorders, characterized by a predominant cerebellar syndrome, that can afflict other neurological systems. The number of known genes associated with disorders is constantly expanding with the use of Next Generation Sequencing (NGS). Originally associated with autosomal recessive SCA16 (SCAR16), homozygous variants in the STUB1 gene have recently been linked to autosomal dominant SCA48 (SCA48) in some patients.
Methods: A 45-year-old male was referred due to cognitive changes that began at the age of 31 years (difficulty in sustaining attention and planning tasks). In the past 6 years he additionally presented difficulties in verbal articulation and fine motor coordination, and progressive gait imbalance. His maternal grandparents were consanguineous, and his mother began experiencing progressive gait and cognitive dysfunction when she was 50. Neurological examination highlighted a multiple-domain cognitive impairment, hypermetric saccades, appendicular dysmetria, low-amplitude intention tremor, dystonic posture of the left hand, 4-limb hyperreflexia and wide-based gait.
Results: Blood analysis excluded reversible causes of ataxia and brain MRI-scan showed olivopontocerebellar atrophy. NGS panel showed a new heterozygous variant (c857T>C) in the STUB1 gene (classified as deleterious by the bioinformatic analysis). Segregation study of the variant in the family identified his mother with the same variant.
Conclusion: We present a clinical case of ataxia caused by SCA48, demonstrating the genotypic and phenotypic expansion seen in these patients. The recently reported SCA48 cases show cerebellar and extrapyramidal involvement, as well as cognitive dysfunction, which are also features seen in SCAR16.
Disclosure: The authors have no potential conflict of interest to disclose.

EPO-362

Genotype-phenotype correlation in Italian patients affected by Tuberous Sclerosis

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Background and aims: Tuberous Sclerosis complex (TSC; MIM #191100, MIM #613254) is a rare genetic multisystem disorder characterized by the presence of widespread hamartomatous lesions in multiple systems. TSC is caused by mutations in either TSC1 or TSC2 genes leading to dysfunction of hamartin or tuberin, respectively. In this study, we aimed to investigate the molecular spectrum of TSC genes and evaluate the genotype-phenotype correlation in an Italian study cohort.
Methods: Our series includes 41 familial/sporadic TSC patients, enrolled at Division of Neurology, Neurofibromatosis and Rare Diseases Center of AOU Luigi Vanvitelli and at Division of Pediatric Neurology of Santobono-Pausilipon Children's Hospital. All TSC patients were clinically evaluated according to NIH diagnostic criteria and a combination of targeted next-generation sequencing and multiplex ligation-dependent probe amplification (MLPA) was performed for molecular analysis.

Results: In our study the mutation detection rate was 93%, TSC2 or TSC1 variants were reported respectively in 25 and 13 TSC patients. We identified 25 different pathogenic or likely pathogenic variants and 18% of identified mutation were novel. TSC1 mutations were associated with a less severe phenotype than TSC2. No retinal manifestations were detected in TSC1 patients.
Conclusion: This study offered an important contribution to identify further novel genotype–phenotype correlation in TSC pathogenesis that may improve the management of TSC patients.
Disclosure: The authors declare that the research was conduct in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

EPO-363

Biallelic variants in ARHGAP19 cause mixed demyelinating and axonal polyneuropathy

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Background and aims: Rho GTPases are members of the large superfamily of small GTPase proteins considered as molecular switches in various cellular events. One of the major regulators of Rho GTPases are Rho GTPase-activating proteins (GAPs), which stimulate intrinsic GTPase activity and are important in actin organisation, cellular migration, cycle control and adhesion. We identified 16 individuals from 14 families with biallelic variants in Rho GTPase-activating protein 19 (ARHGAP19) presenting with young age of onset progressive weakness in lower limbs. Nerve conduction studies reveal mixed demyelinating and axonal polyneuropathy.
Methods: We are using in-vitro GAP assays to assess GAP activity in ARHGAP19 mutant proteins, complemented by an in-vivo Drosophila model to test for movement, lifespan and neuromuscular junction integrity.
Results: Ongoing in-vitro GAP assays show that ARHGAP19 has GAP activity towards RhoA but not Rac1 or Cdc42. Three of the mutations found in patients are being tested for their GAP activity and preliminary data suggest a loss of the GAP activity in a frame shift mutation. Visualisation of the endogenous expression pattern of ARHGAP19 ortholog in fly, RhoGAP54D, suggest the protein is expressed in perineural or subperineural glia in the fly brain. Preliminary results indicate that RNAi knockdown of RhoGAP54D in flies reduces both overall movement and startle responses to light-dark transitions.
Conclusion: This is a first association of ARHGAP19 with neurological disease and deep phenotyping analysis in conjunction with the in-vivo animal model and the in-vitro GAP assay will help highlight he importance of the gene in early human brain development and function.
Disclosure: Nothing to disclose.

EPO-364

Clinical and molecular study of familial Infantile Encephalopathy

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Background and aims: IInfantile Encephalopathy (IE) is a group of neuro-developmental disorders. The genetic and clinical heterogeneity of this condition constitutes a major diagnostic and consequently therapeutic challenge. In recent years, next generation sequencing (NGS) technologies enabled the discovery of numerous genes involved in IE. However, the interpretation of a large amount of NGS data is particularly laborious. The aim of this study was to describe the clinical features and the bioiformatics workflow implemented to investigate Tunisian children with familial IE.
Methods: We conducted a retrospective study of a group of 10 unrelated Tunisian families with familial IE over two years (from January 2019 to December 2020). The probands were investigated by whole exome sequencing (WES).
Results: Bioinformatics analysis of 480 prioritized genes were conducted in the 10 VCF files generated. Twenty different variants of interest were identified in 16 distinct genes. They included five likely pathogenic variants, ten variants of uncertain significance, four likely benign variants, and one benign variant. We extended our analysis to other genes associated with IE. We detected five additional variants in six different genes. The mutated genes were implicated in various molecular pathways involving ion channels and protein needed for regulatory and developmental functions. Our study expands the phenotypic and genetic landscape of IE in Tunisia and emphasizes the complexity of genotype-phenotype correlations.
Conclusion: The results of our current study could allow more accurate management of this pathology and may guide the development of a molecular diagnostic strategy for IE in Tunisia
Disclosure: The authors declare no conflict of interest.

EPO-365

An Italian family affected by SCA 45, a rare autosomal dominant cerebellar ataxia

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Background and aims: SCA 45 is a rare autosomal dominant cerebellar ataxia caused by mutations in FAT2. To date three families and two sporadic cases have been described.
Methods: A 41 year-old man presented to our clinic with a history of slowly progressive gait imbalance since the age of 26. His sister, mother, and grandfather had developed gait imbalance between age 30 and 55. He also reported to have intermittent diplopia. On examination the patient had an ataxic gait, dysarthria, impaired smooth pursuit, gaze evoked nystagmus, action and postural tremor of the hands with no bradykinesia or dystonia. SARA score was 12. Eye examination and EMG were normal. Brain MRI revealed cerebellar atrophy. After SCA 1, 2, 3, 6, 7, 8, 12, 17 were ruled out, he underwent an NGS panel and resulted heterozygous for the variant FAT2 c.12798_12799delCT (p.C4267fs*3) which was confirmed by Sanger sequencing and segregated within the family.
Results: FAT2 encodes for a transmembrane adhesion molecule expressed in the cerebellar granule cells and implicated in cerebellar development. So far, all cases reported presented with a slowly progressive late-onset ataxia. Our patient presented with an early onset cerebellar ataxia with postural tremor whereas the other members of the family affected had gait imbalance later in life. The novel variant found is predicted to cause a frameshift and to result in a truncated protein.
Conclusion: Our case suggests that SCA 45 should be considered as a possible cause of autosomal dominant cerebellar ataxia in younger patients as well.
Disclosure: Nothing to disclose.

EPO-366

Hanac syndrome as a cause of cerebrovascular disease in young patient: about a case

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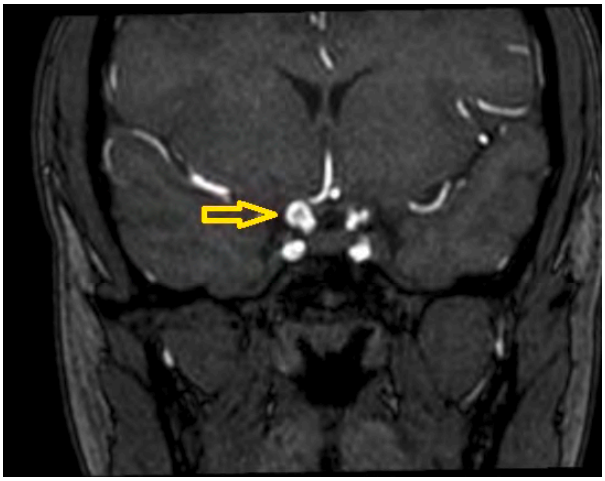
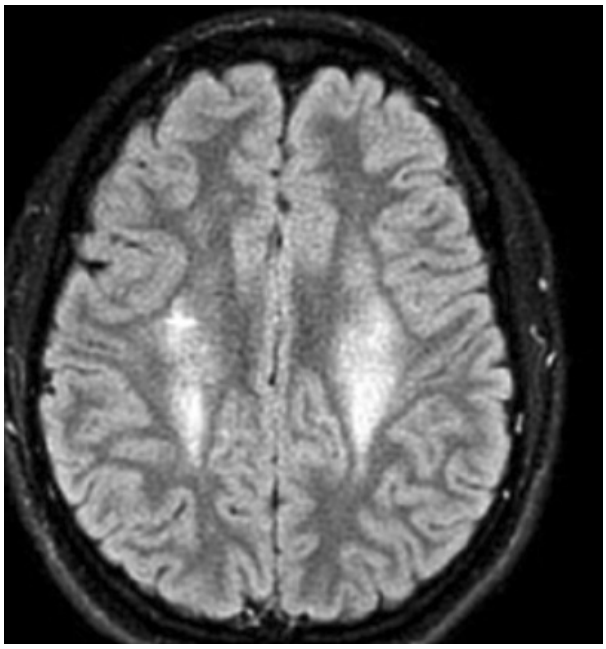
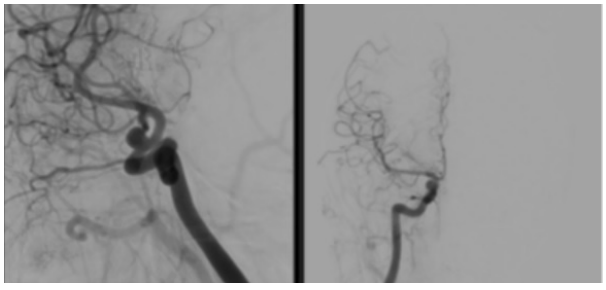
Background and aims: Heterozygous mutations in the COL4A1 gene, which encodes the alpha-1 subunit of type IV collagen, is an extremely rare cause of cerebrovascular disease in young patients. Among its phenotypic spectrum is the HANAC syndrome (hereditary angiopathy-nephropathy-aneurysms-muscle cramps syndrome), a multisystem condition that manifests as small and large vessel cerebrovascular disease, accompanied by ocular and nephrological abnormalities, and myalgias.
Methods: Description of a clinical case.
Results: We present the clinical case of a 23-year-old patient. She is admitted to Neurology due to refractory intense holocranial headache. A cerebral AngioMR was performed, showing a 5mm aneurysm in the ophthalmic region of the right ICA (Figure 1), and severe leukopathy (Figure 2). Diagnostic arteriography is performed (Figure 3). On examination, the presence of bilateral microcornea and a history of cataract intervention stand out. There is no family history. The genetic study showed the mutation c.2317G>A p.(Gly773Arg) in heterozygosity in the COL4A1 gene. The patient is diagnosed with HANAC syndrome.



Saccular aneurysm dependent on the ophthalmic region of the right ICA (yellow arrow). Coronal plane 3D TOF MR sequence.



Axial plane MRI FLAIR sequence. Severe leukopathy is seen in both corona radiata.



Diagnostic arteriography of right carotid aneurysm. Oblique (left) and AP (right) projection.

Conclusion: Genetic diseases individually represent a rare etiology of cerebrovascular disease. However, taken together, they represent a significant percentage of the causes of stroke in young patients. Among them we find the HANAC syndrome, which is produced by heterozygous mutations in the COL4A1 gene.
Disclosure: Nothing to disclose.

EPO-367

Exploring of shared genetic architecture between Alzheimer's disease and multiple sclerosis

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Background and aims: Neuroinflammation is involved in early and late disease phases of Alzheimer's disease (AD). Recent GWAS data revealed several immune-linked genetic variants and molecular pathways linked to proinflammatory interleukins and cytokines in AD pathology. Multiple Sclerosis (MS) is a chronic central nervous system immune-mediated disease with both genetic and environmental risk factors. Here we investigated shared genetic susceptibility between AD and MS, to identify pathological mechanisms between neurodegeneration and the immune system.
Methods: We analysed GWAS for late-onset AD (Wightman et al., 2021, n cases=64549, n controls=634442) and MS (n cases=14802, n controls=26703, IMSGC, 2019). We used statistical genetics methods as gaussian causal mixture modelling (MiXeR) for characterisation of genetic architecture and overlap between the two disorders. The conditional/conjunctional false discovery rate framework (cFDR) was used to identify specific shared genetic loci. Functional annotation was performed with FUMA and Open Targets.
Results: We showed comparable polygenicities for AD and MS and genetic overlap with 20 % of shared trait-influencing variants despite negligible genetic correlation (rg=0.03). Around 1.8 thousand were identified by MiXeR as associated variants. cFDR analysis identified 16 shared genetic loci. Annotated genes were enriched in molecular signalling pathways linked to inflammation and neuron structure.
Conclusion: The current results provide evidence for a polygenic overlap between AD and MS, beyond genetic correlation. The shared loci between AD and MS suggest the important role of the immune system and neurodegeneration in the pathophysiology of disorders, and highlight new opportunities for future studies.
Disclosure: No special disclosures. This work was supported by an RCN grant 324252.

EPO-368

RNA studies in neurogenetical disorders: a new diagnostic tool beyond Next Generation Sequencing.

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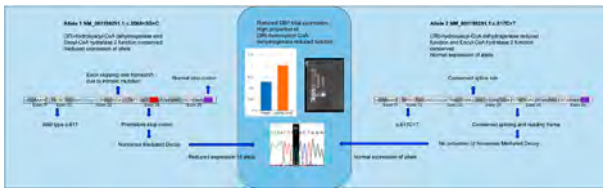
Background and aims: Next Generation Sequencing (NGS) has expanded the diagnostic field of neurogenetical disorders. However, inconclusive results require further studies to confirm pathogenicity of the variants found.

Here, we show two examples where blood-derived RNA was employed to confirm diagnosis.
Methods: Written informed consent was obtain for genetical studies. The effect on splicing was studied through SpliceAI software. Blood RNA was purified and complementary DNA (cDNA) was obtained through reverse transcription. Final time PCR was run and Biodonostia Genomics Platform performed Sanger sequentiation of PCR products. Quantitative PCR (qPCR) were performed in order to measure expression levels.
Results: Patient 1 is a 41 years-old male with sensorineural deafness, intellectual disability, sensorimotor neuropathy and cerebellar ataxia. Whole exome sequencing showed two variants in HSD17B4 gene related to Perrault syndrome: c.817C>T, (pathogenic) and c.2068+5G>C (considered of unknown significance). As the mutation was in the exon-intron boundary, impaired splicing was hypothesized. SpliceAI predicted exon skipping; consequently, a premature stop codon would arise and Non-Sense Mediated Decay would degrade RNA. qPCR and Sanger sequencing confirmed reduced RNA expression of the splice-site mutation allele (Fig.1). Patient2 is a 66 years-old male with frontotemporal dementia. NGS panel showed a mutation in TBK1 (c.229-3_231delinsTCAG) predicted to impaired splicing. Careful revision showed the mutation probably produces a codon loss and, consequently, the absence of Thr79, previously considered pathogenic. Sanger sequencing of blood cDNA confirmed this hypothesis (Fig.2)



Schematic view of the mutations in HSD17B4 found in patient 1. Experiments showed reduced expression of the allele carrying the splicing-site mutation.

Schematic view of the mutation found in TBK1. Although predicted to affect splicing, careful revision show the effect of ACA deletion, resulting in absence of Thr79 which has been previously described as pathogenic.

Conclusion: RNA studies are cost-effective, relatively easy and very useful in selected patients and they should be included in hospital's genetic departments.
Disclosure: No conflicts of interest.

EPO-369

The Role of Bdnf Pathway in Energy Homeostasis deficit in Smith-Magenis syndrome mice

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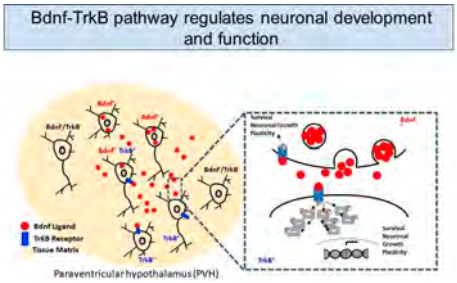
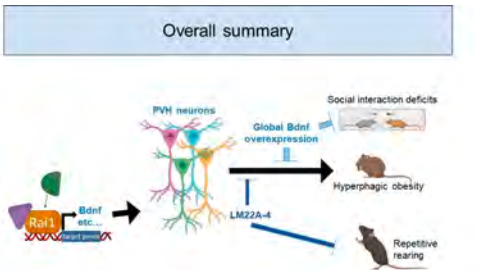
Background and aims: Severe hyperphagia, metabolic defect, and obesity are debilitating features of Smith-Magenis syndrome (SMS), a monogenetic disorder caused by haploinsufficiency of retinoic acid induced 1 (RAI1). Rai1 regulates the transcription of neurodevelopmental genes including brain-derived neurotropic factor (Bdnf). Bdnf is downregulated in the hypothalamus of SMS mice. We further analyzed the contribution of Bdnf signalling in SMS pathology and therapeutically targeting Bdnf pathway.



Schematic for the Bdnf-TrkB Pathways

Methods: We first performed reverse phase protein analyses (RPPA) using a cocktail of antibodies that probe downstream of Bdnf-TrkB pathway. Next, we generated Rai1 conditional knock out (cKO) model (Rai1-deletion in Bdnf producing neurons) to decipher the function of Rai1 in a discrete set of Bdnf-producing cells, which regulates energy homeostasis in the hypothalamus. We explored the therapeutic potential of targeting Bdnf downstream signalling by using a pharmacological agent, LM22A-4 (a TrkB partial agonist).
Results: We found multiple Bdnf downstream targets to be downregulated in SMS mice. Loss of Rai1 from Bdnf-producing cells contributes to obesity in SMS by selectively altering fat deposition. 3-weeks old cKO mice also showed reduced neuronal excitability in the PVH. Our drug treatment data demonstrate that LM22A-4 treatment significantly reduces the body weight in SMS mice and delays the onset of obesity. Moreover, this reduction in body weight is followed by improved blood leptin and lipoprotein levels in the treatment group.
Conclusion: Our work shows the pathological contribution of Bdnf pathways in SMS and demonstrate that targeting Bdnf signaling has a potential to ameliorate obesity associated with SMS.



Summary of results

Disclosure: We declare no confilict of interest.

EPO-370

Neuropsychiatric symptoms in Friedreich's ataxia assessed by the Mild Behavioral Impairment Checklist (MBI-C)

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Background and aims: Neuropsychiatric symptoms (NPS) are common in hereditary ataxias. In Friedreich's ataxia (FRDA), depressive symptoms were previously reported, but little is known about other NPS. The MBI-C is a questionnaire assessing NPS in early stages of neurodegenerative diseases. Using the MBI-C, we aimed to assess the presence and severity of NPS in FRDA and examine their relationship with disease severity.
Methods: 27 FRDA patients and 37 healthy controls (HC) were recruited at the Centre of Hereditary Ataxias. Close informants of all participants filled in the MBI-C. Disease severity was assessed by the Scale for the Assessment and Rating of Ataxia (SARA), and the scale of the Activities of Daily Living (ADL).
Results: Mean MBI scores in FRDA and HC were 6.70 (SD=8.70) and 2.59 (SD=3.20) respectively. 25.9% of FRDA patients had at least one MBI symptom compared to 18.9% HC. Prevalence of specific NPS in FRDA was 25.9% (vs. 18.9% HC) for decreased motivation, 55.6% (vs. 32.4%) for emotional dysregulation, 48.1% (vs. 37.8%) for impulse dyscontrol, 18.5% (vs. 8.1%) for social inappropriateness and 11.1% (vs. 13.5%) for psychotic symptoms. Patients had significantly higher score only in the emotional dysregulation domain (p=0.026). ADL correlated with motivation (r=0.39, p=0.044) and emotional dysregulation (r=0.39, p=0.048). SARA did not correlate with any MBI-C score.
Conclusion: NPS are common in FRDA, particularly in the affective domain, are linked to impairment of ADL but not ataxia severity. NPS should be addressed in clinical care due to their potential impact on quality of life and the possibility for therapeutic intervention.

Disclosure: Supported by Charles University Grant Agency (GAUK) projects No. 224522 and 309121 and project National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107). The authors are members of the European Reference Network for Rare Neurological Diseases (ERN-RND).

EPO-371

Broadening the clinical spectrum of brain-lung-thyroid syndrome. The first patient treated with bipulmonary transplant

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Background and aims: Benign hereditary chorea is part of the "brain-lung-thyroid syndrome", which is caused by mutations in the NKX2.1 gene (also known as TTF1). This gene plays an important role in the embryological development of the brain (ventral telencephalon and hypophysis), lungs and thyroid gland. Pathogenic variants in NKX2.1 have been associated with chorea, hypothyroidism, and lung or thyroid carcinomas.
Methods: We describe the case of the first patient treated with bipulmonary transplantation for lung interstitial fibrosis in the context of a "brain-lung-thyroid syndrome" associated with NKX2.1 and review the clinical spectrum of the disease reported in the literature.
Results: We report the case of a 42-year-old woman who presented delayed motor development and previously undiagnosed choreoathetosic movements since early childhood. Subclinic hypothyroidism was found when she was 30. At 38 years of age, she developed an interstitial lung disease which progressively worsened until requiring lung transplantation. In the lung explant, mucinous adenocarcinoma was discovered in both lungs, with differences in the genetic biomarkers; no lymph nodes were affected. Given the atypical presentation and the combination of clinical signs, the diagnosis was reconsidered. Exome sequencing identified a pathogenic variant in NKX2.1 gene (frameshift mutation). Four more cases of lung cancer in relation to NKX2.1 mutations have been reported, none of them were considered elective to surgery.

Figure 1.- Timeline of the disease development and clinical manifestations. ILD= Interstitial lung disease

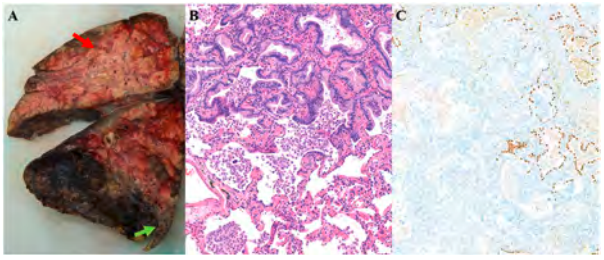

Figure 2.- A. Macroscopic sample of the lung explant. Whitish areas correspond to the lung adenocarcinoma (red arrow) and fibrous tissue in the lung base (green arrow). B,C. Microscopic view of the mucinous adenocarcinoma (upper half). and TTF1 staining.

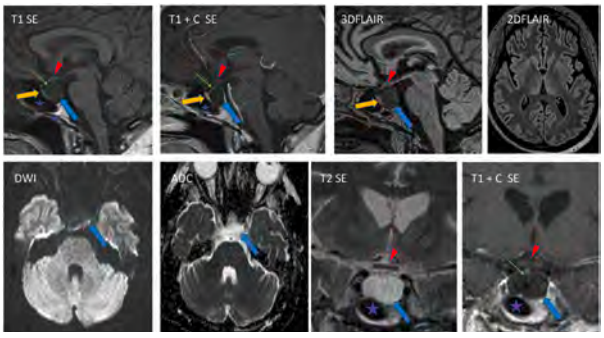

Figure 3.- Intrasellar cystic structure (blue arrow) that causes anterior displacement of the adenohypophysis (orange arrow) and bilateral hyperintensity of the thalamus in FLAIR. Pituitary stalk (green arrow). Optic chiasm (Red arrow).

Conclusion: The brain-lung-thyroid syndrome has a broad clinical spectrum. This case-report expands the clinical spectrum and presentations leading to suspect this rare disease. To our knowledge, this is the first patient treated with lung transplantation.
Disclosure: No conflicts of interest to disclose.

EPO-372

Hereditary ataxias: diagnostic yield with Next-Generation Sequencing

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Background and aims: Hereditary ataxias (HAs) are a group of progressive monogenic rare neurodegenerative disorders characterized by a wide spectrum of ataxia-dominated phenotypes. Despite the identification of many causative genes, up to 50% of HAs cases still remain without molecular diagnosis, mainly due to their vast clinical and genetic heterogeneity. Massive parallel next-generation sequencing (NGS) analysis broadened our knowledge of HAs genetic aetiology, consequently stimulating the trend towards genetically specific therapies. In this study we aimed to assess the diagnostic yield of NGS panel and exome analysis in the clinical practice of our setting.
Methods: A cohort of 100 patients with a clinical diagnosis of HA but no molecular confirmation was studied. NGS panel (26 genes) and/or clinical exome sequencing (CES) were performed in the case of inconclusive first-line genetic tests for spinocerebellar ataxias (SCA1-3, 6-8,12,17), DRPLA, Friedreich's ataxia (FRDA) or phenotype-guided specific single gene sequencing.
Results: By means traditional genetic tests a molecular diagnosis was achieved in 35% of patients. Of 65 patients with HAs of indeterminate genetic origin, 36 underwent new molecular evaluations: in 12 of 36 (33,3%) known pathogenic mutations or putative pathogenic variants were found, using NGS panel and CES. Furthermore, in 30,6% of patients (11/36) one or more variants of unknown significance were detected.
Conclusion: Overall, we present daily practice evidence that for one third of the patients with a clinical diagnosis of HA, but no molecular diagnosis on routine genetic testing, a definitive diagnosis can be reached with NGS approach.
Disclosure: The authors have no conflicts of interest to declare.

Cerebrovascular diseases 3

EPO-373

Analysis of clinical characteristics and functional outcome in patients with cervical artery dissection.

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Background and aims: Cervical artery dissections (CAD) are responsible for 20-25% of ischaemic strokes in young patients. Non-traumatic dissections are the most frequent and, although their cause is unknown, it is believed to be due to a weakness of the arterial wall.
Methods: We conducted a retrospective review of patients with CAD admitted in our hospital between 1-1-2011 and 31-12-2022. We recorded baseline clinical features, treatment, functional outcome, and mortality rate.
Results: We identified 32 cases of CAD (20 carotid/ 12 vertebral); mean age was 48.3 years and 67.7% were men. Four patients (13%) had a history of physical effort. The average baseline NIH Scale score was 3.87 (range, 0-19). Code stroke was activated in 15 patients. Six patients (18.75%) were treated with intravenous thrombolysis and 10 (31.25%) with acute endovascular treatment, 7 of them with stent placement. Five of these patients received both treatments; at 3 months, functional independence (modified Rankin Scale scores 0-2) was achieved by 90% of the patients. One patient died. The average mRS scores for each subgroup were the following: thrombolysis + endovascular treatment 2.2 points, only thrombolysis 1 point, and only endovascular treatment 2.4 points.
Conclusion: Cervical artery dissection is an uncommon cause of ischaemic stroke, which tends to occur in younger patients compared to other aetiologies. Reperfusion therapies appear to be safe in these patients, but more studies are needed to confirm this.
Disclosure: The authors declare no conflict of interest.

EPO-374

Carotid web as a possible cause of ipsilateral ischemic stroke of undetermined origin: experience in a tertiary hospital

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Background and aims: Carotid web (CW) has been observed in cases of embolic strokes of undetermined origin (ESUS). We hypothesize it might be the responsible of the formation of emboli, given no other plausible cause is found. Our objective was to determine the optimal management of these patients by analyzing baseline patient characteristics, acute-phase treatment, functional status at 90 days, secondary prevention, and stroke recurrences.
Methods: Retrospective single-center observational study of a prospectively recorded database from 2017 to 2022 of patients with acute ischemic stroke (AIS) and ipsilateral CW in a tertiary hospital. Patients with a diagnosis of AIS and confirmation of CW in digital subtraction angiography were included. Data regarding baseline characteristics, diagnostic study, presence of recurrence and secondary prevention were recorded.
Results: 12 patients were included, with a median age of 50 years. 1 had a previous stroke. 10 (83%) underwent mechanical thrombectomy (MT), 4 of them with combined intravenous thrombolysis. The diagnostic study revealed 1 patient with atrial fibrillation (AF), 2 with a patent foramen ovale (PFO), 1 with an antiphospholipid syndrome, and 8 with a negative study. Carotid stenting was placed in 7 patients, 1 received acenocumarol (coexistence of PFO and pulmonary thromboembolism) and 1 rivaroxaban (AF) and single antiplatelet therapy. No recurrences were observed.
Conclusion: In our series, CW was the only finding in 58% of patients, being the probable cause of stroke. Although there is no consensus on secondary prevention management, carotid stenting could be a safe and effective alternative.
Disclosure: The authors declare they have no conflict of interest.

EPO-375

Strokes mimics and chameleons on the prehospital level in Emergency Center of Bishkek, Kyrgyzstan

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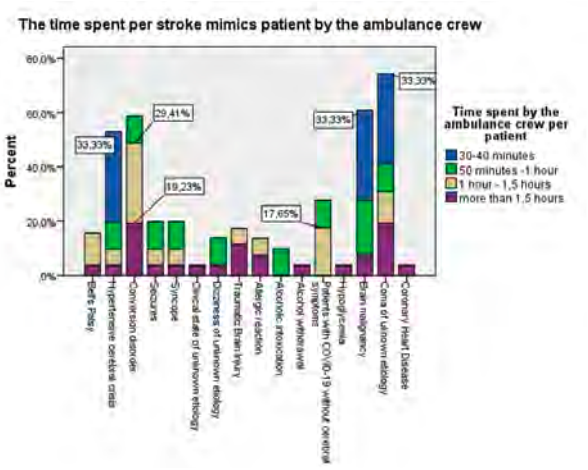
Background and aims: In Kyrgyzstan which is on the way of the thrombolytic therapy implementation and where there is the lack of trained emergency service personnel for stroke recognition and management, early and accurate diagnosis of stroke and differentiating it from stroke mimics is an important task for healthcare. We aimed to identify and describe stroke mimics patients among all the patients with the stroke code.
Methods: We analyzed 535 medical records of patients with a stroke code at the Emergency Medical Center of Bishkek, Kyrgyzstan. We described demographics, clinical and logistical parameters of stroke mimics patients. Comparisons of continuous variables between stroke and stroke mimics patients were made with Independent Samples Test and ANOVA.

Results: There were 10,1% patients with stroke mimics and they were significantly younger: median age was 57 (56;75) while for stroke patients median age was 65 (45;69), p=0,003. Stroke mimics were represented by conversion disorder (19,3%), coma of unknown etiology (15,79%), brain malignancy (8,7%) and others. Stroke mimics patients with seizures and syncopes tend to call to emergency services earlier (median time 0,9 and 1,4 hours) compared to patients with alcohol withdrawal and cardiological diseases (167 hours). Ambulance crew spent around 1-1,5 hours in 30% examining the patients with stroke mimics and in 18% in patients with COVID-19.
Conclusion: New implemented order for the obligatory NIHSS evaluation of the all patients with stroke code will improve diagnostics and may shorten time of the crew spent with stroke mimics patients.
Disclosure: Nothing to disclose.



EPO-376

Tendencies of public stroke knowledge in Vilnius

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Background and aims: Stroke remains the common cause of death and disability in the world. A visible decline in disabling outcomes can be attributed to the increasing frequency of reperfusion therapies. Stroke recognition and urgent admission of patients to specialized stroke centres after the onset of first stroke symptoms are essential for treatment outcomes. This study aims to evaluate public stroke awareness and its change since 2019.
Methods: An anonymous cross-sectional study, involving 802 Vilnius residents was conducted in 2019 and 2022. The closed-ended questionnaire was used. Statistical analysis was performed with SPSS software, with a significance level of $p<0.05$.
Results: Stroke as an acute cerebrovascular disorder was identified by 83.3% of the respondents in 2022 (less than a 1% increase since 2019). At least one correct warning sign of stroke was reported by 98.7% of respondents (96.4% in 2019). The most mentioned symptoms of stroke were one-sided face, arm or leg sensory disturbances, paralysis or weakness (90.0%) and speech disorder (83,3%) – 82.1% and 81.5% respectively in 2019. Only 58% (45.4% in 2019) of respondents reported visual impairment as a stroke symptom. Females have better knowledge of stroke than males ($p<0.05$).
Conclusion: Stroke awareness is improving since 2019 in Vilnius. Women have better knowledge of stroke compared to men. Visual impairment is the least known stroke symptom. Therefore, BE-FAST campaigns should be directed to the target audience through the most used informational means to provide reliable information and be more gender sensitive.
Disclosure: Nothing to disclose.

EPO-377

Opalsky syndrome secondary to medulla oblongata hemorrhage: case report and review of the literature

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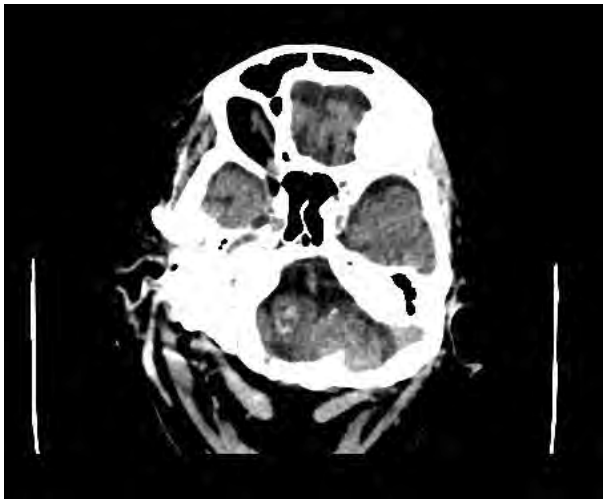
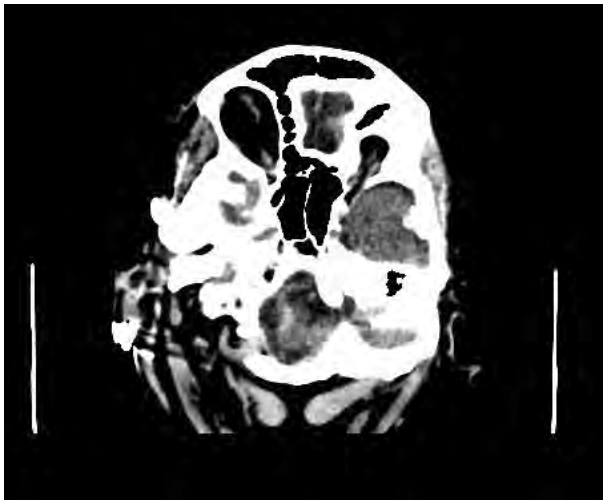
Background and aims: Opalsky syndrome (or sub-bulbar syndrome) was first described by A. Opalsky in 1946, as the presence of a lateral medullary syndrome (Wallemberg syndrome) and ipsilateral hemiplegia. It can be explained by the involvement of the ipsilateral corticospinal tract after the piramidal decussation, and it is considered as a variant of Wallemberg Syndrome.
Methods: We describe a case of Opalsky Syndrome secondary to medulla oblongata hemorrhage. We performed a literature review in PubMed of previous publications on Opalsky Syndrome and the different etiologies reported.
Results: A 80-year-old woman with moderate cognitive decline under heparin treatment due to deep vein trombosis 1 month before, presented with a 3-days history of right leg weakness followed by dysphagia, dysarthria and headache. Neurological examination revealed moderate dysarthria, downbeat nystagmus, right-sided Horner Syndrome (with partial ptosis and miosis), right facial palsy, right limbs 4/5 hemiparesis and left limbs hypoesthesia. Urgent CT showed bleeding in the right margin of medulla oblongata. Urgent blood analysis and EKG were normal. 48h hours later the patient died due to respiratory insuficiency. Literature describe over 62 Opalsky Syndrome with different etiologies: ischemic (53) due to atherotrombosis or vertebral artery dissection (6), vertebral artery giant-cell arteritis (1), cavernome bleeding (1), brainstem tumors (2), multiple sclerosis lessions (2), infective demyelinating event due to scrub typhus (1) or lateral compression by megadolicobasilar artery (1).



Axial CT: Bleeding in the right margin of medulla oblongata



Axial CT: Medulla oblongata hemorraghe

Conclusion: Infarcts are the most common etiology of Opalsky Syndrome. To our knowledge this is the second Opalsky Syndrome secondary to hemorraghe described in the literature.
Disclosure: The authors declare no conflicts of interest.

EPO-378

Telemedical acute stroke management improves performance and patient outcome: evaluation of the NEVAS stroke network

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Background and aims: Timely acute stroke management improves functional outcome considerably. In countryside hospitals without stroke specialization, telemedical consultation by comprehensive stroke centers is an effective concept to provide timely treatment decision making and improve clinical performance.
Methods: In this study, clinical data of stroke patients were collected for the years 2014-2020 from three regional hospitals of the Neurovascular Network of Southwest Bavaria with telemedical stroke support by our centre. Door-to-imaging and door-to-needle times as well as the modified ranking scale (mRS) at discharge were analyzed over the years to examine if performance and clinical outcome improve over time through participation in the network.
Results: The number of admitted stroke patients nearly doubled between 2014 and 2020 with a mean thrombolysis rate of 15%. The percentage of door-to-imaging time <30 and <60 min for all stroke patients declined over time, presumably due to the increasing patient number. However, for thrombolysis candidates, the percentage of door-to-imaging and door-to-needle times <30 and <60 min increased over time. Door-to-needle time was slightly lower comparing thrombolysis indication by the local neurologist vs. telemedicine while improving over time for both scenarios. The percentage of thrombolysed patients with mRS 0-2 at discharge increased significantly (79% in 2020 vs. 59% in 2014). There was no substantial difference in critical time intervals or mRS at discharge during the pandemic year 2020 compared to previous years.
Conclusion: Telemedicine networks can significantly improve stroke care in rural hospitals with limited experience through timely thrombolysis indication by telemedical neurovascular expertise and continuous on-site training of professionals.
Disclosure: No disclosure.

EPO-379

Basilar Artery Occlusion strokes in patients admitted to the Neurological Clinic of Pisa: a retrospective analysis

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Background and aims: Basilar artery occlusion (BAO) is a subtype of stroke burdened by high mortality and disability. The aim is to analyze a cohort of patients with BAO, admitted to the Neurological Clinic of Pisa between January 2001 and December 2021, in order to individuate anamnestic, clinical or neuroradiological features, as well medical treatment, related to the outcome at 90 days, defined by the modified Rankin Scale (mRS).
Methods: The endpoint was mortality or significant disability at 90 days. We performed a binary logistic regression with the significant variables ($p<0.05$) at the univariate analysis.

Results: We have analysed 74 patients (37 males) with BAO admitted to our Unit in the selected timeframe. The median age was 72 years. 50 patients (67.6%) had hypertension, 56 (75.7%) atherosclerosis, 6 (8.1%) previous strokes/TIA, 17 (23%) diabetes, 10 (13.5%) tabagism, 14 (18.9%) atrial fibrillation, 32 (43.2%) structural cardiopathies. During hospitalization, 24 (32.4%) developed dysphagia, 20.3% infections, 8.1% ICH, 29% required intubation, and 8.1% tracheostomy. NIHSS at discharge was 0-10 in 65 (87.8), >10 in 9 (12.2). 18 patients received medical therapy, 11 systemic fibrinolysis, and 45 endovascular treatment. The 90 days mortality occurred in 5 (6.7%), while functional dependance (mRS 3-5) in 22 (29.7%). Dysphagia ($p = 0.01$), atrial fibrillation ($p = 0.03$), atherosclerosis ($p=0.04$) and NIHSS score at discharge ($p < 0.01$), were related to the endpoint.
Conclusion: The importance of primary prevenction (especially AF and atherosclerosis) and the management of complications during hospitalization, are crucial to avoid mortality and disability.
Disclosure: Nothing to disclose.

EPO-380

Total antioxidant status(TAS) in the serum of patients with acute ischemic stroke(AIS) -Is constant attention warranted?

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Background and aims: The impact of oxidative stress on neuronal injury in ischemic stroke has been a focus of stroke research. The aim of this study was to estimate TAS in the serum of patients with AIS within 2-5 days after symptom onset in northeastern Poland.
Methods: 175 patients with AIS, including 85 who received thrombolysis/thrombectomy, and 88 healthy controls were studied. TAS in the serum was measured spectrophotometrically using Randox kits and clinical details were collected from medical records.
Results: 57.2% of patients with AIS had TAS values outside the reference range (1.3-1.77mmol/L). TAS correlated with BMI index, hemoglobin values,and Cd/Pb molar ratios. TAS levels were higher in LVD than in CE/SVD ($p=0.043$) according to the TOAST classification. No significant differences in TAS concentrations were found between AIS patients and healthy controls ($p=0.41$). In patients with AIS, no statistically significant variations were observed with atrial fibrillation, smoking status, T2DM, or administered treatment (intervention vs.conservative). A linear model indicated that conservative treatment had a significantly higher TAS (0.79). A generalized linear regression model showed that higher BMI index, male gender, and LVD etiology were significant predictors of elevated TAS. No association of TAS was found with demographics, NIHSS(lowest values:21-42)/MRS scales,stage of atherosclerosis, brain lesion size,CRP,homocysteine,uric acid,fibrinogen,or lipid profile.
Conclusion: Patients in the initial phase of ischemic stroke show no change in blood TAS concentrations compared to controls, suggesting that at onset, they have an effective antioxidant defense which is depleted over time. The investigation has revealed the potential of using antioxidants for stroke-related oxidative stress.
Disclosure: Nothing to disclose.

EPO-381

Acute Cerebrovascular Accident during the pandemic of a new coronavirus infection in the Ural Federal District

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Background and aims: Acute cerebrovascular accidents (ACVA) are the main causes of death and disability in the population. The study of identifying signs of morbidity with acute cerebral circulation in the context of a pandemic of a new coronavirus infection COVID-19 is an urgent task. Purpose - to conduct a comparative analysis of the primary incidence of ACVA, including transient ischemic attacks (TIA), in the adult population of Russia, the Urals Federal District (UFD) and the constituent entities of the Russia during the pandemic of a new coronavirus infection.
Methods: The primary incidence of transient cerebral ischemic attacks, intracerebral and other intracranial hemorrhages, cerebral infarctions and strokes, not specified as hemorrhage or infarction, was studied. A comparative analysis of the primary incidence of ACVA in the adult population in the UFD and in individual subjects of the district during the 2020 pandemic was carried out relative to the average long-term indicators for 2015-2019.
Results: During the COVID-19 pandemic, the levels of primary incidence of certain ACVA in the whole Russia and the UFD decreased in relation to the average long-term indicators of 2015-2019 in all classes (table).
Conclusion: In real clinical practice, in a pandemic, healthcare resources are more directed towards combating COVID-19, which may affect the statistical indicators of the incidence of stroke. The data obtained require further confirmation by continuous dynamic monitoring of the epidemiology of stroke.

Table. The incidence of selectivity of cerebrovascular accidents in the Russian Federation, Ural Federal District, and also in consideration of the Ural Federal District (per 100,000 adults)

	Average annual level	2020 year	2020 growth to standard deviation (percentage)
All acute cerebrovascular accidents			
Russian Federation	399,9±7,4; Kv3,9	371,1	-7,2
Ural federal district	421,2±15,0; Kv3,6	378,1	+10,2
Kurgan district	483,9±46,8; Kv9,7	414,2	-14,4
Sverdlovsk district	541,6±35,1; Kv6,5	480,3	-11,2
Tyumen region without autonomous okrug	366,3±24,9; Kv6,2	391,9	+1,9
Khanty-Mansi Autonomous Okrug – Yugra	239,9±8,9; Kv3,6	220,6	-9,0
Yamalo-Nenets Autonomous Okrug	198,2±13,4; Kv27,0	201,4	1,6
Chelyabinsk district	379,1±12,8; Kv3,4	335,2	-11,6
Stroke, unspecified as hemorrhage or infarction			
Russian Federation	29,4±6,1; Kv20,7	20,2	-31,3
Ural federal district	10,8±1,7; Kv15,7	10,5	-2,8
Kurgan district	22,3±17,6; Kv78,7	5,1	-77,1
Sverdlovsk district	13,7±1,7;Kv12,2	15,5	13,1
Tyumen region without autonomous okrug	2,1± 3,4, Kv159,8	0,9	-57,1
Khanty-Mansi Autonomous Okrug – Yugra	6,9±2,1, Kv30,9	8,3	20,3
Yamalo-Nenets Autonomous Okrug	11,9±4,4, Kv31,5	6,5	-45,4
Chelyabinsk district	9,7±1,9, Kv19,5	11,4	17,5
Transient cerebral ischemic attacks [attacks] and related syndromes			
Russian Federation	49,3±1,5, Kv3,1	36,3	-26,4
Ural federal district	55,1±2,2, Kv4,5	39,3	-28,7
Kurgan district	65,2±7,3, Kv11,2	53,6	-17,8
Sverdlovsk district	69,3±8,6, Kv12,4	50,8	-26,7
Tyumen region without autonomous okrug	48,5±5,4, Kv11,2	26,7	+44,9
Khanty-Mansi Autonomous Okrug – Yugra	39,5±3,4, Kv8,7	32,4	-18,0
Yamalo-Nenets Autonomous Okrug	31,5±12,7, Kv40,2	30,7	-2,5
Chelyabinsk district	47,9±4,8, Kv10,0	31,6	34,0
Intracerebral and other intracranial hemorrhage			
Russian Federation	42,8±1,0, Kv2,3	39,0	-8,9
Ural federal district	44,8±1,8, Kv4,0	41,0	-8,5
Kurgan district	58,0±5,0, Kv8,6	61,8	5,7
Sverdlovsk district	52,3±3,4, Kv6,5	47,7	-8,8
Tyumen region without autonomous okrug	52,8±2,4, Kv4,5	52,4	-0,8
Khanty-Mansi Autonomous Okrug – Yugra	51,1±7,2, Kv23,0	23,8	+24,5
Yamalo-Nenets Autonomous Okrug	30,4±8,8, Kv29,1	32,2	6,3
Chelyabinsk district	37,1±1,9, Kv5,1	32,2	-13,2
Cerebral infarction			
Russian Federation	278,4±14,4, Kv5,2	275,6	-1,0
Ural federal district	310,5±14,6, Kv4,7	287,3	-7,5
Kurgan district	338,1±16,2, Kv10,7	294,2	+13,1
Sverdlovsk district	405,7±29,2, Kv7,2	366,3	-9,7
Tyumen region without autonomous okrug	295,9±29,7, Kv10,0	311,9	5,4
Khanty-Mansi Autonomous Okrug – Yugra	162,4±6,2, Kv3,8	156,1	-3,9
Yamalo-Nenets Autonomous Okrug	124,5±35,9, Kv28,8	132,0	6,0
Chelyabinsk district	284,4±13,2, Kv5,3	260,0	-8,6

Disclosure: Nothing to disclose.

EPO-382

Moyamoya angiopathy in a Norwegian patient cohort: Characteristics and outcome

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Background and aims: Moyamoya angiopathy (MMA) is a rare intracerebral steno-occlusive, progressive vasculopathy. Increasing awareness of MMA in European populations has impacted on the incidence recently. This is the first description of a Norwegian MMA cohort.
Methods: A retrospective analysis of consecutive patients with MMA, treated with revascularization surgery or followed conservatively at Oslo University Hospital, between January 2010 to October 2021, was performed.
Results: We identified 63 MMA patients, 56 (89%) had moyamoya disease (MMD) and 7 (11%) moyamoya syndrome. 47 (75%) were females. Mean age for symptom onset was 36 (SD 15.6) years. The majority, 41 (65%), were of Caucasian ethnicity, followed by Asian 15 (24%), African 6 (9.5%) and Hispanic 1 (1.5%). Verified familial MMD occurred in 1 (1.5%) of patients. An acute clinical presentation occurred in 24 (38%) of patients, on imaging ischemic lesions were noted in 22 (35%) and hemorrhagic in 9 (14%). Cerebral vasculitis was initially misdiagnosed in 6 (9.5%) of patients. Revascularization treatment was performed in 30 (48%) patients. Mean years of follow-up was 8 (SD 6.9). At baseline, 29 (46%) were employed, vs. 18 (29%) at last follow-up (p <0.001). Initially, 55 (87%) had modified Ranking Scale ≤2 vs. 47 (75%) at last follow-up (p<0.001). Mortality for the cohort was 5 (7.9%) during a total of 498 years of follow-up.
Conclusion: MMA patients in our cohort had a decline in work capacity and functional independency over time. Our results underscore the importance of long-term follow-up and support of MMA patients.
Disclosure: Nothing to disclose.

EPO-383

Delayed neurological improvement in acute ischemic stroke patients treated with intravenous rtPA

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Background and aims: The aim was to investigate the phenomenon of neurological improvement delayed beyond the first 24 hours from admission in acute ischaemic stroke patients with special emphasis on intravenous thrombolysis.
Methods: This retrospective registry-based analysis included patients admitted with first-ever non-minor (NIHSS at least 4) ischaemic stroke within 24 hours from onset to a single tertiary stroke centre from January 2009 to December 2015. Patients treated with mechanical thrombectomy were excluded. Significant neurological improvement was defined as an 8-point reduction in the NIHSS score or reaching a score of 0 or 1. We compared neurological improvement at 24 h and day 7 in patients treated and not-treated with intravenous rtPA.
Results: Of N=463 included patients, n=316 (68%) received rtPA and n=147 (32%) not. There were no differences in median age, gender and baseline NIHSS (10 vs 9). Patients from the rtPA group had lower NIHSS at 24 h (5 vs 8, p=0.005) and day 7 (3 vs 5, p=0.024). Significant neurological improvement from baseline to 24 h was more frequent in the rtPA group (28% vs 10% p<0.001). However, the proportion of patients with significant improvement at day 7 not achieving improvement within the first 24 hours, was similar (22% vs 19%, p=0.493).
Conclusion: Delayed significant neurological improvement that takes effect beyond the first 24 hours from admission occurs in about 20% of acute ischaemic stroke patients with non-minor symptoms. Intravenous rtPA seems not to have an effect on this phenomenon.
Disclosure: We have no financial interests relevant to the submitted publication.

EPO-384

Causal evidence of anterior cingulate cortex function: an experimental study in patients with stroke in the frontal lobe

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Background and aims: The anterior cingulate cortex (ACC) is responsible for task regulation. ACC dysfunction has been linked to a wide spectrum of neuropsychiatric disorders, such as apathy, depression and Parkinson's disease. The Reward Positivity (RewP), an event-related brain potential (ERP), reflects the impact of midbrain dopamine signals on ACC and is a potential biomarker for depression. The RewP is thought to be generated in the ACC. The aim of this study is to (1) investigate the impact of ACC damage on task regulation and (2) localize the source of the RewP.
Methods: Patients with frontal lobe stroke are recruited at Ghent University Hospital, Belgium (recruitment started April 2021). Participants perform the coffee-tea task (CTT), a hierarchical sequence task, and the virtual T-maze task (vTMT) while scalp EEG is recorded. We compare data outcomes between ACC lesions and lesions in other parts of the frontal lobe using voxel-based lesion symptom mapping (VLSM). Beck Depression Inventory (BDI) is used to assess the prevalence of depression in this population.
Results: We have currently recruited 50 patients: mean age 61,4 (±13,3), 23 female. 24 participants (48,9%) successfully completed the CTT. Six patients (12%) had a BDI score greater than 20 and suffered from clinical depression. Average RewP was smaller for the group with rostral ACC lesions. VLSM-maps will be presented at the conference.
Conclusion: Preliminary analysis did not show a contribution of ACC lesions to worse performance of the CTT or higher BDI score. Preliminary ERP-analysis suggested rostral ACC as potential source of the RewP.
Disclosure: Nothing to disclose.

EPO-385

The prediction model for all cause of mortality after stroke

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Background and aims: Stroke is the second leading cause of mortality. Although it is important to stratify high-risk patients after acute ischemic stroke, few studies reported the risk stratification system for ischemic stroke. We aimed to develop a prediction model specific for ischemic stroke using machine learning (ML).
Methods: 3,413 patients were admitted within 7 days after ischemic stroke from 2014 to 2019. We developed a total of seven ML based prediction model composed of patient's demographics, laboratory results, clinical and imaging characteristics of stroke. We also developed a compact model by utilizing the top 10 key factors of the best-performing model.
Results: All cause of mortality was developed in 136 (3.98%) patients in the entire cohort. The CatBoost based prediction model showed the best discriminatory power for high-risk patients, and outperformed the other ML algorithms (Table). The compact model was not inferior to the best performing model using all features.

Table. Summary of Performance according to various ML model

Models	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Internal validation						
Support Vector Machine	0.645	0.4779	0.752	0.074	0.972	0.741
Decision Tree Classifier	0.760	0.698	0.696	0.087	0.982	0.696
Random Forest	0.829	0.770	0.751	0.117	0.987	0.752
AdaBoost	0.725	0.770	0.750	0.116	0.987	0.751
XGBoost	0.818	0.857	0.282	0.038	0.983	0.301
LightGBM	0.781	0.857	0.282	0.038	0.983	0.301
CatBoost	0.803	0.610	0.797	0.111	0.980	0.789
Compact model	0.802	0.610	0.797	0.111	0.980	0.790

Conclusion: We demonstrated that the ML-based predictive model to predict all cause of mortality after ischemic stroke.
Disclosure: Nothing to disclose.

EPO-386

Timing of (code) stroke in southern Spain

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Background and aims: Stroke onset is influenced by circadian rhythms. Spain, with more daylight hours, different daily schedules and customs such as "siesta", could have a different hourly distribution for stroke onset than other European countries. Objective: To describe the temporal distribution of code stroke in southern Spain.
Methods: Descriptive analysis of the local registry of code stroke between 2018 and 2022.
Results: 1,677 stroke code activations were recorded, 88.1% of them considered ischemic strokes at the time of admission (after discarding bleeding, space-occupying lesions and other diagnoses). A peak can be seen in the activation of code stroke between 11:00am and 1:59pm. Taking only wake-up strokes into account, this peak is maintained but another one appears at 8:00-8:59am. Excluding wake-up strokes, starting at 7:00am there is an increase in incidence of onset ischemic stroke symptoms, which reaches its maximum at 10:00-10:59am, gradually

decreasing throughout the day towards a minimum at 3:00-3:59am. 39.40% of not wake-up ischemic strokes occur between 9:00am and 13:59pm. Considering only wake-up ischemic strokes, in which onset time is unknown, 11:00pm to 12:59am are the most frequent hours in which the patient was last seen asymptomatic. The indication for reperfusion therapy (thrombolysis and/or thrombectomy) is more frequent between 11:00am and 2:59pm.
Conclusion: In our population, we consider the time of not wake-up ischemic strokes from 9:00am to 1:59pm and the time when the patient was last seen asymptomatic in wake-up strokes from 11:00pm to 12:59am. This results in arrivals to the emergency room between 8:00am and 1:59pm.
Disclosure: Nothing to disclose.

EPO-387

Utility of External loop recorder cardiac rhythm monitoring in Cryptogenic stroke: An institutional experience

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Background and aims: Cryptogenic strokes (CS) consist of 30% of total strokes. These can be caused by Paroxysmal Atrial fibrillation(PAF), which is not detected in acute settings. Prolonged ECG monitoring may improve the detection of PAF
Methods: This was a single centre, prospective, longitudinal, observational study conducted at a tertiary care centre over 18 months. Consecutive patients of acute ischemic stroke (AIS) admitted in the study period were included. All patients were extensively evaluated for Stroke etiology (Routine investigations, ECG, CT angio head and neck, 2D echo, 24 hour holter monitoring). Patients with initial negative workup were considered as CS and extended loop recorder(ELR) (72 hours) was planned. All patients were followed up for 90 days on outpatient basis or by telephonic interview. mRS and Barthel index (BI) were calculated on admission, on discharge and after 90 days
Results: 113 subjects were enrolled. 61 subjects were identified as cryptogenic stroke and underwent ELR monitoring for 72 hours. After this monitoring 3 subjects (4.9%) were found to have AF, which were not found during routine evaluation by ECG or 24 hour holter monitoring Patients with AF had poorer NIHSS on admission, worse GCS, larger strokes and longer hospital stay compared to the non AF. mRS at discharge and after 90 days did not show any significant difference between patients with or without AF. BI was significantly worse for the patients with AF
Conclusion: In AIS, 72-hour ECG monitoring improves the detection rate of silent PAF
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 3

EPO-388

Efgartigimod Demonstrates Consistent Improvements in Patients With gMG Regardless of Prior Treatment Failures

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Background and aims: In ADAPT, treatment with efgartigimod (a human IgG1 antibody Fc-fragment that blocks neonatal Fc receptor) resulted in clinically meaningful improvements in a broad population of anti-acetylcholine receptor antibody positive (AChR-Ab+) patients with generalised myasthenia gravis (gMG). We assessed efficacy of efgartigimod in a subset of AChR-Ab+ ADAPT patients with refractory gMG, defined as prior exposure to ≥2 immunosuppressive therapies or treatment with ≥1 immunosuppressive therapy and requiring plasma exchange or intravenous immunoglobulin multiple times within 1 year prior to study inclusion.

Methods: Patients received treatment cycles of 4 weekly intravenous infusions of efgartigimod (10 mg/kg) or placebo, with subsequent cycles initiated based on clinical evaluation. Baseline characteristics and proportion of patients achieving responder status were evaluated for refractory patients. Outcome measures included MG-ADL and QMG scores, with responder status defined as ≥2- and ≥3-point improvements for MG-ADL and QMG, respectively, for ≥4 consecutive weeks (with first improvement ≤1 week after last infusion).

Results: In refractory patients (AChR-Ab+), baseline characteristics were balanced between groups, with mean (SD) MG-ADL scores of 9.2 (1.95) for efgartigimod-treated patients and 8.8 (1.69) for placebo-treated patients (Table 1). More efgartigimod-treated patients (67.5%, n=27/40) were MG-ADL responders compared to placebo-treated patients (31.7%, n=13/41; P=.0029; Figure 1A). QMG results followed a similar pattern (Figure 1B). Common adverse events were mostly mild-moderate and included headache, nasopharyngitis, nausea, diarrhoea, and upper respiratory/urinary tract infections.

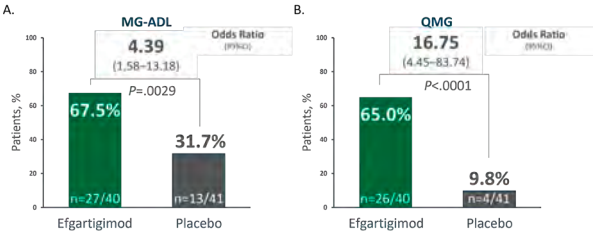

Figure 1: Proportion of MG-ADL (A) and QMG (B) responders in refractory AChR-Ab+ patients.

	Efgartigimod (n=40)	Placebo (n=41)
Age, mean, y (SD)	43.2 (13.89)	48.5 (14.95)
Female, n (%)	30 (75.0)	26 (63.4)
Time since diagnosis, mean, y (SD)	9.59 (7.62)	10.13 (8.07)
MG-ADL score, mean (SD)	9.2 (1.95)	8.8 (1.69)
QMG score, mean (SD)	15.9 (5.71)	15.4 (4.67)
MGFA class at screening, n (%)		
Class IIA	9 (22.5)	8 (19.5)
Class IIB	8 (20.0)	8 (19.5)
Class IIIA	11 (27.5)	10 (24.4)
Class IIIB	12 (30.0)	12 (29.3)
Class IVA	0	3 (7.3)
Prior treatment with steroids, n (%)	39 (97.5)	41 (100.0)
Prior treatment with NSISTs, n (%)	39 (97.5)	37 (90.2)

Refractory was defined as prior exposure to ≥2 immunosuppressive therapies or treatment with ≥1 immunosuppressive therapy and requiring plasma exchange or intravenous immunoglobulin multiple times within 1 year prior to study inclusion.

Table 1: Baseline demographics and clinical characteristics in refractory AChR-Ab+ patients.

	Efgartigimod (n=40)	Placebo (n=41)
AEs,[a] n (%)	29 (72.5)	34 (82.9)
SAEs, n (%)	2 (5.0)	4 (9.8)
Discontinued due to AEs, n (%)	1 (2.5)	2 (4.9)

Table 2: Safety data in the overall population. AE, adverse event; SAE, serious adverse event. aMost AEs were mild to moderate in severity.

Conclusion: Similar to results in AChR-Ab+ patients with gMG studied in ADAPT, efgartigimod demonstrated consistent and statistically significant improvements across outcome measures in patients with refractory gMG.

Disclosure: Multiple relationships financial and non-financial nature for authors CR, FS, JLdB, JV, SH, TV, VB, HM, EB, RK, SS, PU, NG, JV, RM and JFH Jr. stated at point of presentation.

EPO-389

A Real-life experience with Eculizumab and Efgartigimod in generalized Myasthenia Gravis patients.

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Background and aims: Eculizumab, a complement active monoclonal antibody, is reimbursed in Italy for anti-acetylcholine receptor antibody positive (AChR-Ab+) patients showing persistent symptoms, despite therapy with corticosteroids (CS) and ≥2 non-steroidal immunosuppressants (NSISTs). Efgartigimod, a neonatal Fc receptor blocker, is available in Italy through an expanded access program and treatment can be administered to both AChR-Ab+ and seronegative patients.
Methods: We included patients receiving either Eculizumab or Efgartigimod as part of our clinic practice and retrospectively collected data on their MG status using the MG activities of daily living (MG-ADL), quantitative MG scale (qMG), previous and current therapies, adverse events, and concomitant medication use.
Results: We enrolled 10 patients treated with Eculizumab and 12 with Efgartigimod. Demographics are shown in Table 1. Overall, MG-ADL decreased by -6.9 points ($p<0.001$), and qMG by -5.9 ($p<0.001$). Eculizumab reduced the MG-ADL by -6.6 points ($p=0.002$; Figure 1A), and the qMG by -7.4 ($p<0.001$; Figure 1B). Efgartigimod reduced the MG-ADL by -7.3 points ($p<0.001$; Figure 1A), and the qMG by -4.7 ($p<0.001$; Figure 1B). MG-ADL responders were 19 (86.4%), qMG responder were 19 (86.4%). Small non significant differeces emerged in the responder rate between treatments (Figure 2A). Mean prednisone reduction was -13.75 mg for the Eculizumab treated group ad -8.5 in the Efgartigimod group ($p=0.339$; Figure 2B).

Table 1. Baseline Demographics

Variable	Eculizumab (n=10)	Efgartigimod (n=12)	Total (n=22)
Gender (F/M)	5/5	10/2	12/10
AChR-Ab+	10	6*	16
Age	59.5±13.3	55.3±10.8	57.2±11.9
Previous Py use	9	12	21
Previous CS use	9	12	21
Previous NSIST = 0	2	4	6
Previous NSIST ≥1	8	8	16
Previous NSIST ≥2	8	4	12
Previous NSIST ≥3	2	0	2
Follow-up days (median)	116	84	91
MG-ADL	10.7±3.2	10.3±4.0	10.5±3.6
qMG	17.2±6.0	16.8±4.6	17.0±5.2

AChR-Ab+ = anti-acetylcholine receptor antibody positive; PY = Pyridostigmine; CS = Corticosteroids; NSIST = Non-steroidal Immunosuppressants; MG-ADL = Myasthenia Gravis Activities of Daily Living scale; qMG = Myasthenia Gravis quantitative scale. For gender significance is derived from a Fisher exact test, for Age, MG-ADL, qMG from a Mann-Whitney test. All comparisons were not significant. * 6 patients treated with Efgartigimod were seronegative, of these 2 were anti-MuSK-Ab+.

Table 1

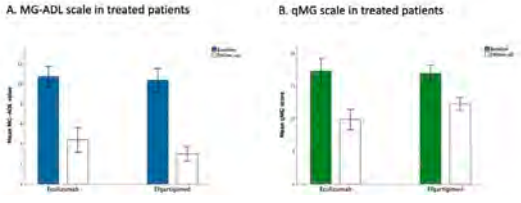

Figure 1

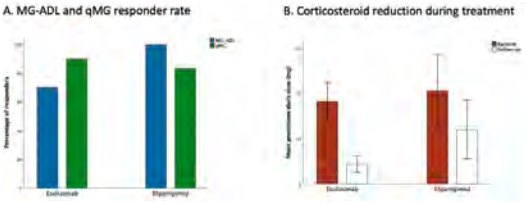

Figure 2

Conclusion: Eculizumab and Efgartigimod proved to be both effective treatments in a real world setting. They reduced MG-ADL and qMG in difficult to treat gMG patients. Responder rate was higher than previously reported in phase III trials.
Disclosure: FS received speaker honoraria from Alexion Pharmaceuticals, Inc, argenx, Biogen, Mylan, Novartis, Roche, Sanofi, and Teva; received honoraria from Alexion Pharmaceuticals, Inc, Almirall, argenx, Avexis, Biogen, Forward Pharma, Lexeo Therapeutics, Merk, Novartis, Pomona, Roche, Sanofi, and Takeda for consulting services; and served as PI in clinical trials supported by Alexion Pharmaceuticals, Inc, argenx, Immunovant, Novartis, Prilenia, and Sanofi. Other authors do not report disclosures.

EPO-390

Efficacy of innovative therapies in Myasthenia Gravis: review and meta-analysis.

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Background and aims: Therapy of Myasthenia Gravis (MG) is undergoing a profound change with new treatments being tested. These include: the complement inhibitors Eculizumab and Ravulizumab (humanized monoclonal antibodies), and Zilucoplan (self-administered peptide); the neonatal Fc receptor (FcRn) blockers Efgartigimod (human Fc-fragment), and Rozanolixizumab (sc-infused monoclonal antibody).
Methods: We present a meta-analysis of phase III trials with available efficacy results. In a second analysis round, we also included placebo-controlled trials with Rituximab. We assessed statistical heterogeneity across trials with Cochrane Q test and I2 values. We pooled mean differences with the random effect model. We derived treatment efficacy after 26 weeks of treatment with Eculizumab and Ravulizumab, 28 days with Efgartigimod, 43 days with Rozanolixizumab, 12 weeks with Zilucoplan, and after 16, 24 or 52 weeks with Rituximab.
Results: We observed an overall mean MG-ADL change of -2.17 points (95% CI -2.67, -1.67; $p<0.001$) as compared to placebo, without a significant difference between complement inhibitors and anti-FcRns ($p=0.16$; Figure 1A). The qMG change was -3.46 (95%CI -4.53, -2.39; $p<0.001$), with a higher reduction with FcRns (-4.78 vs -2.60; $p<0.001$;

Figure 1B). Rituximab did not significantly impact on MG-ADL (-0.92, CI95% -2.24, 0.39; p=0.17; Figure 2A), or qMG (-1.9, 95%CI -3.97, 0.18, p=0.07; Figure 2B).

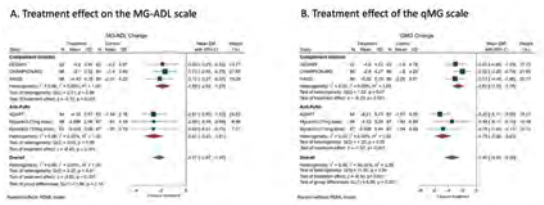

Figure 1. MG-ADL and qMG changes during treatment

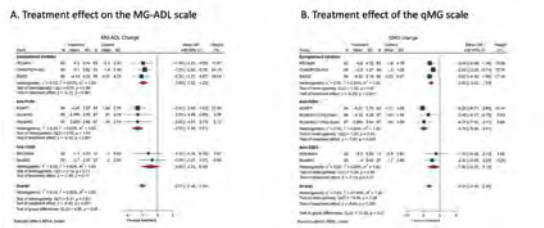

Figure 2. MG-ADL and qMG changes during treatment in the model including Rituximab

Conclusion: Anti-complement and FcRn treatments proved to be both effective in MG patients, whereas Rituximab did not show benefit in AChr-Ab+ patients. With the limitations of this meta-analysis, including efficacy time-points, FcRN treatments showed a short-term higher effect on the qMG.

Disclosure: FS received speaker honoraria from Alexion Pharmaceuticals, Inc, Biogen, Mylan, Novartis, Roche, Sanofi, and Teva; received honoraria from Alexion Pharmaceuticals, Inc, Almirall, argenx, Avexis, Biogen, Forward Pharma, Lexeo Therapeutics, Merk, Novartis, Pomona, Roche, Sanofi, and Takeda for consulting services; and served as PI in clinical trials supported by Alexion Pharmaceuticals, Inc, argenx, Immunovant, Novartis, Prilenia, and Sanofi. All other authors report no disclosures related to this abstract.

EPO-391

Rozanolixizumab in muscle-specific kinase autoantibody-positive myasthenia gravis: Further analyses from MycarinG study

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Background and aims: Muscle-specific kinase autoantibody-positive (MuSK-Ab+) generalised myasthenia gravis (gMG) is usually more clinically severe than acetylcholine receptor autoantibody-positive (AChR-Ab+) gMG. The Phase 3 MycarinG study analysed rozanolixizumab in patients with AChR-Ab+ or MuSK-Ab+ gMG.

Methods: MycarinG (MG0003/NCT03971422) randomised adults with Myasthenia Gravis Foundation of America Class II–IVa, AChR-Ab+ or MuSK-Ab+ gMG to weekly rozanolixizumab 7mg/kg, 10mg/kg or placebo for 6 weeks. The primary endpoint was Day 43 change from baseline (CFB) in Myasthenia Gravis Activities of Daily Living (MG-ADL).

Results: 200 patients (21 MuSK-Ab+) were randomised to rozanolixizumab 7mg/kg (n=66 [5 MuSK-Ab+]), 10mg/kg (n=67 [8]) or placebo (n=67 [8]). Among patients with MuSK-Ab+ gMG, a higher proportion experienced prior MG crisis and a lower proportion had thymectomy than the overall population, and their baseline MG-ADL score was higher (Table 1). Day 43 least-squares mean CFB in

MG-ADL for 7mg/kg, 10mg/kg and placebo groups were –7.28, –4.16 and 2.28, respectively, in patients with MuSK-Ab+ gMG and −3.37, −3.40 and −0.78 in the overall population. MG-ADL reduction in patients with MuSK-Ab+ and in overall population are shown in Figure 1. Mean percentage CFB in total immunoglobulin G (IgG) and IgG4 for patients with MuSK-Ab+ gMG and the overall population are presented in Table 2. Treatment-emergent adverse events occurred in 81.3% (7mg/kg), 82.6% (10mg/kg) and 67.2% (placebo) patients in the overall population and most were mild-to-moderate in severity.

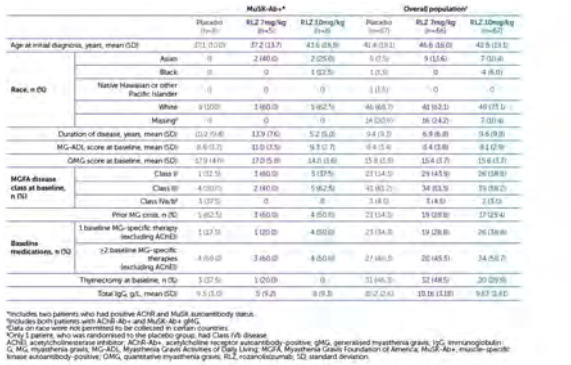

Table 1. Baseline characteristics of patients with MuSK-Ab+ gMG and in the overall population

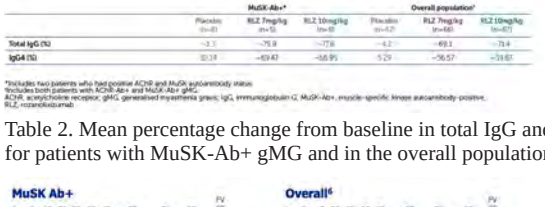

Table 2. Mean percentage change from baseline in total IgG and IgG4 for patients with MuSK-Ab+ gMG and in the overall population

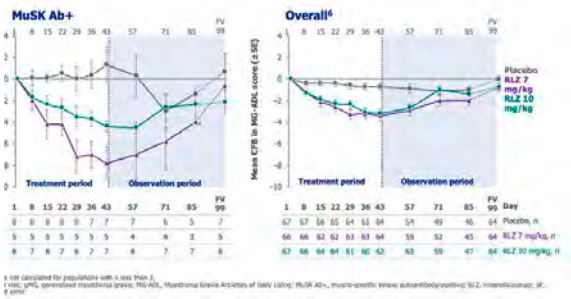

Figure 1. Mean change from baseline in MG-ADL in (A) patients with MuSK-Ab+ gMG and (B) the overall population

Conclusion: Rozanolixizumab lowered total and subclass IgG levels and improved MG-specific outcomes in MuSK+ gMG, consistent with the overall study population. Funding: UCB Pharma.

Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation.

EPO-392

RevEal the burdeN on daily life for myotonic dyStrophy patients due to myotoniA: the ENSA survey.

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Background and aims: Myotonia is a symptom of myotonic dystrophy (DM) type 1 and 2. This can be debilitating and affects patients' everyday living, with a significant burden on Quality of Life (QoL) (1). Impact of DM on QoL has been evaluated (2,3), however, the specific contribution of myotonia remains unclear. The ENSA survey will assess the impact of myotonia on DM patients' daily lives.

Methods: Patients living in Europe, UK and North America, aged ≥18 years with a confirmed diagnosis of DM1/DM2, (or caregivers) will be invited to complete an anonymised online survey. Questions will explore the patient's description of DM symptom onset, time to medical consultation, the nature, frequency and location of myotonia, muscle weakness, fatigue, daytime sleepiness, gastrointestinal, and cardiorespiratory symptoms, along with disease management, treatment history and impact on daily life.

Results: Findings will be available in Q2-2023 and will aim to provide insight into the burden of myotonia on the daily life for DM patients, as well as increasing understanding of symptoms to support future clinical-trial outcome measures.

Conclusion: The ENSA survey will quantify the impact of myotonia on DM1 and DM2 patients' daily life and raise awareness of the need for appropriate management.

References: 1. Diaz-Manera J, et al. EMJ 2021;6[2]:37-46. 2. Rakocevic Stojanovic, S et al; J. Neurological Sciences, 2016;365, 158-161. 3. Landfeldt, E et al; Patient, 2019; 12(4): 365–373.

Disclosure: Zozulya-Weidenfeller is employed by Lupin. Other authors received honoraria from Lupin as consultants during the ENSA creation.

EPO-393

An unusual myopathy caused by a novel mutation in PNPLA2 gene

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Background and aims: The PNPLA2 gene encodes adipose triglyceride lipase, involved in adipose tissue triglyceride hydrolysis. Mutations of this gene are associated with neutral lipid storage disease with myopathy (NLSDM), a rare autosomal recessive condition.
Methods: Case report.
Results: Our case refers to a 35-year-old man history of severe acute heart failure by the age of 28, being identified a dilated myocardiopathy that required an implantable cardioverter-defibrillator implantation. His parents were consanguineous. He had no complaints of muscular weakness but had myalgias with intense physical exercise. On the neurological examination he had only a slight winged scapula, more evident on the left side. On blood workup he presented a high creatinine kinase level (200-800 U/L). A lipid deposition on the leukocytes known as Jordans anomaly was found on the blood smear. Abdominal CT and ultrasound were unremarkable. The muscle biopsy revealed a lipid accumulation on the muscle fibers, mainly on type 1 fibers. A genetic panel for myopathies revealed a novel homozygous pathogenic variant in the PNPLA2 gene (c.792del). He initiated bezafibrate 200mg 2id, which was suspended given the absence of therapeutic effect. He has been recently submitted to a successful heart transplant, from which he has been recovering uneventfully.
Conclusion: Our case of NLSDM seems to be singular as it started as a severe de novo dilated myocardiopathy, with subclinical involvement of skeletal muscle, associated with a novel mutation in PNPLA2 gene. The prognosis seems to be favourable, but it is limited by the cardiac involvement.
Disclosure: Nothing to disclose.

EPO-394

Patients in the Pompe Registry who switched from alglucosidase alfa to avalglucosidase alfa: Real-world experience

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Background and aims: Introduction: Marketing authorization for avalglucosidase alfa (AVAL) has been received in several countries for Pompe disease. Demographic and clinical characteristics of patients with Pompe disease who received alglucosidase alfa (ALGLU) for <5 versus ≥5 years before switching to AVAL are reported.
Methods: Real-world data were obtained from the Pompe Registry (NCT00231400), an international, observational, voluntary registry of patients with Pompe disease. For this analysis, eligible patients had ≥1 ALGLU treatment record immediately pre-switch to AVAL. Demographics, treatment duration and dose, plus respiratory, ambulatory, and biomarker measures are summarised pre-switch and, where data are available, for the last assessment post-switch.
Results: As of 2 December, 2022, data were available for 81 patients with late-onset Pompe disease (LOPD) and 8 with infantile-onset Pompe disease (IOPD); characteristics and treatment histories are summarised (Table 1). For patients with LOPD, last respiratory, ambulatory, and biomarker assessments pre-switch are summarised (Table 2) and for patients with both pre- and post-switch assessments these data are compared (Table 3). The preliminary results indicate an overall stabilisation in clinical outcomes following switch from ALGLU to AVAL, as well as improvement in the levels of biomarkers associated with disease burden, although more data will be needed from future data cuts to confirm these observations.

Parameter	IOPD (N=8)	LOPD: Time on alglucosidase alfa before switch to avalglucosidase alfa < 5 years (N=26)	LOPD: Time on alglucosidase alfa before switch to avalglucosidase alfa ≥ 5 years N=55)
Sex, male, n (%)	3 (38)	12 (46)	31 (56)
Region, n (%)			
North America	2 (25)	26 (100)	46 (84)
Europe, Middle East, and Africa	5 (63)	0	7 (13)
Japan and Asia-Pacific	1 (13)	0	2 (4)
Age at diagnosis, mean±SD, years	0.4±0.30	32.4±22.29	33.7+21.59
Age at alglucosidase alfa initiation, mean±SD, years	0.5±0.29	33.3±22.76	37.6±21.34
First dose on alglucosidase alfa, 20 mg/kg qow,* n (%)	7 (88)	24 (100)	53 (100)
Last dose on alglucosidase alfa 20 mg/kg qow,* n (%)	5 (63)	23 (92)	41 (77)
Age at switch to avalglucosidase alfa, mean±SD, years	11.0±5.15	36.1±23.05	49.0±20.31
Time on avalglucosidase alfa, mean±SD (median [min, max]), months	5.4±8.98 (3.2 [0.0, 27.0])	6.7±20.36 (1.1 [0.0, 104.7])	3.5±3.79 (2.7 [0.0, 13.7])
First dose on avalglucosidase alfa 20 mg/kg qow,* n (%)		19 (73)	44 (80)
First dose on avalglucosidase alfa 40 mg/kg qow,* n (%)	6 (75)		
Last dose on avalglucosidase alfa 20 mg/kg qow,* n (%)		20 (77)	44 (80)
Last dose on avalglucosidase alfa 40 mg/kg qow,* n (%)	6 (75)		

*Most common dose for each group is shown; nominal dose 20 mg/kg (actual range: 14–27 mg/kg), nominal dose 40 mg/kg (actual range: 28–52 mg/kg); percentages based on number of patients with dose available. IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; qow, every other week; SD, standard deviation.

Table 1 Patient characteristics and treatment history (data cut-off: 2 December, 2022)

Parameter	LOPD: Time on alglucosidase alfa before switch to avalglucosidase alfa	
	< 5 years	≥ 5 years
FVC (upright) % predicted, mean±SD (median [min, max])	71.2±19.08 (76.0 [34.0, 104.0]) (n=17)	55.1±24.89 (50.0 [9.4, 124.0]) (n=52)
FEV_1 (upright) % predicted, mean±SD (median [min, max])	71.3±18.35 (74.0 [36.0, 100.0]) (n=16)	56.1±23.58 (50.0 [9.5, 121.0]) (n=50)
MIP, mean±SD (median [min, max]), cmH_2O	58.0±31.70 (59.0 [20.0, 120.0]) (n=11)	50.8±30.89 (43.0 [12.0, 134.0]) (n=35)
MEP, mean±SD (median [min, max]), cmH_2O	137.7±158.58 (84.5 [38.0, 571.0]) (n=10)	63.2±43.61 (52.5 [10.0, 246.0]) (n=30)
6MWT, mean±SD (median [min, max]), m	490.4±170.03 (491.0 [216.0, 869.0]) (n=11)	311.0±109.93 (316.5 [85.0, 500.0]) (n=30)
Urine Glc_4/Hex_4, mean±SD (median [min, max]), mmol/mol creatinine	4.6±2.12 (4.2 [1.6, 9.7]) (n=19)	12.3±20.83 (4.7 [1.6, 110.4]) (n=37)
Serum CK, mean±SD (median [min, max]), U/L	448±286 (366 [129, 976]) (n=18)	544±519 (411 [51, 2803]) (n=47)

*Data for infantile-onset Pompe disease patients not presented due to the small number of patients who had initiated avalglucosidase alfa at data cut-off.
6MWT, 6-minute walk test; CK, creatine kinase; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GLC_4, glucose tetrasaccharide; Hex_4; hexose tetrasaccharide; LOPD, late-onset Pompe disease; MEP maximal expiratory pressure, MIP, maximal inspiratory pressure; SD standard deviation.

Table 2 Last respiratory, ambulatory, and biomarker assessments for patients with LOPD* pre-switch from alglucosidase alfa to avalglucosidase alfa (data cut-off: 2 December, 2022)

Parameter	Patients, n	LOPD switch patients with assessments at both timepoints		
		Last assessment prior to switch	Last-post switch assessment (<1 year)	Change between visits
FVC (upright) % predicted, mean±SD (median [min, max])	16	60.4±23.45 (64.5 [25.0, 104.0])	61.5±23.99 (65.5 [19.0, 99.0])	1.1±5.09 (−1.0 [−6.0, 9.8])
FEV_1 (upright) % predicted, mean±SD (median [min, max])	16	61.8±22.67 (61.5 [28.0, 100.0])	63.3±24.31 (65.0 [22.0, 104.0])	1.5±6.13 (0.0 [−8.0, 13.0])
MIP, mean±SD (median [min, max]), cmH_2O	8	43.0±33.89 (31.0 [12.0, 120.0])	48.9±28.09 (43.5 [21.9, 107.0])	5.9±20.65 (−1.5 [−13.0, 49.2])
MEP, mean±SD (median [min, max]), cmH_2O	5	56.0±47.67 (42.0 [18.0, 138.0])	65.4±41.92 (46.0 [31.0, 126.0])	9.4±36.49 (−7.0 [−12.0, 73.8])
6MWT, mean±SD (median [min, max]), m	16	362.4±149.11 (392.5 [85.0, 640.0])	353.4±174.70 (401.0 [31.0, 650.0])	−8.9±66.15 (4.5 [−197.0, 80.0])
Urine Glc4/Hex_4, mean±SD (median [min, max]), mmol/mol creatinine	22	6.8±6.09 (4.4 [1.6, 25.0])	3.7±2.44 (2.8 [1.5, 10.8])	−3.1±5.67 (−0.8 [−19.3, 3.5])
Serum CK, mean±SD (median [min, max]), U/L	27	472.2±314.14 (424 [51, 1212])	390.8±273.93 (362 [61, 1105])	−81.4±194.56 (−21 [−735, 259])

*Data for patients with infantile-onset Pompe disease not presented due to the small number of patients who had initiated avalglucosidase alfa at data cut-off.
6MWT, 6-minute walk test; CK, creatine kinase; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GLC_4, glucose tetrasaccharide; Hex_4; hexose tetrasaccharide; LOPD, late-onset Pompe disease; MEP maximal expiratory pressure, MIP, maximal inspiratory pressure; SD standard deviation.

Table 3 Respiratory, ambulatory, and biomarker assessments pre- and post-switch (<1 year) from alglucosidase alfa to avalglucosidase alfa for patients with LOPD* who have both assessments (data cut-off: 2 December, 2022)

Conclusion: The Pompe Registry will continue to accrue data for patients switching from ALGLU to AVAL. Post-switch data will support the understanding of AVAL's effectiveness on respiratory and ambulatory outcomes and biomarker levels in the real-world setting.
Disclosure: Funding: Sanofi.

EPO-395

A Study Examining The Concordance Between Patient And Physician Assessment Of The MG-ADL

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Background and aims: Myasthenia Gravis (MG) is a rare, IgG-driven, autoimmune disease affecting vision, breathing, limb strength, and bulbar functioning. The most widely used primary endpoint in clinical trials is the MG-Activities of Daily Living (MG-ADL) scale, in which neurologists assesses patients on 8 symptoms. In contrast, real-world evidence studies often ask patients to complete the MG-ADL themselves. The objective of this study was to assess the concordance between the patient- and neurologist-reported MG-ADL scores.
Methods: An observational study was conducted in Italy and Germany, recruiting MG patients entering the hospital via emergency services or via a scheduled appointment. The MG-ADL was completed by patients at home and by neurologists during the consultation, in random order within 2 days (range 2-6) of each other. Concordance between the patient- and neurologist-reported MG-ADL assessments was calculated with Gwet's agreement coefficient for the 8 items, and with Intraclass Correlation Coefficients (ICC) for the total score.
Results: The ICC for the MG-ADL total score was 0.94 (95%CI 0.89-0.95), based on data from 137 adult MG patients and their neurologist, demonstrating excellent concordance. Gwet's AC showed substantial to almost perfect agreement for 7 items and moderate agreement for 1 item (eyelid droop). Neurologists assessed the patient's total symptom severity 0.6 points higher on a range of 0-24 (average 8.1 vs. 7.5 MG-ADL total score, respectively).

MG-ADL Items	Gwet's AC (p-value)
Chewing	0.77 (p<0.0001)
Double vision	0.74 (p<0.0001)
Breathing	0.73 (p<0.0001)
Rise from a chair	0.69 (p<0.0001)
Talking	0.66 (p<0.0001)
Swallowing	0.66 (p<0.0001)
Brush teeth or comb hair	0.58 (p<0.0001)
Eyelid droop	0.46 (p<0.0001)
	ICC (95% CI)
MG-ADL total score	0.94 (0.89-0.95)

Abbreviations: MG-ADL = myasthenia gravis activity of daily life score, ICC = intraclass correlation coefficient, CI = confidence interval

Table 1. Gwet's AC and ICC for item level and MG-ADL score

Conclusion: Excellent concordance of the assessment of MG symptoms with the MG-ADL was found between patients and neurologists. This evidence supports patient self-administration of the MG-ADL in MG-related clinical practice and research.
Disclosure: FS has received speaking honoraria and honoraria for attendance of advisory boards from Alexion and argenx BV. AM has received speaker honoraria, consulting fees or financial research support from Alexion, Argenx BV, Grifols, Hormosan, Janssen, Octapharma, and UCB. He serves as chairman of the medical advisory board of the German Myasthenia Gravis Society RM has received speaking honoraria from Biomarin, Alexion and UCB, served on advisory boards for Alexion, argenx BV and UCB and received support for congress participation from Merck, Teva and Biogen. SP is an employee of argenx BV, the sponsor of the study SD, owner of SHE, has been commissioned by argenx, the sponsor of the study, and is a member of the EuroQol Group. NT is an employee of SHE. MFJ is a paid consultants for argenx, the sponsor of this study, and received grant support from them.

EPO-396

Real-world experience with eculizumab in Japanese patients with myasthenia gravis: Post-marketing surveillance data

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Background and aims: Eculizumab (complement C5 inhibitor) is approved in Japan for treatment of adults with anti-acetylcholine receptor antibody-positive (AChRAb+) generalised myasthenia gravis (gMG) whose symptoms are difficult to control with high-dose intravenous immunoglobulin therapy or plasma exchange.

Methods: This interim analysis of post-marketing surveillance data assessed the effectiveness and safety of eculizumab in Japanese adults with gMG. Clinically meaningful response (≥3-point reduction in Myasthenia Gravis-Activities of Daily Living total score vs baseline) was evaluated at timepoints up to 104 weeks after eculizumab initiation in the analysis population overall and by patient and disease characteristics. Oral corticosteroid use was assessed. Safety was evaluated by recording adverse events.

Results: Data were available for 231 patients; the effectiveness analysis set comprised 223 patients. For patients with both baseline and follow-up data, 99/172 (57.6%), 104/167 (62.3%), 70/108 (64.8%) and 43/61 (70.5%) achieved clinically meaningful response at 12, 26, 52 and 104 weeks, respectively, after eculizumab initiation. Responder rates were similar and maintained through 104 weeks across analysed subgroups (Table). In patients receiving oral corticosteroids there was a trend towards reduced corticosteroid use and an increased proportion receiving ≤5 mg/day with continued eculizumab treatment (Figure). No new safety signals were observed.

Conclusion: The analysis findings align with previous real-world data, demonstrating eculizumab's sustained effectiveness and consistent safety profile in adults with AChRAb+ gMG, regardless of patient or disease characteristics. The observed reduction in concomitant oral corticosteroid use, also consistent with other real-world experiences, underlines the benefit of C5 inhibition in these patients.

Characteristic	MG-ADL responders, n/N (%)[a] Week 12	Week 26	Week 52	Week 104[b]
Sex				
Female	70/118 (59.3)	71/110 (64.5)	47/70 (67.1)	33/45 (73.3)
Male	29/54 (53.7)	33/57 (57.9)	23/38 (60.5)	10/16 (62.5)
Age at MG diagnosis (years)				
<50	59/103 (57.3)	65/102 (63.7)	47/68 (69.1)	28/39 (71.8)
≥50	40/69 (58.0)	39/65 (60.0)	23/40 (57.5)	15/22 (68.2)
Age at eculizumab initiation (years)				
≥18 to <40	20/32 (62.5)	22/35 (62.9)	14/23 (60.9)	10/15 (66.7)
≥40 to <65	53/96 (55.2)	58/93 (62.4)	42/59 (71.2)	24/33 (72.7)
≥65	26/44 (59.1)	24/39 (61.5)	14/26 (53.8)	9/13 (69.2)
Time from MG diagnosis to eculizumab initiation (years)				
≤2	30/45 (66.7)	33/43 (76.7)	21/30 (70.0)	13/15 (86.7)
>2 to ≤6	25/56 (44.6)	31/60 (51.7)	18/33 (54.5)	17/24 (70.8)
>6 to ≤14	28/42 (66.7)	23/35 (65.7)	16/26 (61.5)	6/13 (46.2)
>14	16/29 (55.2)	17/29 (58.6)	15/19 (78.9)	7/9 (77.8)
Inpatient/outpatient at eculizumab initiation				
Inpatient	28/38 (73.7)	27/35 (77.1)	18/24 (75.0)	11/15 (73.3)
Outpatient	71/134 (53.0)	77/132 (58.3)	52/84 (61.9)	32/46 (69.6)
History of thymoma				
Yes	50/76 (65.8)	48/67 (71.6)	36/44 (81.8)	20/25 (80.0)
No	49/95 (51.6)	56/99 (56.6)	34/63 (54.0)	23/35 (65.7)
Unknown	0/1 (0.0)	0/1 (0.0)	0/1 (0.0)	0/1 (0.0)
Severity of MG at first dose (MGFA classification)				
IIa	18/34 (52.9)	18/36 (50.0)	12/27 (44.4)	4/12 (33.3)
IIb	15/29 (51.7)	18/31 (58.1)	15/23 (65.2)	7/8 (87.5)
IIIa	26/40 (65.0)	29/39 (74.4)	13/18 (72.2)	10/13 (76.9)
IIIb	12/26 (46.2)	11/21 (52.4)	8/12 (66.7)	6/8 (75.0)
IVa	11/15 (73.3)	8/14 (57.1)	8/9 (88.9)	8/9 (88.9)
IVb	7/10 (70.0)	9/11 (81.8)	7/10 (70.0)	3/5 (60.0)
V	10/16 (62.5)	11/13 (84.6)	7/7 (100.0)	5/5 (100.0)
Unknown	0/2 (0.0)	0/2 (0.0)	0/2 (0.0)	0/1 (0.0)
Comorbidity				
Yes	70/120 (58.3)	76/118 (64.4)	52/80 (65.0)	28/41 (68.3)
No	29/52 (55.8)	28/49 (57.1)	18/28 (64.3)	15/20 (75.0)

The effectiveness analysis set (n=223) comprised all patients with ≥1 completed case report form at 26 weeks, except patients who received eculizumab in the REGAIN primary study (NCT01997229) or its open-label extension (NCT02301624). Data for each post-baseline timepoint are presented for those patients who had data at both baseline (eculizumab initiation) and the follow-up timepoint.

[a]MG-ADL responders were defined as patients with an MG-ADL total score improvement of ≥3 points vs. baseline (eculizumab initiation). [b]At time of data cut-off, 161 patients in the effectiveness analysis set were continuing treatment with eculizumab, of whom 82 had been treated for ≥2 years. MG, myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America.

Table: MG-ADL responder rates at Weeks 12, 26, 52 and 104 after eculizumab initiation in the overall population and according to patient and disease characteristics (effectiveness analysis set).

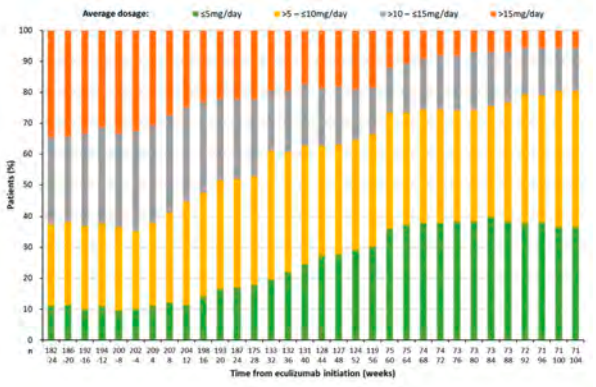

Figure: Mean corticosteroid use (daily dose) by time from eculizumab initiation.

Disclosure: Funded by Alexion Pharma GK, AstraZeneca Rare Disease

EPO-397

Diaphragmatic ultrasound:a promising tool for respiratory assessment in Facioscapulohumeral muscular dystrophy (FSHD)

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Background and aims: A restrictive respiratory impairment has been described in up to 40% of patients affected by Facioscapulohumeral muscular dystrophy (FSHD), one of the most prevalent muscular dystrophies in adults. Spirometry may underestimate early respiratory alterations in these patients, as inspiratory muscle impairment may occur before Forced vital capacity (FVC) variation. Ultrasonography has recently emerged as a non-invasive tool to assess the main inspiratory muscle, the diaphragm. The aim of this study was to thoroughly characterize the respiratory function of a small cohort of FSHD comparing spirometric and ultrasonographic data.

Methods: Genetically confirmed adult FSHD patients were enrolled. US diaphragmatic thickness at the end of a normal expiration (basal-DT), after a maximal inspiration (max-DT) and diaphragmatic excursion were calculated. The difference between max-DT and basal-DT represented "diaphragmatic thickening". FVC, forced expiratory volume in first second (FEV1), total lung capacity (TLC) and residual volume (RV) were also assessed by spirometry. Values were compared to normative data.

Results: Twenty FSHD patients (14 male and 6 female) were enrolled. Asymmetric abnormalities were found on US evaluation in 9 patients (45%), especially in diaphragmatic kinetic: median "diaphragmatic thickening" was 1,8 mm (range 0-4,6). A smaller portion of patients showed alteration on spirometric indexes. Inspiratory dysfunction with low TLC was detected in 5 (25%) patients, three of whom also displayed a restrictive pattern with a low FVC.

Conclusion: This pilot study suggests that diaphragmatic US could be a promising technique to identify early inspiratory dysfunction in FSHD patients and these results need to be confirmed in larger cohort.

Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the abstract and there is no financial interest to report.

EPO-398

IT engineered "smart-shoes" to digitally assess gait dynamics in FSHD patients

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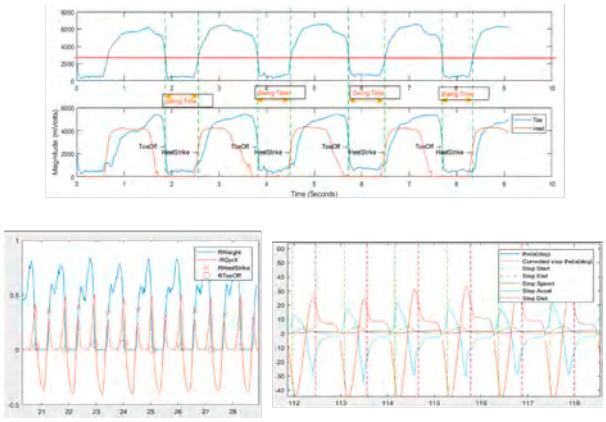
Background and aims: Facioscapulo-humeral muscular dystrophy is one of the most common myopathies in adult patients. Clinical trials are finally approaching also for FSHD, prompting understanding of molecular causes of clinical differences and precise phenotyping of different phenotypes, in order to identify suitable outcome measures. To highlight early signs of gait disturbances in FSHD patients without clinically detectable involvement of the lower leg, we tested the sensitivity of biosensors-featured "smart-shoes". The smart-shoes are integrated in the InGene2.0 software framework, which includes sections for collection of neurological examination, functional motor tests, muscular MRI, genetic data, muscle biopsies. Algorithms for artificial intelligence-mediated analysis and integration of data is applied to the whole software.

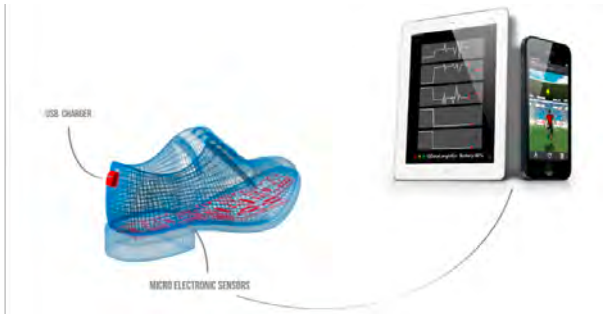
One of the smart shoes model, which is comfortably worn by patients and aesthetically indistinguishable from normal shoes.

Methods: We evaluated FSHD adult patients at baseline and for a 12-months follow-up period and in comparison to healthy controls. Variables collected by the smart shoes are speed gait, plantar pressures, joint angles. The tests included 6MTW, TUG, 10m run and time to climb and descend four stairs.
Results: The shoes are worn comfortably by the patients and can correctly and continuously detect the desired data. A worsening trend in patients' performance was found, although not statistically significant.



Real time collection of data during the tests is available on screen

Conclusion: Application of wearable devices such as the smart shoes could not only deliver digitized data on a personalized basis but also apply to a novel model of tele-monitoring of patients in daily life. The smart shoes will be tested on more patients, also with evident impairment of lower leg. Application of the smart shoes on a wider cohort is needed to validate our preliminary data.



The smart shoes could be integrated in e-health systems and help tele-monitoring of patients.

Disclosure: The authors have no disclosures to declare.

EPO-399

SRPKs in inflammatory muscle diseases

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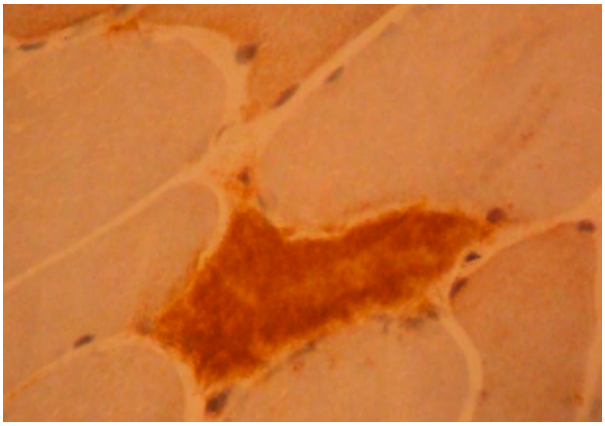
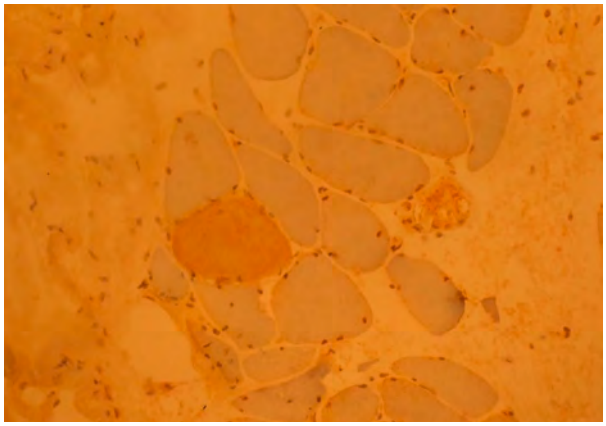
Background and aims: Idiopathic inflammatory myopathies (IIMs) consist an heterogeneous group of chronic autoimmune muscle diseases. Their pathogenetic mechanisms are not fully understood. Serine-arginine protein kinases (SPRKs) are a subgroup of serine-threonine protein kinases that phosphorylates substrates rich in Ser-Arg/Arg-Ser dipeptide repeats. Since many splicing factors contain RS domains, SRPKs play a major role in cell function via phosphorylation of these factors and therefore regulating alternative mRNA splicing. They have been implicated in oncogenesis but there are no data related to other disorders like autoimmune disorders.
Methods: Aiming to study the possible role of SRPKs on autoimmune disorders we sought to determine their expression on striate muscles in healthy individuals and patients with IIMs. We performed immunohistochemistry on frozen sections from muscle biopsies with diverse diagnosis, including dermatomyositis (DM), polymyositis (PM), sporadic inclusion body myositis (sIBM), immune-mediated necrotizing myopathy (IMNM), and myositis associated with antisynthetase syndrome (ASS).
Results: The results revealed an upregulation of both SRPK1 and SRPK2 in the cases with IIMs compared to healthy individuals. Interestingly only muscle fibers expressing other inflammatory markers showed this upregulation in SRPKs.





Conclusion: This results reveal a possible role of SRPKs in IIMs and possibly in other autoimmune disorders, apart from oncogenesis.
Disclosure: No conflict of interest.

EPO-400

The challenging interpretation of RYR-1 gene variants in three unrelated families.

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Background and aims: RYR-1 gene (Ryanodine Receptor type 1, 19q13.9) encodes a sarcoplasmic reticulum receptor, acting as a calcium release channel. RYR-1-related disorders encompass different conditions including central core disease (CCD), susceptibility to malignant hyperthermia and also asymptomatic hyperCKemia. The high phenotypic variability and the great number of emerging genetic variants require expertise and caution for their interpretation and clinical relevance.
Methods: We analyzed three families referred to our Unit with previously unreported RYR-1 heterozygous variants. An extensive phenotyping was performed through clinical examination, laboratory tests and, when available, muscle biopsy and magnetic resonance.
Results: Our cohort included a total of 8 patients, whose average age at first clinical evaluation was 39.1 years old [11-54]. The subjects taken into consideration were: father and daughter (Family A); three siblings (Family B); and mother and two sons (Family C). For each family a unique "in silico" pathogenic variant was identified, but different phenotypes were observed. In family A, the daughter presented a classical clinical and histopathological phenotype of CCD, while the father only mild signs of proximal weakness. In Family B and C, only one member showed clinical, histopathological, imaging, and laboratory characteristics of CCD, while the others' examinations resulted negative, except for a mild increase in serum Creatin kinase in one subject.
Conclusion: Our findings underline the complexity to interpret RYR-1 variants and to explain the genetic results and the clinical implications for a clinician. It also suggests possible incomplete penetrance or other genes' influence on RYR-1 mutated patients' phenotype.
Disclosure: The authors have no interests to disclose.

Motor neurone diseases; Muscle and neuromuscular junction disorder

EPO-401

Smartphone-based cough data in amyotrophic lateral sclerosis: a potential predictor of functional disability

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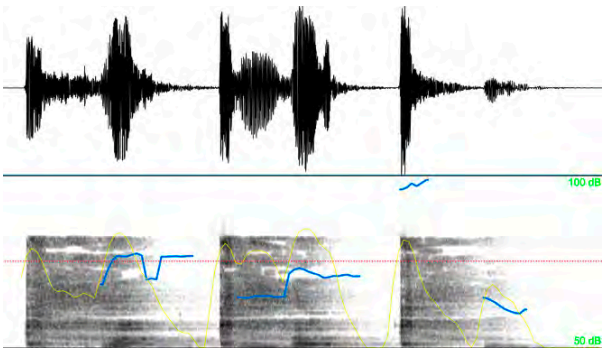
Background and aims: Amyotrophic lateral sclerosis (ALS) leads to severe functional disability. Cough depends on both respiratory and bulbar integrity. Correlations between cough sounds and ALS clinical features have been rarely performed. We aimed to assess the relationship between cough (and vocal) sound characteristics with respiratory and bulbar functions in ALS.

Methods: Single-center, cross-sectional and case-control study, consecutively collected on-demand cough recordings in ALS patients using a smartphone. The Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) was performed by a speech therapist. A quantitative acoustic analysis was conducted using time and frequency signal processing on the recordings. Correlation coefficients and multiple linear regression models were used.

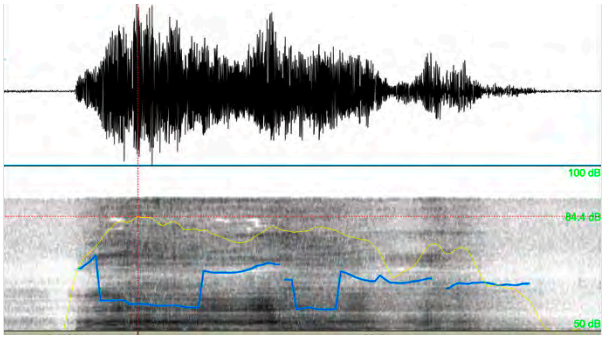
Results: We recruited 30 ALS patients: 19 females; mean age 61.36; mean 35 months disease duration; 10 with bulbar-onset; and a 37.5 mean ALSFRS-R total. Data from 20 controls were also included. Adjusting to age and gender, our results revealed clear differences between patients and controls on 9 (out of 31) cough sound features. The results revealed main difference between the two groups on sound frequency – significantly lower in ALS (p=0.003 for zero-crossing rate) – likely due to paralysis of laryngeal/bulbar muscles. The distance between signal peaks and sound energy were best correlated to ALSFRS total (p<0.001 and p=0.003, respectively) – demonstrating that worse patients have less intense cough sounds (likely due to respiratory impairment). We are now increasing our controls; and correlating findings with CAPE-V.



Healthy control cough bouts sounds: Signal in the time domain (upside); Signal in the frequency domain (downside).

Conclusion: Our results suggest that cough features could emerge as predictors of ALS functional evaluation, at the convenience of using a smartphone.

Disclosure: Nothing to disclose.



ALS patient cough bouts sounds: Signal in the time domain (upside); Signal in the frequency domain (downside).

EPO-402

Preliminary data on safety and efficacy of Risdiplam treatment in a small cohort of adult 5q spinal muscular atrophy

A. Nanni[1] , G. Milella[1], G. Piccirilli[1], M. Ucci[1], S. Idrissi[1], A. Fraddosio[1], A. Introna[1], V. Scacco[2], M. Megna[2], I. Simone[1], E. D'Errico[1]

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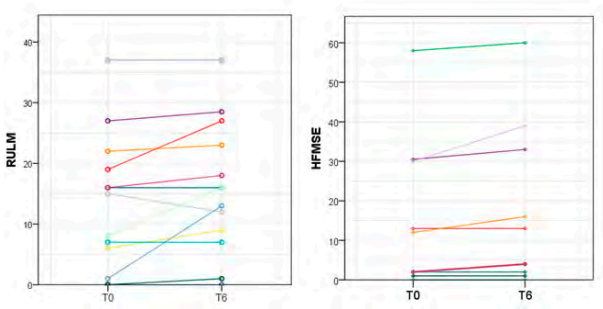
Background and aims: Risdiplam is an oral small-molecule drug recently approved for the treatment of Spinal Muscular Atrophy (SMA). It increases functional SMN (survival motor neuron) protein by modifying pre- mRNA splicing of the gene SMN2. Aim of the study was to investigate safety and efficacy of Risdiplam in our adult cohort of SMA patients.

Methods: Inclusion criteria were: clinical and molecular diagnosis of SMA2/SMA3; starting Risdiplam in adulthood; availability of clinical data and specific motor scale [Hammersmith Functional Motor Scale Expanded (HFMSE); Revised Upper Limb Module (RULM), six minute walking test (6MWT)] at treatment baseline (T0) and after 6 months (T6).
Results: We included 16 patients (10 SMA 2 and 6 SMA3), 41 years median age at first administration (IQR 21-54). HFMSE increased significantly from T0 to T6 (median values: 2, IQR: 0-13 vs 3, IQR: 0-15, p=0.026). The RULM significantly improved from T0 to T6 (median values: 15, IQR: 6-21 vs16, IQR: 9-26, p=0.024). No changes in 6MWT were detected at T6 in walking patients. Eleven patients (69%) were classified as responders at T6. Among all demographic and clinical variables, only the number of SMN2 copy was directly associated with clinical improvement (p=0.023). The one mild adverse effect was reversible diarrhoea in 18% of patients, requiring drug discontinuation. No severe-adverse events were reported.
Conclusion: Our data highlight the efficacy of Risdiplam even in the first six months of treatment, regardless of age/gender/functional clinical status at baseline and SMA type. Number of SMN2 copies influence positively clinical improvement.
Disclosure: Simone IL and E. D'Errico received grants from Biogen and Roche for educational events. All other authors have not disclosures.

		Median (IQR) or N. of patients (%)
Age at sampling (years)		41 (32-47)
Sex	Female	10 (62.5%)
	Male	6 (37,5%)
SMN2	2	5 (31,3%
	3	9 (56,3%)
	4	4 (12,5%)
Age at onset (months)		14 (9-36)
HFMSE	T0	2 (0-13)
	T6	3 (0-15)
RULM	T0	15.50 (6-21)
	T6	16.00 (9-26)



EPO-403

Clinical characteristics in amyotrophic lateral sclerosis with Sub-Saharan Africa ancestry

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Institute of Physiology, Instituto de Medicina Molecular-JLA, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal

Background and aims: Studies concerning epidemiological and clinical data of amyotrophic lateral sclerosis (ALS) in middle and low-incoming countries, including Sub-Saharan Africa (SA), are scarce. We attempted to characterize an ALS cohort with SA ancestry but followed in our ALS clinic in Lisbon.
Methods: A hospital-based retrospective study was conducted, including a total of 1633 ALS patients followed longitudinally. Patients were divided in two groups: SAALS (SA ancestry) and PALS (Portuguese ancestry). We looked for phenotype, genotype and prognosis.
Results: Thirty patients (1.8%) patients (15 men) were included in the SAALS group, with a median onset age of 51.5 years (15-73) and a predominant spinal-onset phenotype (23 patients, 76.7%). No patient had dementia. In this group onset age was lower ($p < 0.001$), and diagnostic delay longer (16 vs. 11 months, p=0.004). No other significant differences were found, including onset-region, familial history of ALS/FTD, rate non-invasive ventilation use or riluzole treatment. Ancestry was not an independent predictor of survival. C9orf72 repeat expansion testing was negative in SAALS group. One patient had a heterozygous FUS mutation identified by single-gene testing.
Conclusion: SAALS is a specific ALS population with a younger onset. Survival was not dependent on the ancestry. Regular follow-up and treatment in a specialized ALS Centre could explain the differences in survival between our results and previous data from African countries.
Disclosure: Nothing to disclose.

EPO-404

Epidemiology and comorbid disease of Spinal and bulbar muscular atrophy in South Korea

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Background and aims: Spinal and bulbar muscular atrophy (SBMA), also known as Kennedy's disease is caused by the increased CAG repeats in the Exon 1 of the androgen receptor. SBMA affects approximately 1:40,000 ~1:300,000 male people worldwide. The aim of this study was to investigate the prevalence and comorbidity of SBMA using Korean National Health Insurance database.
Methods: We conducted a retrospective cohort analysis of patients with the G12.25 code, registered from January 1, 2016 to December 31, 2019. Concomitant morbidity was assessed using various disease codes.
Results: A total of 294 SBMA patients with a G12.25 diagnosis were identified in the database during 2016-2019. The prevalence in South Korea of 2019 was 0.8:100,000. Comorbidities identified in more than 80% of SBMA were M79 (84%, Other soft tissue disorders), E78 (88.4%, Disorders of lipoprotein metabolism and other lipidemia), K30 (89.1%, Dyspepsia), K21 (90.5%, Gastro-oesophageal reflux disease), M54 (91.2%, Dorsalgia), J30 (92.2%, Vasomotor and allergic rhinitis), J20 (93.5%, Acute bronchitis), and K29 (99.7%, Gastritis and duodenitis). Of the 294 SBMA patients, 25 (8.5%) had accompanying cancer. The most common cancer was gastric cancer (5 patients).
Conclusion: According to our study, the prevalence of SBMA in South Korea is 0.8:100,000. In addition, there was increased association of dyslipidemia was found in 89% of the SBMA patients with accompanying cancer in 8.5%.
Disclosure: The authors have no disclosures.

EPO-405

Benchmarking care for adults living with spinal muscular atrophy (SMA) in Europe

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Background and aims: Spinal muscular atrophy (SMA) is a rare neuromuscular disease, leading to loss of motor milestones and reduced life expectancy. Individuals with SMA require complex care from a multidisciplinary team of healthcare professionals. Recommendations on standards of care (SoC) in SMA were updated before pharmacological treatments were widely available and are primarily focused on paediatric patients. SoC recommendations focused on the needs of adults are required. In partnership, F. Hoffmann-La Roche Ltd and SMA Europe are conducting a benchmarking project to assess how care is provided for adults living with SMA in 23 European countries, to identify gaps and to make recommendations for solutions and policy changes to improve SoC and quality of life for adults with SMA.
Methods: The study is being conducted in three phases: Phase 1: Reaching consensus on data collection methodology and benchmarking indicators. Phase 2: Collection and analysis of data from published sources; a structured survey targeting clinical experts, and semi-structured phone interviews with patient organisations. Phase 3: Summarisation of results, highlighting key gaps, best practices and recommendations. An expert committee of patients and healthcare professionals will advise on the project.
Results: Here we describe the study design of the project, focussing on the development of benchmarking indicators and data collection.
Conclusion: This study will help to identify care gaps for adults living with SMA in Europe. These results can be used by healthcare professionals, patient advocacy groups and policy makers to develop solutions to help improve SoC and quality of life.
Disclosure: This study is funded by F. Hoffmann-La Roche Ltd, Basel, Switzerland and is being conducted in partnership with SMA Europe. Data collection and analysis are being conducted by Hall and Partners, UK, and Weber Shandwick, Belgium, respectively. Writing and editorial assistance was provided by Chrysalis Medical Communications UK, in accordance with Good Publication Practice (GPP2022) guidelines (https://www.ismpp.org/gpp-2022). Data collection, analysis and medical writing support are funded by F. Hoffmann-La Roche Ltd.

EPO-406

Acoustic voice analysis as a useful tool to discriminate different ALS phenotypes.

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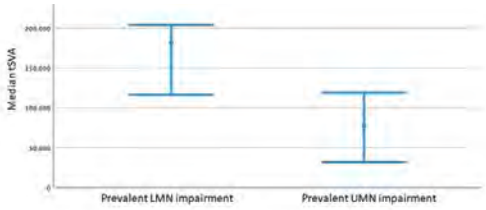
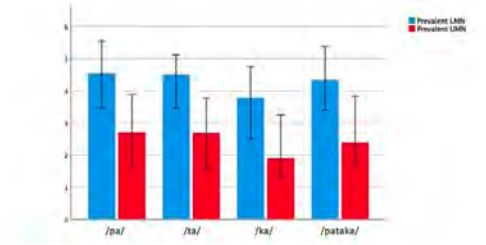
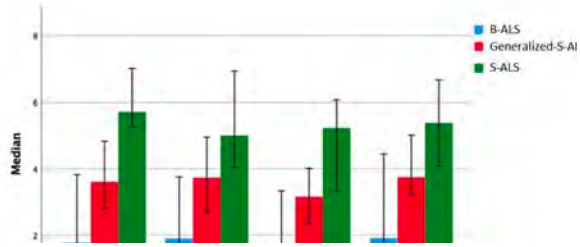
Background and aims: The assessment of upper (UMN) and lower motor neuron (LMN) impairment in bulbar regions remains still challenging in amyotrophic lateral sclerosis (ALS) patients. Particularly, there is a lack of quantitative measures able to discriminate spastic (UMN-impairment) by flaccid (LMN-impairment) dysarthria. Aim of the study was to evaluate acoustic voice analysis as useful tool to discriminate ALS phenotypes.

Methods: Thirty-six ALS patients were recruited (excluding severe dysarthrics). Patients' articulatory and motor speech production abilities were evaluated using the following acoustic parameters: Triangular Vowel Space-Area (tVSA), Alternating Motion Rates (AMR) and Sequential Motion Rates (SMR). The above-mentioned measures were tested in patients with prevalent UMN (pUMN) and LMN (pLMN) impairment (using the median of the Penn Upper Motor Neuron Scale-PUMNS, as a cut-off) and then in patients with bulbar-onset (B-ALS), with spinal-onset without bulbar symptoms (S-ALS) and with spinal-onset and bulbar symptoms at clinical evaluation (generalized-S-ALS).







Results: ALS patients with pUMN showed significantly lower values of tVSA, AMR and SMR than pLMNs. Among all the acoustic parameters, tVSA exhibited higher accuracy in discriminating patients with pUMN and pLMN (AUC: 0.83, CI:0.707–0.965, p<0.001). No differences were found in tVSA according to the site of onset. B-ALS patients showed significantly lower values of AMR and SMR compared to generalized-S-ALS and in turn, these latter exhibited lower values of the above-mentioned acoustic measures compared to S-ALS.
Conclusion: The acoustic voice analysis might be a useful tool to discriminate spastic by flaccid dysarthria and to incept the degree of bulbar involvement in ALS disease.
Disclosure: The authors have nothing to declare.

EPO-407

Ten-year Longitudinal Natural History and Prognosis in Amyotrophic Lateral Sclerosis in Southern Germany

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Background and aims: The ALS registry Swabia is an epidemiologic registry in Southern Germany covering a source population of 8.4 million inhabitants. We describe a 10 year follow-up of natural history and time to key clinical milestones (non-invasive ventilation (NIV), tracheostomy with invasive ventilation (TIV), percutaneous endoscopic gastrostomy (PEG)) and survival.
Methods: Between 10/2010 and 12/2020, n=1,171 people with ALS (pwALS) participated with annual follow-up. Three hundred forty-four pwALS were genetically tested.
Results: Overall, mean age at onset was 65.8 ± 11.2 years, 59.3% were male. Spinal/bulbar onset was observed in 65.3%/29.8%. A family history of ALS was reported by 6.2%. Median diagnostic delay was 7 months. 21.4% of pwALS used antidepressants at baseline and 73.5% Riluzole. Cumulative 5-year incidence for NIV, TIV, PEG and death was 28%/4%/17% and 83%, respectively. Median survival was 21.4 months (Q1 10.3, Q3 41.1). Thirty pwALS carried a C9ORF72, three a SOD1 mutation. C9ORF72 pwALS differed in age (61.3 ± 10.8) and onset (bulbar 40%) and had a faster progression (ALS-FRS-R -0.99/month versus -0.76/month in the entire cohort) with reduced survival. Each SOD1 pwALS had spinal onset and a positive family history, in contrast to C9ORF72 pwALS (50% with positive family history). Median diagnostic delay was 4 months in C9ORF72 and 3 months in SOD1 pwALS.
Conclusion: In Germany, TIV is rare while NIV/PEG is used in >25%/>15% of pwALS within 5 years. Riluzole treatment is regular and antidepressants used in up to 30%. Median survival was 21.4 months. Genetic forms alter clinical course and survival.
Disclosure: Specific data analysis in this investigator-initiated registry was supported by Biogen Inc. Biogen had no role in study design, and data collection within the registry, but gave input to the specific protocol, statistical analysis plan, and data interpretation for this project, and reviewed the final version of the abstract.

EPO-408

NIPA1 (GCG), NOP56 (GGCCTG) and NOTCH2NLC (GGC) expansion analysis in Italian Amyotrophic Lateral Sclerosis patients

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Background and aims: The discovery of hexanucleotide repeats expansion (RE) in C9Orf72 as the major genetic cause of ALS and the association between intermediate repeats in ATXN2 with the disorder suggest that repetitive sequence in the human genome plays a significant role in ALS pathophysiology. In this study, we aimed to define the frequency of REs in NIPA1, NOP56 and NOTCH2NLC genes; disclose the probable role of this expansion in ALS disease and the potential associations between phenotypes and the size of REs.
Methods: The REs were screened by both repeat-primed PCR and PCR-fragment analyses in 302 El Escorial diagnosed ALS patients. The distribution of repeats in the ALS cohort was evaluated and compared to a group of 197 healthy controls matched for age, gender, ethnicity. The chi-square test, Fisher exact test, Student's t-test and the Odd Ratio (OR) were used for statistical analysis.
Results: The REs distribution between ALS and control cases were similar (Fig. 1) with the presence of only a few borderline cases. There is a moderate association between long REs length and different clinical features such as age at onset, sex, site of onset, and family history.

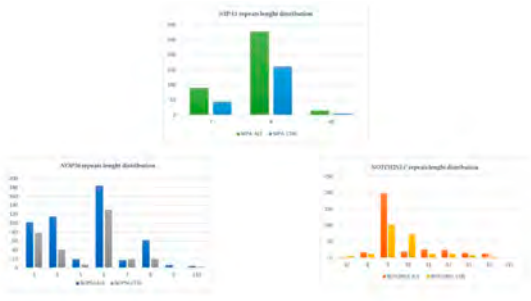

Fig 1

Conclusion: This study is the first to screen a cohort of ALS patients from southern Italy to evaluate the role of REs in the NIPA1, NOP56 and NOTCH2NLC genes in disease pathogenesis. Our results highlighted an extremely rare pathogenic REs in this gene not allowing an association with the disease.
Disclosure: The Authors disclose any conflicts of interest related to the manuscript.

EPO-409

Retinal degeneration in Amyotrophic Lateral Sclerosis phenotypes – preliminary data from a longitudinal study.

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Background and aims: Retinal measurements are biomarker candidates for many neurological diseases, but their significance in Amyotrophic Lateral Sclerosis (ALS) remains unestablished. We investigate retinal degeneration in ALS and its different phenotypes, its value as a progression biomarker and its prognostic implications.
Methods: Retinal Nerve Fiber Layer (RNFL) and Ganglion Cell Layer (GCL) are measured by Optical Coherence Tomography in 61 ALS patients and 12 healthy controls. Visual evoked potentials testing and cognitive assessment of ALS subjects are conducted concurrently, together with clinical examination, disease history collection, ALS-Functional Rating Scale (ALS-FRS) administration and blood collection for neurofilament (Nfl) levels determination. All tests are repeated after 12 months to detect progression. The latest available vital status information is used for analysis.
Results: When compared with controls, ALS subjects show lower mean GCL thickness in both eyes (right/left: 78,24/77,13 vs 83,5/83 μm – p 0,052/0,047) and global minimum GCL thickness (68,15 vs 78,17 μm – p 0,026). RNFL also shows thinning, without reaching statistical significance (right/left: 89,39/89,57 vs 94,66/95,41 μm – p 0,116/0,084). Preliminary longitudinal analysis on 15 subjects reassessed after 12 months only shows left-eye GCL thinning (mean/minimum 78,67/71,73 vs 74,47/69,90 μm – p 0,014/0,077).
Conclusion: We detected GCL thinning transversally and longitudinally, confirming retinal degeneration as a neurodegeneration marker. Broader analysis, including additional follow-up data, will explore the relationships between such phenomenon and different motor and cognitive involvement patterns, progression rate and Nfl levels.
Disclosure: The authors declare no competing interests. This work was supported by grants of the Italian Ministry of Health to Luca Diamanti (2021-2022).

EPO-410

Validity and Reliability of a New Clinical Myotonia Rating Scale for Non-Dystrophic Myotonia

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Background and aims: The severity of myotonia is difficult to assess without the use of a standardized and validated tool.
Methods: The Clinical Myotonia Rating Scale (CMRS) was evaluated in Myotonia Congenita (MC) and Paramyotonia Congenita (PMC) patients during the randomised cross-over double-blind mexiletine vs placebo MYOMEX trial. The CMRS comprises two consecutive sections: a myotonia severity scale rated on the patient's clinical exam and a disability scale rated on the patient's opinion on daily activities. The CMRS was assessed by two different investigators at baseline and by one of them (always the same for each patient) at the end of each treatment period. Interrater reliability was estimated by weighted Kappa coefficients. Intraclass correlation coefficients (ICC) were calculated for the global scores (GS). Bland & Altman methods were also used. Spearman correlation coefficients were estimated for correlations with the stiffness score using visual analogue scale (VAS) and the Individualized Neuromuscular Quality of Life (INQoL) self-questionnaire.
Results: 13 MC patients and 12 PMC patients were evaluated at six centres. Kappa ranged between -0.02 and 0.82. The highest interrater agreement was for eyelid blinking frequency and respiratory muscle intensity items (0.73 95%confidence interval [0.54;0.91] and 0.72 [0.45;0.98] respectively) as well as for hygiene and getting dressed (0.82 [0.59;1.00] and 0.73 [0.45;0.98] respectively). The ICC severity score was 0.54 and the ICC disability score - 0.65. The severity GS was strongly correlated with both the VAS (0.70, $p \leq 0.001$) and the INQoL (0.67, $p \leq 0.001$).
Conclusion: The CMRS is a promising scale and requires further validation in myotonic disorders.
Disclosure: Savine Vicart, Yann Pereon, Sabrina Sacconi and Bertrand Fontaine have received consulting fees from Lupin for other initiatives.

EPO-411

Expert group recommendations for cardiac assessment of non-dystrophic myotonic adult patients treated with mexiletine

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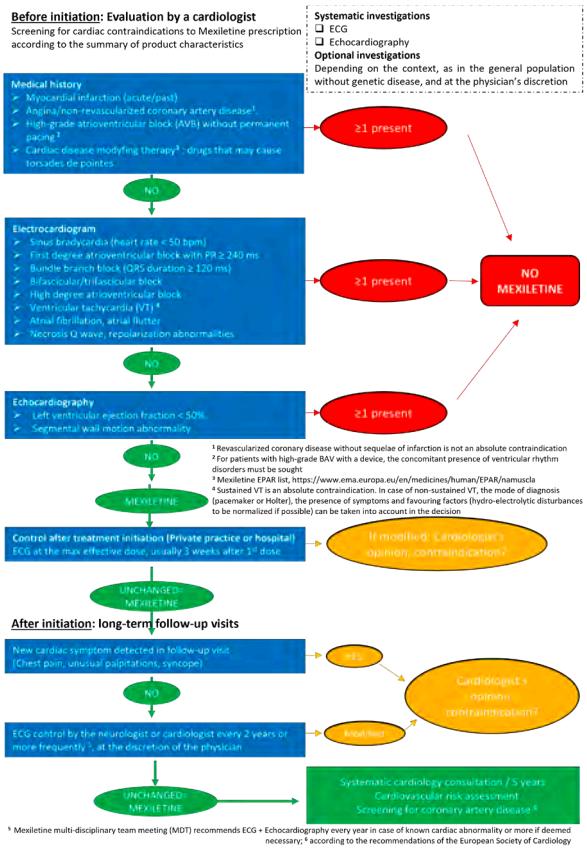
Background and aims: Mexiletine (NaMuscla™) is indicated for the symptomatic treatment of myotonia in adults with non-dystrophic myotonia (NDM). A cardiac assessment is required as mexiletine may have a pro-arrhythmic effect. Long-term safety data supporting use of mexiletine in patients with NDM combined with the extensive clinical experience of an expert group resulted in creation of an algorithm for cardiac monitoring of NDM patients treated with Mexiletine.
Methods: To define the treatment algorithm, several workshops with experts including 3 neurologists and 5 cardiologists from different French neuromuscular reference centres were set up. These workshops aimed to define the screening and surveillance tools required to avoid cardiac

events in mexiletine-treated patients. The recommendations are based on the summary of product characteristics (SmPC), a review of the literature on the safety of mexiletine-treated NDM patients and on the expertise of the authors.

Results: The expert group concluded that the cardiac safety profile of mexiletine in NDM patients appears similar to that of the general population. Therefore, NDM patients treated with Mexiletine should be monitored as any patient treated with a class 1b anti-arrhythmic. Cardiac assessment should be performed before initiation of mexiletine and at least every 2 years under treatment (Figure 1).



Mexiletine prescription algorithm in patients with NDM

Conclusion: An algorithm for cardiac safety monitoring in patients with NDM treated with mexiletine has been developed to assist the neurologists and cardiologists managing these patients.

Disclosure: All authors declare consulting fees from Lupin.

EPO-412

Rozanolixizumab responder and minimal symptom expression rates in generalised MG: Pooled Phase 3 and extension studies

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Background and aims: The Phase 3 MycarinG (MG0003/NCT03971422) trial demonstrated efficacy of one 6-week cycle of rozanolixizumab in generalised myasthenia gravis (gMG). We assessed consistency of cyclical rozanolixizumab efficacy and safety over time.

Methods: After 6 weeks of weekly rozanolixizumab/placebo in MycarinG, patients entered MG0004 (NCT04124965: ≤52 weeks of weekly rozanolixizumab) or MG0007 (NCT04650854: initial 6-week cycle; subsequent cycles administered on symptom worsening as determined by investigator's discretion, e.g. Myasthenia Gravis Activities of Daily Living [MG-ADL] increase ≥2/Quantitative Myasthenia Gravis [QMG] increase ≥3; "symptom-driven cycles") (Figure 1). Efficacy pool: data for patients with ≥2 symptom-driven cycles pooled across MycarinG, MG0004 (first 6 weeks) and MG0007 (interim analysis); safety pool: data for patients with ≥1 cycle across MycarinG (symptom-driven) and MG0007 (fixed/symptom-driven).

Results: 127 patients received ≥2 symptom-driven cycles of rozanolixizumab 7mg/kg (initial dose, n=69) or 10mg/kg (initial dose, n=58). MG-ADL change from baseline to Day 43, responder rates at Day 43 for MG-ADL, Myasthenia Gravis Composite and QMG and minimal symptom expression at any visit were consistent across cycles (Figure 2, Table). Treatment-free intervals (time from previous dose to first dose in symptom-driven cycle 1) were <4 weeks for 9.0%, 4–13 weeks for 59.3%, 13–26 weeks for 13.8% and ≥26 weeks for 4.2% of patients, with similar proportions at the next cycle. Treatment-emergent adverse events (most mild to moderate) occurred in 77.4% and 91.6% of patients receiving ≥1 cycle of rozanolixizumab 7mg/kg and 10mg/kg.

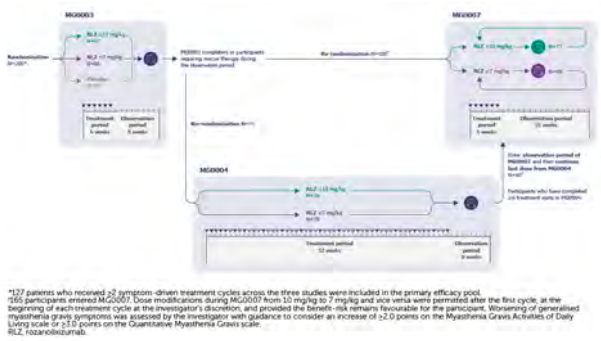
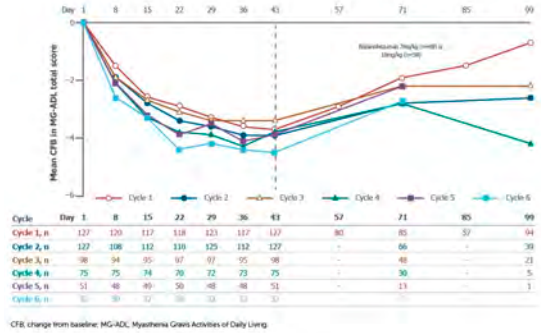


Figure 1. Pooled analysis design



Cycle	Day 1	8	15	22	29	36	43	57	71	85	99
Cycle 1, n	127	120	117	118	123	117	127	80	85	57	94
Cycle 2, n	127	108	112	110	125	112	127	-	66	-	39
Cycle 3, n	98	94	95	97	97	95	98	-	48	-	23
Cycle 4, n	75	75	74	70	72	73	75	-	30	-	5
Cycle 5, n	51	48	49	50	48	48	51	-	13	-	1
Cycle 6, n	31	30	32	30	33	32	33	-	-	-	-

Figure 2: Mean CFB in MG-ADL score per cycle, in patients who received ≥2 symptom-driven cycles of rozanolixizumab

Proportion of MG-ADL, MGC and QMG responders and proportion achieving MSE in patients who received ≥2 symptom-driven cycles of rozanolixizumab

	Cycle 1 n/N (%)	Cycle 2 n/N (%)	Cycle 3 n/N (%)	Cycle 4 n/N (%)	Cycle 5 n/N (%)	Cycle 6 n/N (%)
responders*	**94/127** (74.0)	**95/127** (74.8)	**63/98** (64.3)	**55/75** (73.3)	**40/51** (78.4)	**23/32** (71.9)
responders†	**93/127** (73.2)	**95/127** (74.8)	**68/98** (69.4)	**55/75** (73.3)	**35/50** (70.0)	**22/31** (71.0)
responders‡	**87/127** (68.5)	**78/125** (62.4)	**63/97** (64.9)	**51/74** (68.9)	**30/51** (58.8)	**21/32** (65.6)
	35/127 (27.6)	**34/127** (26.8)	**25/98** (25.5)	**24/75** (32.0)	**17/51** (33.3)	**13/32** (40.6)

Table: Proportion of MG-ADL, MGC and QMG responders and proportion achieving MSE in patients who received ≥2 symptom-driven cycles of rozanolixizumab

Conclusion: Rozanolixizumab efficacy was maintained over symptom-driven cyclical treatment and multiple endpoints. Funding: UCB Pharma.

Disclosure: This study was funded by UCB Pharma. Detailed author disclosures will be provided in the oral/poster presentation

EPO-413

Attenuated total reflection-Fourier transform infrared spectroscopy (ATR-FTIR) in muscle diseases

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Background and aims: Inherited muscle diseases are a heterogeneous group of clinical conditions, characterized by histological and functional abnormalities of skeletal muscle. Attenuated Total Reflectance (ATR) is one of the sampling technologies used for infrared spectroscopy and, as a rapid and non-destructive technique, it is increasingly used in different biological applications. The aim of this study was to evaluate whether the biochemical profile determined by the ATR-Fourier transform infrared (FTIR) spectroscopic technique would allow to distinguish patients affected by late-onset Pompe disease (LOPD), Becker muscular dystrophy (BMD), limb-girdle muscular dystrophies (LGMD), and healthy subjects (HS).

Methods: A total of 40 participants were included: 11 LOPD, 10 BMD, 10 LGMD, 9 HS. For ATR-FTIR, muscle samples were cut at 10 μm in cross-section and placed onto diamond/ZnSe crystal for spectral analysis.

Results: The results obtained show that the spectroscopic fingerprint embeds sufficient information to allow a correct classification of the majority of participants in three groups: dystrophic (BMD and LGMD) and metabolic (LOPD) myopathies, healthy subjects (accuracy 88.4±7.1%). The ATR-FTIR analysis was also effective in classification rates using a two-class model: LOPD vs LGMD (accuracy 95.7±3.2%), LOPD vs BMD (accuracy 82.9±4.6%) and LOPD vs BMD+LGMD (accuracy 93.4±3.0%).

Conclusion: In conclusion, our data suggest that ATR-FTIR profile is a reliable diagnostic biomarker for LOPD, BMD and LGMD. Future directions will include evaluating its role as a prognostic biomarker in these genetic diseases, also analyzing biofluids, and the ability of this technique to shed light on the underlying pathogenic mechanisms.

Disclosure: The authors declare no conflict of interest.

EPO-414

A case of late-onset Congenital Myasthenic Syndrome associated to PREPL heterozygotic mutation

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Background and aims: We report the first case of a late-onset CMS associated with a heterozygous missense variant in Prolyl-Endopeptidase-Like (PREPL) gene.

Methods: Biochemical tests, muscle MRI, electrodiagnostic testing, muscle biopsy and NGS.
Results: A short 52-years-old Italian male with clinical onset in the first decade with impaired ocular motility and diplopia. From third decade he developed bilateral eyelid ptosis, slowly progressive fatigability and weakness in the upper and lower limbs. Neurological examination showed bilateral ophthalmoparesis, shoulder-girdle hypotrophy and weakness, mild weakness of iliopsoas, rectus femoris and hamstring muscles and reduced ROTs. Fatigability tests were positive. CPK was normal. Electrodiagnostic testing showed a pathological repetitive nerve stimulation, a pathological single fiber EMG finding and a myopathic pattern on EMG with normal nerve conductions. The dosage of anti-AChR-Abs, anti-MuSK-Abs and anti-LRP4-Abs resulted negative and also the chest CT. Muscle MRI showed no significant changes. Muscle biopsy showed a slight myopathic changes (marked variability in size, nuclear centralizations and a prevalence of type I fibers). CMS was suspected and we started Pyridostigmine with benefit. We performed whole-exome sequencing and found a heterozygous missense variant in the PREPL gene: c.473T>C (p.Ile158Thr).
Conclusion: PREPL deficiency is a rare autosomal recessive inherited congenital myasthenic syndrome characterized by neonatal hypotonia, feeding problems, neuromuscular symptoms and growth deficit. In almost all cases is caused by biallelic deletion/duplication in PREPL gene. However, the function of this gene remains unknown. In our patient we found only one PREPL mutation, which might explain his clinical picture of CMS with a milder and later clinical expression.
Disclosure: Nothing to disclose.

Headache 3

EPO-415

Patients with Suspected Idiopathic Intracranial Hypertension: Is there a Reliable Score to Predict the Opening Pressure?

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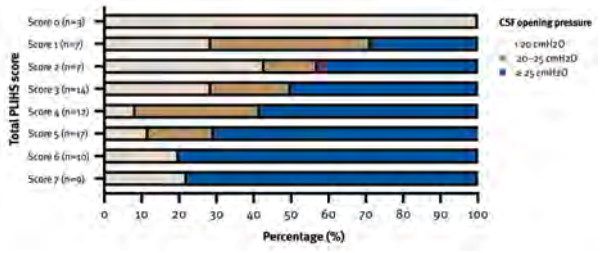
Background and aims: The Pre-Lumbar Puncture Intracranial Hypertension Scale (PLIHS) was reported to identify patients with suspected idiopathic intracranial hypertension (IIH) and high likelihood of pathologically raised opening pressure (≥25cmH2O). However, external validation is missing.
Methods: Patients from the Vienna IIH database who underwent diagnostic lumbar puncture for suspected IIH were applied the PLIHS (papilledema [Frisén grade II or higher], tinnitus, empty sella sign, distension of perioptic subarachnoid space, BMI ≥30; range 0–7; cut-off ≥3 points).
Results: We included 79 patients (87.3% female, mean age 36.0 years [12.2], median BMI 31.2 [27.5–37.1]), with 58.2% having opening pressure of ≥25cmH2O. Median PLIHS score was 4 (range 0–7), and it differed between patients above and below 25cmH2O (5 [1–7] vs. 3 [0–7]; p=0.001). AUC for predicting opening pressure ≥25cmH2O was 0.71 (95% CI 0.60–0.83) and did not differ from the reported one (0.84, 95% CI 0.78–0.90)1. Observed and reported sensitivities (89.1% vs. 87.4%), NPV (70.6% vs. 78.6%) and PPV (66.1% vs. 76.4%) were comparable, whereas observed specificity was lower (36.4% vs. 61.7%; p=0.029). PLIHS ≥3 points was associated with a nearly 5-fold increased risk for ≥25cmH2O (OR 4.69; 95% CI 1.46, 15.07; p=0.010), while from single PLIHS parameters only papilledema (OR 5.08; 95% CI 1.93, 13.36; p<0.001) and BMI ≥30 (OR 3.40; 95% CI 1.32, 8.79; p=0.012) were associated with elevated opening pressure.



Distribution of total PLIHS score in relation to CSF opening pressure.

Conclusion: In patients with suspected IIH, the PLIHS displays only moderate diagnostic accuracy with low specificity. It could potentially be improved by adding quantitative measures (OCT, orbital ultrasonography).
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-416

CLUSTER HEADACHE DECREASES LIFE EXPECTANCY: A 40-YEAR LONGITUDINAL STUDY

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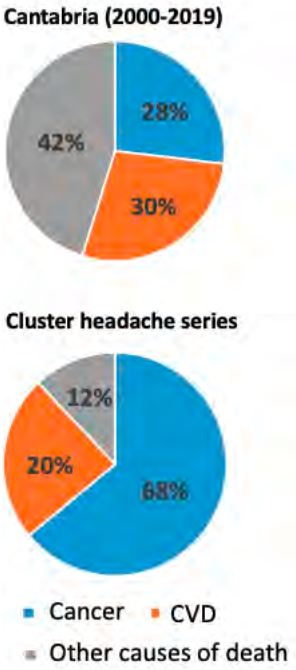
Background and aims: Cluster headache is the most frequent trigeminal-autonomic headache and one of the most disabling pains that exist. Patients affected by this entity frequently present unhealthy lifestyle habits. Given its relatively low prevalence, there are few data on the morbimortality associated with this pathology.
Methods: Our aim was to assess the morbimortality of cluster headache by calculating years of potential life lost (YPLL) in the patients included in a cluster headache registry of a tertiary hospital in Spain since 1974. Data were compared with those expected for the adjusted general population of our region according to the "Encuesta Nacional de Salud".
Results: There were 25 deaths among the 162 patients included. 21 of them (84%) lived fewer years than the expected mean for their sex and year of death, with a mean of 13.7 YPLL (SD 9.3).Cancer was the most frequent cause of death, and it was significantly more frequent among individuals with cluster headache than in the general population of our region (68% vs 28.5% p<0.001). Cardiovascular diseases were the second reason for death in this series. The percentage of male smokers was significantly higher among individuals with cluster headache than in the general population or our region (p=0.0095).

Subject	Age of death	YPLL	Cause of death
1	74	6	Cancer
2	78	2	Cancer
3	63	12	Cancer
4	72	8	Cancer
5	64	16	Suicide
6	69	11	Cancer
7	63	17	Cancer
8	72	8	Cancer
9	76	4	Cancer
10	56	24	Cancer
11	66	14	Cancer
12	77	8	Cancer
13	62	18	Cancer
14	75	10	Cardiovascular disease
15	69	11	Cancer
16	43	37	Drugs
17	50	30	Cancer
18	63	17	Cancer
19	76	4	Cancer
20	76	4	Cancer
21	59	26	Cardiovascular disease

YPLL and cause of death of patients who died prematurely in our series



Causes of death in our region (Cantabria) and ir our cluster headache series

Conclusion: Cluster headache patients who died of our series presented an average of almost 14 YPLL, mostly due to cancer followed by cardiovascular disorders. Tobacco could play an essential causal role, so it is essential to establish measures aimed at controlling unhealthy lifestyle habits in this population since the time of diagnosis.
Disclosure: Nothing to disclose.

EPO-417

Clinical predictors of good outcome in refractory chronic cluster headache treated with occipital nerve stimulation

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La Paz University Hospital, Madrid, Spain

Background and aims: Occipital nerve stimulation (ONS) is a surgical treatment with good clinical evidence for the treatment of refractory chronic cluster headache (rCCH). However, the irregular response rate reported in different studies, and the associated cost make it necessary to investigate predictors of response.
Methods: We conducted a cross-sectional study through a review of the medical records of rCCH patients in our Headache Clinic. Epidemiological, clinical, and outcome variables were described.
Results: Twenty rCCH patients were treated with ONS. A good clinical outcome (at least three severe attacks per week that impact quality of life despite preventive or symptomatic treatment) was observed in 35.0% (7/20). Headache comorbidity, history of alcohol consumption or opioid use, and comorbid psychiatric disorders did not differ between patients with good and poor outcome after surgery. Age of onset, diagnostic delay, and time to surgery was also similar. Patients with good outcome presented less frequently a sense of restlessness or agitation (71.4% vs 100%, p=0.042), seasonal exacerbations (0.0% vs 61.5%, p=0.005), active tobacco use (50.0% vs 100%, p=0.021) and comorbid pain conditions such as fibromyalgia or chronic pain of traumatological origin (0.0% vs 46.2%, p=0.032).
Conclusion: Some clinical characteristics such as the absence of ictal restlessness and seasonal exacerbations may be related to a good outcome after ONS surgery in rCCH patients. Comorbid chronic pain conditions could be related to poor outcome, such as active tobacco use. Comorbidity with other headache disorders, opioid abuse, and diagnostic delay were not associated with poor outcome.
Disclosure: JA Membrilla has received honoraria as a consultant and speaker for TEVA and Novartis. Lilly, TEVA and Novartis have funded JA Membrilla's research and teaching activities. Boston Scientific, Lilly and TEVA have collaborated with JA Membrilla for his registration at scientific meetings.

EPO-418

Chronic cluster headache: description of epidemiology, clinical features, and treatment in a tertiary hospital

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Background and aims: Cluster headache (CH) is a relatively rare primary headache disorder in which large series of the chronic form are lacking. In this study, we aimed to describe the characteristics of chronic CH (CCH) patients.
Methods: We conducted a cross-sectional study through a review of the medical records of CCH patients in our Headache Clinic. Epidemiological, clinical, treatment, and outcome variables were described.
Results: From a series of 87 CH patients, 34 (39.1%) had CCH. Women represented 35.3% (12/34). Diagnostic criteria of refractory CCH (as defined by the European Headache Federation Consensus statement) were met in 76.5% (26/34). The mean age at diagnosis was 38.0 (SD 11.8), with a median diagnostic delay of 4.5 years (1.0-9.5). All patients underwent verapamil and topiramate treatment, being discontinued in 50.0% (17/34) in both cases. Lithium was used in 67.7% (23/34) and discontinued in 78.3% (18/23). OnabotulinumtoxinA was initiated in 85.3% (32/34) but discontinued in 46.9% (15/32). Most treatment discontinuations were due to inefficacy. Occipital nerve stimulation (ONS) was implanted in 58.8% (20/34), with 45.0% (9/20) remaining active. Further data on pharmacological and neurosurgical therapies are described. At the date this work was conducted, 55.9% (19/34) had poor clinical outcomes (having at least three severe attacks per week). In the remaining 44.1% (15/34), ONS was the treatment that achieved improvement in most cases (46.7%, 7/15).
Conclusion: CCH is not uncommon in some Headache Clinics, meeting refractoriness criteria in most cases. Half of the patients have poor prognosis, with ONS being the treatment with the best outcomes.
Disclosure: JA Membrilla has received honoraria as a consultant and speaker for TEVA and Novartis. Lilly, TEVA and Novartis have funded JA Membrilla's research and teaching activities. Boston Scientific, Lilly and TEVA have collaborated with JA Membrilla for his registration at scientific meetings.

EPO-419

Neck pain and migraine: clinical characterization of an often overlooked symptom

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Background and aims: Neck pain is increasingly recognized as a symptom which often accompanies migraine attacks. It is, however, rarely listed among the classical migraine symptoms. We aim to describe the relationship between migraine and neck pain: its prevalence, timing within the attack, severity relatively to other symptoms, and efficaciousness of abortive medications in treating this symptom.
Methods: Questionnaires were distributed in a headache clinic after informed consent was obtained. All patients were 18 years old or older and had a diagnosis of episodic or chronic migraine with or without aura according to ICHD-III. Demographic and clinical information was collected. Standard descriptive and inferential statistics were employed.

Results: Fifty patients were included, 86.0% female, with a mean age of 44.7 ± 12.7 years, 38.0% of which fulfilled criteria for migraine with aura. Average number of migraine attacks per month was 9.4 ± 7.2 days and 64,0% used some preventive treatment. 60.0% of all patients reported neck pain as one of their symptoms. Of these, 50.0% rated it as one of their three most bothersome symptoms, 53.3% reported neck pain onset to be simultaneous with headache and 73.3% noticed an improvement when using abortive medication. Neck pain prevalence did not differ between the groups diagnosed with migraine with and without aura (68.4% vs 54.8%, p=0.341).
Conclusion: Neck pain is a frequent and bothersome symptom of migraine, even if often overlooked by physicians. Direct inquiry about this symptom may help us to better understand the migraine burden and improve the quality of life of patients.
Disclosure: Nothing to disclose.

EPO-420

HEADWORK a tool for monitoring MABs efficacy on work disability in migraine patients

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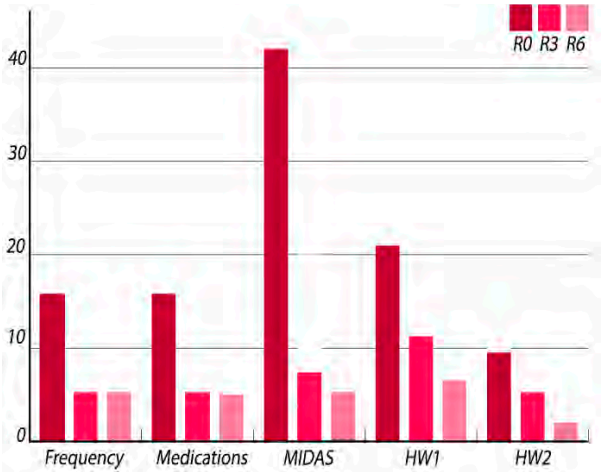
Background and aims: The efficacy of Monoclonal antibodies (MABs) is generally assessed with disease related metrics, but is crucial to evaluate the impact on the global burden of migraine. HEADWORK (HW) is a tool, developed to assess the work disability of migraineurs. Aim of this study was to test HW on migraine patients treated with MABs.
Methods: We enrolled 69 patients treated with MABs at the Headache Centres of "C.Besta" (Milan) and "C.Mondino" (Pavia). They were assessed with the HW questionnaire at baseline and at the 3rd (M3) and 6th month (M6) of treatment. HW questionnaire consists: "Work-related difficulties" (HW1); "Factors contributing to work-related difficulties" (HW2).
Results: Population: 15 M and 54 F, mean age (49.5y±8.6), mean age at onset of disease (18y±7), mean duration of disease (34y±11.6). We observed a marked and consistent reduction in 'classical' indicators: monthly migraine days (15±5.7 at baseline, 5±5.8 at M3, 6±6.2 at M6), medications per month (15±8.7 at baseline, 5±12.1 at M3, 6±6.6 at M6), MIDAS (41±43.2 at baseline, 6.5±11.3 at M3, 5±13 at M6), HIT-6 (66±2.8 at baseline, 59±8.7 at M3, 59±8.2 at M6). HW scores paralleled: HW1 (20±8.1 at baseline, 11±9 at M3, 7±8.2 at M6), HW2 (9±6 at baseline, 5±4.8 at M3, 3±3.8 at M6).



Results

Conclusion: Our data show that HW reveals a trend parallel to classic clinical indicators during MABs treatment. HW appears a suitable tool to assess migraine-related work disability in these patients.
Disclosure: Nothing to disclose.

EPO-421

Migraine patients need increased amounts of sleep during attacks to maintain neurological functioning

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Background and aims: There is a clear, but unexplained association between migraine and sleep. Migraine patients frequently describe increased sleep need during migraine attacks, and that sleep can ease the attack. In this study we investigated the effect of insufficient sleep in migraine, in order to explain why migraine patients have increased need for sleep during attacks.
Methods: Fifty-four migraine patients were examined both after two nights of eight-hour habitual sleep and two nights of four-hour restricted sleep. We recorded short interval intracortical inhibition (SICI), intracortical facilitation (ICF), and beta event related desynchronisation (beta-ERD) and synchronisation (beta-ERS). The effect of sleep condition and time after attack end or postictal versus interictal phase were evaluated in linear mixed models.
Results: SICI ($p = 0.041$) and beta-ERS ($p < 0.001$) were more reduced, and beta-ERD ($p = 0.002$) more increased after sleep restriction the shorter time that had elapsed since the previous attack. For the postictal phase within 24 hours after attack end specifically, SICI ($p = 0.013$) was more reduced and ICF (ICF 8, $p = 0.003$; ICF 10, $p = 0.021$) more increased after sleep restriction.

Conclusion: Insufficient sleep during or shortly after migraine attacks result in a dysfunction in GABAergic inhibition. This inhibitory alteration resembles that previously described in healthy subjects after total sleep deprivation. Thus, migraine patients have increased need for sleep during migraine attacks to maintain normal neurological functioning.

Disclosure: The authors declare that there is no conflict of interest relevant to this abstract.

EPO-422

Migraine-related stigma and its association with seeking care and migraine disability: Results from OVERCOME (EU) Study

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Background and aims: Migraine is a debilitating neurological disease associated with several consequences including migraine-related stigma. Here, we describe the frequency of migraine-related stigma and its association with seeking care, quality of life (QoL) and migraine-related disability.

Methods: The ObserVational survey of the Epidemiology, tReatment and Care Of MigrainE Europe [OVERCOME (EU)], is a cross-sectional, population-based survey (Oct-2020 to Feb-2021), conducted in Germany and Spain, as part of an overarching study program including the US and Japan. As part of the survey, patients reported their experiences with migraine-related stigma and were categorised, based on responses, to yes (sometimes/often/very often) or no (rarely/never). Results are summarised with descriptive statistics.

Results: OVERCOME (EU) respondents (N=20,756) had a mean age of 40.4 years, 60.3% were female. Migraine-related stigma was experienced by 32.6% (n=6760; Fig.1A). This cohort were more likely to hesitate seeking care (48.3%) than those who rarely/never experienced migraine-related stigma (30%; Fig.1B). Experiencing migraine-related stigma was associated with poorer QoL (MSQ-role function-restrictive 52.3[20.3] vs 68.0[20.6]) and higher headache days/month (HDs/M; mean[SD]=4.7[5.5] vs 3.5[4.5]; Figs.2). A greater proportion of those with migraine-related stigma compared to those without reported 15+ HDs/M (7.2% vs 4.1%), severe disability (MIDAS IV score=21+: 34.9% vs 16.0%) and severe interictal burden (MIBS Score=5+: 66.8% vs 34.2%; Figs.1B, 3).

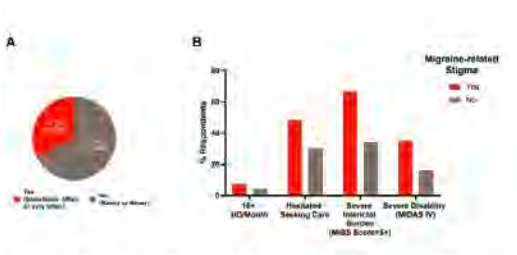

Figure 1. Proportion of respondents who experienced migraine-related stigma (A) and associated migraine characteristics (B). N=20,756. HD/month: headache days per month; MIBS: Migraine Interictal Burden Scale; MIDAS: Migraine Disability Assessment Score; N: number of total respondents; n: number of respondents per group.

Figure 1. Proportion of respondents who experienced migraine-related stigma (A) and associated migraine characteristics (B).

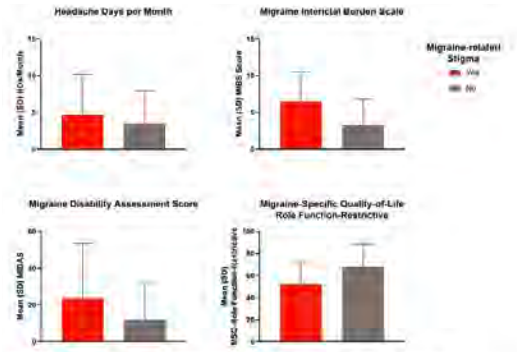

Figure 2. Migraine characteristics of OVERCOME (EU) survey respondents categorised based on experience of migraine-related stigma (yes or no). MIBS: Migraine Interictal Burden Scale – Score 0 = None; Score 1-2 = Mild; Score 3-4 = Moderate; Score 5+ = Severe. MIDAS: Migraine Disability Assessment Score – MIDAS I (score 0-5) = Little or No Disability; MIDAS II (score 6-10) = mild disability; MIDAS III (score 11-20) = moderate disability; MIDAS IV (score 21+) = severe disability; HD/Month: headache days per month. MSQ-RFR: Migraine-Specific Quality of Life Questionnaire-Role Function-Restrictive - Scale-0-100, where scores approaching 100 indicated better quality of life.

Figure 2. Migraine characteristics of OVERCOME (EU) survey respondents categorised based on experience of migraine-related stigma (yes or no).

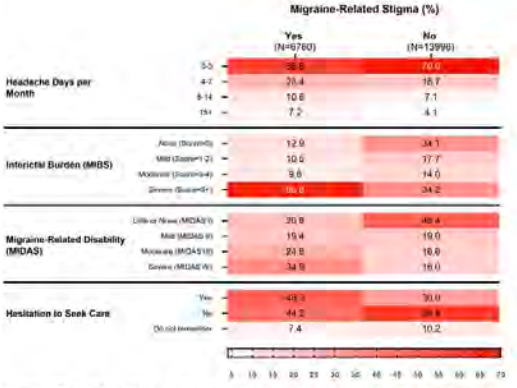

Figure 3. Distribution of respondents within migraine characteristic groups based on experience of migraine-related stigma. Heatmap displays percentage of respondents who experienced migraine-related stigma (yes) or rarely/never experienced migraine-related stigma (no) within specified groups relating to migraine characteristics. MIBS: Migraine Interictal Burden Scale; MIDAS: Migraine Disability Assessment Score; N: total number of respondents.

Figure 3. Distribution of respondents within migraine characteristic groups based on experience of migraine-related stigma.

Conclusion: In OVERCOME (EU), experiencing migraine-related stigma was associated with hesitation seeking care, higher HDs/M, poorer QoL and severe disability – specifically interictal burden. Migraine-related stigma remains a prevalent issue, further understanding and action are required to reduce its occurrence and improve patient QoL.
Disclosure: DN, AZ, SG and GD are employees and minor shareholders of Eli Lilly and Company. JP reports: serving on advisory boards for Allergan-Abbvie, Amgen-Novartis, Lilly, and TEVA; serving as speaker / on speaker boards for Allergan-Abbvie, Amgen-Novartis, Eli Lilly and Company, and TEVA; grant support for research or education from Allergan and Lilly; and serving on the editorial board for Headache. SE reports: grant support from Novartis, Teva, Perfood, Lilly and Lundbeck; serving as speaker / on advisory boards for Lilly, Lundbeck, Novartis, Perfood and Teva.

EPO-423

Evolution of migraine attack duration

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Background and aims: Migraine is a prevalent neurological disorder characterized by disabling headache attacks. Although headache days/per month is well studied among migraine patients; evolution of attack duration (hours) along in years is not fully investigated to our knowledge. There is lack of study investigated attack duration related factors and tendencies particularly among adults.
Methods: We hypothesized that due to accumulated attacks through years and decades, migraine attack duration could be prolonged. We grouped patients according to attack duration (short (4-12 hours), medium duration (13-24 hours) and long duration (>24 hours)) and evaluated related factors and tendencies.
Results: The study group consisted 694 patients. Long attack duration (>24 hours) group were significantly older ($p<0.001$). We observed a significant lineer association with increasing age and attack duration. Longer attacks observed more common at females ($p=0.007$). Headache days frequency per month were similar between groups. Headache history (for months) were significantly differed for long attack group ($p<0.001$). This feature also showed a lineer association similar to age of patients (median values for groups 60, 72, 120 moths respectively). The long attack groups' pain intensity was significantly higher than others ($p<0.001$).
Conclusion: This study reveals migraine attack duration is significantly changing with age of sufferer and disease course. This novel finding supports attack duration evolution throughout the life. This is the first study explicitly reveals attack duration's association with patient age and disease duration among adults.
Disclosure: This study reveals headache attack duration is evolutioning with accumulated attacks. This promising finding could lead to new studies and further studies are needed.

EPO-424

Effectiveness and safety of CGRP-mAbs in migraine related to mitochondrial diseases

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Background and aims: Migraine affects nearly 55% of patients with mitochondrial disease (MD), with attacks which are difficult to treat compared to other migraine patients. Migraine mechanisms, characterized by the imbalance between brain demand and energy resources, may be shared also by patients with MD, where dysfunctional glucose metabolism works as a key pathophysiological substrate for migraine attacks. To date, migraine response to monoclonal antibodies acting on CGRP (CGRP-mAbs) in patients with MD is unknown.
Methods: Monthly subcutaneous galcanezumab 120 mg have been administered as preventive treatment in two women with genetically proven neuropathy, ataxia, and retinitis pigmentosa syndrome (NARP) and progressive external ophthalmoplegia (PEO), suffering from chronic migraine, respectively without and with medication overuse. Patients underwent a monthly follow-up for six months to assess galcanezumab effectiveness, safety and tolerability.
Results: After the third Galcanezumab administration, both reported a significant improvement in monthly migraine days (from an average of 20 to 2 migraine, and from an average of 22 to 14 respectively in the patient with NARP and PEO), headache intensity, number of pain-killers intake and pain-killers response. We cannot exclude that CGRP-mAbs may act not only peripherally modulating CGRP-induced meningeal vessels vasodilation and neurogenic inflammation but also within the trigeminal ganglion, modulating, through CGRP pathway inhibition, the dysfunctional neuronal glycolytic metabolism.
Conclusion: CGRP-mAbs could represent an effective and safe preventive therapeutic strategy in patients with genetically proven mitochondrial disease complaining migraine attacks. Future studies with a larger sample of patients will further support our observations.
Disclosure: Nothing to disclose.

EPO-425

Serum alpha and beta-CGRP levels in chronic migraine patients before and after CGRP monoclonal antibodies

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Background and aims: To analyse the evolution of alpha and beta-CGRP circulating levels throughout the treatment with CGRP monoclonal antibodies (mAb) in chronic migraine (CM) patients.
Methods: We recruited CM patients beginning mAb treatment along with sex and age paired healthy controls (HC). Blood was extracted before initiation of mAb, at two-weeks (M0.5) and three months (M3) after first dose in CM, always in migraine-free periods, and once for HC. Determinations of alpha and beta-CGRP serum content were carried out using ELISA kits specific for detection of each isoforms.
Results: We assessed 96 CM and 78 HC. Baseline alpha-CGRP levels were significantly (p=0.019) elevated in CM (54.6±32.5 pg/mL) compared to HC (45.2±27.5 pg/mL) and normalized over the course of mAb treatment (M0.5: 47.4±27.8 pg/mL; M3: 46.0±29.0 pg/mL) (Fig. 1). Absolute decrease of alpha-CGRP throughout the treatment significantly correlated with the decrease in monthly headache days (p=0.02) (Fig. 2). Negative modulation of alpha-CGRP significantly associated with positive treatment outcome scores at the Patient Global Impression of Change scale (p<0.01) (Fig. 3) and with stop fulfilling analgesic overuse criteria (p<0.01). Beta-CGRP levels did not differ at baseline between CM patients (4.6±3.5 pg/mL) and HCs (4.5±2.6 pg/mL) nor was modulated by mAb treatment (M0.5: 4.6±3.1 pg/mL; M3; 4.5±2.9 pg/mL).

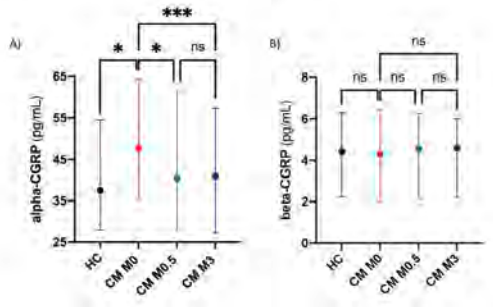

Figure 1.. Circulating levels of A) alpha-CGRP and B) beta-CGRP in healthy controls (HC) and patients with CM at baseline (CM M0), at two-weeks (CM M0.5) and at three-months (CM M3) after first dose of mAb treatment.

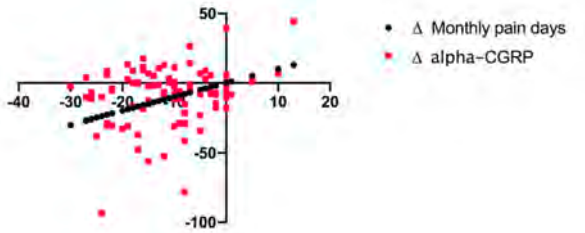

Fig. 2. XY plot showing the correlation between Δ monthly pain days (x axis) and Δ alpha-CGRP in pg/mL (y axis)

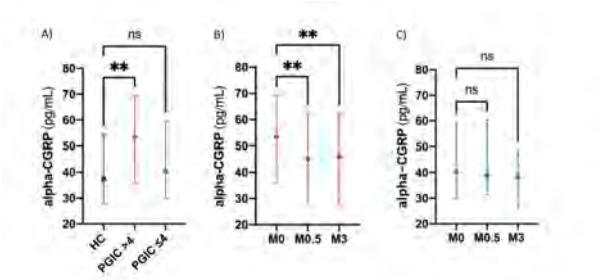

Fig. 3. Circulating levels of alpha-CGRP in: A) healthy controls (HC), patients with CM with a PGIC score >4 (PGIC>4) and those with a score >4 (PGIC>4) at baseline. B) patients with CM with PGIC score >4 at baseline (CM M0), at two-weeks (CM M0.5)

Conclusion: Treatment with mAB, regardless of its target, is able to progressively normalize basally increased alpha-CGRP levels in CM and this effect correlates with efficacy measures, which supports a role of this neuropeptide as the first CM biomarker.
Disclosure: This work was supported by grants from the Instituto de Salud Carlos III (PI20/01358), IDIVAL (INNVAL 20/25) and Lilly grant I5Q-NS-O002.

EPO-426

Clinical phenotypes in chronic migraine: Principal component analysis in the Italian National Headache Registry (RICe)

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Background and aims: The clinical heterogeneity of migraine raises the need of phenotypical classification to support the diagnostic-therapeutic process. This could be particularly important when considering chronic migraine (CM) and medication overuse headache (MOH) due to their high socio-economic impact. Migraine diagnostic criteria (ICHD-3) mainly focus on attack characteristics; this study aims to use a nationwide database to refine the characterization of patients subgroups.
Methods: A principal component analysis (PCA) was performed on 1238 patients diagnosed with migraine with or without aura, CM or MOH and included in the Italian Registry of Headaches (RICe Study) between April 2020 and March 2021.
Results: We extracted 3 components from categorical variables: the first inversely correlated the diagnosis of CM and MOH with the presence of migraine diagnostic criteria, while in the second one they were directly correlated, describing a group of "typical" patients; the initial localization of pain and the presence of high pain intensity and allodynia were associated in the third one. Considering

the quantitative variables, 2 components were extracted: the first related to age, BMI and monthly migraine days (MMD); the second was correlated with pain intensity.
Conclusion: A group of patients suffering from CM or MOH would be less identifiable through the migraine diagnostic characteristics, resulting in problems of underdiagnosis. Another group presents a significant association between BMI, age, and MMD, thus revealing possible risk factors for chronification. Further studies could evaluate the association between these phenotypes and other relevant characteristics (impact on daily life and on therapeutic efficacy).
Disclosure: No disclosures to declare.

EPO-427

Patient-reported outcomes and burden in resistant and refractory migraine: results from the REFINE study

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Background and aims: We assessed the burden of resistant (RES) and refractory (REF) migraine – defined according to the 2020 European Headache Federation criteria – in a real-world setting, according to patient-reported outcomes (PROMs).
Methods: The REFINE study is an observational, multicenter, international study which aim is to compare baseline characteristics, comorbidities, and PROMs of patients with RES, REF, and non-resistant and non-refractory migraine (NRNR).
Results: We included 612 patients with a median age of 46 years (IQR=37-55), of which 340 (55.6%) with NRNR migraine, 228 (37.3%) with RES, 44 (7.2%) with REF. Individuals with RES and REF migraine reported higher number of monthly migraine days compared with those with NRNR (median=10, IQR=5-16 vs. median=15 IQR=10-20 and median=16, IQR=10.5-25; p<0.001). In RES and REF groups, PROMs also revealed higher presence of anxiety (HADS_A scale; p<0.001) and depression (HADS_D scale; p<0.001) symptoms and poorer sleep quality (ISI score; p<0.001) compared with NRNR. RES and REF individuals reported higher impact of migraine on daily life (HALT score; p≤0.001) when compared to NRNR subjects (table1).
Conclusion: RES and REF are associated with relevant migraine burden, confirmed by the migraine frequency and PROM scores.
Disclosure: Nothing to disclose.

	Total (n = 612)	Non-resistant and non-refractory migraine (n = 340; 55.6%)	Resistant migraine (n = 228; 37.3%)	Refractory migraine (n = 44; 7.2%)	p-value
HIT-6 score, median (IQR)	62 (57-66)	62 (57-66)	65 (61-68)	66 (61-70)	≤0,001
HALT score, median (IQR)	31 (13-65)	20 (7-46)	50 (23-81)	60 (31-115)	≤0,001
HADS score - anxiety symptoms, median (IQR)	8 (5-11)	7 (4-10)	9 (5-12)	9 (5-12)	≤0,001
HADS score - depression symptoms, median (IQR)	6 (3-9)	5 (2-8)	8 (4-10)	10 (6-13)	≤0,001
ISI score, median (IQR)	9 (4-15)	8 (3-13)	11.5 (4-16)	13 (7-17)	0,006

Table 1. Patients reported outcomes measures (PROMs) scores reported as medians (IQR).

Neuroimmunology 3

EPO-428

Antineuronal antibodies of unknown significance: assesing risk of cancer in a Spanish reference laboratory cohort

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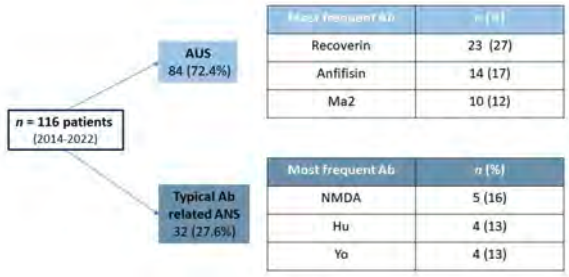
Background and aims: Widespread use of commercial assays has increased the detection of autoantibodies (Ab) related to autoimmune neurological syndromes (ANS). However, they also often reveal antibodies of unknown significance (AUS), apparently not related to a suspected ANS. We aim to describe the oncological risk of these cases.

Methods: Retrospective study including patients with positive results for intracellular or cell surface Ab detected in serum and/or cerebrospinal fluid in a reference laboratory of a Spanish tertiary hospital between 2014-2022. AUS were defined as the presence of Ab in the absence of a concordant ANS. Ab were classified into high/intermediate/low-risk of paraneoplastic neurological syndromes (PNSs) according to updated Graus criteria. Clinical records were reviewed for any tumour detection at acute phase and after two-year follow-up. We compared tumour detection rate between patients with AUS and those with typical Ab-mediated neurological syndromes.

Results: We included 116 patients (54.3% men, 61.6±17.5 years). The most frequent Ab was anti-Recoverin (20.7%). Fifty-eight patients (50%) had a high-risk Ab. The most frequent syndrome was autoimmune encephalitis (9.5%). Twelve patients (10.3%) had a high paraneoplastic-risk syndrome, and 77 (66.4%) low-risk or non-autoimmune disorders. We identified 83 (71.6%) patients with AUS. A novel cancer was detected in 37.9% of patients, being less frequent in patients with AUS (OR=0.34, p=0.017). When only high-risk Ab were considered, AUS also presented less tumour association than remaining Ab (OR=0.22, p=0.005).

Paraneoplastic risk	Type of antibody	Total (*n*)
High	Yo	9
	Sox1	3
	Tr	3
	Hu	6
	CV2	9
	Anfifisin	15
	Ma2	12
	Ri	1
Intermedium	NMDA	6
Low	CASPR2	2
	GAD65	7
	LGI1	5
Undetermined (not included in Graus criteria)	Recoverin	24
	Titin	9
	Zic4	5

Distribution of antibodies in our cohort, classified according to Graus criteria into high risk for paraneoplastic neurological syndromes (>70% with an underlying malignancy), intermedium (30-70%), and low risk (<30%).



Most frequent antibodies found in each group. AUS: antibodies of unknown significance. Ab: antibody. ANS: autoinmune neurological syndromes.

Tumour detection rate in each group: in the whole cohort (A), and considering only high-risk antibodies (B).

Conclusion: In our cohort, AUS were less likely to be related to cancer development. Ab testing should be directed by clinical presentation to avoid misdiagnosis.

Disclosure: Nothing to disclose.

EPO-429

Epigenetic characterization of monocyte-derived microglia (MDMi) differentiation and ATP-driven innate immune memory

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Background and aims: Microglia are the brain's immune regulators. The dysregulated microglia activation observed across neurologic diseases may result from consecutive stimuli, in which a previous insult would pre-condition subsequent responses. Purinergic signalling is considered to be implicated in neuropathology and high ATP levels have been shown in settings like epilepsy. The functional characterization of human microglia is ethical and technically challenging. The MDMi in vitro model is promising due to its speed, scalability, low-cost, and replication of main microglial features. We developed an MDMi culture and investigated ATP-driven preconditioning in microglia activation.
Methods: Peripheral blood monocytes were from healthy donors using CD14+ microbeads. MDMi cells were obtained by incubating monocytes in serum-free conditions supplemented with cytokine cocktail. MDMi were treated with ATP and posteriorly LPS. Cells were characterized by optic microscopy, flow cytometry, RT-PCR, ELISA and DNA methylation using Infinium MethylationEPIC BeadChips.
Results: MDMi showed elongated and ramified morphology and upregulation of canonical markers at day 7. Differentially methylated positions (DMPs) between MDMi and monocytes were enriched for binding motifs of microglia lineage transcription factors, like PU.1 and IRF8. MDMi cells treated with LPS showed higher pro-inflammatory activation when previously conditioned with ATP. Such was accompanied by DNA methylation reprogramming of immune-related pathways, adrenergic receptor binding and nucleotide phosphorylation.
Conclusion: MDMi carry microglial epigenetic microglial traits, which validates it as a valuable model to study microglia. Unbalanced microglia activation may be modulated by an ATP-driven epigenetic reprogramming. A better characterization of these mechanisms would be a step forward in understanding microglia's role in neuropathology.
Disclosure: Nothing to disclose.

EPO-430

Prevalence, clinical profiles, and prognosis of Stiff-person syndrome in Japanese nationwide survey

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Background and aims: To elucidate epidemiological, clinical, immunological profiles, and treatment of stiff-person syndrome (SPS) in Japan.
Methods: A nationwide epidemiological survey was conducted using an established method. Data processing sheets were randomly sent to all specialist departments of internal medicine, neurology, pediatrics, psychiatry, and neurosurgery throughout Japan to identify patients with SPS who were seen between January 2015 and December 2017.
Results: The estimated number of patients with SPS was 257 (95% confidential interval [CI]: 161-354), and the prevalence was 0.2 per 100,000 (95% CI, 0.13-0.28). Detailed clinical profiles were available for 55 patients. The median age at onset was 51 years (range, 7–83 years) and 41 (75%) were female. Of these, 58% had Classic SPS, 25% had stiff-limb syndrome (SLS), and 18% had SPS-plus. Autoantibodies were positive in 68% patients; glutamic acid decarboxylase-65 (GAD65) antibodies in 44%, α1 subunit of glycine receptor antibodies in 20%, and γ-aminobutyric acid-B receptor antibodies in 4%. After immunotherapies, the median modified Rankin score (mRS) was 2 at the last visit. The coexistence of type 1 diabetes mellitus was independent risk factor for poor outcome (mRS $\geq$3) in GAD65 -positive patients (Odds ratio, 16.0, 95%CI 2.8–139.9, p=0.001).
Conclusion: This study provides current epidemiologic and clinical status of SPS in Japan. GAD65 antibodies were most frequent, however, their titers were not correlated with the response to therapies. The outcome of SPS was generally favorable, but more aggressive immunotherapies may be necessary for patients associated with type 1 diabetes.
Disclosure: All researchers report no disclosures.

EPO-431

White matter alterations in a mouse model of anti-NMDAR encephalitis by active immunization

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Background and aims: Anti-NMDA receptor (NMDAR) encephalitis is a neurological disorder that associates with neuropsychiatric manifestations caused by antibody-mediated internalization of the receptor. Studies with advanced imaging show extensive changes in white matter integrity in most patients. Antibodies from patients have been shown to alter NMDAR function in cultured oligodendrocytes. Here, we aim to explore the pathogenic mechanisms of white matter alterations by active immunization.
Methods: 8-week-old female C57BL/6J mice were immunized at days 1 and 28 with 200 µg of the GluN1 356-385 peptide or saline along with AddaVax adjuvant and Pertussis Toxin. NMDAR antibodies in serum and CSF were determined by cell-based assays, and the effects of the antibodies were assessed with confocal brain tissue immunohistochemistry. Behavioural alterations were assessed with a standard panel of tests: Novel Object Location test (memory), Pre-Pulse Inhibition (psychotic-like behaviour), and Tail Suspension Test (depressive-like behaviour).
Results: Compared with control mice, those immunized with GluN1 356-385, showed decreased Myelin Basic Protein (MBP) clusters in the corpus callosum, as well as striatum and cerebellum white matter. These findings were associated with the presence of NMDAR antibodies and a significant decrease in synaptic NMDAR clusters in the brain. Accompanying symptoms included memory deficit, acute psychotic-like behaviour, and chronic depressive-like behaviour.
Conclusion: This model of active immunization causes alterations of the white matter and confirms previous studies with the model of passive transfer of patients' antibodies. The model will help to determine the immunobiology of the disease and how pharmacological interventions can be used as an adjuvant to immunotherapy.
Disclosure: J. D. receives royalties from Euroimmun for the use of NMDAR as an antibody test.

EPO-432

Immunomodulatory aspects of therapeutic plasma exchange in neurological disorders – a pilot study

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Background and aims: Plasma exchange (PLEX) represents a rescue therapy for autoimmune disorders. While used for several neurological indications, investigations on the immunomodulatory effects of PLEX have been sparse. We aimed to explore changes in antibodies, cytokines and lymphocytes associated with therapeutic PLEX.
Methods: We included 10 patients (3 women, average age: 55 ± 19 years) that underwent PLEX for various neurological autoimmune disorders between 2020 and 2022. We assessed various pathogen-specific antibodies, total immunoglobulin levels (IgM, IgA, IgG; IgG1/2/3/4), interleukin-6 concentrations (IL-6, pg/mL) and main lymphocyte subset counts (cells/µL) prior to PLEX (pre-PLEX), immediately after PLEX (post-PLEX) and four weeks later (follow-up/4wk). We calculated proportional changes of pathogen-specific antibody levels and absolute changes of total immunoglobulins, IL-6 and lymphocyte subsets referenced by their respective pre-PLEX baseline values.
Results: Pathogen-specific antibody levels were reduced by 86% ($p < 0.05$) post-PLEX and recovered to 55% ($p < 0.05$) at follow-up/4wk. Similar, total IgG (and subclasses 1-4), IgA and IgM were reduced by 86% ($p < 0.05$) post-PLEX and recovered to 80% ($p < 0.05$) after 4 weeks. We found no effects on B- and T-cell counts. The average IL-6 increased from 4.0 pg/ml (95% CI, 0.5 – 7.7) to 18.9 pg/ml (95% CI, 2.9 – 34.9, $p = 0.071$) at post-PLEX.

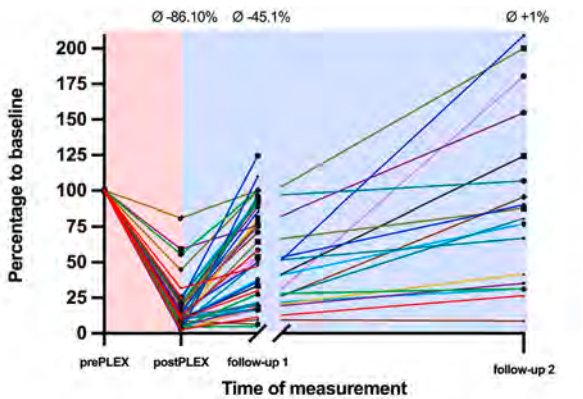

Fig. 1. Impact of PLEX on pathogen-specific antibody levels

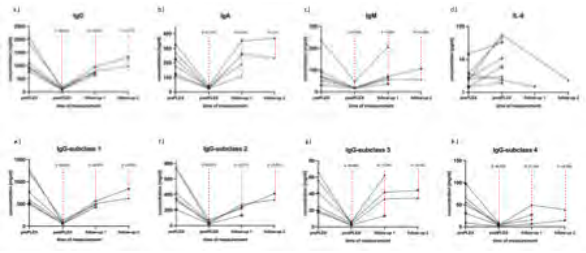

Fig. 2: Impact of PLEX on immunoglobulins IgA/IgM/IgG

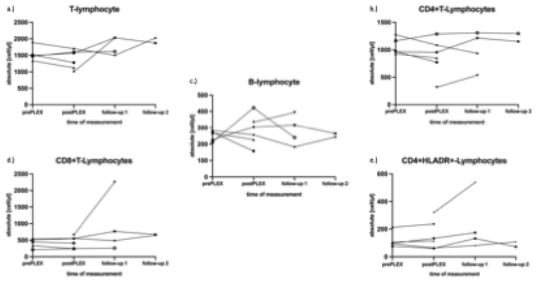

Fig. 3 Impact of PLEX on main lymphocyte subsets

Conclusion: PLEX effects a profound but transient reduction of circulating antibodies. While this indicates no loss of control for pathogens, it has also implications on the treatment strategy of the underlying autoimmune disorder. The impact on IL-6 needs further investigation.
Disclosure: Nothing to disclose.

EPO-433

Autoimmune Encephalitis and Long-Term Cognitive and Functional Outcomes

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Background and aims: Autoimmune encephalitis (AE) comprises a heterogeneous group of inflammatory brain diseases. The extent of dysfunction varies, and it may persist in the long-term. However, few studies have detailed the cognitive and functional outcomes of these patients.
Methods: We carried a single-centre observational cross-sectional study, including ≥18-yo patients diagnosed with EA both with autoantibodies and with definite seronegative limbic encephalitis, at a Portuguese tertiary centre (January 2007-December 2021). A neuropsychological evaluation and questionnaires to assess functional status were applied in a scheduled appointment. For cognitive scales, impairment was considered below 1.5sd from normative values.
Results: All 13 patients were independent according to the modified Rankin Scale, however, Functional Assessment Inventory in Adults and the Elderly identified functional impairment in 5 (38.5%). Only 4 patients (30.8%) had an entirely normal neuropsychological evaluation. Five patients (41.7%) showed cognitive impairment on MoCA. Seven patients (58.3%) showed impairment in at least one memory test; the same holds for executive functions. Older age at disease onset correlated with higher functional disability, lower MoCA, and higher verbal memory and executive impairment. Also, higher CSF protein counts correlated with impaired verbal memory and executive functioning tasks.
Conclusion: Although most times subtle, we found frequent multimodal impairment in this AE population, especially in older individuals. Disability and cognition ought to be systematically screened in this setting.
Disclosure: The authors declare no conflict of interest.

EPO-434

Characterization of Subclinical Spinal Cord and Optic Nerve MRI Lesions in the N-Momentum Trial

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Background and aims: Neuromyelitis optica spectrum disorder (NMOSD) causes inflammatory attacks on the optic nerve (ON), spinal cord (SC), and brain/brainstem. Subclinical MRI findings have unknown significance therefore we evaluated the frequency, prognosis, and response to inebilizumab (INEB).
Methods: Gadolinium-enhancing (Gd+)T1 and T2 weighted MRI of SC, ON, and brain/brainstem were performed at baseline and RCP end (Week 28) in participants without NMOSD attack. Serum glial fibrillary acidic protein (sGFAP) concentrations were determined using single-molecule array assay.

Results: 134 participants with full neuroaxis MRI and no NMOSD symptoms at RCP end, 20(15%) had asymptomatic Gd+T1-SC lesions, and 65(49%) had asymptomatic Gd+T1-ON lesions. Subclinical Gd+T1 lesions in the SC/ON were shorter in length(mm) than attack-related lesions: SC p=0.08, ON p<0.001. Total Gd+T1 and T2 subclinical SC-lesions were less frequent with INEB than Placebo at RCP end; mean(±SE): Placebo=0.74(0.50,1.09), INEB=0.27(0.20,0.35). The frequency of new subclinical SC and ON lesion formation decreased with continued INEB over the open-label period. More participants with subclinical T2-lesions in the SC (but not ON) had a 2-fold change increase in sGFAP from baseline vs. those without lesions, p<0.001. Subclinical Gd+T1 and T2 lesions in SC were associated with domain-specific attacks in the following year: Gd+T1, p<0.0001; T2, p=0.03.
Conclusion: Subclinical Gd+T1 ON lesions are more frequent than SC lesions. The total length of subclinical Gd+T1 ON/SC lesions was smaller than attack-associated lesions. The subclinical lesions predicted future attacks for the SC but not the ON. Both ON and SC lesion formation frequencies were reduced with repeated inebilizumab treatment.
Disclosure: FP Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi Genzyme, Teva, Guthy-Jackson Char Found, German Res Council (DFG Exc 257), German Compet Network for MS, OCTIMS study comittee JLB MedImmune, Alexion, Antigenomycs, BeiGene, Chugai, Clene Nanomed, Genentech, Genzyme, Reistone, Roche, Imcyse, TG, Alexion, Novartis, NIH JJC Roche, UCB, Horizon HPH Bayer, Biogen Idec, Celgene Receptos, CSL Behring, GeNeuro, Genzyme, Horizon, MedDay, MedImmune, Merck Serono, Novartis, Roche, Sanofi, TG Thera HJK NRF of Korea, Aprilbio, Eisai, Alexion, Aprilbio, Altos Biologics, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll BioPharma, Handok, Horizon, Kolon LS, Medimmune, Merck Serono, Mitsubishi Tanabe, Novartis, Roche, Sanofi Genzyme, Teva-Handok, UCB KF AbbVie, Asahi Kasei, Biogen, Chugai, Eisai, Merck, Mitsubishi Tanabe, Novartis, Ono, Roche, Sumitomo Dainippon, Takeda, Teijin, UCB, Horizon, Ministry of Edu Sci and Tech of Japan, Ministry of Health, Welfare, Labour of Japan OA German Research Found (DFG), German Ministry of Edu and Res (BMBF), Bayer, Biogen, Genzyme, Horizon, Novartis, Teva, Almirall, MedImmune, Merck Serono, Roche BAC Alexion, Atara, Autobahn, Avotres, Biogen, Boston, EMD Serono, Gossamer, Hexal/Sandoz, Horizon, Immunic AG, Neuron23, Novartis, Sanofi, Siemens, TG Thera, Therini, Genentech DMC, KRP, MAS Horizon The study and analyses funded by Horizon.

EPO-435

Proteomic fingerprint to understand treatment response and long-term outcome in anti-NMDAR encephalitis

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Background and aims: Anti–N-Methyl-D-Aspartate receptor encephalitis (anti-NMDARE) is a neurological disorder caused by pathogenic antibodies affecting NMDA receptors. It is a life-threatening disease and many patients end up on the intensive care unit. Despite its severity, most patients ultimately improve with immunotherapy, albeit recovery is prolonged and often incomplete. Biomarkers to predict treatment response and outcome are scarce and their discriminative value is limited, making treatment decisions difficult and expert opinion only. We aim to 1) identify immunological pathways relevant in anti-NMDARE (apart from the antibodies), and 2) identify biomarkers to better predict treatment response and outcome.
Methods: We investigated the CSF proteome from 29 untreated anti-NMDARE patients using SomaScan, a proteomic platform able to detect ~1,350 proteins including low abundant proteins, and compared these to 15 healthy controls. Difference in expression was confirmed using Luminex. Pathway analysis was performed by String and Ingenuity.
Results: Preliminary results indicate that the expression of TNF sR-II and sL-Selectin was upregulated in anti-NMDARE (median 57,032 vs 17,487RFU and 106,482 vs 46,636RFU, respectively, both p<0.0001)), especially in those with a poor prognosis. Upregulation was confirmed by Luminex (median concentration 1,037 vs 135pg/ml and 11,600 vs 4,113pg/ml, respectively, both p<0.0001). This upregulation was joined by alterations in related pro-inflammatory cytokines (e.g. IL6) and chemokines (e.g. CXCL8) in anti-NMDARE patients.
Conclusion: The proteomic footprint identified pathways involved in the pathophysiology of anti-NMDARE, allowing testing of targeted biomarkers by easier, high-throughput methods. This proof-of-principle study opens the road towards better understanding of anti-NMDARE and development of tailored treatments for anti-NMDARE patients.
Disclosure: I do not have a conflict of interest.

EPO-436

Immunomodulatory effects of diroximel fumarate on T cells subsets during experimental autoimmune neuritis in Lewis rats

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Background and aims: Diroximel fumarate is an immunomodulatory drug, approved for the treatment of multiple sclerosis. In view of the limited therapeutic options for human polyneuritis, we used the animal model of experimental autoimmune neuritis(EAN) in the Lewis rat to study the effects of diroximel fumarate on autoimmune inflammation through T cells in the peripheral nervous system.
Methods: EAN was induced by immunization with the neuritogenic peptide (amino acids 53-78) of P2 myelin protein. Clinical course, nerve conduction studies, histological analyses of the peripheral nerves and the intestinal immune system as well as rt-PCR analyses were performed with a focus on pro inflammatory VLA-4 / CXCR4 and TGFb / Smad 7 axes.
Results: Preventive treatment beginning at the day of immunization with DRF given at 90 mg/kg twice daily by oral gavage significantly ameliorated clinical neuritis by reducing demyelination and axonal degeneration in the nerve conduction studies. Histology revealed a significantly lower degree of inflammatory infiltrates in the sciatic nerves. Furthermore VLA-4 / CXCR4 and TGFb / Smad 7 axes, which become activated through the early EAN phase are both modulated through DRF both in the peripheral nerve and the intestinal immune system (jejunum), thereby mediating its immunomodulatory properties.
Conclusion: We conclude that DRF modulates the immune system in EAN through reduction of the proninflammatory properties of the VLA-4 / CXCR4 axis, which mediates inflammatory infiltration in the peripheral nerves and TGFb / Smad 7 axes, which increases proinflammatory potential of peripheral T cells both in the intestinal immune system and the peripheral nerves.
Disclosure: The authors report no disclosures.

EPO-437

Small fiber involvement and macrophage-dependent axonal pathology in the rat model of experimental autoimmune neuritis

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Background and aims: Experimental autoimmune neuritis (EAN) is a common animal model for acute human immune-mediated polyneuropathies. Although already established in 1955, a number of pathophysiological mechanisms in the peripheral nervous systems still remain unknown. We provide an extensive characterization of EAN progression in Lewis rats, including new insights into the integrity of small nerve fibers, neuropathic pain and macrophage activation.
Methods: Acute EAN was induced with P253-78 peptide and consequently investigated using the CatWalk XT, electrophysiological and histopathological analyses, qPCR, dorsal root ganglia outgrowth studies as well as the von Frey hair and Hargreaves test. For the longitudinal set up, rats were sacrificed at d10 (onset), d15 (peak), d26 (recovery), d29 (late recovery).
Results: We confirmed the classical T-cell and macrophage driven inflammation and the primarily demyelinating nature of the EAN. The dual role of macrophages in EAN is implicated by the high number of remaining macrophages throughout disease progression. Furthermore, different subpopulations of macrophages based on Cx3cr1, Pf4 and Mgl1 expression were identified. In addition, a modulation of the sensory system in EAN was detected. An outgrowth of small fibers in the plantar skin at onset and peak of the EAN went parallel to the development of an acute hyperalgesia mediated through transient receptor potential vanilloid 1 modulation.
Conclusion: Our data depict EAN as a primary demyelinating disease with implicated axonal damage, small unmyelinated fiber impairment throughout the disease progression course and the pivotal role of macrophages in the effector and during the recovery stage.
Disclosure: Nothing to disclose.

EPO-438

Meningeal carcinomatosis or neurological immune-related adverse event? A diagnostic challenge in the ICI-treated patient

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Background and aims: Immune Checkpoint Inhibitor drugs (ICIs) can be associated with neurological immune-related adverse events (n-irAEs) such as polyradiculoneuritis. Leptomeningeal carcinomatosis (LC), a rapidly fatal cancer

manifestation, can mimic polyradiculoneuritis by involving spinal roots. Here, we present two challenging cases of ICI-treated patients with polyradiculoneuritis and LC.
Methods: Data were collected from medical records. Cerebrospinal fluid (CSF) histology was performed by cytospin followed by May-Grunwald Giemsa staining.
Results: Case 1: 67 yo man with pulmonary adenocarcinoma treated with pembrolizumab presented with progressive numbness, weakness in his legs and cranial neuropathy. Spine MRI showed nerve roots contrast-enhancement with pseudonodular aspect. Case 2: 47 yo man with renal-cell carcinoma treated with nivolumab presented with distal painful dysesthesia in his legs. Spine MRI showed contrast enhancement of nerve roots at the cauda equina. Both patients showed a long disease course (14 and 2 months) and inflammatory signs on CSF (cells: 43 and 77 cells). Cytospin identified rare likely cancerous cells with increased cytoplasm-nucleus ratio and intense basophilia. Both patients were treated with high-dose steroids, with poor response, and restarted ICI-treatment. Patient 1 died after 3 months, while patient 2 is still on follow-up.
Conclusion: LC diagnosis is challenging. In our cases, the long disease duration could be explained by the effect of ICIs on LC, whereas the inflammatory signs detected in CSF likely reflect the ICI-increased immune response against the tumor localized into the spinal roots. In this scenario, continuation of ICIs is crucial to support the anti-tumoral response.
Disclosure: I have no conflict of interest to declare.

EPO-439

Targeting the gut-brain axis to dampen neuroinflammation using a murine model of multiple sclerosis

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Background and aims: Multiple sclerosis (MS) and its animal model, the experimental autoimmune encephalomyelitis (EAE), are demyelinating diseases of the central nervous system (CNS). Both are mediated by auto-reactive CNS-specific T lymphocytes activated in the periphery. Gut microbiota is an emerging factor involved in MS pathogenesis that needs further characterization. We hypothesize that myelin-specific T lymphocytes, in particular Th17 subsets, acquire their encephalitogenic properties by interacting with the gut microbiota during colonic lamina propria infiltration in the EAE adoptive transfer model.
Methods: We used a broad-spectrum antibiotic cocktail to unravel the impact of gut microbiota in the EAE Th17 cell adoptive transfer murine model and characterized immune cells from the colon by flow cytometry and RNA sequencing. Next, we treated myelin-specific Th17 cells with microbiota-derived metabolites from mouse fecal filtrates to decipher their impact on Th17 cells using flow cytometry. Feces were characterized for metabolomics by UPLC-MS/MS.
Results: Antibiotic treatment attenuates EAE adoptive Th17 cell transfer disease and reduces CNS-specific Th17 cell infiltration in the CNS. It decreases their pathogenic signature and their pro-inflammatory cytokine and chemokine receptor expression. Gut-derived fecal filtrates treatment of myelin-specific Th17 cells enhances their pathogenicity in a microbiota-dependent manner. Furthermore, adoptive transfer of Th17 cells exposed to fecal filtrates increases EAE disease severity.
Conclusion: We propose that the interaction between adoptively transferred Th17 cells and microbiota-derived metabolites induces a pathogenic switch in the colon and enhances their migratory abilities leading to increase neurological disease severity.
Disclosure: CP has participate to advisory boards for Biogen, Merck, Novartis, Roche none related to this work Author Details

EPO-440

Etiology of optic neuritis (ON) in the tropics.

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Background and aims: ON, an inflammatory demyelinating optic neuropathy, has heterogeneous etiologies, which include CNS inflammatory demyelinating disorders such as multiple sclerosis (S, NMOSD and myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD), systemic autoimmune diseases (SLE, Sjogren's), post viral demyelination (post viral ON and ADEM) as well as infections such as tuberculosis and viruses. The purpose of this study was to evaluate the causes of ON in the tropics.
Methods: Clinical, radiological data, immunological tests performed, cerebrospinal fluid analysis, visual evoked potentials (VEPs) and results of all relevant tests of patients presenting with ON was prospectively collected. Patients were categorised according to the final diagnosis.
Results: The final diagnosis in 131 patients who presented with ON was as follows: MS-22, NMOSD-24, MOGAD-20, idiopathic ON-39, post-viral ON-3, ADEM-1, recurrent ON (with negative aquaporin-4 and MOG antibody)-2, idiopathic neuroretinitis-6, chronic relapsing inflammatory optic neuropathy (CRION)-7, Vogt Koyanagi Harada syndrome-1 and infection in 6 (tubercular meningitis-4 and

dengue-2) patients. Along with post-viral ON, six patients with CNS inflammatory disorders (2 each with MS, NMOSD and MOGAD) had prior history of viral infection. Mean age of MS, NMOSD and MOGAD patients was 26.8, 42 and 26.5 years respectively.
Conclusion: MS, NMOSD and MOGAD together formed a large proportion (50.4%) of ON whereas infection related (post-viral, ADEM and infectious ON) were just 10.6%. Preceding viral infection was seen even in 4.6% patients with CNS inflammatory disorders. Average age of patients with NMOSD was much higher than MS and MOGAD.
Disclosure: Nothing to disclose.

EPO-441

Nasal administration of anti-CD3 monoclonal antibody improves cognition in mouse models of Alzheimer's disease

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Background and aims: Alzheimer's disease (AD) is a neurodegenerative disorder in which microglial cells change from a homeostatic (M0) to a neurodegenerative (MGnD) phenotype and become activated, contributing to neuroinflammation and cognition decline. We have shown in several mouse models of central nervous system (CNS) inflammation that nasal administration of anti-CD3 monoclonal antibody localizes to the cervical lymph nodes where it induces IL-10-producing Treg cells that migrate to the CNS to control inflammation by inducing a MGnD phenotype. Here, we investigated whether nasal anti-CD3 would improve cognition in APP-PS1 and 3xTg mice, which are wildly used for evaluating the cognitive dysfunction.
Methods: Nasal anti-CD3 or isotype control were administered at a dose of 10mcg/mouse, 3x/week for 2 months (APP-PS1) or 5 months (3xTg) and then tested for cognition using the Y-maze and the Morris water maze. Mice were then euthanized, and brains removed for microglial cell sorting and transcriptomeic analysis.
Results: We found that nasal anti-CD3 improved short-term memory in 10-month-old APP-PS1 mice and both short- and long-term memory in 6-month-old 3xTg mice compared to isotype control treated groups. Improvement in cognition was associated with a downregulation of microglial genes associated with neurodegeneration and an upregulation of microglial homeostatic genes. In addition, CD4+ T cells were detected in the AD mouse brains by flow cytometry and immunohistochemistry.
Conclusion: To conclude, our results suggested that nasal anti-CD3 may constitute a novel microglial modulating immunotherapy to treat AD.
Disclosure: Nothing to disclose.

EPO-442

PERIPHERAL NERVOUS SYSTEM ADVERSE EVENTS ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS

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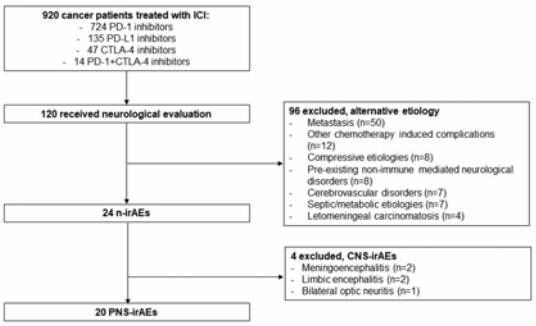
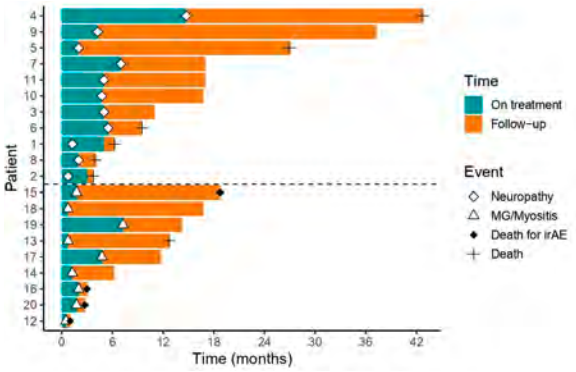
Background and aims: Immune checkpoint inhibitors (ICIs) represent an effective cancer immunotherapy yet are associated with immune-related adverse events (irAEs). The aim of this study was to characterize irAEs involving the peripheral nervous system (PNS-irAEs) in a real-world cohort of ICI-treated patients.
Methods: Cancer patients treated with ICIs between January 2014 and March 2022 were included. Patients with PNS-irAEs were identified and divided into two groups: (1) cranial/peripheral neuropathies and (2) myasthenia gravis (MG) and/or myositis. Clinical characteristics and outcomes, measured with the modified Rankin Scale (mRS), were compared among the two groups.
Results: Among 920 ICI-treated patients, 20 patients (2.17%) developed a PNS-irAEs. The median latency from ICI exposure was 8.8 weeks. Eleven patients developed a neuropathy: polyneuropathy (n=4), cranial neuropathy (n=3), small-fiber neuropathy (n=3), brachial plexopathy (n=1). Nine patients presented MG and/or myositis: concomitant MG and myositis (n=6), isolated myositis (n=2), exacerbation of MG (n=1). Immunosuppressive treatment and/or ICI withdrawal determined a significant clinical improvement, expressed by a mRS reduction, in the neuropathy group (p=0.004), but not in the MG/myositis group (p=0.11). Overall, death due to irAEs occurred in four patients (20%), all with MG/myositis. Compared to patients with neuropathies, those with MG/myositis had a shorter latency onset (p=0.036), developed more frequently concomitant non-neurologic irAEs (p=0.028) and showed a higher mortality rate (p=0.026).
Conclusion: In our large cohort of ICI-treated patients, 2.17% developed PNS-irAEs. Compared to patients with neuropathies, those with MG/myositis had a more aggressive clinical course, characterized by earlier onset, worse response to treatment, and higher mortality.



Patients' selection. CNS-irAEs: central nervous system immune-related adverse events; CTLA-4: cytotoxic T-lymphocyte antigen 4; ICI: immune checkpoint inhibitor; n-irAEs: neurological immune-related adverse events; PD-1: programmed cell death 1; PD-L1 pro



Swimmer plot graph that shows the duration of ICI treatment (blue part of the bar) and total follow-up time (orange part of the bar) in patients with ir-neuropathies (above the dotted line) and ir-MG/myositis (under the dotted line). The onset of the PNS-

Disclosure: Funding: the present study has no funding sources. Conflict of Interest: Prof. Andrea Ardizzoni reports research grants from Celgene, BMS, Ipsen, Roche; honoraria for advisory board participation from BMS, MSD, ROCHE, AstraZeneca, Eli-Lilly. Dr. Francesco Gelsomino reports personal fees from AstraZeneca and honoraria for advisory board participation from Eli-Lilly. The other authors have no conflict of interest to declare.

Clinical neurophysiology; Neurological manifestation of systemic diseases; Neuro-ophthalmology/neuro-otology

EPO-443

"All Tibial Foot": an integrative neurophysiological and neuroradiological study.

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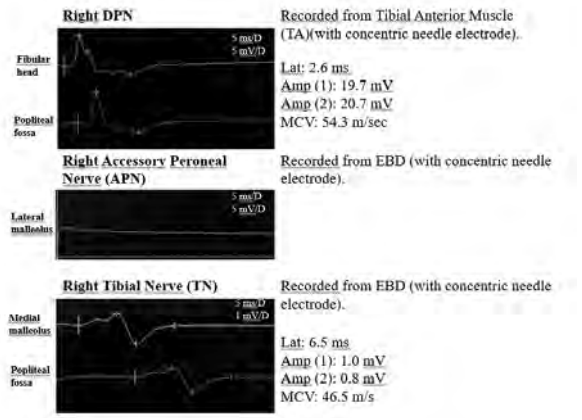
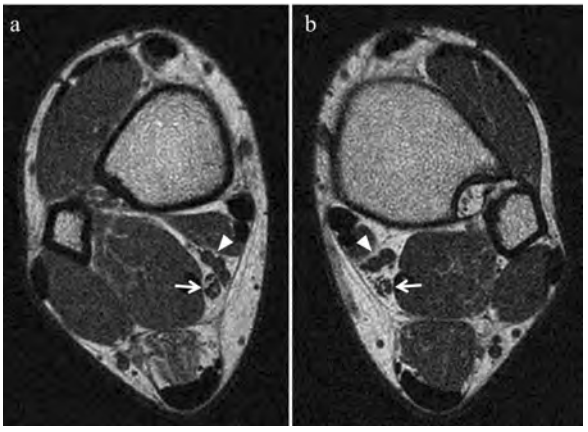
Background and aims: A highly rare anatomic variant is here reported. We presented the case of a patient with the right foot totally innervated by TN. This condition is known as "All Tibial Foot" and it has been reported in only three cases.

Methods: Our study is the first to analyze "All Tibial Foot" with concentric needle electrode nerve conduction study, avoiding the hypothesis of a volume conducted potential mimicking a CMAP response. Neuroradiological study of this rare anatomic variant has not previously been performed.

Results: A 39-year-old man was admitted to our department. Neurological examination showed right gastrocnemius hypertrophy. Patients underwent EMG and nerve conduction study, which was performed with needle electrodes. The absence of right DPN CMAP recorded on EDB was observed. Nevertheless, normal CMAPs were found stimulating DPN recorded on Tibial Anterior (TA) muscle at fibular head and at popliteal fossa. A needle nerve conduction study excluded the presence of APN. A normal DPN CMAP was obtained stimulating TN at ankle and at popliteal fossa and recording on EBD. DPN Sensory Nerve Action Potentials (SNAP) recorded between first and second toes and Sural SNAPS were also normal. Neuroimaging studies (MRI and ultrasound evaluation) confirmed right gastrocnemius hypertrophy, showing a normal representation of DPN and TN nerves and of TA and EDB muscles bilaterally. A diagnosis of right "All Tibial foot" was made.



The ENG study that highlights a Tibial Foot pattern of motori innervation.



Axial T1-weighted turbo spin-echo images of the right (a) and left (b) ankle. The TN (white arrows) located behind the posterior tibial artery and vein (white arrowheads). Normal morphology of EBD muscles (red arrowheads).

Conclusion: Clinicians should considerate "All tibial foot" variant, in addition to APN variant or EBD aplasia, when DPN CMAP is not recorded from EBD.

Author and year	Admission diagnosis	Age	Sex	DPN stim. at ankle; rec from EDB	DPN stim at fibular head; rec from EDB	DPN stim at popliteal fossa; rec from EDB	APN stim at lateral malleolus; rec from EDB	DPN stim at fibular head; rec from TA	TN stim at ankle; rec from EDB	TN stim at popliteal fossa; rec from EDB	DPN sensitive stim at ankle; rec between first and second toes	SPN stim at lateral calf; rec from lateral malleolus	SN stim at lateral calf; rec from posterior lateral malleolus	Other EMG/ENG evidence
Yamashita et al. (1994)[7]	Encephalitis	23	M	Not recorded*	Not recorded*	Not recorded*	Not recorded*	Normal CMAP*	Normal CMAP*	Normal CMAP*	Normal SNAP*	Normal SNAP*	Normal SNAP*	None
Linden et al. (1994)[8]	Erectile disfunction	62	M	Not recorded*	Not recorded*	—	Not recorded*	Normal CMAP*	Normal CMAP*	Normal CMAP*	—	—	—	Martin Gruber anastomosis
Glocker et al. (1995)[9]	Traumatic lesion of common peroneal nerve	19	F	Small CMAP*	Small CMAP*	—	Not recorded*	—	Normal CMAP*	Normal CMAP*	—	—	—	Denervation in TA
Battiato et al. (2022)	Transient ischemic attack	39	M	Not recorded*	Not recorded*	Not recorded*	Not recorded*	Normal CMAP*	Normal CMAP*, Small CMAP*	Small CMAP*	Normal SNAP#	Normal SNAP#	Normal SNAP*	None

Legend DPN: Deep Peroneal Nerve; APN: Accessory Peroneal Nerve; TN: Tibial Nerve; SPN: Superficial Peroneal Nerve; SN: Sural Nerve; EDB: Extensor Digitorum Brevis (EDB) muscle; TA: Tibial Anterior muscle; CMAP: compound motor action potential; SNAP: sensory nerve action potential. *recorded with surface electrode; #recorded with concentric needle electrode.

Nerve conduction studies of "All Tibial Foot" in four reported cases, from 1994 to 2022.

Disclosure: In the interest of transparency, i declare the absence of relationships/activities/interests related to the manuscript.

EPO-444

Is there any effect of migraine on the symptoms and recovery of BPPV?

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Background and aims: The purpose of our study was to determine whether migraine has any influence on the severity of vertigo and dizziness, as well as the quality of life, in patients with BPPV.
Methods: A total of 128 BPPV patients were recruited for this prospective cohort study, 64 of whom had migraine (39.1 (10.2) years; 55 females, 9 males) and 64 without migraine (44.6 (9.5) years; 36 females, 28 males). At baseline, the participants filled out a sociodemographic form, Vertigo Symptom Scale(VSS), Vertigo Dizziness Imbalance Symptom Scale(VDI-SS) and Health related quality of life scale(VDI-HRQoLS), Beck Depression Inventory(BDI), Beck Anxiety Inventory(BAI), Motion Sickness Severity Scale, Headache Impact Test(HIT-6), Migraine Disability Assessment Scale(MIDAS). All patients were asked to complete the clinical scales again at the one-month follow-up visit.
Results: The VSS scores were higher in migraine group both at the baseline (19.5(10.7) vs. 11.3(8.5); p<0.001) and 1 month follow-up (10.9(9.3) vs. 2.2(2.7); p<0.001). The VDI-SS scores indicates that the migraine group had higher dizziness levels of dizziness at the baseline (61.9% vs. 77.3%; p<0.001) and one month later (78.9% vs. 93.7%; p<0.001). According to the VDI-HRQoLS scores, the quality of life was impaired in patients with migraine at the baseline (77.4% vs. 91.8%; p<0.001) and one month after (86.3% vs. 97.6%; p<0.001).
Conclusion: Patients with both BPPV and migraine tend to experience more severe vertigo and dizziness and have a greater impact on their quality of life compared to those with BPPV alone.
Disclosure: Clinicians are recommended to inquire migraine when they are taking a history from the patient with BPPV. Patients with both migraine and BPPV may require special attention during their treatments.

EPO-445

Dissociation between the blink-to-visual-threat reflex and the visual field

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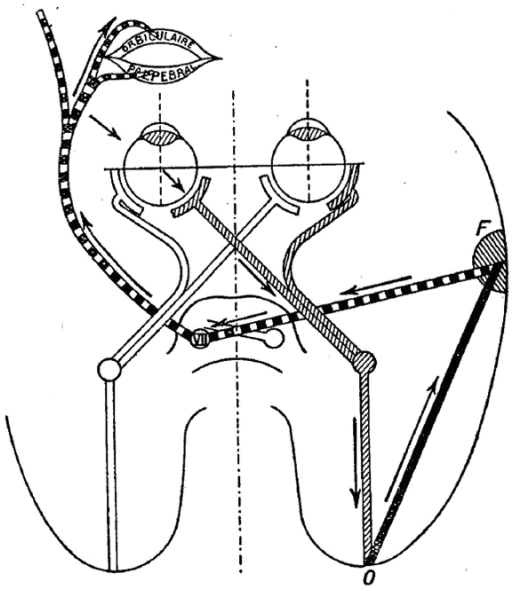
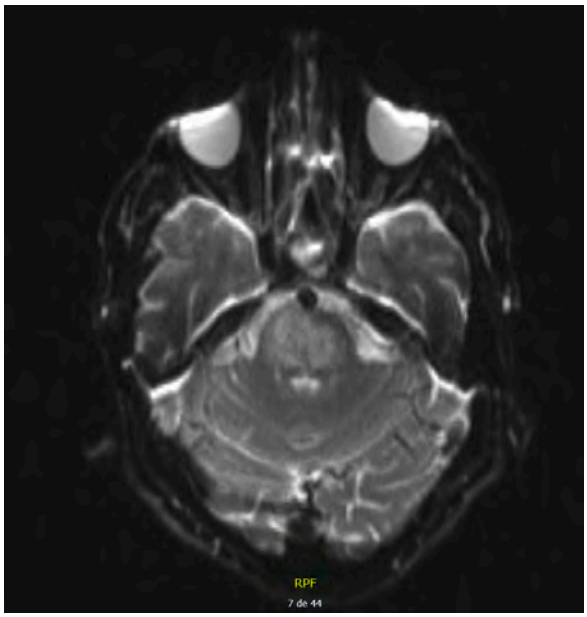
Background and aims: The blink-to-visual-threat reflex is a neurological examination maneuver often used to roughly assess visual fields in patients unable to communicate. However, its reflex arc is long and complex, and it includes not only visual pathways but also motor pathways, from the retina to the orbicularis oculi muscle. Thus, the absence of the blink-to-threat reflex doesn't always mean a visual field defect.

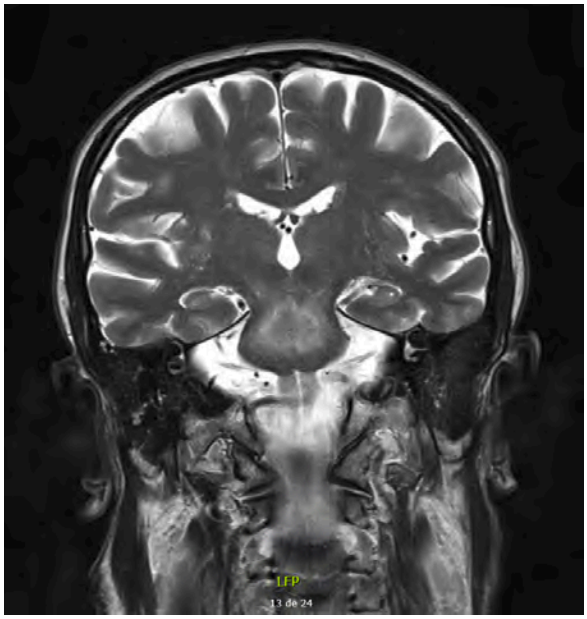


Schematic representation of the reflex arc of the blink reflex to visual threat (adapted from Rademaker and Garcin, 1934)

Methods:N/A
Results: A 69-year-old male was admitted to the ER for sudden onset of left hemiparesis and anarthria. CT scan and angio-CT had no acute lesions, but they documented a proximal occlusion of the basilar artery. The patient underwent mechanical thrombectomy with significant remaining stenosis. He was admitted to the ICU, intubated, and later tracheostomized. The patient recovered gradually, presenting with left hemiplegia, peripheric type left facial palsy, severe dysphagia, and blink-to-threat reflex absent bilaterally. He was still able to follow commands, even in response to visual stimuli. MRI imaging didn't document any occipital lesions, although it revealed acute ischemic lesions that covered nearly the entirety of the transversal section of the pons and right postero-lateral portion of the mesencephalon. These lesions, while not part of the visual pathways, resulted in a lesion of the efferent pathways of this reflex arc, which lead to its bilateral suppression.



MRI - DWI



MRI - T2

Conclusion: This case portrays a dissociation between the absence of blink-to-visual-threat reflex and visual field integrity, which must be taken into account. While useful, this reflex must be interpreted carefully in its clinical context.

Disclosure: Nothing to disclose.

EPO-446

Painful ophtalmoplegia and visual loss – when patients with acute rhinosinusitis see the neurologist

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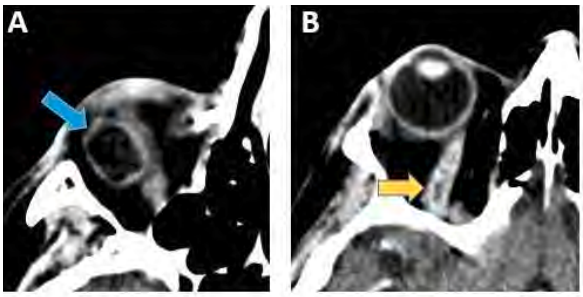
Background and aims: Orbital cellulitis is a complication of acute rhinosinusitis with the development of potentially severe neurological deficits such as opthtalmoplegia and loss of vision. Septic cavernous sinus thrombosis and intracranial dissemination are fearful evolutions.

Methods: We report two clinical cases of orbital cellulitis related to acute rhinosinusitis with subsequent extension of the infection in the cavernous sinus or intracranially.

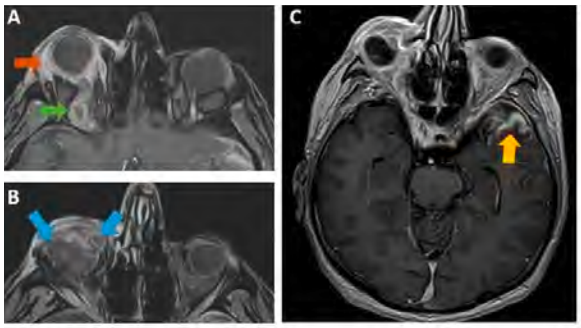
Results: Clinical case 1. A 62 year-old male patient presented to the hospital for periorbital pain, ptosis, and loss of vision in the right eye with sudden onset. Clinically, painful complete ophtalmoplegia, chemosis, proptosis and loss of vission were noticed. Contrast-enhanced CT scan revealed right orbital cellulitis with orbital abscesses, ophtalmic vein thrombosis and sphenoidal rhinosinusitis. MRI revealed multiple small left temporal and parietal abscesses. Intravenous antibiotic treatment and low-molecular-weight heparin were started. Clinical case 2. A 45 year-old male patient, with COVID and type 2 diabetes, presented for left facial pain followed by loss of vision and ptosis of the left eye. Clinically, left painful ophtalmoplegia, loss of vision, maxillary and ophtalmic trigeminal hypoesthesia were noticed. Contrast-enhanced CT scan and MRI revealed left orbital cellulitis with orbital abscesses, partial cavernous sinus thrombosis and pansinusitis. Surgery with drainage of the left paranasal sinuses was performed, intravenous antibiotics and anticoagulation were initiated. One month later, both patients did not clinically aggravate but ophtalmoplegia and visual loss persisted.

Conclusion: Rapid diagnosis and initiation of appropiate treatment are crucial to prevent devastating consequences in complicated acute rhinosinusitis.

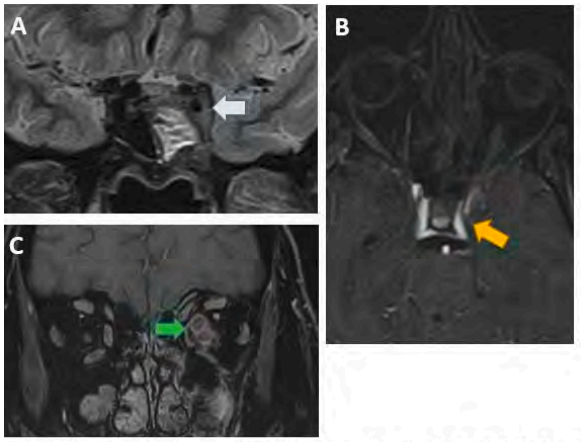
Disclosure: -



atient 1 – Figure 1: Contrast-enhanced CT scan reveals orbital abscess with ring enhancement (image A, blue arrow) and superior ophthalmic vein thrombosis with illing defect (image B, yellow arrow).



atient 1 – Figure 2: Contrast-enhanced MRI reveals the superior ophthalmic vein thrombosis with filling defect and nlargement (image A - green arrow), orbital cellulitis with diffuse inflammation and proptosis (image A- brown rrow), multiple orbital abscesses with ring enhancement (image B - blue arrows) and parenchymal abscess in the emporal lobe with contrast enhancement (image C - yellow arrow)



Patient 2 – Figure 1: Brain MRI reveals the partial cavernous sinus thrombosis with thickening of the cavernous sinus (image A – white arrow), partial filling defect (image B – yellow arrow) and multiple orbital abscesses with ring enhancement (image C – green arrows).

EPO-447

Late-onset Fabry disease due to p.F113L mutation: clinical profile of the first Italian cluster

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[1]Department of Medical and Surgical Sciences, Magna Græcia University of Catanzaro, Catanzaro, Italy, [2]Regional Epilepsy Centre, Great Metropolitan "Bianchi-Melacrino-Morelli Hospital", Reggio Calabria, Italy, [3]Great Metropolitan Hospital "Bianchi-Melacrino-Morelli", Cardiology Department, Reggio Calabria, Italy

Background and aims: The GLA c.337T>C (p.F113L) is a known pathogenic mutation associated to late-onset Fabry disease (LOFD). A founder effect was demonstrated in a large cohort of predominantly cardiac LOFD in the Portuguese region of Guimarães. Herein we report an in-depth description of clinical and biochemical phenotype of a cluster of five Italian families living in Calabria, Southern Italy, with LOFD caused by p.F113L mutation.
Methods: Five index males with p.F113L mutation with at-risk relatives were identified and underwent biochemical and genetical screening test. Multidisciplinary clinical and instrumental evaluations were performed on mutation's carriers.
Results: Twenty-seven (12 M, 15 F) individuals with GLA mutation were identified (table). Sixteen (59.2%) subjects (M: 8/12; F: 8/15) had clinical or instrumental cardiac manifestations. Notably, myocardial fibrosis was found in 7/8 (87.5%) patients, of whom 2 under 40 years old. Seven patients (all females) complained of acroparesthesias. Renal manifestations occurred in 10 (37%) patients (M: 4/12; F: 6/15), angiokeratomas in 9 (33.3%) subjects (M: 2/12; F: 7/15). Stroke occurred in 4 (14.8%) patients (M: 3/12; F: 1/15). White matter lesions were detected in 12/19 (63.1%) patients (M: 4/7; F: 8/12) and occurred in 40% of subjects under 40 years old.

Demographical and clinical characteristics	All patients (n: 27)	Male (n: 12)	Female (n: 15)
Age at diagnosis (years; mean±SD)	53.8±19.1	53.8±19.9	53.8±19.0
Mean plasma Lyso-GB3[1] (ng/mL; mean±SD)	3.1±2.6	6.3±1.7	1.4±0.4
Cardiac manifestations	16 (59.2%)	8 (66.7%)	8 (53.3%)
Myocardial ischemic events (n, %)	2 (7.4%)	2 (16.7%)	0
Heart failure (n, %)	7 (25.9%)	5 (41.7%)	2 (13.3%)
LVH[2] (n, %)	12 (60%)	6 (66.7%)	6 (54.5%)
LGE[3] (n, %)	7 (87.5%)	2 (100.0%)	5 (83.3%)
Arrhythmia (n, %)	7 (25.9%)	3 (25%)	4 (26.7%)
Neurological and neuropsychiatric manifestations	14 (51.8%)	5 (28.3%)	9 (60%)
Stroke (n, %)	4 (14.8%)	3 (25%)	1 (6.7%)
WML[4] (n, %)	12 (63.1%)	4 (57.1%)	8 (66.6%)
Brain haemorrhage[4] (n, %)	1 (5.2%)	1 (14.3%)	0
Acroparesthesias (n, %)	7 (25.9%)	0	7 (46.7%)
Carpal tunnel syndrome[5] (n, %)	3 (15%)	0	3 (23.1%)
Polyneuropathy[5] (n, %)	2 (10%)	1 (14.3%)	1 (7.7%)
Dysautonomia (n, %)	6 (22.2%)	3 (25%)	3 (20%)
Anxiety/depression (n, %)	3 (11.1%)	0	3 (20%)
Renal manifestations	10 (37%)	4 (33.3%)	6 (40%)
Albuminuria/proteinuria (n, %)	10 (37%)	4 (33.3%)	6 (40%)
Kidney failure (n, %)	3 (11.1%)	0	3 (20%)
Angiokeratomas (n, %)	9 (33.3%)	2 (7.4%)	7 (46.7%)
Eye manifestations	4 (14.8%)	1 (8.3%)	3 (20%)
Cornea verticillata (n, %)	1 (3.7%)	0	1 (6.7%)
Cataracts (n, %)	3 (11.1%)	1 (8.3%)	2 (13.3%)
Sensorineural deafness (n, %)	3 (11.1%)	0	3 (20%)
Pulmonary manifestations (n, %)	2 (7.4%)	1 (8.3%)	1 (6.7%)
Gastrointestinal manifestations (n, %)	4 (14.8%)	1 (8.3%)	3 (20%)

LVH: left ventricular hypertrophy; LGE: late-gadolinium enhancement.
Performed 20/27 (7 M and 13 F); [2]cardiac imaging performed in 20/27 (9 M and 11 F); [3]cardiac MRI performed in 8/27 patients (2 M and 6 F); [4]brain imaging erformed in 19/27 patients (7 M and 12 F); [5]ENG performed in 20/27 patients (7 M and 13 F).

Demographical, clinical and instrumental features of subjects with the GLA p.F113L mutation.

Conclusion: This study demonstrates that GLA p.F113L mutation is also present in Southern Italy. Disease manifestations are frequent in both sexes and may occur early in life. Cardiac involvement represents a core manifestation in Portuguese families as well as in our cohort, while neurological and renal manifestations are more frequent in the Italian cluster.
Disclosure: All authors report no disclosure.

EPO-448

The Use Of Optical Coherence Tomography In Clinical And Subclinical Optic Neuritis

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Background and aims: Despite the high prevalence of clinical(CON) and subclinical(SON) optic neuritis in multiple sclerosis(MS), current diagnostic criteria do not consider optic neuritis as evidence for dissemination in space. Optical coherence tomography(OCT) may be a useful tool to confirm CON and detect SON, and therefore contribute to MS diagnosis.
Methods: Objectives: To sought the utility of OCT in confirming CON and detecting SON, and to compare OCT and clinical data between eyes with CON, SON and with no optic neuritis (NON). Methodology: Retrospective analysis of MS patients. Eyes were separated into 3 groups: CON(acute visual event with concordant exam, >6m apart from OCT), SON(retinal nerve fiber layer(RNFL) or ganglion cell layer(GCL) difference between eyes >6micron and/or significant RNFL and GCL loss on deviation/color maps in one or both eyes) and NON(none of the above).
Results: We included 125 patients(244 eyes)(mean age 37.97±11.73 years, 65.6% (n=82) females). OCT detected SON in 11.5% (n=28) of eyes and confirmed the presence of CON in all CON eyes(23.8% (n=58)). The remaining 158 (64.8%) eyes were NON. Disease duration, EDSS, and number of relapses in the last 2 years, were similar between groups. There were no differences in mean RNFL (p=0.91), and mean GCL (p=0.94) between CON and SON eyes. Mean RNFL thickness correlated inversely with disease duration (R=-0.161, p=0.012).
Conclusion: OCT confirmed the occurrence in all previous CON and further detected SON in 10% of eyes. There were no differences between CON and SON eyes, suggesting that the OCT criteria here used for classifying SON are probably picking real optic neuritis.
Disclosure: Nothing to disclose.

EPO-449

Neurosarcoidosis: a rare disease with many facets

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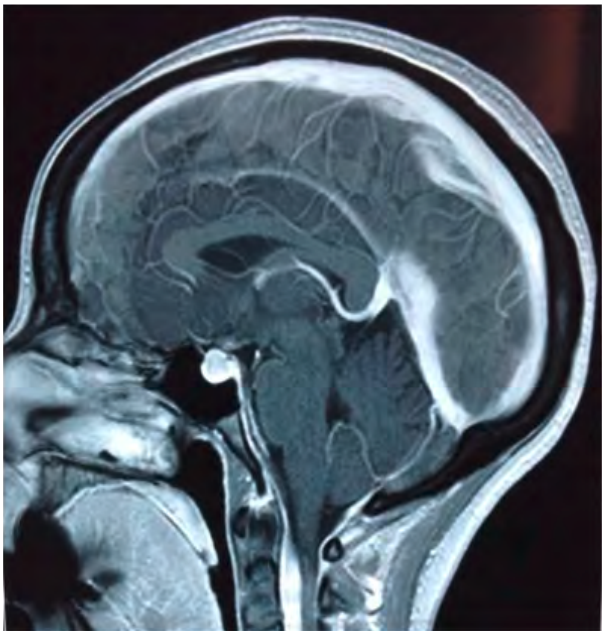
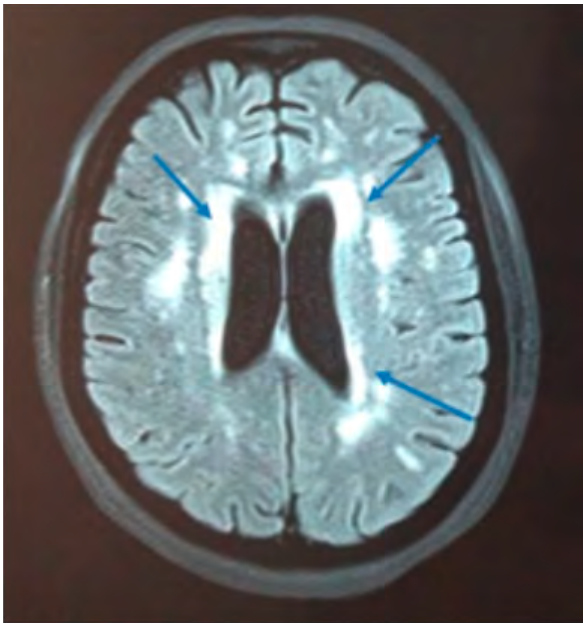
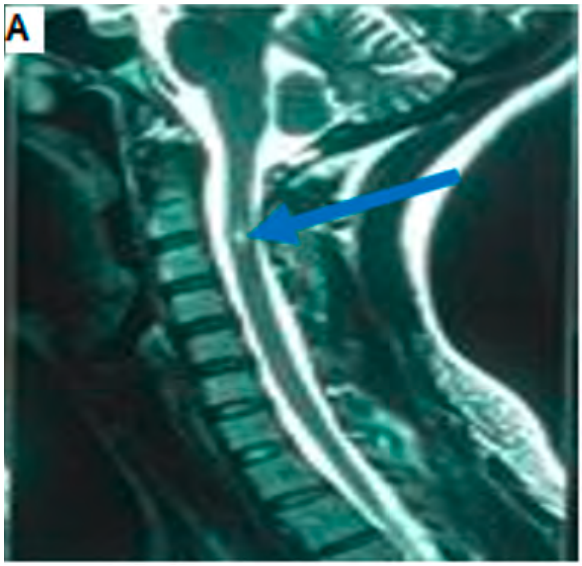
Background and aims: Sarcoidosis is an immune-mediated disease characterized by granulomatous inflammation. Neurosarcoidosis (NS)can involve the central nervous system or the peripheral nervous system or both. Our aim is to describe the clinical and radiological manifestations of NS in tunisian patients.
Methods: We conducted a descriptive and retrospective monocentric study of 38 patients with neurosarcoidosis, followed in the internal medicine and neurology departments at the Military Hospital of Tunis over a period of 20 years from 1997 to 2017.
Results: Thirty-eight patients met the inclusion criteria for NS , all patients underwent a magnetic resonance imaging (MRI) of the brain and spinal cord . Central neurological involvement was present in 33 patients (86.8%). Cranial nerve involvement was found in 10 patients (26.3%), the peripheral nervous system was affected in 5 patients (13.1%) , and ten patients had at least two types of involvement.







Conclusion: Although sarcoidosis commonly affects the lungs, eyes, liver and lymph nodes, neurological involvement can be observed and can sometimes be the only manifestation of the disease.
Disclosure: Nothing to disclose.

EPO-450

No effects of sleep deprivation on brain excitability in a threshold tracking TMS study

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Background and aims: Sleep deprivation was reported to increase the risk of epileptic seizures in healthy individuals, to have antidepressant effects and to influence cortical excitability explored using conventional transcranial magnetic stimulation (TMS). However, these studies included a limited number of TMS modalities and a limited number of inter-stimulus intervals (ISIs); moreover, no studies were performed using threshold tracking TMS (TT-TMS). This study aimed to investigate the effects of sleep deprivation on cortical excitability using TT-TMS and a wide range of ISIs.
Methods: 13 healthy subjects (age 24-59), sleep deprived for at least 24 hours, have been included. The local ethical committee approved the study (1-10-72-171-22). The following paired-pulse TT-TMS methodologies have been applied using the QtracS software and automated QTMSG-12 recording protocols: short- and long interval intracortical inhibition (SICI and LICI), short and long interval facilitation (SICF and ICF) and short-latency afferent inhibition (SAI). The recording was obtained from the abductor pollicis brevis (APB) muscle and using a MagStim/Bistim TMS device and a figure-of-eight coil.
Results: There was no significant difference in SICI, ICF, LICI or SAI at any of the ISIs. For the presentation results will be updated with further individuals.
Conclusion: At this stage, our results do not show any effect of sleep deprivation TMS cortical excitability measurements. As the automated TT-TMS reduces the intra- and inter-day variability better than conventional TMS measurements, this can explain the results of our study in comparison to the literature.
Disclosure: Nothing to disclose.

EPO-451

Dizziness in Postural Orthostatic Tachycardia Syndrome - is there a migrainous component?

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Background and aims: Postural tachycardia syndrome (PoTS) is a chronic condition characterised by increase in heart rate on prolonged standing. A variety of symptoms and comorbidities is recognised including dizziness and also migraine. Much of the dizziness in PoTS is likely due to direct orthostatic effects, however this study looked for evidence of other mechanisms for dizziness in this population.
Methods: This was a retrospective review of 85 patients with PoTS attending a tertiary Neuro-otology clinic undergoing standardised detailed assessments (validated symptom questionnaires, history/physical examination, neuro-otological diagnostics (pure tone audiometry PTA, video head impulse test VHIT, videonystagmography VNG and caloric testing).
Results: 85 patients were included (Mean age 35 years +/-12, 92% were female). 85% had migraine and 29% had a phenotype of vestibular migraine. Visual motion intolerance was present in 41% and 47% experienced true rotational vertigo. Physical examination was limited in a minority (23%) by comorbidity (chronic pain), or symptom provocation. PTA was abnormal in 36%, VHIT was abnormal in 2%, and 38% had abnormal caloric testing. 49% of cases were offered migraine management advice and 54% were offered vestibular rehabilitation.
Conclusion: Dizziness in patients with PoTS can be complex and multifactorial. There are likely to be multiple potential mechanisms including vestibular migraine and minor head injuries from syncope, and this may be a mechanism for some of the findings. Further prospective in a more representative population evaluation is recommended. Clinicians seeing patients with PoTS need a systematic approach to dizziness to identify and treat non-cardiac causes.
Disclosure: Nothing to disclose.

EPO-452

Efficacy and safety of tiomolibdate choline in Wilson disease: 96-week results from an ongoing phase 3 study

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Background and aims: Patients with Wilson disease (WD) in the open-label randomised phase III FoCus trial (NCT03403205) underwent 48 weeks (W) of treatment with the oral, copper-binding agent, tiomolibdate choline (INN: tiomolibdic acid; ALXN1840) or standard-of-care (SoC). All patients completing 48W were offered participation in an extension and were evaluated for copper mobilisation, neurologic signs/symptoms, and safety during 96W of tiomolibdate treatment.

Methods: At enrollment, 214 patients (aged >=12 years) were randomised to tiomolibdate (15mg every-other-day to 60mg daily) or SoC (penicillamine, trientine and/or zinc) for 48W. 178 patients enrolled in the extension (tiomolibdate only) were evaluated over 96W following the first dose of tiomolibdate (baseline). Prespecified endpoints were directly measured non-ceruloplasmin bound copper (dNCC) and Unified WD Rating Scale (UWDRS) Parts II and III. UWDRS scores were stratified by presence of baseline neurologic symptoms (score >0).

Results: At baseline, 123 (69.1%) patients had received SoC for >=18 months; 67 and 134 had total scores on UWDRS Part II >0 and Part III >0, respectively. dNCC remained stable between W48–96 (Figure 1). At W96, least squares mean changes from baseline in UWDRS Parts II and III were –1.0 (95% confidence interval: –1.4,–0.5) and –4.2 (–5.6,–2.9), respectively, and in patients with score >0, –2.6 (–3.8,–1.5) and –5.5 (–7.2,–3.7), respectively, suggesting improvement (Figure 2). Safety data are shown in Table 1; no deaths occurred in the extension.

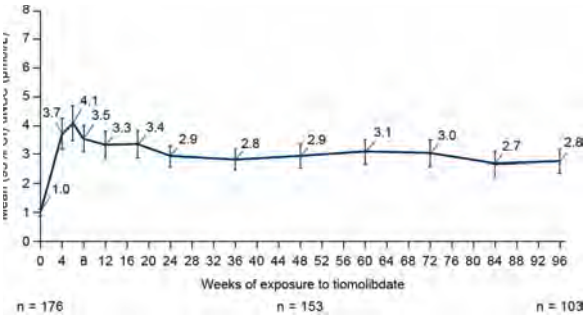

Figure 1. dNCC by week after initiation of tiomolibdate

	Patients enrolled in extension phase N = 178; PY = 349.5		
	n (%)	Number of events	Events per 100 PY
Any AE	156 (87.6)	999	44.6
Any SAE	35 (19.7)	63	10.0
Drug-related AE*	83 (46.6)	226	23.7
Drug-related SAE*	5 (2.8)	5	1.4
AE leading to withdrawal of study drug	10 (5.6)	12	2.9
Death†	0 (0.0)	0	0.0
AE by severity			
Grade 1	145 (81.5)	715	41.5
Grade 2	88 (49.4)	242	25.2
Grade 3	28 (15.7)	40	8.0
Grade 4	2 (1.1)	2	0.6
Grade 5	0 (0.0)	0	0.0
	Worst post-baseline laboratory value, by severity grade (CTCAE)		
	Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)	Grade 4, n (%)
ALT (n=176)	64 (36.4)	11 (6.3)	14 (8.0)	3 (1.7)
GGT (n=176)	42 (23.9)	27 (15.3)	15 (8.5)	5 (2.8)
Triglycerides (n=174)	68 (39.1)	24 (13.8)	10 (5.7)	5 (2.9)
Cholesterol (n=174)	89 (51.1)	9 (5.2)	6 (3.4)	0
Neutrophils (n=174)	1 (0.6)	36 (20.7)	12 (6.9)	4 (2.3)

*Assessed as drug-related by investigator

† 2 patient deaths – both assessed by investigators as unrelated to study treatment – occurred during the primary evaluation period; these are not captured here because the analysis included only patients who entered the extension phase

AE: adverse event; ALT: alanine aminotransferase; CTCAE: Common Terminology Criteria for Adverse Events; GGT: gamma-glutamyltransferase; PY: person-years; SAE: serious adverse event.

Table 1. Safety – weeks 0–96 after first exposure to tiomolibdate

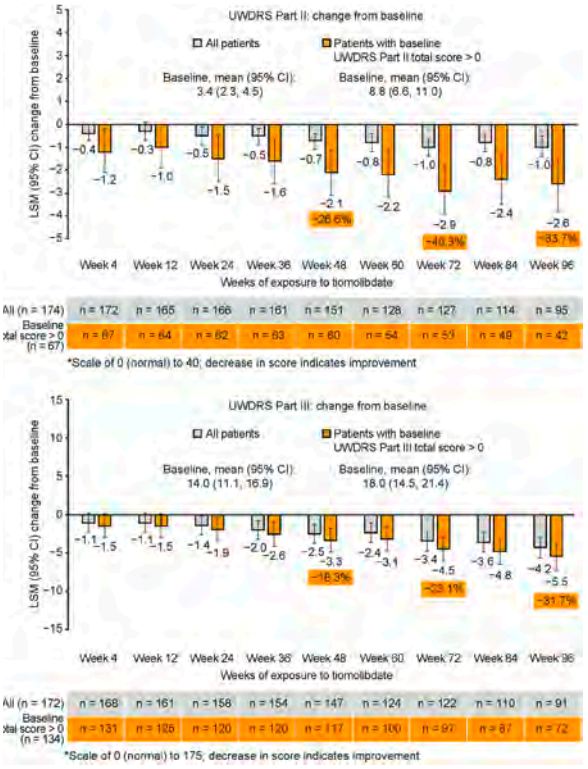

Figure 2. UWDRS Part II (patient/caregiver-assessed) and Part III (neurologist-assessed):* change from baseline

Conclusion: Treatment with tiomolibdate over 96W was generally safe and well-tolerated and was associated with sustained copper sequestration and improvement in neurologic symptoms.
Disclosure: This study was sponsored by Alexion, AstraZeneca Rare Disease.

EPO-453

A digital platform for neurovisual rehabilitation

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Background and aims: Rehabilitation of visual deficits is crucial for improving cognitive and motor functions and quality of life, however, the possible influence of visual-sensory and ocular motor disorders on the patient's outcome is often ignored in neurorehabilitation. Sensory and motor aspects of visual system may be the target of neurovisual rehabilitation.
Methods: A digital rehabilitative platform was designed to include specific tasks for each deficit: Saccadic tasks in patients with diplopia. Benton's line and antisaccade task are designed for peripheral visual field deficits and Unilateral Spatial Neglect (USN) rehabilitation. Visual search and visual sequential search tasks, visual recognition and identification of figures, 2-3D shapes, objects, facial expression recognition and colors (Stroop test) are designed for rehabilitation of visual perception, visual attention and visual agnosia. The platform is accessible to both clinical and remotely . A report of each rehabilitation cycle allows a constant monitoring of patient results but it is also used for different statistics and for addressing the work to each individual patient customizing its reports at various levels of difficulty.
Results: We tested 46 patients: 21 patients with central visual deficits: 9 patients with diplopia, 2 patients with USN, 3 patients with hemianopia and 7 patients with visual perception deficits. The results showed a significant improvement in subjective and objective visual functions.
Conclusion: Neurovisual rehabilitation platform represents a valid instrument for rehabilitation of visual deficits in neurological patients, allowing the clinician to personalize and monitor the treatment's progression and ensuring an easily accessible instrument for patients.
Disclosure: Nothing to disclose.

EPO-454

Effects of ageing on hand muscles

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Background and aims: Hand function decreases with age, due to a reduction in functional motor units, joint degeneration, and neural control. We aimed to investigate the effect of age on different hand muscles using compound muscle action potential (CMAP) amplitude and neurophysiological index (NI), which combines CMAP amplitude, distal motor latency (DML) and F-waves frequency.
Methods: We studied data from adult subjects without neuromuscular disorders. CMAP amplitude, DML and F-wave frequency were obtained for abductor pollicis brevis (APB), first dorsal interosseous muscle (FDI), and abductor digiti minimi (ADM). CMAP and NI from each muscle were analysed. Focal nerve lesion was excluded. Age groups were defined by median and interquantile ranges (IQRs). Lower limit values were defined by the 5th percentile. We used Kruskal–Wallis one-way analysis, Pearson correlation and linear regression for testing age-dependence measurements.
Results: We included 164 subjects; 85 (52%) were women with a median age of 56.0 years (IQR 41.0-72.8). No gender differences were observed, except for FDI CMAP amplitude (12.6 versus 11.1, $p<0.001$) and FDI NI (3.1 versus 2.8, $p=0.041$), which were higher in men. Median and lower limit cut-off values differed significantly between age groups for all neurophysiological measurements ($p<0.001$). APB, FDI and ADM CMAP amplitudes decreased around 0.07, 0.05 and 0.03mV/year, respectively. APB, FDI, and ADM NI decreased around 0.03, 0.02 and 0.01/year, respectively.
Conclusion: CMAP and NI are both age-dependent, confirming an age-related loss of motor units in hand muscles. However, age-dependent changes in APB and FDI are more markedly possibly related to a higher user-effect.
Disclosure: Nothing to disclose.

EPO-455

Dural arteriovenous fistula as the cause of intracranial hypertension

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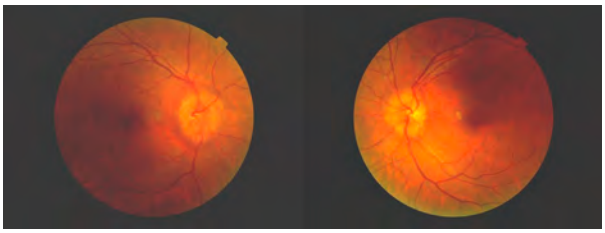
Background and aims: Dural arteriovenous fistula (DAVF) is an abnormal shunt between the arterial and venous systems located within the dura. Presenting symptoms of DAVF are variable and can develop intracranial hypertension in about 8% of that. We describe a patient with intracranial hypertension due to DAVF.

Methods: A 55-year-old female presented with a 5-month history of bilateral transient visual obscurations which occur with postural provocation.

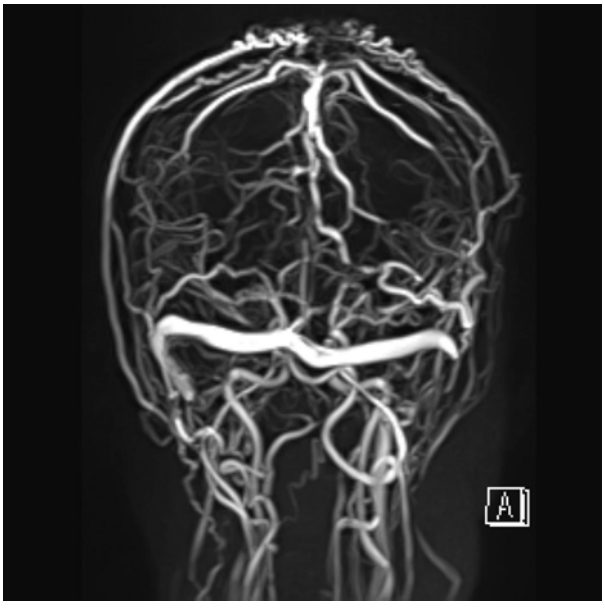
Results: Visual acuity was 20/20 in each eye, and visual field tests demonstrated enlarged blind spot with peripheral field constriction in the right eye. Fundus examinations showed bilateral papilledema with Frisen Grade 3. There was no mass-like lesion in brain computed tomography, and lumbar puncture showed an opening pressure of 380 mmH2O with normal CSF contents. Magnetic resonance venography showed stenosis of the left transverse sinus with a suspicious DAVF in the right transverse sinus. Transfemoral cerebral angiography (TFCA) confirmed a DAVF of the right transverse sinus with arterial supply from the posterior meningeal artery. The left transverse sinus was markedly narrowed. After Onyx embolization of a DAVF and venous stenting of the left transverse sinus, her symptoms was gradually improved. Bilateral papilledema also disappeared in a 1-month follow-up fundus examination.

Conclusion: Clinician should be aware of alternate causes of intracranial hypertension such as DAVF. Our case highlights a critical role of endovascular intervention in managing intracranial hypertension secondary to DAVF.

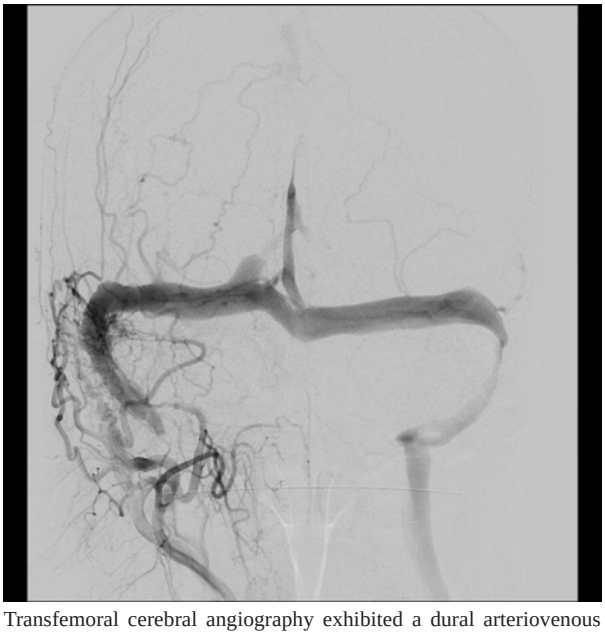
Disclosure: We have no disclosure of any competing interest.



Fundus photography disclosed bilateral papilledema with Frisen Grade 3.



Magnetic resonance venography showed stenosis of left transverse sinus with a suspicious dural arteriovenous fistula in the right transverse sinus.



Transfemoral cerebral angiography exhibited a dural arteriovenous fistula of the right transverse sinus with severe stenosis of left transverse sinus.

EPO-456

Ocular Neuromyotonia In Thyroid Eye Disease

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Background and aims: Ocular neuromyotonia (ONM) consists of abnormal tonic spasms of the extraocular muscles, manifesting as intermittent diplopia. While usually associated with chronic nerve compression and radiation, it has been rarely described in thyroid eye disease (TED).
Methods: Case report
Results: A 61-year-old male with a history of seropositive generalized myasthenia gravis with no ocular involvement, developed binocular vertical diplopia exclusively in upgaze. Exam showed mild limitation of supraduction of the right eye, eyelid retraction and exophthalmos ipsilaterally. Orbit CT revealed tendon-sparing enlargement of the right inferior more than the superior rectus muscle and of the left medial rectus muscle, and blood panel revealed low levels of thyroid-stimulating hormone (0.004 uUI/ml), and raised levels of free thyroxine (1.8 mg/ml), free triiodothyronine (8.0 pg/ml), TSH receptor antibodies (5.0 U/L), and thyroid stimulating immunoglobulin (2.2 U/L), consistent with TED. Treatment with methylprednisolone pulses, thiamazole and selenium was initiated. 1 year later, the patient reported multiple daily attacks of intermittent binocular vertical diplopia also occurring in straight and downgaze. On exam, during an attack, there was tonic downward deviation of the right eye and complete limitation of right supraduction lasting ~1 minute. Between attacks, there was no vertical misalignment in straight gaze and only partial limitation of right supraduction. A diagnosis of ONM was made. Treatment trials with carbamazepine and lacosamide have been unsatisfactory so far.
Conclusion: Despite its rarity, ONM should be considered in TED. Lack of response to voltage-gated sodium channel blockers in our case, suggests the presence of pathomechanism(s) other than ephaptic transmission.
Disclosure: The authors have no relevant financial or non-financial interests to disclose.

EPO-457

The origin of slow saccadic eye movements in Steinert's disease

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Background and aims: Myotonic dystrophy type 1 (DM1) or Steinert's disease is a multisystemic disorder with great phenotypical variability. Oculomotor disturbances in DM1 may be the result of peripheral (neuromuscular) or central dysfunction, e.g. due to the well known lesions in brain MRIs of many Steinert patients. We investigated whether the slowing of saccades has a myopathic/myotonic or a central neural origin.
Methods: Horizontal saccades and the fast vestibulo-ocular reflex (VOR) were examined in 9 DM1 patients and 15 controls by means of video-oculography and video head-impulse testing
Results: Peak velocity-to-amplitude ratios were lower in DM1 patients as compared to controls (19.6 deg/s vs 23.1 deg/s, $P<0.001$, respectively). Moreover, the VOR gain was decreased in patients, as well (0.78 vs 0.98, $P<0.01$). Importantly, there was a strong linear correlation between saccadic velocity and fast VOR movements ($R2=0.941$, $P<0.001$).
Conclusion: Patients with DM1 exhibit slow saccadic eye movements, accompanied by a reduced VOR gain. These results indicate that the patients' oculomotor dysfunction involving various fast eye movement types, is not due to central (supranuclear) causes, but occurs in the context of extraocular muscle dysfunction.
Disclosure: Nothing to disclose.

Movement disorders 3

EPO-458

Spinocerebellar ataxia autosomal recessive type 10 misdiagnosed as a Multiple System Atrophy Type C: a case report.

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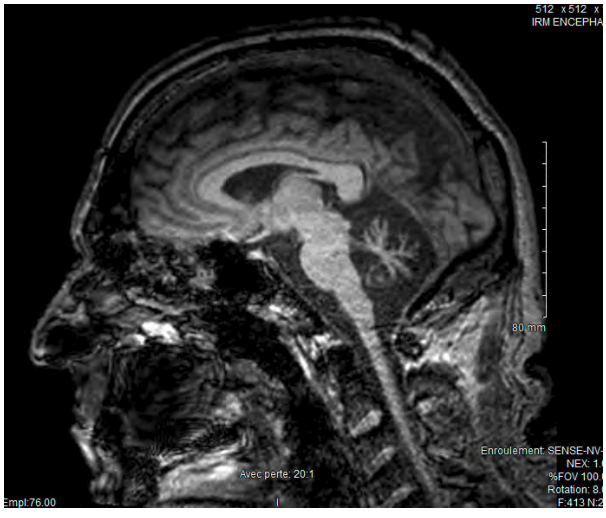
Background and aims: Spinocerebellar ataxia autosomal-recessive type 10 (SCAR 10) is a very rare cause of slowly pro-gressive cerebellar ataxia caused by mutations of ANO10 gene.
Methods: Here we present the case of a 51-years-old man who manifested a gait and balance problem over the past year. The patient had no previous medical disorders and his family history was unremarkable. The neurological examination revealed an ataxic gait, a dysarthric speech, bilateral dysmetria, mild bradykinesia, lateral and vertical nystagmus and abnormally vivid tendon reflexes in the four limbs. Furthermore, the patient reported erectile dysfunction and urinary urgency that improved after beginning an alpha-blocker. The tilt test demonstrated no signs of dysautonomia. The patient performed an MRI that showed significant atrophy of cerebellum and pons, while there was no involvement of dopaminergic pathways at DATSCAN. A polysomnography showed the presence of a nocturnal stridor.
Results: This clinical picture led to the conclusion for a possible MSA type C. However, over the next 12 years, the clinical picture was essentially stable apart from the onset of severe spasticity. The patient also developed a moderate dysphagia. Considering the absence of frank dysautonomia signs and the slow progression of symptoms an NGS analysis was performed and finally, a composite heterozygous genetic mutation of the gene ANO10 (p. Ala74pro e p.Phe171ser) was found.



Cerebellar atrophy

Conclusion: This is a very unusual case of an adult-onset cerebellar ataxia misdiagnosed as a MSA type C. This case is an example of how important it is to always question a
Disclosure: I have no financial disclosure or conflicts of interest with the material presented in this manuscript.

EPO-459

Abstract withdrawn

EPO-460

Is working memory training success in Parkinson's disease determined by cortical thickness and white matter lesions?

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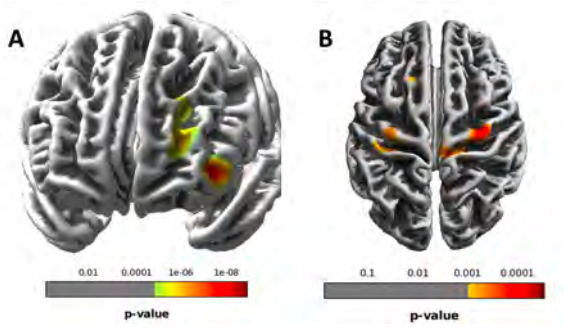
Background and aims: Patients with Parkinson's Disease (PD) are highly vulnerable for cognitive decline. Therefore, early cognitive training interventions may be crucial for long-term preservation of cognition. While prediction of intervention responsiveness is important for tailored treatment, the influence of structural brain properties, specifically cortical thickness (CT) and white matter lesions (WML), on training success has not been studied. Thus, we aimed to evaluate the influence of CT and WML on working memory training (WMT) success in cognitively unimpaired patients with PD.
Methods: Behavioral and structural imaging (T1, FLAIR) data of 46 patients with PD, 21 of which engaged in home-based adaptive digital WMT, were analyzed. The relationships of demographic, disease-related and cognitive measures with CT and WML (number and volume of lesions) were estimated. For the intervention group, the effect of CT and WML on training success was investigated.
Results: Generally, increasing age had a negative effect on the brain indicated by more WML and less CT. Sex had an effect on CT in the right frontal cortex only (CT in females > males). Interestingly, when corrected for age and sex, disease duration was positively correlated with CT in right middle frontal gyrus. For cognition, better executive function performance at baseline was associated with greater CT in pre-central gyrus. CT and WML were neither correlated to any other demographic, disease-related or cognitive measure at baseline, nor to the responsiveness to WMT.



A: Positive correlation between disease duration and cortical thickness. B: Positive correlation between executive function performance at baseline and cortical thickness.

Conclusion: While structural brain properties might influence cognitive performance at baseline, they do not seem to determine WMT success in this patient cohort.
Disclosure: Nothing to disclose.

EPO-461

Prevalence of Headache on a Cohort of Patients With Parkinson's Disease

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Background and aims: Our aim was to assess the lifetime and last year prevalence and the phenomenology of the headache in a cohort of PD patients in comparison with control subjects (Ctrl).
Methods: We recruited 80 patients (36 F; 44 M) and 76 Ctrl (37 F; 39 M) comparable for age, sex and education. All participants underwent Beck Depression Inventory scale and a questionnaire assessing the presence of a history of headache and days with headache during the last year, describing characteristics of pain as well. Only patients were clinically evaluated by the motor section of Unified PD Rating Scale (UPDRS-III) and Hoehn and Yahr (HY) scale.
Results: No significant difference was observed in the overall prevalence of lifetime migraine among PD patients (30%; 5 M/9 F; p=0.387) compared to Ctrl (39%; 6 M/12 F; p=0.178), as well as the prevalence of tension-type headache (TTH) between the two groups (70% vs 61%; p=0.619). Migraine prevalence was significantly higher among women in both groups (11% M vs 25% F; p=0.067; 15% M vs 32% F; Ctrl: p=0.016). We found higher occurrence of headache family history (40% vs 13%; p=0.004), more common headache remission with age (p<0.001), particularly after the onset of motor symptoms (23%; p=0.037), among PD subjects rather than Ctrl.
Conclusion: PD does not seem to act as a risk factor in the development of headache, but the dopaminergic pathway degeneration might affect the severity and duration of the attacks and favor the improvement and remission of the headache in these patients.
Disclosure: Nothing to disclose.

EPO-462

Gender differences regarding non-motor symptoms in Parkinson's disease patients

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Background and aims: Parkinson's disease is a chronic progressive neurodegenerative disorder whose main hallmarks are motor symptoms such as bradykinesia, rigor, tremor, and postural instability. Several years before motor, various non-motor symptoms may be observed, such as depression, pain, fatigue, loss of smell, low blood pressure. The aim of this cross-sectional study was to investigate gender differences in non-motor symptoms in patients with Parkinson's disease.
Methods: This study included patients with idiopathic Parkinson's disease treated at the Osijek College Hospital. A demographic questionnaire, non-motor symptoms questionnaire (NMSQ) and autonomic dysfunction questionnaire (SCOPA-AUT) were used to assess clinical presentation.
Results: We studied 96 idiopathic PD patients (35 women and 61 men). Patients did not differ in age or disease duration. We found no difference in age at disease onset (60.1 years in women and 61.1 years in men) between the sexes. Among non-motor symptoms, we observed urinary urgency (P = 0.05) and feelings of anxiety and panic (P = 0.008) more frequently in women and decreased or increased sexual desire in men (P = 0.05). There was no statistically significant sex difference in other non-motor symptoms. In autonomic functions, the only difference was in thermoregulatory functions (P = 0.03), which were more impaired in women. No significant gender difference was found in the other five domains or in the total score.
Conclusion: Age of onset did not differ between genders. Symptoms such as urinary urgency, thermoregulatory dysfunction, anxiety and panic are more common in women, while decreased or increased sexual desire is more common in men.
Disclosure: The authors have nothing to disclose.

EPO-463

Apomorphine Sublingual Film for OFF episodes in PD: Impact on Orthostatic Hypotension during Dose-Optimization

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Background and aims: Apomorphine sublingual film (SL-APO) has been shown to be an effective and generally well-tolerated on-demand treatment for OFF episodes in patients with Parkinson's disease (PwPD) [1, 2]. Several dopamine agonists have been associated with orthostatic hypotension (OH). Objective: To assess the impact of SL-APO on the occurrence of OH during dose-optimization, based on blood pressure (BP) readings and adverse event (AE) reporting in two pivotal trials (CTH-300 and CTH-302).
Methods: SL-APO was optimized in PwPD and OFF episodes to obtain an effective and tolerable dose. Patients' BP was measured before and 1h after SL-APO intake when they visited clinics during the dose-optimization phase. We post-hoc analyzed OH-related AEs, BP readings, and their co-occurrence.
Results: At 652 dose-optimization visits from 240 patients, mean BP readings before and after SL-APO intake were comparable. In these visits, the frequency of OH appearing after SL-APO intake was similar to the frequency of OH occurring at pre-dosing only. Correspondingly, visits with reported OH-related AEs (5.4% of total visits) were accompanied by OH, based on BP readings, at a comparable frequency before and after SL-APO intake only (see Table).

Results Table

	Pre-dose	Post-dose
Supine BP (μ±SEM, mmHg)	138.7±0.7 mmHg systolic BP, 81.5 ±0.4 mmHg diastolic BP	139.7±0.8 mmHg systolic BP, 82.0 ±0.4 mmHg diastolic BP
Standing BP (μ±SEM, mmHg)	135.0±0.7 mmHg systolic BP, 81.9 ±0.4 mmHg diastolic BP	136.4±0.8 mmHg systolic BP, 82.7 ±0.5 mmHg diastolic BP
Difference between standing and supine BP (μ±SEM, mmHg)	-3.6±0.5 mmHg systolic BP, 0.5±0.3 mmHg diastolic BP	-3.3±0.5 mmHg systolic BP, 0.7±0.3 mmHg diastolic BP
visits with OH based on BP readings (n, %)	52/652, 8.0%*	51/652, 7.8%**
visits with OH-related AE and OH based on BP readings (n, %)	4/652, 0.6%*	5/652, 0.8%**

* considered when OH occurred only at pre-dose and not at post-dose
** considered when OH occurred only at post-dose and not at pre-dose

Table

Conclusion: Overall, SL-APO did not affect general BP readings nor the frequency of OH as assessed by those readings during dose-optimization at in-clinic visits (co-occurring with or without reported OH-related AEs). 1. Olanow et al., Lancet Neurol. 2020; 19(2):135-144. 2. Stocchi et al., Mov Disord 2022; 37(Suppl 1, abstract 781).
Disclosure: This study has been supported by BIAL - Portela & C[a], S.A.

EPO-464

A role of transcranial sonography in dystonia and tremor: a possible insight into underlying pathophysiology?

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Background and aims: The association between tremor and dystonia has been recognized for over 100 years, but many uncertainties remain concerning possible shared underlying pathophysiology of these disorders. The discrimination between these conditions in clinical setting is still challenging and reliable biomarkers are needed. Transcranial sonography (TCS) is an easily available, non-invasive and inexpensive tool providing information about the morphology of the brain and it's been proven useful in the differential diagnosis of different movement disorders. The aim of this study was to investigate changes in TCS in patients with focal dystonia (FD) with or without tremor and to assess its role as a potential tool in differentiating these conditions.
Methods: Our study included 92 FD patients who were regularly monitored and treated at the Clinic of Neurology, University Clinical Center of Serbia. They were assessed for the presence of TCS changes.
Results: .The study included 92 FD patients, among them 31 had either head tremor or head and arm tremor combined. There were no clinically significant changes in echogenicity of the substantia nigra (SN) between the groups, neither in diameter of the third ventricle. However, TCS revealed significantly higher prevalence of hyperechogenic nucleus lentiformis (LN) ($p < 0.05$) in patients with FD and tremor (Table 1).

N=92	Focal dystonia without tremor (N=61)	Focal dystonia with tremor (N=31)	p (<0.05)
SN echogenicity (cm2)*	0,15±0,05	0,16±0,07	0,72
Third ventricle diameter (mm)*	6,03±2,13	6,10±2,09	0,89
LN hyperechogenicity (Y or N)£	11:50 (18:82%)	12:19 (39:61%)	**0,03**
SN hyperechogenicity (Y or N)£	19:38 (33:67%)	11:18 (36:64%)	0,67
Brainstem raphe (grade 0 or 1)£	25:33 (43:57%)	9:20 (31:69%)	0,35

*Mean values ± SD, £ number of patients with percentage in brackets, p < 0.05.

Table 1. TCS findings in patients with focal dystonia with and without tremor

Conclusion: The LN hyperechogenicity was more prevalent in patients with FD presenting with tremor. This result could suggest a possible role of LN in pathogenesis of tremor, but also highlight possible pathophysiological mechanism shared with dystonia. However, further investigation on a larger sample is needed.
Disclosure: Nothing to disclose.

EPO-465

Sleep quality and autonomic dysfunction in a-synucleinopathies

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Background and aims: Clinical observations suggest that the presence of dysautonomia can worsen RBD symptoms and vice versa in Parkinson's Disease. We aimed to determine whether PD patients with RBD have more severe dysautonomia and whether sleep quality is correlated with autonomic dysfunction in PD. Cardiovascular autonomic control was assessed through heart rate variability (HRV) analysis, a non-invasive method quantifying the activity of the two branches of the ANS.
Methods: We enrolled 15 PD patients (8 RBD+, 7 RBD-), at the Neurology Unit of Policlinico Hospital, Milan. ECG and respiratory traces were recorded for 10 minutes in supine position; subsequently, a segment of 250 ± 50 beats was selected for the HRV spectral and symbolic analysis. Sleep quality was evaluated using a wireless monitoring patch for 1 night (RootiRx; 3 channels: ECG, thoracic effort and actigraphy). Questionnaires for subjective evaluation of sleep quality and autonomic symptoms were administrated.
Results: PDSS score negatively correlated with LF/HF, an index of sympathetic modulation, suggesting that sleep impairment is related to a sympathetic predominance. Low sleep efficiency and higher Wake time After Sleep Onset (WASO) scores were associated with higher sympathetic modulation (0V%) and reduced parasympathetic modulation (2UV%). Moreover, RBD+ patients had higher COMPASS-31 scores and worse sleep quality, assessed by PDSS.
Conclusion: Our preliminary data showed that altered sleep quality is significantly associated with cardiovascular sympathetic predominance in PD patients and that RBD+ patients have severer global autonomic dysfunction. Overall, this suggests that the link between altered sleep and autonomic dysfunction in PD should be more deeply investigated.
Disclosure: The authors have nothing to disclose.

EPO-466

Heterogeneity in congenital disorders of glycosylation (CDG): a case series

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Background and aims: Congenital disorders of glycosylation (CDG) are multisystemic diseases due to defects in synthesis and attachment of glycoproteins/glycolipid glycans, with onset in infancy and high prevalence of neurological symptoms.
Methods: Retrospective case series.
Results: Case 1: A 28 years-old man with PMM2-CDG (AR), who presented delayed psychomotor development and over time also cerebellar syndrome, strabismus, microcephaly and other bone deformities. He had special education, but could not pursue a job. On MRI (27-years) there was cerebellar atrophy and T2/FLAIR hyperintensities in caudate and posterolateral thalami. Case 2: A 22 years-old man with MAN1B1-CDG (autosomal recessive), currently on special needs school, who had delayed developmental milestones, cerebellar syndrome by the age of 8 years, scoliosis, bone hypermobility and later generalized dystonia. MRI (8-years) disclosed mild posterior periventricular hypersignal in T2/FLAIR. Case 3: A 24 years-old man with SLC35A2-CDG (X-linked) with normal psychomotor development and stature.
Conclusion: Our cases highlight the range of severity of CDG. The four patients have a predominant neurological and bone phenotype, with patient 4 also having significant psychiatric symptoms.
Disclosure: No disclosures.

EPO-467

Transferrin as a possible CSF biomarker in neurodegenerative proteinopathies

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Background and aims: Transferrin is one of the key proteins involved in iron homeostasis within the CNS. Impaired iron homeostasis can induce toxic protein oligomers and abnormal intracellular aggregates; the aggregation of a-synuclein and tau protein has been shown in vitro to be triggered by iron. The aim of this study was to determine whether cerebrospinal fluid (CSF) levels of transferrin differ between patients with PD, MSA, PSP, CBD and healthy controls or in general between α-synucleinopathies and tauopathies.

Methods: CSF transferrin levels were compared between groups of patients suffering from PD (n=77), MSA (n=24), PSP (n=24), CBD (n=7) and HC (n=90) and subsequently between the groups of α-synucleinopathies (n=101) and tauopathies (n=31). Mann-Whitney U test and Spearman correlation analysis were used for statistical analysis; tests were performed at a significance level of 0.05.
Results: A significantly lower CSF transferrin level (p=0.012) was present in the PD group when compared to HC. Significantly higher CSF level of transferrin was found in the group of tauopathies when compared to α-synucleinopathies (p=0.024).
Conclusion: Transferrin cannot enter the brain from the blood directly, and the iron transport in the brain is mediated by transferrin synthesized by oligodendrocytes and choroid plexus epithelial cells. CSF transferrin levels, which varies depending mutually on the amount of iron in the brain, may reflect differences between underlying pathophysiology of neurodegenerative proteinopathies; transferrin therefore might be one of the CSF biomarkers useful for their differential diagnosis. Supported by: the European Regional Development Fund - Project ENOCH (No. Z.02.1.01/0.0/0.0/16_019/0000868) and IGA-LF-2022-014
Disclosure: There is nothing to disclose.

EPO-468

RFC1 intronic repeat expansion in Serbian patients with sporadic and seemingly autosomal recessive cerebellar ataxias

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Background and aims: Autosomal recessive intronic repeat expansion in the gene for replication factor C subunit 1 (RFC1) has been described as a common cause of late-onset sporadic cerebellar ataxia associated with sensory neuropathy and vestibulopathy. The aim of this study was to investigate the presence of pathogenic expansions in the RFC1 gene in patients with sporadic and seemingly autosomal recessive ataxia from the Serbian population.
Methods: The study included 96 patients with sporadic or seemingly recessive ataxia in whom symptomatic and most frequent hereditary ataxias (SCA1, 2, 3, 6, 7, 17 and Friedreich's ataxia) were excluded. RFC1 mutation analysis was performed by duplex PCR and Sanger sequencing. Biallelic expansions are not amplifiable by standard PCR and don't harbor the wildtype AAAAG repeat motif.
Results: We identified biallelic pathogenic repeat expansion of the AAGGG motif in the RFC1 in five out of 96 patients with late-onset ataxia (5.2%). The age at onset of individuals with expansion was 46-58 years and they all had gait ataxia and absent reflexes on lower extremities, while three patients had dysarthria. Most patients had oculomotor abnormalities such as broken smooth pursuit, downbeat and gaze-evoked nystagmus. One patient had dystonic head tremor. All patients reported chronic cough. Nerve conduction studies showed signs of sensorimotor neuropathy in all five patients and four of them had cerebellar atrophy on MRI, while two patients suffered from vestibulopathy.
Conclusion: Biallelic mutations in the RFC1 are a relatively frequent cause of late-onset sporadic ataxia with neuropathy. Additionally, they may present with oculomotor abnormalities, vestibulopathy, and dystonia.
Disclosure: We have nothing to disclose.

EPO-469

Depicting a single-center cohort of Friedreich ataxia

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Background and aims: Friedreich ataxia (FA) is a common recessive ataxia, with a wide spectrum of neurological and extra-neurological involvement. We aimed at characterizing the phenotype and genotype of a series of patients.
Methods: Unicentric prospective study, since 2017. Patients identified from an institutional ataxia database. Data collection and analysis performed on RedCap.
Results: Seventeen patients (12 families) were identified (58.8% male). Mean age-of-onset was 14.7±12.2 yrs, including one late-onset (LOFA) and one very late-onset (VLOFA) case. Seven probands (41.2%) had family history of FA, 2 families (11.8%) were known to be consanguineous. Presenting signs/symptoms were gait instability (64.7%), neuropathy (29.4%) and epilepsy (5.9%). Besides cerebellar syndrome in all, 76.4% had pyramidal signs and 52.9% segmental dystonia. Eight patients (47.1%) developed hypertrophic cardiomyopathy and 5 (29.4%) diabetes mellitus. The commonest MRI finding was cervical spinal atrophy (29.4%). Mean age at diagnosis was 22.2±14.6 years. Six patients (35.3%) were homoallelic, with a mean GAA repetition of ~800 [min:607; max:923]. When heteroallelic, repeat number was ~351 [90; 850] for the smaller and ~832 [707; 973] for the larger allele. Mean (GAA)n correlated with earlier age of onset (rS = -0.820, p<0.001). After a follow-up of 15.1±9.4 years, mean SARA was 21.4±12.4. Two patients died.
Conclusion: We highlight the presence of atypical forms, with late-onset or epilepsy, which may lead to diagnostic delay. The relatively high frequency of FA carriers in our general population (1/158) may explain the reduced proportion of known consanguineous cases in our cohort.
Disclosure: The authors have nothing to disclose.

EPO-470

Parkinson's Disease Burden and Device-Aided Therapy Utilization: Interim Results From the PROSPECT Observational Study

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Background and aims: As Parkinson's disease (PD) progresses, motor complications make it increasingly difficult for many patients to manage symptoms with oral anti-parkinsonian medications. We present interim outcomes of an ongoing international observational study evaluating clinical and economic outcomes, and treatment patterns of patients with PD whose symptoms are inadequately controlled with their current therapy.

Methods: PROSPECT (a PRospective Observational Study to evaluate the disease Progression and burdEn of disease of PD patients inadequately Controlled by conventional Therapy) is an ongoing 24-month study. PROSPECT enrolled adults (aged >=30 years) with idiopathic PD who had inadequately controlled motor symptoms (>=2.5 hours/day 'Off' time) despite optimisation of oral medications and were not receiving device-aided therapy (DAT). Interim 12-month outcomes are reported.

Results: This interim analysis includes 90 patients; the mean (SD) age was 68.7 (8.8) years, time since PD diagnosis was 8.7 (5.0) years, time since first motor fluctuation was 6.5 (5.0) years, and daily 'Off' time duration was 5.0 (2.7) hours (Table). By month 12 DAT was offered to 40.3% of patients (n/N=27/67), of whom 29.6% (n/N=8/27) initiated DAT (Figure). Patients who refused DAT reported needing more time to decide and feeling insecure with the procedure. At month 12, the average (SD) change in daily 'Off' time from baseline was −0.3 (1.8) hours (n=50) for patients remaining on oral anti-parkinsonian medication.

Characteristic	All Patients N = 90
Age, years, mean (SD)	68.7 (8.8)
Sex, n (%)	
Males	47 (52.2)
Duration of PD, years, mean (SD)	8.7 (5.0)
Time since first motor fluctuation, years, mean (SD)	6.5 (5.0)
Daily 'Off' time[a], hours, mean (SD)	5.0 (2.7)
History of levodopa-induced dyskinesia[b], n (%)	41 (45.6)
Duration of levodopa-induced dyskinesia, years, mean (SD)	4.3 (3.8)
Use of at least one PD medication, n (%)	77 (85.6)
Amantadine derivatives	22 (24.4)
Istradefylline	9 (10.0)
Dopa and dopa derivatives	70 (77.8)
Dopamine agonists	61 (67.8)
Dopaminergic agents	1 (1.1)
Monoamine oxidase B inhibitors	45 (50.0)
Other dopaminergic agents	26 (28.9)
Tertiary amines	1 (1.1)

PD, Parkinson's disease.
[a]'Off' time is reported as the average normalised 'Off' time, based on a 16-hour waking day, using the Hauser PD diaries completed by patients during the 3 days prior to each study visit.
[b]Obtained from medical reports.

Table. Baseline Demographics and Disease Characteristics

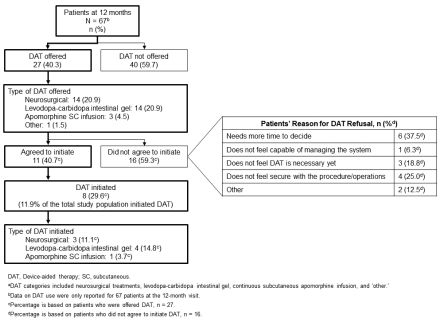

Figure. Patients' initiation of DAT, reported at 12 months.

Conclusion: Despite having a high initial burden of PD symptoms and no improvement in 'Off' time at month 12, most physicians and patients chose to remain on oral medications.

Disclosure: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication, and agreed to submit this abstract to the European Academy of Neurology (EAN) 2023 Congress for consideration as an oral presentation or poster. No honoraria or payments were made for authorship. AbbVie and authors thank all the trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Morgan Gingerich, PhD, of JB Ashtin, and funded by AbbVie.

EPO-471

Orthostatic Hypotension in Parkinson's Disease: Is there a role for Locus Coeruleus Magnetic Resonance Imaging?

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Background and aims: Orthostatic Hypotension (OH) is a common and debilitating non-motor symptom in Parkinson's disease (PD) but the mechanisms underlying its development remain largely elusive. Peripheral and central noradrenergic denervation are both likely to play a key role. Locus coeruleus (LC) is the main noradrenergic nucleus of the brain and its early degeneration in PD has been put in relation with a variety of non-motor symptoms, including OH, but with inconsistent results.
Methods: In a case-control study we compared the MRI-LC parameters (LC signal intensity -LC ratio- and the estimated number of voxels -nVox) in 11 PD patients with OH (PD-OH+) versus 11 without OH (PD-OH-), matched for sex, age and disease duration. We also tested for correlations between subject's LC-MRI features and orthostatic drop in systolic blood pressure (SBP).
Results: PD-OH- and PD-OH+ did not differ significantly based on demographics and clinical characteristics, except for blood pressure measurements and cardiovascular score in the SCOPA-AUT questionnaire. LC ratio and nVox were significantly lower in PD patients compared to the LC-MRI parameters of 52 age-matched healthy volunteers, while no differences were observed between PD-OH- and PD-OH+. Additionally, no correlation was found between the MRI-LC measures and the orthostatic drop in SBP or the clinical severity of autonomic symptoms.
Conclusion: Our results failed to indicate a link between the LC MRI features and the presence of OH in PD but confirmed a marked alteration of LC signal in PD patients.
Disclosure: We have nothing to disclose.

EPO-472

Functional disorders in Parkinson's disease patients with deep brain stimulation – a case series

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Background and aims: Functional neurologic disorders (FND) are disorders with a neurologic presentation but without a clear organic cause. They mostly present as symptoms mimicking actual disorders and can have an organic background, making their proper diagnosis especially challenging. A specifically interesting phenomenon is the emergence of FMDs in patients with Parkinson's disease (PD) with deep brain stimulation (DBS). We report 3 such cases.
Methods: We present three patients that were treated at the Clinic for Neurology in Rijeka and presented with FND-s after DBS. First is a 62-year old female patient with billateral STN-DBS that presented with severe right-sided tremor, the second is a 54-year old male with STN-DBS that presented with extreme „stiffness", hypophonia and a history of dopamine abuse and the third is a 50-year old bilateral STN-DBS patient that presented with bilateral leg weakness which would emerge only in walking, but not in other activities.
Results: After using broad diagnostic methods and excluding other potential causes for the symptoms, we utilized a multidisciplinary approach including physical therap and work therapy, psychological support as well as methods such as „sham" stimulation, distraction and suggestion, achieving a beneficial therapeutic effect in the end and the improvement of the symptoms over time.
Conclusion: FND-s pose a challenging diagnostic and therapeutic problem in modern neurology and even more so in patients with underlying conditions such as PD, especially in those with DBS. A multidisciplinary approach should be utilized when treating these complex patients and for the best therapeutic effect.
Disclosure: Authors have nothing to disclose.

Epilepsy 3

EPO-473

Biallelic Pathogenic Variants in RARS2 Cause Progressive Myoclonus Epilepsy and Variable Epilepsy Phenotype

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Background and aims: Biallelic pathogenic variants of RARS2 are associated with pontocerebellar hypoplasia type 6 (PCH6) typically manifesting with vermian hypoplasia and refractory seizures1. We aim to characterize the epilepsy phenotype of individuals with RARS2 mutations.
Methods: we included patients carrying pathogenic variants of RARS2, referred to our Institute. All patients underwent a comprehensive electro-clinical work-up.
Results: we selected 4 individuals (mean age 29,5±1,29 years) carrying compound heterozygous mutations of RARS2 [NM_020320 m1:c.1A>T(p.Met1 Leu), m2:c.1544A>G(p.Asp515Gly); m3:c.1586+3A>T, m4:c.1366C>T(p.Arg456Cys); m5:c.1305+1G>A, m6:c.1026G>A(p.Met342Ile)]. One variant is novel. The mean age at seizure onset was 12,08±16,19 months. One patient presented with myoclonic and GTCS evolving in status epilepticus, 2 with spasms, one with tonic and GTCS. A transient response to vitamin B6 was documented in one individual. With disease progression, 2 patients developed multiple seizure types, 2 showed myoclonic and GTCS, respectively. Two individuals with earlier age at onset showed microcephaly, spastic tetraparesis, profound intellectual disability (ID) and cortical blindness. Interictal EEG showed a severe slowing of background activity with multifocal epileptiform abnormalities. Brain MRI highlighted the typical pontocerebellar atrophy. The other 2 patients manifested a milder phenotype with moderate ID, cerebellar signs and action myoclonus, resembling Progressive myoclonus epilepsy (PME). Interictal EEG showed epileptiform discharges predominant posteriorly and a photoparoxysmal response. Brain MRI was normal.
Conclusion: Biallelic pathogenic variants of RARS2 cause mitochondrial encephalopathy with variable inter and intra-family severity: from classic PCH6 to a milder PME phenotype. Pontocerebellar atrophy is not a mandatory feature. Our data widen the epilepsy phenotype of RARS2, to include PME.
Disclosure: The authors have no disclosures.

EPO-474

Psychogenic Non-epileptic Seizures – Semiology, Time and the Role of a Multidisciplinary Follow-up

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Background and aims: Psychogenic non-epileptic seizures (PNES) are relatively common, however, factors that predict prognosis are still largely unknown.
Methods: We selected a group of patients with documented-PNES on video-electroencephalogram monitoring between 2012-2021 with follow-up data. Data on demographics, previous medical history, PNES semiology, time to diagnosis, medications, and type of follow-up were collected. PNES evolution was dichotomized as improvement (resolution/decreased frequency) and absence of improvement (maintenance/worsening frequency). Statistical analysis was performed to find prognostic factors.
Results: A total of 31 patients were included, 26 females, mean age 43,0±14, years. Mean time to diagnosis was 12,6±11,3 years. Mean follow-up time post-diagnosis was 3.1±2.9 years. Patients were followed in the outpatient clinic of neurology (n=27), psychiatry (n=21) and/or psychology (n=8). Seventeen patients improved (2 complete remissions); nine had no improvement. Patients with multiple PNES semiologies were less likely to improve (p=0.012). Sixteen patients reduced anti-seizure medications (ASM): this was more common in those with multiple PNES semiologies (p=0,023), in the presence of ictal-cry (p=0,033) and in patients with follow-up in psychology (p=0,040). Time to diagnosis was inversely related to degree of ASM reduction (p=0,011). There were no statistically significant differences in prognosis relating to: sex, age, education level, employment status, comorbidities (epilepsy/psychiatric diseases) or medications.
Conclusion: In our cohort, although PNES remission was rare, more than half of patients improved. Multidisciplinary follow-up, namely psychological intervention, seem to have an impact on the reduction of unnecessary medications. Although multiple PNES semiologies seem to predict a worse prognosis ASM reduction was still possible in these patients.
Disclosure: Nothing to disclose.

EPO-475

Late-onset epilepsy in cerebral amyloid angiopathy patients: a case-control study

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Background and aims: Sporadic cerebral amyloid angiopathy (CAA) is characterized by amyloid deposition in the walls of leptomeningeal and small cortical arteries of the central nervous system [1]. Epileptic seizures at CAA onset have been rarely reported and their prevalence is unknown. Given the high frequency of CAA in elderly population and the epileptogenic role of cortical hemorrhagic lesions, it may be hypothesized that CAA can explain a proportion of late-onset epilepsies of unknown etiology. This study aims to assess the prevalence of CAA in patients with late-onset (>50years) epilepsy of unknown or vascular etiology and in age-matched nonepileptic controls.
Methods: We included subjects with late-onset epilepsy and controls affected by other neurological conditions. All subjects underwent MRI (1.5 Tesla) including blood-sensitive sequences. In the epilepsy group, MRI had to be performed within 60 days from epilepsy onset. To evaluate differences between groups, a Chi-squared test was performed. We also calculated odds ratio (OR).
Results: We included 54 patients with late-onset epilepsy (29 males, mean age 70.3±8.7 years) and 128 age-matched controls (76 males, mean age 71.4±9.8 years). A diagnosis of probable CAA according to Boston criteria 2.0 [2] was done in 14.8% (8/54) of patients with late-onset epilepsy and in 3.1% (4/128) of the control group. This difference was statistically significant (p=0.01). OR for seizures in CAA vs. non-CAA was 5.4 (95% CI:1.55-18-8)
Conclusion: In our case-control study, the prevalence of CAA resulted significatively higher in patients with late-onset epilepsy, suggesting a significant association between probable CAA diagnosis and late-onset epilepsy.
Disclosure: Nothing to disclose.

EPO-476

Prognostic patterns and long-term seizure outcome of non-surgically treated patients with focal cortical dysplasia

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Background and aims: Focal cortical dysplasia (FCD) represents a relative common cause of surgically remediable focal epilepsy. However, some patients may not undergo surgery for multiple reasons, and little is known regarding their long-term prognosis. In this study, we aimed to investigate prognostic patterns and long-term seizure outcome in cohort of non-surgically treated FCD patients.
Methods: Data from patients with focal epilepsy followed from 1975 to 2022 were retrospectively reviewed. We included patients with an imaging diagnosis of FCD who did not undergo surgical treatment due to their choice or clinical reasons, followed-up for more than 5 years from epilepsy diagnosis.
Results: Thirty-eight patients were included. The median age was 49.5 years (Interquartile range [IQR] 36-62] and the median follow-up was 11.5 years (IQR 8-18) (table 1). Surgery was not performed because of bilateral seizures (n= 4, 10.5%), involvement of eloquent brain areas (n=10, 38% of patients), patient's choice (n=7, 18.4%) or lack of drug-resistance (n=7, 18.4%). The most common prognostic pattern was non-remitting course (n=20, 52.6% of patients), followed by relapsing-remitting and late-remission patterns (18.4% each), and by early remission (10.5%) (figure 1). Remission patterns were associated with a parietal localization of FCD, whereas no remission course with focal seizures with impaired awareness and epileptiform abnormalities on baseline EEG ($p < 0.05$).

Clinical characteristics of the population (n=38)		
Variable		**n**
Gender	Male, n (%)	20 (52.6)
	Female, n (%)	18 (47.4)
Age (median, [IQR]); years	49.5 [36-62]	
Age at epilepsy onset (median, [IQR]); years	10 [4-18]	
Follow-up (median, [IQR]); years	11.5 [8-18]	
FCD localization	Frontal, n (%)	16 (42.1)
	Parietal, n (%)	8 (21.1)
	Temporal, n (%)	14 (36.8)
Prognostic patterns	No remission, n (%)	20 (52.6)
	Relapsing-remitting, n (%)	7 (18.4)
	Early remission, n (%)	4 (10.5)
	Late remission, n (%)	7 (18.4)
EEG abnormalities	Normal, n (%)	6 (15.8)
	Focal slowing, n (%)	5 (13.2)
	Epileptiform abnormalities, n (%)	27 (71)
Seizure frequency at last follow-up	Daily, n (%)	6 (15.8)
	Weekly, n (%)	9 (23.7)
	Monthly, n (%)	7 (18.4)
	Annually, n (%)	5 (13.2)
	No seizures, n (%)	11 (28.9)

Table 1 - Clinical characteristics of the population

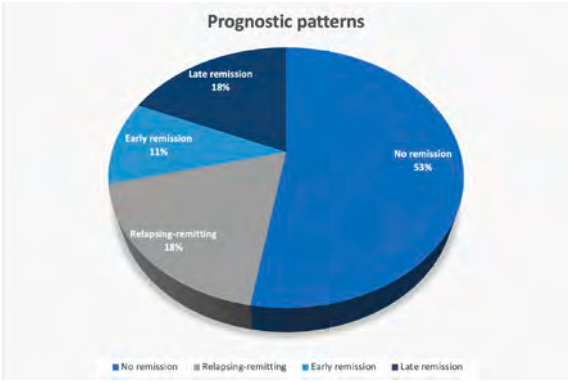

Figure 1 - Prognostic patterns

Conclusion: Our study highlights the prognostic patterns of non-surgically treated FCD patients and provides some electroclinical factors associated with long-term outcome.
Disclosure: Nothing to disclose.

EPO-477

Inflammatory cytokines, synaptic proteins and oxidative stress in children with epilepsy: A cross sectional study.

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Background and aims: Oxidative stress, inflammatory cytokines and synaptic proteins play a pivotal role in the pathogenesis of epilepsy. The study explored the underlying mechanism of excitotoxicity with respect to the roles of interleukin-1β (IL-1β), IL-6, α-synuclein, neuron-specific enolase (NSE), C-reactive protein (CRP) and free radicals.
Methods: Eighty-five children from 9 months to 12 years of age with epilepsy were compared to healthy controls (n=70) in this study. The concentrations of CSF NSE, 1L-1β, IL-6, α-synuclein and CRP were measured by specific ELISA methods. Saliva parameters for free radicals were analyzed.
Results: Mean salivary values of peroxidase and SOD activity increased by 19 % as compared to the controls. The lower plasma Nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) level in epileptic group was highly significant as compared to controls. The mean concentrations of NSE, IL-1β, Il-6 and CRP in the epileptic group showed a significant increase ($P < 0.05$) as compared with the control group. The mutual correlations of NGF, NSE, α-synuclein, 1L-1β, IL-6 and CRP were also analyzed. Results inferred that there were positive correlations between the markers and seizure severity and frequency.
Conclusion: Our results provide insights into high rate of oxidative metabolism coupled with increased inflammatory cytokines in pediatric epilepsy. The results support the possibility of using an appropriate selection of serum cytokine for early diagnosis and emphasize the need to standardize quantitative methods for serum analysis. Our findings also contribute to the ongoing efforts toward identification of early biological markers specific to subphenotypes of epilepsy.
Disclosure: Nothing to disclose and nothing to declare no conflict among the authors.

EPO-478

Admission neutrophil-to-lymphocyte ratio predicts need for ICU admission in Status Epilepticus

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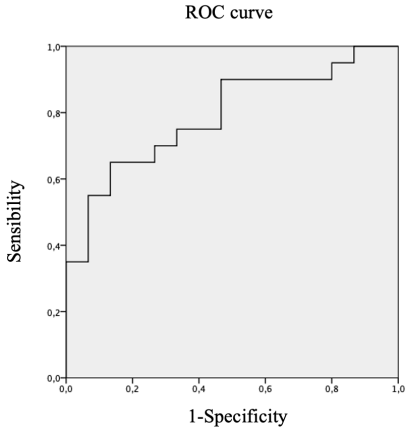
Background and aims: Status epilepticus (SE) is a time-dependent neurological emergency characterized by a high mortality and morbidity rate, and high healthcare costs associated. The introduction of reliable prognostic markers into clinical practice could be useful in rapidly identifying critically-ill patients. The current study evaluates the correlation between admission neutrophil-to-lymphocyte ratio (NLR) and need for ICU admission.
Methods: In this retrospective observational cohort study we enrolled consecutive patients with a diagnosis of SE from 1st January 2022 and 31st December 2022. Anagraphic data, STESS, NLR and SE etiology and semeiology were collected. Multivariate analyses were conducted to test the association of NLR with the need for Intensive Care Unit (ICU) admission and 30-day mortality. Receiver operating characteristic (ROC) analysis was performed to identify the best cutoff for NLR to identify patients who will need ICU admission.
Results: A total of 35 patients were enrolled in our study. Demographic data are reported in table 1. NLR was correlated with the need for ICU admission at stepwise multivariate (OR= 1.787 CI (1.141-2.799); p=0.011). Thirty days mortality was correlated with STESS (OR= 6.391 CI (1.965-2.079); p=0.002), but not with NLR. ROC analysis identified an NLR of 7.0 as the best cutoff value to discriminate the need for ICU admission (area under the curve [AUC]=0.790; p=0.004; Youden's index=0.430; sensitivity, 70.0%, specificity, 73.3%).



Receiver operating characteristic (ROC) analysis

Sex n (%)	
M	11 (31.4%)
F	24 (68.6%)
Age (y)	69 (64 – 83)
STESS	4.2 (3 – 5)
Clinical presentation n (%)	
CSE	7 (20.0%)
NCSE	28 (80.0%)
ICU admission n (%)	20 (57.1%)

Demographic characteristics of the included sample (n = 35). Medians (IQRs) and proportions as appropriate. CSE = Convulsive Status Epilepticus, NCSE = Non-Convulsive Status Epilepticus, IQRs = Interquartile Range (25th -75th percentile).

Conclusion: In patients with SE admission NLR could be a predictor of the need for ICU admission. Serum biomarkers could be considered to implement clinical prognostic scores in SE.
Disclosure: Nothing to disclose.

EPO-479

Long-term outcome of Status Epilepticus: The relationship between aetiology and the risk of subsequent epilepsy

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Background and aims: The aim of our study was to evaluate the incidence of late seizure (LS) in a cohort of first-ever Status Epilepticus (SE) survivors.
Methods: Retrospective monocentric study of adults patients with a SE who were consecutively admitted to the Modena Academic Hospital (Italy), from September 2013 to March 2022. Post-anoxic episodes and patients with a previous diagnosis of epilepsy were excluded. Kaplan–Meier survival analyses were used to calculate the probability of seizure freedom following the index event, whereas a Cox proportional hazard regression model was used to identify outcome predictors.
Results: Patients were included, 280 (66%) of whom survived at 30 days from SE onset. Overall, 55 out of 280 patients (19.6%) developed LS or experience SE recurrence (mean follow-up: 29.8 months). For the majority of cases (36/55; 65%), the first relapse occurred within the first year of follow-up, whereas the cumulative probability of seizure freedom was 84% and 68% at 12 months and 5 years, respectively. The risk of LS was significantly higher after SE due to structural aetiologies (HR 1.84 95% CI 0.98 – 3.43), or in case of early prominent motor episodes with evolution into non-convulsive SE (HR 2.86 95% CI 1.31 – 6.27).
Conclusion: after a first-ever SE, the cumulative probability of seizure freedom remained high up to 5 years from the index event. However, in case of SE due to structural aetiologies, and in case of motor SE evolving to NCSE, patients may be at higher risk of relapsing, especially within 12 from SE.
Disclosure: Nothing to disclose.

EPO-480

Prolongation of cortical sleep spindles during hippocampal interictal epileptiform discharges in epilepsy patients

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Background and aims: Memory deficits are frequent among patients with epilepsies affecting the temporal lobe. Hippocampal interictal epileptic discharges (hIED), the presumed epileptic exaggeration of sharp wave-ripples (SWR) are known to contribute to memory dysfunctions, but the potential underlying mechanism is unknown. The precise temporal coordination between hippocampal SWRs and corticothalamic spindles during sleep is critical for memory consolidation. In the present study we aimed to assess the influence of hIEDs on neocortical spindles.
Methods: Methods We analyzed the spindle characteristics (duration, amplitude, frequency) of 21 epilepsy patients implanted with foramen ovale (FO) electrodes during a whole night sleep. Scalp sleep spindles were categorized based on their temporal relationship to hIEDs detected on the FO electrodes. Three groups were created: (i) spindles coinciding with hIEDs, (ii) spindles “induced” by hIEDs, and (iii) spindles without hIEDs co-occurrence.
Results: We found that spindles co-occurring with hIEDs had altered characteristics in all measured properties, they lasted longer, had higher amplitude and their frequency

range shifted towards the higher frequencies. Also hIED-induced spindles had identical oscillatory properties with spindles without any temporal relationships with hIEDs.
Conclusion: We investigated the effect of hippocampal IEDs on neocortical spindle activity and found spindle alterations in cases of spindle-hIED co-occurrence, but not in cases of hIED-initiated spindles. We propose that this is a marker of a pathologic process, where IEDs may have direct effect on spindle generation. It could mark a potential mechanism where IEDs disrupt memory processes, and also provide a potential therapeutic target to treat memory disturbances in epilepsy.
Disclosure: None of the authors has any conflict of interest to disclose.

EPO-481

What do 90-99% responder rates mean in patients treated with cenobamate: results from an open label extension study

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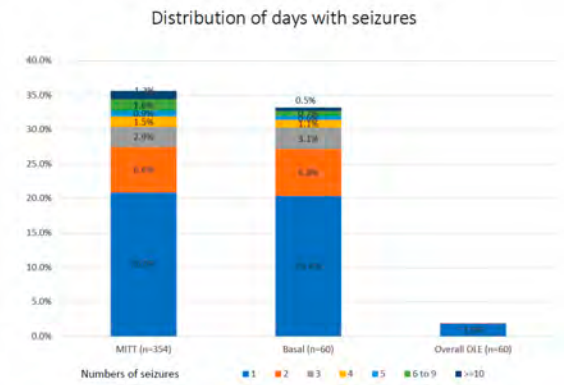
Background and aims: Cenobamate is an antiseizure medication (ASM) approved in Europe as adjunctive therapy for adults with inadequately controlled focal seizures. Maintained seizure freedom is the goal of epilepsy treatment, however, it is not always possible to achieve. Here we analyze the long-term 90-99% responder population during the whole C017 open label extension (OLE) study.
Methods: Adults with focal seizures despite treatment with 1-3 concomitant ASMs completed the double-blind treatment and entered the CO17 OLE study. A Post-hoc analysis was performed in patients who achieved responder rates ≥90% but did not achieve seizure freedom to quantify seizure-free days during the whole OLE.
Results: 17% (60/354) of participants achieved 90-99% responder rates during the length of their participation in the OLE study (median 291.3 weeks). 90- 99% responders had a median duration of epilepsy of 24 years compared to 23 years for the mITT (modified Intention to treat) population. Baseline seizure frequency was 8.75 for 90-99% responders vs 9.5 for mITT. The proportion of days with seizures during the baseline period was similar in both populations: 43.3% (27/60) of the 90-99% responders were seizure free for 99% of the days and more than 90% (55/60) were seizure free for at least 95% of the days. 90-99% responders had one seizure 1.9% of the days, two seizures 0.2% of the days, and >2 seizures less than 0.05% of the days.
Conclusion: While seizure freedom is the goal of epilepsy treatment, the ≥90% seizure reduction obtained with cenobamate, might be also an optimal long-term outcome. This outcome measure may be used in other ASM studies.
Disclosure: The original study (NCT01866111) was supported by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini S.p.a. (Rome, Italy).



EPO-482

Focal adenosine A1 receptor activation through photopharmacology as a potential treatment for drug-resistant epilepsy

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Background and aims: The inhibitory adenosine A1 receptors (A1Rs) possess potent seizure-suppressive effects. However, A1R agonists cannot be administered systemically due to severe side-effects. Local A1R activation could be achieved with photopharmacology, which provides control over the activity of a drug using light. In this study, photocaged cyclopentyladenosine (pcCPA; an inactivated A1R agonist) is being tested in vivo as a potential epilepsy treatment.
Methods: The possibility to activate pcCPA in vivo was first studied by investigating effects on hippocampal evoked potentials (EPs). Healthy mice were implanted with an optrode in the hippocampus through which light was delivered after intracerebroventricular (ICV) injection of pcCPA. Effects were compared to those of ICV injection of the active compound CPA. To test the effect of local pcCPA activation on hippocampal seizures, epileptic mice received an injection of pcCPA through a cannula implanted above the lateral ventricle after which light was delivered via an optrode implanted in the hippocampus. The occurrence of

seizures was compared before and after the intervention.
Results: Local illumination in the hippocampus after ICV injection of pcCPA resulted in suppression of hippocampal EPs, similar to that obtained with administration of CPA, indicating successful activation of A1Rs. In a pilot study with epileptic mice, ICV administration of pcCPA combined with hippocampal illumination suppressed the occurrence of seizures.
Conclusion: This study provides proof of concept that local activation of A1Rs can be achieved in vivo using photopharmacology. The first results with pcCPA in epileptic mice show that this approach could be effective for suppressing seizures.
Disclosure: Nothing to disclose.

EPO-483

Interim analysis of adjunctive perampanel as 2nd or 3rd anti-seizure medication from the observational PERPRISE study

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Background and aims: Prospective data on perampanel use in Germany mainly consist of late adjunctive therapy for refractory epilepsy. In this interim analysis from a subset of patients in PERPRISE (PERampanel in patients with PRImary or SEcondarily generalised seizures; NCT04202159), we compared those receiving perampanel-only adjunctive therapy as the 2nd versus 3rd anti-seizure medication (ASM).
Methods: PERPRISE is a multicentre, prospective, observational, non-interventional study to evaluate perampanel as the only adjunctive to current ASM monotherapy or as a substitute for one ASM during dual therapy. Patients (>=18 years) with focal or idiopathic generalised epilepsy who had >=1 focal to bilateral tonic-clonic seizure (FBTCS) or generalised tonic-clonic seizure (GTCS) within 3 months prior to inclusion were eligible. The Interim Analysis Set (IAS) includes patients who received >=1 dose of perampanel and attended or discontinued prior to the 6-month visit. Endpoints include retention rate, response rate, seizure-freedom rate and safety.
Results: As of 25 November 2021, 38 patients in the IAS were receiving adjunctive perampanel as 2nd (n=13) or 3rd (n=25) ASM. Retention rates were 92.3% and 84.0%, respectively, compared with 78.0% in the overall IAS (Figure 1). Response rates were comparable between 2nd or 3rd ASM groups for FBTCS+GTCS (Figure 2). However, seizure-freedom rates varied with the number of previous ASMs (Figure 3). Treatment-emergent adverse events (TEAEs) were reported in 48.0% of patients in the IAS; 7.0% reported serious TEAEs.
Conclusion: These data demonstrate favourable retention and seizure-freedom rates with perampanel-only adjunctive therapy as the 2nd or 3rd ASM for FBTCS and/or GTCS.

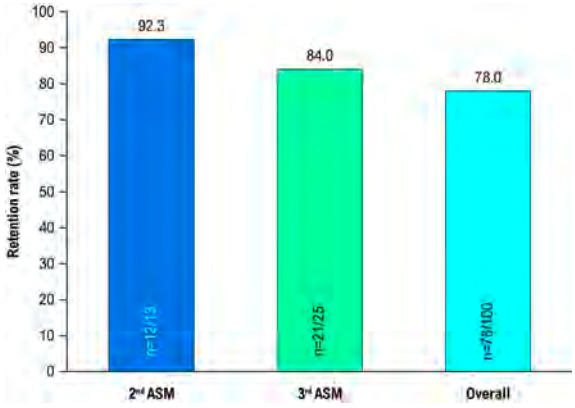

Figure 1. Retention rate of perampanel as 2nd or 3rd ASM administered as only adjunctive therapy at 6 months compared with the overall population (Interim Analysis Set)

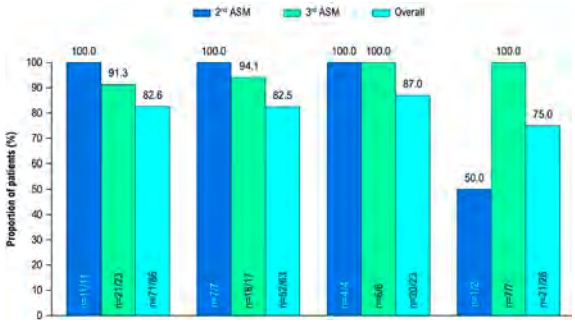

Figure 2. Response rate of perampanel as 2nd or 3rd ASM administered as only adjunctive therapy by seizure type at 6 months compared with the overall population (Interim Analysis Set)

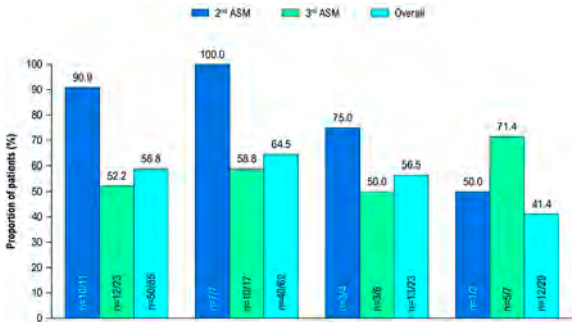

Figure 3. Seizure-freedom rate of perampanel as 2nd or 3rd ASM administered as only adjunctive therapy by seizure type at 6 months compared with the overall population (Interim Analysis Set)

Disclosure: This study was funded by Eisai GmbH. Bernhard J Steinhoff has received speaker honoraria from Angelini, Arvelle Therapeutics, Desitin, Eisai, GW Pharmaceuticals, Tabuk Pharmaceuticals, Teva and UCB Pharma; and has served as a paid consultant for Angelini, Arvelle Therapeutics, B. Braun Melsungen, Eisai, GW Pharmaceuticals and UCB Pharma. Tobias Goldmann is an employee of Eisai GmbH. Yaroslav Winter has received honoraria for educational presentations and consultations from Arvelle Therapeutics, Bayer AG, BIAL, Eisai, LivaNova, Novartis and UCB Pharma.

EPO-484

Psychiatric Comorbidities and Their Relationship With Quality of Life and Stigmatization in Patients With Epilepsy

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Background and aims: This prospective study aims to evaluate comorbid psychiatric diseases and stigmatization in patients with epilepsy, by investigating their relationship with clinical and sociodemographic data, to determine their effects on patients' quality of life and perceived stigma.
Methods: 300 patients were evaluated aged between 18-65 and diagnosed with epilepsy in the epilepsy outpatient clinic. Demographic, clinical, laboratory and, imaging features were assessed. Patients were classified using the International League Against Epilepsy's 2017 Classification of Epilepsy Syndromes and Seizures. Symptom Check List (SCL90-R), Quality of Life in Epilepsy Scale (QOLIE-10), and Perceived Stigma Scale were applied to all patients. Patients having SCL90-R general symptom index ≥ 1 were assessed using the Mini International Neuropsychiatric Interview by psychiatrists. The frequency of psychiatric comorbidities, relationship of comorbid psychiatric disorders with quality of life, and stigmatization in epilepsy patients were evaluated.
Results: Psychiatric comorbidities were found in 24% (n=64) of epilepsy patients. Mood (18.7%, n=50) and anxiety disorder were the most common (10.4%, n=28). The frequency of seizures (p=0,004), number of antiepileptics (p=0,015), previous epilepsy surgery and psychiatric disorder (p<0,001), high perceived Stigma (p<0,001), and QOLIE-10 (p<0,001) scores were all correlated to psychiatric comorbidities.
Conclusion: This study showed that a history of psychiatric disease, poor quality of life, and high perceived stigma were the most significant predictors of psychiatric comorbidities in epilepsy patients. This suggests that screening patients for comorbid psychiatric conditions in epilepsy outpatient clinics is critical to reduce psychosocial issues, economic burden of stigmatization, and improving quality of life.
Disclosure: The authors declare no conflicts of interest.

EPO-485

Re-operation after failed first epilepsy surgery: Our clinical experience

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Background and aims: Resective epilepsy surgery can lead to sustained seizure control in up to 70-80% of selected patients whereas seizure recurrence is about 20-30% after first epilepsy surgery. The aim of this retrospective study is to evaluate re-operated patients' clinical features, EEG/MRI findings and their seizure outcome.
Methods: We included consecutive patients who were re-operated between the years 1995-2018. The clinical characteristics, EEG findings, seziure outcome and the reason for second epilepsy surgery were analyzed.
Results: There were 620 patients who underwent resective epilepsy surgery. Twenty-seven(12 female, 15 male) patients(4.35%) re-operated after failed first surgery. The mean time between second and first surgery was 3±2.72, mean age of the re-operated patients were 18(3-35). Sixteen of the patients had focal cortical dysplasia, two patients had mesial temporal sclerosis three of them had neuroectodermal tumor and others were dual pathologies(FCD+MTS) and reactive gliosis. Tailered resection, anterior temporal lobectomy, corpus callosotomy and disconnection were the re-operation types. Most common pathologies were FCD type 2(n=6), type 3(n=5) and type 1(n=3). Engel classification after second epilepsy surgery were class 1 in 10 and class 2 in 8 patients end 70% of the patients in Engel1 group had FCD. Five patients couldn't be reached seizure information after re-operation.
Conclusion: Re-operation is possible after failed first surgery and some patients have chance for seizure freedom after it. Patients should be re-evaluated for the re-operation after first epileptic surgery who have consistant auras, continuation of the seizures, different auras and/or seizures.
Disclosure: Nothing to disclose.

EPO-486

Access to health care in patients with epilepsy in Latin America

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Background and aims: The lifelong prevalence of epilepsy in Latin America and the Caribbean (LAC) stands at an average of 17.8 per 1,000 inhabitants. The treatment gap is greater than 50%, thus more than half are not receiving any type of care. Our objective was to assess the access to epilepsy care in LAC.
Methods: We conducted a cross-sectional survey regarding access to care of people with epilepsy in LAC. Neurologists and epilepsy specialists were surveyed either by mail or in-person during the XII Latin American Epilepsy Congress in Medellin, Colombia from October 1st to 4th, 2022.
Results: 98 of 101 physicians answered our survey in person. Information was obtained from 17 countries in

LAC, 37,8% epilepsy specialists and 62.2% neurologists. 85% of physicians reported issues accessing education and work for people with epilepsy. 62.1% countries had prenatal care programs. 78% of physicians reported a high cost of care as the main access barrier. EEG was available in 94.5% countries and CT scan in 82.7%. 54% countries did not have legislation related to access to epilepsy surgery and 85.6% physicians reported there is no information available regarding this treatment.
Conclusion: There is a low prevalence of educational and work opportunities for patients with epilepsy in LAC. Government support is weak, as evidenced by a low prevalence of preventive measures for epilepsy. Most countries have access to neurologists and diagnostic equipment, yet with high cost of ASM. There is a need for improved access in the treatment, evaluation, and education of epilepsy in LAC.
Disclosure: Nothing to disclose.

EPO-487

Obstetric and neonatal outcome in women with epilepsy – a single center study in Poland.

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Background and aims: Pregnancy in women with epilepsy can be challenging due to the known teratogenicity of some antiseizure medication (ASM) and the risk associated with seizures during pregnancy.
Methods: We retrospectively reviewed the medical records of 190 pregnancies in 127 women with epilepsy treated in our outpatient clinic over the years 2010-2022.
Results: The average age at delivery was 30.1 years (±4.4). 78.3% of patients were on monotherapy and the majority were prescribed ASMs with low teratogenic potential (78.3%). Levetiracetam and lamotrigine were the most commonly used (70, 37.0% and 63, 33.3%). Valproic acid was used in 31 pregnancies (16.4%), topiramate in 11 (5.8%). Seizures during pregnancy occurred in 87 cases (46.5%) – more often in women on polytherapy (25, 29.1% versus 12, 12.0%; p= 0.009). Furthermore, seizures during the postpartum period (45, 56.3% versus 15, 15.8%; p<0.001) and caesarean section were more frequent (55, 73.3% versus 48, 55.8%; p=0.022) in this group. Among all pregnancies, there were 12 miscarriages (6.4%) and 6 cases (3.2) of termination of pregnancy. The majority delivered by caesarean section -103 cases (64.0%). Low birth weight (<2,500g) was detected in 13 newborns (11.3%), low Apgar score (≤7) in 9 (5.9%). 107 women (68.2%) decided to breastfeed - fewer in the polytherapy group (42.9% versus 74.2%, p=0.001)
Conclusion: Due to the use of new antiepileptic drugs with low teratogenic potential, most of the patients in our group gave birth to healthy children, and the percentage of congenital defects was low.
Disclosure: Nothing to disclose.

MS and related disorders 5

EPO-488

Association of multi-sensor derived motor features with established functional outcomes in people with MS

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Background and aims: Sensor-based measurements promise an accurate, objective, and reliable assessment of motor function in people with multiple sclerosis (PwMS). Within our study validating smartphone-based digital biomarkers (dreaMS, NCT05009160), we investigate the association of motor features derived by a multi-sensor inertial motion capture system with established functional outcomes.

Methods: Study participants were equipped with an 18-sensor inertial motion capture system (Xsens MVN) and performed the following tests in our outpatient clinic: Timed-up-and-go (TUG), 30-second walk, chair-rising, stair-climbing, and tandem walk. Signals captured by this system underwent automatic pre-processing, segmentation, and feature extraction (Figure 1). We examined correlations between these motor features and the Neurostatus-Expanded Disability Status Scale (EDSS), timed 25-foot walk (T25FW), and self-reported MS walking scale (MSWS-12).

Results: We included 52 PwMS (40 female [77%], mean age 45.9±11.1 years, median disease duration 11.2 years [range 0.2-37.1], median EDSS 2.0 [range 0-6.0], median T25FW 4.6s [range 3.3-13.2], and median MSWS-12 8.3% [range 0-100]). The strongest correlations were found for chair-rising (T25FW Pearson r=0.66 [95% CI 0.46-0.80], EDSS r=0.52 [0.28-0.70]), stair-climbing (T25FW r=0.57 [0.33-0.74], MSWS-12 r=0.50 [0.24-0.69]), and TUG (T25FW r=0.51 [0.24-0.71], MSWS r=0.43 [0.15-0.65]), see Figure 2.

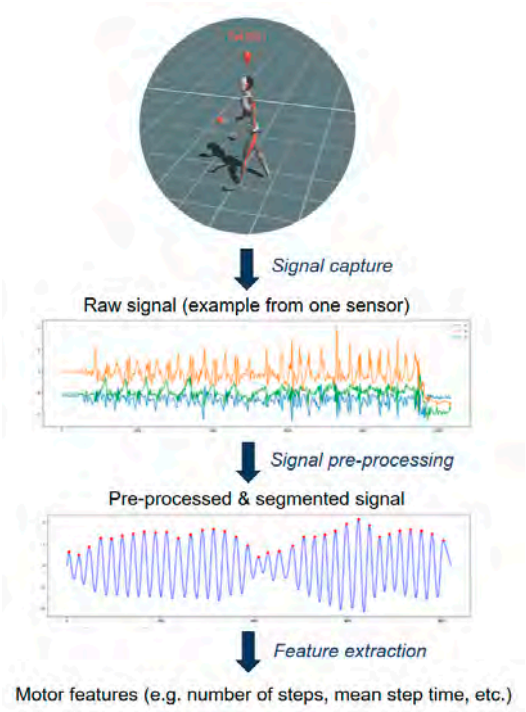

Figure 1. Processing of 18-sensor motion-capture system

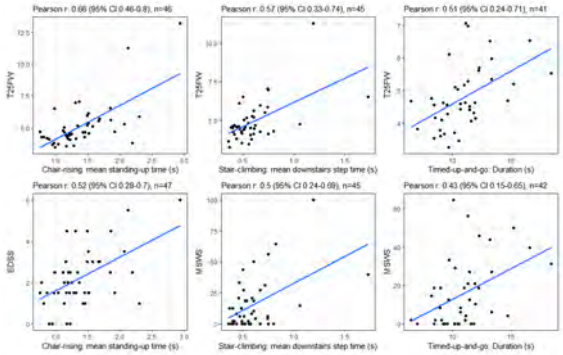

Figure 2. Best correlations of multi-sensor derived motor features with reference tests

Conclusion: Precise ground truth datasets for diverse motor tests can be generated with a multi-sensor motion capture system in the clinic. Extracted motor features show strong correlations with established functional outcomes in PwMS. Exploring this relation will inform further cross-validation with features derived from smartphone sensors that can be easier and more frequently applied in patients' natural environment.

Disclosure: T.W. nothing to disclose. A.E. is an employee of Healios AG. L.K.: fees for board membership, consultancy or speaking, or grants in the past 3 years from Actelion, Advancell, Allozyne, Bayer, Bayhill, Biogen Idec, BioMarin, CSL Behring, Eli Lilly EU, Genmab, GeNeuro SA, Gianni Rubatto Foundation, Glenmark, Merck Serono, MediciNova, Mitsubishi Pharma, Novartis, Novartis Research Foundation, Novo Nordisk, Peptimmune, Roche, Roche Research Foundation, Santhera, Sanofi-Aventis, Swiss MS Society, Swiss National Research Foundation,

Teva Pharmaceutical Industries Ltd, UCB, and Wyeth. O.R. is an employee of Healios AG. C.G.: (i) advisory board and consultancy fees from Actelion, Novartis, Genzyme and F. Hoffmann-La Roche; (ii) speaker fees from Biogen and Genzyme-Sanofi; (iii) research support by F. Hoffmann-La Roche Ltd.. J.L.: research grants from Novartis, Biogen and Innosuisse (Swiss Innovation Agency), honoraria for advisory boards and/or speaking fees from Novartis, Roche and Teva.

EPO-489

Abstract withdrawn

EPO-490

Serum Neurofilaments are a reliable biomarker to early detect PML in Multiple Sclerosis patients

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Background and aims: The earliest detection of progressive multifocal leukoencephalopathy (PML) is crucial in Natalizumab (NTZ)-treated Multiple Sclerosis patients. This study aims to assess serum Neurofilaments (sNFL) to early detect PML in longitudinal patients' follow-up

Methods: sNFL were retrospectively measured in the four PML cases occurred at CRESM, in samples collected from one year before PML onset, at PML onset, during PML and in post-PML follow-up. Levels were interpreted according to reference values. sNFL were also measured in 45 NTZ-treated patients in NEDA-3 status.

Results: Different PML onsets were observed: in 3 patients brain MRI revealed radiological-PML signs followed by different clinical manifestations; one patient showed a clinical onset confirmed by MRI. sNFL were analyzed during the different PML phases: 1)up to 4 months before PML onset: sNFL values were in the normal range in all patients (median 8.7 pg/ml, range 6.2-10.7). 2)within 3 months before PML onset: sNFL were elevated in all samples (median 17.5 pg/ml, range 15.1-81.0). 3)PML onset: sNFL were elevated (median 67.6 pg/ml, range 11.1-148.8). 4)PML/IRIS: the peak of sNFL (median 82.3 pg/ml, range 20.5-272.9) was observed. 5)Post-PML: sNFL levels demonstrated a decrease (median 13.20 pg/ml, range 9.3-30.6), but were still elevated in 2 patients according to reference values. Median sNFL values in NEDA-3 patients were 4.5 pg/ml (range 2.2-9.6).

Conclusion: Elevated sNFL were observed at radiological/clinical PML onset, but also prior to the onset. During PML recovery, sNFL weren't normalized in all samples, suggesting ongoing neuronal degeneration. sNFL represent a reliable biomarker to early detect and monitor PML.

Disclosure: Nothing to disclose.

EPO-491

New insight of gender effect on cognitive profile of a cohort of early Multiple Sclerosis patients

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Background and aims: Gender seems to influence disease phenotype and evolution in people with Multiple Sclerosis (PwMS). With our study we aimed to investigate the interplay between gender and fatigue on cognitive performances in early PwMS.

Methods: 200 PwMS (F: 64%, mean ± SD age 38.2±12.42 years, EDSS median, IQR= 2, 0-5.0) were enrolled at the diagnosis. All subjects underwent Selective Reminding Test (SRT), Spatial Recall Test (SPART), Symbol Digit Modalities Test (SDMT), Paced Auditory Serial Additional Test (PASAT-2, PASAT-3), Word List Generation (WLG) and Stroop Color-Word Interference Test (ST) for cognition; Fatigue Severity Scale (FSS) was used to report fatigue. Cognitive performances were compared between different groups using Chi-squared, Mann-Whitney-U test, and multivariate regression analysis, as appropriate.

Results: In our cohort the proportion of PwMS with cognitive impairment varied across different tests, from 3.1% in SPART-D to 8% in SRT. Fatigue was reported in 25% of PwMS. Female subjects had worse scores at SRT-LTS ($p=0.002$), SPART ($p=0.001$), SDMT ($p=0.009$), PASAT-3, ($p<0.0001$), PASAT-2 ($p<0.0001$) and STROOP ($p=0.039$). PwMS with fatigue had worse performances in STROOP ($p=0.002$) , PASAT-3 ($p=0.14$) and PASAT-2 ($p=0.004$). Multivariate analysis confirmed the predictive values of gender for impairment in SRTLTS, SPART-D and SDMT.

Conclusion: In MS previous studies, conducted some years postdiagnosis, showed male sex to be a significant predictor of worse cognitive impairment, except for visuospatial memory. This last, appears to be the more compromised cognitive domain in female subjects in our cohort at disease beginning.

Disclosure: Dr. Oggiano, Biasi, Guerra T, Guerra S, Vitobello, Iaffaldano A, Taurisano and Bianco have nothing to disclose. Dr Manni has served on scientific advisory boards for Merck Serono, Sanofi Genzyme and Roche. Prof Paolicelli, Prof Trojano and Prof Iaffaldano have served on scientific advisory boards for Biogen, Novartis, Roche, Merck and Genzyme, and they have received speaker honoraria from Biogen Idec, Merck, Roche, Teva, Sanofi-Genzyme and Novartis.

EPO-492

Leptomeningeal Enhancement in Stem Cell Transplantation Treated Multiple Sclerosis and in Other Neurological Diseases

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Background and aims: In multiple sclerosis (MS) Leptomeningeal Enhancement (LME) is a MRI marker of leptomeningeal inflammation. Aims of this study were to assess the frequency and number of LME in patients affected by MS and Other Neurological Diseases (OND), and to evaluate whether previous treatment with Autologous Hematopoietic Stem Cell Transplantation (AHSCT) determined differences in this marker.

Methods: Monocentric study in patients affected by MS or OND who in the period 2020-2022 performed one 3T brain MRI with a standardized protocol, including a post-contrast FLAIR. For a subset of AHSCT patients follow-up MRI scans, including one before treatment, were analyzed.

Results: Fifty-eight MS (40 Relapsing Remitting [RR-MS], 18 Progressive [Pr-MS]) and 12 OND patients were included. Among MS patients, 24/58 (41%) underwent AHSCT (MS AHSCT group) and the remaining 34 received approved treatments (MS CTRL; Table 1). At least one LME was identified in 20/58 (34%) MS and in 7/12 (58%) OND patients (p=0.112). No differences in the frequency of LME positive patients between the MS AHSCT (10/24, 42%) and MS CTRL group were observed (10/34, 29%) (p=0.405). However, in the MS AHSCT group we identified a direct correlation between LME number and age at AHSCT, but not at MRI (R=0.44). Furthermore, in the longitudinal pilot study (n=4), one LME disappeared following AHSCT in one case.

	MS AHSCT n=24		MS CTRL n=34		
	median	(range)	median	(range)	p value
Age at MRI, years	46	(29-57)	44.5	(22-74)	0.874
Disease duration, years	17	(6-31)	14.5	(0-52)	0.420
Progressive phase duration, years	6	(1-24)	6	(1-8)	0.620
Treatment duration, years	13	(5-26)	10	(0-25)	0.017
Duration of treatment with second-line DMTs, years	8.5	(3-14)	6	(0-11)	0.048
EDSS at MRI	3.5	(1-7)	4	(0-7)	0.536
Number of DMTs received prior to MRI	4	(2-7)	2	(0 – 5)	<0.001
Age at AHSCT, years	42.5	(27-53)	-	-	-
	n	(%)	n	(%)	p value
Gender, female	20	(83%)	20	(58%)	0.082
MS phenotype: RR-MS	16	(67%)	24	(70%)	0.312
Patients receiving treatment at MRI	0	(0%)	19	(56%)	<0.001

Table 1: Clinical-demographic characteristics of MS patients in the MS AHSCT (Multiple Sclerosis Autologous Hemopoietic Stem Cell Transplantation) and MS CTRL (Multiple Sclerosis Control) groups.

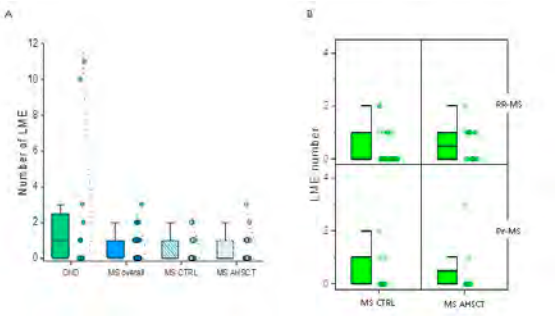

Figure 1. Median (interquartile range) number of LME in the MS and OND groups. (A) The MS cohort is further stratified according to the previous exposure to AHSCT (A) and MS form (B).

Conclusion: Based on our results AHSCT may halt the formation of new LMEs, reinforcing the indication of early use of this treatment and of high efficacy disease modifying therapies targeting inflammation.

Disclosure: Nothing to disclose.

EPO-493

Sensorineural hearing loss (SNHL) as the initial manifestation of Multiple Sclerosis with acoustic Uhthoff phenomenon

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Background and aims: Albeit uncommon, SNHL may be a manifestation of Multiple Sclerosis (MS), even less often at disease onset, and can be sudden, progressive, unilateral, bilateral or a/symmetric. Disruption of hearing neural pathways (plaques involving from brainstem to the auditory cortex) is the proposed mechanism, but inner ear involvement is also suggested. Uhthoff phenomenon is a transient worsening of neurological function, usually visual, related to increases in core body temperature.
Methods: A 20-year-old woman consulted for sudden hearing loss, tinnitus and aural fullness in the right ear for 2 weeks. The neurological examination showed horizontal nystagmus at the right gaze and upper limb pyramidalism. Audiometry test showed right SNHL of 60%. 1.5 T MRI showed T2 periventricular and subcortical hyperintensities suggesting MS.
Results: Immunologic analysis was normal. High-dose intravenous corticosteroids were indicated for 5 days, with substantial improvement (100% recovery in audiometry). CSF oligoclonal bands were positive. Six months later, a MRI showed new hyperintensities establishing MS diagnosis. During the follow-up, she reported numerous brief episodes of hearing worsening and aural fullness with hot temperatures or during exercise.
Conclusion: Neurologists should be aware of the auditory MS manifestations that over time can occur in 25%, predominantly with lesions in the medullary tegmentum. Sudden SNHL can be the sentinel presentation as clinical isolated syndrome, with a good chance of complete recovery with steroids or plasmapheresis. Temperature-sensitive conduction blockade of partially demyelinated axons is the most widely accepted mechanism of Uthoff. To our knowledge, this is the first report of acoustic Uhthoff phenomenon in MS.
Disclosure: Authors declare no conflicts of interest.

EPO-494

Accuracy of multiple sclerosis diagnostic criteria in detecting perivenular de-myelination visualized in vivo by MRI

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Background and aims: In multiple sclerosis (MS) diagnosis, caution is needed in cases carrying red flags (MS-plus). To assess the performance of the diagnostic criteria in the setting of MS-plus, perivenular topography of the lesions, a cardinal and highly specific pathological feature of MS noninvasively detectable by brain MRI, was used as a "reference standard".
Methods: Cases of typical relapsing-remitting (RR) MS (n= 28), RR MS-plus (n=59), and non-MS cases carrying MS-like brain white matter lesions (WML; n=32) received one brain MRI including conventional and FLAIR* images. PVL number/WML number (PVL-f) and conventional lesion characteristics were evaluated. For evaluating the performance of the MS diagnostic criteria, a PVL-f threshold selected by ROC analysis of the typical RRMS and non-MS cases was then applied to the MS-plus cases.
Results: Typical MS cases had a median PVL-f of 91% (range 67–100%), non-MS of 23% (range 0-89%, $p<0.00001$), and MS-plus of 55% (range 8–100%, $p=0.001$). The 52% PVL-f threshold selected by ROC analysis was exceeded by 28 (100%) of the typical RRMS cases and 1 non-MS (3%; $p<0.00001$) indicating 98% accuracy of the diagnostic criteria when compared to PVL-f. However, only 32 (53%) of the MS-plus cases had PVL-f >52% ($p=0.001$), corresponding in these cases to 68% nominal accuracy of the diagnostic criteria. In patients with low PVL-f, atypical brain lesions and cerebrovascular comorbidities were common.
Conclusion: In the setting of MS-plus, incorporating PVL-f analysis into the MS diagnostic criteria could remarkably improve diagnostic accuracy.
Disclosure: Prof Massacesi received: - educational unrestricted support from Biogen; Sanofi-Genzyme; Novartis Roche and Merck-Serono; - honoraria for scientific lectures, scientific consultation, or participation in advisory boards from Biogen; Novartis; Sanofi-Genzyme; Roche; Mylan; Merck- Serono. - research grants (recipient: University Dept.) from Sanofi-Genzyme; Biogen; Roche; Merck-Serono; Novartis

EPO-495

K index improves MS diagnosis and supports the differential diagnosis between MS and MS-like syndromes

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Background and aims: Despite validated diagnostic criteria, MS diagnosis is sometimes difficult because of MS-like clinical and/or radiological syndromes. K-index (K-index = CSF/serum K-free light chains divided by CSF/serum albumin) is a CSF biomarker, that can easily and quickly be assayed through an automatic technique that, unlike oligoclonal bands (OB) assay, releases quantitative results. To date its role in diagnostic process is controversial.
Methods: We analyzed pts with MS according to fulfillment of the 2011 McDonald diagnostic criteria and other inflammatory/vascular CNS diseases (nMS) who underwent to CSF analysis in our MS Centre. CSF biomarkers OB and K-index were analyzed. Pts were then classified according to OB presence (OB+), K-index >6,49 (k-index+) and, when magnitude susceptibility weighted images (SWI) were available, Central Vein Sign >50% (CSV+).
Results: 106 pts were included, 62 pts (58,5%) MS and 44 pts (41,5%) nMS. Frequencies of CSF biomarkers are reported in table 1-2. A subgroup of 40 pts with 3T MRI (n= 25 MS and n= 15 nMS) was also analyzed. 14/25 MS pts and 1/15 nMS pts were OB+K-index+CVS+ and 1/25 MS and 8/15 nMS pts were OB-K-index-CSV-. The inclusion of K-index in addition to OB improved the specificity (0,8 vs 0,7). The specificity of the diagnosis was higher when CVS was included (0,93) despite a lower sensitivity (0,56 vs 0,77) compared to only OB evaluation.
Conclusion: In clinical practice the combination of CSF biomarkers (OB and K-index) with MRI marker (CVS) could be a good approach to minimize misdiagnosis.
Disclosure: The authors declare that they have no conflict of interest.

Table 1. **MS** (62 pts)

K index	BO	Totale	%
+	+/-	53	85,5%
+/-	+	48	77,4%
+	+	46	74,2%
+	-	7	11,3%
-	+	2	3,2%
-	-	7	11,3%

+/- = independent from biomarker result

Table 2. **nMS** (44 pts)

K index	BO	Totale	%
+	+/-	14	31,8%
+/-	+	13	29,5%
+	+	9	20,5%
+	-	5	11,4%
-	+	4	9,1%
-	-	26	59,1%

+/- = independent from biomarker result

EPO-496

Wearing Off Phenomenon in MS Patients in Treatment With Monoclonal Antibodies: Clinical and Biological Implications

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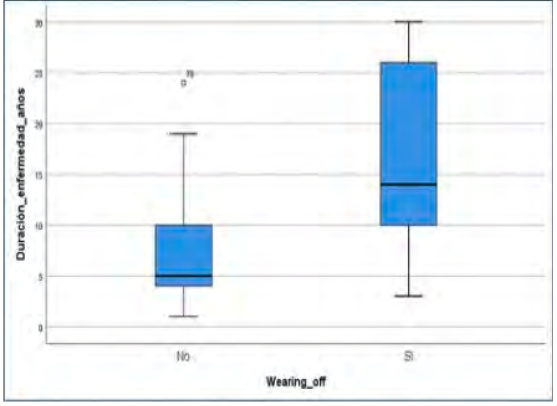
Background and aims: Multiple Sclerosis(MS)patients treated with monoclonal antibodies occasionally report some symptoms before the next dose of treatment called"wearing off phenomenon"that relate to drug "exhaustion".This phenomenon is called "wearing-off phenomenon"and its clinical relevance is controversial.Our objective is to analyze the prevalence of the wearing-off phenomenon in our MS patients who use natalizumab and ocrelizumab, describe the clinical phenomenon and investigate the. associated factors as well as possible etiologies.

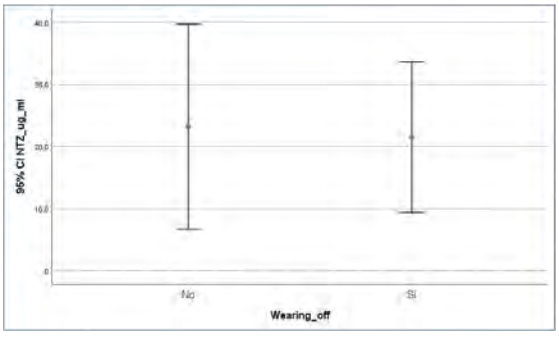
Methods: Cross-sectional study in MS patients treated with natalizumab and ocrelizumab.A survey on the wearing off phenomenon is provided to the patients. We correlated this phenomenon with different clinical factors: evolution time, age, EDSS, relapses, concentration of the drug in blood of Natalizumab and CD19+ count in Ocrelizumab patients. We use statistical package SPSS v.25.

Results: The frequency of wearing off is higher with Natalizumab (48%) than with Ocrelizumab(25%)with significant differences(chi square, p=0.043).The most common symptom if wearing off is fatigue. No significant association between relapses, age, baseline EDSS or progression between patients with and without wearing off was observed in the two drugs. In Ocrelizumab there is no association with wearing off, CD19+,or NfLs, and with Natalizumab there is no relationship with serum levels of Natalizumab. Only association in Ocrelizumab and EDSS month 36 relapsing MS, and time of evolution of the disease in progressive forms(U Mann Whitney p<0.05).

Conclusion: Although the perception of wearing off is not uncommon in MS patients treated with monoclonal antibodies, its association with disease evolution and impact on clinical and analytical biomarkers has not been demonstrated in our sample

Disclosure: Nothing to disclose.





EPO-497

Ocrelizumab use in the real-world experience: data from a hot spot area for Multiple Sclerosis

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Background and aims: Despite the growing use of Ocrelizumab, data of the real-world experience are limited. Aim of this study was to examine the OCR use in primary progressive (PP) and relapsing remitting (RR) patients categorized as naïve and switchers, also evaluating predictors of treatment response and adverse infusion events (AIEs).

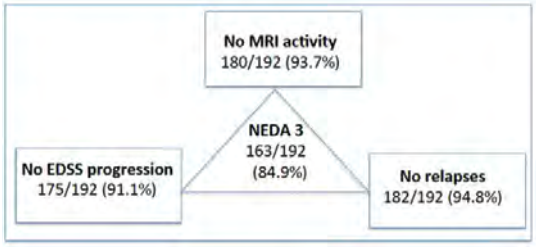
Methods: MS patients exposed to OCR between 2016 and 2022 were considered. NEDA-3 status at 24 months was evaluated for RR patients; determinants of NEDA 3 and AIEs were explored by regression analyses.

Results: The sample included 421 patients, of which 33 (7.9%) were PP and 388 (92.1%) RR. Among these, 67(17.3%) were naïve, while the switchers from I° and II° line DMTs were 199 (51.3%) and 122 (31.4%), respectively. OCR use as exit strategy from Natalizumab has been reported in 25 JCV+ patients. Among these, 6 patients presented with MS reactivation in the first 12 months, despite the short latency to OCR initiation (3.4 ± 2.0 months). NEDA 3 status after 24 months was calculated for 192 RR patients and achieved by 163(84.9%), with lower age (p=0.05) and ARR in the year prior OCR (p=0.005) emerged as determinants. AIEs occurred in 128 (30.4%) patients; a relationship with previous allergic diathesis (p=0.001), reported for 37 (8.8%) patients, was observed,

while the short protocol administration, used for 279 (66.8%) patients, was not related.

	Total MS patients (421)		RRMS		
	PPMS (33)	RRMS (388)	Naive (67; 17.3 %)	Switchers from I°line DMTs (199; 51.3%)	Switchers from II°line DMTs (122; 31.4%)
Male Gender	17 (51.5%)**	132 (34%)	30 (44.7%)	62 (31.1%)	40 (32.8%)*
Age at OCR initiation (years)	53.0 ± 9.0**	42.4 ± 10.1	40.1 ± 10.8	43.7 ± 10.4	41.7 ± 9.1
MS duration at OCR initiation (years)	16.2 ± 11.7*	13.1± 8.6	3.9 ± 6.2	13.6 ± 8.4	16.0 ± 6.6
EDSS score at OCR initiation	6.1± 0.9**	3.3 ± 2.2	2.4 ± 1.7*	3.5 ± 2.2	3.3 ± 2.2
OCR exposition (months)	22.4 ± 11.1	25 ± 15.3	23.5 ± 11.8	25.6 ± 17.6	24.7 ± 12.9

Demographic and clinical features of progressive and relapsing remitting patients exposed to ocrelizumab, categorized as naive or switchers from I° and II° line DMTs.



Different components of NEDA 3 status at 24 months of OCR exposure (192 MS patients)

NEDA 3					
	B	Sig.	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Age at OCR initiation (ys)	-0.048	**0.058**	,953	,906	1,002
ARR in the year prior OCR	-0.653	**0.005**	,520	,332	,817
MS duration	0.024	0.417	1,024	,966	1,086
EDSS at baseline	0.055	0.624	1,057	,847	1,318
Naive	0.438	0.476	1,549	,464	5,167

Predictors of therapeutic response of MS patients exposed to 24 months of OCR (192 subjects)

Conclusion: OCR is confirmed as a high efficacy option for naïve and switchers patients. Further real-world data are needed to understand its efficacy and safety in different patients' groups.

Disclosure: Mellino P has received travel grants from Sanofi. Lorefice L, Frau J, Coghe G and Cocco E, have received honoraria for consultancy or speaking from Biogen, Novartis, Sanofi Genzyme, Serono, Teva, and Almirall. Pilotto S. has received travel grants from Biogen, Teva and Bristol Myers Squibb. Barracciu M has nothing to disclose.

EPO-498

Transorbital Ultrasound for Morphological and Haemodynamical Assessment of Optic Nerve in Multiple Sclerosis

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Background and aims: Changes of the optic nerve (ON) reflect the overall pathology in multiple sclerosis (MS). Transorbital ultrasonography (TOUS) is a promising tool for detecting ON changes after exposure to optic neuritis. We aimed to explore ON haemodynamic in addition to morphological changes in a sample of MS patients.

Methods: Sixty-seven MS patients (Thompson diagnostic criteria) were included in this preliminary study: 53 women and 14 men aged 41.6 (11.3) and 40.1 (11.0) (p=ns) years. EDSS score was 0-2.5 in 47 (70.1%) and >2.5 in 20 (14.9%) subjects. ANCOVA was used to investigate the association between US morphological (ON diameter (OND) at 3 and 5 mm from papilla, ON sheath diameter (ONSD) at 3 mm from papilla and myelination index (MI) ratio), a history of optic neuritis, controlling for sex and EDSS.

Results: Out of 134 eyes no history of optic neuritis was recorded in 89 (66.4%), while at least 1 episode was recorded for 45 (33.6%). A higher proportion of affected eyes among women (86.4%) than men (13.6%) was observed (p=ns). OND – at 5 mm from papilla especially - and ONSD at 3 mm were significantly reduced in ONs with optic neuritis. MI ratios were higher in affected vs unaffected eyes. Mean ON diameters were lower in patients with higher EDSS score, irrespective of history optic neuritis. Mean flow velocity was reduced in affected eyes for all principal arteries explored.

Conclusion: TOUS and Doppler US examination can detect ON changes in MS, showing potential for prognostic marker.

Disclosure: The authors have nothing to disclose.

Table 1

US parameters	Marginal means (95% CIs) Eye with optic neurities	Unaffected fellow eyes	p^a
OND3 (mm)	2.87 (2.78, 2.96)	2.99 (2.93, 3.05)	***0.031***
ONSD3 (mm)	4.47 (4.33, 4.61)	4.56 (4.46, 4.65)	*0.266*
ONSD5 (mm)	4.77 (4.60, 4.93)	4.88 (4.76, 4.99)	***0.030***
MI ratio (mm)	0.940 (0.928, 0.952)	0.937 (0.928, 0.945)	***0.009***
OA MFV (cm/sec)	18.97 (17.33, 20.61)	19.50 (18.35, 20.66)	***0.008***
CRA MFV (cm/sec)	7.47 (6.97, 7.97)	7.75 (7.40, 8.10)	*0.473*
PCA MFV (cm/sec)	17.44 (15.80, 19.09)	18.66 (17.50, 19.82)	*0.522*

[a]ANCOVA: dependent variables history of ON is the fixed factor; covariates: sex, EDSS (0-2.5 vs >2.5)
US=Ultrasound; ON=optic nerve; OND3=ON diameter at 3mm from papilla; ONSD3= ON sheath diameter at 3mm from papilla; ONSD5= ON sheath diameter at 5mm from papilla; MI=myelination index; OA=Ophthalmic Artery; CRA=central retinal artery; PCA=posterior ciliary artery; MFV=mean flow velocity.

EPO-499

Family Functioning and Multiple Sclerosis: preliminary data of a multicentric Italian project

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Background and aims: Multiple Sclerosis (MS) may influence family functioning, with effects on both marital relationships and parental bonding. Our aim is to evaluate family functioning and related factors in patients with MS and their families.

Methods: A dedicated platform has been used for filling in the questionnaires for MS patients and their families. As controls, we selected families with no subjects referring chronic diseases. Socio-demographic and clinical information were preliminary collected. Administered questionnaires included: (1) the short form of the Family Assessment Measure Third Edition (FAM3); (2) the Hospital Anxiety and Depression Scale (HADS); (3) the Multidimensional Scale of Perceived Social Support (MSPSS); Dyadic Adjustment Scale (DAS) and the Inventory of Parent and Peer Attachment (IPPA).

Results: 129 MS patients, 93 family members (21 aged between 13 and 20 years), and 210 control subjects (100 aged between 13 and 20 years) completed the online questionnaires. Sociodemographic characteristics are displayed in table 1. MS family members showed to be more anxious than control subjects (p= 0.0016) and MS partners had a higher degree of dyadic agreement (on finances, leisure time, home organization) than control subjects (p= 0.0167). Young people with age between 13 and 20 years, who have at least one member with MS in their family, had higher quality attachments with significant others (both parents and peers), as assessed with the IPPA (Table 2).

Conclusion: MS may affect the psychological state and family functioning by making MS family members more anxious, but also make more compliant partners and mature adolescents.

Disclosure: The authors have no conflicts of interest or disclosures in connection with this article.

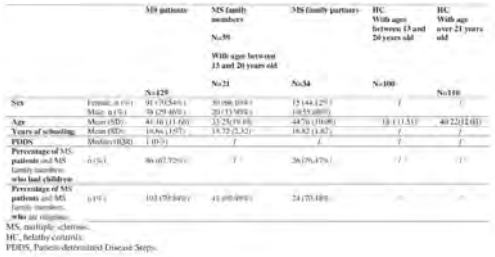

Table 1. Sociodemographic characteristics of MS patients and their family members and partners.

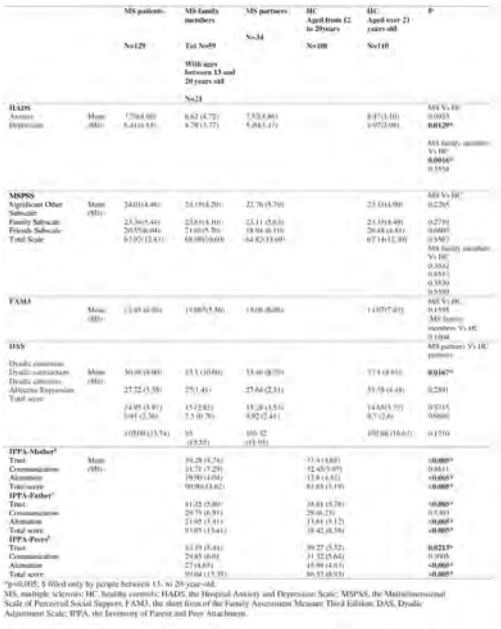

Table 2. The results of questionnaires in MS patients, MS family members and Healthy controls with no subjects with chronic diseases in their families.

EPO-500

Depressive symptoms and monoaminergic network changes in multiple sclerosis: a longitudinal study

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Background and aims: Growing evidence suggests that depression in multiple sclerosis (MS) patients might be a symptom with a neurobiological basis rather than a mere consequence of the disability accumulation. This study aimed to investigate whether the development of depressive symptoms in MS is associated with monoaminergic functional network changes.
Methods: Forty-nine MS patients and 27 healthy controls (HC) underwent clinical and 3.0T resting state (RS) functional MRI assessment at baseline and after 1.6 year median follow-up (interquartile range=1.0-2.1 years). Depressive symptoms were evaluated at both time points using the Montgomery-Asberg Depression Scale (MADRS); MS patients were included if their baseline MADRS was <9 (i.e., no depression). Monoaminergic-related RS functional connectivity (FC) was derived by independent component analysis, constrained to PET atlases for dopamine, noradrenaline and serotonin transporters.
Results: Fourteen (29%) MS patients developed depressive (D) symptoms at follow-up, while 35 (71%) remained not depressed (ND). At baseline, MS patients showed decreased RS FC vs HC in all three PET-guided monoaminergic networks in frontal, cingulate and cerebellar cortices, and increased RS FC in parieto-occipital regions. ND-MS patients showed limited RS FC changes over time. Conversely, D-MS patients showed a widespread RS FC decrease over time in the PET-guided dopamine network, mainly in orbitofrontal, middle occipital, anterior cingulate and precuneal cortices (all significant at time-by-group interaction analysis), and in occipital regions. They also presented decreased RS FC over time in parahippocampal and occipital regions of the PET-guided noradrenaline network.
Conclusion: Specific patterns of monoaminergic networks changes were associated with development of depressive symptoms in MS patients.
Disclosure: The authors have nothing to disclose.

EPO-501

Influence of cardiorespiratory fitness and neuroinflammation on hippocampal volume in multiple sclerosis

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Background and aims: The hippocampus is characterized by neuroplasticity and neurogenesis also in adulthood. Neuroinflammation and cardiorespiratory fitness (CRF) may influence hippocampal integrity by modulating the processes promoting neurogenesis and neuroprotection that contribute to the preservation of functions. Here, we investigated whether higher CRF may limit the detrimental effects of neuroinflammation on hippocampal volume in the main multiple sclerosis (MS) clinical phenotypes.
Methods: Brain structural MRI scans and maximum oxygen consumption (VO2max), a proxy of CRF, were acquired from 81 MS patients (27 relapsing-remitting [RR] and 54 progressive [P]), and 45 age- and sex-matched healthy controls (HC). T2-hyperintense white matter lesion volume (T2-LV) and choroid plexuses volume (CPV) were quantified as neuroinflammatory measures. Association of demographic, clinical, neuroinflammatory and CRF measures with normalized brain, gray matter, hippocampal and thalamic volumes in RRMS and PMS patients were assessed using Shapley and best subset selection regression.
Results: For most volumetric outcomes, largest portions of variance were explained by T2-LV (variable importance [VI]=9.4-39.4) and CPV (VI=4.5-26.2). VO2max explained the largest portion of variance of normalized hippocampal volume in RRMS patients (VI=16.9) and was retained as a relevant predictor (Std. β=0.374, p=0.023) together with T2-LV (Std. β=-0.330, p=0.016), while explaining a small amount of variance of this outcome in PMS subjects (VI=0.1) and of all the other volumetric outcomes in both groups (VI from 0.3 to 2.2).
Conclusion: By exerting beneficial neurotrophic effects, a higher CRF may have a specific neuroprotective role for the hippocampus mainly in the early phases of MS.
Disclosure: The authors have nothing to disclose.

EPO-502

Eculizumab in AQP4+ neuromyelitis optica spectrum disorder: 3 years of data from Japanese post-marketing surveillance

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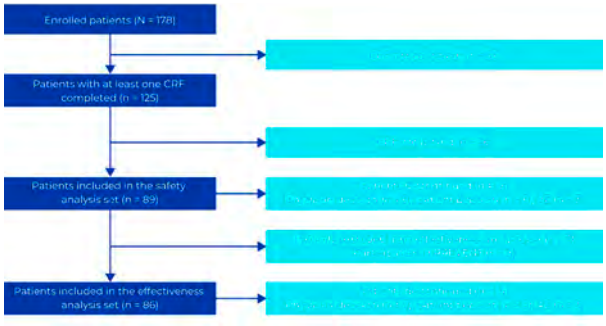
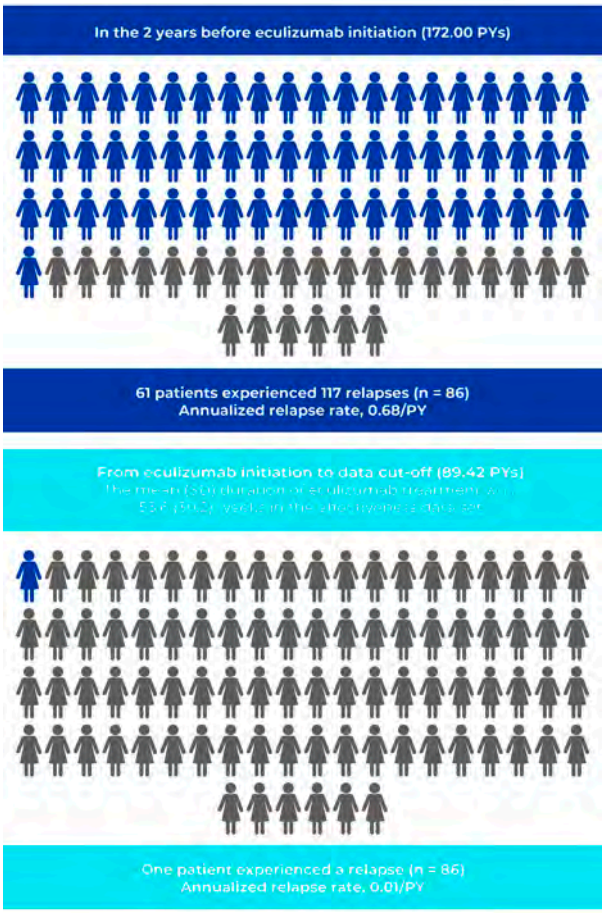
Background and aims: Eculizumab (ecu) is approved in Japan for prevention of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) relapse and is undergoing mandatory post-marketing surveillance (PMS) of real-world use.
Methods: This PMS interim analysis assessed long-term safety and effectiveness of ecu in Japanese patients (pts) from approval (November 2019) to data cut-off (October 2022).
Results: The safety set comprised 89/178 pts; 16 discontinued (9 physician decisions, 8 patient decisions, 3 adverse events [AEs]). Overall, 62 AEs (25 deemed treatment-related) were observed in 31 pts; of these 62 AEs, 40 were serious AEs (14 deemed treatment-related), observed in 22 pts. No meningococcal infections occurred. The effectiveness set comprised 86 pts. In the 2 years (172.00 patient years [PY]) before ecu, relapse rate was 0.68/PY; 28 pts (32.6%) had 1 relapse, 33 pts (38.4%) had ≥2 relapses. During ecu treatment (89.42 PY), relapse rate was 0.01/PY (1 relapse). In the 6 months before ecu, 46 pts (53.5%) were receiving immunosuppressant therapy (IST), whereas during 6–12 months after ecu, 25 pts (44.6%) were receiving IST. The proportion of pts taking prednisolone >10 mg/day decreased from 44.2% at 24–20 weeks before ecu treatment to 18.2% and 11.2% at 52–56 and 100–104 weeks after ecu, respectively.



Patient disposition



Incidence of relapses before and after eculizumab initiation

Table 1. Summary of patients with treatment-related AEs

Event, n (%)	Safety analysis set (n = 89)
Any treatment-related AE	15 (16.9)
Any treatment-related SAE	8 (9.0)
Gonococcal infection	2 (2.2)
Bacteraemia	1 (1.1)
Cellulitis	1 (1.1)
Meningitis bacterial	1 (1.1)
Meningitis herpes	1 (1.1)
Pneumonia	1 (1.1)
Bacterial sepsis	1 (1.1)
Device related infection	1 (1.1)
Pulmonary hypertension	1 (1.1)
Systemic lupus erythematosus	1 (1.1)
Cystitis haemorrhagic	1 (1.1)
Renal impairment	1 (1.1)
Pyrexia	1 (1.1)

AE, adverse event; SAE, serious adverse event.

Summary of patients with treatment-related AEs

Conclusion: In a real-world setting, ecu was highly effective in preventing relapses and well tolerated in Japanese pts with AQP4+ NMOSD, consistent with findings from the PREVENT study. The observed reduction in IST use, also aligned with other real-world experiences, underlines the benefits of C5 inhibition in these pts.
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CSL Behring, Daiichi Sankyo, Eisai, Kyorin, Mitsubishi Tanabe Pharma, Novartis, Otsuka, Roche, Takeda, Teijin Pharma, research scholarships from AbbVie, Boehringer Ingelheim, Chugai Pharmaceutical, Daiichi Sankyo, EA Pharma, Eisai, Japan Blood Products Organization, Mitsubishi Tanabe Pharma, Otsuka, Shionogi, Sumitomo Pharma, Teijin Pharma and Tsumura, and grants from Biogen, the MEXT of Japan and the MHLW. IN: personal fees from Alexion Pharma GK, Chugai Pharmaceutical, Biogen Japan, Mitsubishi Tanabe Pharma, Novartis and Takeda, and grants from LSI Medience, the MEXT and the MHLW of Japan. HY: personal fees from Alexion Pharma GK, Biogen Japan, Chugai Pharmaceutical, Mitsubishi Tanabe Pharma and Novartis, and grants from the MHLW of Japan. YM: personal fees from Alexion Pharma GK, Biogen Japan and Chugai Pharmaceutical. KO and KH: employees of, and hold stock in, Alexion Pharma GK, AstraZeneca Rare Disease. KF: personal fees and other support from AbbVie, Asahi Kasei Medical, Biogen, Chugai Pharmaceutical, Eisai, Merck Biopharma, Mitsubishi Tanabe Pharma, Novartis, Ono, Roche, Sumitomo Dainippon, Takeda, Teijin Pharma, UCB and Viela Bio and grants from the MEXT of Japan and the MHLW of Japan.

MS and related disorders 6

EPO-503

Spasticity Plus Syndrome model in Multiple Sclerosis: an operative approach in a real life cohort

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Background and aims: Spasticity Plus Syndrome (SPS) has been recently conceptualised to enclose several symptoms that might coexist with spasticity in Multiple Sclerosis (MS). In this study we aimed to test the SPS model through a web-based tool exploring the symptomatic profile of a cohort of patients with MS relying on patients reported outcomes (PROs).
Methods: A web-based questionnaire was sent to MS patients followed at the MS Center of Tor Vergata University to assess the symptomatic burden of spasticity, spasms, pain, fatigue, sleep disorders, depression, bladder and bowel dysfunctions and sexual disturbances. The impact of each symptom on daily life was rated from 0 to 5 and symptoms ≥ 3 were considered for the analysis.
Results: Analysing 400 questionnaires we found that frequency of fatigue was 64%, depression 46%, spasticity 33%, pain 25%, spasms 19%, bladder 37% and bowel 21% dysfunctions, sexual disturbances 30%, sleep disorders 31%. Defining SPS as the association of spasticity or spasms plus at least one symptom among pain, urinary dysfunction and fatigue, SPS was detected in 26% of patients with EDSS ≤ 2.5 and in 24% with EDSS 3-4 and 50% with EDSS >4.
Conclusion: Our PROs-web-based questionnaire confirms the validity of SPS model in a real-life setting and provides an operative frame to assess SPS model. Moreover, our analysis shows that SPS can be found also in patients with low disability. Adoption of this self-reported SPS questionnaire in clinical practice might allow an earlier detection of SPS and prompt an innovative model of care.
Disclosure: All authors report no disclosures relevant for the purpose of this manuscript.

EPO-504

Prophylaxis of HBV reactivation in multiple sclerosis patients treated with ocrelizumab

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Background and aims: There are some recommendations starting antiviral prophylaxis to prevent hepatitis B virus (HBV) reactivation in the case of immunosuppressive treatment for hematologic and oncologic diseases.
Methods: 62 MS individuals qualified for OCR therapy were enrolled in the prospective study. Serum HBV surface antigen (HBsAg), anti-HBV core antigen (anty-HBcAg total) and HBV-DNA were evaluated before OCR therapy and after administration of prophylactic agents for HBV reactivation: nucleosid(t)e analogs (PA-HBV).
Results: Positive anty-HBcAg total and negative HBsAg were found in 4 patients with primary progressive multiple sclerosis (PPMS) and in 4 individuals with relapsing-remitting (RRMS). Oral treatment with PA-HBV: entecavir (0.5 mg/day) and tenofovir (245 mg/day) were included in 7 patients and in 1 individual, respectively. The time from starting PA-HBV therapy to initiation of ocrelizumab treatment was 31.4±17.5 [days]. The number of OCR infusion was 3.0±1.0. Mean value of anty-HBcAg total was 5.5±4.4 [ratio] at baseline and 4.59±3.4 during OCR therapy after PA-HBV administration. Serum hepatic parameters (aspartate;-alanine aminotransferase bilirubin) were 20.1±3.2; 26.1±15.9 [U/L] and 7.6±2.7 [umol/l], repectively. HBsAg and HBV-DNA were not detected.
Conclusion: OCR therapy is related to the risk for HBV reactivation. However, additional treatment with PA-HBV prevent HBV viral replication in MS patients. No hepatic impairments and side effects were observed after PA-HBV administration. While tenofovir was found as potent inhibitor of Epstein-Barr virus reactivation, it seems an appropriate therapeutic approach in MS patients.
Disclosure: Authors declare no conflicts of interest.

EPO-505

Evaluation of paramagnetic rim lesions as a marker of disability

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Background and aims: In multiple sclerosis (MS) brain lesions with a paramagnetic rim (PRL) detected by brain MRi are considered a biomarker of chronic inflammatory active lesions and their presence seems to correlate with disability accumulation.
Methods: MS patients under treatment and with disease activity (n=119) were included (RR, n= 99; SP, n= 20). Each of them received one 3T MRi scan with 3D-EPI susceptibility weighted image (SWI) for the detection of PRLs. MRi data were analyzed with the clinical characteristics by descriptive and multivariate analysis. T2 lesion load was obtained in 99 patients using MIPAV, while brain volumes were evaluated by FreeSurfer software.
Results: Overall, the patients with PRL were 73/119 (61,3%), average PRL number/patient = 3,3 (1-18).

Bivariate and multivariate analysis between PRL presence and baseline clinical and demographic parameters showed association with EDSS. Multiple linear regression analysis showed close correlation between EDSS and PRL number (r= 0,34; p= 0,00001) in the RR patients, but not in the SP patients. Moreover, presence of just one PRL seem associated to the total brain volume changes independently from the total T2 lesion.

Conclusion: Presence of PRLs correlates with disability. One single PRL seems sufficient to increase high EDSS development risk and brain atrophy independently from T2 lesion load. No correlation was observed at the higher EDSS values in SP patients, despite a higher PRL number/patient, probably because of a ceiling effect.

Disclosure: Nothing to disclose.

EPO-506

Medically unexplained symptoms are common in women in tertiary neurological healthcare center: a survey study

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Background and aims: Persons with suspicious onset of multiple sclerosis (MS), 18-67% do not fulfil diagnostic criteria of MS. Although some of them are diagnosed with other neurological diagnoses, most of them remain undiagnosed and are often not followed-up in healthcare. In our previous study, persons with undetermined diagnosis (PwUD) showed signs of impaired cognition and reduced quality of life. In this study, we invited PwUD to answer a survey to further characterize this cohort.

Methods: The studied cohort of suspected MS included 271 patients in a tertiary neurological healthcare center who were prospectively followed for 40 months (range 31-52). PwUD (n=72) answered a questionnaire based on Epidemiological Investigation of MS (EIMS), a population-based case-control study using incident cases of MS and a control population aged 16-70 years. For each case, two controls were randomly selected from the Swedish national population registry, matched by age, gender and residential area.

Results: The response rate was 83% and 61% reported persisting MS-like symptoms. The proportion of PwUD in the studied cohort was 20.3%. Compared to PwMS and/or controls, PwUD consisted of more women with non-Swedish origin, had more children and higher education. There were more non-smokers among PwUD and they consumed less alcohol. PwUD reported higher occurrence of autoimmune disease (Table).

Study	Sahlgrenska	EIMS			
Case-control status	PwUD	PwMS	P value[1]	Controls	P value[2]
Total	72	256		531	
Age of onset (mean, SD) Age of onset (median, range)	34.3 (9.4) 33.0 (16-56)	33.5 (10.0) 32.0 (12-62)	0.7		0.4
Age at study inclusion (mean, SD) Age at study inclusion (median, range)	38.5 (9.7) 37.5 (20-60)	37.5 (10.9) 36.0 (17-70)	0.2	38.3 (11.2) 37.0 (17-69)	0.1
Women (n, %)	57 (79)	175 (68.4)	0.06	364 (68.6)	0.05*
Swedish[3] (n, %)	44 (61)	192 (75)	0.006*	382 (72)	0.02*
Currently living with an adult (n, %) Lived with an adult 5 years ago (n, %)	52 (72) 49 (68)	192 (76) 184 (73)	0.4 0.3	385 (77) 379 (76)	0.3 0.06
Children (n, %) Number of children (mean, SD)	53 (74) 1.4 (1.0)	130 (52) 1.0 (1.1)	0.002*	314 (63) 1.2 (1.2)	0.09
Autoimmune disease[4] (n, %)	21 (29)	41 (16)	0.002*	78 (15)	<0.001*
Heredity for AI disease[5] (n, %)	46 (64)	190 (74)	0.05	379 (71)	0.06
University (n, %) Number of terms (mean, SD) Exam (n, %)	45 (62) 4.2 (5.3) 41 (57)	114 (45) 3.3 (4.3) 66 (26)	0.002*	242 (46) 3.3 (4.2) 144 (27)	0.003*
Ever smoking[6] (n, %)	29 (39)	138 (54)	0.08	230 (43)	0.9
Current smoking[9] (n, %)	13 (19)	76 (30)	0.03*	116 (22)	0.4
Past smoking[10] (n, %)	16 (23)	62 (24)	0.6	114 (21)	0.98
Number of pack years (mean, SD)	2.3 (5.9)	3.5 (6.6)	0.1	2.7 (6.1)	0.5
Snuff use (n, %)	13 (18)	43 (17)	0.6	93 (18)	0.7
Exercise[11] at inclusion (mean, SD)	2.5 (1.1)	2.5 (1.0)	0.6	2.6 (0.9)	0.9
Exercise 5 years ago (mean, SD)	2.6 (1.1)	2.7 (1.0)	0.5	2.7 (1.0)	0.7
Low intake of fatty fish[12] (n, %)	7 (10)	44 (18)	0.2	93 (18)	0.1
Alcohol drinkers (n, %)	47 (65)	178 (70)	0.3	360 (68)	0.4
Gram alcohol/week (mean, SD)	29.8 (37.2)	45.3 (66.9)	0.04*	53.0 (98.7)	0.04*
Tiredness[13] (mean, SD)	16.5 (5.1)	15.7 (4.1)	0.4	14.4 (3.9)	<0.001*
Trust[14] outside home (mean, SD)	1.4 (0.6)	2.3 (1.0)	<0.001*	2.2 (1.0)	<0.001*
Trust at home (mean, SD)	1.5 (0.9)	1.7 (0.9)	0.2	1.6 (0.8)	0.2
Economy[15] (mean, SD)	1.4 (0.7)	1.5 (0.9)	0.5	1.5 (0.8)	0.5

1=p value for difference between PwUD and PwMS; 2=p value for difference between PwUD and controls;
Differences in variables between categories of case-control status were assessed using one-way analysis of variance (ANOVA) for continuous variables and the Kruskal-Wallis test (Mann-Whitney U test) for categorical variables.

3=born in Sweden with parents who have not immigrated from outside Sweden; 4= autoimmune disease except MS; 5=heredity for any of the mentioned autoimmune diseases; 6=ever smoking before index; index=year of disease onset among cases and corresponding controls, or first disease symptoms among non-cases; 9=smoking at index; 10=past smoking at index; 1 pack year=20 cig smoked daily during 1 year; 11=exercise was given a value between 1 (lowest exposure) and 4 (highest exposure); 12=fish intake never or seldom (less than monthly); 13=each of the seven questions on tiredness was given a number ranging between 1 (disagree) and 4 (agree), an index ranging between 7 and 28 was created by adding the numbers together, questions 1, 3, 5 and 7 were reversed; 14= feelings of trust (TrustOTR) were given a value between 1 (agree) and 4 (disagree); 15=question on money was given a value between 1 and 4, a higher value indicates financial problems.

Table: Characteristics of PwUD, PwMS and controls.

Conclusion: Approximately 20% of persons investigated for suspected MS had undetermined neurological diagnosis. PwUD seemed to have higher performance but reported lower quality of life. Although the diagnostic workup did not reveal a specific diagnosis, almost one third of PwUD reported other autoimmune diagnosis than MS.

Disclosure: LN has received honoraria for lecture from Biogen, Merck, Novartis, Teva, and has served on advisory boards for Merck, Sanofi, Janssen. JL has received travel support and/or lecture honoraria and has served on scientific advisory boards for Biogen, Novartis, and Sanofi Genzyme; and has received unconditional research grants from Biogen and Novartis. TO has academic grants from the Knut and Alice Wallenberg foundation, the Swedish Research Council and the Swedish Research Council; has received lecture and/or advisory board honoraria, as well as non-restricted MS research grants, from Biogen, Novartis, Sanofi and Merck on projects not related to the one reported here.

EPO-507

Persistence with Botulinum Toxin Treatment for Spasticity Symptoms in Multiple Sclerosis

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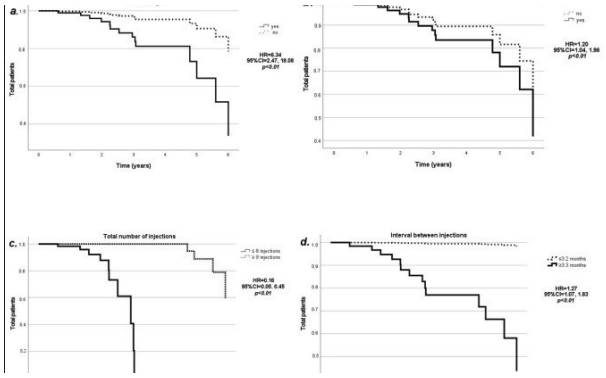
Background and aims: Botulinum toxin (BT) is an effective treatment for spasticity symptoms in multiple sclerosis (MS). We aim to evaluate the rate of discontinuation of BT treatment and the correlation with MS, spasticity, and injection variables.
Methods: This retrospective study on 3-year prospectively collected data included 122 MS patients. We collected MS clinical variables (disease durations, Expanded Disability Status Scales [EDSSs], disease-modifying treatments [DMT], and Symbol Digit Modalities Tests), modified Ashworth scales [MASs], concomitant treatments, and injection variables (formulation, dose, number of injections, and intervals between injections).
Results: A total of 14 patients discontinued BT. In the Cox regression model including the MS clinical variables, the probability of BT discontinuations increased in patients with DMT changes (HR = 6.34; 95%CI = 2.47, 18.08; p < 0.01) and with impaired SDMTs (HR = 1.20; 95%CI = 1.04, 1.96; p < 0.01). In the model including the spasticity variables, there were no associations between BT discontinuation and MAS or other spasticity treatments. In the model including the injection variables, the probability of discontinuation decreased by 80% for each cumulative injection (HR = 0.16; 95%CI = 0.05, 0.45; p < 0.01), but increased by 1% for each additional day over the 3-month interval between injections (HR = 1.27; 95%CI = 1.07, 1.83; p < 0.01).



Kaplan–Meier curves showing the rate of BT discontinuation in relation to the DMT changes (a); impaired SDMT (b); total number of injections (c); interval between injections (d); HR, 95%CI, and p-values are shown from from the Cox regression models.

		BT Continuation (*n* = 108)	BT Discontinuation (*n* = 14)	*p*-Value
Age, years		50.1 ± 9.4	44.0 ± 10.6	0.02 *
Sex, females		46 (42.6%)	6 (42.8%)	0.98
Follow-up duration, years		2.7 ± 1.5	3.0 ± 1.5	0.47
Disease duration, years		14.4 ± 8.3	13.1 ± 9.1	0.58
EDSS		5.8 ± 1.2	5.4 ± 1.3	0.26
DMT	None	9 (8.3%)	0 (0%)	0.30
	Low/Medium efficacy	35 (32.4%)	3 (21.4%)	
	High efficacy	64 (59.3%)	11 (78.6%)	
DMT change		29 (26.8%)	2 (14.3%)	0.64
SDMT, adjusted score		38.0 ± 11.3	35.4 ± 17.5	0.37
SDMT, impaired		40 (37.0%)	6 (42.8%)	
MAS, highest score		1.8 ± 0.5	1.9 ± 0.5	0.77
Concomitant spasticity treatments		48 (44.4%)	6 (42.8%)	0.91
BT formulation	Botox	39 (36.2%)	7 (50.0%)	0.56
	Dysport	45 (41.6%)	4 (28.6%)	
	Xeomin	24 (22.2%)	3 (21.4%)	
BT dose, uDU		263.4 ± 157.0	225.0 ± 131.19	0.38
BT changes		28 (25.9%)	4 (28.6%)	0.83
Total number of BT injections		10.3 ± 5.5	8.1 ± 5.6	0.17
Interval between BT injections, months		3.1 ± 0.4	4.9 ± 1.3	<0.01 *

Demographic, MS, spasticity, and injection variables. The p-values show the differences between the MS patients continuing or discontinuing the BT injections, using a t-test, a chi-square test, or a Fisher's exact test, as appropriate.

Conclusion: BT discontinuation was associated with concomitant MS-related issues, which should be accounted for when planning injections. The interval between injections should be kept as short as possible to reduce discontinuation in the long term.
Disclosure: The authors declare no conflict of interest.

EPO-508

Safety and Efficacy of Tolebrutinib from the Long-term Extension Study in Relapsing Multiple Sclerosis: 2.5-Year Results

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Background and aims: In the phase 2b trial (NCT03889639), brain-penetrant Bruton's tyrosine kinase inhibitor tolebrutinib was well-tolerated and elicited dose-dependent reductions in new gadolinium-enhancing T1 and new/enlarging T2-lesions in participants with relapsing multiple sclerosis. This study reported safety and efficacy at Week (W) 120 in long-term safety (LTS) extension (NCT03996291) of the phase 2b trial.
Methods: In double-blind LTS Part-A, participants continued receiving tolebrutinib 5, 15, 30, or 60mg/day until phase 3 dose selection (60mg/day). In open-label Part-B, participants received tolebrutinib 60mg/day. Safety was assessed via adverse events (AEs). Efficacy outcomes included annualised relapse rate (ARR) and change in Expanded Disability Status Scale (EDSS) score from baseline.

Results: As of July 7th, 2022, 107 (85.6%) participants had ongoing treatment. Reasons for treatment discontinuation were perceived lack of efficacy (n=5), progressive disease (n=4), participant's decision (n=3), AEs (n=3), immigration (n=2), and planned pregnancy (n=1). At W120, no new safety signals were observed. Most common treatment-emergent AEs (TEAEs) were COVID-19 (24.8% [31/125]), headache (13.6% [17/125]), nasopharyngitis (12.8% [16/125]), upper respiratory tract infection (11.2% [14/125]), cystitis bacterial, arthralgia and back pain (7.2% each [9/125]), and pharyngitis (6.4% [8/125]). There was no observed tolebrutinib dose effect for TEAEs or serious AEs (Part-A) and no safety signals emerged upon switching to tolebrutinib 60mg/day. In participants receiving tolebrutinib 60mg/day for >=8 weeks (n=124), ARR was 0.20 (95%CI: 0.14-0.28) and 73.4% remained relapse-free. Mean EDSS remained stable to W120.
Conclusion: Through LTS extension W120, tolebrutinib 60mg/day continued demonstrating favourable safety profile with low ARR and stable disability. FUNDING: Sanofi.
Disclosure: Jiwon Oh: Consulting or speaking fees (Biogen Idec, BMS, EMD Serono, Novartis, Roche, and Sanofi) and research support (Biogen Idec, EMD Serono, and Roche). Sana Syed, Tong Li, Naji Salloum, Timothy J. Turner: Employees of Sanofi (may hold shares and/or stock options in the company). Robert J. Fox: Consulting fees (AB Science, Biogen, Celgene, EMD Serono, Genentech, Greenwich Biosciences, Immunic, Janssen, Novartis, Sanofi, and TG Therapeutics) and research support (Biogen, Novartis, and Sanofi).

EPO-509

Hemibody paroxysmal dystonia as the first manifestation of multiple sclerosis

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Background and aims: Movement disorders (MD) are relatively frequent in multiple sclerosis (MS). Paroxysmal dystonia (PD) is among the most prevalent MD in MS, but rarely a first manifestation.
Methods: Clinical case report of a patient admitted to the emergency room with PD.
Results: A 32-year-old male, former smoker, with benign papillary urothelial neoplasm, was admitted with episodes of painless involuntary right wrist and metacarpophalangeal flexion with fingers extension; and right knee extension, plantar flexion, and toe flexion, with cramp-like pain in hallux. He reported 5-8 episodes/day, lasting around 30 seconds, some occurring during sleep, with complete remission of symptoms between episodes and no other focal neurological signs. He also referred right hemibody tingling sensation, starting 3 months before, with progressive worsening. Head CT and CT-angiography, and blood analysis including metabolic, autoimmune, and infectious panels were unremarkable. Onconeuronal and antineuronal antibodies were negative. He had a clinical event during EEG, without paroxysmal activity. He was started on 0,5mg clonazepam. 15 days later he was asymptomatic, without symptoms recurrence since then. Brain MRI revealed T2 hyperintense/T1 hypointense left precentral circumvolution, left midbrain and multiple small juxta-cortical, deep, and juxtaventricular white matter lesions; without gadolinium enhancement nor diffusion restriction; suggestive of a demyelinating/inflammatory aetiology. Spinal MRI was normal. CSF analysis was normal except for oligoclonal bands presence. The patient was diagnosed with MS (McDonald 2017 criteria) and is being treated with interferon beta-1b.
Conclusion: The left precentral circumvolution or the left midbrain demyelinating lesions may have caused erratic activation of corticospinal axons explaining the right hemibody PD.
Disclosure: Nothing to disclose.

EPO-510

Multiple sclerosis treatment and holistic patient care: Consensus of the Spanish Society of Neurology

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Background and aims: The management of patients with multiple sclerosis (MS) is complicated and entails several challenges, both in diagnosis and treatment. The growing number of disease-modifying therapies (DMTs) available, the scarcity of accurate biomarkers to predict their effectiveness and safety, and individual patient preferences make therapeutic decision-making very complex. The objective of the study was to offer a set of recommendations on the complete management of the MS patient in clinical practice.
Methods: The recommendations were developed following the Delphi method and taking into consideration the latest scientific evidence and the limitations of existing resources.
Results: The recommendations address nine dimensions, including early diagnosis, early start of DMT, escalation versus early start of high-efficacy DMT, face-to-face and remote follow-up, suboptimal response detection, patient perspective, biomarkers, pregnancy, and vaccination. Early treatment is recommended when possible. The classic terminology of treatment lines is obsolete, since the so-called "second line" DMTs are high-efficacy drugs that can be used as the first treatment option, depending on the patient characteristics and disease. It is also recommended to assess the patient experience using validated tools. Most potential biomarkers are not yet considered useful or feasible enough for routine use, further validation and standardization is required.
Conclusion: This consensus is intended to be a useful tool to improve and standardize MS patient management in clinical practice in Spain.
Disclosure: The authors declare fees for lectures, consultations, assistance to congresses, advisory meetings, personal compensation, teaching or research from: Actelion, Alexion, Almirall, Aventis, Bayer, Bial, Biogen Idec, BMS, Bristol Myers Squibb, Celgene, Daiichi Sankyo, Genzyme, GW Pharma, Janssen, Merck, Novartis, Roche, Sandoz, Sanofi, Teva, UCB Pharma and Viatris.

EPO-511

Association of upregulated serum miR-34a-5p with enhancing lesions and lower brain volumes in early Multiple Sclerosis

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Background and aims: Different circulating microRNAs (miRs) have recently emerged as candidate biomarkers in Multiple Sclerosis (MS). This cross-sectional study investigates the association between a panel of candidate miRs expression in serum samples of patients with recent MS diagnosis and disease course, lesion load and brain volumes.
Methods: 51 patients (33 females) aged 18-40 years recently (≤2 years) diagnosed with MS were consecutively enrolled in the study; a brain MRI scan performed between 6 months before and 1 month after inclusion was mandatory. Clinical and demographic variables were collected, and T2-lesion, global brain, white matter (WM) and gray matter (GM) volumes, and presence of gadolinium-enhancing (Gd+) lesions were assessed. Serum levels of miR-15b-5p, miR-27a-3p, miR-30b-5p, miR-34a-5p, miR-122-5p, miR-128-3p, miR-196b-5p, miR-326-3p, miR-432-5p, miR-155-5p, miR-223-3p, miR-140-5p were detected by Real-Time PCR and expressed as ratio of each miR level to a normalizer.
Results: Mean age at diagnosis was 33.3±6.18 years. Mean EDSS was 1.5±1. 45 patients had relapsing-remitting MS, 6 had primary progressive MS. Serum miR-34a-5p level was higher in patients with Gd+ lesions (mean 0.29±0,50 vs 0.07±0.25, p=0.005); miR-34a-5p was also inversely correlated with global brain volume (r= –0.46, p=0.001) and with WM volume (r= –0.44, p=0.002). In addition, miR-128-3p was inversely correlated with global brain volume (r= –0.31, p=0.034) and GM volume (r= –0.31, p=0.035).
Conclusion: Serum miR-34a-5p could be related to biological mechanisms underlying overt inflammation with blood-brain barrier disruption in MS; longitudinal studies are required to assess the possible link of miR-34a-5p and miR-128-3p with brain atrophy in MS patients.
Disclosure: Nothing to disclose.

EPO-512

Ocrelizumab dose-interval extension: a new approach to decrease adverse events while maintaining efficacy

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Background and aims: Ocrelizumab, one of the most effective treatments for MS, can induce side effects such as lymphopenia, low IgG count, infections and decreased response to vaccines. To decrease adverse events while maintaining efficacy, time-interval extension between infusions has been proposed.
Methods: 71 patients from the Hôpital Pitié-Salpetrière in Paris and the IRCCS Besta in Milan, were recruited. 44 patients were treated with an extended dose-interval (EDI) (one infusion at 9 months) after at least 2 years of treatment, while 27 patients followed standard protocol (SDI, 6 months +/- 10 days). Data about ARR (mean annualised relapse rate), EDSS (expanded disability status scale), MRI activity, PI (progression index), lymphocytes count, CD19+ and IgG were collected.
Results: No statistically significant differences were found between the two groups at treatment beginning concerning EDSS, MS type, number of previous treatments, age and sex ($p>0.05$; C.I. 95%). No statistically significant differences concerning ARR, MRI outcomes and PI ($p>0.05$, C.I. 95%) were found between the two groups. Infection incidence was higher in the SDI group, even though not statistically significant ($P=0.34$; $Z=-0.42$). A slightly higher percentage of patients in the SDI group developed hypogammaglobulinemia (EDI 31.8%; SDI 33.3%, $p>0.05$).
Conclusion: Extending time between infusions doesn´t affect treatment efficacy, while incidence of immunological AE shows a decreasing trend. However, given the importance of the topic longer studies with greater MS population should be conducted
Disclosure: Dr. Papeix, has received consulting or travel fees from Alexion , Biogen, Novartis, Roche, Sanofi-Genzyme, Teva and Merck Serono, none related to the present work. Dr Brambilla received honoraria for speaking from Novartis and Sanofi-Genzyme, and for traveling from Sanofi-Genzyme, Merck-Serono, Coloplast, and Roche. She acted as an Advisory Board member for Novartis, Sanofi-Genzyme, Biogen, Merck-Serono, and principal investigator in trials for Roche and Merck-Serono. Dr Mantegazza acted as an Advisory Board member of Biomarin. He received funding for traveling and honoraria for speaking from Sanofi-Aventis, Grifols, Teva, Bayer, Biomarin, Alexion, Argenx. He is involved as principal investigator in clinical trials for Alexion, Merck Serono, Hoffman-La Roche, Teva, Biogen, Biomarin, Almirall, Novartis, Genzyme, Catalyst. Dr Crisafulli received travel grants from Merk and Novertis. Dr Confalonieri has received honoraria from Novartis and Biogen, has received funding for travel from Merck Serono, Biogen Idec, Teva, Mylan and Roche. Dr Perugini has no disclosures No funding was received for the present study

EPO-513

Metabolomic profile changes during pregnancy and puerperium in Multiple Sclerosis

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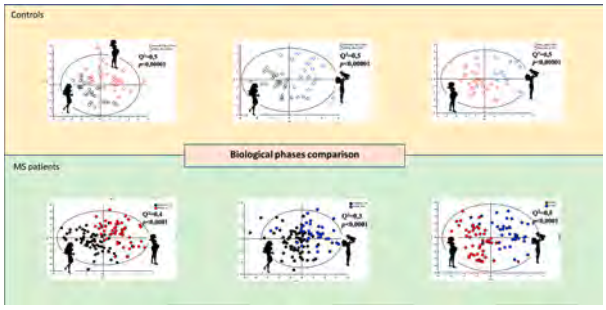
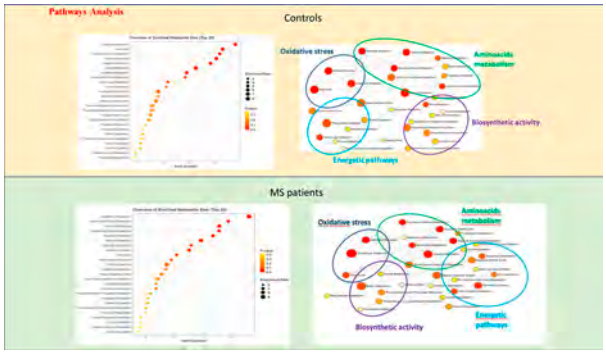
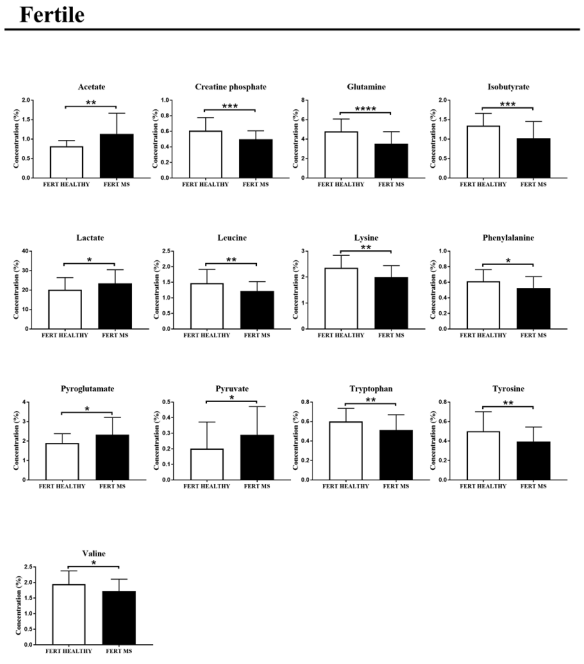
Background and aims: Pregnancy represents a protective condition for women with Multiple Sclerosis (MS) but is often accompanied by post-partum disease reactivation. The present study aims at evaluating possible metabolomic changes of MS women compared to healthy women (HCs) during the fertile phase, pregnancy, and puerperium.
Methods: Serum samples from women with MS and HC during fertile life, pregnancy and puerperium were collected and analyzed by high-resolution nuclear magnetic resonance spectroscopy. Univariate and multivariate statistics as well as pathways' analysis were performed.
Results: Samples of 155 MS women free from disease modifying treatments (68 during fertile life, 49 during pregnancy, 38 during puerperium; mean age 33.8±4.7) and 68 HCs (28 during fertile life, 26 during pregnancy, 14 during puerperium; mean age 31.8±4.5) were analyzed. Significant metabolic differences resulted by the comparison of the three different biologic phases were found in both MS ($R^2X=0,5$; $R^2Y=0,5$; $Q^2=0,3$; $p<0,00001$) and HC samples ($R^2X=0,5$; $R^2Y=0,7$; $Q^2=0,4$; $p<0,00001$), with altered pathways principally related to biosynthesis activity, oxidative stress, energetic pathways and aminoacidic metabolism. After comparison between HC and MS samples at each phase, a significant metabolomic difference in fertile life ($R^2X=0,4$; $R^2Y=0,4$; $Q^2=0,3$; $p<0,00001$) was found. An increase in tryptophan levels has been reported in postpartum MS women.



Description of the metabolic Patterns after comparing different biologic phases in MS patients and HCs



Pathway analysis in MS patients and HCs



Metabolomic differences in MS patients and HCs in the fertile phase

Conclusion: The comparison between MS and HCs revealed that the main metabolomic differences are driven by the disease state during fertile phase. Despite the presence of the disease state, the metabolomic changes related to the presence of the foetus seem to prevail on the metabolomic signature connected to MS.

Disclosure: Pilotto S. has received travel grants from Biogen, Teva and Bristol Myers Squibb. Lorefice L, Fronza M, Fenu G, and Cocco E, have received honoraria for consultancy or speaking from Biogen, Novartis, Sanofi Genzyme, Serono, Teva, and Almirall. Other co-authors have nothing to disclose. We acknowledge Fondazione di Sardegna for financial support.

EPO-514

Predictive role of spinal cord MRI in multiple sclerosis: a monocentric real-world experience

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Background and aims: The 2021 Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) group consensus has confirmed the importance of spinal cord MRI acquisition for MS diagnosis, while spinal cord MRI monitoring is not recommended due to technical, time and cost limitations. Here we investigate the frequency of spinal cord and brain lesion load changes and their association with clinical activity, also exploring how changes in spinal cord MRI acquisition influence disease modifying treatment (DMT) choice and switch.

Methods: 1.5T brain and spinal cord MRI scanners were acquired from each patient at two timepoints spaced by at least 6 months. Radiological activity was defined as new, enlarged or gadolinium-enhancing (Gd+) lesions and clinical and demographic data were collected. Descriptive and multivariate analyses were performed.

Results: 201 relapsing-remitting MS (RRMS) patients were enrolled (145 women and 56 men, mean age: 42.5±12.1 years, mean EDSS-score:2.7±1.9). 44 (21.9%) patients presented both clinical and MRI activity, while 84 (41.8%) patients had asymptomatic MRI activity, with worsening limited to spinal cord in 16 (8%) cases. An association between spinal cord MRI activity and the occurrence of clinical relapses within 3 months after MRI was observed (p=0.024) independently of brain MRI activity. Spinal cord MRI activity resulted a determinant for DMT switch in patients with stable brain lesion load (p=0.021) and without clinical activity (p=0.003), respectively.

Worsening of brain and spinal cord MRI, and Gd+ enhancing lesions (WB+: worsened lesions in brain MRI; WSC+: worsened lesions in spinal cord MRI; GD+B: Gd+ enhancing lesions in brain MRI; GD+SC: Gd+ enhancing lesions in spinal cord MRI).

DMTs	MS Patients (201)	DMTs exposure (months) at MRI	Clinical MS activity at MRI	MRI activity (new T2 lesions/Gd+)	Concomitant clinical and MRI activity
First Line	110 (54.7%)	39.7 ± 31.6	Yes 39/201(19.4%) Intragroup 39/110 (35.4%)	Yes 44/201 (21.9%) Intragroup 44/110 (40%)	Yes 22/201(10.9%) Intragroup 22/110 (20%)
Interferon beta	30 (14.9%)				
Glatiramer Acetate	23 (11.4%)				
Teriflunomide	9 (4.5%)				
Dimethyl-fumarate	48 (23.9%)				
Second Line	57 (28.4%)	28.5 ± 27.3	Yes 20/201(10%) Intragroup 20/57 (35.1%)	Yes 21/201 (10.4%) Intragroup 21/57 (36.8%)	Yes 11/201 (5.5%) Intragroup 11/57 (19.3%)
Fingolimod	11 (5.5%)				
Alemtuzumab	8 (4%)				
Cladribine	6 (3%)				
Ocrelizumab	30 (14.9%)				
Natalizumab	2 (1%)				
No DMTs	34 (16.9%)		Yes 20/201(10%) Intragroup 20/34 (58.8%)	Yes 19/201 (9.5%) Intragroup 19/34 (55.9%)	Yes 11/201 (5.5%) Intragroup 11/34 (32.3%)

Descriptive statistics of disease modifying treatment (DMT) exposure and clinical and MRI activity at MRI acquisition.

	Clinical activity within 3 months after MRI in patients without brain MRI activity (N=138)		DMTs shift in patients without brain MRI activity (N=138)		DMTs shift in patients without clinical activity (N=155)	
	Beta	*P value*	Beta	*P value*	Beta	*P value*
Age at study time	0.002	0.902	-0.034	0.315	-0.052	0.029
Disease duration	-0.014	0.636				
EDSS at study time					0.254	0.056
DMDs exposure (months)	0.003	0.465	0.012	0.213	0.011	0.035
Gd+ spinal cord lesions	1.113	0.024				
New spinal cord lesions			2.292	0.021	1.482	0.003
Enlarged spinal cord lesions			2.792	0.046		

Multivariate analysis models between clinical activity and DMT switch (independent variables) and spinal cord radiological activity while controlling for demographic and clinical variables in specific population subgroups (p value<0.05).

Conclusion: Our results support the utility of spinal cord MRI monitoring in MS. The definition of standardized protocols for the application of MRI in evaluating spinal cord changes is needed given its prognostic and therapeutic implications.

Disclosure: Pilotto S. has received travel grants from Biogen, Teva and Bristol Myers Squibb. Lorefice L, Fenu G, and Cocco E, have received honoraria for consultancy or speaking from Biogen, Novartis, Sanofi Genzyme, Serono, Teva, and Almirall. Other co-authors have nothing to disclose.

EPO-515

Risk factors of Dimethyl fumarate-associated lymphopenia

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Background and aims: Dimethyl fumarate (DMF) is a disease-modifying treatment (DMT), approved for treatment of relapsing-remitting multiple sclerosis (RRMS). Treatment with DMF results in a reduction in clinical (annual relapse rate) and MRI activity, but is associated with a reduction in absolute lymphocyte counts. Some patients even develop severe (Grade II/III) lymphopenia under 500 lymphocytes/mikroliter during treatment. Moreover, patients with lymphopenia exhibit a higher risk of progressive multifocal leukoencephalopathy (PML). At the same time, recent studies also suggest that lymphopenia might be associated with further reduction of relapse rate and MRI activity within DMF treated patients.

Methods: In this study, we retrospectively studied the clinical and laboratory data of RRMS patients treated with DMF in our outpatient clinic. The aim was to identify risk factors of Grade II/III lymphopenia during DMF treatment.

Results: 42 out of 144 patients developed Grade II/III lymphopenia. Patients with lymphopenia were significantly older, had a higher overall JC virus titer (indicative of increased PML risk) and the absolute lymphocyte count at baseline was lower. Furthermore, lymphopenic patients received a higher number of immunomodulatory therapies before DMF initiation.

Conclusion: DMF is one of the most used DMT for RRMS. A frequent reason for discontinuation of treatment with DMF is severe lymphopenia. We identified age and absolute lymphocyte count at DMF initiation, as well as a positive JC virus status as possible risk factors to develop lymphopenia under DMF treatment.

Disclosure: Nothing to disclose.

EPO-516

Real World Experience With Early Treatment With Cladribine in Mild-Moderate Relapsing Multiple Sclerosis

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Background and aims: Cladribine is indicated for patients with highly active relapsing multiple sclerosis (RMS), but real world-evidence remains scarce.
Methods: Prospective collection of clinical, radiological and safety variables in RMS patients treated with Cladribine from October 2018 to December 2022 in a specialized MS centre.
Results: We included 68 patients treated with a first cycle of cladribine, of whom 43 received a second cycle. Median (IQR) age at treatment initiation was 37.2 (30.5–43.3) years. Time from MS diagnosis to first dose was 1.55 (0.26–9.80) years. Cladribine was mainly administered in naïve (55.9%) or first-switch (17.7%) patients, even if older than 50 years (14.7%). At baseline, MS was considered mainly as mild-moderate (median [range] of 1 [0-3] relapse in the previous year and only 8.8% of patients with >50 T2 lesions). Annualized relapse rate (ARR) was decreased by 86.4% and 95.2% after one and two years, respectively. NEDA-3 was achieved in 35.1% and 66.7% in years first and second, respectively. NEDA-3 at first year was 43.2% whenever first two months (until full onset of action) were excluded. Two patients received additional cycles but treatment was subsequently discontinued due to lack of efficacy. All adverse events reported were considered mild, with an incidence rate of infections of 76.7 per 100 patient-years. Lymphopenia was frequent and mild-moderate, with no cases of grade 4 lymphopenia.
Conclusion: In our cohort, cladribine showed an excellent benefit-risk ratio, with a high efficacy and safety in patients with early MS, including older patients and/or with mild-moderate activity.
Disclosure: FRJ received research grants and travel support for speaking engagements from Janssen, Novartis and Sanofi-Genzyme.

EPO-517

Virtual Patient Simulation Improves Performance in Distinguishing MS Severity and Making Holistic Therapy Choices

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Background and aims: It can be challenging for neurologists to select appropriate multiple sclerosis (MS) diagnostic investigations, distinguish severity, and make appropriate treatment choices including newer therapies. We used patient simulation, engaging neurologists in a practical learning experience to assess performance in making these choices.
Methods: This CME-certified virtual patient simulation consisted of 2 patient cases presented in a platform allowing neurologists to conduct assessments and complete open-field entries, choosing from an extensive database of diagnostic and treatment options reflecting the scope and depth of actual practice. After each decision, learners received clinical guidance (CG) based on current evidence and faculty recommendations. Clinical decisions were compared pre- and post-CG using a 2-tailed paired t-test to determine P values (P<.05 is significant). Rationales for clinical decisions were collected in real time. Data were collected July-December 2022.
Results: 145 neurologists completed case 1 and 72 completed case 2. Statistically significant improvements in diagnosis including MS severity, and appropriate treatment choice were observed (Figures). In case 1, 15% chose a novel S1P-Receptor modulator (RM) due to ease of use, disease activity and efficacy; 85% did not mainly due to unfamiliarity with use. In case 2, 31% chose a novel S1P-RM due to efficacy and disease activity; 69% did not mainly due to unfamiliarity with use or unavailability on formulary; in addition, 13% chose ofatumumab primarily due to efficacy and disease activity.

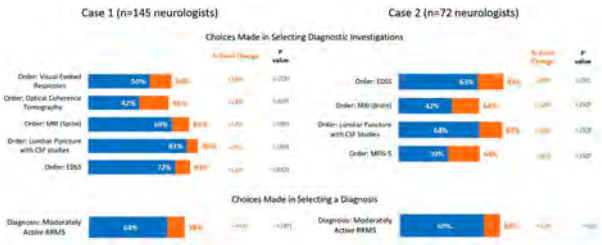

Figure 1.

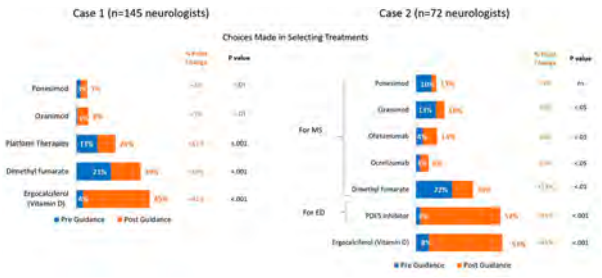

Figure 2.

Conclusion: These results demonstrate the success of immersive, online simulation education in improving performance in selecting appropriate investigations, diagnosis, and treatments according to patient characteristics.
Disclosure: Nothing to disclose.

ePosters

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Cerebrovascular diseases 4

EPO-518
Abstract withdrawn

EPO-519
Skeletal muscle changes and statokinetic instability in the patients with chronic cerebral circulation insufficiency

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Background and aims: The assessment of the relationship between skeletal muscle status and statokinetic instability (SI) in the patients with chronic cerebral circulation insufficiency (CCCI).
Methods: Patients with CCCI (n=64) were categorised as having SI (n=33) and without SI (n=31) by the data of computerized static stabilometry using the parameters: the ellipse area (EA) and the quality of balance function (QBF). The appendicular lean mass index (ALMI) was measured using dual-energy X-ray absorptiometry. Maximum grip strength was measured using a digital handgrip dynamometer. Muscular performance status was evaluated using the Short Physical Performance Battery (SPPB).
Results: It was found that more pronounced skeletal muscle changes in the patients with SI in CCCI was evidenced by significant loss of lean muscle mass (ALMI), reduced handgrip strength as well as the functional decline (decrease of SPPB score) compared to the subjects without SI in CCCI and healthy controls. There was no significant difference in muscle status in the patients without SI in CCCI and the healthy controls (Table 1). The significant positive correlation ($p<0.05$) between QBF and ALMI (R=0.42), grip strength (R=0.39) and SPPB score (R=0.45) were found.

Variable	Patients with SI in CCCI (n=33)	Patients without SI in CCCI (n=31)	Healthy controls (n=30)
	1	2	3
male/female	15(45,5)/18(54,5)	12(38,7)/19(61,3)	13(43,3)/17(56,7)
age (years)	63,0±7,5	61,1±8,1	60,3±8,4
ALMI man (kg/m^2)	7,27 [7,05; 7,56] $p_{1,3}$=0,008 $p_{1,2}$=0,006	8,09 [7,84; 9,29] $p_{2,3}$>0,05	8,05 [7,79; 8,91]
ALMI woman (kg/m^2)	5,83 [5,24; 6,17] $p_{1,3}$=0,004 $p_{1,2}$=0,023	6,78 [6,15; 8,46] $p_{2,3}$>0,05	7,28 [6,84; 7,67]
Maximum grip strength man (kg)	31,0 [29,5; 31,5] $p_{1,3}$=0,013 $p_{1,2}$=0,011	38,5 [33,0; 43,0] $p_{2,3}$>0,05	39,0 [35,5; 40,0]
Maximum grip strength woman (kg)	24,0 [22,0; 30,0] $p_{1,2}$=0,012 $p_{1,3}$=0,003	31,5 [28,5; 34,5] $p_{2,3}$>0,05	32,7 [30,0; 36,0]
SPPB-test (score)	9,0 [9,0; 10,0] $p_{1,2}$=0,003 $p_{1,3}$=0,001	12,0 [11,0; 12,0] $p_{2,3}$>0,05	12,0 [12,0; 12,0]
Confirmed sarcopenia by EWGSOP2 criteria	12 (36,4) $p_{1,2}$=0,045	3 (9,7)	-
Severe sarcopenia by EWGSOP2 criteria	3 (9,1)	-	-
Notes: Values are means (± SD), median [interquartile range] or numbers (percentages). *p*-values was based on the Mann-Whitney U test and the chi-square			

Table 1 – Characteristics of the patients included

Conclusion: Skeletal muscle changes typical for sarcopenia was associated with the SI in CCCI detected by static stabiloplatform. These findings add new information about the significant role pathology of the muscular system in the occurrence of SI in CCCI and suggest new therapeutic targets.
Disclosure: Nothing to disclose.

EPO-520

The real-life reliability of modified rankin scale used in stroke unit and rehabilitation ward

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Background and aims: Modified Rankin Scale (mRS) is the gold standard for measuring stroke-related disability in clinical trials and everyday practice. Inter-observer variability may be considered as a source of bias in retrospective observational studies. It may also depend on the clinical background of the assessing physician. Our aim was to assess real-life consistency between stroke unit physicians (SUP) and rehabilitation medicine physicians (RMP) using mRS in patients transferred directly to rehabilitation ward (RW).
Methods: We enrolled 50 consecutive acute stroke patients transferred within the same hospital from tertiary SU to RW. Patients were scored in mRS by SUP and RMP at the day of transfer. Reference mRS score (REF) was obtained by a single blinded stroke physician using Rankin Focused Assessment form to guide the interview.
Results: mRS score was reported for all patients admitted to RW and n=34 patients discharged from SU. The overall agreement was 76.5% between SUP and RMP (kappa 0.58), 73.5% between SUP and REF (kappa 0.89), and 70.6% between RMP and REF (kappa 0.50). Similar agreement was observed for RMP and REF in the whole sample of n=50 patients (66.7%, kappa 0.48). Patients with REF mRS score of 2 (n=6) were often scored 3 both by SUP (4/6) and RMP (5/6). In patients with REF mRS of 3 and 4 there was no clear tendency towards overrating disability levels.
Conclusion: The reliability of mRS assessment done for the purpose of everyday practice is modest and does not seem to depend on the clinical background of assessing physician.
Disclosure: Nothing to disclose.

EPO-521

Stroke and troponin, a comparison between treated and not treated patients in wake up stroke (WUS)

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Background and aims: The Stroke-heart syndrome (SHS) has been identified as a frequent complication of acute stroke characterized by a cardiac injury following the cerebrovascular event. It is thought that could be caused by a cytokines storm involving the sympathetic system. Wake up stroke (WUS) may be linked to similar pathophysiology. The aim of this study was to compare the maximum troponin level reached between WUS and no-WUS patients (treated and no treated with reperfusion therapy) looking at the OCSP classification.
Methods: We analyzed anamnestic and clinical data of 408 patients admitted in the Stroke Unit of Trieste between January 2021 and October 2022 with an acute ischemic stroke. For each patients we followed the troponin levels until the maximum level reached. Moreover we collect also the site of lesion if it was in anterior circulation (ACI), posterior circulation (POCI) or lacunar (LACI) infarction.
Results: In general, troponin level over 18 ng/l (99th percentile of our laboratory test) in the treated cohort was 48% in n-WUS and 46% in WUS, instead the same parameter in non treated patients was 37% in n-WUS and 29% in WUS (any significant differences with $p<0.05$). The comparison between the no-WUS and WUS patients in each OCSP subgroup lesion type, none of them have a significant difference in troponin rise ($p<0.05$).
Conclusion: More study are needed to understand the complex relationship between WUS and cardiac injury after an ischemic stroke. We didn't find any difference in WUS and no-WUS patient in treated and no treated patients in each OCSP subgroup.
Disclosure: Nothing to disclose.

EPO-522

TIA management in Trieste: Day Hospital admission is effective as a Stroke Unit assessment?

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Background and aims: Transient ischemic attack (TIA) management is still challenging. It is know that TIA needs a rapid access in clinics or Stroke Unit (SU) or in ED (emergency departement). We decided to evaluate if our DH (day hospital) evaluation has the same effectiveness in reducing recurrence rate of ischemic events confronting to the SU work up.
Methods: This is a 4-years restrospective study (between January 1 2018 and December 31 2021) including all the confirmed TIAs in the Trieste province from ED, DH, SU. For each patients we look at the recurrence rate of an ischemic event <90 days and >90 days and the overall mortality rate.
Results: We collect data of 490 patients referred to our ED/outpatients/SU. 53 Patients were discharged with a diagnosis of TIA from SU, 227 from the ED and 210 from DH. Comparing the effectiveness in preventing new ischemic events within 90 days and beyond 90 days between SU and DH patients, no significant difference was found in all the endpoints considered ($p<0.05$).

Patients' characteristics	SU (53 pt)	DH (210 pt)	p value
Age (years)	76 (66-81)	73 (62-81)	p>0.05
Sex, n (%)			
Male (M)	23 (44%)	111 (53%)	p>0.05
Female (F)	30 (56%)	99 (47%)	
Recurrence rate < 90 days	2 (3,5%)	3 (1,6%)	p>0.05
Recurrence rate > 90 days	6 (11%)	13 (6%)	p>0.05
Overall mortality rate	5 (9%)	12 (6%)	p>0.05

Table 1: comparison between the outcomes after a SU and DH evaluation

Patients' characteristics	ED (227 pt)
Age (years)	82 (74-88)
Sex, n (%)	
Male (M)	100 (44%)
Female (F)	127 (56%)
Recurrence rate < 90 days	14 (6%)
Recurrence rate > 90 days	18 (8%)
Overall mortality rate	44 (19%)

Table 2: outcomes after only a ED evaluation

Conclusion: There is a no defined TIA management in practice guidelines. We found a similar recurrence rate <90days and beyond 90 days between a DH evaluation and a SU assessment.
Disclosure: Nothing to disclose.

EPO-523

The use of TMS-hdEEG as an advanced neurophysiologic tool in patients with acute and chronic stroke

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Background and aims: Structural lesions lead to functional alterations of brain activity beyond the site of neuronal loss. This can be studied either by observing spontaneous activity or by assessing brain reactivity to direct perturbations.
Methods: Considering recent evidence, here we exploited this second option and performed a neurophysiological assessment based on Transcranial Magnetic Stimulation coupled with high density EEG recordings (TMS-hdEEG) in a group of twelve stoke patients affected by focal ischemic lesions both during their stay in the stroke unit as well as during rehabilitation.**Results:** Perilesional cortical stimulations were characterized by low frequency responses associated with an extracranial marker of the transient suppression of neuronal activity both in the acute and chronic phase. Longitudinal assessment revealed a reduction of such alterations following physical therapy. Notably, the renormalization of the EEG responses to TMS was found proportional to patients' clinical improvement.**Conclusion:** We confirmed previous evidence of altered local perilesional reactivity following focal brain injury. Importantly, the association between the reduction of such alterations following rehabilitation with the patients' clinical improvement suggests a causal link between the two. More in general, our findings demonstrate the feasibility of advanced neurophysiological assessments by TMS-hdEEG in stroke unit facilities, thus paving the way for an early, neurophysiologically-informed planning of appropriate interventions based on neuromodulation strategies and physical rehabilitation protocols.
Disclosure: I declare that all the participants to this study don't have conflict of interest.

EPO-524

Comparison of the predictive value of hematological factors and ABCD2 in predicting transient ischemic attack recurrence

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Background and aims: Cerebral vascular accidents (CVA) or strokes are major causes of morbidity and mortality worldwide. Although, previous research has been paid to detecting patients with transient ischemic attack (TIA) who are at higher risk of developing CVA since up to 20% of ischemic strokes have been preceded by TIA.
Methods: 465 patients were referred to Razi Hospital in Birjand with TIA between 2019 and 2021, and their ABCD2 scores and hematology factors were recorded.
Results: The mean age in transient ischemic stroke was 67.14±8.94 and non-transient ischemic stroke was 64.925±14.33 years. The mean age did not differ between the two groups (t=1.14, p=0.25). It was determined in the past medical history, hypertension (p<0.001) and hyperlipidemia (p=0.01) in the two groups of transient ischemia and non-ischemia are significantly different. The median MCH levels in the transient ischemic group (30.0 [28.9–31.5]) were significantly higher than in the transient non-ischemic group (29.3 [28.2–30.6]). Other blood factors were not significantly different between the two groups. The median level of systolic and diastolic blood pressure in the transient ischemic stroke group was significantly higher than in the non-transient ischemic stroke group (p<0.05). The ABCD2 index in the transient ischemic stroke group (6.0 [5.0–6.0]) was significantly higher than the non-transient ischemic stroke group (4.0 [3.0–5.0], p<0.001).
Conclusion: ABCD2 score, along with blood factors in patients who presented with TIA after 3 months of follow-up, can be a suitable indicator for the possibility of TIA recurrence in this group of patients, although it is recommended to do more research on this index.
Disclosure: There is nothing to disclose in regards to transparency, relationships/activities/interests related to the manuscript.

EPO-525

Using DRAGON score for prediction of outcome in patients receiving intravenous thrombolysis for acute ischemic stroke

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Background and aims: In everyday clinical practice, neurologist usually rely on their own experience in predicting functional outcome and mortality in patients with acute ischemic stroke (AIS). Predictive scales represent objective outcome measures. DRAGON score is a 10-point system, consisting of 6 variables which are available immediately on admission. We aimed to test DRAGON score in prediction of favorable functional outcome in patients treated with IVT for AIS.
Methods: This retrospective cohort study included patients treated with intravenous thrombolysis for acute ischemic stroke in 10-year period. Variables constituting DRAGON score were collected from medical histories. Favorable outcome was defined as functional independence (mRS 0-2).
Results: Total of 397 patients received IVT for AIS. Functional independence was achieved in 54.9% of cases. Out of 6 variables entering DRAGON score, 4 showed predictive value in our sample. The DRAGON score showed highly statistically significant positive correlation of mean to high intensity with mRS after 3 months (p=0.000, Spearman's ρ=0.580). Values of DRAGON score below 5 predict favorable functional outcome with sensitivity of 82% and specificity of 72%.
Conclusion: Tested score showed significant positive correlation with functional outcome, as well as good predictive value. Using simple, reliable and cost-free tools like DRAGON score can help us predict outcome in patients treated with IVT for AIS.
Disclosure: Nothing to disclose.

EPO-526

Moving from CT to MRI paradigm in acute ischemic stroke: effects on time metrics and revascularization rates and safety

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Background and aims: Neuroimaging is necessary before intravenous thrombolysis (IVT) and endovascular treatment (EVT) for acute ischemic stroke (AIS). Both CT and MRI are possible first-line approaches in the acute setting. In May 2018, we switched from CT to MRI as first line imaging for suspected AIS. Here, we aimed at retrospectively assessing the effects of this paradigm change on revascularisation metrics and safety.
Methods: From the Acute STroke Registry and Analysis (ASTRAL) we selected identical number of patients during the MRI-first-period (05/2018–08/2022) and the preceding CT-first-period. We compared outcome measures in the two periods by univariate and multivariate analysis.
Results: We assessed 1,131 consecutive thrombolyzed and 662 thrombectomized patients. After switching the imaging-paradigm, 80% of patients underwent MRI. Median door-to-needle-time was 31min (IQR=24–48) in the CT-period vs. 43min (IQR=33–58) in the MRI-period (+12 min, puniv<0.01), while door-to-groin-time was unchanged (-3 min, puniv=1). In the CT vs. MRI periods, rates of missed thrombolysis opportunities were respectively 3.1% vs. 0.8% (puniv<0.01); rates of symptomatic intracranial haemorrhage (SICH) after IVT were numerically, but non-significantly, lower (5.6% vs 3.2%, padj=0.07) and SICH after EVT(±IVT) were similar (6.5% vs 4.2%, padj=0.21). Disability at 3 months was unaffected for both IVT and EVT-treated patients (common adjusted odds ratio for favourable Rankin shift 1.23,95%CI=0.96–1.58; p=0.1 and 0.93,95%CI=0.67–1.29, p=0.674 respectively).
Conclusion: In our comprehensive stroke centre, transition from CT to MRI as first-line imaging before revascularizing AIS reduced the rates of missed thrombolysis opportunities. We observed longer door-to-needle and stable door-to-groin times during the MRI-period. Safety (SICH) and 90-day disability were not affected.
Disclosure: Costanza Maria Rapillo received a Research Fellowship Grant from EAN to conduct her research project at Lausanne University Hospital - CHUV.

EPO-527

Investigating Temporal Muscle Thickness (TMT) as a predictor of functional outcome after acute ischemic stroke treatment

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Background and aims: Measurement of temporal muscle thickness (TMT) has been introduced as an easily obtainable surrogate marker to identify patients at risk of sarcopenia, known to be a major cause of disability and frailty, especially among the elderly. Reliability of TMT as a tool to identify sarcopenic patients has been confirmed in a mixed stroke population (ischemic and hemorrhagic) but there isn't available data regarding its relationship with ischemic stroke outcome after acute phase treatment.
Methods: TMT of patients who underwent revascularization was measured on brain CT images acquired upon arrival in the ER. Modified Rankin Scale (mRS) scores at 3 months represented the main endpoint of functional outcome. Patients were further divided into two groups: at-risk vs not-at-risk of sarcopenia. Univariate and multivariate analyses were performed to assess the significance of mean TMT as predictor of functional outcome.
Results: Patients with unfavorable outcomes at 90 days (mRS >3) had lower values of mean TMT (4.9 vs 5.6 mm, p=0.02), as well as the subgroup of patients who passed away (n=17, 13.5%; 4.1 vs 5.6 mm, <0.001). In the multivariate analysis, neither mean TMT nor belonging to the at-risk of sarcopenia group were confirmed as independently associated with worse outcomes.
Conclusion: A trend in higher frequencies of very severe outcomes for patients at-risk of sarcopenia undergoing revascularization treatments for acute ischemic stroke was identified. Actual evidence fully supports treatment of this frail population according to established guidelines. Further investigations are needed to verify if sarcopenia may be an independent prognostic factor.
Disclosure: Nothing to disclose.

EPO-528

Clinico-radiological profile at admission and hemorrhagic risk in cardioembolic stroke under anticoagulant therapy

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Background and aims: Hemorrhagic transformation (HT) is a potential complication of cardioembolic stroke, even more in patients under anticoagulant treatment (AC). Our aim was to assess HT risk in acute cardioembolic stroke patients continuing AC based on their clinico-radiological profile at admission.

Methods: Retrospective observational study of acute cardioembolic stroke patients admitted to a Stroke Center between 2014 and 2021 who were maintained on AC therapy after admission at the physician's discretion. We describe clinical and radiological characteristics on admission non-contrast and CT-angio (blinded assessment) including ASPECTS, presence of leukoaraiosis and intracranial occlusion, mechanical thrombectomy (MT) performance and unsuccessful recanalization (TICI 0-2A) after MT. We used cross-tables to compare these variables with the incidence of HT during hospitalization.

Results: We identified 189 patients (age mean 78.4±8.8 years), initial NIHSS median (IQR) 5 (3–11) points. ASPECTS median (IQR) 10 (8–10) points. Leukoaraiosis was present in 121 (64%) patients, and medium-large vessel occlusion in 66 (34.9%). MT was performed in 28 (14.8%) patients, 8 of them (28.6%) with unsuccessful recanalization. HT during admission occurred in 24 (15.6%) patients, but only 2 (1.1%) presented with neurological worsening. There were not significant differences regarding ASPECTS, leukoaraiosis, intracranial occlusion, MT, or unsuccessful recanalization between patients with and without incident HT.

Conclusion: In our study, only 1.1% of patients with recent cardioembolic stroke who maintained AC presented symptomatic HT. None of the radiological variables analyzed increased HT risk. Further prospective studies are needed to confirm the safety of AC continuation in these patients.

Disclosure: Nothing to disclose.

EPO-529

Reporting from the real world: Health benefits of successful recanalization in acute stroke

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Background and aims: Stroke caused by large vessel occlusion is associated with severe disability, dependency and death. Although thrombectomy is the standard treatment, benefit stems from reperfusion/recanalization. We aim to model the effects of successful recanalization in quality of life and mortality in a lifetime horizon.

Methods: Patients from a Portuguese tertiary center were included from 2016–2021 if they underwent thrombectomy and were followed or deceased in the center. Expanded Thrombolysis in Cerebral Infarction (eTICI) 2b/2c/3 were considered successful recanalization. Modified Rankin Scale (mRS) was collected, and EuroQol-5dimensions-5levels at 3 and 12 months was used in a subset of patients from 2021–2022. We developed a Markov Model (software TreeAge Pro©) with cycles considering background mortality from life tables and specific mRS mortality. Quality-adjusted life years (QALYs) with 95% prediction intervals (95%PI) were calculated using patient simulation.

Results: We included 311 subjects, median age 75 (20 to 96) years, median National Institute of Health Stroke Scale 18 at admission. One-year mortality was 34.7% for successful and 52.2% for unsuccessful recanalization. The model predicted a mean of 4.30 (95%PI 4.10–4.51) QALYs for successful recanalization and 2.69 (95%PI 2.52–2.86) QALYs for unsuccessful, per patient. For patients ≤65 years the results were 9.83 (95%PI 9.54–10.12) and 6.01 (95%PI 5.77–6.25) QALYs, respectively, and for >65 years were 1.85 (95%PI 1.75–1.94) and 1.22 (95%PI 1.14-–1.30) QALYs.

Conclusion: Unsuccessful thrombectomy dramatically decreases lifetime QALYs, with relevant gains from better recanalization. Our results are in line with a published meta-analysis where a 65-year-old person with eTICI 3 has 6.73 QALYs.

Disclosure: PhD grant from CUF Healthcare.

EPO-530

Stroke-related delirium in patients undergoing revascularization treatments: a retrospective, observational study.

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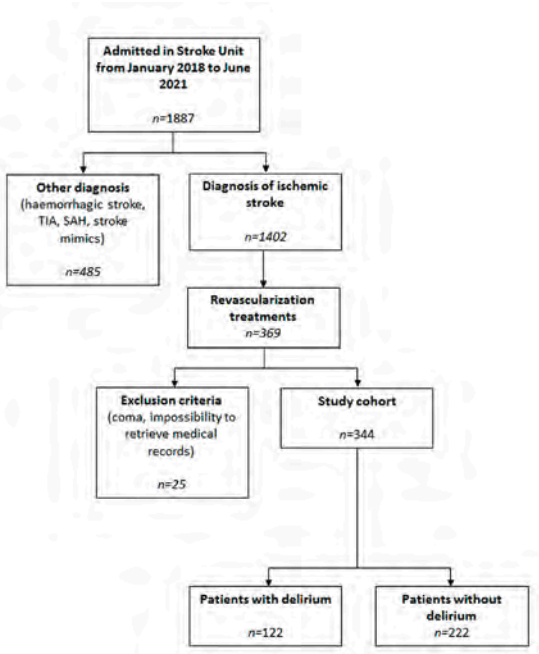
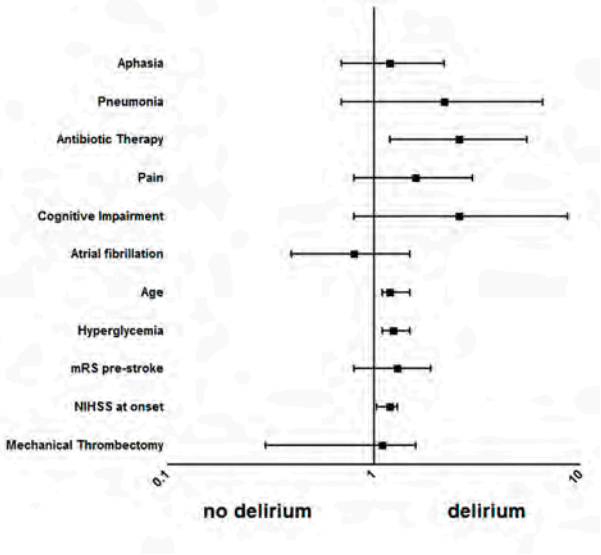
Background and aims: Delirium is a complex neuropsychiatric disorder, which often complicates acute illnesses, including acute stroke. The aims of the present study were to evaluate the prevalence and risk factors of delirium in stroke patients undergoing revascularization treatments, and to assess its impact on stroke outcome.

Methods: We retrospectively reviewed the clinical charts of patients admitted to the Stroke Unit of Policlinico Gemelli from 2018 to 2021. Inclusion criteria were: ischemic stroke; treatment with thrombolysis and/or mechanical thrombectomy. Exclusion criteria were: impossibility to retrieve medical records; coma. Delirium was diagnosed based on the DSM-V criteria by reviewing nurse and medical records.

Results: The study cohort consisted of 344 patients. Mean age was 73.63±12.93. Mechanical thrombectomy was performed in 161(46.8%) patients, thrombolysis in 270(78.5%), both in 87(35.6%). Delirium prevalence was 122/344 (35.5%). In the univariate analysis, delirium was associated with aphasia (p<0.033), atrial fibrillation (p<0.022), hyperglycemia at stroke onset (p<0.001), use of central nervous system acting drugs (p=0.029), cognitive impairment (p<0.025), pain (p=0.033), pneumonia (p<0.001), antibiotic therapy (p<0.001). Patients with delirium had higher NIHSS at stroke onset (p<0.001), and after treatment (p<0.001). In the multivariate analysis, risk factors for delirium were age (OR=1.03; 95% C.I.=1.01–1.06; p=0.039), NIHSS at onset (OR=1.09; 95% C.I.=1.03–1.15; p=0.003), antibiotic therapy (OR=2.56; 95% C.I.=1.18–5.52; p=0.017), hyperglycemia (OR=1.02; 95% C.I.=1.01–1.02; p=0.001). Patients with delirium were less often discharged home (p<0.001), had prolonged hospitalization (p<0.001) and increased 90-days disability (p<0.001).



Study flow chart



Multivariate logistic regression analysis.

Conclusion: Delirium is a frequent complication in acute stroke patients undergoing revascularization treatments and negatively affects the outcome of stroke.

Disclosure: Nothing to disclose.

EPO-531

Evaluating the antiplatelets use before intravenous infusion of rtPA for AIS

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Background and aims: Antiplatelet therapy is one of the most frequent therapies used in prevention of cardiovascular events. The aim of this study is to evaluate the effects of prehospital antiplatelet therapy (AP) before thrombolysis and to assess the rate of intracranial hemorrhage (ICH) and functional outcome in patients with acute ischemic stroke (AIS).
Methods: Retrospective study from a hospital based registry and medical records of the patients admitted to the Department of Neurology, County Clinic Hospital Brasov, over a course of a 36-month period starting in March 2019. We identified patients who had taken at least one dose of any APs within the previous 24 hours before thrombolysis. They were divided into groups based on AP drug, single versus dual AP treatment (DAPT).
Results: A total of 526 patients received rtPA for AIS. The use of any AP was not associated with an increased rate of ICH (20.8% vs 20.94%) with ICH more frequent in the DAPT group. Patients on any AP had a better functional outcome that those without pre stroke AP-treatment (60% vs 51.87%, p=0.265). In addition, significant difference was noted in the rate of good outcome in patients with ICH and pre stroke AP when compared with patients that presented ICH without AP treatment (46.15% vs 32.14%, p=0.04).
Conclusion: Our study didn't show a statistically significant correlation between the risk of ICH and antiplatelet use before intravenous thrombolysis. Patients with AIS and AP had a good a better functional outcome following thrombolysis.
Disclosure: Nothing to disclose.

EPO-532

The Oslo Study of Visual Impairment after Stroke - StrokeVIS

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Background and aims: Studies have shown that up to 60% of patients have some form of new visual impairment after stroke (Rowe et al., 2019). In the annual report of the Norwegian Stroke Register from 2021, only 16% of stroke patients were registered with visual impairment. Notably, this figure is significantly lower than expected from the literature and indicates a significant under-reporting and/or under-diagnosis. The Oslo study of visual impairment (StrokeVIS) intends to measure the prevalence of visual impairment after stroke, validate a Norwegian version of the VISA screening tool (Rowe et al., 2020) and evaluate vision outcomes of acute stroke patients.
Methods: Consenting patients, who fulfill the exclusion and inclusion criteria, will undergo a baseline neuro-ophthalmological examination by an experienced orthoptist, and this expert examination will function as the prevalence as well as a comparable "gold standard". Within 24hrs, the Vision Impairment Screening Assessment (VISA) tool is administered by a nurse. Participating nurses undergo short instruction but are otherwise untrained in vision diagnostics. Patients will attend a 90-day follow-up with reassessments by the same orthoptist, including automated perimetry, and clinical neurological assessments by a neurologist (NIHSS, MOCA and Modified Ranking Scale score).
Results: So far, 62 patients have been included. Recruitment is still ongoing at Oslo University hospital, with a completion date of October 2023 and at least 100 patients to be included.
Conclusion: Preliminary findings indicate feasibility for the use of VISA as a screening tool, for visual impairment after stroke, in Norway.
Disclosure: Nothing to disclose.

Neurogenetics 2

EPO-533

Pyridostigmine for treatment of neuromuscular deficits in PURA syndrome; a gloablly expanding obervation

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Background and aims: PURA syndrome is a rare central nervous system disorder caused by heterozygous variants in the PURA gene. However, several phenotypic features suggested a peripheral/NMJ source of weakness and clinical improvement in treatment with pyridostigmine was reported in one published case. We questioned if this treatment response is generalizable, in patients from multiple countries and with different PURA variants, across the 3 PURA functional domains.
Methods: Observational study with patients from the US and Europe. Approval from local thical committees were obtained, as applicable. Pyridostigmine was administered in a dosis 3 to 7 mg/kg, in divided doses 4 to 6 times, under the supervision of the local, treating neurologist. Before and after treatment observations were compared.
Results: 5 patients from 3 countries were studied. Further patients are included and the number will be update upon presentation. All patients showed an improvement after pyridostigmine, including neurodevelopmental improvements, as evidenced by achievement of new developmental milestones in some cases. Treatment response over time seemed to be sustained and was not restricted to variants in any single functional domain in the PURA protein. No major side effects, including bradycardia, were noted.
Conclusion: Pyridostigmine treatment response in PURA syndrome neuromuscular deficits is generalizable, and not limited to PURA variants in any one functional domain in this small observational study. Additional studies are needed to corroborate these findings with greater confidence.
Disclosure: Nothing to disclose.

EPO-534

A relatively common cause of hereditary motor neuropathy due to a founder mutation in VWA1

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Background and aims: Recently, rare biallelic variants in VWA1 encoding Von Willebrand factor A domain containing 1 were identified as a cause of a subtype of hereditary axonal motor neuropathy. The allele frequency of the most common pathogenic VWA1 variant p.(G25Rfs*74) is estimated to be around 1/1,000 in European populations. Since its first description in early 2021, 34 patients from 23 families, including 17 patients from the UK or western Europe, have been reported in the literature.
Methods: We present the clinical features and variants of 10 newly diagnosed patients from European-, and non-European ancestries along with reviewing all the previously reported patients.
Results: Age of onset varied from childhood to adulthood. Disease progression was slow, and ambulation largely preserved. Clinical presentation included foot deformities, proximal and distal muscle weakness predominantly of the lower limbs, and upper motor neuron signs without any sensory involvement. In some cases, myopathic changes were observed in the muscle biopsy and muscle imaging. Two patients had abnormal brain MRI with white matter abnormalities and one patient presented with dysmorphic features.
Conclusion: Biallelic variants in VWA1 may be responsible for up to 1% of hereditary motor neuropathy cases in the European population. Therefore, early molecular testing for VWA1 variants needs to be considered in patients with unexplained hereditary motor neuropathy. With the expected increase in newly diagnosed cases of VWA1-related neuropathy in the coming years, a foundation will be established to raise public awareness and support clinical collaboration and research in this field,.
Disclosure: HH was funded by the MRC (MR/S01165X/1, MR/S005021/1, G0601943), the National Institute for Health Research University College London Hospitals Biomedical Research Centre.

EPO-535

Identifying of circulating miRNAs as novel emerging biomarkers in Neurofibromatosis type 1

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Background and aims: In recent years is emerging the field of circulating miRNAs as tumor-associated biomarkers that reflect cancer dynamics, malignant potential and drug resistance. We investigated differentially expressed miRNAs (DEmiRNAs) to distinguish patients affected by Neurofibromatosis type 1 (NF1) with classical phenotype from NF1 patients showing a more severe clinical picture.
Methods: The study includes 126 NF1 patients, enrolled at Division of Neurology of AOU Luigi Vanvitelli and diagnosed based on the NIH Consensus Conference criteria of 1988. Clinical subgroups have been classified: NF1 patients with classical phenotype (G1); NF1 patients with G1 features plus systemic complications (G2); NF1 patients with G1 features with diagnosis of MPNST (G3); NF1 patients with G1 features plus multi-apparatus involvement and neurological malignancies (G4); NF1 patients with G1 features, plus multi-apparatus involvement and other tumours (G5). The miRNA expression levels were measured by small non coding RNA sequencing (sncRNA-Seq) using serum pooling approach, followed by RT-qPCR in the entire NF1 cohort.
Results: Our findings showed 87 DEmiRNAs involved in the neurological and psychological diseases, organismal injury, cancer, developmental, skeletal and muscular disorders. A concordance expression pattern between sncRNA-Seq and qRT-PCR data for seven DEmiRNAs was found.
Conclusion: NF1 is characterized by a highly clinical variability. Our results revealed novel and noninvasive potential circulating biomarkers of NF1 disease and related clinical complications. Further validation analysis in other NF1 patients are needed.
Disclosure: The research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-536

Real-world data from risdiplam treatment of SMA patients

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Background and aims: The latest novel disease-modifying therapy for spinal muscular atrophy is risdiplam, which is an orally bioavailable mRNA splicing modifier which increases systemic SMN protein concentrations by improving SMN2 gene transcription. In clinical trials, risdiplam improved motor functions with acceptable safety in SMA patients. The population treated with risdiplam in over 20 countries, up to age 60 represents real-world clinical practice.
Methods: In our centre we follow up 56 SMA patients. 30 of them receive nusinersen and 18 are treated with risdiplam through an early access program. In this cohort we follow 9 men and 9 women between ages 5 and 51 years (median 31,8 years, 22–28 months follow-up). 3 patients have SMA1, 14 SMA2 and 1 person has SMA3. In our cohort 16 patients have 3 SMN2 copies, 2 patients have 2 copies. All of them have severe kyphoscoliosis, 2 patients had spinal stabilization surgeries. Two patients use NIV, 2 have invasive ventilation. All patients are wheelchair-dependent, 3 are non-sitters. In 16 patients motor function was followed by RULM.
Results: RULM scores were between 0 and 28 and they increased or stayed stable in 11 cases (68.75%). Transient increases and decreases were also observed. Adherence is excellent and we also see a positive psychological effect. 6 patients had transient diarrhea, but we observed no significant side effects.
Conclusion: Risdiplam is well-tolerable and safe. In adult patients, even stagnating motor function is considered a positive result compared to natural history of disease. Further follow-up is necessary to detect clinically relevant changes.
Disclosure: At the point of abstract submission, I have nothing to disclose, but there might be an industrial sponsor.

EPO-537

Plasma miRNAs expression in a large family of healthy controls, presymptomatic and symptomatic TARDBP carriers

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease without effective treatment. The diagnosis of ALS includes the detection of early symptoms and, as the disease progresses, muscle weakness and atrophy spread to other parts of the body. Several studies highlight the miRNA's role in ALS pathology by describing their deregulation in various biological fluids, such as plasma.
Methods: In this study, we selected 15 tissue- and disease-specific circulating miRNAs involved in targeting TARDBP or binding TDP-43 during their biogenesis/mature form (Table 1) able to classify symptomatic (n=7), presymptomatic (n=8) TARDBP-G376D carriers and healthy members (n=13) belonging to a large ALS family. The differential expression of selected circulating miRNAs was verified by qRT-PCR in our cohort (Figure 1). Statistical analysis for comparing three groups was performed.

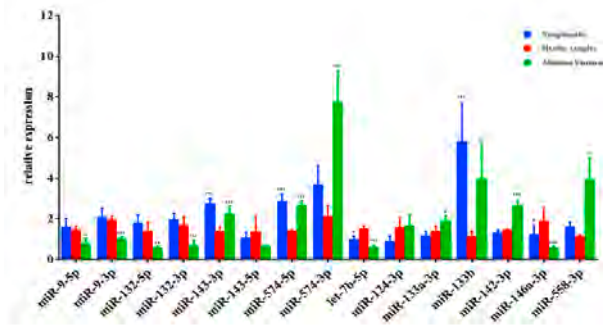

Figure 1

Results: Table 1 displays all miRNAs differentially expressed in family members. Five out of 15 miRNAs were significantly dysregulated between healthy control and patients. Furthermore, 13 out of 15 miRNAs were significantly dysregulated in presymtomatic carriers; eight miRNAs are deregulated exclusively in this group.

miRNA	Fold change (mean ± SD)	
	Symptomatic	Mutation Carriers
miR-9-5p	1.55 ± 0.48 p=0.57	**0,72 ± 0,30 p= 2*10⁻⁴**
miR-9-3p	2.03 ± 0.49 p= 0.40	**0.94 ± 0.18 p= 10⁻⁴**
miR-132-5p	1,74 ±0,48 p=0.09	**0.52 ± 0.13 p= 7*10⁻⁴**
miR-132-3p	1.88 ± 0.41 p= 0.37	**0.62 ± 0.32 p= 10⁻⁴**
miR-143-3p	**2.70 ± 0.31 p= 10⁻⁴**	**2.16 ± 0.49 p= 10⁻⁴**
miR-143-5p	1 ± 0.34 p= 0.57	0.57 ± 0.09 p= 0.12
miR-574-5p	**2.8 ± 0.43 p= 10⁻⁴**	**2.62 ± 0.28 p= 10⁻⁴**
miR-574-3p	3.61 ± 1.02 p=0.12	**7.65 ± 1.67 p= 10⁻⁴**

Table 1

Conclusion: This study shows miRNAs differentially expressed between clinical conditions suggesting that miRNA dysregulation may be used as an early prognostic biomarker for ALS. Interestingly, miR-574-3p, -133B and -558-3P were identified as significantly overexpressed in presymptomatic individuals compared with healthy members, suggesting that the expression of this miRNA is associated with TARDBP mutation. Additionally, -124-3p was significantly deregulated in patients when compared with presymptomatic carriers which supports the correlation of miRNA-133b expression with the progression of TARDBP-associated disease.
Disclosure: The authors disclose any conflicts of interest related to the manuscript.

EPO-538

Pathogenicity of mutation in MT-ND1 (m.3796A>G) in a family with "Leber Hereditary Optic Neuropathy Plus Phenotype"

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Background and aims: Leber Hereditary Optic Neuropathy (LHON) is a mitochondrial disease presenting with subacute loss of vision. Prevalence is around 1 in 30,000. Some patients suffer from a broader spectrum of symptoms such as movement disorders, neuropathy, ataxia, psychiatric disturbances, mental retardation, often named a Leber plus disease. The three most common pathogenic variants demonstrated in 90-95% of LHON are in MT-ND1 (m.3460G>A), MT-ND4 (m.11778G>A) and MT-ND6 (m.14484T>C). Counseling is complicated by the varying penetrance and influence of environmental factors such as tobacco smoking.
Methods: We present a family of 29 relatives, descending

from a woman who suffered from blindness, mental slowness and prominent cerebellar ataxia.
Results: Nine out of nineteen females (mean age 28y) and six out of ten males (mean age 25y) suffer from vision loss, compatible with LHON. Eight out of nineteen females and three out of ten males suffer from cerebellar ataxia. Seven out of nineteen females and two out of ten males complaint of muscle cramps. One patient has muscular fatigue with muscle biopsy showing a mitochondrial complex I deficiency. Four out of nineteen females and three out of ten males demonstrate mental slowness. Only one affected male family member has kids, all asymptomatic. In all affected, the m.3796A>G variant was found in MT-ND1, a mutation previously described in a patient with adult-onset dystonia, spasticity, and myopathy.
Conclusion: This family demonstrates the variability of symptoms, disease-severity and penetrance that is associated with the "LHON plus phenotype". We believe that the identified mutation m.3796A>G in MT-ND1 , an important subunit in complex I of oxidative phosphorylation that is involved in LHON, is likely pathogenic and explanatory for the observed phenotype.
Disclosure: Nothing to disclose.

EPO-539

Plasma neurofilament light chain concentration in RFC1-Related Disease: a multicentre cross-sectional study

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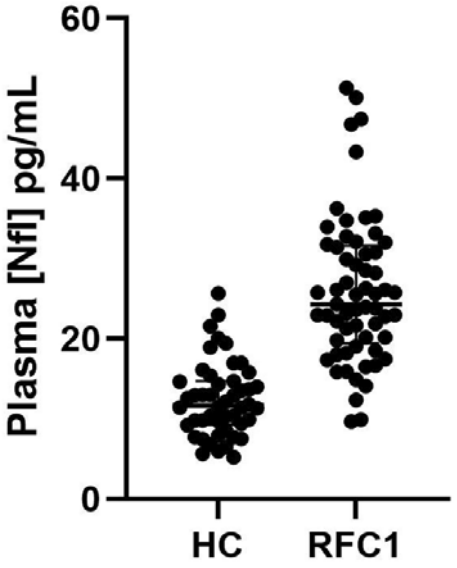
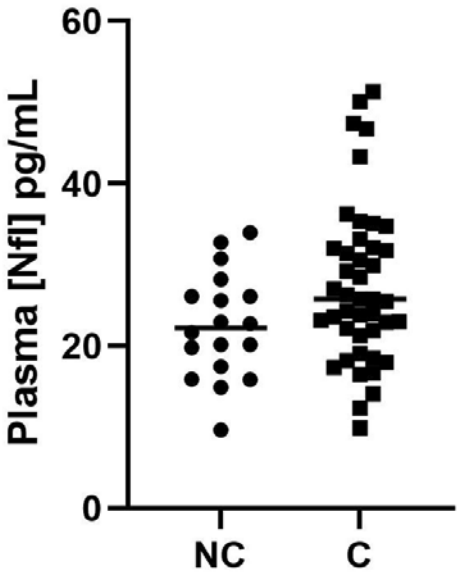
Background and aims: Recently, biallelic intronic AAGGG repeat expansions in the replication factor complex subunit 1 (RFC1) gene have been identified as the cause of cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS) and a frequent cause of late-onset ataxia and sensory neuronopathy. Disease severity and course appear to be highly variable and, given the lack of insight into the pathomechanisms of the disease, no potential biomarker has been identified yet. Neurofilament light chains (NfL) are a promising biomarker in both central



Significantly increased plasma NfL concentration in RFC1 CANVAS and disease spectrum patients compared to healthy controls (HC).



Significantly increased plasma NfL concentration in patients with clinical cerebellar involvement (C) compared to patients without cerebellar dysfunction (NC).

Conclusion: Serum NfL concentration was significantly higher in RFC1 CANVAS and disease spectrum patients than in HCs. Longitudinal studies are warranted to investigate the possible role of serum NfL in disease monitoring.
Disclosure: The authors have no relevant interests to disclose.

EPO-540

Diagnostic yield of whole-exome sequencing for dystonia patients: single tertiatry center experience

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Background and aims: Advent of next-generation sequencing has greatly impacted gene discovery and enabled more genetic diagnoses of dystonia than ever before. Our aim was to assess the clinical impact of whole-exome sequencing in our tertiary centre.
Methods: Our study cohort includes patients from the Clinic of Neurology at the Clinical Hospital Centre Rijeka, referred to genetic testing from 2020 to 2022. Exome sequencing was performed at the Clinical Institute of Genomic Medicine, UKC Ljubljana using standardized protocols and using a determined hereditary dystonia gene panel. Identified variants were classified according to the ACMG and AMP 2015 joint consensus recommendation, along with ACGS recommendations where applicable.
Results: We have performed exome sequencing in 20 patients. Causative pathogenic and likely pathogenic mutations have been confirmed in 7 patients (35%, GNAO, CHD8, GNAL, YY1, KMT2B and GNB1), while variants of uncertain significance (VUS) were found in 2 patients (10%, ADCY5 and SPG7). Additonally, one patient has confirmed carriership of classically recessive genes (5%, UPB1). Regarding dystonia type, the diagnostic yield for generalized dystonia was 77.7%, with one additional VUS finding (11.1%). In segmental dystonia there was one VUS and one carriership, while in focal dystonia there was no findings.
Conclusion: Genetic testing using whole-exome sequencing is recommended for dystonia patients, especially in generalized and segmental dystonia, which is in line with previous findings in the literature. This enables a complete and accurate genetic diagnosis in patients, which has real-life implications given the younger patient population.
Disclosure: There are no financial conflicts of interest to disclose for all authors.

EPO-541

Analysis of a new case of the IRF2BPL mutation syndrome: a rare neurological phenotype of a rare disease.

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Background and aims: Variants in interferon regulatory Factor 2-binding protein-like (IRF2BPL) gene are associated with neurodevelopmental delay, seizures, and other neurological manifestations, such as ataxia, dystonia, ocular disturbances and spasticity. We report a nonsense IRF2BPL variant in an individual with neurological impairments starting in adolescence with psychomotor regression.
Methods: Case report and non-systematic literature review.
Results: A 32-year-old male, presented appropriate cognitive and motor progression until the age of 12, when he quit school due to learning difficulties. At age 15 presented dysarthria and gait ataxia. At age 22 magnetic resonance imaging (MRI) revealed cerebellar atrophy. After 5 years of clinical stability, tendency to fall and dysarthria aggravated. At age 32, the deficits included proximal spastic paraparesis, hyperreflexia, mixed spastic and ataxic gait, dysmetric eye saccades, dysphagia, dysarthria, and progressively voider and scarcer speech. At this stage, MRI showed mild cerebellar atrophy. Genetic testing detected a nonsense c.499C>T (p.Gln167*) heterozygous variant of IRF2BPL gene, described as pathogenic, compatible with a dominant autosomal developmental regression syndrome with motor impairment, aphasia and seizures. A genetic consultation was required to examine the family members.
Conclusion: There are only 28 previously reported cases of pathogenic IRF2BPL mutations, and this case was never described before, to the extent of the authors knowledge. The nonsense variants are typical associated with more severe presentations. The IRF2BPL gene is involved in normal neuronal function, and may be important in other organ systems.
Disclosure: The authors declare no conflict of interests.

EPO-542

Identification of genetic networks highlights a risk trajectory linking Mild Cognitive Impairment to Alzheimer's disease

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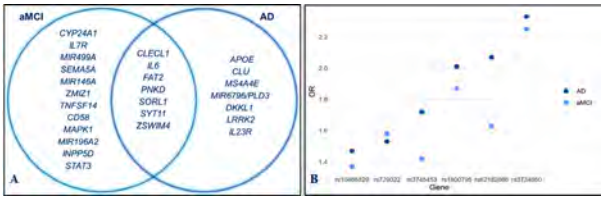
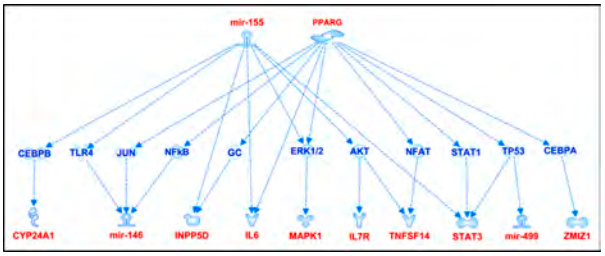
Background and aims: Mild Cognitive Impairment (MCI) and sporadic Alzheimer's Disease (AD) are multifactorial conditions resulting from a complex crosstalk among multiple molecular and biological processes. The study aimed at investigating genetic variants, which may represent susceptibility, prognostic biomarkers or multi-target treatment options for MCI and AD.

Methods: The study included 371 patients (217 amnesic MCI and 154 sporadic AD) and 503 control samples. Open Array technology was utilized to screen patients for a panel of 120 Single Nucleotide Polymorphisms (SNPs). Successively, the data were analysed by statistical, bioinformatics and machine-learning approaches.

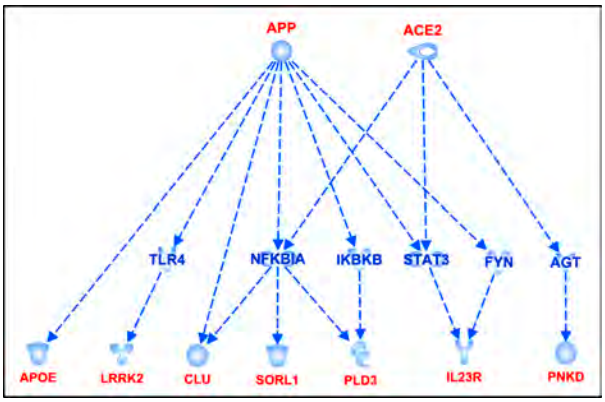
Results: As a result, 21 SNPs were associated with aMCI and 13 variants with sporadic AD. In particular, seven SNPs (rs10466829, CLECL1; rs1800795, IL6; rs3734050, FAT2; rs62182086, PNKD; rs11218343, SORL1; rs729022, SYT11; rs3745453, ZSWIM4) shared between both conditions, reported higher risk values in AD than in aMCI, suggesting the existence of a risk trajectory linking aMCI to AD. In addition, the study highlighted significant interactions among genes and miRNAs that participate in the signalling networks of APP (p=9.04*10–4), ACE2 (p=2.00*10–4), miRNA-155 (p=1.76*10–5) e PPARG (p=1.36*10–4), which have been involved in neuroinflammatory and neurodegenerative contexts underlying MCI and AD.



A. Venn diagram showing shared and specific genes associated with aMCI and sporadic AD. B. Illustration of the risk values (Odd Ratio, OR) of the variants that are slightly higher in AD patients with respect to the aMCI group.



Interaction among genes associated with AD and the APP and ACE2 signalling networks.



Interaction among genes and miRNAs associated with aMCI and the signalling networks of miR-155 and PPARG.

Conclusion: Overall, the present study identified several SNPs associated with aMCI and sporadic AD, among which seven SNPs were shared between both conditions and highlighted the existence of a risk trajectory linking aMCI to AD. These results may be relevant for the development of multi-target treatments and the evaluation of the individual risk for aMCI and progression towards AD.

Disclosure: Nothing to disclose.

EPO-543

A family from Turkey with congenital myasthenia and hereditary polyneuropathy

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Background and aims: Congenital myasthenia is caused by genetic defects of the neuromuscular junction proteins. The possible symptoms are, apnea attacks during feeding, weak crying, ptosis, in the neonatal period or exercise intolerance in childhood. Here, we report a large family with congenital myasthenia displaying heterogeneous neurological symptoms in affected family members, some of whom also have polyneuropathy.
Methods: The index case is a 44-year-old woman who was followed up for 15 years with ptosis in the neonatal period and fatigue in childhood. A detailed family history disclosed common occurrence of consanguineous marriages in the family. Three patients had complaints compatible with congenital myasthenia(IV-1,IV-6,V-5) and three patients had only neuropathic symptoms(III-12,IV-5,IV-7), one of whom(IV-6) had both complaints(Figure1). We performed a detailed electrophysiological and genetic analysis in this family.
Results: We determined decrement after repetitive stimulation of accessory and facial nerves, suggesting a postsynaptic type of neuromuscular junction disorder in patients with myasthenic symptoms and a demyelinating polyneuropathy with conduction blocks in patients with neuropathic symptoms. Two pathogenic variants were identified in the CHRNE gene of the index patient using WES analysis (c.1336del;p.Asp446ThrfsTr61, inherited from the father and c.1219+2T>G;splice region, inherited from the mother). The segregation results of Sanger analysis

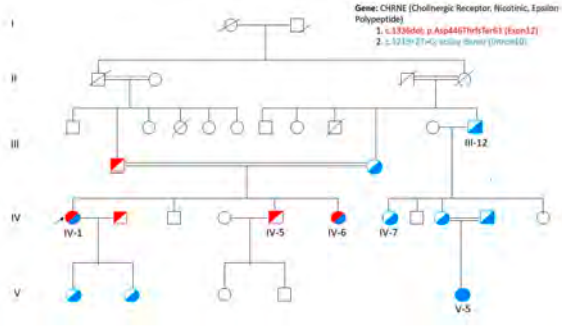

Figure1

Conclusion: The co-occurrence of congenital myasthenia and polyneuropathy is probably an incidental finding in this family due to high frequency of consanguineous matings on one hand and the high ethnic heterogeneity of the population under investigation on the other hand. The presence of conduction blocks in familial polyneuropathy is an interesting finding.
Disclosure: Electrophysiological study samples will be included in the final presentation.

EPO-544

The role of patient representatives in the optimization of Patient Care Pathways at European level: the PKU experience

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Background and aims: In defining and optimising patient care pathways (PCPs) the role of patient representatives (PRs) is very important; it is crucial in the contest of rare diseases where the complexity of the disorders is higher, co-morbidity and multi-organ involvement are present, multidisciplinary care is needed, and patients may experience inequality in the access to specialised diagnostic/treatment procedures. In this work we have analysed the role of PRs in the design and optimization of Phenylketonuria's (PKU) PCP.
Methods: We applied RarERN PathÓ methodology to PKU PCP within the Value of Treatment (VOT) for Rare Brain Disorders project (European Brain Council). PRs of PKU Associations of Ireland and Germany were involved. The PCPs in place in centers of excellence (COE) were analysed, and patients provided input through a semi-structured questions survey exploring organization of care and perception of criticalities when receiving healthcare services. A first draft of the optimized PCP for PKU was discussed in a plenary meeting attended by neurologists and PRs. Finally, PRs were requested to provide additional suggestions through a second ad-hoc survey.
Results: PRs contributed to the design of an optimized PCP, providing unique information on the main organizational challenges in COEs and on the coordination of care between COE and non-hospital care at European level.
Conclusion: To formally involve PRs in the co-design of the PCP is necessary because it allows to complement clinicians' perspective about "ranking" and "weight" of what really matters throughout the PCP. PKU case is particularly interesting in this respect.
Disclosure: The study received financial support from Biomarin.

EPO-545

RARS2-related encephalopathy: a case of ataxia-epilepsy due to a novel splicing variant and review of the literature

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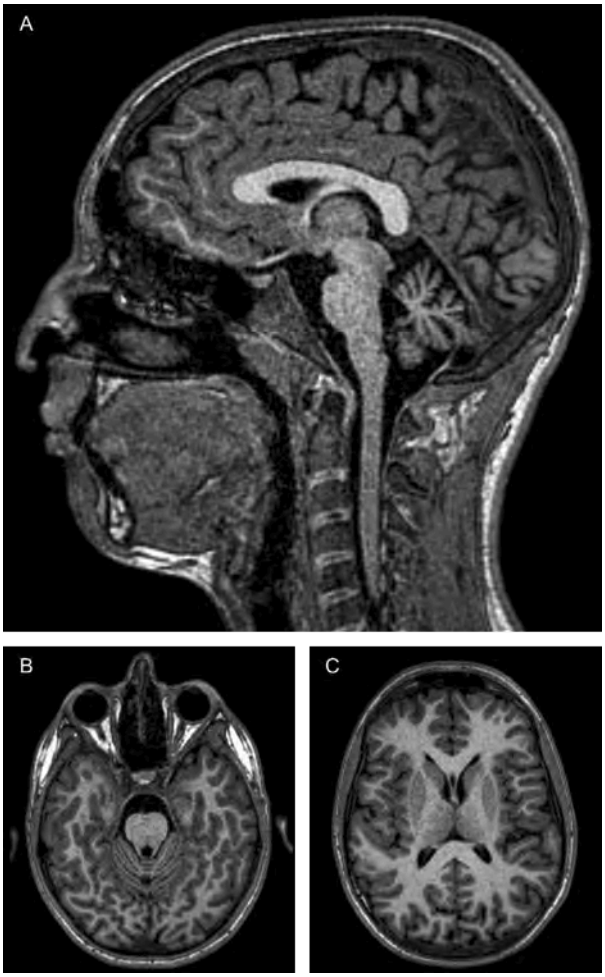
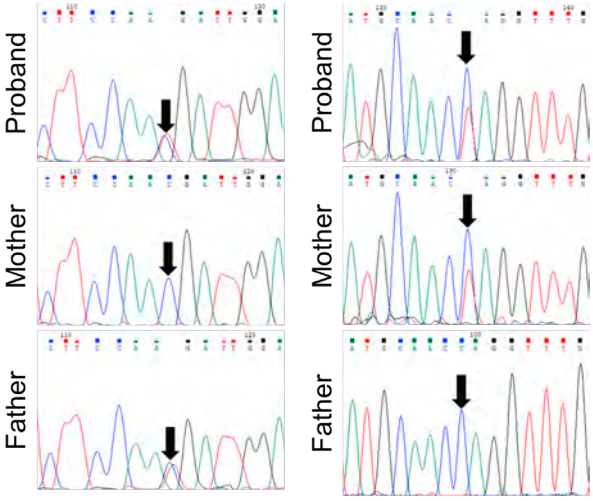
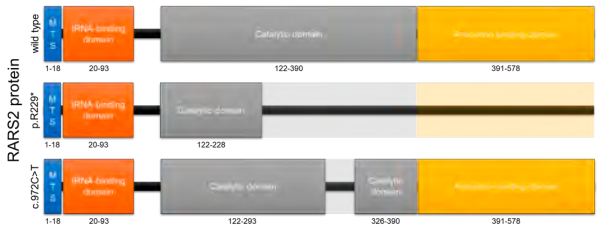
Background and aims: Biallelic RARS2 mutations cause a rare epileptic encephalopathy with 70 reported cases. We report a new case, notable for a novel splicing variant and a mild phenotype with late onset, ataxia, and mild epilepsy.
Methods: A 15 year-old-male patient was clinically evaluated by neurologists with additional training in pediatric neurophysiopathology and movement disorders. Electroencephalogram (EEG) and brain magnetic resonance imaging (MRI) were performed. A whole-exome sequencing (WES) was performed and followed by segregation analysis with Sanger sequencing. Respiratory chain activity (RCA) was assessed on peripheral lymphocytes.
Results: The patient presented at 3 years with language delay and ataxia, and had a severe epileptic crisis at 13 years. He now displays mild intellectual disability, dysarthria, tremor, and ataxia. His EEG showed paroxysmal abnormalities at 3 Hz on fronto-temporo-occipital regions while his brain MRI showed isolated vermis cerebellaris atrophy. His RCA is normal. WES revealed two compound heterozygous mutations in RARS2: a nonsense (p.Arg229*) and a novel synonymous variant (c.972C>T) that determines the skipping of exon 11 (gnomAD allele frequency: 0.000004; ACMG criteria: PP3,PM2,BP6,BP7). Reviewing the literature on RARS2-related encephalopathy, we observed a strong correlation between the genotype and the phenotype severity including onset, survival, neurological and systemic involvement, neuroradiological and biochemical profiles, histopathological and functional characterizations.



T1-weighted brain MRI with a sagittal slice evidencing vermis cerebellaris atrophy (A), an axial slice evidencing cerebellar vermis and mesencephalon (B), and an axial slice evidencing conserved forebrain (C).



Sanger sequencing on DNA of the patient and his parents evidencing the c.685C>T (p.Arg229*) variant in the proband and his father and the c.972C>T variant in the proband and his mother.



Wild type and mutated RARS2 protein with the premature interruption of translation at the amino acid 228 due to the p.Arg229* nonsense mutation and the loss of the 32 amino acids of the catalytic domain of the enzyme encoded by exon 11.

Conclusion: A prompt genotypic characterization of patients with infantile-onset epilepsy and additional characteristics, such as ataxia and intellectual disability, may allow an early genetic diagnosis of RARS2-related encephalopathy and predict the phenotype, improving diagnostic counselling, follow-up, and assistance.

Disclosure: The authors declare no conflict of interest.

Cerebrovascular diseases 5

EPO-546

Tenecteplase in central retinal artery occlusion study (tencraos)

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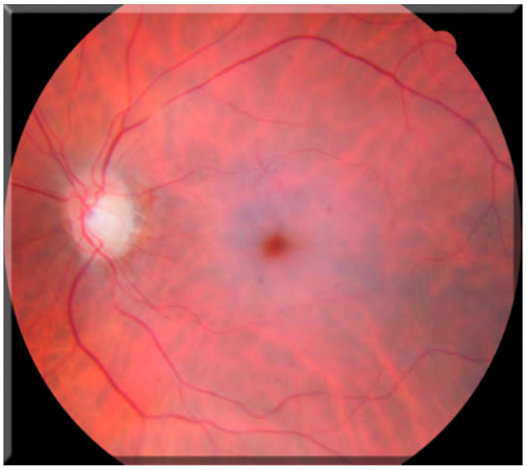
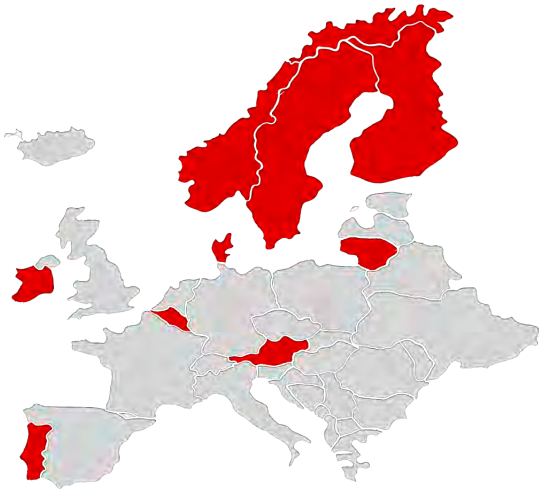
Background and aims: Central retinal artery occlusion (CRAO) is an ophthalmologic emergency that bears a high risk of permanent blindness. No evidence-based treatment is currently available. Whether prompt reperfusion with thrombolytic agents can improve the outcome in CRAO, as proved in ischemic stroke, remains unanswered. The main aim is to assess the effect of systemic tenecteplase within 4.5 hours of onset of central retinal artery occlusion.



Retina changes in a patient with CRAO

Methods: The trial is an ongoing prospective, randomised-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25 mg/kg + placebo vs. ASA + placebo (2 arms with 1:1 block randomisation). Patients are recruited after an ophthalmologist has confirmed CRAO and they can be treated within 4.5hrs. After observation in the stroke unit, patients will be re-examined by an ophthalmologist and a neurologist as an out-patient at 30 and 90-day follow-up. The primary outcome is the proportion of patients with ≤0.7 logMAR best-corrected visual acuity (BCVA) in the affected eye at 30 days after treatment, representing an improvement in BCVA of at least 0.3 logMAR.

Results: 9 countries are participating with more than 30 centres. Currently there are 6 countries activated for recruitment. We have recruited 29 patients so far, 6 in Norway and 2 in Finland. Updated figures will be presented.



European map of participating countries

Conclusion: Inclusion will continue until 78 patients have been randomised. All patients have been included within the strict parameters of the study without any serious adverse events.

Disclosure: Nothing to disclose.

EPO-547

Safety of tenecteplasa vs. Alteplasa in stent implantation in the acute ischemic stroke

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Background and aims: The use of intravenous fibrinolysis in patients who required stenting in the acute phase of the stroke with antiplatelet agents could increase the risk of bleeding. The objective of our study is to compare the safety of the use of tenecteplase (TNK) vs alteplase (rTPA) prior to stent implantation.
Methods: Retrospective observational single-center study. We evaluated patients between January 2021 and October 2022 treated by mechanical thrombectomy and stenting in the acute phase. They were subdivided into 3 groups based on whether they received intravenous fibrinolysis with TNK, rTPA, or without fibrinolysis.
Results: 34 patients with a mean age of 67.31 years (SD 17.16), 40% women, were included. 33.3% (12/34) received TNK, 20% (6/34) TPA, and 46.67% (16/34) did not undergo fibrinolysis. The NIHSS mean prior to treatment was 13 and the ASPECTS mean 8, with no significant differences between the groups. In 29/30 a satisfactory recanalization was achieved with TICI≥2b and in 19/34 an extracranial stent was placed. 3 patients treated with TNK and 1 with rTPA presented intracranial hemorrhage (OR=1.67, p=0.69), being symptomatic in the patient who received rTPA (OR=0.15, p=0.26). Among those treated with TNK vs those who did not receive fibrinolysis, there were no differences in asymptomatic hemorrhagic transformation (OR=1.44, p=0.69) or in symptomatic hemorrhage (OR=0.24, p=0.37).
Conclusion: In our series, the use of TNK prior to mechanical thrombectomy with stent implantation in the acute phase of stroke was shown to be safe and did not significantly increase the risk of symptomatic intracranial haemorrhage.
Disclosure: The authors did not receive funds, grants, or other support from any organization for the submitted work.

EPO-548

How Stressed Are the Patients and Caregivers Following an Acute Stroke? – A Study Protocol.

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Background and aims: Stroke is the third leading cause of death worldwide and a main cause of disability. Not only does it affect stroke survivors, but also their informal caregivers. Caregiver burden was previously associated with depression and low quality of life (QoL) of both, caregiver and the stroke survivor. However, a uniform methodology of assessment of caregiver burden has yet to be defined.
Methods: Aims: This study aims to evaluate stress, QoL, depression, anxiety as part of the overall caregiver burden following an acute stroke.
Results: We plan to conclude a longitudinal study of 150 stroke-survivor caregiver dyads. The assessments will be done immediately after stroke, at 3 and 12 months. To evaluate amount of stress, we will use the Perceived Stress Scale 10 (PSS-10) and combine that with the analysis of biological parameters that have been associated with chronic stress (hair cortisol. CRP, LDL, fasting glucose, HbA1c and blood pressure). Short form 36 (SF-36), Stroke Impact Scale (SIS-3.0) and EuroQol-5 (EQ5DL) will be used to determine QoL. Furthermore, we aim to assess anxiety (Hamilton Anxiety Scale / HAM-A), depression (Patient Health Questionnaire 9 / PHQ-9) and sexual behavior (Sexual Behavior Questionnaire SBQ-G) along with caregiver burden (Zarit Burden Interview / ZBI). Besides descriptive statistics, we aim to quantify the association between stroke parameters in patients and their caregivers' stress, thus multiple linear regression models will be fitted.
Conclusion: We aim to comprehend the burden of stroke patients and their caregivers, and establish prevention programs to reduce stress and enhance the QoL.
Disclosure: All authors have no financial conflicts to disclose. The financing of the project has yet to be defined.

EPO-549

Mitochondrial dysfunction in patients with cervical artery dissection: RNA-sequencing data analysis

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Background and aims: CeAD is the leading cause of ischemic stroke at a young age. It is based on undifferentiated connective tissue dysplasia. GWAS didn't establish significant genetic variants, which suggests epigenetic dysregulation. Research goal is to evaluate differentially expressed genes in peripheral blood in patients with CeAD relative to healthy volunteers.
Methods: Peripheral blood from 29 patients with CeAD (mean age 38.1±4.13; female-68.97%) and 18 healthy volunteers (mean age 30.1±6.65; female-66.67%) were collected into EDTA tubes, 1,500 µl aliquots were used for RNA extraction using the RNeasy Mini Kit. 1,000 ng of the RNA (RIN>7.0) were used to prepare each RNA-seq library with the TruSeq Stranded Total RNA Library Prep Gold kit. RNA-sequencing was performed on the Illumina© NovaSeq 6000. The depth of sequencing was 30-50 million paired-end reads per sample. 67%–82% of reads were aligned to the human reference genome using Hisat2. Counting reads in features is done with htseq-count. After TMM normalization, DE analysis was performed in EdgeR (CeAD vs Norma, adj.p-value <0.05, |logFC|>1.0). GSEA was conducted on the Reactome, KEGG and GO databases.
Results: DE analysis revealed >8,000 differentially expressed genes for CeAD relative to norma, LDHB was the most significant (LogFC - 3.6961, adj.p-value 7.1705e-17). GSEA determined the dysregulation of mitochondrial pathways (ATP-synthesis and heat production – adj.p-value 1.165896e-14, TCA-cycle and electron transport chain - adj.p-value 4.672472e-13) and cell-to-extracellular matrix signaling, RNA-processing, innate immunity.

Volcano plot demonstrates results of DE analysis for patients with CeAD relative to healthy volunteers

Conclusion: Mitochondrial metabolism, RNA processing and cell-to-ECM signaling play significant role in pathogenesis of CeAD and connective tissue dysplasia as its main cause.
Disclosure: Nothing to disclose.

EPO-550

Intensive lipid-lowering therapy for secondary stroke prevention: experience from a comprehensive stroke centre

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Background and aims: Updated guidelines for secondary ischemic stroke (IS) prevention suggest strict LDL cholesterol (LDLc) targets. The most established targets are <55 mg/dl for atherothrombotic stroke and <70 mg/dl for other subtypes. We present our lipid-lowering management experience in a comprehensive stroke centre.
Methods: Observational, descriptive study of a prospective cohort of patients with IS admitted to a Stroke Unit between July and October 2020. Demographic, clinical and laboratory data were collected at admission and after 5-month follow-up. Compliance with cLDL goals was assessed.
Results: A total of 152 patients (44.1% women, 70.9±13.9 years old) were included. 42 (27.6%) had TIA, and 110 (72.4%) IS. 30 were atherothrombotic, 46 cardioembolic and 57 of undetermined source. LDLc levels at admission were 97.1±38.0 mg/dl. 68 patients (44.7%) were receiving statin treatment (only 6 high-intensity statins, 15 Ezetimibe-combinations). Treatment was optimised in 120 patients (78.9%), including every atherothrombotic IS, prescribing 26.7% high-intensity statins, 50% Ezetimibe-combinations, and 1 PCSK-9 inhibitor in this group. LDLc was reduced by 31.2±37.9 mg/dl at follow-up (95% Cl=22.9–34.8, p=0.0001). LDLc objective <70 mg/dl was achieved in 81.1% of patients, whereas 83.3% of atherothrombotic IS attained LDLc <55 mg/dl. There was 5.3% of poor treatment adherence and 9.8% of adverse effects.
Conclusion: Early use of high-intensity statins and Ezetimibe-combinations improved adherence to new cLDL targets. Low abandonment rates and few adverse effects were observed.
Disclosure: Nothing to disclose.

EPO-551

CAA and amyloid PET: quantitative analysis in a sample of patients with probable CAA

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Background and aims: The diagnostic criteria of CAA do not include the use of amyloid PET (a-PET). Being able to arrive at a diagnosis in advance of overt manifestations of CAA would be beneficial to avoid risk factors such as anticoagulation.
Methods: We recruited 7 patients who met the Boston Criteria 2.0 for probable CAA and underwent brain MRI, a-PET, and neuropsychological tests. Lumbar puncture and genetic analysis were also performed. We accomplished a quantitative analysis of the a-PET data after automated segmentation in 18 brain regions (Table 1).
Results: A total of 126 values expressing aβ burden were evaluated. If we exclude the cerebellum, only 9 brain regions (8%) have no pathological deposition (Table 2); 4 out of 9 were localised in the same area of post-hemorrhagic encephalomalacia. The occipital lobe showed variable amyloid load values, but 3 out of 14 occipital regions (21%) were also affected by encephalomalacia; in these same regions the lowest deposition was identified. The lateral temporal lobe (Figure 1) showed higher aβ load than the medial one. The prefrontal cortex, cingulate, precuneus and parietal lobe had bilateral uniform aβ deposition in excess of the norm.

	Sex	Age at diagnosis	Aβ 40 (CSF) (7755 - 16715)	Aβ 42 (CSF) (> 640)	Aβ 42 / Aβ 40 (CSF) (0.068 - 0.115)	p-tau (CSF) (21.5 - 56.5)	total tau (CSF) (146 - 404)	MMSE	Time between MMSE and a-PET
PT1	F	69	NE	NE	NE	NE	NE	20	173
PT2	F	70	5128	245	0,05	34.1	286	22	6
PT3	F	78	7019	234	0,03	114.8	781	24	55
PT4	M	74	3557	128	0,04	66.8	408	29	131
PT5	F	48	4355	270	0,06	36.4	337	29	42
PT6	F	74	NE	NE	NE	NE	NE	28	-7
PT7	F	79	NE	NE	NE	NE	NE	21	125
		70 ± 9.72 (mean ± SD)						25 ± 3.61 (mean ± SD)	75 ± 63.5 (mean ± SD)

Table 1. Demographic, clinical and biomolecular characteristics. Abbreviations: Aβ = amyloid beta; CSF = cerebrospinal fluid; MMSE = mini mental state examination; NE = not executed; p-tau = phospho-tau; PT = patient; t-tau = total-tau.'

Patient	Parietal lobe (right)	Parietal lobe (left)	Lateral temporal lobe (right)	Lateral temporal lobe (left)
PT1	9,57	7,89	7,96	7,15
PT2	5,56	5,18	6,21	7,2
PT3	6,19	6,41	8,01	8,05
PT4	6,85	5,18	1,62	5,93
PT5	8,76	8,49	9,65	6,67
PT6	4,78	4,71	6,67	5,13
PT7	6,19	6,05	9,58	10,2

ALG	N°	%	N°	%
grade 3	4	28,6	8	57,1
grade 2	10	71,4	5	35,7
grade 1	0	0,0	0	0,0
grade 0	0	0,0	1	7,1

Patient	Sensorimotor cortex (right)	Sensorimotor cortex (left)	Mesial temporal lobe (right)	Mesial temporal lobe (left)
PT1	8,43	7,57	2,36	2,85
PT2	2,95	2,91	3,24	3,52
PT3	1,44	2,46	1,43	2,63
PT4	4,04	3,44	-0,13	2,98
PT5	6,29	6,36	5,35	2,21
PT6	2,29	1,02	1,83	0,15
PT7	3,06	1,84	2,88	3,31

ALG	N°	%	N°	%
grade 3	2	14,3	0	0,0
grade 2	3	21,4	1	7,1
grade 1	6	42,9	9	64,3
grade 0	3	21,4	4	28,6

Patient	Occipital lobe (right)	Occipital lobe (left)	Cerebellum (grey matter)	Cerebellum (whole)
PT1	4,76	3,97	1,91	3,05
PT2	4,33	4,43	0,36	0,41
PT3	2,39	2,74	-0,86	0,15
PT4	-2,24	4,42	0,64	0,68
PT5	10,30	8,17	1,23	1,03
PT6	6,38	-0,54	0,30	0,53
PT7	4,99	5,82	-0,94	-0,73

ALG	N°	%	N°	%
grade 3	2	14,3	0	0,0
grade 2	7	50,0	0	0,0
grade 1	3	21,4	1	7,1
grade 0	1	7,1	13	92,9

Table 1. Values from quantitative a-PET analysis. The severity of amyloid load has been conventionally classified from grade 0 to grade 3, represented with different colours. Areas of recent or previous l-ICH are shown in red font.

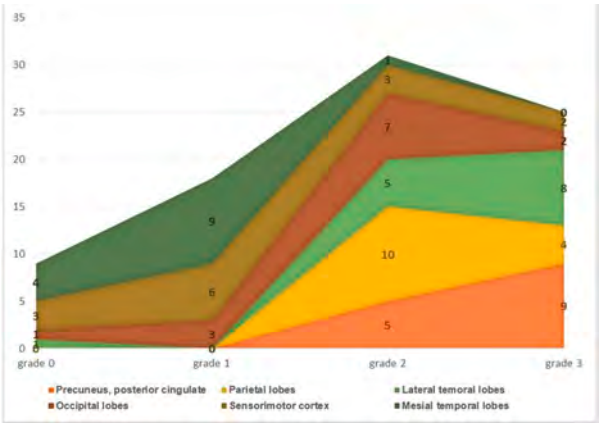

Figure 1. Distribution of severity of amyloid load at a-PET in six different brain regions according to ALG (Amyloid Load Grading): values below 2 (grade 0), values between 2 and 4 (grade 1), values between 4 and 7 (grade 2), values above 7 (grade 3).

Conclusion: Our preliminary results demonstrate concordance between diagnosis and a-PET quantitative results. However, due to the wide variability of CAA pathological and radiological phenomena, it is imperative to ensure a complementary qualitative analysis by a nuclear radiologist. Only a study with a large cohort of patients with clinically overt CAA may allow the adaptation of a-PET protocols to this pathology.
Disclosure: Nothing to disclose.

EPO-552

Effect of the extended thrombectomy time window on survival and quality of life – experiences from Szeged, Hungary

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Background and aims: The thrombectomy time window can be extended up to 24 hours. The aim of our research is twofold: to summarize the results of thrombectomies performed between 6–24 hours after the onset of symptoms, and to identify predictors that can predict the unfavorable outcome.
Methods: In 2020-2021, we processed the data of 90 patients who underwent thrombectomy at Szeged with stroke symptoms of 6–24 hours. Demographic and clinical data were analized, the 90-day mortality, the functional outcome, and the correlation of these parameters with the technical success of the thrombectomy. Correlation between the individual parameters and the outcome was peformed using SPSS and MatLab.
Results: The average age of the patients was 73.03 years (⌖11.85 SD), 48.88% of the patients were outside of the region of Szeged, tandem occlusion occurred in 13%. Sixtyeight percent of the thrombectomies were technically successful, the average score on the 90-day modified Rankin scale was 3 (⌖2 SD), the 90-day mortality was 30%. Higher age, previous stroke in medical history, severity of stroke, technical success of the thrombectomy, atrial fibrillation, lack of prior antiaggregant and thrombolysis treatment together can predict a poor clinical outcome with 93% specificity and 72% sensitivity.
Conclusion: While the practical application of the extended time window leads to more patients who can benefit from effective stroke care, our real world data analysis warrants further investigation to better identify a subgroup of patients to reduce mortality and further improve functional outcome.
Disclosure: Nothing to disclose.

EPO-553

Markers of damage to the blood-brain barrier and brain in cerebral small vessel disease and Alzheimer's disease

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Background and aims: It is believed that the comorbidity of cerebral small vessel disease (cSVD) and Alzheimer's disease (AD) is the cause of mixed cognitive impairments (CI). At the early stages, their comorbidity could not be confirmed by laboratory signs. This study was aimed at finding markers to differentiate cSVD and AD.
Methods: The study included 68 cSVD patients (61.0±8.6; m. 60.3%) with dysexecutive (26%), amnestic (7.2%) and mixed (66.8%) CI types and 17 AD patients (65.2±8.3; m. 35.3%). The following markers of damage to the blood-brain barrier and brain were investigated in blood serum (BS) and cerebral spinal fluid (CSF) with ELISA: matrix metalloproteinases (MMP) 2 and 9, tumor necrosis factor (TNF) alpha, tissue-type plasminogen activator (tPA), fibrinogen, neurofilament light chains (NEFL), glial fibrillary acidic protein (GFAP), neuron-specific enolase (NSE). Statistical analysis was performed with Mann-Whitney U test and receiver operating characteristic (ROC) curves analysis (SPSS v26).
Results: The levels of TNFalpha in BS and CSF and GFAP in CSF were significantly higher in cSVD patients ($p<0,001$) (Fig. 1). Differential markers of cSVD from AD were BS TNFalpha >9.95 pg/ml (0.99; CI 0.96-1.0), CSF TNFalpha >7.1 pg/ml (0.99; CI 0.99-1.0), CSF GFAP >1.03 ng/mL (0.92; CI 0.86–0.98) with sensitivity and specificity of threshold values >70% (Fig. 2).

Fig 1. The levels of TNFalpha in BS and CSF and GFAP in CSF in patients with cSVD (blue) and AD (orange)

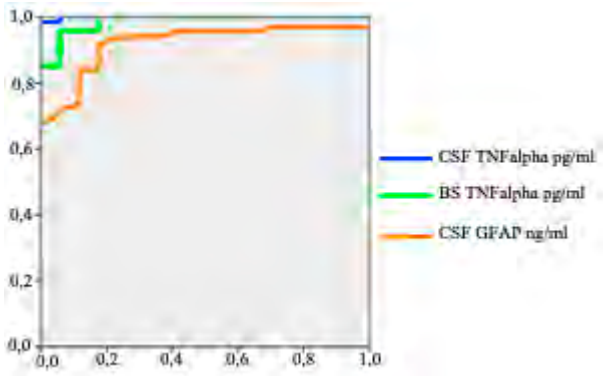

Fig 2. ROC curve analysis for markers of blood-brain barrier permeability and neurodegeneration in cSVD and AD

Conclusion: The established differential predictors indicate a high significance of TNFalpha-supported neuro-inflammation and astrocytic GFAP-reactivity in cSVD. Found threshold values can be used in AD with white matter hyperintensity to clarify isolated and mixed form with cSVD.

Disclosure: Supported by the Russian Foundation for Basic Research, project no.22-15-00183

EPO-554

Markers of blood-brain barrier permeability, lymphangiogenesis and neurodegeneration in cerebral small vessel disease

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Background and aims: This study aimed to calculate the predictive value of circulating markers associated with leading mechanisms of cerebral small vessel disease (cSVD).

Methods: The study included 68 cSVD patients (61.0±8.6; men 60.3%) with cognitive impairments of varying severity and 26 healthy participants (HP) (59.9±6.7; men 38.5%). The following indicators were determined in blood serum by ELISA: the markers of blood-brain barrier (BBB) permeability (matrix metalloproteinases (MMP) 2 and 9, tumor necrosis factor (TNF) alpha, tissue-type plasminogen activator (tPA), fibrinogen), lymphangiogenesis (vascular endothelial growth factor (VEGF) C) and neurodegeneration (neurofilament light chains (NEFL), glial fibrillary acidic protein (GFAP), neuron-specific enolase (NSE)). Statistical analysis was performed with Mann-Whitney U test, receiver operating characteristic (ROC) curves and Pearson's correlation analysis (SPSS v26).

Results: The level of all studied markers in cSVD patients was significantly different from HP. The highest areas under the ROC curve were determined for VEGF C (0.93, CI 0.87–0.98), MMP 2 (0.93, CI 0.87–0.98), MMP 9 (0.99, CI 0.99–1.00), TNF alpha (0.96, CI 0.91–1.00), GFAP (0.82, CI 0.73–0.90) with sensitivity and specificity of threshold values >70% for all of them (Fig. 1). The GFAP level correlated with the levels of TNF alpha (r=0.447), MMP 9 (r=0.554), VEGF C (r=0.430).

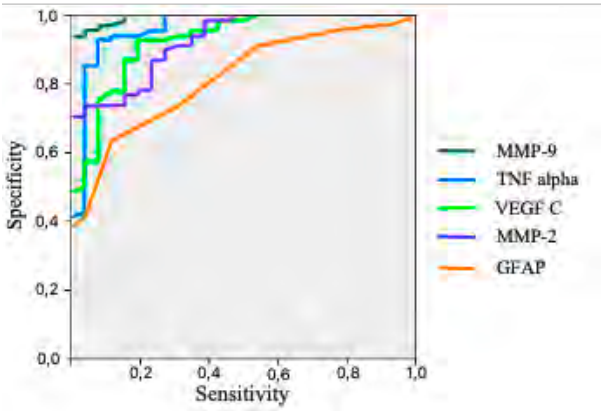
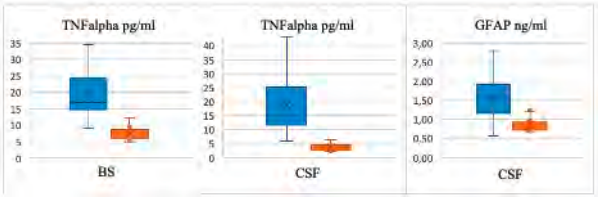


Fig 1. ROC curve analysis for markers of BBB permeability, lymphangiogenesis and neurodegeneration in cSVD

Conclusion: The analysis of GFAP associations suggests the determining role of TNF alpha, MMPs 2, 9 and VEGF C in damage and maintenance of high BBB permeability and GFAP-associated neuroinflammation and neurodegeneration and the possibility of using them in the cSVD diagnosis.

Disclosure: This study was supported by the Russian Foundation for Basic Research, project no. 22-15-00183.



EPO-555

Challenges Of Acute Ischemic Stroke Associated With Left Ventricular Thrombus: A Single-Center Experience.

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Background and aims: Left ventricular thrombus (LVT) is a known complication in patients with myocardial infarction (MI), mainly in anterior MI [1]. LVT is a rare cause of cardioembolic ischemic stroke (IS) and may remain undetected, as “embolic stroke of undetermined source (ESUS)”[2]. Transthoracic echocardiography (TTE) is the main investigation: intravenous contrast administration increases its sensitivity for LVT detection. Cardiac Magnetic Resonance Imaging (MRI) has a high sensitivity and specificity for the thrombus delineation [3].
Methods: A retrospective analysis of 2,792 consecutive patients with acute IS, admitted to the Stroke Unit of the University of Messina, between 2014 and 2022, LVT was reported in fifteen patients. 12 patients had a diagnosis of “cardioembolic IS”, due to TTE LVT detection. Three patients were discharged with the ESUS diagnosis and underwent cardio-MRI.
Results: The cardiological assessment with TTE showed an apex hypo-akinesias and reduced left ventricular ejection fraction (LVEF<50%) in all patients. In twelve patients, TTE detected LVT; in three patients, TTE showed LVT risk factors, so they performed cardio-MRI, which revealed mural thrombosis. All patients were treated with vitamin K antagonists for a period of a minimum of 3–6 months up to thrombus resolution.
Conclusion: LVT is a rare cause of cardioembolic IS, and therefore a correct diagnostic-therapeutic pathway is of the utmost importance [4]. Whether there is high clinical suspect of LVT and TTE findings of left ventricular dysfunction, cardio-MRI should be performed when other methods are not diagnostic.
Disclosure: The authors have no financial interest to report and did not receive any fundings.

EPO-556

Thrombolytic and Endovascular Treatment Experience in Patients Over 85 Years of Age with Acute Ischemic Stroke

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Background and aims: Intravenous thrombolytic treatment(IVT) and endovascular treatment(EVT) are important in acute ischemic stroke(AIS). There is insufficient literature data regarding the safety of IVT and EVT in the elderly.We wanted to share our experiences with IVT and EVT in patients aged 85 years and older with aII.
Methods: 25 patients with acute ischemic stroke over the age of 85 were included in our study. Multiple risk factors,treatments used,admission and discharge NIHSS scores, door-to-needle and symptom-door times, complications after the procedure, discharge and 3rd month mRS scores were recorded.
Results: IVT was performed in 32% of the patients,EVT in 20% and both IVT and EVT in the remainder. Complications did not develop in 16 (64%) patients,asymptomatic intracranial hemorrhage (ICH) was observed in 5 (20%) and symptomatic ICH was observed in 2 (8%) patients.13 (52%) patients had a good outcome (mRS 0–2) at discharge.Hospital mortality rate was calculated as 24%. Our third month mortality rate at was 28%.Factors associated with poor outcome at 3 months (mRS 3–6); high entry NIHSS score (p=0.005), presence of symptomatic and asymptomatic ICH (p=0.048) and presence of more than one vascular risk factor (p=0.041). These results showed that aII can be effectively treated in this age group with IVT and EVT.It is noteworthy that third month mRS scores were found between 3–6 in all patients who developed symptomatic or asymptomatic ICH.

Relationship between patient characteristics and 3rd month mRS score

	3. month mRS 0-2	3. month mRS 3-6	P value
Symptom-Door Time	145,56±48,31	191±136,95	0,351
Admission NIHSS Score	9,11±5,33	15,87±4,01	**0,005**
Door-to-needle Time	89,22±43,16	109,67±71,35	0,63
Door-to-needle Time (categorical)			
≤60 minutes (n=9)	3	6	1
>60 minutes (n=15)	6	9	
Complication			
None (n=16)	9	7	
Asymptomatic bleeding (n=5)	0	5	**0,048**
Symptomatic bleeding (n=2)	0	2	
Other (n=2)	0	2	
Use of Antiaggregant or	4	5	0,671
Anticoagulant Drugs	5	11	
Var (n=9)			
Yok (n=16)			
Hypertension			
Var (n=19)	7	12	1
Yok (n=6)	2	4	
Diabetus Mellitus			
Var (n=5)	1	4	0,621
Yok (n=20)	8	12	
Atrial fibrillation			
Var (n=11)	3	8	0,677
Yok (n=14)	6	8	
Coronary artery disease			
Var (n=5)	1	4	0,621
Yok (n=20)	8	12	
Multiple risk factors			
Var (n=13)	2	11	**0,041**
Yok (n=12)	7	5	

Thrombolytic and Endovascular Treatment Experience in Patients Over 85 Years of Age with Acute Ischemic Stroke

Conclusion: In conclusion,it can be said that IVT and EVT applications are effective and safe in elderly patients with all.
Disclosure: We are of the opinion that IVT and EVT is safe in elderly patients and patient-based evaluation is important.

EPO-557

Aphasia due to acute stroke treated with the tablet-based speech therapy app Neolexon®: a randomized controlled trial.

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Background and aims: Aphasia is a common symptom in acute stroke patients, which has severe impact on both functional independence and quality of life. Current guidelines recommend face-to-face speech therapy as early as possible after stroke onset. Speech therapy smart devices are a promising approach to complement face-to-face logopaedics and are suitable for self-training purposes. We hypothesize, that speech therapy assisted by the tablet-based app Neolexon® is superior to standard logopaedics (NCT04080817).
Methods: We aim to enroll 180 adult German native-speaking patients with aphasia due to acute stroke and ≤13 points in the Language Aphasia Screening Test (LAST). Probands are dichotomized into three groups based on their LAST scale and randomly assigned (1:1) to receive either standard speech therapy or standard speech therapy and Neolexon®-therapy. Patients will be visited four times within three months during hospital stay and rehabilitation. Study visits comprise both comprehensive neurological and speech therapy examinations. Primary outcome is defined by a 10% mean difference in the change of percentile rank of the Bielefelder Aphasie Screening (BIAS) after three months. Secondary outcomes include quality of life, scale in Becks Depression Inventory and modified Rankin Scale after three months.
Results: From July 2021 up to now we enrolled n=62 patients, of which n=24 completed their last study visit. We aim to present preliminary results of ongoing analysis.
Conclusion: The Neolexon® application could be a beneficial complementary tool in speech therapy. This trial is suitable to provide evidence for computer-supported speech therapy in acute stroke patients with aphasia.
Disclosure: All authors report no conflicts of interest related to the presented research.

EPO-558

1-year outcome of mechanical thrombectomy in the oldest old

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Background and aims: Little is known about stroke treatment and one-year outcomes in the oldest old stroke population.
Methods: We analysed data from acute ischemic stroke (AIS) patients with large vessel occlusion treated by mechanical thrombectomy (MT) admitted to the Comprehensive Stroke Center at the University Hospital in Krakow, Poland, between 2019 and December 2021. The study was approved by the Ethical Committee. Only the patients who gave written consent were included. We studied 34 parameters readily available within 24 hours after AIS including demographics, stroke risk factors, thrombolytic treatment and several clinical and biochemical parameters. Outcome measure was the modified Rankin score (mRS) at 1-year after stroke. mRS≤2 defined good outcome and mRS=6 - death.
Results: During a study we registered 2,554 AIS patients, 1,788 (70%) patients agreed to participate of whom 593 (33.2%) received MT. IVT proceeded MT in 325 cases (54.8%). 1-year follow-up was available for 564 (95.11%) patients. We identified 16 patients aged ≥90 years. Oldest old patients as compared to others differed in gender distribution (females: 87.5% vs 45.1%, p<0.01) and had significantly more often atrial fibrillation (56.3% vs. 27.9%, p=0.014). 1-year mortality was similar between the studied groups (50% vs 30,1%, p=0.089), however, good outcome was noted less often the oldest old (31.3% vs. 61.7%, p=0.014).
Conclusion: MT in the oldest old as compared to others seems to be similarly effective in terms of 1-year mortality; still, 1/3 of the oldest old remains independent after 1-year follow up.
Disclosure: ERA-NET-NEURON/21/2020 iBioStroke grant

EPO-559

Comparison of characteristics and outcomes between acute ischemic stroke patients with different heart failure

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Background and aims: Acute ischemic stroke (AIS) can be complicated by heart failure involving preserved ejection fraction (HFpEF) or reduced ejection fraction (HFrEF), and whether prognosis differs between the two types of patients is unclear. We compared the clinical characteristics and outcomes of the two types of patients at 3 months after stroke.
Methods: We retrospectively analyzed patients who, between 1 January 2018 and 1 January 2021, experienced AIS that was complicated by HFrEF or HFpEF. All patients had been prospectively registered in the Chengdu Stroke Registry. Poor outcome was defined as a modified Rankin Scale (mRS) score of 2–6 at 3 months. Univariate and binary logistic regression was used to assess whether HFpEF was associated with significantly worse prognosis than HFrEF.
Results: Among the final sample of 108 patients (60.2% men; mean age, 73.08±10.82 years), 75 (69.4%) had HFpEF. Compared to HFrEF patients, those with HFpEF were older (p=0.002), were more likely to have chronic kidney disease (p=0.033) and to experience poor outcome (p=0.022). After adjustments, HFpEF was associated with significantly greater risk of poor outcome than HFrEF (OR 4.05, 95%CI 1.19–15.26, p=0.03). However, rates of hemorrhagic transformation or mortality at 3 months after AIS did not differ significantly between the two types of heart failure (all p>0.05).
Conclusion: Patients with AIS involving HFpEF may experience worse outcomes than those with HFrEF and therefore may require special monitoring and management. Our findings need to be verified in large prospective studies.
Disclosure: The authors declare no conflicts of interest.

EPO-560

Risk factors for osteoporosis in Korean adult stroke over 60 years old survivors

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Background and aims: Many studies examined the relationship between osteoporosis and stroke. However there are little study about risk factors of osteoporosis in stroke patients. We assumed that osteoporosis and stroke are more closely related beyond the previously known risk factors of osteoporosis. Therefore, we investigated the prevalence of osteoporosis among stroke survivors and analyze the risk factors for osteoporosis in an elderly Korean stroke population.
Methods: This study retrieved data contained in the 7th Korea National Health and Nutrition Examination Survey (KNHANES) for a population-based sample of stroke patients. Total 328 patients were included in this study and we compared two group, stroke with osteoporosis and without osteoporosis.
Results: The high prevalence of osteoporosis was observed among women, unemployed, low-educated people, and rheumatic arthritis patients. Contrary to our expectations, the study showed that those with higher average alcohol consumption and smokers had a lower prevalence of osteoporosis. After adjusting for sex and age, the study showed no statistical significance between the prevalence of osteoporosis in relation to education level and employment and smoking status. When adjusting for all variables, there was no statistical significance except for females and patients with rheumatic arthritis and cardiovascular disease.
Conclusion: The risk factor of osteoporosis in stroke patients may differ from that in non-stroke patients. Furthermore, stroke itself can be a more significant risk factor than other factors for osteoporosis. The main contributions of this study are this is the first study to evaluate the risk factors of osteoporosis in stroke patients using KNHANES data.
Disclosure: Nothing to disclose.

Higher cortical functions; Neuroinformatics; Neuro-oncology; Neurotoxicology/occupational neurology; Spinal cord and root disorders

EPO-561

Copper deficiency related myelopathy

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Background and aims: Myelopathy is a frequent reason for acute adult neurology admission and is an important cause of disability. The objective of this case report is to highlight a rare and treatable cause of non-compressive myelopathy. Acquired copper deficiency resembles subacute combined degeneration of the cord due to B12 deficiency and responds to copper replacement.
Methods: We present a case of a patient with progressive myelopathy who subsequently required admission. The biochemical and radiological features of acquired copper deficiency are discussed.
Results: A 74 year female presented to the outpatient clinic in February 2021 with slowly progressive distal sensory loss, poor balance and walking difficulty. Examination revealed a mild spastic quadriparesis with impaired distal sensation, marked proprioceptive loss and sensory ataxia. After 6 months, she was using a wheelchair. A microcytic anaemia with normal ferritin was noted. MRI spine showed a long segment of high T2 intrinsic posterior cord signal from C2-T3, therefore inflammatory and metabolic causes were considered. B12 level, CSF, EEG and nerve conduction studies were normal. An empirical course of intravenous methylprednisolone was given without improvement. Serum copper was low at 3.2 micromol/L (normal 12-26 micromol/L). Her walking improved with intravenous followed by oral copper replacement. She was later found to be using zinc containing denture cream which was stopped.
Conclusion: Serum copper levels should be checked early in the investigation of non-compressive myelopathy. Zinc containing denture cream affects copper absorption and can deplete serum copper levels.
Disclosure: The authors have no disclosures.

EPO-562

In the eye of the neurologist: distinct prognosis profiles in FND inpatients

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Background and aims: Functional neurological disorder is a frequent reason for neurology and psychiatry referrals and clinicians could be challenged by the management and follow-up of the disorder. FND patients represent a heterogenous population, however there has been little research whether there are different patient profiles, especially regarding adherence to the diagnosis and prognosis.
Methods: We developed a subjective, seven item clinician graded prognostic outcome score (POS) combining items relevant to diagnosis adherence and objective potential prognostic. We used latent class analysis with score items as indicators to examine patient profiles in a cohort of consecutive FND inpatients.
Results: Regarding diagnosis adherence and potential prognosis, we found the existence of two distinct FND patient profiles based on the proposed subjectively graded prognostic outcome score. In the neurologist's eye there is one profile of good diagnosis adherence and better potential prognosis and one profile of poor diagnosis adherence and potentially worse prognosis.

Table 1. Population characteristics			
		Count	% of total
Gender	Female	33	71,7%
FND manifestation	PNES	28	62,2%
	Motor or sensitive manifestation	14	31,1%
	Cognitive manifestation	3	6,7%
Neurological comorbidities	None	22	48,9%
	Epilepsy	9	20,0%
	Traumatic brain injury or stroke	3	6,7%
	Epilepsy due to brain damage	5	11,1%
	Headaches	3	6,7%
	Peripheral nervous system pathology	1	2,2%
	Intellectual deficiency	2	4,4%
Psychiatric comorbidities	None	29	64,4%
	Anxiety	7	15,6%
	Depression	6	13,3%
	Anxiety and Depression	3	6,7%
Term used for final diagnosis	No particular term	11	23,9%
	Psychogenic	27	58,7%
	Somatoform	3	6,5%
	Functional	5	10,9%
FND related ER visits in the previous year	No	40	88,9%
FND related hospitalizations in the previous year	No	43	95,6%

Table 1. Population characterics

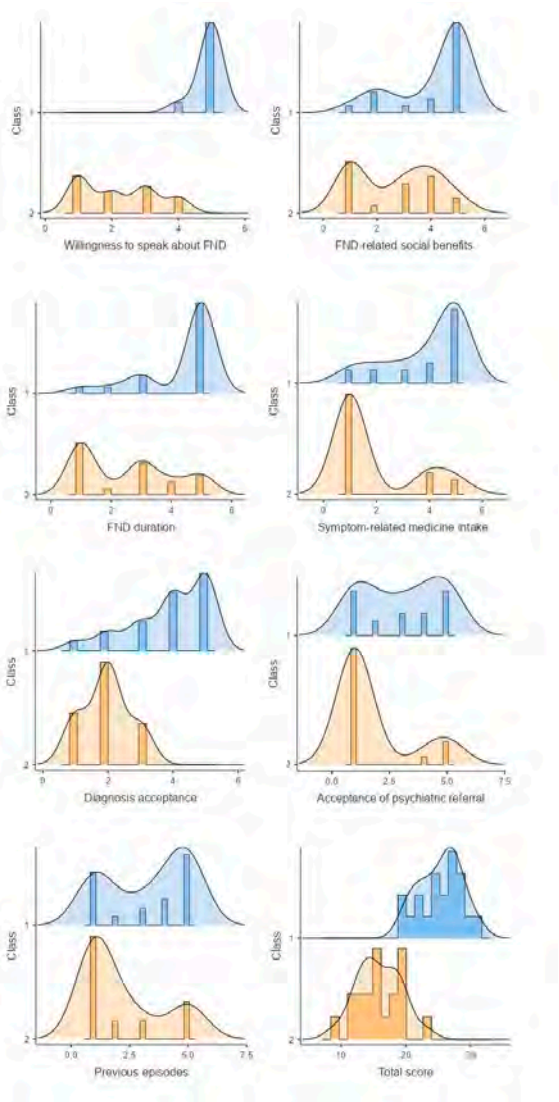

Figure 1. Histograms of LCA Indicators and total score between-class distribution

Conclusion: The POS score is a promising tool for the estimation of FND prognosis. Future research is needed to correlate patient profiles to the outcome and confirm the validity of the POS score in a larger, prospective cohort.
Disclosure: Nothing to disclose.

EPO-563

Vismodegib in Neoplastic Meningitis from Sonic Hedgehog (SHH)-Activated Medulloblastomas: a Case Report.

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Background and aims: Vismodegib is a SHH-inhibitor that proved to be effective in locally-recurrent SHH-activated medulloblastoma. However, whether vismodegib is effective in case of neoplastic meningitis (NM) as well has not been assessed so far. Here, we present a case of a patient with NM from SHH-activated medulloblastoma who showed a dramatic response to vismodegib.
Methods: (not applicable)
Results: A 34-year-old patient was diagnosed with a SHH-activated cerebellar medulloblastoma in 2015. He underwent gross-total resection, cranio-spinal radiotherapy (RT) and 5 cycles of lomustine, vincristine and cisplatin. Then, he remained disease-free until October 2021, when the MRI showed a new single contrast-enhanced nodule in the spine (T10), which was treated with stereotactic RT. However, the following MRI showed a diffuse leptomeningeal involvement, with new multiple linear and nodular lesions. The CSF cytology confirmed the presence of neoplastic cells. Therefore, in April 2022 vismodegib (150 mg daily) was started. The treatment was well tolerated, except for increased creatine phosphokinase (CTCAE v3.0 grade 1). After only 2 months of therapy, a reduction of the meningeal enhancement was seen on MRI, and after 4 months all nodular and linear lesions disappeared. Similarly, CSF cytology became negative after 4 months of treatment. Treatment is still ongoing, with an enduring response on MRI.
Conclusion: To our knowledge, this is the first report of an adult patient with NM from SHH-activated medulloblastoma achieving a complete response with vismodegib. Data from larger series are needed to confirm the effectiveness and safety of vismodegib in case of leptomeningeal spread.
Disclosure: I have no disclosures.

EPO-564

Posterior reversible encephalopathy syndrome in a COVID vaccine associated Guillain-Barré syndrome.

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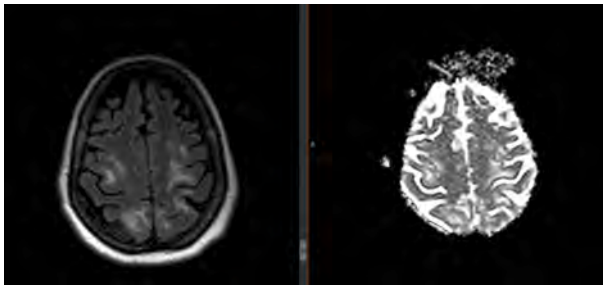
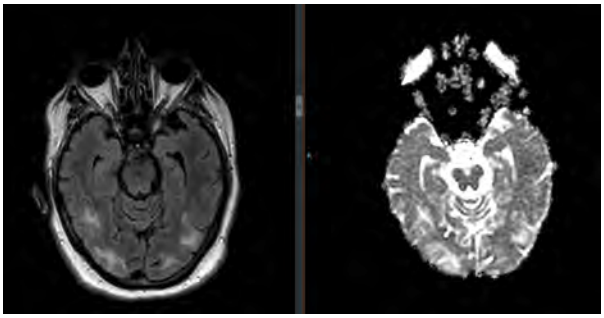
Background and aims: Posterior reversible encephalopathy syndrome (PRES) and Guillain-Barré syndrome (GBS) are two uncommon neurologic entities in the general population, and their overlap, although rare, has been reported. Most authors theorize that the dysautonomia observed in GBS patients might trigger blood pressure changes causing PRES, however forms and time of presentation vary amongst cases, blurring this linear causality.
Methods: We present a novel case admitted in our hospital and review the existing literature.
Results: We describe the case of a 67-year-old woman that three weeks after receiving the first dose of a viral vector COVID-19 vaccine presented with distal paraesthesia in all four limbs, dizziness, instability and altered gait. Six days before admission she experienced sharp back pain and had noticed high blood pressure in her residence. Initial neurological exam showed severe distal weakness, global hyporeflexia, sensory loss in glove and stocking pattern and autonomous gait was impossible. Additionally, our patient presented an altered mental status with tendency towards somnolence that fluctuated during her hospital stay and later developed visual hallucinations. GBS diagnosis was confirmed by CFS and neurophysiological tests. MRI showed symmetric subcortical vasogenic oedema in occipital, parietal, and frontal lobes, that suggested a concomitant PRES. During hospitalization she received intravenous immunoglobulins and physical therapy with partial motor improvement.



Parietal and frontal subcortical oedema suggestive of PRES; FLAIR and aADC sequences.



Occipital subcortical oedema suggestive of PRES; FLAIR and aADC sequences.

Conclusion: Although the physio-pathological base of the co-occurrence of these two neurologic syndromes still requires further analysis, our case adds to the existing evidence of the association between them and the need to consider PRES in GBS cases with atypical neurological manifestations.
Disclosure: None of the authors present any conflict of interest in this case.

EPO-565

Predicting brain metabolism in elderly patients with cognitive impairment using deep learning

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Background and aims: Image-to-image translation algorithms can generate highly precise synthetic images from real images. Usage of such methodology to predict brain development is currently uncharted territory. Regional decline in brain metabolism can aid in the differential diagnosei of neurodegenerative diseases. As such, FDG-PET, quantifying brain metabolism, presents a promising target for a proof-of-principle study of medical imaging time series prediction. Here, we aim to predict future FDG-PET scans from FDG-PET data acquired in year zero and year one using a convolutional neural network (CNN).
Methods: We identified elderly (≥55 years) participants from the Alzheimer's Disease Neuroimaging Initiative who received FDG-PET scans in three consecutive years. A CNN was implemented and trained on scans from year zero and year one to generate a prediction for the scan of the second year. The performance of the CNN was evaluated on a holdout sample using mean absolute error (MAE) and structural similarity (SSIM).
Results: Preliminary results suggest that second-year scans can be predicted with low reconstruction error (small MAE, high SSIM) when using data from individuals with high

likelihood of neurodegeneration-associated changes on FDG-PET, i.e., individuals with pending conversion to, or an existing diagnosis of Alzheimer's disease.
Conclusion: We report that future FDG-PET scans can potentially be predicted from existing FDG-PET data. If successful on a larger scale, our model may be relevant for data augmentation in scientific longitudinal studies, as well as provide insights into the development of brain metabolism in relation to neurodegenerative diseases.
Disclosure: Nothing to disclose.

EPO-566

Clinical-MRI Dissociation in Spinal Cord Sarcoidosis: A Case Report.

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Background and aims: The diagnosis of spinal cord sarcoidosis can be particularly challenging when not accompanied by clinically overt systemic involvement. Herein we describe a rare case of longitudinally extensive spinal cord sarcoidosis incidentally disclosed during the diagnostic work-up for intermittent diplopia.
Methods: The clinical presentation and diagnostic approach leading to the diagnosis of spinal cord sarcoidosis are presented.
Results: A 53-year-old man presented after one month of intermittent diplopia that resolved spontaneously. Neurological examination revealed diffuse hyperreflexia, bilateral Trömner sign, diplopia evocable after fatigability on the left gaze. Brain MRI revealed some abnormalities in the upper cervical spinal cord. Spinal cord MRI disclosed a longitudinally extensive T2-hyperintense lesion from C1 to D1, with patchy gadolinium enhancement. Negative testing for aquaporin-4 and myelin oligodendrocyte glycoprotein antibodies by cell-based assay (fixed and live, respectively). Lumbar puncture showed mild pleocytosis (12 white blood cells/mm^3), elevated proteins (70mg/dL; normal range, <40mg/dL). Chest CT revealed mediastinal lymphadenopathy, with associated intense FDG uptake on positron emission tomography. Transbronchial needle aspiration of a lymph node revealed non-caseating granulomatous inflammation, consistent with probable neuro-sarcoidosis. The patient was followed untreated for 3 months with stability of the spinal cord lesion on MRI. After he developed numbness in both hands and Lhermitte's phenomenon. Intravenous methylprednisolone was administered followed by slow tapering of oral, with prompt resolution of symptoms and marked improvement of the spinal cord abnormalities.

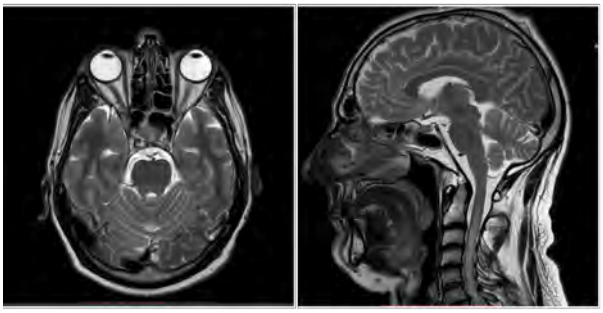


Figure 1. Axial (A) and sagittal (B) T2-weighted images of the brain did not show brain abnormalities, but reveal an extensive cervical spinal cord lesion.

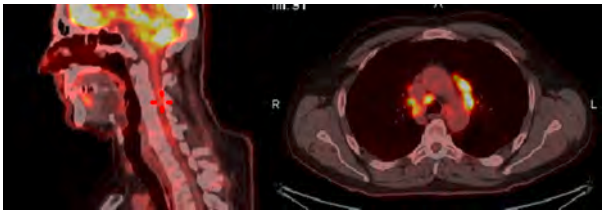
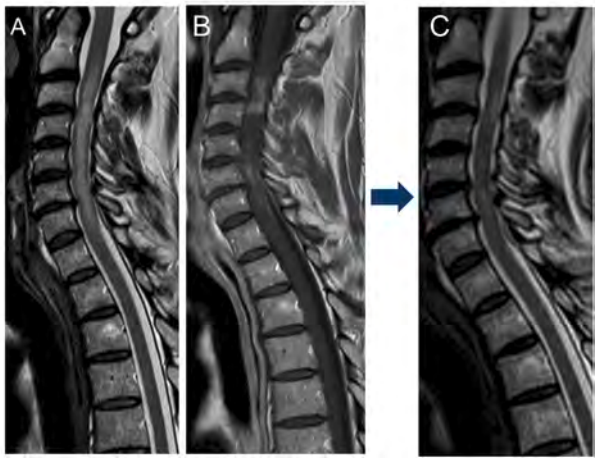


Figure 2. 18F-FDG PET/CT demonstrated hypermetabolic activity of the cervical spinal cord lesion (A), and mediastinal lymphnodes (B).

Conclusion: A marked clinical-MRI dissociation (i.e., extensive MRI abnormalities accompanied by only mild clinical manifestations) is a big clue for diagnosis.



On admission, a longitudinally extensive T2-hyperintense lesion (A), associated with patchy gadolinium enhancement (B). The spinal cord lesion resolved nearly completely after treatment with corticosteroids (C).

Disclosure: All authors had no disclosures.

EPO-567

Default mode network activity during attention switching in intracranial EEG

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Background and aims: The Default Mode Network (DMN) is one of the intrinsic brain networks playing a crucial role in many cognitive functions. First discovered as a resting state network, DMN was later shown to be activated not only during mind wandering but also in tasks requiring internally oriented attention. On the contrary, DMN is deactivated during external attention demanding tasks, thus its activity is often anti-correlated with other brain networks, such as Dorsal Attention Network (DAN). However, the neuronal mechanisms of DMN/DAN switching remain unclear.
Methods: We investigated the interplay between DMN and DAN during an attention switching task using intracranial EEG (iEEG) recorded in a large cohort of 25 epilepsy patients. The iEEG is a useful tool to study brain network dynamics, as it reflects the local neuronal activity in the vicinity of the intracerebral electrodes with millisecond precision.
Results: We found a robust representation of the attention switching in the alpha power (8–12 Hz) of the iEEG. In particular, the alpha power of DMN was strongly attenuated in the internal attention task and increased during the task requiring external attention, while the DAN showed exactly the opposite pattern of activations.
Conclusion: Given that the alpha power is often referred to as the idling rhythm, our results are thus in line with generally accepted concept of DMN/DAN dynamics. Uncovering the detailed neuronal mechanisms of attention switching may also have profound implications for various neurological and psychiatric diseases in which the network dynamics are compromised.
Disclosure: This research was supported by GACR grant 20-21339S and GAUK grant 272221

EPO-568

Scwannomas: Neuro-glial Interaction and Molecular Therapy

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Background and aims: Neurofibromatosis is a disease from the group of phakomatoses. This term unites group of three diseases: neurofibromatosis type I (NF1), neurofibromatosis type II (NF2), schwannomatosis, neurofibromas, and scoliosis. Schwannoma is a tumor that arises from the Schwann cells of the nerve sheath. It can be either malignant or benign. This type of oncology is diagnosed infrequently, in about 7% of cases of all soft tissue sarcomas. It is observed mainly in middle-aged people, more often in males. So far, there have been only surgical methods for removing these tumors. The aim of our work was to analyze the possibilities of treatment using molecular genetic methods for the treatment of schwannomas in animal genetic models.
Methods: Knock-out mice were obtained by disruption of Nf1 gene. Organ and tissues genesis were dependent of neurofibromin encoded by this gene. Glial fibrillar acid protein (GFAP) as marker of glial cells metabolite and neuron-specific enolase (NSE) as neuronal functions protein were evaluated.
Results: After development of shwannomas on mice legs we used adeno-associated serotype 1 virus (AAV1)-based vector delivering N-terminal of the TRK-fused gene. In result of 7 passages of virus vector delivering to experimental mice the sizes of 4 schwannomas were considerably reduced. After course of molecular treatment activity of GFAP and NSE was markedly decreased.
Conclusion: Mouse model of Neurofibromatosis I and II and schwannomatosis seems to be a good target for molecular therapeutic approaches.
Disclosure: Nothing to disclose.

EPO-569

Outcomes of tailored psychotherapy for dissociative seizures in a developing functional neurology service

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Background and aims: Dissociative seizures (DS) can cause distress and disability comparable to that caused by epileptic seizures. There is growing evidence to suggest psychological therapy can be effective in treating DS, although the treatment approaches are varied.
Methods: We analysed outcomes from a functional neurological disorders service in the North West of England offering short term psychotherapy to consecutive eligible patients with a diagnosis of DS. Patients were assessed for clinical and psychological variables before and after psychotherapy using the GAD-7 screening score for generalised anxiety disorder, the Work and Social Adjustment Scale (WSAS) to assess functional status, the PHQ-15 somatic symptoms scale, PHQ-9 depression score and PCLC PTSD symptom score.
Results: 86 patients (67 female) were referred for psychotherapy with a clinical diagnosis of DS. The mean number of therapy sessions was 5.94 (95% CI 5.04 to 6.84). Patients had significant improvements in GAD-7 sumscores ($Z=-2.549$, $p=0.011$), PHQ-15 ($p=0.028$), PHQ-9 ($Z=-3.202$, $p<0.001$) as well as PCLC PTSD symptom scores ($Z=-2.288$, $p=0.022$), comparing pre and post treatment values. Whilst there was a reduction in the median WSAS scores comparing pre and post treatment values (30 to 22.5), this difference was not significant ($Z=-1.932$, $p=0.053$). DS frequency improved in 67.4% of patients (95% CI 52.0% to 80.5%).
Conclusion: Although this is an observational study, findings support the notion that tailored psychotherapy is a clinically effective intervention to improve psychological status, quality of life and dissociative seizure frequency in a real-world clinical setting.
Disclosure: Nothing to disclose.

EPO-570

Manganism: a toxidrome to be remembered

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Background and aims: Manganese (Mn) is an abundant element in nature, but its neurotoxicity (manganism) is uncommon. It usually occurs after occupational or iatrogenic exposures to Mn. Manganism produces an extrapyramidal case that resembles Parkinson's disease due to a special tropism for the basal ganglia, with a typical brain magnetic resonance image (MRI): hypersignal on T1 sequence of both globus pallidus.
Methods: Description of a manganism's case.
Results: A 55 year old male was admitted with acute onset parkinsonism. Brain MRI showed basal ganglia ischemia and T1 hyperintensity of both globus pallidus, suggestive of Mn deposit. Accidental exposure to insecticide products containing Mn in a domestic greenhouse was verified, thus establishing the diagnosis of manganism. Parkinsonism was resolved within a few weeks, and later the patient developed an apathetic-abulic syndrome secondary to basal ganglia ischemia, showing a steady improvement after treatment with neuropsychological stimulation, fluoxetine and homotaurine.
Conclusion: We present a clinical case of manganism, epidemiologically atypical and showing infrequent and complex semiology. Manganism should always be considered in the differential diagnosis of a patient with acute parkinsonism, looking for a possible exposure to the toxin and having a high level of clinical suspicion. The most recent evidence suggests that Mn could have a molecular and neuropathological tropism on the basal ganglia and perhaps be related to the onset and development of Parkinson's disease.
Disclosure: Authors have no conflicts of interest to declare.

EPO-571

Spinal Arteriovenous Fistula (sAVF): An underrecognized cause of Longitudinally Extensive Transverse Myelitis (LETM)

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Background and aims: LETM causes acute paraparesis or paraplegia with a broad differential, including mainly inflammatory diseases. SAVF is a rare and potentially treatable cause of LETM, with devastating consequences if left untreated.
Methods: We present a case of LETM due to sAVF, along with a systematic review of the literature. We searched MEDLINE for LETM and sAVF cases, identifying 752 and 671 articles, respectively. Finally, 106 articles for LETM and 20 articles for sAVF were included.
Results: A 57-year-old previously healthy man, presented with subacute flaccid paraparesis, hypoesthesia below knees and urinary retention. Spine MRI revealed LETM from the 7th to the 12th thoracic vertebra, with concomitant dilated perimedullary vessels and T2 flow-voids. DSA depicted a sAVF at 3rd Lumbar artery level, which was subsequently embolized with excellent clinical response. In our review, we found 246 LETM cases (Mean age: 40 years, 129 Women-52%). The most common causes were NMOSD (32%), Infections (30%) and systematic Autoimmune diseases (13%). Only 3% of LETM cases were attributed to sAVF. Then, we searched for cases with sAVF, identifying 842 patients (Mean age: 58 years, 677 Men-80%). The most common clinical findings were sensory-71%, motor-60% and sphincter disturbances-31%. Myelopathy on MRI was found in 70% of patients. Surgery was the treatment of choice in 76%, while clinical improvement was established in 1/3 of the patients.
Conclusion: The diagnosis of sAVF is challenging and thus a high clinical and radiological suspicion is needed, especially among middle-aged men with LETM. Early diagnosis and minimally invasive intravascular interventions guarantee a favourable prognosis.
Disclosure: Nothing to disclose.

EPO-572

Mes-CoBraD: an open-source research platform for integrated data collection and analysis

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Background and aims: Complex brain disorders (CoBraD), as represented in Epilepsy, Neurocognitive and Sleep disorders, have high prevalence, individually and in combination, leading to disability and high socioeconomic burden. The "Multidisciplinary Expert System for the Assessment & Management of Complex Brain Disorders (MES-CoBraD)" is an international interdisciplinary project combining Real-World Data and developing a platform providing a comprehensive toolset with advanced functionalities for research and diagnosis. The main goal is to streamline and simplify the workflows of gathering, sharing and processing data, using existing mature tools, and organizing them in a common environment.
Methods: Nine Work Groups (WG) in four categories (Complex Brain Disorders, Real-World Data, Science of Science, and Socioeconomics) are working in tandem to ensure interoperability between clinical and technical requirements of the project.
Results: We structured a pilot data collection protocol including clinical history, neuroimaging, neurophysiology, neuropsychology and biomarkers (blood and hair). The platform supports data sharing by creation, sanitisation, anonymisation, harmonisation and upload of datasets on a common data-lake environment. Several open-source and tailormade tools are included, designed to address advanced research needs. The platform integrates several general statistics functions and machine learning algorithms, based on the acquired data, and used in a workflow management system, forming an expert system to support research and diagnostic processes.
Conclusion: The MES-CoBraD platform provides tools for harmonized data collection and analysis through a single unified environment. Users without significant technical experience or available computational resources will be able to share, review and analyze their data in a unified ecosystem.
Disclosure: Multidisciplinary Expert System for the Assessment and Management of Complex Brain Disorders (MES-CoBraD), is funded with a European Union's Horizon 2020 grant; ID: 965422

EPO-573

Tricky Feeding Artery in a Patient with Progressive Gait Disorder

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Background and aims: Dural arteriovenous fistulas (DAVF) are the most common type of vascular malformation of the spinal cord and may cause myelopathy through venous hypertension. The clinical evolution is slowly progressive and the diagnosis can be inferred from the Magnetic Resonance Imaging (MRI) appearance. The aim of our report is to present the case of a patient with progressive gait disorder in which DAVF was suspected.
Methods: A 62 years old patient, known with a history of back injury five years prior, was admitted for gait disorder and bilateral asymmetric lower limb weakness and paresthesia with onset in the past two years and slow progression. Spinal MRI revealed T2 bright signal enlargement of the spinal cord at the level of T9–T12 vertebrae and conus medullaris with para-medullary flow voids suggestive of venous hypertensive myelopathy. Thus, a spinal DAVF was suspected. An MR angiography of the spinal cord showed enlarged serpiginous peri-medullary vessels, as well as one enlarged vessel around left L5 nerve root. Digital subtraction angiography with selective catheterization of the internal iliac arteries was performed showing DAVF at L5-S2 level with arterial feeder originating in the right iliolumbar artery.
Results: Super-selective microcatheterization permitted endovascular occlusion of the supplying artery through injection of embolic material. Upon discharge seven days later there was marked improvement of the symptoms.
Conclusion: The feeding artery of a DAFS can be elusive and MR angiography can guide the endovascular management of such vascular malformations, which may require injection of arteries as far as internal iliac branches.
Disclosure: I make no disclosures.

Headache 4

EPO-574

Microvascular involvement in migraine: an optical coherence tomography angiography study

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Background and aims: The aim of this study was to evaluate the microvasculature of the macula and the optic nerve by optical coherence tomography angiography (OCTA) in patients affected by migraine with aura (MA) and without aura (MO), compared to healthy controls (HC).
Methods: We collected data from ocular and orthotic examinations, including eye motility, intraocular pressure, best-corrected visual acuity, objective refraction, fundus examination, macular and optic disk OCTA examination. The following OCTA parameters were recorded: macular, inside disc, peripapillary, disc whole image, fovea choriocapillaris, fovea, parafovea vessel densities (VD); peripapillary, fovea, parafovea and macular full retinal thickness, and foveal avascular zone (FAZ) parameters. Clinical and demographical data were collected.
Results: We included 56 eyes from 28 patients with a diagnosis of MO, 32 eyes from 16 patients with a diagnosis of MA, and 32 eyes from 16 HC. The FAZ area was 0.230 ±0.099 mm^2 in the MO group, 0.248±0.091 mm^2 in the MA group and 0.184±0.061 mm^2 in the control group. The FAZ area was significantly larger in the MA group than in the HC group (p=0.007). The foveal choriocapillaris VD was significantly lower in MA patients (63.6±2.49%) when compared with MO patients (65.27±3.29%) (p=0.02).

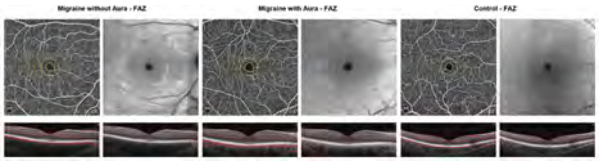

Figure 1: Representative macular optical coherence tomography angiography (OCTA) scans of migraine with aura (MA), without aura (MO), and healthy controls (HC) participants. The foveal avascular zone (FAZ) area is circled in yellow. The mean FAZ area was

Figure 2: Representative macular optical coherence tomography angiography (OCTA) scans of migraine with aura (MA), without aura (MO), and healthy controls (HC) participants. The foveal choriocapillaris vessel density (VD) decreased in MA patients.

Conclusion: An impairment of retinal microcirculation can be detected in patients with MA, as demonstrated by the enlargement of FAZ. The study of choroid circulation may reveal microvascular damage in MA patients. OCTA is a useful non-invasive screening tool for the detection of microcirculatory disturbance in patients with migraine.
Disclosure: Nothing to disclose.

EPO-575

Neuralgias of trigeminal terminal branches in a headache unit

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Background and aims: International Classification of Headache Disorders, III Edition (ICHD-III) did not include neuralgias of trigeminal terminal branches previously considered in ICHD-II: nasociliary, supraorbital or other terminal branch neuralgias. We aim to analyse incidence and characteristics of these disorders in a headache registry.
Methods: Prospective observational study evaluating patients diagnosed as nasociliary neuralgia (code 13.5 in ICHD-2), supraorbital neuralgia (13.6) or other terminal branch neuralgias (13.7) attended in a headache unit from January-2008 to January-2023. We collected demographic and clinical data.
Results: We included 108 patients (71 females, 37 males) out of 8,728 attended in our unit during the inclusion period (1.2%). Age at onset was 47.4±18.7 years (6–89). Latency between onset and diagnosis was 34.4±68.5 months (1–420). Among the entities independently considered in ICHD-2, we diagnosed 5 nasociliary and 43 supraorbital neuralgias. Among those included among other terminal branches, most frequent neuralgia was auriculotemporal (28 cases). We also identified patients with supratrochlear (9 cases), infraorbital (8), lacrimal (8), mental (6), and infratrochlear (1) neuralgias.
Conclusion: Neuralgias of trigeminal terminal branches are not uncommon in a headache unit. Diagnostic delay observed in our series indicates a need for increasing their understanding, which, in our opinion, has not been facilitated by having been withdrawn from ICHD-3. We suggest that supraorbital and auriculotemporal neuralgias are considered independently in next editions of ICHD and that the entity "neuralgia of other terminal branches" is reintroduced.
Disclosure: No potential disclosures related to this work.

EPO-576

Head-to-head study on efficacy and safety of Monoclonal Antibodies Against Calcitonin Gene-Related Peptide for Migraine

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Background and aims: Monoclonal antibodies targeting the CGRP pathway (mAbs) have shown effectiveness, safety and tolerability in clinical trials both episodic and chronic migraine. However, there are no prospective real-world studies intending to compare their efficacy and safety. Aim of the study is to compare the effectiveness and safety of Galcanezumab, Fremanezumab and Erenumab for the treatment of chronic and episodic migraine, through real world data.

Methods: This is a prospective observational study comparing the effective and safety of Galcanezumab, Fremanezumab and Erenumab for the treatment of 140 chronic and episodic migraine patients. Framenezumab, Erenumab or Galcanezumab were administered for 12 months. The mean monthly days with headache, MIDAS score, and adverse events were evaluated during the run-in period and every three months by reviewing standardized paper patient headache diaries.

Results: We found a mean reduction of migraine monthly days from baseline of -12.152 (-9.821,-14.482) in the Galcanezumab group, -13.021 (-10.806,-15.237) in the Fremanezumab group, -11.784 (-9.440,14.127) in the Erenumab group (for all p<0.001). We found a mean reduction of MIDAS score of -33,273 (-26,857,- 39,689) in the Galcanezumab group, -36,542 (-30,563,- 42,520) in the Fremanezumab group, -31,946 (-25,631, 38,261) in the Erenumab group (for all p<0.001). We found no significant differences between mAbs in the reduction of mean monthly days with headache, and MIDAS score.

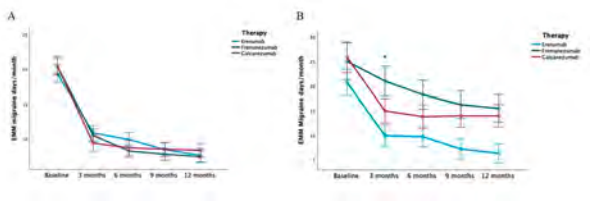

Figure 1 Monthly migraine days in Erenumab, Fremanezumab and Galcanezumab patients (A) and in Medication Overuse Headache patients (B)

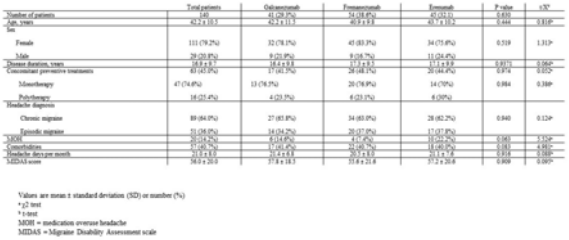

Table 1 Baseline demographic and clinical characteristics

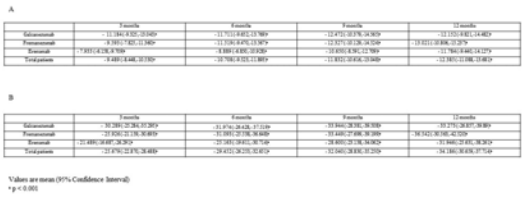

Table 2 Monthly migraine days and MIDAS score reduction compared to baseline

Conclusion: Our results confirm the therapeutic benefits of anti-CGRP mAbs. There is no evidence that suggests that one antibody may be superior to the others in terms of effectiveness, both in chronic and episodic patients.

Disclosure: Cinzia Valeria Russo received personal compensation from Sanofi Genzyme and Merck Serono.

EPO-577

Anti-Calcitonin Gene-Related Peptide Monoclonal Antibodies for the Treatment of Vestibular Migraine.

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Background and aims: Vestibular Migraine (VM) is considered the most common cause of recurrent vertigo for which specific treatments are missing. Monoclonal antibodies against CGRP, are effective in preventing migraine. Since CGRP is also detected in human cochlear and vestibular organs it may also play a role in vestibular physiology.

Methods: This is a prospective observational cohort study, aiming at evaluating the efficacy of Erenumab, Framenezumab or Galcanezumab for the treatment of fifty VM patients. We assessed mean monthly days with headache and dizziness/vestibular symptoms, pain intensity and migraine-related clinical burden occurring for 18 months.

Results: Response to treatment was excellent as 90% of patients had at least a 50% reduction in vertigo frequency, 86% had at least a 50% reduction in headache frequency, and 80% a MIDAS reduction of at least 50%. Overall, 78% of patients had a concomitant reduction of all three parameters. Mean monthly days with dizziness/vestibular symptoms showed an overall significant decrease from a mean of 10.3 at baseline to 0.8 days (CI 95% 0.1, 1.5; $p<0.001$) after twelve months ($F=27.588$; $p<0.001$).

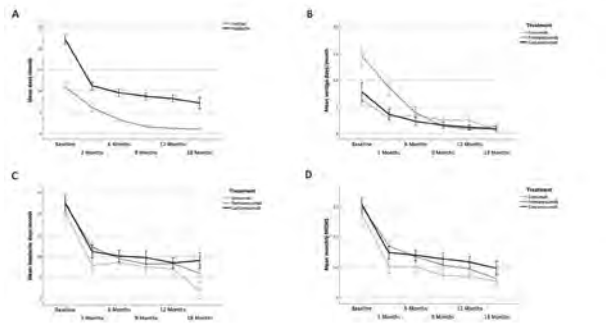

Figure 1 Mean monthly days with vestibular symptoms and headache (A) and differences in vertigo (B), headache (C) and MIDAS (D) in three different anti CGRP Mab

Patients	N = 50
Age	45.0 ± 13.3
Gender	
Female	39 (78.0)
Male	11 (22.0)
Disease duration, years	18.7± 10.9
Concomitant oral preventive treatments	18 (36.0)
Monotherapy	13 (72.0)
Polytherapy	5 (28.0)
Pervious preventive classes failure	2.3 ± 0.8
Vertigo (days per month)	10.3 ± 9.2
Headache (days per month)	20.9 ± 7.3
MIDAS	52.8 ± 19.9

Values are mean ± standard error (SE) or number (%)
MIDAS migraine disability assessment scale

Table 1 Demographic and baseline headache characteristics of patients

Conclusion: We show that anti-CGRP mAbs may be effective in the treatment of Vestibular Migraine. Their use should be encouraged early in the disease course to allow for a better symptom control and quality of life improvement.

Disclosure: Cinzia Valeria Russo received personal compensation from Sanofi Genzyme and Merck Serono.

EPO-578

Chasing the smoking gun without success – no evidence of cortical spreading depression in migraine without aura

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Background and aims: There is uncertainty about whether the cortical spreading depolarization (CSD) causes the migraine headache. The susceptibility weighted imaging (SWI) is the part of magnetic resonance imaging (MRI) protocol that depicts the cerebral veins and likely reflects the CSD. The aim was to assess the frequency of SWI changes in migraine without aura and compare it to migraine with aura and controls.
Methods: 300 patients were included when they (i) presented with an acute neurological deficit or headache, (ii) had a brain MRI, and (iii) had a discharge diagnosis of migraine aura, migraine without aura or controls (n=100 per group).
Results: In the migraine with aura group, SWI asymmetry was found in 26% (95%CI 18–35), significantly more than in patients with migraine without aura (3%, 95%CI 1–8, p<0.001). There was no difference between patients with migraine without aura and controls (7% (95%CI 3–14), p=0.19). After adjusting for age, sex, arterial hypertension and hyperlipidemia, the SWI asymmetry was still significantly more frequent in migraine with aura compared to pooled migraine without aura and controls (adjustedOR 6, 95%CI 1.98–19, p=0.001).
Conclusion: Our findings argue against the notion of CSD as part of the pathophysiology of migraine without aura.
Disclosure: No relevant disclosures to the abstract.

EPO-579

Weather impact on migraine: an Emergency Department retrospective study

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Background and aims: Migraine is a relapsing, remittent pleomorphic disorder characterized by recurrent attacks that may be triggered or precipitated by several factors. About half of migraineurs identified weather conditions changes as a trigger for the headache onset, or as a cause of worsening of ongoing headache symptoms. Aim of the present study was to assess the influence of some meteorological parameters on migraine attacks.
Methods: We retrospectively evaluated the clinical data of all patients with headache who presented to the Emergency Room (ER) of Policlinico Gemelli from 20th March 2010 to 20th March 2012. Primary and secondary headaches were classified according to the International Headache Society (IHS) criteria. Weather data were obtained from the Italian National Weather Service, analyzed, and correlated with clinical data, using Spearman's correlation coefficients.
Results: During the 24 months period, 1,615 patients with migraine without aura and 127 with migraine with aura were admitted to the ER. Number of emergency admissions were directly correlated with the increase of temperature compared to the previous day and the humidity level two days before the attack, and inversely correlated with the atmospheric pressure two days before.
Conclusion: Our data confirm that a subgroup of migraineurs is highly sensitive to variations of meteorological factors. We could hypothesize that any variation of weather parameters may interfere with neuronal excitability of the trigeminal-vascular system directly, or with structures to it correlated, facilitating the onset of attacks. Alternatively, it could be possible that quantitative variations of trigger factors may enhance the response of migraineurs to environmental stimuli.
Disclosure: The authors report no disclosures relevant to the manuscript.

EPO-580

Headache location and response to greater occipital nerve block – is posterior location required? A real-world study

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Background and aims: Selection criteria for greater occipital nerve block (GONB) for migraine are unclear. The present study aims to report the relationship between headache location and efficacy of GONB.
Methods: We included consecutive migraine patients treated according to clinical indication with GONB in the Headache Center of Avezzano-L'Aquila. Patients received bilateral local injections of methylprednisolone 40 mg/lidocaine 10 mg. We reported the median decrease in monthly migraine days (MMDs) and headache intensity (HI) (ranging 0–10) during the month following the first-ever GONB compared with the previous month. We performed chi-squared or Wilcoxon-Mann-Whitney tests to assess outcomes according to migraine pain location.
Results: We included 52 patients (84.6% female). Pain location was anterior (frontal/temporal) in 32 patients (61.5%), posterior (parietal/occipital) in 9 (17.3%) and diffuse in 11 (21.2%). Overall, median MMDs decreased from 20 (95% CI, 10–30) to 9 (IQR 6–20; p=0.006) while median HI decreased from 8 (IQR 7–9) to 6 (IQR 5–8; p<0.001). MMD decrease was not different in patients with anterior location (-5 median days, IQR -14 to -0.5) than in those with posterior (-2; IQR -5 to 0) or diffuse location (0 median days, IQR -1.5 to +1; p=0.164). Median HI decrease was -1.5 (IQR -3 to 0) in patients with anterior, -1 (IQR -3 to 0) in those with posterior, and -2 (IQR -3 to -1.5) in those with diffuse location (p=0.737).
Conclusion: According to our data from a limited population, the decrease in MMD and in HI after GONB is independent from pain location.
Disclosure: No disclosure to declare.

EPO-581

Infodemiology of cluster headache seasonality: A proof of concept by a Google Trends analysis

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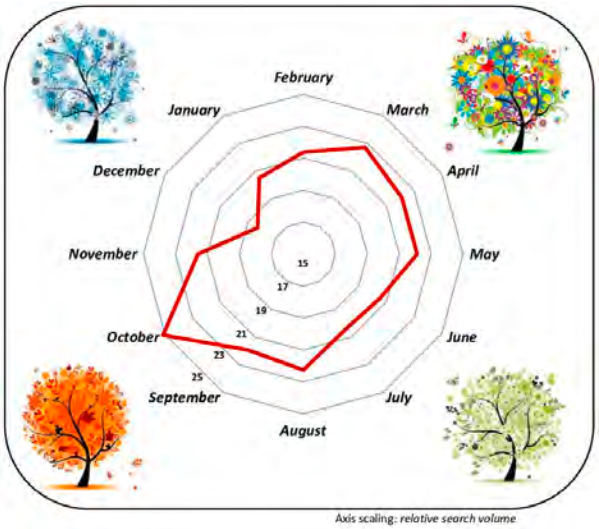
Background and aims: Cluster headache is commonly reported to follow an annual pattern with a peak in the spring and a second peak in autumn. Patients with headache frequently use search engines, such as Google, to look for terms related to their disease, creating trend data that can be analyzed with Google Trends. Indeed, Google Trends has been used for surveillance studies and can provide indirect estimates of the burden of diseases and symptoms. The present cross-sectional study investigated the seasonality of searches for "cluster headache" in the northern and southern hemispheres using 10 years of Google Trends data.
Methods: The term "cluster headache" or its translation in the 10 most spoken languages in the world was searched on Google Trends to obtain relative search volumes, in order to compare variations in searches across periods. Twentyeight countries were selected according to the following criteria: (1) a relative search volume of >40 for the term for cluster headache; and (2) a population of at least 5 million inhabitants. For statistical purposes, countries were grouped in relation to hemisphere. Relative search volumes were extracted from January 2012 to January 2022 and analyzed according to two subgroups based on meteorological seasons.
Results: A seasonal trend for in searches for cluster headache was found worldwide exhibiting higher relative search volumes in spring and autumn compared with summer and winter.



Radar chart showing the seasonality of Google Trends search volumes for the term "cluster headache," with two peaks in spring and autumn.

Term	Country	Search volume	Inhabitants
Cluster headache	United Kingdom	76	68.7 million
Cluster headache	South Africa*	69	61.0 million
Cluster headache	Australia*	68	25.8 million
Cluster headache	Philippines	62	112.9 million
Cluster headache	Nepal	61	29.9 million
Cluster headache	Canada	57	38.5 million
Cluster headache	United Arab Emirates	56	9.3 million
Cluster headache	New Zealand*	53	5.1 million
Cluster headache	Pakistan	47	230.9 million
Cluster headache	Jordan	46	10.8 million
Cluster headache	Singapore	40	5.6 million
Cluster headache	United States	40	335.4 million
Cefalea en racimos	Cuba	100	11.2 million
Cefalea en racimos	Costa Rica	59	5.1 million
Cefalea en racimos	Spain	51	46.8 million
Cefalea en racimos	Mexico	45	132.4 million
الصداع العنقودي	Saudi Arabia	100	35.8 million
Cefaleia em salvas	Brazil*	100	216.0 million
Cefaleia em salvas	Portugal	92	10.3 million
Sakit kepala cluster	Indonesia*	100	280.2 million
Sakit kepala cluster	Malaysia	52	33.3 million
Algie vasculaire de la face	France	64	65.6 million
Céphalée de Horton	Canada	100	38.5 million
Céphalée de Horton	France	87	65.6 million
Céphalée de Horton	Belgium	87	11.5 million
群発頭痛	Japan	100	125.6 million
Кластерные головные боли	Russia	100	146.0 million
Кластерные головные боли	Kazakhstan	60	19.7 million
Cluster-Kopfschmerz	Germany	100	84.3 million

Relative search volumes for the term "cluster headache" for each selected language, extracted from January 2012 to January 2022.

Conclusion: Higher search volumes for the term during the meteorological seasons of spring and autumn clearly reflect a circannual pattern of cluster headache occurrence, representing new evidence for its seasonality.
Disclosure: I have no disclosure.

EPO-582

Fremanezumab adherence & persistence along with past & concomitant migraine medication use: PEARL 3rd interim analysis

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Background and aims: Suboptimal adherence to oral migraine preventive treatments is common. Consequences include patients cycling across various preventive treatments and reduced treatment effectiveness. This analysis provides real-world data on patient adherence to and persistence with fremanezumab for migraine prevention.

Methods: PEARL (EUPAS35111) is an observational, prospective, Phase IV study, evaluating the effectiveness of fremanezumab for migraine prevention in adults with episodic or chronic migraine (EM, CM). This third interim analysis was conducted when all patients had completed ≥6 months of treatment. Patient data included past-preventive and concomitant migraine medication use, fremanezumab adherence (administration within ±5 days of due date) and persistence (continued administration, unless required to discontinue) using daily headache diaries.

Results: Among 968 patients (EM, 33.1%; CM, 66.9%), the most common past-preventive migraine treatments were anticonvulsants, beta-blockers, and tricyclics (Table 1). Most patients (64.7%) used concomitant migraine medication; 51.3% used acute and 33.2% preventive - tricyclics (6.0%), beta-blockers (6.0%), and anticonvulsants (5.6%) being the most common. The mean number of days with concomitant triptan use decreased within one month of treatment and persisted over time (Figure 1). Over time, the proportion of patients receiving their fremanezumab dose within +/–5 days of their due date decreased progressively, but persistence was largely maintained (Figure 2).

Past-preventive medication class	Total use			Mean duration of use, months, n
	Total patients (N=968), n (%)	EM patients (N=320), n (%)	CM patients (N=648), n (%)	
Anticonvulsants	665 (68.7)	256 (80.0)	409 (63.1)	11.0
Beta-blockers	590 (61.0)	187 (58.4)	403 (62.2)	9.2
Tricyclics	552 (57.0)	163 (50.9)	389 (60.0)	10.0
Calcium channel blockers	371 (38.3)	168 (52.5)	203 (31.3)	6.9
Onabotulinumtoxin A	344 (35.5)	37 (11.6)	307 (47.4)	17.8
Angiotensin II receptor antagonists	149 (15.4)	10 (3.1)	139 (21.5)	9.1
Valproic acid	135 (13.9)	48 (15.0)	87 (13.4)	9.1
Erenumab	85 (8.8)	21 (6.6)	64 (9.9)	11.6
Galcanezumab	4 (0.4)	1 (0.3)	3 (0.5)	4.0

Table 1: Past-preventive medication in patients with migraine. CM, chronic migraine; EM, episodic migraine.

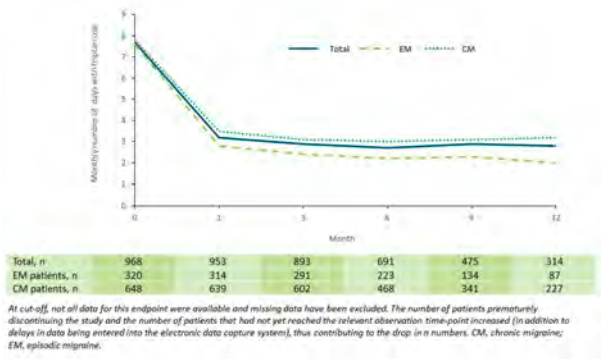

Figure 1: Monthly number of days with concomitant acute migraine medication (triptans) use by migraine type.

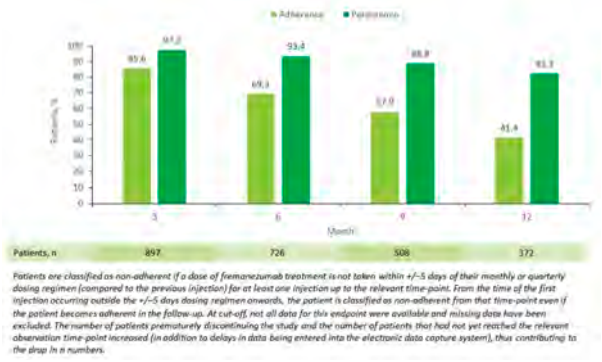

Figure 2: Adherence to and persistence with the fremanezumab treatment schedule over Months 3, 6, 9 and 12 post-initiation.

Conclusion: The proportion of patients receiving their fremanezumab dose for migraine prevention within their ±5-day administration window decreased over time, while treatment persistence was more stable. Sustained reductions in concomitant triptan use suggest patients maintain efficacy with fremanezumab despite fluctuations in adherence (as defined in this study).

Disclosure: Funded by Teva Pharmaceuticals.

EPO-583

Impact of fremanezumab on headache intensity and duration of remaining migraine attacks: PEARL 3rd interim analysis

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Background and aims: The duration and pain intensity of migraine attacks can directly impact patient outcomes, including quality of life and healthcare resource utilisation.
Methods: PEARL (EUPAS35111) is an observational, prospective, Phase IV study, evaluating the effectiveness of fremanezumab for migraine prevention in adults with episodic or chronic migraine (EM, CM). This third interim analysis was conducted when all enrolled patients had completed >=6 months of treatment. Daily patient headache diaries were used to record patient data, including the impact of fremanezumab initiation on monthly migraine days (MMD, primary outcome), and headache severity and duration of remaining migraine attacks over 12 months (secondary outcomes). Headache severity was measured using an 11-point Numerical Rating Scale (NRS, 0=no pain; 10=worst pain possible).
Results: The full analysis set included 968 patients (EM, 33.1%, CM, 66.9%). In patients with available data, mean MMD decreased from 14.6 days at baseline to 6.1 days at Month 12 after fremanezumab initiation. The monthly mean duration of the remaining attacks decreased from 8.4 hours at baseline to 6.1 hours at Month 12 (7.7 to 5.2 hours for EM; 8.8 to 6.5 hours for CM [Figure 1]). The monthly mean NRS score decreased from 6.8 at baseline to 5.1 at Month 12, with a similar trend in patients with EM and CM (Figure 2).

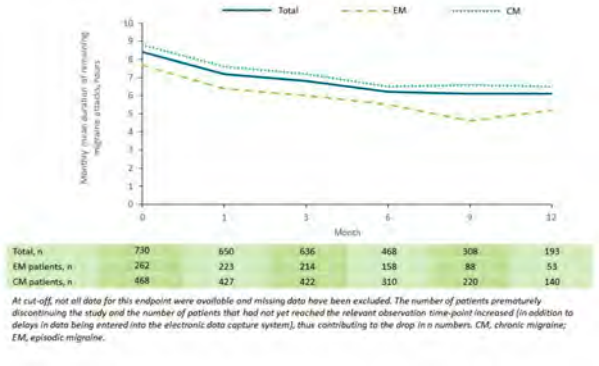

Figure 1: Monthly mean duration of remaining migraine attacks, by migraine type.

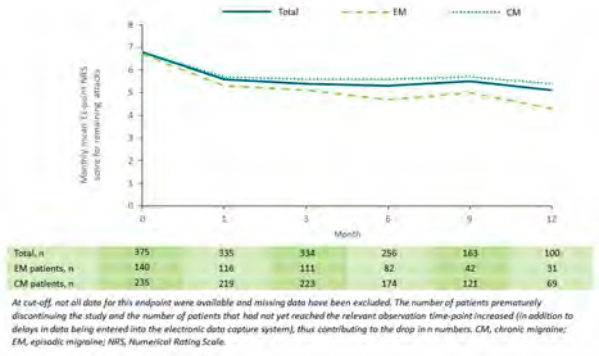

Figure 2: Monthly mean 11-point NRS score for peak headache severity, by migraine type.

Conclusion: This analysis demonstrated that, in addition to reducing MMD, fremanezumab treatment reduced the duration and mean pain intensity of migraine attacks in patients with EM and CM.
Disclosure: Funded by Teva Pharmaceuticals.

EPO-584

Trpa1 gene polymorphism involvement in migraine pathogenesis

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Background and aims: TRPA1 expressed in trigeminal neurons are one the key receptors in migraine pain, same as TRPV1, which single nucleotide polymorphism (SNP) rs8065080, as we previously found, may serve as a potential biomarker of migraine chronification risk. Recent studies suggested that SNPs rs11988795, rs920829, rs13255063 of TRPA1 gene have a protective function against neuropathic pain. However, TRPA1 SNPs has not been tested in migraine yet. Here was evaluated the genotype frequency distribution of rs11988795, rs920829, rs13255063 in the TRPA1 gene in healthy individuals and patients with episodic (EM) and chronic migraine (CM) to test the influence of the SNPs on susceptibility to these forms of migraine.

Methods: The study included 127 patients with migraine (40 EM and 31 CM) and 56 healthy controls. DNA from peripheral blood was used to test TRPA1 SNPs using allele-specific PCR.

Results: The distribution of genotypes of the rs13255063 TRPA1 in EM and in CM differed significantly from control (p=0.003 and p=0.0002), (Table 1). Notably, both in EM and CM groups in contrast to control one, the frequency of AA genotype associated with higher pain threshold doubly decreased, while TT genotype emerged, known as a risk factor for neuropathic pain (Fig.1). Two other SNPs did not show any significant differences.

SNP, genotypes	Control n (%)	Episodic migraine, n (%)	Chronic migraine n (%)
rs11988795			
GG	20 (36)	24 (60)	15 (48)
GA	32 (57)	16 (40)	16 (52)
AA	4 (7)	0	0
rs920829			
GG	32 (57)	31 (78)	23 (74)
GA	20 (36)	9 (22)	8 (26)
AA	4 (7)	0	0
rs13255063			
AA	45 (80)	19 (48)	16 (52)
AT	11 (20)	15 (37)	11 (35)
TT	0	6 (15)	4 (13)

Table 1. Genotypes distribution of rs11988795, rs920829, rs13255063 in TRPA1 gene in the control group, episodic and chronic migraine patients

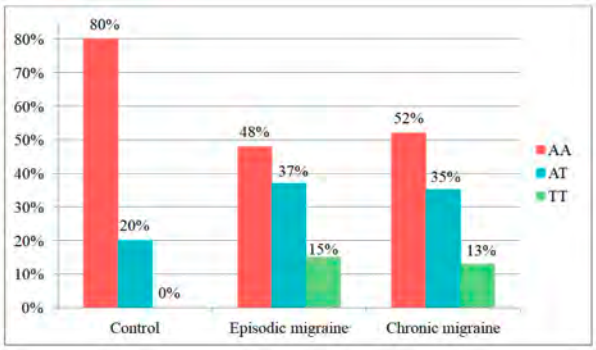

Fig. 1. TRPA1 rs13255063 genotypes distribution in the control group, episodic and chronic migraine patients

Conclusion: This study confirms an association of TRPA1 gene with migraine and indicates an involvement of TT genotype of rs13255063 in pathogenesis of disease, both in case of episodic and chronic forms.

Disclosure: This work was supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).

EPO-585

Pain-modulation system in patients with episodic migraine and medication overuse headache: offset analgesia paradigm

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Background and aims: The offset analgesia (OA) phenomenon refers to the disproportionately large decrease in the perceived pain following a slight decrease in intensity of a noxious warm stimulus, as expression of activation of the endogenous pain-modulation system, whose dysfunction is supposed to be involved in the pathophysiology of migraine and medication overuse headache (MOH). Aim of this study was to investigate pain processing mechanisms in patients with episodic migraine (assessed during the different phases of the migraine cycle) and MOH by using the OA paradigm,

Methods: 40 patients with episodic migraine, 10 patients with MOH, and 15 healthy control subjects were enrolled. All subjects underwent an experimental paradigm (3 stimulus offset trials and 3 constant temperature trials based on the individual heat pain threshold). Both the trigeminal area (supraorbital region) and an extratrigeminal site (ipsilateral hand) were tested.

Results: An absent OA phenomenon was observed in patients with MOH when testing the trigeminal area. No significant differences in the OA phenomenon were observed between patients with episodic migraine. Group comparisons during the constant trial showed a significant difference between episodic migraine patients evaluated in the interictal vs peri-ictal phase: marked habituation to the stimulus was observed only in patients in the ictal and pre-ictal phase.

Conclusion: A dysfunction in the endogenous pain-modulation system could play a pathophysiological role in patients with MOH. Changes in habituation and sensitization phenomena in response to thermal stimuli were also observed throughout the migraine cycle, suggesting a complex interplay between different aspects of painful sensations processing in migraine.

Disclosure: Nothing to disclose.

EPO-586

Effectiveness And Safety Of Monthly Versus Quarterly Fremanezumab For Migraine Prevention: A Real-Life Pilot Study

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Background and aims: Fremanezumab, an anti-CGRP monoclonal antibody, is available in two dosing options for migraine prevention: 225 mg monthly and 675 mg quarterly. This study aimed to compare the effectiveness and safety of monthly versus quarterly fremanezumab in a real-life setting.

Methods: 48 migraine patients were prospectively enrolled. All participants completed a three-month treatment period, receiving fremanezumab monthly or quarterly (25 versus 23, respectively); 44 completed a six-month treatment period (26 versus 18). Two patients switched from quarterly to monthly fremanezumab after three months. Demographic data were collected at baseline. Clinical variables, including monthly headache days (MHD) and migraine days (MMD), monthly acute medication days (AMD) and pills (AMP), headache intensity on NRS, HIT-6, and MIDAS scores were recorded at baseline and after three (M3) and six (M6) months of treatment. Adverse events (AEs) were also investigated at M3 and M6. Within and between-group differences in treatment effectiveness were assessed at M3 and M6 using Wilcoxon and mixed-effect ANOVA tests.

Results: After 3 months of treatment as well as after 6 months, both groups had a significant reduction of MHD, MMD, AMP, AMD, NRS, HIT-6 and MIDAS scores. AEs were reported by three patients of the quarterly group at M3 and by one patient of the monthly group at M6. Between-group differences in clinical outcomes at each time-point were not statistically significant.

Conclusion: Both monthly and quarterly fremanezumab resulted to be effective for migraine prevention; no significant difference between the two dose regimens emerged. Also, a similar safety profile was observed.

Disclosure: The authors declare no competing interests.

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EPO-587

Light sensitivity in myasthenia gravis: frequency, clinical characteristics and impact on the quality of life

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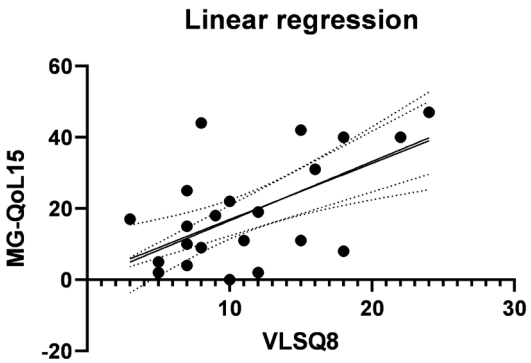
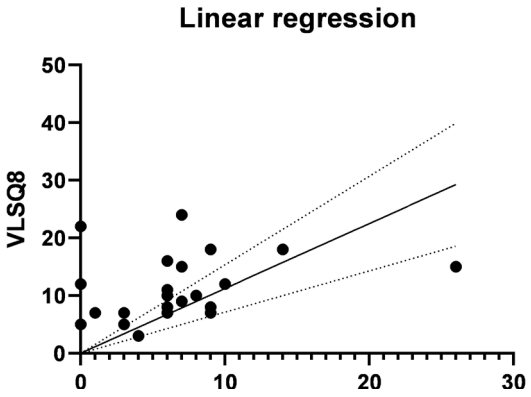
Background and aims: Dysfunction of extraocular muscles is common in myasthenia gravis (MG) and most patients develop ptosis and/or diplopia during the disease course. Light sensitivity (LS) (a.k.a. photophobia) is a frequently reported symptom among patients with MG, but it has not been thoroughly investigated. The aim of this study was to assess the frequency, the clinical characteristics and the impact on the quality of life of LS in MG patients.
Methods: In this prospective observational study, we enrolled patients with diagnosis of MG, consecutively admitted at the Fondazione Policlinico Universitario A. Gemelli in Rome from December 2021 to December 2022. Inclusion criteria were age ≥18 years, diagnosis of MG with Acetylcholine Receptor antibodies and ocular involvement. Exclusion criteria were migraine, ophthalmological and psychiatric comorbidities. The severity of LS was assessed by the Visual light sensitivity Questionnaire-8 (VLSQ-8). Each patient with MG was evaluated with the QMG, MG-ADL and MG-QoL-15 scales.
Results: 59 patients with MG (males=40, 67.7%) and 50 healthy subjects (males=24, 48 %) were recruited. The frequency of photophobia was higher in MG patients (23/59, 38.9%), compared with controls (0, 0%) ($p<0.0001$). Linear regression analysis showed that the severity of LS of MG patients was associated with a lower health-related quality of life and a more severe disease as assessed by both MG-ADL ($p<0,0001$) and QMG scores ($p<0,0001$).





Conclusion: LS represents a frequent and disabling symptom of MG, it has an impact on the quality of life of patients. The cause of LS in MG warrants further investigation.
Disclosure: The authors declare tey have no relevant or material financial interests that relate to the research.

EPO-588

Detection of Potential Pathogenicity of Glutamate Decarboxylase Antibodies in Patients with Stiff Person Syndrome

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Background and aims: Stiff-person syndrome (SPS) is a rare autoimmune disease characterized by painful spasms and rigidity. Antibodies (abs) to the intraneural enzyme glutamate decarboxylase (GAD) are most frequently found in SPS. Their pathogenic significance is discussed controversially. If GAD abs are pathogenic, they should reach their intracellularly located antigen. With the following experiments, we investigated whether GAD abs can be internalized in GAD65 transfected HEK293 cells.
Methods: We performed internalization assays on fixed HEK293 cells. HEK293 cells were transfected with plasmids containing GFP-tagged GAD65-DNA, incubated with commercial GAD abs, fixed with 4% formaldehyde and permeabilized with triton X-100. After incubation with secondary antibodies, fluorescence signals were detected. We then performed internalization assays on living HEK293 cells without fixation. Instead, living HEK293 cells were pre-treated with chloroquine to influence membrane permeability.
Results: An average of 31±0.8 % of the HEK293 cells were successfully transfected. We then quantified the colocalization of GAD-DNA and GAD abs of the overall GAD plasmid transfection rate: In fixed HEK293 cells, the colocalization rate was 11%, and 37% when permeabilized with triton. In living HEK293 cells, GAD abs were internalized into 21% of cells with, and in 0% of cells without chloroquine pre-treatment.
Conclusion: GAD abs were only internalized and reacted with GAD65 in fixated and permeabilized cells but not in living, untreated cells. Further investigations are necessary to find out whether GAD abs can be internalized into live neurons and linked to the impairment of GAD and GABAergic neurons to provide more effective therapeutic approaches.
Disclosure: No conflict of interest.

EPO-589

Use of fluid biomarkers in ongoing Clinical Trials on Multiple Sclerosis (MS)

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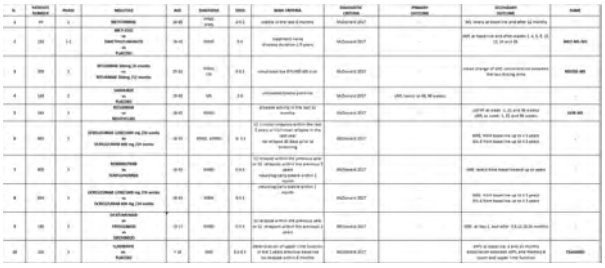
Background and aims: The present study aimed to describe the state of art of fluid biomarkers use in ongoing MS clinical trials.
Methods: A review of 600 ongoing protocols in the clinicaltrials.gov database was performed. The trials enrolled subjects with a diagnosis of RRMS, SPMS and/or PPMS according to Revised McDonald Criteria 2017 or RMS according to Lublin et al. 2014. The presence of CSF (c) or blood (b), either plasma (p) or serum (s), biomarkers among the primary and/or secondary study outcomes was assessed.
Results: Overall, 5% of ongoing studies on MS adopted CSF or blood biomarkers. They were mostly adopted as secondary outcomes in phase 3–4 clinical trials to support the potential disease modifying properties of the intervention. Most studies evaluated sNfL, some considered pNfL or cNfL. A small number considered novel biomarkers of neuroinflammation and neurodegeneration as sGFAP/cGFAP, bIL-6, sChi3L1, and/or inflammatory biomarkers: sVCAM, sMAdCAM, sCXCL13.



Description of selected clinical trials in which fluid biomarkers were evaluated as primary or secondary outcome (part 1).

Description of selected clinical trials in which fluid biomarkers were evaluated as primary or secondary outcomes (part 2).

Description of selected clinical trials in which fluid biomarkers were evaluated as primary or secondary outcomes (part 3).

Conclusion: Considering the numerous ongoing clinical trials in MS, still a small number considers fluid biomarkers as outcome measures, thus testifying the distance from clinical practice. Fluid biomarkers were prevalently considered in studies evaluating the effectiveness of approved second line therapies. Almost all clinical trials evaluating new drugs, particularly BTK-inhibitors considered fluid biomarkers, suggesting a future clinical utility in assessing the effectiveness of these treatments. Nevertheless, the cost-effectiveness in the "real word" remains to be clarified. NfLs have been also used to monitor disease progression after natalizumab suspension in stable patients, cladribine efficacy after anti-CD20 discontinuation, and the efficacy of AHSCT compared to medical treatment.
Disclosure: Nothing to disclose.

EPO-590

Anti-adenylate kinase-5 autoimmune encephalitis - the important role of clinical suspicion

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Background and aims: Anti-adenylate kinase-5 (anti-AK5) encephalitis is a recently described non-paraneoplastic autoimmune limbic encephalitis, characterized by severe amnesia, psychiatric symptoms, and rarely seizures. It is poorly responsive to immunotherapy.
Methods: Clinical case description.
Results: A healthy 72-year-old man presented with a two-week history of progressive confusion and disorientation. Neurological examination revealed severe anterograde amnestic syndrome with marked short-term memory impairment. Brain MRI showed bilateral temporal lobe T2/FLAIR hyperintensities, relatively symmetric, with heterogeneous contrast-enhancement (Figure 1). EEG showed diffuse slow-wave activity, without epileptiform activity. CSF evaluation revealed five nucleated cells, hyperproteinorrachia, and intrathecal oligoclonal band synthesis; bacteriological and virological analysis were negative. Routine panels of CSF/serum antineuronal antibodies were negative. There was no evidence of malignant neoplasm or autoimmune comorbidities. Considering the diagnosis of autoimmune encephalitis, the patient was started on IV corticosteroid, followed by IV immunoglobulin. Despite initial improvement, there was clinical and imagiologic worsening six weeks later. Since imagiological and clinical features were compatible with anti-AK5 encephalitis, immunofluorescence antibody studies were reviewed and a pattern suggestive of anti-AK5 antibodies was identified in rat tissue (Figure 2). Anti-AK5 antibodies in CSF and serum were later confirmed by immunoblot. Despite treatment with plasmapheresis and rituximab, severe memory impairment persisted. Brain lesions evolved to mesio-temporal atrophy.

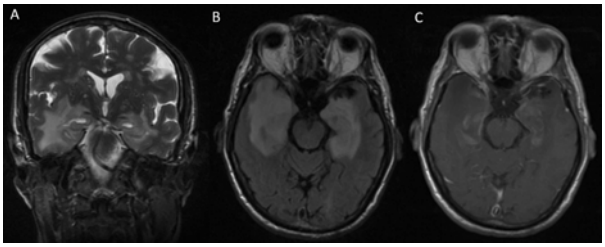

Fig. 1 Coronal T2 (A) and axial FLAIR (B) brain MRI showing bilateral hyperintense medial temporal lobes, and axial T1 brain MRI with gadolinium (C) showing bilateral heterogeneous contrast enhancement.

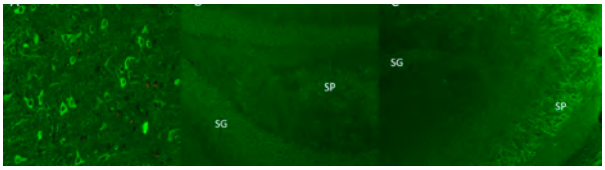

Fig. 2 Indirect immunofluorescence, serum sample. (A) Monkey cerebrum - cytoplasmic positivity of cortex neural (x400) (B, C) Rat hipocamppus, immunofluorescence localized to the granular neurons of the dentate gyrus (SG) and pyramidal cells (SP) (x100).

Conclusion: We report a new case of anti-AK5 encephalitis with the typical clinical course of severe subacute amnestic syndrome. We want to emphasize the importance of expanding antibodies' investigation in presumed autoimmune encephalitis, particularly for the detection of recently described antibodies that might be absent from routine panels.
Disclosure: Nothing to disclose.

EPO-591

Anti-DPPX encephalitis: clinical characterization and outcome of 11 new patients

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Background and aims: Anti-dipeptidyl-peptidase-like protein-6 (DPPX) encephalitis was first described in 2013 and, since then, only 65 cases have been reported. We aimed to characterize a new series of patients with anti-DDPX encephalitis from a clinical and outcome perspective.
Methods: Retrospective nationwide study of patients tested positive for anti-DPPX antibodies in the French referral centre.
Results: Of 11 identified patients, 7(63%) fulfilled the typical triad of weight loss, cognitive impairment and hyperexcitability. Additionally, 9(82%) had cerebellar involvement, 3(27%) diarrhea, 7(64%) mood disorders, 3(27%) brainstem involvement, 3(27%) sleep disorders and 2(18%) dysautonomia (Figure 1). 5(45%) cases had an abnormal brain MRI, mainly cerebellar atrophy (3/5, 60%). CSF analysis revealed pleocytosis in 2(18%), high protein levels in 4(36%) and positive oligoclonal bands in 6/8(75%). All patients except a recent diagnosis (10/11, 91%) were treated with immunotherapy: 8(72%) patients received first line immunotherapy (IT) (median delay from onset 18 months, range 2–180) and 8(72%) received second line IT (median delay from onset 15 mohs, range 8–181). Four patients (36%) experienced relapsntes during follow-up. Figure 2 depicts the evolution of the modified Rankin score (mRS) of 10 patients with disability information between onset and last visit. Improvement of at least one mRS point was observed in 4/10(40%) and stabilization in 3/10(30%) patients. The median follow-up was 45 months (2-219).

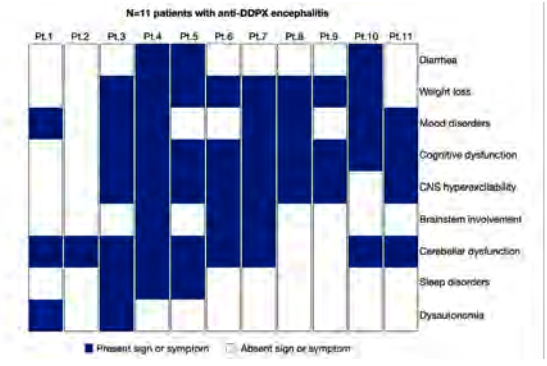

Figure 1. Distribution of signs and symptoms in the cohort of patients with anti-DPPX encephalitis.

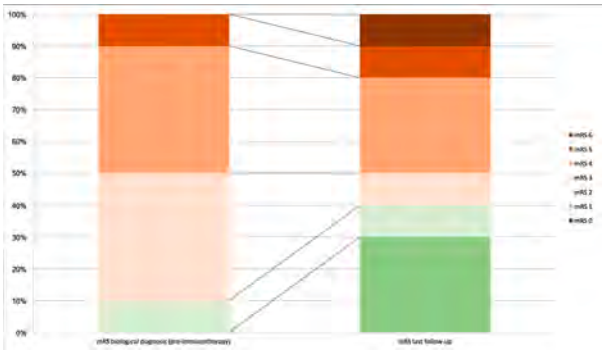

Figure 2. Evolution of the modified Rankin score from neurological onset to last visit.

Conclusion: Anti-DPPX encephalitis recognition is crucial as we observed that, even in cases of delayed administration, most patients improved or stabilized following immunotherapy.
Disclosure: Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero.

EPO-592

Therapeutic Plasma Exchange and Double Filtration Plasmapheresis in neuroimmune diseases as the first treatment option

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Background and aims: Therapeutic plasma exchange (TPE) and double filtration plasmapheresis (DFPP) are therapeutic modalities that are used in the management of severe neuroimmune disorders. High-dose intravenous immunoglobulins is an alternative treatment for these patients but it's significantly more expensive. The American Society for Apheresis accepted TPE as first line treatment for some severe neuroimmune conditions, like: acute Guillain-Barre Syndrome, Myasthenia Gravis and chronic inflammatory demyelinating polyneuropathy.
Methods: We reviewed medical records of 82 patients with severe autoimmune neurological diseases requiring TPE or DFPP, treated in our hospital during a 4-year period (from 2019 to 2022). We analysed the efficacy, side effects and complications of these procedures on specific scales.
Results: The prevalent neuroimmune conditions treated in our centre, were: Guillain-Barre Syndrome (47%), Myasthenia Gravis (25%), neuromyelitis optica (5%) and chronic inflammatory demyelinating polyradiculoneuropathy (5%). The mean number of TPE sessions/patient and DFPP sessions/patient was 3.8 (range 3–5) and 2.5 (range 2–4), respectively. The most common systemic complications of plasma exchange were: dyselectrolytemia (48% of patients), hypocalcemia (38% of patients), and hypotension (8% of patients). Infection/sepsis, produced by prolonged immobilization, developed in 20% patients. These systemic complications were completely reversible. No mortality was directly generated by these therapeutic procedures. After completing the plasma exchange sessions, 80% of the patients had clinical neurological improvement, 20% had no improvement.
Conclusion: Based on the results of our center, we conclude that plasmapheresis represents a first option in the treatment of autoimmune diseases, being a relatively safe procedure with mild complications and good clinical outcome.
Disclosure: Nothing to disclose.

EPO-593

Quality of Life in patients with Susac Syndrome – Identifying themes and pitfalls

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Background and aims: Susac syndrome (SuS) is a neuroimmunological disease characterized by encephalopathy, hearing impairment and visual disturbances. This may have an impact on the patients' quality of life (QoL). To date, no studies have investigated QoL in SuS. This study aims to investigate generic and disease specific QoL and to map disease related themes in patients with SuS.
Methods: 10 patients (3 men, 7 women, average age 38 years) were recruited via the Neurology department of the Antwerp University Hospital. After obtaining written informed consent, patients filled in two questionnaires: EQ-5D-5L and NeuroQoL. Results were analysed using a t-test. Patient's experiences during daily life were explored in a semi-structured interview to identify relevant themes. Questionnaires and interviews were triangulated within the epistemological concept of pragmatism.
Results: Preliminary results show that responses from the questionnaires were comparable to the general population (EQ-5D-5L) and were less severe than the average response in a neurological population (NeuroQoL). The following themes were influential: Emotional Health, Social Network and relatives, Financial burden, Impact on activities, Symptoms and Treatment.
Conclusion: SuS has a considerable impact on the patient and their environment during the diagnosis phase, the follow-up and in case of relapse. Triangulation shows that the included questionnaires underestimate the burden placed upon these patients. Improving QoL may be possible via interventions focusing on the aforementioned themes.
Disclosure: No specific conflicts of interest to disclose.

EPO-594

Extracellular vesicles from Peripheral B cells may contribute to pathogenesis and be a biomarker of Multiple Sclerosis.

G. Torres Iglesias, M. Fernández-Fournier, D. Piniella-Alcalde, F. Laso-García, M. Gómez-de Frutos, M. Lopez, L. Botella, B. Chamorro, S. Sánchez Velasco, R. Gallego, J. Pozo, I. Puertas, A. Tallón, E. Diez-Tejedor, M. Gutiérrez-Fernández, L. Otero-Ortega
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Background and aims: To investigate whether extracellular vesicles (EVs) mediate exchange of myelin autoreactive antibodies from peripheral B cells to the CNS and analyze whether myelin antibodies could act as diagnostic biomarker in MS.
Methods: Circulating B cell-derived EVs from blood and cerebrospinal fluid (CSF) of MS patients were isolated by precipitation and immunoisolation, their anti-myelin antibody content was analyzed by Elisa. The effect of circulating EV-derived autoantibodies on demyelination was studied in vitro. Whether myelin antibodies carried EV reach oligodendrocytes in patients was also evaluated. Influence of disease activity and disease-modifying therapies in the content of antibodies in blood B cell-derived EVs of MS patients was examined.
Results: This study enrolled 136 MS patients and 39 healthy controls. EV-autoreactive myelin antibodies released by peripheral B cells were identified in the blood of MS patients, but not in the CSF. We also have identified a cut-off value of 3.95 ng/ml of MBP autoantibodies in EVs derived from blood peripheral B cells with a 95.2% sensitivity and 88.2% specificity which allow to differentiate MS patients from healthy controls. These myelin antibody-loaded vesicles induced demyelination in oligodendrocytes in vitro. EV-derived myelin antibodies were found in oligodendrocytes from MS patients. Disease activity nor disease-modifying therapies did not affect the antibody content in blood peripheral B cells-derived EVs of MS patients.
Conclusion: Blood peripheral reactive immune cells could contribute in remote to the pathogenesis of MS by using EVs as antibody delivery nano-system. Furthermore, EV-derived myelin antibodies could have a role as minimally invasive diagnostic biomarker in MS.
Disclosure: This work was sponsored by the FIS PI21/00918 project from the Spanish Ministry of Health—Carlos III Health Institute (ISCIII) and the European Regional Development Fund (FEDER Funding), Miguel Servet (CP20/00024 to Laura Otero-Ortega) Miguel Servet (CPII20/00002 to María Gutiérrez-Fernández), a predoctoral fellowship (FI17/00188 to Mari Carmen Gómez-de Frutos; FI18/00026 to Fernando Laso-García), a Río Hortega (CM20/00047 to Elisa Alonso-López) from the Carlos III Health Institute Health Care Research Fund and was co-funded by the European Regional Development Fund (ERDF).The authors declare that they have no competing interests.

EPO-595

Neural and lymphocyte-derived extracellular vesicles as biomarkers for treatment response in Multiple Sclerosis.

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Neurological Sciences and Cerebrovascular Research Laboratory, Department of Neurology, Neuroscience Area Hospital La Paz Institute for Health Research IdiPAZ, La Paz University Hospital, Universidad Autónoma de Madrid, Madrid, Spain

Background and aims: The benefit of each disease modifying treatment (DMTs) for individual patients in MS is unknown, which makes clinical decision-making a complex process. Previous studies of our group showed that DMTs alter circulating Extracellular Vesicles (EVs) in MS patients. Here, we aim to investigate whether circulating EVs could show potential for therapeutic response monitoring in MS treated patients.
Methods: EVs specifically derived from neurons, oligodendrocytes, B and T lymphocytes were isolated from blood of 36 MS patients before DMT initiation and after 3 months. Over the course of 12 months, treatment response was monitored by: 1) disease activity by clinical relapses and new lesions in magnetic resonance; 2) motor and cognitive progression independent of relapse activity (PIRA) 3) relapse-associated worsening (RAW). Motor and cognitive progression was measured using the Expanded Disability Status Scale (EDSS) and symbol digit and 9-hole peg test (9HPT).
Results: Patients with no evidence of disease activity (NEDA) showed higher size of B cell-derived EVs compared to those with activity of disease (p=0.015). Analyzing motor progression, patients with EDSS-associated RAW showed lower levels of B cell-derived EVs (p=0.05) and patients with 9HPT-associated PIRA had smaller size oligodendrocyte-derived EVs (p=0.001). Patients showing cognitive progression had lower levels of T cell-derived EVs (p=0.018). While bigger size B-cell derived EVs were found in patients cognitive PIRA (p=0.041), smaller B-cell derived EVs were associated to those patients with cognitive RAW (p=0.028).
Conclusion: Circulating EVs derived from oligodendrocyte, B and T cells may play an important role as biomarkers for treatment response in MS patients.
Disclosure: This work was sponsored by the FIS PI21/00918 project from the Spanish Ministry of Health—Carlos III Health Institute (ISCIII) and the European Regional Development Fund (FEDER Funding), Miguel Servet (CP20/00024 to Laura OteroOrtega) Miguel Servet (CPII20/00002 to María Gutiérrez-Fernández), a predoctoral fellowship (FI17/00188 to Mari Carmen Gómez-de Frutos; FI18/00026 to Fernando Laso-García) from the Carlos III Health Institute Health Care Research Fund and was co-funded by the European Regional Development Fund (ERDF). The authors declare that they have no competing interests

EPO-596

Neuropathological findings in CASPR2-encephalitis. Report of 2 cases.

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Background and aims: Antibodies against contactin-associated protein-like 2 (CASPR2) are associated with phenotypically heterogeneous autoimmune encephalitis. Detailed neuropathological studies have been reported in only two patients, and in one of them, the findings were unclear due to severe hypoxic changes.
Methods: We describe the neuropathological findings of two patients with CASPR2-encephalitis who died at 3 months and 3 years from disease onset, respectively. Antibodies were determined by immunohistochemistry and in-house cell-based assays in a reference laboratory.
Results: Patient 1: a 48-year-old male developed Morvan's syndrome progressing over 3 months. Both CASPR2 and LGI1 antibodies were found in serum and CSF, and brain MRI showed bilateral mesotemporal abnormalities. Despite immunotherapy with methylprednisolone and IVIg, the patient died of cardiac arrest in the context of severe dysautonomia. Autopsy revealed a malignant thymoma and pontine and cortical tauopathy involving neurons and astrocytes, without overt inflammatory changes. Patient 2: a 68-year-old man with cardiomyopathy, developed rapidly progressive short-term memory deficits. CSF and MRI studies were unremarkable except for the presence of CASPR2 in CSF and serum. Steroids led to transient cognitive improvement, followed by clinical fluctuations that ultimately stabilized for 2 years under rituximab treatment. He died from heart failure, and the autopsy revealed selective atrophy in hippocampal CA1, without inflammatory infiltrates, and stage III of argyrophilic grain disease in mesotemporal regions.
Conclusion: Neuropathological findings in these 2 different stages of CASPR2-encephalitis do not reveal prominent inflammatory changes. In contrast, different patterns of tauopathy were found. Whether these findings are causally related or purely coincidental remains unknown.
Disclosure: Nothing to disclose.

EPO-597

Hu-antibodies autoimmunity in patients without detectable cancer

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Background and aims: Anti-Hu paraneoplastic neurological syndromes are almost invariably associated to lung cancer. However, up to 3% of cases may present without an underlying malignancy. We aimed to characterize this non-paraneoplastic subset in a cohort of anti-Hu patients.
Methods: Retrospective nationwide study of patients tested positive for Hu-antibodies in the French Reference Centre.
Results: Among 466 included patients, 54 (12%) had a previously known cancer at the onset of neurological symptoms, 295 (63%) had a subsequent oncological diagnosis, 84 (18%) did not but had less than 2 years follow-up and 33/466 (7%) remained cancer-free 2 years after onset (Figure 1). We compared 295 patients developing a proved cancer versus 33 cancer-free patients after 2 years follow-up. Cancer-free patients had a lower median age (54 vs 64 years, p=0.002), a less frequent history of smoking (77% vs 97%, p=0.001), coexistent neural antibodies (3% vs 20%, p=0.01) and hyperproteinorrachia (38% vs 73%, 0.0001). They also had a longer median delay to Hu-antibodies detection (12 vs 3 months, p<0.001), more common involvement of limbic (51% vs 25%, p=0.003) and myenteric areas (33% vs 13%, p=0.003; Figure 2), more frequent modified Rankin score <4 at diagnosis (45% vs 21%, p<0.001) and longer survival (Figure 3). Imaging findings suggestive of a possible regressed tumour were observed in 13/33 (39%).

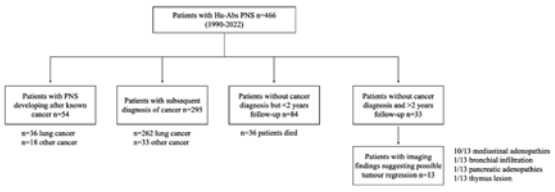

Figure 1. Flowchart of the study.

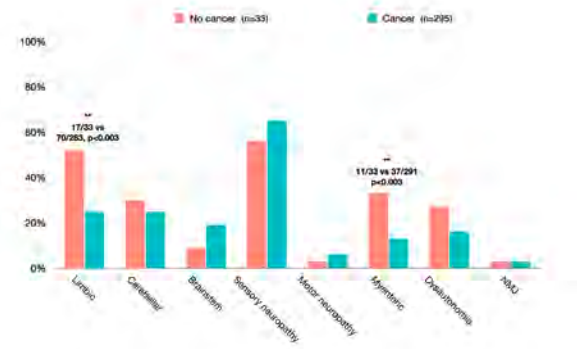

Figure 2. Clinical area involvement in patients with or without cancer.

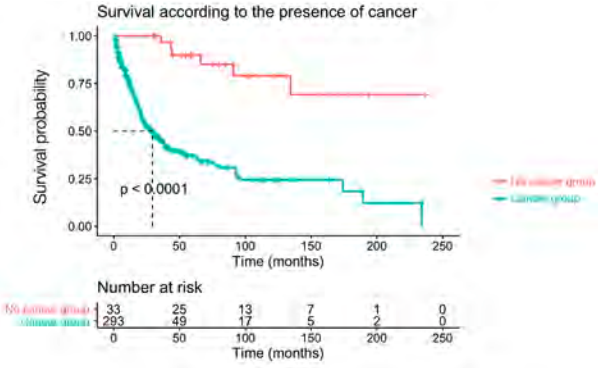

Figure 3. Survival analysis according to the presence of a cancer.

Conclusion: Patients with Hu-antibodies remaining cancer-free after a long follow-up have distinct features despite not presenting with a specific clinical phenotype. However, whether these patients had a regressive cancer or represent truly idiopathic cases remains unknown.

Disclosure: Macarena Villagrán-García received a research fellowship grant from the Spanish Foundation Alfonso Martín Escudero. Antonio Farina received a research fellowship grant from the European Academy of Neurology.

EPO-598

Myelin Oligodendrocyte Glycoprotein antibody associated disorder in neuro-Behçet's disease: differential diagnosis

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Background and aims: Myelin oligodendrocyte glycoprotein associated disorder (MOG-AD) diagnosis could be difficult when other autoimmune comorbidities can mimick its presentation.

Methods: We hereby report the case of a 54 years-old woman with a history of Behçet's disease (HLA-B51 positivity, recurrent oral aphthosis, skin ulcers and positive pathergy reaction) since adolescence.

Results: In September 2013 she developed paraparesis, urinary retention, headache and emesis. She was admitted to a Neurology Department, where Magnetic Resonance Imaging (MRI) showed T2-hyperintense brainstem lesions with contrast enhancement, and a transverse myelitis from T2 to T11. Cerebrospinal fluid (CSF) analysis revealed elevated leukocytes and protein and one oligoclonal band. Excluded infectious CNS diseases, high-dose intravenous methylprednisolone (IVMP) was administered, with partial recovery. A diagnosis of probable neuro-Behçet's disease (NBD) was made. The patient was stable until 2020, when she experienced a new clinical (nausea and speech disturbances) and MRI (cortical lesions with mild oedema in left temporal lobe) relapse. She was admitted to our Neurology Department: the complete diagnostic workup was unremarkable, except for MOG-IgG positivity, detected using fluorescence-activated cell sorting. She was diagnosed as MOG-AD. At the subsequent two-year follow-up, serum MOG-IgG were constantly detected.

Conclusion: NBD occurs in less than 10 % of patients with Behçet's disease, and its parenchymal type can manifest with clinical and MRI findings similar to MOG-AD. The recurrence of MOG-IgG positivity, longitudinally extensive spinal cord lesions and partial response to IVMP, guided, over time, our diagnosis. Distinguishing MOG-AD from other CNS inflammatory diseases is mandatory for treatment decision-making.

Disclosure: Dr. Vitobello, Dr. Oggiano and Dr. Bianco have nothing to disclose. Dr Manni has served on scientific advisory boards for Merck Serono, Sanofi Genzyme and Roche. Prof. Trojano received honoraria for consultancy or speaking from Biogen, Sanofi Aventis, Merck Serono, Novartis, Genzyme, TEVA, and Bayer-Schering and research grants from Merck Serono, Biogen, and Novartis. Dr. Iaffaldano A., Prof Paolicelli and Prof Iaffaldano P. have served on scientific advisory boards for Biogen, Novartis, Roche, Merck and Genzyme, and they have received speaker honoraria from Biogen Idec, Merck, Roche, Teva, Sanofi-Genzyme and Novartis.

Neuroimaging; Neurosonology

EPO-599

Impact of rater experience on detecting MRI features of idiopathic intracranial hypertension

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Background and aims: In idiopathic intracranial hypertension (IIH), MRI features (empty sella (ES), optic nerve sheath distension (ONSD), optic nerve tortuosity (ONT), posterior globe flattening (PGF) and transverse sinus stenosis (TSS)) are promising diagnostic markers.

Methods: In patients with definitive IIH and routine cranial MRI performed during diagnostic work-up, we compared ratings in real-world setting by radiologists with unknown awareness of IIH-MRI-features with a junior neuroradiologist aware of features but without special training and a senior neuroradiologist with experience in IIH imaging (gold-standard).

Results: In 84 IIH patients (88% female, mean age 33.5 years), 78.6% had ≥1 IIH-MRI-feature and 60% had ≥3 features with ONSD most frequent (64.3%) followed by TSS (60.0%), ONT (46.4%), ES (44.4%) and PGF (23.8%). Compared to gold standard, IIH features were described significantly less frequently in routine MRI reports (≥1 feature 64.3%, ≥3 features 15.7%, ONSD 28.6%, ONT 13.1%, PGF 4.8%, TSS 42.9%, p<0.01 respectively) except for ES (42.9%, p=0.9). Specific referral question regarding IIH increased detection rates in routine reports, but ONSD, ONT and PGF were still significantly lower than by gold standard. Contrary, rating by a neuroradiologist without special training produced significantly higher frequencies of ≥1 / ≥3 MRI features (95.2% and 72.5%, p<0.01 respectively), ONSD (81.0%, p<0.01) and ONT (60.7%, p<0.01), but not ES (47.6%), PGF (29.8%) and TSS (68.1%).

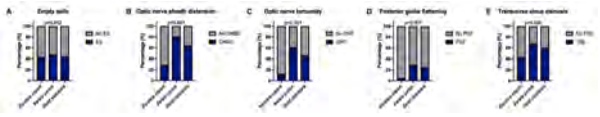

Figure 1

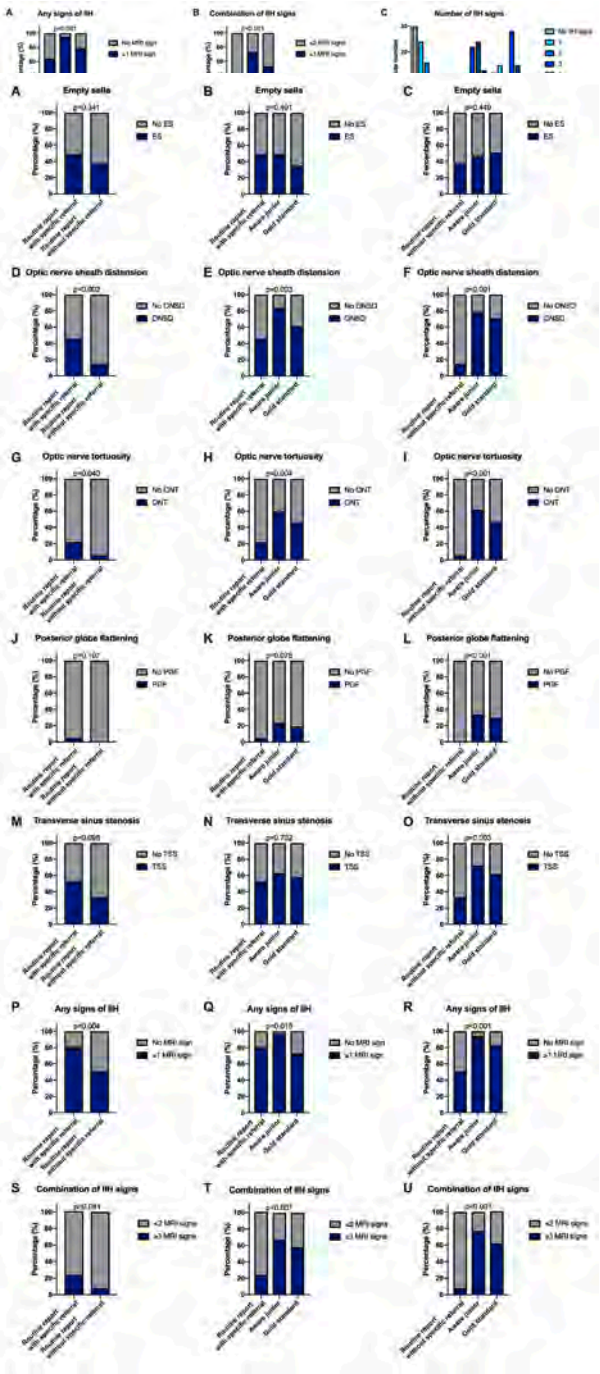

Figure 3

Conclusion: MRI features are underestimated in routine MRI reports and partly overestimated by less experienced neuroradiologists. Reevaluation of MRI scans by an

experienced rater (and to a lesser degree specific referral question) improves diagnostic accuracy.
Disclosure: GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPO-600

Frailty is associated with hippocampal atrophy in cognitively unimpaired older individuals

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Background and aims: Frailty (FI)has been associated with an increased risk of dementia (1)(2).The aim of the present study was to investigate the association between frailty, operationalized through a FI and hippocampal volume in cognitively intact subjects.
Methods: Sociodemographic, clinical, biological and neuroimaging data of 291 cognitively unimpaired individuals were obtained from the Alzheimer's Disease neuroimaging Initiative (ADNI) database phase 2. Clinical variables collected at screening and baseline visits were used to develop a 40-items FI (3). A linear regression model was then performed to explore the association between FI and hippocampal volume, adjusting for age, sex, education, ApoE status, CSF Aβ-42 and CSF P-tau. Sensitivity analyses were conducted using a modified 28-items FI
Results: Participants included in the study had a mean age of 73 (SD 6.0) years, mean education of 16.6 (SD 2.5) years, and 54% of them were women.The mean score of the 40-items FI was 0.18 (SD 0.08). In the multi-adjusted model, a statistically significant association between the 40-items FI and the reduction of hippocampal volume was observed (ß -0.15, 95%CI -0.28, -0.02, p=0.02). The association remained significant even considering the 28-items FI (ß -0.11, 95%CI -0.20, -0.01, p_0.03).
Conclusion: The results show that FI correlates with a reduction of hippocampal volume, an in vivo biomarker of neurodegeneration, independently from chronological age and traditional pathological lesions. Frailty contributes to hippocampal atrophy. Further studies are needed to clarify the relationship between frailty, neurodegeneration, and other biomarkers of dementia
Disclosure: Nothing to dislose.

EPO-601

Biochemical pathways involved in higher resilience in Parkinson's disease

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Background and aims: The emerging concept of resilience in Parkinson's disease (PD) aims to explain variations in symptom severity and progression rates in patients with a comparable extent of neurodegeneration. While several lifestyle factors and neurobiological underpinnings have recently been associated with slower disease progression, the biochemical basis of higher resilience is still unknown.
Methods: Using data from the PPMI database, high and low resilience groups were defined by residuals derived from a regression model predicting the motoric symptom severity by the dopamine transporter signal. In a preliminary gene set enrichment analysis (GSEA) we used protein abundances, quantified by slow off-rate modified aptamers, of 40 low and 50 high reserve patients. Gene sets were considered as of interest by an FDR<25%. We aim to apply an unsupervised machine learning algorithm in a bigger cohort to further investigate and validate the identified pathways of interest. Before clustering patients based on metabolome and proteome data, we will apply a feature selection algorithm. Finally, the difference in cluster expression scores across motor reserve categories and their influence on motor symptom progression will be investigated.
Results: Or preliminary results suggest higher resilience to be related to upregulated iron transport and homeostasis as well as inflammatory pathways. Low reserve, in contrast, seems to be associated with increased apoptotic processes. Further, cytochrome C was identified as a potential metabolite of interest.
Conclusion: In conclusion, identifying altered metabolites, proteins, or whole biochemical pathways might help to point out novel interventional targets.
Disclosure: I have nothing to disclose.

EPO-602

Effects of deep brain stimulation on functional connectivity in Parkinson's disease

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Background and aims: Deep-brain stimulation in the subthalamic nucleus (STN-DBS) is a prosperous surgical treatment for Parkinson's disease (PD). Research findings indicate that STN-DBS affects functional brain connectivity, however, with diverse results (Mueller 2013, Zhang 2021). Using a relatively large cohort, we inspected the impact of DBS in brain connectivity of PD patients.

Methods: Connectivity of 104 PD participants (age 59.5±7.9 y; 34 fem, disease duration 15.1±6.3 y) was measured with functional magnetic resonance imaging (fMRI) in STN-DBS ON and OFF state. Eigenvector centrality (EC) and global correlation (GCOR) maps were estimated using LIPSIA software and CONN toolbox, respectively, for each individual in both states. The contrast of STN-DBS ON-OFF was computed with SPM12 across all subjects as well as for female and male patients independently.

Results: Significant STN-DBS ON-OFF EC increase was found in male participants confirming the findings of Mueller 2013 (Fig 1). The contrast was shown in left and right premotor and parietal cortex, and right insula. No significant connectivity differences were found in females. The reversed contrast across all 104 PD patients demonstrated brain network centrality decrease in the left and right entorhinal cortex with both centrality measures EC and GCOR (Fig 2).

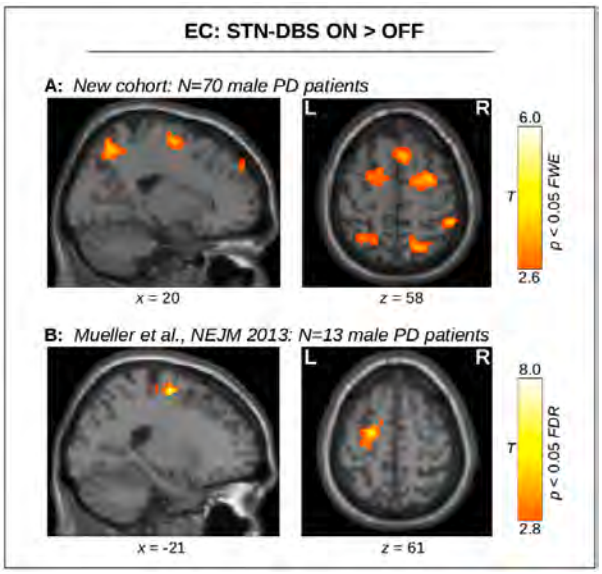

Figure 1. Significant STN-DBS ON-OFF EC increase in a group of male PD participants. The new cohort (A) is verifying the former finding (B).

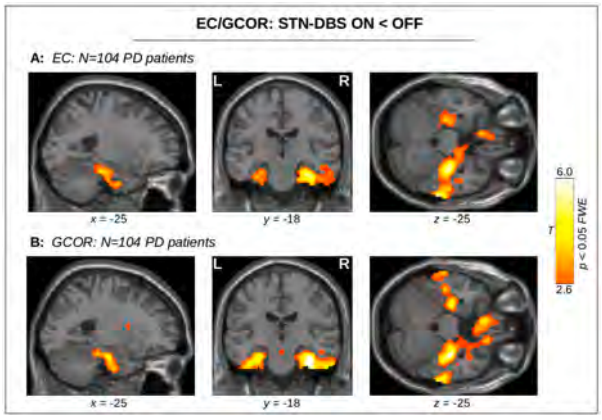

Figure 2. Significant STN-DBS ON-OFF EC decrease illustrated in brain slices of all PD participants (n=104). EC and GCOR results are aligned.

Conclusion: The analysis illustrated EC increase in several cortical regions of male individuals. Profound centrality decrease was shown in all groups indicating an association between STN-DBS and hippocampal connectivity.

Disclosure: Supported by a grant of the National Institute for Neurological Research, Czech Republic, Programme EXCELES (ID project No. LX22NPO5107) and the Charles University: Cooperatio Program in Neuroscience.

EPO-603

Paramagnetic rim lesions lead to pronounced diffuse periplaque white matter damage in multiple sclerosis

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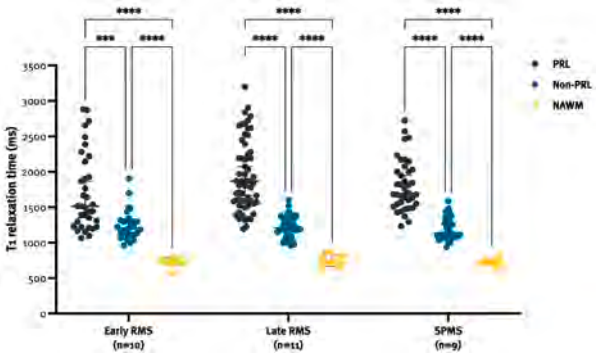
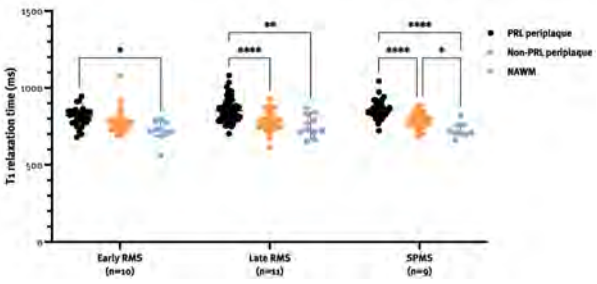
Background and aims: Paramagnetic rim lesions (PRLs) are a novel imaging biomarker, indicating a more severe disease course and earlier conversion to secondary progressive multiple sclerosis (SPMS).
Methods: We performed a cross-sectional, retrospective study on MS patients who underwent 3T MRI. Patients were grouped into early relapsing MS (eRMS) (disease duration (dd) ≤1 year), late RMS (lRMS) (dd ≥10 years), and clinically definite SPMS by Lorscheider et al. (dd ≥10 years). T1 relaxation times were measured by the quantitative "SyMRI" technology in PRLs and non-PRLs, their corresponding periplaque areas, and normal-appearing white matter (NAWM).
Results: Thirty patients were included (mean age 39.5 years [SD 11.0], 73.3% female, median EDSS 2.3 [range 0–6.0]). 135 PRLs and 107 non-PRLs were identified, 5 (16.7%) patients having no PRLs (2 eRMS, 2 lRMS, 1 SPMS). T1 relaxation times in PRLs were significantly longer compared to non-PRLs (eRMS: 1,705 vs. 1,245, lRMS: 2,011 vs. 1,223, SPMS: 1,811 vs. 1,200; p<0.001) (Figure 1). The PRL periplaque area showed significantly longer T1 relaxation times compared to the non-PRL periplaque area and NAWM in lRMS (857 vs. 789, p<0.0001; 857 vs. 752, p=0.0043) and SPMS (864 vs. 792; 864 vs. 727; p<0.0001). In eRMS, longer T1 relaxation times were observed only between the PRL periplaque area and NAWM (811 vs. 720, p=0.0124) (Figure 2).



PRLs showed longer T1 relaxation times compared to non-PRLs and NAWM.



The PRL periplaque area showed longer T1 relaxation times compared to the non-PRL periplaque area and NAWM.

Conclusion: PRLs are more destructive than non-PRLs and lead to pronounced diffuse periplaque WM damage which explains the more rapidly progressive clinical disability in patients with PRLs.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-604

Quantification of Thalamic Volume in Multiple Sclerosis: From the Multicenter INNI Dataset Towards Clinical Application

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Background and aims: Thalamic atrophy has been found since the earliest phases of multiple sclerosis (MS). Aim of this study was to obtain a reliable segmentation of the thalamus in MS by comparing existing automatic methods.
Methods: 141 relapsing-remitting MS and 69 healthy controls (HC) with baseline and 1-year 3D T1-weighted, T2-weighted and diffusion weighted (DW) MRI were collected from the Italian Neuroimaging Network Initiative. From DWI, fractional anisotropy (FA) maps were derived for the FSL-MIST multimodal segmentation. FSL-FIRST v5.0.9 and Freesurfer v6.0 were also compared. The agreement among the results of the pipelines and the effect sizes in differentiating between MS and HC were assessed. In patients, correlations with age, disease duration, EDSS and T2-hyperintense lesion volume (LV) were evaluated.
Results: At baseline, FIRST and MIST showed the highest significant agreement for thalamic volumes ($R=0.87$, $p<0.001$), with the highest effect size for MIST (Cohen's $d=1.11$). At baseline, FIRST showed the highest significant correlations with age (-0.36, $p<0.001$), EDSS ($R=-0.3$, $p<0.001$), T2-hyperintense LV ($R=-0.4$, $p<0.001$) and disease duration ($R=-0.2$, $p=0.02$). At follow-up, MIST showed the lowest variability in estimating thalamic volume changes (TVC) for HC (standard deviation=1.07%) in comparison to the other pipelines, and the highest effect size (Cohen's $d=0.21$). In MS, only MIST TVC showed a significant correlation with T2-hyperintense LV change ($R=-0.22$, $p=0.01$).
Conclusion: We found that the use of a multimodal approach increased robustness of the longitudinal results and a better capability to detect small variations of thalamic volumes, as shown by the results for MIST.
Disclosure: This study was partially supported by Fondazione Italiana Sclerosi Multipla with a research fellowship (FISM 2019/BR/009) and a research grant (FISM2018/S/3).

EPO-605

MRI abnormalities in stiff person syndrome

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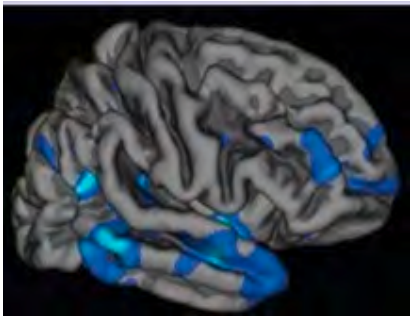
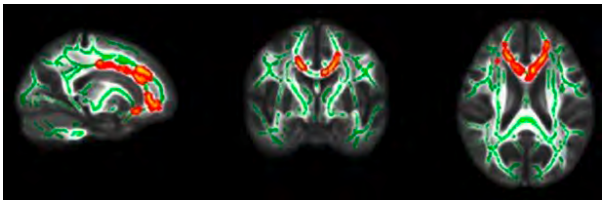
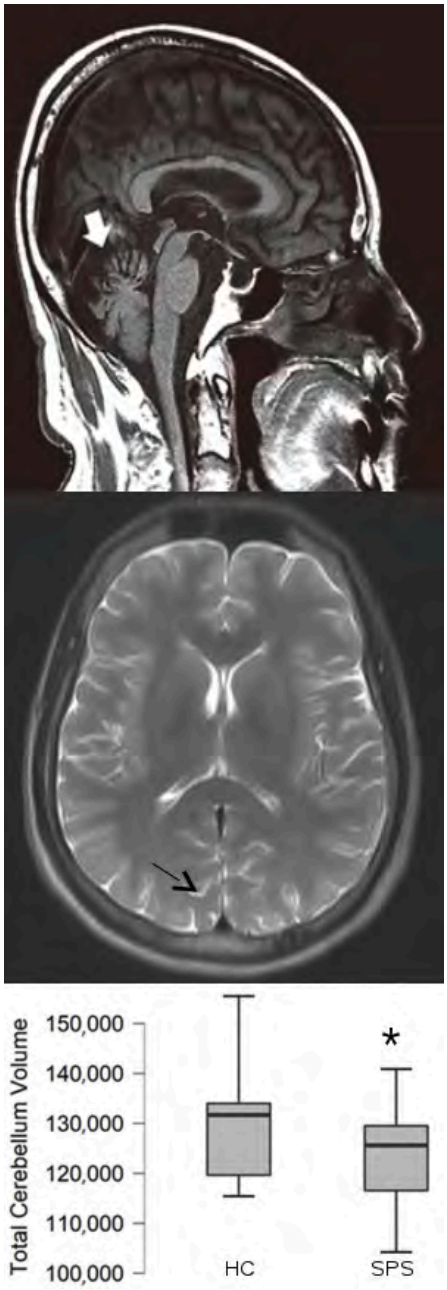
Background and aims: Stiff-person-syndrome (SPS) is a chronic autoimmune disease which mainly affects the central nervous system with spasms and stiffness, pain and psychological comorbidities. The diagnosis remains challenging due to the variety of symptoms, and conventional brain imaging contribution to the diagnosis is often limited. Magnetic resonance imaging (MRI) studies on SPS are lacking so far.
Methods: 25 SPS patients were examined by a neurologist, underwent questionnaires about chronic pain and were compared to 25 sex and age matched healthy controls (HC). MRI was performed at 3 Tesla. For each participant we included a structural sequence, diffusion tensor imaging, resting-state functional MRI and proton magnetic resonance spectroscopy in the insular cortex.
Results: SPS patients had lower cortical thickness bilaterally in the prefrontal cortex in the region of superior frontal gyrus (SFG) in comparison to healthy controls. SPS patients indicated chronic pain in the GCPS. There was a negative correlation between the individual extent of pain according to the GCPS and cortical thickness in the bilateral SFG. GABA spectroscopy in the insular cortex revealed lower GABA in the SPS cohort compared to the HCs.



SPS patients show lower prefrontal and temporal cortical thickness



SPS patients had lower fractional anisotropy bilaterally in the prefrontal cortex



SPS patients with higher GAD antibody titer show more cerebellar atrophy

Conclusion: This study provides a comprehensive radiological description of the pain pathology associated with GAD positive SPS, using advanced MRI analyses. The findings of the SPS patients in cortical thickness match those of patients with chronic pain and social anxiety disorder. The radiological peculiarities of the patients in our cohort, by identifying the precise structures affected, can provide a better understanding of the pathophysiology and the development of the chronic pain.
Disclosure: Nothing to disclose.

EPO-606

Multishell diffusion-weighted MRI characterization of chronic active lesions in Multiple Sclerosis

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Background and aims: Chronic active Multiple Sclerosis (MS) lesions, seen on susceptibility-weighted MRI as Paramagnetic Rim Lesions (PRL), are associated with increased clinical disability and axonal damage. Diffusion MRI (dMRI) can characterize in vivo PRL's tissue damage, however the tissue microstructure specificity of dMRI models is limited. Here, we characterized PRL's microstructure using 4 different models, including one novel dMRI model: Microstructure Fingerprinting (MF).
Methods: 367 lesions (202 PRL and 165 non-PRL) were segmented in 44 MS patients (27 relapsing-remitting, 11 secondary progressive, 6 primary progressive). For each lesion, we calculated volume, quantitative T1 values and diffusion parameters (Table 1) derived from 4 dMRI models: Diffusion Tensor Imaging (DTI), Neurite Orientation Dispersion and Density Imaging (NODDI) and DIstribution of Anisotropic MicrOstructural eNvironments in DWI (DIAMOND) and MF.
Results: PRL were bigger ($p<0.001$) and featured higher T1-values ($p<0.001$) vs non-PRL. DTI and DIAMOND models showed lower fractional anisotropy, higher mean diffusivity and radial diffusivity in PRL vs non-PRL ($p<0.001$). NODDI and MF models showed lower neurite density index and weighted fibre volume fraction ($p<0.001$), suggesting overall impaired axonal integrity/density in PRL vs non-PRL (Table, Figure).

	PRL *Mean ± SD*	**non-PRL** *Mean ± SD*	*p*
Volume, mm^3	228,673 ± 290,301	102,998 ± 112,540	< 0,001
T1, ms	1529,872 ± 284,678	1236,189 ± 217,452	< 0,001
DTI_AD, mm^2/s	0,00101 ± 0,00018	0,00096 ± 0,00019	< 0,001
DTI_FA	0,35872 ± 0,11089	0,44450 ± 0,12704	< 0,001
DTI_MD, mm^2/s	0,00074 ± 0,00014	0,00064 ± 0,00013	< 0,001
DTI_RD, mm^2/s	0,00060 ± 0,00015	0,00047 ± 0,00014	< 0,001
NODDI_fExtra	0,58044 ± 0,10657	0,48462 ± 0,10705	< 0,001
NODDI_NDI	0,27335 ± 0,08745	0,33077 ± 0,10099	< 0,001
NODDI_fIso	0,14599 + 0,10826	0,18461 ± 0,09603	< 0,001
NODDI_odi	0,25121 ± 0,08352	0,23366 ± 0,07619	0,097
DIAMOND_wAD, mm^2/s	0,00182 ± 0,00029	0,00175 ± 0,00028	0,018
DIAMOND_wFA	0,54310 ± 0,12855	0,63083 ± 0,13551	< 0,001
DIAMOND_wMD, mm^2/s	0,00107 ±0,00016	0,00095 ± 0,00017	< 0,001
DIAMOND_wRD, mm^2/s	0,00070 ± 0,00018	0,00054 ±0,00020	< 0,001
MF_frac_CSF	0,26621 ± 0,15471	0,20683 ± 0,14503	< 0,001
MF_frac_ftot	0,73357 ± 0,15500	0,79317 ± 0,14503	< 0,001
MF_fvf_tot	0,14803 ± 0,06889	0,20792 ± 0,08798	< 0,001
MF_wfvf	0,19508 ± 0,06413	0,25581 ± 0,08374	< 0,001

Table: Mean volume, T1 times and diffusion parameters of DTI, NODDI, DIAMOND and MF models for PRL and non-PRL lesions. Abbreviations: DTI_AD: DTI Axial Diffusivity DTI_FA: DTI Fractional Anisotropy DTI_MD: DTI Mean Diffusivity DTI_RD: DTI Radial Diffusivity NOD

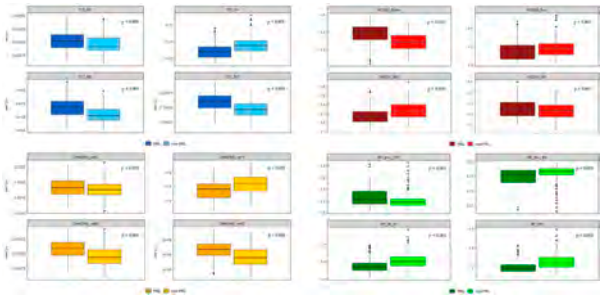

Figure: Boxplot of average DTI (blue), NODDI (red), DIAMOND (yellow) and MF (green) dMRI model parameters in PRL and non-PRL lesions. Abbreviations: DTI_AD: DTI Axial Diffusivity DTI_FA: DTI Fractional Anisotropy DTI_MD: DTI Mean Diffusivity DTI_RD: DTI Radial D

Conclusion: Consistent with previous data, we show that PRL are characterized by higher axonal damage when compared to non-PRL. Results derived from the MF model are in line with those obtained with DTI, NODDI and DIAMOND, suggesting that this novel dMRI model can be used to study MS lesion pathology. As an advantage, the MF model framework allows further methodological improvement, using more accurate white matter-diffusion simulations.

Disclosure: Authors have no relevant disclosures related to this submission.

EPO-607

Retinal ischemia due to different stages of atherosclerosis

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Background and aims: Ischemic stroke (IS) and retinal ischemia (IR) share similar vascular risk factors, but differ in response to intravenous thrombolysis and the risk for subsequent stroke or restroke. High resolution orbital color-coded sonography (OCCS) is an easy to use diagnostic tool in the diagnosis of this small vessel. This study characterized the cardiovascular risk profiles of patients with central retinal artery occlusion (CRAO).

Methods: We performed a retrospective analysis on the detailed cardiovascular risk factors and neuroimaging data in 94 patients with IR. CRAO were further divided based upon their appearance on OCCS as hyperechoic, termed ssCRAO ("spot sign") or hypoechoic (heCRAO). Statistical analyses were performed with Kruskal-Wallis, Mann-Whitney-U and $\chi 2$ testing. P-values were corrected for multiple testing and considered significant if < 0.05.

Results: 26 patients were diagnosed as heCRAO and 68 as ssCRAO. Patients with ssCRAO were significantly older. Male patients were overrepresented in the cohort as whole. ssCRAO was associated with more severe atherosclerosis whereas heCRAO patients had more echolucent atherosclerosis. The presence of atrial fibrillation did not differ statistically significant between the subgroups and most patients with atrial fibrillation were on ongoing oral anticoagulation while suffering CRAO.

Conclusion: Based upon these findings, we postulate that emboli in atherosclerosis may be one of the most important, if not the main embolic source, for IR. By contrast, the contribution of atrial fibrillation in IR etiology remains questionable. These findings have implications for secondary stroke prevention suggesting more intense treatment of atherosclerotic risk factors.

Disclosure: Nothing to disclose.

Movement disorders 4

EPO-608

Extensor dystonia in young-onset Parkinson's disease

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Background and aims: Extensor dystonia (ED), in the form of retrocollis or extensor truncal dystonia (ETD), has been scarcely reported in idiopathic Parkinson's disease (PD). Studies suggest an increased presence in advanced stages of PD but its exact prevalence remains unknown (Kashihara et al. 2013; Thiel et al. 2022). We describe three cases of ED in young-onset PD.
Methods: A search was conducted in our outpatient database for PD patients who presented ED at any point during their follow-up.
Results: Three female patients (of ages 65, 66, and 69) with PD onset at ages 44, 47 and 52, respectively, fulfilled above criteria. The first two underwent bilateral subthalamic deep brain stimulation (DBS) at 11 and 14 years from PD onset. One had retrocollis only during off periods and responded to oral dopaminergic drugs and later to DBS. The other had continuous ETD that worsened during off periods with a clear tendency to arching the back but was able to walk unassisted. The third patient had painful ETD that conditioned severe postural instability and multiple falls. Botulinum toxin injection in mainly affected muscles showed only partial response. She needed a walking frame and was dependent for basic activities.

Figure: 66 year old female patient with off period retrocollis.

Conclusion: ED significantly affects quality of life and motor function of PD patients. Most reported cases are from young-onset PD but systematic studies to determine prevalence and associations are lacking. As these cases suggest, different mechanism might be involved, and treatment should be individualized.
Disclosure: We have no actual or potential conflict of interest in relation to this presentation.

EPO-609

Abstract withdrawn

EPO-610

Enrolment characteristics for patients entering a Phase 3 study of subcutaneous levodopa/carbidopa infusion with ND0612

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Background and aims: The BouNDless study (NCT04006210) compared the efficacy, safety, and tolerability of subcutaneous levodopa/carbidopa (LD/CD) as an investigational ND0612 24-hour infusion versus oral immediate-release (IR)-LD/CD in patients with Parkinson's disease (PwP) experiencing motor fluctuations. Here we report patient enrollment characteristics; primary results will be available in 2023.
Methods: Following screening, PwP on ≥4 doses/day of oral LD/dopa-decarboxylase inhibitor (LD ≥400mg/day) and experiencing ≥2.5h daily OFF-time were consented and enrolled. They entered a 4-6 week open-label adjustment period during which oral LD formulations and COMT inhibitor doses were converted to equivalent doses of IR-LD/CD and then adjusted to optimal clinical effect.

Patients then entered an 4-6 week open-label ND0612 conversion period in which IR-LD/CD was replaced by ND0612 (LD/CD dose up to 720/90mg/day) with adjunct IR-LD/CD, as required, and adjusted until this combination regimen was optimal. Patients then entered a 12-week, double-blind, double-dummy period, during which they were randomized (1:1) either to their optimized regimen of ND0612 infusion (plus IR-LD/CD), or to the optimized IR-LD/CD-only regimen.

Results: Enrollment characteristics of randomized patients (n=259) were similar to other clinical trials in PwP experiencing motor fluctuations refractory (mean±SD age: 63.5±9.0y; 63.7% male; diagnosed 9.6±4.3y; motor fluctuations 4.5±3.3y, mean OFF time 6.1±1.7h). Levodopa equivalent daily doses at enrollment were 1029mg; 86% patient were receiving adjunct Parkinson's medications, mainly dopamine agonists (63%).

Conclusion: Enrollment characteristics of patients randomized in the BouNDless trial are consistent with those observed in other clinical studies in PwP experiencing motor fluctuations.

Disclosure: Funded by NeuroDerm. Olivier Rascol, Alberto Albanese, Aaron Ellenbogen, Joaquim Ferreira, Tanya Gurevich, Sharon Hassin, Jorge Hernandez-Vara, Stuart Isaacson, Karl Kieburtz, Peter LeWitt, Lydia Lopez Manzanares, C. Warren Olanow, Rajesh Pahwa, Werner Poewe, Harini Sarva, Fabrizio Stocchi, Alberto Espay, and Navin Giladi are members of the BouNDless study group. Tami Yardeni, Liat Adar, Laurence Salin, Nelson Lopes, Nissim Sasson, and Ryan Case are employed by NeuroDerm.

EPO-611

Dystonia management in four European countries: evaluation of patients' experience

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Background and aims: A long time for diagnosis and treatment of dystonia was reported. The aim of present study was to evaluate dystonia management from patients' own experience in four European countries with different health care systems regarding the delivery of services and education.

Methods: Dystonia survey was undertaken using a structured on-line questionnaire to assess patients' own experience of dystonia management and treatment in Croatia, Italy, Germany and the UK. The questionnaire was composed of 30 questions divided into three parts: part I. general questions part II. specific questions as disease duration, type of DS, experience with a first initial visit to GP etc.; part III. type of therapy, satisfaction/discontinuation of therapy.

Results: A total of 1,645 patients responded to survey: 379 (12.2%) from Croatia, 340 (10.9%) from Germany, 175 (5.6%) Italy and 751 (24.1%) from UK. Women outnumbered men in all countries cervical dystonia was the most prevalent type. Most patients (around 50%) from all countries were 41-50/51-60 years old. Although most patients across countries were diagnosed within 2 years since the first symptoms, significant number waited more than 10 years (7–15%). In comparison to UK participants Italian and Croatian patients reported shorter time to diagnosis. Croatian patients have experienced a 'more adequate' initial GP assessment.

Conclusion: Sub-analysis of Germany, Italy and the UK did not show significant differences in the current state of dystonia management among countries, although significant difference exists in the healthcare system.

Disclosure: Nothing to disclose.

EPO-612

CACNA1A variant can be associated with generalized dystonia

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Background and aims: Mutations in the CACNA1A gene have been correlated with episodic ataxia type 2, spinocerebellar ataxia type 6, and familial hemiplegic migraine type 1. Dystonia is not enlisted among the typical clinical manifestations of CACNA1A mutations. We report the case of a patient with a novel missense mutation of the CACNA1A gene presenting headache, head and arm tremor, slowly progressive dystonia associated with episodic painful focal dystonic attacks.

Methods: A 57-year-old woman was referred because of neck dystonia associated with head and arms tremor since the age of 15 years. At the age of 47, in 2012, she presented an increase in tremor amplitude led to suspect of essential tremor. In 2019 she showed mild dysarthria, right torticollis with dystonic head tremor and both arms, and gait with dystonic head posture. Moreover, she reported paroxysmal dystonia attacks (3–4 per week) of the lower extremities, occurring without apparent provoking factors.

Results: Dystonia's genetic panel showed a heterozygous mutation in the CACNA1A gene (NM_023035.2:c.1630C>T p.(Arg544Trp). In 2020 due to worsening dystonia,, she underwent evaluation for Gpi-DBS surgery. However, a brain MRI showed cortical atrophy, and she was excluded.

Conclusion: CACNA1A mutations are associated with a broad spectrum of neurological manifestations, with a frequent overlap of headache and neurological signs related to the involvement of the cerebellum. Few dystonic symptoms have been reported so far; however, the link between dystonia and CACNA1A mutations is increasingly evident, although the prevalence, incidence, and pathogenesis still need to be elucidated.
Disclosure: Nothing to disclose.

EPO-613

Au nanoclusters loaded with GLP-1 agonist as a potential treatment for Parkinson's Disease

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Background and aims: Parkinson's Disease (PD) is the second most common neurodegenerative disease worldwide. To date, the drugs used for PD are only designed to treat symptoms and ultimately, patients will develop a cumulative disability and neuronal loss. In previous studies exendin-4, a glp1 agonist tested in PD mice models was found to improve neurotoxin-induced motor alterations and chronic inflammation in the brain. In order to aim for success in drug transportation and take advantage of the neuroprotective effects of previously reported effects of gold nanoparticles we treated SH-SY5Y cells with Au loaded -4 nanoclusters with exendin on a PD cell model.
Methods: To evaluate the effect of the nanosystem four groups were tested and treated for 72 hours. DAPI staining, Neurite length measurements, and LDH assays were performed on the groups. XRD, TEM, and FTIR microscopy were used for nanoparticle characterization.
Results: When analyzed with TEM and XRD techniques, the gold nanoparticles showed a 1–3 nm size. The nanosystem exendin-nanoparticle reversed the oxidative damage in a PD SH-SY5Y cell model. Following light microscopic analyses, the stained cells with DAPI showed similar cell survival compared to the control cell group. The nanosystem displayed neuronal protection on the 6-OHDA PD model.
Conclusion: GLP-1 agonists combined with nanotechnology have not yet been studied in Parkinson's Disease before, we hope to open a new research perspective into the treatment options for PD. Targeting mitochondrial and oxidative stress relief while using nanotechnology might improve the therapeutic treatment for PD patients and help provide better medical results.
Disclosure: Nothing to disclose.

EPO-614

Absent significant association of oral levodopa with polyneuropathy in Parkinson's disease

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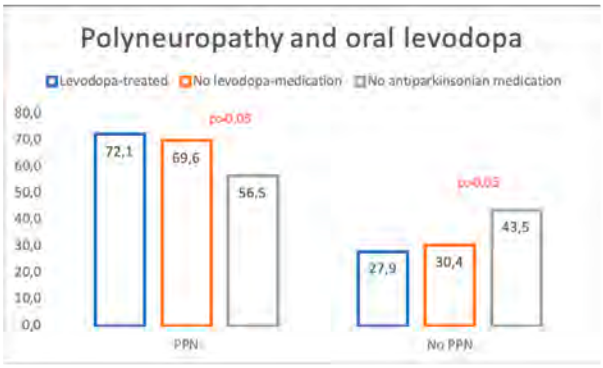
Background and aims: Peripheral polyneuropathies (PPN) have a prevalence of about 8–10% in the elderly in general population. Some studies suggest an increased prevalence of PPN in patients with Parkinson's disease (PD) and an association of PPN with oral levodopa treatment.
Methods: We assessed clinical and electrophysiological data of 692 consecutive patients with idiopathic PD, admitted to our clinic between 2016 and 2019.
Results: Of 692 patients, 73,26% had clinically PPN, mostly a sensory or sensorimotor axonal, moderate or severe one. Of 623 patients (90.02%) received diverse antiparkinsonian medication, 567 (91.0%) had oral levodopa. Of 69 patients with no antiparkinsonian medication, 57 (82.61%) had PPN. Of the patients receiving oral levodopa, 409 (72.13%) had PPN ($p>0.05$). Of the 56 patients, receiving diverse antiparkinsonian medication other than levodopa, 39 (69.4%) had PPN. ´Vitamin B12 blood levels below 300pg/ml were more common in PPN-positive PD patients (40.62% at the time point of PPN first diagnose) than in PPN-negative PD patients (23.78%). 40.0% of levodopa-naive PD patients had low blood level of the vitamin B12, compared to 40.46% of levodopa-treated PD patients ($p>0.5$). In tested patients without antiparkinsonian medications at all, 38.18% patients had low vitamin B12 blood level.
Conclusion: Peripheral polyneuropathy is very common in Parkinson's disease patients. Typically, it is a moderate or severe, sensory or sensorimotor axonal polyneuropathy. A low vitamin B12 blood level was more common in PPN-positive PD patients. No significant association between oral levodopa or other antiparkinsonian medication and PPN in PD patients was found.
Disclosure: Nothing to disclose.



EPO-615

Challenges in Wilson´s disease therapy: therapy initiation, compliance, comorbidities and survival

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Background and aims: The aim of the study is to highlight the challenges in long-term treatment of patients with Wilson´s disease occurring during their entire life-span.
Methods: In a combined retrospective and cross-sectional mono-centric study demographical, treatment related and clinical and biochemical data were extracted from the charts of 110 patients with Wilson´s disease.
Results: Rapid recovery of liver dysfunction and prolonged recovery of neurological symptoms were observed after initiation of WD-specific therapy with up to 900mg DPA and up to 1,200mg Trientine during the first two years of treatment. During the course of treatment about one third of the patients presented with compliance problems reaching from low adherence to medication regimens to complete cessation of medication with lethal outcome. More than 20% of the patients had mild to moderate side effects of WD-specific treatment and more than 70% of the patients developed neurological and non-neurological comorbidities interfering with WD. About 4% of the patients developed malignancies as hepatocellular carcinoma. In contrast to previous reports life-expectancy in WD appears to be reduced.
Conclusion: Throughout their entire life-span patients with WD have to face a variety of challenges and need careful therapy monitoring.
Disclosure: The authors declare no conflicts of interest associated with this research work.

EPO-616

First-year Treatment Intensity and Prognosis in Early Parkinson's Disease: A Retrospective, Longitudinal Study in Israel

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Background and aims: Given Parkinson´s disease (PD) heterogeneity, it is challenging to find associations between patients' characteristics and prognosis. We compared long term disease prognosis among people with Parkinson's Disease (PwPD) by treatment intensity in the first year after PD diagnosis.
Methods: This population-based, retrospective cohort study utilised data from a large health plan in Israel. Members were included if they had ≥1 PD diagnosis between 2005–2010. Index date was defined as the earliest PD diagnosis or anti-PD therapy initiation. PwPD were required to have ≥5 years' membership in the health plan prior to index date and up to 10 years of follow-up. Study population was divided into low and high treatment intensity groups based on levodopa-equivalent daily dose status during the first year post-index date (low [mild], <600 mg; high [intensive], ≥600 mg). Survival, comorbidities, and symptoms were evaluated and compared.
Results: We identified 2,525 eligible PwPD (mean [SD] age, 74.5 [10.7] years; males, 55.9%). Of those, 292 (11.6%; mean age, 75.4 [8.8] years; males, 65.1%) were intensively treated during the first year post-index date; 2,233 (88.4%, mean age, 74.4 [10.9] years; males, 54.7%) were mildly treated (Table). Compared with mild treatment, intensive treatment was associated with increased probability of death at 10 years (p<0.0001) (Figure). Additional results are forthcoming.

Table. Age and sex for overall PD population and by LEDD status in the first year

Characteristic		Low Dose (Mild Treatment) <600 mg LEDD n = 2233	High Dose (Intensive Treatment) >=600 mg LEDD n = 292	*P* value[a]
Age at index date	Mean (SD)	74.4 (10.9)	75.4 (8.8)	.074
	<55 (%)	113 (5.1)	11 (3.8)	.007
	55-65 (%)	286 (12.8)	19 (6.5)	
	65-75 (%)	641 (28.7)	100 (34.2)	
	>=75 (%)	1193 (53.4)	162 (55.5)	
Sex	Male (%)	1222 (54.7)	190 (65.1)	.001

[a]The statistical tests used were *t* test for continuous variables and chi square test for categorical variables.
LEDD, levodopa-equivalent daily dose.

Table. Age and sex for overall PD population and by LEDD status in the first year

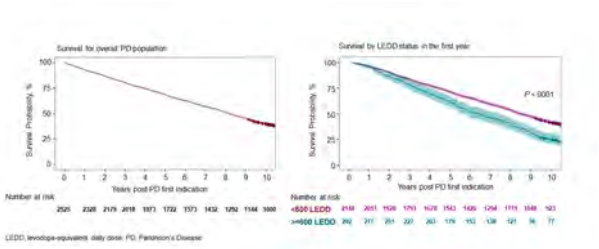

Figure. Survival curves for the overall PD population and for patients stratified by LEDD status in the first year.

Conclusion: PwPD who received intensive treatment early after diagnosis had a worse disease prognosis. The epidemiologic assessment of the early stages of PD in PwPD may help define diverse subgroups who may benefit from more timely and targeted therapeutic interventions.
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EPO-617

Motor resonance in early Parkinson's disease. A Near-Infrared Spectroscopy and EEG study

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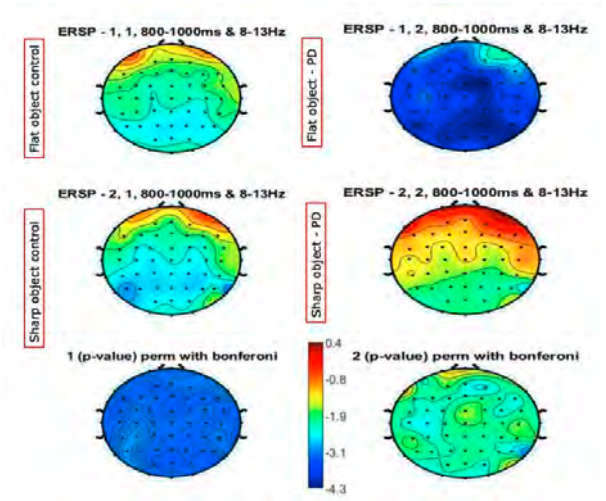
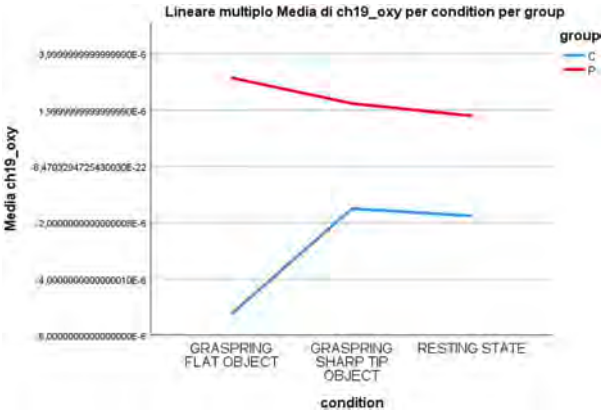
Background and aims: The observation of action seems to involve the generation of the internal representation of that same action in the observer, a process named Motor Resonance (MR).
Methods: The objective of this study was to verify whether an experimental paradigm of action observation in a laboratory context could elicit cortical motor activation. We recruited 21 early Parkinson's disease (PD) patients and 22 controls. Inclusion criteria for PD patients were diagnosis of Idiopathic PD at Hoehn-Yahr stage I-II, age between 40 and 80 years, MMSE>23, and absence of significant visual deficits. Participants were instructed to simply observe (Observation-only session) or to respond (Time-to-contact detection session) at the instant the agent performed a grasping action toward a graspable or ungraspable object. We used functional Near-Infrared Spectroscopy (fNIRS) with 20 channels on the motor and premotor brain areas and event-related desynchronization of alpha-mu rhythm.
Results: In both groups, response times were more accurate in graspable than ungraspable object trials, suggesting that motor resonance is present in PD patients. In the Time-to-contact detection session, the oxyhemoglobin levels and alpha-mu desynchronization prevailed in the graspable vs ungraspable object trials. In the resting state, the alpha mu desynchronization was more evident in PD patients than in controls.



EEG 8–13 Hz frequencies scalp distribution during observation session



f-NIRS, ΔHbO2 in channel 19 (grasping flat, grasping sharp tip, resting state)

Conclusion: This study demonstrates the preservation of MR mechanisms in early PD patients. The action observation finalized to a consequent movement can activate cortical networks in patients with early PD, suggesting early rehabilitation interventions taking into account specific observation paradigms, preceding motor production.
Disclosure: The authors declare no competing interests.

EPO-618

Changes in principal caregiver mood affects the mood of the Parkinson disease patient. The vicious cycle of illness.

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Background and aims: Although many studies have analyzed what factors contribute to caregiver burden in Parkinson´s disease (PD), there is currently no knowledge about how the status of the caregiver could impact the patient. The aim of this study was to analyze how the change in the caregiver´s status influences PD patients.

Methods: PD patients and their caregivers who were recruited from January/2016 to November/2017 from 35 centers in Spain from the COPPADIS cohort were included in the study (V0). They were evaluated again at 2-year follow-up (V2). Caregivers completed the Zarit Caregiver Burden Inventory (ZCBI), Caregiver Strain Index (CSI), Beck Depression Inventory-II (BDI-II), and EUROHIS-QOL 8-item index (EUROHIS-QOL8) at V0 and V2. Multivariate models were used to analyze the impact of the change from V0 to V2 (Δ) on the caregiver´s status over the change in the patient´s status.

Results: ΔBDI-II and ΔEUROHIS-QOL8 in the caregiver predicted ΔBDI-II (β=0.32; p<0.0001; R2=0.71) (Table 1) and ΔEUROHIS-QOL8 (β=0.39; p<0.0001; R2=0.68) in the patient (Table 2), respectively. Variables related to the caregiver were not associated with changes in the patient´s health-related QoL (ΔPDQ-39 [[39-item Parkinson's disease Questionnaire]) or autonomy for activities of daily-living (ΔADLS [Schwab & England Activities of Daily Living Scale]).

Conclusion: The change in the caregiver´s mood and global QoL was associated with the change in the patient´s mood and global QoL, respectively, independently of other variables of the disease influencing both patient´s aspects.

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	Univariate analysis			Multivariate analysis		
	β	95% CI	p	β	95% CI	p
Caregiver						
Δ BDI-II	0.42	0.40 – 0.77	<0.0001	0.32	0.27 – 0.67	<0.0001
Δ ZCBI	0.19	0.05 – 0.28	0.006	0.10	-0.02 – 0.22	0.125
Δ CSI	0.14	0.03 – 1.33	0.039	-0.03	-0.89 – 0.50	0.576
Δ EUROHIS-QOL8	-0.21	-7.97 – -1.67	0.003	0.20	1.74 – 8.13	0.003
Patient						
Δ EUROHIS-QOL8	0.22	0.07 – 0.40	0.006	-0.56	-9.34 – -5.95	<0.0001
BDI-II at baseline	0.19	-0.14 – -0.01	0.035	-0.36	-0.64 – -0.32	<0.0001

Dependent variable: change in the PD patient from V0 to V2 (Δ) in the BDI-II total score. β standardized coefficient and 95% IC are shown. [a], univariate analysis; [b], multivariate analysis (Durbin-Watson test=2.11; R^2=0.71). Only significant variables (p<0.01) from the patient in the multivariate analysis are shown. Covariates from the patient included were the change from V0 to V2 (Δ) in LEDD, UPDRS-III-OFF, UPDRS-IV, FOGQ, PD-CRS, NMSS, PDSS, QUIP-RS, NPI, VAS-PAIN, VAFS, ADLS, PDQ-39SI, EUROHIS-QOL8, and the score on the BDI-II at baseline.

ADLS, Schwab & England Activities of Daily Living Scale; BDI-II, Beck Depression Inventory-II; CSI, Caregiver Strain Index; FOGQ, Freezing Of Gait Questionnaire; LEDD, levodopa equivalent daily dose; Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD-CRS, Parkinson´s Disease Cognitive Rating Scale; PDQ-39, the 39-item Parkinson's disease Questionnaire Summary Index; PDSS, Parkinson's Disease Sleep Scale; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAS, Visual Analogue Scale; ZCBI, Zarit Caregiver Burden Inventory.

Table 1. Effect of changes in the caregiver over the change in mood in PD patients from the COPPADIS cohort after 2-year follow-up (n=192).

	Univariate analysis			Multivariate analysis		
	β	95% CI	p	β	95% CI	p
A) Δ PDQ-39SI						
Caregiver						
Δ BDI-II	0.19	0.10 – 0.62	0.006	0.16	0.01 – 0.54	0.047
Δ ZCBI	0.28	0.16 – 0.46	<0.0001	0.03	-0.13 – 0.20	0.671
Δ CSI	0.20	0.41 – 2.15	0.004	0.04	-0.72 – 1.20	0.818
Δ EUROHIS-QOL8	0.01	-3.89 – 4.64	0.863	0.13	-0.33 – 7.74	0.072
Patient						
Δ UPDRS-III	0.41	0.37 – 0.73	<0.0001	0.20	0.06 – 0.43	0.008
Δ NMSS	0.57	0.16 – 0.25	<0.0001	0.29	0.05 – 0.15	<0.0001
Δ ADLS	-0.48	-0.62 – -0.36	<0.0001	-0.25	-0.39 – -0.10	0.001
PDQ-39 at baseline	-0.20	-0.32 – -0.05	0.005	-0.20	-0.29 – -0.06	0.002
B) EUROSHIS-QOL8						
Caregiver						
Δ BDI-II	-0.14	-0.029 – -0.001	0.039	0.24	0.01 – 0.04	0.001
Δ ZCBI	-0.04	-0.011 – 0.006	0.530	0.02	-0.00 – 0.01	0.679
Δ CSI	-0.09	-0.078- 0.016	0.201	-0.03	-0.06 – 0.03	0.604
Δ EUROHIS-QOL8	0.41	0.454 – 0.878	<0.0001	0.39	0.49 – 0.89	<0.0001
Patient						
Δ BDI-II	-0.63	-0.053 – -0.037	<0.0001	-0.55	-0.03 – -0.66	<0.0001
EUROHIS-QOL8 at baseline	0.39	0.024 – 0.049	<0.0001	-0.37	-0.65 – -0.36	<0.0001

Dependent variable: change in the PD patient from V0 to V2 (Δ) in the PDQ-39 (A) and EROHIS-QOL8 (B). β standardized coefficient and 95% IC are shown. [a], univariate analysis; [b], multivariate analysis: A) Durbin-Watson test=2.07; R^2=0.51; B) Durbin-Watson test=2.02; R^2=0.68. Only significant variables (p<0.01) from the patient in the multivariate analysis are shown. Covariates from the patient included were the change from V0 to V2 (Δ) in LEDD, UPDRS-III-OFF, UPDRS-IV, FOGQ, PD-CRS, NMSS, PDSS, QUIP-RS, NPI, VAS-PAIN, VAFS, ADLS, and the score on the PDQ-39SI (A) and EUROHIS-QOL8 (B) at baseline.

ADLS, Schwab & England Activities of Daily Living Scale; BDI-II, Beck Depression Inventory-II; CSI, Caregiver Strain Index; FOGQ, Freezing Of Gait Questionnaire; LEDD, levodopa equivalent daily dose; Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD-CRS, Parkinson's Disease Cognitive Rating Scale; PDQ-39, the 39-item Parkinson's disease Questionnaire Summary Index; PDSS, Parkinson's Disease Sleep Scale; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAS, Visual Analogue Scale; ZCBI, Zarit Caregiver Burden Inventory.

Table 2. Effect of changes in the caregiver over the change in health-related and global QoL in PD patients from the COPPADIS cohort after 2-year follow-up (n=192).

EPO-619

Bilateral staged VIM thalamotomy for essential tremor

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Background and aims: Unilateral MRI-guided focused ultrasound (FUS) VIM thalamotomy has established efficacy in tremor relief. However, data regarding the safety and efficacy of bilateral staged treatments is scarce. We report our preliminary results on the safety and efficacy of bilateral staged FUS VIM thalamotomy in essential tremor (ET) patients with severe medication resistant tremor.

Methods: Five patients underwent bilateral staged FUS VIM thalamotomy. Primary outcome was change in tremor score relative to baseline using the Clinical Rating Scale for Tremor (CRST). Secondary outcome was change in quality of life (QOL) in ET (QUEST) score relative to baseline. Adverse event profile was collected.

Results: Tremor significantly improved following bilateral treatments from a median score of 33 at baseline to median score of 8 at 1 month, following second treatment p=0.006. Quest score improved from a median score of 36 before FUS to a median score of 7 at 1 month, p=0.02. All 5 patients experienced mild transient ataxia that resolved (2 days-12 weeks). One patient reported burning tongue sensation that did not resolved at his 1 month visit. One patient reported asthenia and another reported mild facial nerve palsy, both resolved after 3 weeks.

Conclusion: Our preliminary results suggest that staged bilateral MRI-guided focused FUS thalamotomy is safe and effective. It improves tremor and quality of life of ET patients with severe medication resistant tremor. Larger studies and longer-term follow-up are needed to validate these findings.

Disclosure: Nothing to disclose.

EPO-620

Characterization of gait profiles in patients with atypical parkinsonian syndromes

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Background and aims: Impaired gait and postural instability are common symptoms in atypical parkinsonism. Therefore, an early detection of abnormal gait patterns is important for fall prevention. This prospective, multicentric study aims to systematically characterize gait, clinical and cognitive functions of patients with multiple system atrophy (MSA), progressive supranuclear gaze palsy (PSP) and idiopathic Parkinson's disease (IPD).

Methods: Patients were included with stable medication without comorbidities affecting mobility. All participants were assessed using the MDS-UPDRS for motor function and the Montreal Cognitive Assessment (MoCA) for cognition. To characterize mobility, we used sensor based gait analysis with a standardized test battery including a 20-meter-walk-test and a Timed-Up-and-Go (TUG) test.

Results: We assessed 22 MSA, 19 PSP and 39 IPD patients. MSA and PSP had shorter disease duration (p<0.001) and greater motor impairment (MDS-UPDRS III p<0.001) compared to IPD. PSP patients were cognitively most impaired (MoCA p<0.003). Significant differences in 20-meter-walk-test were detected in stride length (mean (m): MSA=0.93, PSP=1.10, IPD=1.27; p<0.001), gait velocity (mean (m/sec): MSA=0.83, PSP=0.88, IPD=1.14; p<0.001) and heel strike angle (mean (°): MSA=-8.0, PSP= -15.5, IPD=-17.9; p<0.001). Parameters directly correlated with fall frequency. The TUG was completed faster by IPDs compared to MSA and PSP patients (p<0.001).

Conclusion: These preliminary data show significantly impaired gait in patients with atypical parkinsonism, correlating with the severity of motor impairment and the frequency of falls. Sensor-based gait analysis is an effective and rater-independent way to objectify gait disturbances and fall-risk. Especially in the context of clinical trials, this can be used as a supportive outcome measure.
Disclosure: Nothing to declare.

EPO-621

Iron deposition in thalamic subregions in early drug-naïve Parkinson's disease patients with mild cognitive impairment

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Background and aims: Iron deposition using Quantitative Susceptibility Mapping (QSM) has been reported in several cortico-subcortical areas within the dopaminergic pathways in patients with Parkinson's disease(PD)and a relationship with cognitive decline has been proposed. Mild cognitive impairment (MCI) is a common non-motor symptom in PD and is considered a risk factor for development of dementia. We aimed at exploring the QSM signature underling MCI in drug-naïve PD patients, focusing on several areas, particularly on the thalamic subregions.
Methods: 3T MRI images of 59 drug-naïve PD patients (20 PD-MCI and 39 PD-noMCI) were analyzed and compared. QSM values were extracted from several subcortical deep gray matter nuclei and 16 thalamic subregions. A partial correlation analyses were run between MRI metrics and clinical data. A ROC curve was performed to test the ability of QSM values in distinguishing PD-MCI from PD-noMCI.
Results: PD-MCI patients showed higher susceptibility values in right subthalamus, in bilateral inferior pulvinar and in bilateral ventral posterolateral thalamus. Moreover, higher susceptibility values in the thalamus correlated with worse motor/cognitive severity and quality of life in patients. ROC curve analysis showed that QSM values extracted from left inferior pulvinar and right ventral posterolateral thalamus could significantly identify the presence of MCI in drug-naïve PD.
Conclusion: This study provides evidence of higher iron deposition within lateral and posterior regions of thalamus in PD patients with MCI patients compared to those without. These findings may reflect the presence of diffuse neuropathological changes occurring at the disease onset, potentially leading to altered cognitive processing and sensorial perception/integration in PD patients.
Disclosure: Nothing to disclose.

EPO-622

Real-World Local Field Potential Dynamics in Patients with Parkinson's Disease

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Background and aims: To determine spectral peak and band power dynamics over time in patients with Parkinson's disease (PwPD) and deep brain stimulation.
Methods: A total of 26 PwPD (age: 67.0[56.8–73.1] years; sex: 8 females; disease duration: 12.0[7.8–15.0] years) with repeated local field potential (LFP)recordings (days between recordings: 33.9[11.0–65.1] were included in this analysis. PwPD with LFPrecordings within 2-weeks of macroelectrode implant were labeled as Acute (n=12). Peak amplitude and frequency, in addition to alpha, low-beta, high-beta, and gamma band power, were calculated for each hemisphere.
Results: Peaks were detected in 41/51(80.4%) nuclei with recordings at the initial session and 43/51(84.3%) nuclei at follow-up. Of the patients with bilateral implants (n=26), 24(92.3%) at visit 1 and 25(96.2%) at visit 2 had at least 1 hemisphere with an identifiable peak. No differences were seen in peak amplitude (left-hemisphere: p=0.695; right-hemisphere: p=0.162) and frequency (left-hemisphere: p=0.320; right-hemisphere: p=0.576) between visits for the cohort. Right-hemisphere low-beta (p=0.018) and bilateral gamma (left-hemisphere: p=0.036; right-hemisphere: p=0.014) band power demonstrated a significant increase at follow-up. No differences were found in the relative change of peak amplitude, frequency, or band power between patients with acute and chronically implanted macroelectrodes (p>0.05).
Conclusion: Our findings provide early, real-world evidence of LFP peak and band power stability in PwPD. Importantly, peak characteristicsdemonstrated no differences between visits or between patients with acute and chronic macroelectrode implants. Moreover, peak detection was stable across timepoints. These findings have implications as LFPsare proposed to be a biomarker for guiding DBSprograming and novel stimulation patterns.
Disclosure: A. Singer, C. Sannelli and N. Morelli are employees of Medtronic, Minneapolis, MN, USA. A. Fasano, H. Mure, G. Oyama and T. Witt are Principal Investigators of the Medtronic Product Surveillance Registry.

Movement disorders 5

EPO-623

Complications of gastrojejunostomy in patients with Parkinson's disease on levodopa/carbidopa intestinal gel treatment

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Background and aims: One of the treatment options of advanced Parkinson's disease is the administration of levodopa/carbidopa intestinal gel (LCIG) through percutaneous endoscopic gastrostomy with jejunal extension (PEG-J), potentially associated with various complications.
Methods: We retrospectively analyzed complications of inserted PEG-J in patients with LCIG in years 2009-2022 at the 2nd Department of Neurology CU in Bratislava (Movement Disorders Centre).
Results: 80 PEG-J were introduced at our centre, two patients died within 30 days of aspiration bronchopneumonia. Of the remaining 78 patients, 47 patients have completed the treatment – 32 patients died, six patients decided to terminate LCIG at their own request, six for non-cooperation, one for skin phlegmon in the PEG-J insertion area, one for buried bumper syndrome and one for gastrointestinal discomfort. Median (min-max) of LCIG treatment duration was 3 (0–11) years and had 2 (0–9) complications per patient. A total of 190 PEG-J revisions were carried out: 42 cases for the inner tube knotting, 37 for the inner tube disconnecting, 31 for the inner tube occlusion, 19 for the inner tube dislocation, 12 for accidentally pull out of the tube, 11 for leakage in the insertion area, eight for malfunction of connectors, two for leakage of the inner tube and 28 patients for PEG-J wear or the cause of the deterioration has not been identified.
Conclusion: Despite frequent complications with need repetitive gastrofibroscopies, less than 10% of patients were finished the treatment for dissatisfaction.
Disclosure: Nothing to disclose.

EPO-624

Managing Parkinson's Disease during pregnancy: A case report

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Background and aims: Since only 5% of cases of Parkinson's disease (PD) present before the age of 40, pregnancy is a rare but feasible occurrence with only a few cases reported.
Methods: A 38-year-old patient with a familiar PARK6 form of PD diagnosed at 25-year-age became pregnant while receiving 800/100 mg/day of L-DOPA/carbidopa (LD/CD) and 6mg of rotigotine. She became aware of her pregnancy at week 23, while associating significant worsening of motor fluctuations with wearing-off and dystonic postures during off period. LD/CD was increased up to 1200/150 mg/day with significant improvement of symptoms, returning to her previous motor situation. Rotigotine was maintained. At 39 gestational weeks she had a cesarean delivery because of podalic presentation. The newborn showed no malformations and is healthy at 6 months follow-up.
Results: There is little information about the effects of pregnancy on PD. Most studies suggest it can worsen its symptoms due to changes in hormonal production and pharmacological metabolism. Knowledge regarding anti-pakinsonian drugs during pregnancy is very limited, with LD being the first-line treatment since it has not been associated with significant adverse effects. Dopamine agonists are thought to be safe, with no reports of rotigotine usage during pregnancy in PD in the literature.
Conclusion: Pregnancy in PD patients is uncommon, with limited information published about its effects and management. We present the case of a pregnant PD patient who received anti-parkinsonian treatment with no complications during pregnancy or the newborn's health.
Disclosure: The authors report no sources of funding and no conflicts of interest related to this presentation.

EPO-625

First description of Episodic kinesigenic dyskinesia 1 with epilepsy in a large Moroccan family with the PRRT2 mutation

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Background and aims: Episodic kinesigenic dyskinesia 1 (EKD1, MIM≠128200), more commonly called paroxysmal kinesigenic dyskinesia (PKD), is a rare movement disorder disease, very heterogeneous clinically and characterized by recurrent and brief attacks of involuntary movement triggered by sudden voluntary movement without alteration of consciousness

Methods: A large family of Moroccan origin (RBT-ELB), with four affected siblings with suspicion of kinesigenic dyskinesia, was recruited in the department of Clinical Neurophysiology of Hôpital des Spécialités of Rabat (Morocco).

Results: We report the first description of PKD in a Moroccan family with the c.649dupC mutation in PRRT2 gene found in 4 patients. Five affected family members were identified (one female and 4 mans) with age of onset around puberty except for one who presented seizures during his first year of life. PKD manifested as brief ballic and/or dystonic attacks, precipitated by sudden movements with variable severity and frequency amongst affected family members. The consciousness was fully preserved during the attacks. Nevertheless, epileptic manifestations were associated with the dyskinetic attacks in 3 cases. The disease course was favorable using carbamazepine and two patients did not seek pharmacological treatment.

Conclusion: Epilepsy and other paroxysmal disorders have already been described in PKD patients with PRRT2 gene mutation. The epileptic phenotypes frequently reported are infantile convulsions with choreoathetosis syndrome ICCA), benign familial infantile seizures. Interestingly, the index patient experienced an adult-onset epilepsy, in addition to the typical attacks of kinesigenic dyskinesia, which is not a common finding in the literature

Disclosure: Nothing to disclose.

EPO-626

Cardiovascular, pelvic and laryngeal functions in multiple system atrophy: a neurophysiological comparative study

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Background and aims: Cardiovascular dysfunction is a prominent manifestation of autonomic failure in multiple system atrophy (MSA). The electromyographic finding of neurogenic damage of the external anal sphincter (EAS) corroborates Onuf's nucleus degeneration in MSA. Electrophysiology is also useful to detect vocal cord correlates of stridor, which contributes to the poor prognosis of these patients. It is unclear whether the neurodegenerative process evenly involves the different areas underlying the variety of symptoms in MSA. In this retrospective study, we explored the links between the clinical and neurophysiological correlates of vagal and sympathetic cardiovascular impairment, pelvic dysfunction, laryngeal abnormalities, parkinsonism, and cerebellar ataxia in MSA patients.

Methods: 61 patients diagnosed as clinically established MSA performed clinical evaluation, cardiovascular reflex tests, and EAS electromyography. Subgroups of 56 and 42 patients also underwent 24-hour blood pressure monitoring and laryngeal electromyography, respectively. In particular, we identified the presence of neurogenic damage and the specific electromyographic pattern of EAS and vocal cord muscles according to previously published electrophysiological classifications.

Results: The multivariate analyses by means of Spearman's rho coefficient did not show any correlation among parameters deriving from cardiovascular reflex tests, nocturnal blood pressure profiles, electrophysiological features of EAS and vocal cord muscles, and severity of motor impairment.

Conclusion: It could be speculated that the neuronal loss within Onuf's nucleus, intermediolateral cell columns, nucleus ambiguus, striatum and cerebellum might not go in parallel in MSA. The multifaceted neurodegeneration may indeed involve several regions to varying degrees or at different disease stages.

Disclosure: Nothing to disclose.

EPO-627

Subjective quality of life (QoL) in patients with Parkinson's disease (PD) - PDQ39 and SEIQol (5-year follow-up)

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Background and aims: PDQ39 (Jenkinson et al., 1995, 1997) is commonly used tool in PD but often doesn't reflect the subjective QoL (e.g. income, partnership...). In a 5-year follow-up study with PD patients, we compared PDQ39 and SEIQoL (McGee et al., 1991) with respect to acceptance, drop-out rates and the most important domains. We aimed to analyse whether there is a correlation between PDQ-39 and SEIQoL sum-scores. Additionally, we examined the overlap between aspects nominated in SEIQoL and domains captured by PDQ-39.
Methods: 31 patients (9 female, mean age at BL 67.23 (±5.95 years) disease duration 3.87 (±3.98 years)) were analysed and assessed at baseline and over a 5-years. PDQ-39 consists of eight domains, from which a sum-score can be calculated (0=best value, 100=worst possible value). SEIQoL invites each patient to nominate 5 aspects and to weight those. Correlations between PDQ-39 and SEIQoL sum-scores were calculated using Spearman's Rank correlations and mixed linear model (GLMM).
Results: The GLMM showed a significant association of p=0.0402 between PDQ-39 and SEIQoL sum-scores. This significance however vanished once LED was added as a control variable. SEIQoL aspects revealed the relevance of social environment and social relationships. PDQ-39 domains showed the worst score in cognition. SEIQoL: Social environment 14%, autonomy 13%, health 11% PDQ39: cognition 35%, stigma 30%, mobility 12%
Conclusion: The disease-related and individual QoL in this analysis did not overlap. Therefore, both instruments can complimentary be used in QoL research of PD patients.
Disclosure: Nothing to disclose.

EPO-628

Social cognition and emotional processing in functional movement disorders

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Background and aims: It is unknown how potentially altered processing of social information may affect the clinical presentation and severity of functional movement disorders (FMD). Our objective was to assess the social cognition (Theory of Mind) and emotional processing (alexithymia) in FMD patients.
Methods: Twenty one patient with clinically established FMD and 19 age, sex and education matched patients with "organic" movement disorders (OMD) underwent a thorough evaluation of psychiatric and cognitive characteristics. Faux Pas situation recognition stories and images for Reading the Mind in the Eye Test (RMET) were used to assess the ToM, while 20-item Toronto Alexithymia Scale (TAS-20) was used for alexithymia analysis.
Results: Compared to OMD, patients with FMD had higher scores for depression, anxiety, and non-motor symptoms, and lower score of the ACE-R subscale for fluency. FMD group in comparison to OMD had lower scores on recognition of Faux Pas (40.8±23.3 and 57.0±19.2, p=0.022) and Ne-Faux Pas situations (57.9±26.0 and 79.2±18.8, p=0.032), while RMET scores did not differ between groups. Also, FMD patients were more alexithymic in comparison to OMD (58.9±9.1 and 48.9±7.5, p=0.001). The lower scores on fluency, language, and attention ACE-R subdomains correlated with ToM deficiency in FMD. The association of different psychiatric symptoms (anxiety, depression, apathy and non-motor symptoms) with the severity of alexithymia in both study groups was shown.
Conclusion: The results of our study show that impairment of social cognition and altered emotional processing are present in FMD, and may represent a significant etiopathogenetic factor.
Disclosure: Nothing to disclose.

EPO-629

Effect of impulse control disorders and related behaviors in quality of life in Parkinson's disease.

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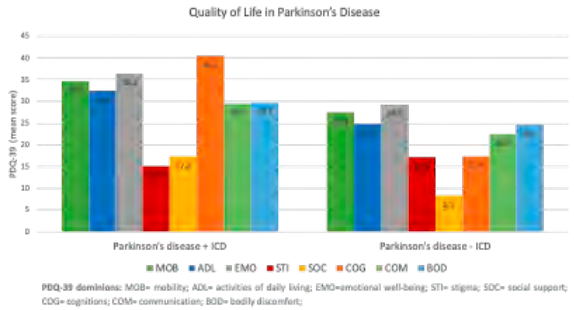
Background and aims: Impulse control disorders (ICD) and related behaviors represent a common psychiatric complication in patients with Parkinson's disease (PD) receiving dopaminergic replacement therapy, particularly dopamine agonists (DA). We aimed to assess the impact of these disabling disorders in quality of life (QoL).
Methods: We performed a cross-sectional study that included 30 patients with PD and ICD (PD+ICD) and 30 patients with PD without ICD (PD-ICD). All 60 patients were previously exposed to DA. Demographic and clinical data were obtained by clinical records and formal interview. The participants underwent a comprehensive neuropsychological evaluation including cognitive assessment, motor and non-motor status, measures of impulsiveness, apathy, ICD, depression, and anxiety. Impact in QoL was assessed by the Parkinson's Disease Questionnaire (PDQ-39).
Results: The mean age of disease onset was 52,8 y.o. in PD+ICD patients and 58,1 y.o. in PD-ICD (p=0,01). Hypersexuality and pathological gambling were the predominant ICD in PD+ICD patients. Scores in QoL were significantly worse in social support and cognition dominions in PD+ICD patients compared with PD-ICD (17,3 vs. 8,3; p=0,02 and 40,4 vs. 17,4; p=0,001 respectively). Non-motor symptoms burden was significantly higher in the PD+ICD group. Prevalence of apathy, impulsiveness, anxiety and depression were also significantly higher in PD+ICD patients. DA dose and subtype did not significantly differed between the 2 groups.
Conclusion: In this study, QoL, non-motor symptoms burden and mood disorders were found to be worse in PD patients with ICD compared to those without ICD. These results highlight the disabling effect of ICD and related behaviors in PD patients wellbeing.
Disclosure: Nothing to disclose.



EPO-630

Alien hand as a transient post-ictal phenomenon – a case series

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Background and aims: Alien limb (AL) refers to involuntary limb activity in which patients report loss of control over the affected limb. Isolated AL is encountered in patients with well-defined lesions, such as stroke or tumour, while in neurodegenerative diseases, AL coexists with other motor and cognitive deficits.
Methods: Clinical evaluation, video recordings and EEG recordings of three patients with post-ictal AL.
Results: 81-yo female was admitted due to epileptic status, caused by an old ischemic lesion in the right temporo-occipital cortex (Figure 1). Postictally, AL was observed in the left arm and leg along with left-sided neglect and Balint syndrome: optic ataxia, oculomotor apraxia and simultagnosia. The symptoms completely subsided after 4 days. 68-yo male was admitted after a series of seizures, caused by an old vascular lesion in the left occipito-parietal cortex (Figure 2). Post-ictal confusion, right arm Todd's paresis and postictal aphasia were followed by right arm AL that continued for 2 days. 81-yo female was admitted due to a convulsive seizure, caused by old ischemic lesions in the left temporo-occipital cortex (Figure 3). Postictal Todd paresis in the right arm was followed by right arm AL which subsided after 2 days. In all cases, prolonged EEG recordings ruled out seizure activity during episodes of AL.

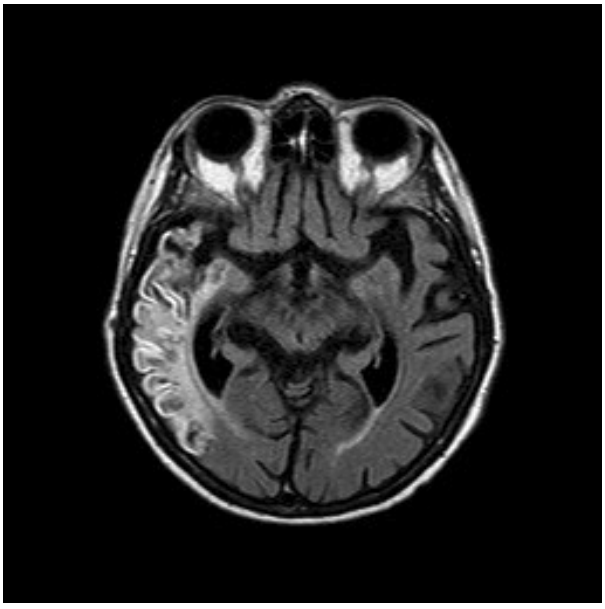

Figure 1: Patient no. 1 - FLAIR sequence showing post-ischemic encephalomalacia in the right occipital and temporo-occipital cortex.

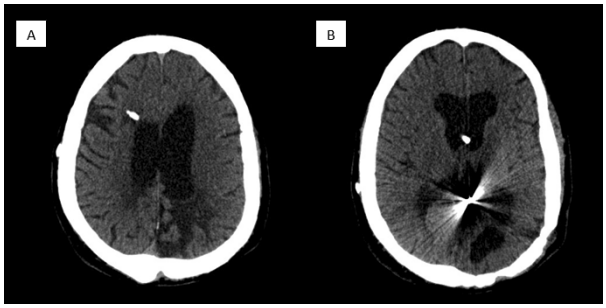

Figure 2: Patient no. 2 - CT scan showing A) encephalomalacia in the left occipito-parietal cortex after aterio-venous malformation (AVM) haemorrhage and B) surgical material near the corpus callosum splenium, left after AVM resection.

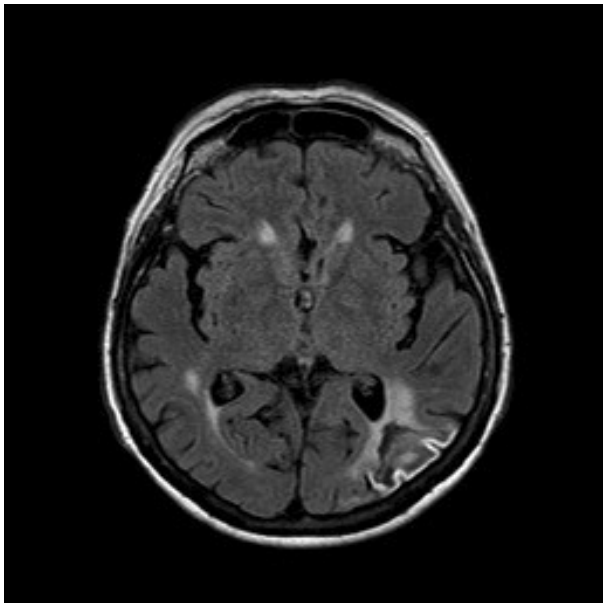

Figure 3: Patient no. 3 - FLAIR sequence showing post-ischemic encephalomalacia in the right temporo-occipital cortex.

Conclusion: Transient post-ictal AL may be observed in patients with posterior cortical lesions. Pathophysiologically, it may arise from postictally suppressed parietal areas, causing disinhibition of the motor areas (transitory disconnection) along with a lack of sense of agency.
Disclosure: Nothing to disclose.

EPO-631

Salivary biomarkers in Parkinson's disease: alpha-synuclein and beyond

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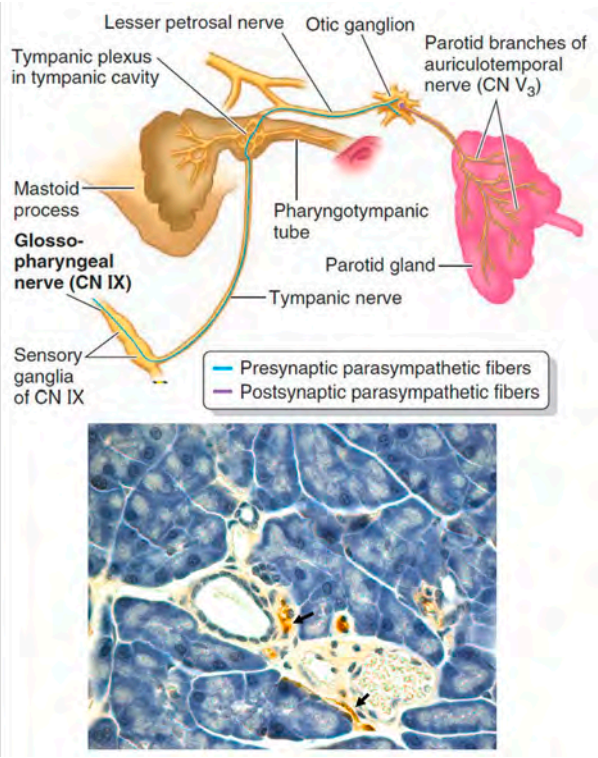
Background and aims: Parkinson's Disease (PD) is characterized by the accumulation of misfolded alpha-synuclein (a-syn) and by the activation of different molecular pathways, converging in neuronal death and synaptic loss. Clinical diagnosis and treatment of PD are hampered by the progressive deterioration of target neuronal circuits and by the mismatch between clinical and neuropathological onset. Molecular biomarkers are of unreplaceable importance to couple neuropathological and clinical features. Saliva is an easily accessible biofluid, whose collection is free of pain and discomfort for the patient and which has recently demonstrated a great potential as source of biomarkers for PD.
Methods: ELISA analysis and Real-Time Quaking Induced Conversion (RT-QuIC) assay have been applied to detect a-syn aggregates, tau aggregation, inflammation and autophagy biomarkers, in the saliva of 80 de novo PD patients and 65 healthy subjects. Molecular data have been correlated with clinical features of PD patients and used for molecular clustering though principal component analysis (PCA).
Results: Reduced levels of total a-syn and increased levels of a-syn aggregates have been demonstrated in the saliva of PD patients by ELISA. Moreover, RT-QuIC assay demonstrated seeding competent a-syn species in the saliva of PD patients and RT-QuIC kinetic parameters correlated with disease severity. Finally, autophagic markers and inflammatory markers were increased in the saliva of PD patients and were responsible of the molecular clustering of PD patients.
Conclusion: Saliva represents a key biofluid candidate for the detection of biomarkers in PD and could be also used for clustering different PD subtypes, improving molecular diagnosis and follow-up.
Disclosure: We have no disclosures.



Schematic representation of the innervation of the parotid gland and alpha-synuclein immunostaining showing the presence of alpha-synuclein positive fibres in the connective storma around the secretory cells of the salivary glands (arrows).

EPO-632

A case report of parkinsonism due to Coxsackie B virus infection

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Background and aims: Since encephalitis lethargica, the pathophysiology of viral parkinsonism has largely remained a mystery. The distinction of directly virus-mediated vs. parainfectious-autoimmune mechanisms is also clinically relevant.
Methods: Case report.
Results: A 73-year-old man without history of neurological symptoms presented with new onset of fatigue, gait disturbance and tremor. Clinical examination showed predominantly axial and only mildly asymmetric parkinsonism with mild cognitive impairment and orthostatic hypotension. Brain MRI showed mild small vessel disease. DaT scan showed decreased tracer uptake in putamen and caudate, predominantly on the right. Cerebrospinal fluid (CSF) analysis revealed pleocytosis (51 cells/µl, 12% neutrophils), elevated protein and absence of intrathecal IgG synthesis. Various neuronal autoantibodies tested negative in serum and CSF. Assuming a parainfectious autoimmune aetiology and while waiting for the viral metagenomics, a steroid pulse with oral tapering was initiated, but showed no benefit apart from improved fatigue. Neither levodopa nor amantadine showed any effect on parkinsonism. Viral metagenomics in CSF was positive for enterovirus, specified by serology as Coxsackie B1 virus. After therapy with intravenous immunoglobulin, however, the patient started to improve. On last follow-up, CSF showed only mildly elevated CSF protein, no pleocytosis and no traces of Coxsackie B virus-RNA.
Conclusion: Differentiating viral parkinsonism from an autoimmune-mediated etiology is challenging but important for treatment strategies. This case highlights the relevance of CSF cytology (the neutrophils were the reason to do viral metagenomics) and the need for better pathophysiological understanding.
Disclosure: There are no financial disclosures or conflicts of interest concerning this research item.

EPO-633

Symptomatic treatment of Huntington's disease (HD) chorea in Polish sites.

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Background and aims: Various drugs are used in management of chorea in HD patients, but there is limited data confirming efficacy. We compared motor symptoms and cognitive competence in HD patients on stable doses of tiapride, olanzapine, tetrabenazine and risperidone for one year.
Methods: We analyzed first-choice drugs for motor symptoms in patients from REGISTRY and Enroll-HD studies of two Polish Sites: Warsaw-IPiN and Poznan. Among 650 subjects (510 from Warsaw-IPiN and 140 from Poznan) we selected 79 patients treated with: tetrabenazine (n=27), tiapride (n=33), olanzapine (n=13) risperidone (n=6) and received stable doses for one year. Total motor score (TMS), chorea and dystonia subscore, cognitive tests at the beginning and after a year were compared.
Results: In all groups except tetrabenazine, changes in total TMS score were insignificant. TMS score significantly increased in a tetrabenazine group △=3.7 pkt, p=0.05 (t-test).Significant reduction in chorea subscore was found in tiapridal group (△=-3.6 pkt, p=0.002 t-test), in other groups was insignificant, buy accompanied with an insignificant increase in dystonia subscore. Patients treated with tetrabenazine characterized with significant decrease of cognitive performance (Stroop interference test △=-3.84, p=0.01, MMSE △=-1.8, p=0.03). In other groups tests results were either insignificantly worser (olanzapine, risperidon) or better (tiapride).
Conclusion: Tiapride, tetrabenazine and olanzapine are the most often first choice drugs in management of chorea in Polish HD Sites: Poznan and Warsaw-IPiN, however their efficacy in one year of observation is insignificant. This could be explained by HD progression and limited neuroprotective effect. Moreover, they may have a negative impact on cognitive abilities.
Disclosure: All authors report no conflict of interests.

EPO-634

Acoustic analysis of speech in Parkinson's disease with motor fluctuations

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Background and aims: Speech disorders of the nature of hypokinetic dysarthria are one of the most common symptoms of PD. The assessment of motor symptoms using non-invasive mobile devices that would enable monitoring of the patient's condition also outside the medical facility may be helpful in precise adjustment of appropriate doses of antiparkinsonian drugs to ensure optimal control of motor symptoms. The aim of the study was to assess the usefulness of speech acoustic analysis in tracking the severity of PD motor symptoms. To achieve the aim of the study, an assessment of the dependence of speech acoustic analysis parameters on the severity of PD motor symptoms was carried out.
Methods: The study involved 27 patients diagnosed with PD based on MDS criteria. Each patient was examined 5 times, at specific times: in the off state and 30-, 60-, 120- and 180-minutes after taking a standard dose of levodopa. At each measurement, speech was recorded, as well as an assessment of the severity of PD motor symptoms in part III of the UPDRS scale.
Results: All patients had a significant decrease in the UPDRS-III score after taking levodopa compared to OFF. In addition, dependencies were obtained that show a decrease in the value of all analyzed acoustic parameters with a decrease in the severity of disease symptoms.
Conclusion: Acoustic analysis of speech parameters is a sensitive marker of the severity of PD motor symptoms and can be used in practice in evaluating the patient's condition, selecting drug dosages and tracking the rate of disease progression.
Disclosure: Nothing to disclose.

EPO-635

Deep-learning-based quantification of the Pull Test for assessment of postural instability in parkinsonian syndromes

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[1]German Center for Vertigo and Balance Disorders, University hospital of Munich, Germany, [2]Department of Neurology, University hospital of Munich, Germany

Background and aims: Postural instability and falls are major complications in advanced Parkinson's disease (PD). Clinical evaluation of postural instability in PD and related movement disorders is most commonly based on the Pull Test (PT) that examines the ability to recover from a backward pull on the shoulder, which closely correlates with patients' risk of falling. Clinical application of the PT suffers, however, from several shortcomings such as lack of consensus on the proper execution and a subjective scoring system that both contribute to a low intra- and inter-rater reliability.
Methods: Here, we seek the potential to objectify the execution and patient performance during PT by means of deep-learning-based multi-person pose estimation applied on RGB-D recordings (Microsoft Kinect Azure) of PT examination in a cohort of healthy individuals (n=16) and exemplary patients with idiopathic and atypical PD.
Results: We demonstrate that our approach enables both, an objective monitoring of PT execution (pull strength) and quantitative assessment of patients' postural responses (pull-to-step latency, number of steps, etc.), and allows to reliably discriminate pathological from healthy performance.
Conclusion: Video-based quantitative PT assessment may thus facilitate increased sensitivity and specificity of clinical assessment of postural instability and risk of falling in PD.
Disclosure: No conflicts of interest to disclose.

EPO-636

The utilization of goal attainment scaling in cervical dystonia

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Background and aims: The heterogeneous manifestation of cervical dystonia (CD) makes the identification of the involved muscles and appropriate dose selection of the gold standard botulinum neurotoxin (BoNT) treatment challenging. Accordingly, the aim of the current study was to adapt goal attainment scaling (GAS), a widely used approach to set up treatment goals in the treatment of spasticity, into the individualised management of CD.
Methods: 38 patients with CD, receiving BoNT under ultrasound (US) guidance with standard injection points to the muscles selected according to the collum-caput (COL-CAP) concept, were involved. GAS, adapted with the inclusion of 11 possible domains, was applied to set up individualised goals with the calculation of initial GAS-T scores. Following at least 4 BoNT injections, patients were reassessed whether they reached the pre-set goals, and the GAS-T scores were calculated again.
Results: The initial GAS-T scores (median: 36.9, range: 22.8–40) significantly improved ($p<0.001$) to the end of the study (the median of final GAS-T scores: 50, range: 25.5–63.6). The major determinative factor whether to reach therapeutic aim of GAS-T score of 50 was that at least 50% of BoNT injections were performed according to the COL-CAP concept AND US guidance (odds ratio: 10.5, 95% confidence interval: 1.95–78.7).
Conclusion: In the lack of published studies in that issue the current was the first to demonstrate the applicability of GAS in setting up individualised therapeutic aims in CD in a measurable way. Furthermore, the utility of the COL-CAP concept AND US-guided injections in the management of CD were confirmed as well.
Disclosure: Nothing to disclose.

EPO-637

Inhibitory theta burst rTMS of the left primary and supplementary motor cortex decreases sway path in orthostatic tremor

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Background and aims: A ponto-cerebello-thalamo-cortical network is the pathophysiological correlate of primary orthostatic tremor (POT). Affected patients often do not respond satisfactory to pharmacological treatment. The objective of this study was to examine the effects of inhibitory rTMS of the left primary motor cortex (M1) and supplementary motor area (SMA) on tremor frequency, intensity, sway path and subjective unsteadiness in POT patients.
Methods: In a cross-over design eight POT patients (mean age 70.2±5.4 years, 4 female) received either rTMS of the left M1 leg area or of the left SMA at the first study session, followed by the respective other condition (SMA or M1) at the second study session 30 days later. Tremor frequency and intensity were examined by surface electromyography of lower leg muscles and total sway path by posturography (foam rubber with eyes closed) before and after each rTMS session. Patients subjectively rated postural stability on the posturography platform after each rTMS session.
Results: Tremor frequency and intensity did not change significantly with M1- or SMA-stimulation despite a tendency towards a decrease in tremor intensity after M1-stimulation (p=0.066). The sway path, however, decreased after M1-stimulation (p=0.001) and SMA-stimulation (p=0.046). Accordingly, POT patients indicated a better subjective feeling of postural stability both with M1-rTMS (p=0.014) and SMA-rTMS (p=0.02).
Conclusion: Non-invasive neuromodulation particularly of the M1 area seems a promising add-on therapy in POT.
Disclosure: Nothing to disclose.

MS and related disorders 7

EPO-638

Adding Animation to Case-based MS Education Improves Neurologists' Knowledge of DMT MoA & Competence in Implementation

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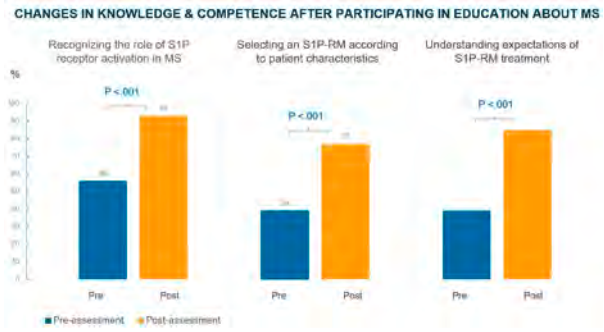
Medscape Education Global, London, UK

Background and aims: Understanding disease modifying therapy (DMT) mechanism of action in multiple sclerosis (MS) and relating this to implementation is important but challenging for neurologists to understand. To tackle this, we combined animation with MS case-based, text-based education.
Methods: Neurologists participated in a text, case-based activity, viewed animations, and completed pre- and post-questions. Educational effect was assessed using a 3-question repeated-pair design with pre-/post-assessment. A paired samples t-test was conducted for significance testing on overall average number of correct responses and for confidence rating, and a McNemar's test was conducted at the learning objective level (5% significance level, $p<0.05$). Cohen's d with correction for paired samples estimated the effect size of the education on number of correct responses. Data were collected from 3/21/2022–6/1/2022.
Results: Overall significant improvements at the aggregate level were seen after participation for neurologists (45% average correct response rate at pre-assessment vs 85% at post-assessment; $p<0.001$, Cohen's d= 1.25, n=61). Highly significant improvements were achieved with regards to the role of S1P receptor activation in MS, how to choose an S1P receptor modulator (RM) according to patient characteristics, and expectations of S1P-RM treatment (figure). After participating, 43% had measurable improved confidence ($p<0.001$), differentiating and selecting an S1P-RM.



Figure

Conclusion: This study demonstrates the success of this combination of educational elements in improving neurologists' knowledge of S1P-RM mechanism and competence in implementation.
Disclosure: Nothing to disclose.

EPO-639

MRI correlates of manual dexterity asymmetry in people with multiple sclerosis

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Background and aims: Motor, sensory and cerebellar symptoms are often lateralized in people with multiple sclerosis (pwMS). Here we explored associations between manual dexterity asymmetry and structural damage in pwMS and their relation to disability.
Methods: Three hundred thirty-four pwMS and 124 healthy controls (HC) underwent 3T MRI acquisition of 3D-T1-weighted and dual-echo sequences, used to extract left and right normalized brain volumes (cortical and deep gray matter and cerebellum) and lesion loads (cerebral and cerebellar). Hand dexterity was evaluated with the nine-hole peg test (NHPT). Asymmetry indexes (AIs) for these measures were calculated by subtracting left and right z-transformed values, determined based on HC group. Correlations between NHPT AI and AIs of structural measures were performed in HC and in pwMS stratified by disability, measured with the Expanded Disability Status Scale (EDSS) (mild=0–3.5; moderate=4.0–5.5; severe≥6.0).
Results: No side-specific lateralization of dexterity impairment or structural damage emerged in the examination of AIs in pwMS. Greater asymmetries (i.e. larger distributions of AIs) were observed in patients with moderate/severe disability, whereas mildly disabled pwMS had distributions similar to HC (see Figure). No correlations between structural and NHPT AIs were found in HC and mildly disabled pwMS. In moderately disabled pwMS NHPT AI correlated with cortical and deep gray matter volume AIs, while in pwMS with severe disability it was associated with cerebellar lesion load AI.

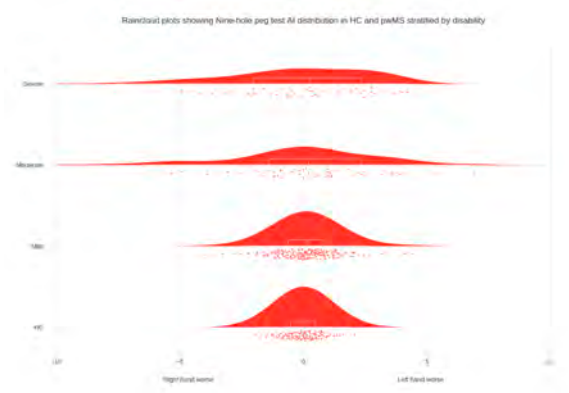

Figure. Raincloud plots showing nine-hole peg test AI distribution in HC and pwMS stratified by disability

Conclusion: Structural asymmetries are associated to asymmetry in NHPT, and both increase with disability in pwMS. Different structural substrates at different levels of disability underlie asymmetry in manual dexterity impairment.
Disclosure: The authors have nothing to disclose.

EPO-640

Structural and functional correlates of disability and gait in multiple sclerosis: focus on the globus pallidus

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Background and aims: The globus pallidus (GP) is divided into an internal (GPi) and an external (GPe) component. Here, we explored in people with multiple sclerosis (pwMS) the added role of studying structural and functional GPi/GPe damage, rather than as a whole, in relationship with clinical measures.
Methods: 60 pwMS and 30 matched healthy controls (HC) underwent 3T MRI including 3D-T1-weighted, dual-echo and resting state (RS) functional MRI. Timed 25-foot walk (T25FW) and Expanded Disability Status Scale (EDSS) were administered. Two operators segmented left and right GP into GPi and GPe starting from FSL FIRST masks (see Figure). Whole-GP, GPi and GPe normalized volumes and T1/T2 ratio were extracted, and seed-based RS functional connectivity (FC) was analyzed.
Results: PwMS had a higher T25FW than HC ($p<0.001$). The GP and its components were not atrophied in pwMS. Compared to HC, pwMS had higher T1/T2 ratio in all GP regions, which correlated with higher EDSS scores. At whole-GP RS FC analysis, pwMS showed decreased connectivity between left GP and right insula and between right GP and frontal cortices. They also showed increased connectivity between right GP and thalamus. When looking at RS FC of pallidal components, pwMS exhibited decreased connectivity between bilateral GPe and frontal cortices, as well as decreased intra-pallidal and increased thalamo-pallidal GPi connectivity. Lower GPe-frontal RS FC correlated with worse T25FW and EDSS scores.
Conclusion: Structural involvement of the GP in pwMS was similar across components. However, GPi and GPe showed specific RS FC alterations, which correlated with walking impairment and global disability.
Disclosure: The authors have nothing to disclose.

EPO-641

Impact of fatigue on spontaneous EEG topographies of patients with Multiple Sclerosis

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Background and aims: Fatigue is a disabling symptom in patients with Multiple Sclerosis (PwMS). Functional Magnetic Resonance Imaging studies demonstrated altered functional brain connectivity in fatigued PwMS (F-PwMS). Our purpose was to evaluate the impact of fatigue on resting-state networks, comparing EEG microstates of F-PwMS, non-fatigued PwMS (noF-PwMS) and healthy controls (HCs).

Methods: We enrolled 44 PwMS and 24 HCs, age and gender-matched. The Modified Fatigue Impact Scale (MFIS) was administered and the high-density EEG was recorded. Patients were divided into F-PwMS (MFIS-score>38, n=32) and noF-PwMS (MFIS-score<38, n=12). Microstates analysis was performed to identify stable scalp potential topographies, which best explained hdEEG variances of all participants. Mean duration (MD), time coverage, occurrence and global explained variance were computed for each map. All parameters of PwMS were standardized with respect to control by calculating the z-score. Differences between F-PwMS vs noF-PwMS were assessed by non-parametric statistical test. A correlation was performed between microstates parameters and fatigue data (alpha=0.05).

Results: We identified six stable scalp potential topographies (A-F). F-PwMS showed a significant decrease in the temporal dynamic of microstate F, and a significant increase in MD of microstate B, compared to noF-PwMS ($p<0.05$). A positive correlation between cognitive fatigue and activation of microstate B was found.

Conclusion: Our findings suggest that F-PwMs have a decreased activity of salience network and an increased activity of visual network, previously associated with microstate F and B respectively. The correlation of microstate B with cognitive fatigue suggests a possible marker for cognitive dysfunctions.

Disclosure: S. Baldini received funding from FISM; A. Sartori received travel grants and/or speaker honoraria from Biogen, Novartis, Merk, Roche, Sanofi, Almirall; L. Rossi, A. Dinoto, A. Favero, A. Bratina, P. Manganotti: nothing to disclose; F. Pasquin received travel grants from Genzyme and Biogen; A. Bosco received travel grants from Biogen and Roche.

EPO-642

Five-Year Safety of Ofatumumab in People Living With Relapsing Multiple Sclerosis

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Background and aims: Previously reported safety data from ALITHIOS open-label extension study for up to 4 years demonstrated that extended treatment with ofatumumab continues to show a favorable safety and tolerability profile in relapsing multiple sclerosis (RMS) participants. Here, we assess the longer-term safety profile of ofatumumab treatment for up to 5 years.

Methods: Participants completing core ASCLEPIOS I/II, APOLITOS and APLIOS clinical trials entered ALITHIOS. We analysed cumulative safety data for up to 5 years (cut-off: 25-Sep-2022) of ofatumumab treatment in the overall (n=1,969), continuous (ofatumumab in core+extension; n=1,292) and newly-switched (teriflunomide in core/ofatumumab in extension; n=677) groups. The analysis included proportion of participants with treatment-emergent adverse events (AEs), serious AEs (SAEs), injection-related reactions (IRRs), serious infections including COVID-19, malignancies, serum immunoglobulin (Ig)G and IgM levels and their association with serious infections.

Results: Overall, 89.9% of patients had ≥1 AEs (exposure-adjusted incidence rate/100 patient-years [EAIR], 124.6) and 14.7% had ≥1 SAEs (EAIR, 4.7) with low incidence of serious infections (5.4%; EAIR, 1.6) and malignancies (1.06%; EAIR, 0.3). Most COVID-19 cases were non-serious (92.3%) and recovered (96.1%) (Table). Overall, 2% of patients had IgG and 30.6% had IgM

Conclusion: Cumulative safety data for up to 5 years indicate that extended treatment with ofatumumab is well-

tolerated, with no new safety risks identified. These data inform physicians on the longer-term safety profile of ofatumumab in people living with RMS.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

Adverse event	Core, ASCLEPIOS OMB (N=946)		Core + extension, Overall OMB, (N=1969)	
	n (%)	EAIR (95% CI)	n (%)	EAIR (95% CI)
Patients with at least one AE	791 (83.61)	188.55 [175.86, 202.16]	1771 (89.9)	124.65 [118.97, 130.59]
Patients with at least one SAE	86 (9.10)	5.39 [4.36, 6.65]	289 (14.7)	4.68 [4.17, 5.26]
AEs leading to discontinuation	54 (5.70)	–	139 (7.1)	–
Infections and infestations	488 (51.58)	51.14 [46.80, 55.88]	1334 (67.75)	40.99 [38.85, 43.25]
Serious infections	24 (2.54)	1.44 [0.97, 2.15]	106 (5.38)	1.63 [1.35, 1.97]
Injection-related systemic reactions	195 (20.61)	15.49 [13.46, 17.83]	508 (25.79)	10.06 [9.22, 10.98]
Injection site reactions	103 (10.88)	7.21 [5.94, 8.74]	243 (12.34)	4.08 [3.60, 4.63]
Malignancies	5 (0.53)	0.32 [0.13, 0.77]	21 (1.06)	0.32 [0.21, 0.48]
Deaths	0	0	9 (0.46)	–

Safety Profile of Ofatumumab for Up to 5 years of Treatment

EPO-643

International Consensus on Smoldering Disease in Multiple Sclerosis using the Delphi Method

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Background and aims: Despite the successful therapeutic suppression of relapses and new MRI lesions, most people with multiple sclerosis (pwMS) experience neurological deterioration. Accumulating data suggest that multiple sclerosis (MS) in addition to being a disease related to acute focal inflammation, involves more widespread, smoldering pathogenic processes that impact the entire central nervous system from early stages of the disease. Understanding and better defining the biology underlying the clinical and radiological manifestations of smoldering pathological processes remain important unmet needs. Greater comprehension of smoldering disease will improve clinical management, promote drug research by identifying new targets, stratifying pwMS for clinical trials and aid pwMS in understanding the causes of disease worsening.

Methods: Fifteen MS experts from eight countries across Europe, US, and Canada convened to develop consensus-driven statements on smoldering disease across multiple domains. They employed the Delphi method to anonymously establish agreement on a 5-point scale with "consensus" defined a priori as >75% who agree or strongly agree.

Results: See Table

Table 1

Statements relating to definition of smoldering disease	Statements relating to disease worsening due to smoldering disease
Smoldering disease is considered an umbrella term characterizing chronic pathobiological processes occurring in the CNS, beyond acute focal inflammation, associated with neurodegeneration leading to clinical worsening in pwMS, that may start early and continues throughout the disease course.	Clinical disease worsening is not just associated with progressive stages of the disease but may be observed at early stages of the disease and throughout the course of MS
Progression independent of relapse activity (PIRA) should be considered primarily a clinical manifestation of smoldering disease and therefore those terms should not be used interchangeably	Disease worsening may be driven by smoldering disease activity, which may be present throughout the disease course (even before clinical features manifest) and may account for physical as well as cognitive dysfunction

Table

Conclusion: This expert panel aims to provide further definitions and recommendations to help raise awareness and educate the neurology community on smoldering disease as well as advise on its implementation into routine clinical practice. Full presentation and publication of all statements with supporting evidence are expected in 2023.

Disclosure: The concepts and contents of this abstract emerged from several meetings facilitated by Sanofi. The experts involved are paid for attending the meetings but not for any writing efforts. Medical writing support was provided by Lionel Thevathasan, MD from LT Associates Ltd who was funded by Sanofi.

EPO-644

Clinical characteristics of late-onset multiple sclerosis: a single centre retrospective cohort study

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Background and aims: Diagnosis of late-onset multiple sclerosis (LOMS), defined as symptom onset at >=50 years of age, is challenging. Despite an aging MS population and evidence of increasing incidence of LOMS, this entity remains scarcely described. We aimed to characterize LOMS patients in a tertiary centre and compare with published data.
Methods: Data was obtained from retrospective review of electronic clinical records. Patients were included if MS diagnosed according to 2017 McDonald criteria and age at symptom onset >=50 years. We retrieved data on demographic, clinical, imaging and laboratory characteristics. We performed a descriptive analysis of the cohort.
Results: We identified 24 LOMS patients, median age at symptom onset of 55.5 years (interquartile range [IQR]=8.75) and at diagnosis of 59 years (IQR=6). Most patients were female (62.5%, female/male ratio=1.7). Relapse-remitting MS (50%) was the most frequent MS subtype, followed by primary progressive MS (41.7%). All patients had registered comorbidities, being hypertension (62.5%) the most frequent. The most common presentation was as isolated medullary syndrome (58.3%). Median EDSS at last follow-up was 4.0 (IQR=2.5). Clinical progression was described in 58.3% and inflammatory activity in 45.8% (median follow-up=3 years, IQR=5). Cervical cord lesions were identified in 62.5% at diagnosis.
Conclusion: In our cohort, LOMS is characterized by high proportion of primary progressive phenotype and frequent medullary involvement, which is in line with previous studies. The high frequency of cardiovascular comorbidities may impact diagnosis and therapeutic decisions. LOMS should be considered in older people with new-onset acute or progressive neurological symptoms.
Disclosure: Nothing to disclose.

EPO-645

piRNA and miRNA in Multiple Sclerosis

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Background and aims: Multiple sclerosis (MS) is a common inflammatory demyelinating disease with a high mortality rate. MS is caused by many candidate genes whose specific involvement has yet to be established.
Methods: In order to establish the possible effect of miRNA and piRNAs on the MS candidate genes, we determined the interaction characteristics using the MirTarget program. Program defines the following features of miRNA and piRNA binding to mRNA: the initiation of the miRNA and piRNA binding to the mRNAs from the first nucleotide of the mRNAs, the localization of the piRNA and miRNA BSs in the 5′UTR, CDS and 3′UTR of the mRNAs, the schemes of nucleotide interactions between piRNAs, miRNAs, and mRNAs, the free energy of the interaction between piRNA and the mRNA.
Results: The piRNA BSs were predominantly located in the 3'UTR and only two genes were located in the 5'UTR and the TNFRSF1A gene in the CDS. The mRNAs of the IL2RA, MGAT5, and ZBTB46 genes each had one piRNA BS, and the mRNA of the MLANA gene had three piRNA BSs. ADAM17, AHI1, EVI5, and TNFRSF1A genes was the target of several piRNAs whose BSs were located with overlapping nucleotides, which we called clusters of BSs.
Conclusion: The piRNA and miRNA target genes were EOMES, ADAM17, AHI1, EVI5, IL2RA, and MGAT5. These genes were most dependent on piRNA and miRNA, and therefore, their associations with the corresponding piRNA and miRNA are the most suitable for use in MS diagnosis.
Disclosure: The EOMES, ADAM17, AHI1, EVI5, IL2RA, and MGAT5 genes were targets for piRNA and miRNA.

EPO-646

Pregnancy effect on disease activity in women treated with cladribrine

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Background and aims: Cladribrine is an oral pulsed therapy for relapsing multiple sclerosis (RMS).Hormonal and immune changes are responsible for the decline of disease activity in the third trimester of pregnancy and disease reactivation in the early post-partum period.To date there are no available studies on the pregnancy effect on disease activity in women with MS who conceived after cladribrine treatment.
Methods: We recruited women of childbearing age with RMS who became pregnant or not after being treated with cladribrine.For both groups, demographic,clinical and radiological data were collected one year before and after treatment to compare the disease activity.
Results: 47 childbearing women mean age 35.05 ys were included. 24 women had a pregnancy after a mean of 1.75 years from the first treatment cycle,5 pregnancies occurred between the first and second cycle.Women with or without pregnancy did not differ for demographics or disease activity pre cladribrine. No significant differences in disease activity post cladribrine were found between women with or without pregnancy (0.12 vs 0.04 for ARR p=0.36; 1.9 vs 1.1 p=0.65 for new T2 lesions and 0.29 vs 0.3 p= 0.60 for new gd+ lesions). No significant differences were found between women with pregnancy occurred between the first and second cycle or after the second cycle.
Conclusion: Pregnancy does not appear to influence disease activity in women previously treated with cladribrine; further studies with larger numbers are needed to confirm this finding and to identify the best timeframe to conceive after cladribine treatment that guarantees to be still protected from reactivation in the post-partum period.
Disclosure: Nothing to disclose.

EPO-647

NEDA-3 achievement in early highly active RR-MS patients treated with Ocrelizumab or Natalizumab

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Background and aims: the use of high-efficacy disease-modifying therapy(HE DMT)at the beginning of the Multiple Sclerosis(MS)may be the best strategy to delay or minimizing neurological damage and progression of the disease in the long term especially for highly active MS patients (HAMS).Natalizumab(NTZ) and Ocrelizumab (OCR) are considered HE DMT with a significant anti-inflammatory effect. Here we investigate the NEDA-3 achievement in naïve patients with HAMS treated with NTZ or OCR after two years of follow-up.
Methods: we retrospectively recruited naïve HAMS patients treated with NTZ or OCR and we collected demographic,clinical and instrumental characteristics before and after starting any treatment in order to compare disease activity, disability progression and NEDA-3 achievement.
Results: we recruited 141 naïve patients (pts) with RR-MS with(mean age 33.2±11.17) treated with NTZ (90 pts) or OCR(51 pts). Comparing disease activity pre and post therapies after six months of re-baseline,we registered a significant reduction of ARR from 1.47 to 0.015 for NTZ and from 1.24 to 0.030 for OCR without significant differences between treatments (p=0.36). Also for gd+ lesions we registered a significant reduction(1.31 vs 0.067 in NTZ and 1.29 vs 0.030 in OCR) without significant differences between treatments (p=0.46). Globally 81.6% of pts were NEDA-3 after two ys of follow-up, 87.3% (95% CI: 77.7–93.0) of NTZ pts and 72.6%(95% CI: 55.4–84.1) of OCR pts (p=0.026).
Conclusion: starting HE DMT with monoclonal antibodies for HAMS could achieve NEDA-3 in a high percentage of patients, however the drivers of response to therapy in this category of patients needs to be further investigated.
Disclosure: Nothing to disclose.

EPO-648

Prospective outcome analysis of multiple sclerosis cases reveals candidate prognostic markers

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Background and aims: Predicting long-term disability outcomes of multiple sclerosis (MS) cases is challenging. We prospectively analysed our previous MS cohort with initial cerebrospinal fluid (CSF) proteomics data to reveal disability markers after 8.2±2.2 years of follow-up.
Methods: Patients with regular follow-up visits were assigned into two groups: those with an age-related MS severity (ARMSS) score ≥5 (unfavourable course group, n=27) and ARMSS score <5 (favourable course group, n=67). A machine learning-based algorithm was applied to reveal candidate poor prognosis-associated initial CSF proteins, which were then measured in an independent MS cohort (verification group, n=40) by ELISA. Additionally, the correlation of initial clinical and radiological parameters with long-term disability was analysed.
Results: CSF alpha-2-macroglobulin (p=0.0015), apo-A1 (p=0.0016), and haptoglobin (p=0.0003) protein levels were significantly higher in the unfavourable course group than in the favourable course group. Among the clinical and radiological parameters, cerebral lesion load (>9 lesions) on magnetic resonance imaging, gait disturbance (p=0.04), and bladder/bowel symptoms (p=0.01) at disease onset were higher in the unfavourable course group, while optic nerve involvement evident on initial magnetic resonance imaging (P=0.002) and optic neuritis (p=0.01) were more frequent in the favourable course group. Correlation analyses between other clinical parameters and protein levels did not disclose reliable findings due to the small number of cases in the subgroups.
Conclusion: Higher levels of CSF alpha-2-macroglobulin, apo-A1, and haptoglobin proteins at disease onset are associated with a poor disease outcome and may have predictive value of long-term disability of MS cases.
Disclosure: Nothing to disclose.

EPO-649

Different initial treatment strategies and their impact on disability progression in Multiple Sclerosis

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Background and aims: Treatment approach in Multiple Sclerosis (MS) is changing. The classic escalation strategy is giving way to an early high-efficacy treatment. This renowned "inversion of the pyramid" is exhibiting promising results in different cohorts. This study aimed to identify how initial treatment strategy could be associated with the progression of disability, specifically the need for walking aid.
Methods: An observational, single-center, retrospective cohort study was conducted, including all patients in an MS center with relapse-remitting MS (RRMS) starting treatment between 2012–2022. Baseline characteristics (gender, age, diagnosis' delay) were assessed, and patients' classification according to treatment strategy for the first 2 years: escalation (ESC); early intensive (EIT); first treatment's efficacy (modest, moderate, high). A multivariate Cox regression was performed to compare the risk of reaching an Expanded Disability Scale Score (EDSS) 6.0.
Results: 303 patients were included: 67.7% were women, mean age at diagnosis was 36.3±11.2 years, mean diagnosis' delay was 2.17±4.474 years. Most patients began treatment with a low-efficacy drug (78.0%) and followed ESC strategy (70.6%). 18 patients reached EDSS 6.0 (5.9%), in a mean interval of 3.83±2.83 years. There was a lower risk in reaching EDSS 6.0 in EIT patients when the first treatment was a moderate or high efficacy drug (HR 0.150, CI 0.039–0.580, p=0.006).
Conclusion: In this cohort, MS patients selected for EIT strategy have a lower risk of disability progression when the first treatment is one of moderate or high-efficacy.
Disclosure: Nothing to disclose.

EPO-650

Does the target NEDA comply with functional measure changes after 2 years in early phase of Multiple Sclerosis?

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Background and aims: Few studies investigated the longitudinal changes of functional measures in people with MS (PwMS) with low disability. The aim of the study is to evaluate after two years of follow-up (2FU) the evolution of clinical and functional measures stratified for NEDA (no-evident-disease-activity).
Methods: We assessed PwMS at baseline and after 2FU: Six Minute Walking Test (6MWT), Timed up and Go test (TUG), Timed-25 Foot Walking (T-25FW), Fatigue Severity Scale (FSS), Twelve-Multiple Sclerosis Walking Scale (MSWS_12), Fullerton Advanced Balance-short (FAB-s), 9-Hole Peg Test (9-HPT), Manual Ability Mesure-36 (MAM-36), Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS).
Results: 57 PwMS were enrolled [baseline: 35F, mean age 38.97 (SD=10.76) years, mean disease duration 2.14 (SD=1.84) years, mean EDSS 1.41), 57 relapsing-remitting MS course; 2FU: mean EDSS 1.83]. At 2FU, 30 PwMS were NEDA (NEDAgroup) while 27 not (noNEDAgroup) In the NEDAgroup the number of PwMS worsened: 14 at 6MWT, 9 at TUG, 13 at FSS, 14 at T-25FW, 9 at MSWS-12, 10 at FAB, 21 at 9-HPT, 5 at MAM-36, 12 at SDMT, 11 at CVLT-II, 8 at BVMT-R. In the noNEDAgroup the number of improved: 9 at 6MWT, 12 at TUG, 14 at FSS, 11 at T-25FW, 10 MSWS-12, 8 at FAB, 12 at 9-HPT, 8 at MAM-36, 10 at SDMT, 14 at CVLT-II, 9 at BVMT-R.
Conclusion: In conclusion, MS subjects classified as NEDA showed a decrease of function in at least one domain at 2FU. Several subjects showed an improvement underline the importance of an extensive clinical evaluation beyond the EDSS.
Disclosure: All authors have no conflict of interest.

EPO-651

Is brain atrophy a good surrogate for cognitive outcomes in Multiple Sclerosis? A meta-regression of randomized trials

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Background and aims: Magnetic Resonance Imaging lesions have been successfully used as primary outcomes for Phase-2 studies in relapsing-remitting Multiple Sclerosis (MS), while it is still challenging to select an optimal outcome to design Phase-2 studies in progressive MS. Up to now brain atrophy was proposed as a "ready-to-use" outcome for progressive MS trials, even if it its role as a surrogate for inflammation and/or neurodegeneration is still not fully clarified. We aim here to evaluate the surrogacy of brain atrophy for cognitive outcomes in MS clinical trials.
Methods: We collected all the 2-year randomized clinical trials in relapsing-remitting and progressive MS reporting data on the treatment effect on brain atrophy and cognition (PASAT-3). We run a meta-regression (weighted on trial size) of the effect of treatment on PASAT-3 and on brain atrophy. The standardized mean difference (Hedges' g) between baseline and follow-up PASAT-3 assessment was used as the main effect size measure on cognition and the log-percentage brain volume change (PBVC) was used as the main effect size measure on brain atrophy.
Results: 10 trials (16 contrasts, 12 vs placebo, 4 vs active treatment) were included. The weighted correlation between the effects on PBCV and cognition was r=0.57. The R2 was 0.32 (p=0.017), indicating that the 32% of variability of treatment effects on PASAT-3 can be explained by the effects on brain atrophy (Figure).

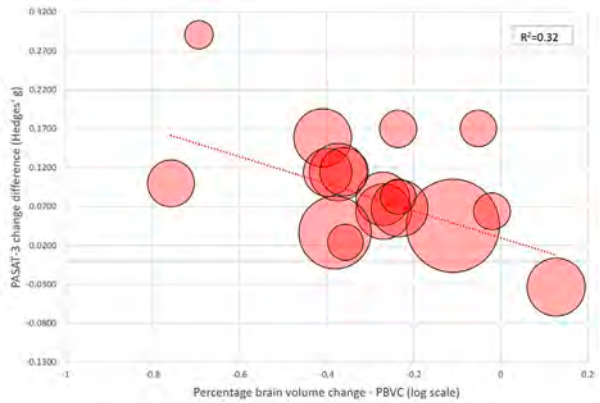

Figure: Association between cognition (PASAT-3) and brain atrophy (PBVC)

Conclusion: Brain atrophy is a good surrogate outcome for treatment effect on cognitive outcomes, despite the limitations related to lack of homogeneity in assessing cognition in MS studies.

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EPO-652

Low serum vitamin D levels are associated with cognitive impairment in multiple sclerosis

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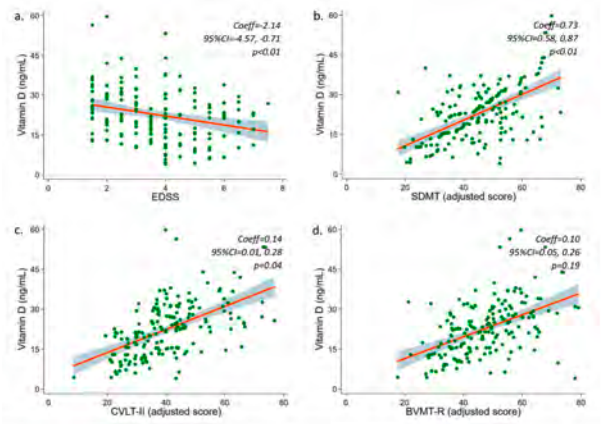
Background and aims: Cognitive impairment (CI) frequently affects people with multiple sclerosis (MS) possibly due to neurodegenerative mechanisms. Low vitamin D levels have been associated with cognitive dysfunction in Alzheimer's and Parkinson's disease, and, in MS, with motor disability and disease activity. We aim to investigate associations between vitamin D and cognitive status in MS.

Methods: In this cross-sectional study, we included 181 MS patients with serum 25-hydroxy-vitamin D measurements using Chemiluminescence ImmunoAssay, and cognitive assessment using Symbol Digit Modalities Test (SDMT), California Verbal Learning Test II (CVLT-II) and Brief Visuospatial Memory Test-Revised (BVMT-R). We collected demographic (age, sex), and clinical variables (disease duration, disease subtype, expanded disability status scale (EDSS), disease modifying treatment (DMT), relapses in previous 12 months, steroid treatment in previous 12 months, concomitant vitamin D supplementation, comorbidities).

Results: At univariate linear regression models, higher levels of vitamin D were associated with higher scores on SDMT (Coeff=0.93; 95%CI=0.81, 1.04; p<0.01), CVLT-II (Coeff=0.68; 95%CI=0.53, 0.83; p<0.01), and BVMT-R (Coeff=0.58; 95%CI=0.43, 0.73; p<0.01), and with lower EDSS (Coeff=-2.16; 95%CI=-3.57, -0.75; p<0.01). At multivariate linear regression models including all demographic, clinical and cognitive variables, we confirmed associations for EDSS (Coeff=-2.14; 95%CI=-4.57, -0.71; p<0.01), SDMT (Coeff=0.73; 95%CI=0.58, 0.87; p<0.01), and CVLT-II (Coeff=0.14; 95%CI=0.01, 0.28; p=0.04), but no association was found for BVMT-R (Coeff=0.10; 95%CI=-0.05, 0.26; p=0.19).



Scatter plots show associations between vitamin D and EDSS (a), SDMT (b), CVLT-II (c), and BVMT-R (d). Coefficients (Coeff), 95% confidence intervals (95%CI, represented as grey shadow), and p-values are reported from multivariate linear regression models

Conclusion: Higher vitamin D levels were associated with better performance in MS on multiple cognitive domains, including attention, information processing speed and verbal memory. Vitamin D possibly affects neurodegenerative aspects of MS.

Disclosure: The authors declare no conflict of interest.

MS and related disorders 8

EPO-653

Czech MS registry ReMuS: Trends in patients initiating their first disease-modifying therapies from 2013 to 2021

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Background and aims: We aimed to describe the trend in the characteristics of patients with multiple sclerosis (MS) initiating their first disease-modifying therapies (DMTs) in the Czech Republic. The secondary objective was to present the Czech national MS registry (ReMuS) with its history, data collection, and scientific potential.

Methods: First, using descriptive statistics, we analysed the characteristics of patients initiating their first DMTs, either platform (including dimethyl fumarate) or high efficacy DMTs (HE-DMTs), each year. Second, a detailed description of the history, data collection, completeness, quality optimising procedures, and legal issues of ReMuS was provided.

Results: Based on the dataset from December 31, 2021, the total number of monitored patients with MS in ReMuS increased from 9,019 in 2013 (referred from 7 of 15 MS centres) to 12,940 in 2016 (already referred from all 15 Czech MS centres) to 17,478 in 2021. In these years, the percentage of patients treated with DMTs in the registry ranged between 76 and 83%, but the proportion of patients treated with HE DMTs changed (from 16.2% in 2013 to 37.1% in 2021). During the follow-up period, a total of 8,491 treatment-naive patients initiated DMTs. The proportion of patients (all MS phenotypes) starting with HE DMTs increased from 2.1% in 2013 to 18.5% in 2021.

Conclusion: An increasing proportion of patients initiating HE-DMTs can bring considerable efficacy to therapy. However, it also carries greater potential risks. Consistent long-term follow-up of patients in real-world clinical practice, which only registries allow, is therefore crucial.

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EPO-654

Pseudotumoral demyelinating lesions of the central nervous system

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Background and aims: Pseudotumoral demyelinating lesions (PDL) of the central nervous system (CNS) are large lesions visualized on magnetic resonance imaging (MRI). We investigated the etiology of PDL of the CNS, clinical and neuroradiological characteristics of inflammatory PDL and tumefactive MS lesions.

Methods: The patients with PDL of the CNS treated at the Neurology Clinic, University of Belgrade between 2018 and 2022. Demographic, clinical and neuroradiological data were collected prospectively and retrospectively using the hospital's digital clinical records and analyzed using descriptive statistics. We have classified PDL according to MAGNIMS criteria

Results: 53 patients with PDL of the CNS were analyzed. Concordance of initial and final diagnoses was 64.2%. Out of these, 29 patients (m:f ratio 1:1.25) had inflammatory demyelinating etiologies, among which 10 (34.5%) had previously established MS, 11 (37.9%) got diagnosed with MS in the later course of disease and 8 (27.6%) met criteria for related demyelinating entities. Solitary lesions were seen in 16 (55.2%) patients while 13 (44.8%) had multiple ones. Out of the 11 patients, who went on to develop MS after initial tumefactive lesion 72.7% demonstrated oligoclonal bands. Out of a.m. 29 patients 58.6% had ring-like lesions, 44.8% parietal lobe as predilection site, and 41.4% sensory disturbance as the presenting symptom of the disease.

Conclusion: MS was the most common cause of parietal and ring-like PDL, but not the exclusive cause. This highlights the importance of a thorough and targeted diagnostic workup that utilizes routine analyses, the whole spectrum of neuroimaging modalities, including repeated MRI scans and advanced methods.

Disclosure: Nothing to disclose.

EPO-655

Abstract withdrawn

EPO-656

Prospective trial of personalized extended dosing of natalizumab by therapeutic drug monitoring in multiple sclerosis

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Background and aims: Extended interval dosing (EID) of natalizumab is a promising strategy for reducing the risk of progressive multifocal leukoencephalopathy (PML) in multiple sclerosis (MS). Personalized EID, in which treatment intervals are extended based on natalizumab concentrations, could be superior in comparison to fixed EID in terms of PML risk and healthcare costs.

Methods: The NEXT-MS trial is an ongoing investigator-initiated prospective non-randomized study containing three groups: personalized EID with an aim natalizumab drug trough concentration of 10 µg/mL (EID10), standard interval dosing (SID) of 4 weeks, and an exploratory group of personalized EID with an aim of 5 µg/mL (EID5). The primary outcome is radiological disease activity on MRI (new/enlarged T2 lesions) comparing the EID10 group to a historical cohort of SID.

Results: In December 2022, median treatment interval was 5 weeks (IQR 5 to 6 weeks) in the EID10 group (n=251). Two participants (1.8 participants/year, n=171) showed radiological disease activity during follow-up, which was comparable to the historical SID cohort (2.3 participants/year, n=88). One participant had a relapse (0.65 participants/year vs 4.1 participants/year in the historical cohort). In the EID5 group (n=66), median treatment interval was 6 weeks (IQR 5 to 7 weeks, 32% extended >6 weeks). One participant (0.51 participants/year) showed radiological disease activity and there were no relapses.

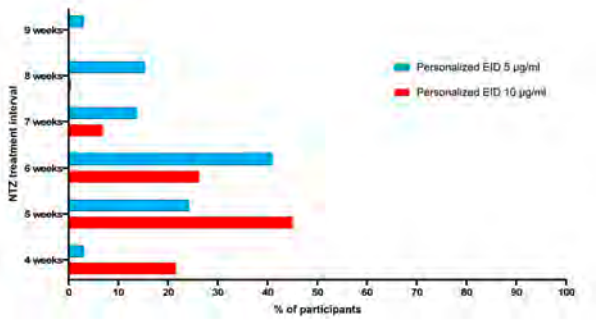

Figure 1: Natalizumab treatment intervals in the personalized EID groups. Percentage of participants in each study group (EID10 in red; EID5 in blue) is displayed on the x-axis. The y-axis indicates the natalizumab treatment interval at last available FU.

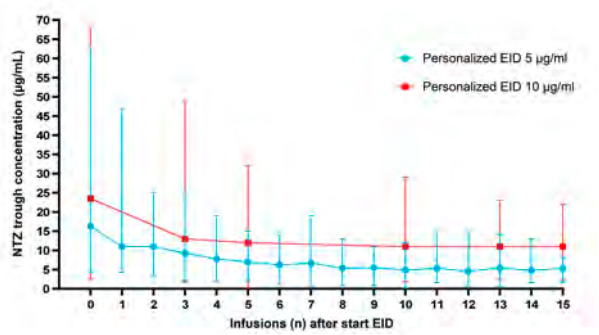

Figure 2: Natalizumab drug concentrations in the personalized EID groups. Values are presented as medians with ranges (min-max). Number of infusions after start of EID are displayed on the x-axis. The y-axis indicates natalizumab trough concentrations.

Conclusion: MS disease activity is adequately controlled with personalized EID of natalizumab. The study will continue in 2023 with an amended study protocol with personalized EID starting from 6 weeks.

Disclosure: This study was kindly funded by the Dutch MS Research Foundation (18-1030), the Brain Foundation Netherlands, and Innovation Fund Healthcare insurers. The funding sources had no further involvement in the study. On behalf of the NEXT-MS study group; A.A. Toorop: nothing to disclose; T. Rispens received funding for research from Genmab; received consulting fees from Novartis; B.M.J. Uitdehaag received research support and/or consultancy fees from Biogen Idec, Genzyme, Merck Serono, Novartis, Roche, Teva and Immunic Therapeutics; J. Killestein received research grants for multicentre investigator initiated trials DOT-MS trial, ClinicalTrials.gov Identifier: NCT04260711 (ZonMW) and BLOOMS trial (ZonMW and Treatmeds), ClinicalTrials.gov Identifier: NCT05296161); received consulting fees for F. Hoffmann-La Roche Ltd, Biogen, Teva, Merck, Novartis and Sanofi/Genzyme (all payments to institution); reports speaker relationships with F. Hoffmann-La Roche Ltd, Biogen, Immunic, Teva, Merck, Novartis and Sanofi/Genzyme (all payments to institution); adjudication committee of MS clinical trial of Immunic (payments to institution only); Z.L.E. van Kempen: nothing to disclose.

EPO-657

Humoral vaccine response and COVID-19 hospitalizations in vaccinated multiple sclerosis patients treated with rituximab

H. Torgauten[1], T. Onyangp[2], E. Hallin[3], T. Serkland[3], S. Skrede[4], R. Cox[4], N. Langeland[4], K. Myhr[1], Ø. Torkildsen[1]

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Background and aims: People with multiple sclerosis (MS) treated with anti-CD20 therapies like rituximab have increased risk of severe COVID-19 disease. Vaccination protects patients from severe COVID-19 disease, but humoral vaccine responses are usually diminished in rituximab treated patients, indicating a need for more clinical data.

Methods: Rituximab-treated patients registered in the National MS Registry, living in Bergen and neighboring municipalities were invited to participate by giving a consent and providing a blood sample 3–12 weeks after ordinary vaccination, i.e. 2 doses, against SARS-CoV-2. Blood samples were analyzed with Enzyme-Linked Immunosorbent assay (ELISA) to detect SARS-CoV-2 specific antibodies with screening test against receptor-binding domain (RBD) and confirmatory Spike IgG-specific ELISA. Patient serum concentration of rituximab were quantified using LC-MS/MS. Registry data from the Norwegian MS registry, and information on hospitalization from patient records were collected and linked to laboratory results.

Results: 140 patients met the criteria and were included in the study. 67% of the included patients had a low or undetectable humoral vaccine response. A total of 10 (7.1%) were admitted for observation and/or treatment for COVID-19 during the observation period. None of the patients were admitted to ICU and there were no deaths.

Conclusion: The majority of rituximab-treated patients with MS had a reduced vaccine response after 2 doses of SARS-cov-2 vaccine. Despite this, only few patients were admitted to hospital and none required ICU treatment. The results indicate that vaccinated patients with MS treated with rituximab have a protective effect despite a low humoral antibody response.

Disclosure: H.Torgauten has nothing to disclose. Ø. Torkildsen has received speaker honoraria from and/or served on scientific advisory boards for Biogen, Roche, Teva, Sanofi-Aventis, Merck and Novartis. R.J. Cox has nothing to disclose. N. Langeland has nothing to disclose. S. Skrede has nothing to disclose. T. Serkland has nothing to disclose. E. Hallin has nothing to disclose. KM. Myhr has received speaker honoraria from Biogen, Roche, Sanofi-Aventis, and Novartis, and participated in clinical trials sponsored by Biogen, Roche, Sanofi-Aventis, and Novartis.

EPO-658

TYSABRI® Observational Program: Long-term Safety and Effectiveness in Relapsing-Remitting Multiple Sclerosis over 15 years

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Background and aims: The Tysabri Observational Program (TOP) is the largest ongoing real-world observational study to inform on long-term safety and effectiveness of natalizumab (NTZ) in relapsing remitting multiple sclerosis (RRMS) in clinical practice.

Methods: Annualized relapse rates (ARRs) for the year prior to NTZ and the period on NTZ (and ≤84 days after the last dose) were compared using a repeated Poisson model. Confirmed Expanded Disability Status Scale (EDSS) worsening and improvement were estimated by Kaplan-Meier analysis. Serious adverse events (SAEs) were assessed at clinical visits.

Results: As of November 2022, TOP included 6,321 patients. At baseline (BL), mean EDSS score was 3.5; 92.6% had prior disease-modifying therapy (DMT) use. A total of 3,993 patients (63.2%) discontinued NTZ; 2,721 (43.0%) withdrew from TOP. Median exposure was 46 (range, 1–191) doses; median follow-up time was 116 (range, 1–200) months. ARR was 2.00 pre-NTZ and 0.18 on NTZ (91.0% reduction, $p<0.001$). For those with BL EDSS scores <3.0 or ≥3.0, ARR decreased by 93.0% ($p<0.001$) and 90.0% ($p<0.001$), respectively. For those with 0, 1, or ≥2 prior DMTs, ARRs were reduced by 93.7% ($p<0.001$), 92.6% ($p<0.001$), and 89.3% ($p<0.001$), respectively. At 15 years, cumulative probabilities of 24-week–confirmed EDSS worsening and improvement were 42.9% and 39.6%, respectively. Overall, 1,122 of 6,321 patients (17.8%) experienced ≥1 SAE (most commonly reported by system organ class: infections and infestations, 320 patients [5.1%]).

Conclusion: This interim analysis of TOP reinforces the consistent effectiveness and established safety profile of NTZ, now assessed over 15 years.

Disclosure: This study is supported by Biogen. LK institutions: Abbvie, Actelion, Auriga Vision AG, Bayer HealthCare, Biogen, Bristol Myers Squibb, Celgene, Desitin, df-mp Monia & Pohlmann, Eli Lilly, EMD Serono, European Union, Genentech, Genzyme, Glaxo Smith Kline, Innosuisse, Janssen, Merck, Minoryx, Neurostatus, Novartis, Roche, Sanofi, Santhera, Senda Biosciences, Shionogi, Swiss MS Society, Swiss National Research Foundation, Teva, and Wellmera AG. TS: Biogen, Novartis. MT: Biogen, Novartis, Roche, Merck, Sanofi, and Teva; MT institution: Biogen, Merck, Roche, and Novartis. HB: Oxford Health Policy Forum; HB institution: Biogen, Merck, Novartis, Roche, UCB Pharma. HW: AbbVie, Actelion, Alexion, argenx, Biogen, Biologix, Bristol Myers Squibb, Cognomed, EMD Serono, Evgen, F. Hoffmann-La Roche, Gemeinnützige Hertie-Stiftung, Genzyme, GlaxoSmithKline GmbH, Idorsia, IGES, Immunic, Immunovant, Janssen, Johnson & Johnson, MedDay, Merck Serono, Novartis, Roche, Sanofi Genzyme, Swiss MS Society, Teva, UCB, WebMD Global. KB, ZS, AD: employees of and may hold stock and/or stock options in Biogen.

EPO-659

Predicting cognitive outcomes using deep learning derived brain age in people with multiple sclerosis

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Background and aims: Cognitive decline affects up to 70% of people with multiple sclerosis (MS). The MRI surrogate marker brain age has been shown to be associated with cognitive performance. We investigated the applicability of a deep learning-based algorithm estimating brain age using T1-weighted images to predict cognitive outcomes in people with MS.

Methods: In total, 67 people with MS from a local prospective longitudinal cohort were included in this study (mean age: 35.6 years, 70% females, mean disease duration 2.9 years, mean follow-up time 4.4 years). T1-weighted MRI data was acquired at two time points. The deep learning model, which was trained on 53,542 structural scans from healthy individuals (age range 3–95), was applied to estimate brain age . Annualized brain ageing and brain age gap (BAG), which is the difference between biological and estimated brain age, was then calculated. The patients underwent extensive cognitive testing, and a sum score for global cognitive function was calculated. Linear regression models were used to investigate the correlations between brain age, annualized brain ageing and cognitive performance.

Results: Annualized brain ageing and the BAG were not associated with the overall cognitive outcomes (t=-1.49, p=0.14 and t=0.50, p=0.61, respectively). However, accelerated annualized brain ageing was associated with reduced processing speed at follow-up (t=-2.17, p=0.03) and with increased verbal fluency score at follow-up (t=-2.06, p=0.04).

Conclusion: BAG did not predict global cognitive performance in our MS cohort. Accelerated annualized brain ageing was associated with reduced processing speed and lower verbal fluency.

Disclosure: Einar Høgestøl received honoraria for lecturing and advisory board activity from Biogen, Merck and Sanofi-Genzyme and unrestricted research grant from Merck. Gro Owren Nygaard, Esten H. Leonardsen reports no diclosures. Synne Brune has received honoraria for lecturing from Biogen and Novartis Elisabeth G Celius has received honoraria for advisory boards and/or speaker honoraria from Almirall, Biogen, Merck KGaA, Roche, Novartis, Genzyme and Teva, and unrestricted research grants from Novartis and Genzyme, and reports personal fees from Biogen, Sanofi, and Novartis, and personal fees from Roche and Merck KGaA.

EPO-660

Clinical utility of serum neurofilament light chains in multiple sclerosis measured by Ella™ versus Simoa™ assays.

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Background and aims: Neurofilament light chains (NfL) are cytoskeletal biomarkers of axonal damage, about 200 times lower in serum (s) compared to cerebrospinal fluid. Ultrasensitive techniques are employed to determine s levels, mostly a single molecule array (Simoa™). We aimed to compare sNfL levels determined with Simoa™ versus another platform, the Ella™, in multiple sclerosis (MS) patients at diagnosis.

Methods: 66 newly-diagnosed relapsing-remitting MS patients (42 females; mean age: 36.7 years, standard deviation or SD=10.4) were enrolled before steroid or disease-modifying treatments. sNfL were determined both with the commercial Ella™ microfluidic platform (Bio-Techne) and Simoa™ on SR-X instrument using NF-light assays (Quanterix).

Results: Mean sNfL levels were 37.6 pg/ml (SD=36.8, range 12–262) with Ella™ and 24.8 pg/ml (SD 34.1, range 3.8–208.4 pg/mL) with Simoa™. We observed a positive correlation between the two measures (Spearman's rank test: R=0.9, p<0.0001), and the Bland-Altman method showed a mean bias of 12.7% with Ella™ overestimating. sNfL did not correlate with gender and age at diagnosis.

Conclusion: sNFL serum levels measured with Ella™ resulted higher compared to Simoa™ in naïve patients. Despite this difference in absolute values, a good correlation between the two assays was demonstrated, showing that Ella™ is reliable to measure sNfL in MS. However, Ella™ and Simoa™ can not be interchanged in longitudinal studies.

Disclosure: The study was partially supported by Roche.

EPO-661

Characterization of ms patients at diagnosis through serum and cerebrospinal fluid biomarkers: preliminary data

E. Virgilio[1], D. Vecchio[1], C. Puricelli[2], S. Perga[2], N. Clemente[3], M. Hassan[3], S. Stangalini[2], E. Boggio[3], A. Appiani[2], L. Gigliotti[3], R. Cantello[1], U. Dianzani[2], C. Comi[4]

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Background and aims: Multiple Sclerosis (MS) is highly heterogeneous. Moreover, multiple disease-modifying treatments (DMTs) are available. Therefore, there is a need for robust fluid biomarkers from diagnosis, for characterization, and to monitor follow-up from early disease stages. Several biomarkers are consolidated, particularly neurofilaments light chains (NFL), but the value of others is less explored.

Methods: We aimed to evaluate the usefulness of different axonal damage and inflammatory biomarkers in cerebrospinal fluid (CSF) and serum in a cohort of 60 newly-diagnosed MS. Samples were obtained at diagnosis. CSF, serum NFL and osteopontin (OPN) were obtained using Ella microfluid platform, CSF total-tau and phosphorylated-tau using CLEIA Luminpulse.

Results: We observed a strong correlation between total-tau and p-tau (rs=0.76, p<0.0001) and between CSF and serum NFL (rs=0.80, p<0.0001) whereas, CSF and serum OPN did not. CSF and serum NFL correlated with total-tau (rs=0.45, p=0.0004 and rs=0.29, p=0.02), and not with p-tau. Patients with higher CSF NFL (rs=0.39 p=0.0019), total-tau (rs=0.27, p=0.03), and OPN (rs0.37 p:0.003) displayed higher EDSS at diagnosis. CSF (p=0.01) and serum NFL (p=0.04) were higher in patients with gadolinium-enhancing lesions and only CSF in patients treated after diagnosis with highly-efficacy DMTs (p=0.049), whereas high CSF OPN was observed in male patients (p=0.02).

Conclusion: Our preliminary data confirm the usefulness of CSF axonal damage biomarkers performed at MS diagnosis. Follow-up data such as disability scores over time and repeat serum dosages are needed. We suggest that a combination of several fluid biomarkers might be useful for a better characterization at diagnosis.

Disclosure: No disclosures related to the present study.

EPO-662

Patient centered outcomes of the ageing population in Multiple Sclerosis compared with the Danish background population

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Background and aims: The fraction of elderly patients with multiple sclerosis (MS) is growing and knowledge about patient-centered outcomes in this population remain sparse. The aim of the study was to compare socioeconomic and comorbidity metrics in aging patients with MS compared to the background population.

Methods: A matched cross-sectional study based on the nationwide population-based Danish Multiple Sclerosis Registry and nationwide public registries. Matching was done 1:10 on sex, age, and region to individuals from a 25% random sample of the background population.

Results: The study population was 8,336 patients with MS and 83,360 matches. The average age was 63.3 years (SD= 8.9) and 68.2% were females. There was no difference between the MS and matches on number of comorbidities (p=0.17), but the MS population had significantly more acute hospitalizations (p<0.0001). The MS population received more social care with a median of 20.5 (Q1–Q3: 5.0–60.5) monthly hours of practical help and 2.0 (Q1–Q3: 1.3–4.1) of personal care (p<0.0001). In the age-group 50–65 years, the proportion of MS patients receiving disability pensions was higher 46.1% versus 13.3 % (p<0.0001), and for those having a job, the annual salary was lower 45,000 € versus 50,000 € (p<0.0001). Progeny of both populations had similar marital status (p=0.26) and level of education (p=0.79).

Conclusion: The ageing population in MS are hospitalized more frequently, receive more social care, and perform worse on socioeconomic metrics compared to the background population. However, the prevalence of comorbidities is equal and progeny of patients with MS perform like those of the background population.

Disclosure: Malthe Wandall-Holm has received speaker honoraria from Novartis and Sanofi. Olivia Sarah Strandbech has nothing to disclose. Melinda Magyari has served in scientific advisory board for Sanofi, Novartis, Merck, and has received honoraria for lecturing from Biogen, Merck, Novartis, Roche, Genzyme, Bristol Myers Squibb.

EPO-663

Patients with benign multiple sclerosis have a much higher risk of disability pension than the background population

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Background and aims: Patients with multiple sclerosis (MS) experience vastly heterogenous disease courses. A subpopulation presents with benign MS (BMS), characterized by limited disability accumulation on the expanded disability status scale (EDSS), however their socioeconomic performance is poorly described. The aim of the study was to investigate the risk of disability pension of BMS patients compared to the background population.
Methods: A cohort study of MS patients of the working age (30–64) from the Danish Multiple Sclerosis Registry. The study period was 1998 to 2021, and matching was done 1:10 on age, sex, educational level, municipality, and calendar year to individuals from a 25% random sample of the Danish background population. We followed individuals to disability pension, censoring or a competing risk, and estimated absolute risk and cause specific hazard ratio (HR) of receiving disability pension.
Results: We identified 1,868 BMS patients with a mean age of 43.1 (SD=8.0) years and 69% were females. Most received a disease modifying treatment (87%) and the mean EDSS was 1.4 (SD=0.9). The absolute risk of receiving disability pension 20 years after disease onset was 13.7% (95% CI: 11.6–16.1) for the BMS-patients, significantly higher than the matches: 3.9% (95% CI: 3.5–4.3), $p<0.001$. Correspondingly, the BMS-patients displayed a fourfold increase in the hazard of receiving disability pension compared with controls, HR: 4.1 (95% CI: 3.4–4.8).
Conclusion: Despite a benign disease course defined by the standard clinical disability metric, EDSS, patients with BMS exhibit a much higher risk of disability pension compared to matches from the Danish background population.
Disclosure: Malthe Wandall-Holm has received speaker honoraria from Novartis and Sanofi. Mathias Due Buron has received speaker honoraria from Novartis. Rolf Pringler Holm has nothing to disclose. Finn Sellebjerg has served on scientific advisory boards for, served as consultant for, received support for congress participation or received speaker honoraria from Alexion, Biogen, Bristol Myers Squibb, H. Lundbeck A/S, Merck, Novartis, Roche and Sanofi Genzyme. His laboratory has received research support from Biogen, Merck, Novartis, Roche and Sanofi Genzyme. Melinda Magyari has served in scientific advisory board for Sanofi, Novartis, Merck, and has received honoraria for lecturing from Biogen, Merck, Novartis, Roche, Genzyme, Bristol Myers Squibb.

EPO-664

Baseline Characteristics in the Tolebrutinib Phase 3 Relapsing Multiple Sclerosis GEMINI 1 and 2 Trials

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Background and aims: GEMINI 1 (NCT04410978) and GEMINI 2 (NCT04410991) are two Phase 3 trials with identical designs, evaluating the efficacy and safety of tolebrutinib, an oral, brain-penetrant, Bruton's tyrosine kinase inhibitor, compared with teriflunomide in participants with relapsing multiple sclerosis (RMS). Our objective is to present baseline characteristics of GEMINI 1 and 2 trial participants.
Methods: GEMINI 1 and 2 are randomised, double-blind, double-dummy, parallel-group, event-driven (6-month confirmed disability worsening) trials in RMS participants aged 18–55 years, with an Expanded Disability Status Scale (EDSS) score $\leq$5.5 at screening and either $\geq$1 documented relapse within the previous year, $\geq$2 documented relapses within the previous 2 years, or $\geq$1 documented gadolinium-enhancing brain lesion on magnetic resonance imaging (MRI) within the previous year. Participants were randomised 1:1 to receive 60 mg oral tolebrutinib or 14 mg oral teriflunomide, once daily.
Results: 1,873 participants were enrolled (974 in GEMINI 1 and 899 in GEMINI 2), with a mean age of 36.7 and 36.4 years, and a mean time since diagnosis of 4.7 and 3.8 years, respectively. The majority were female (67% combined), more than half were treatment-naïve (66%), and the mean number of relapses in the year prior to enrolment was 1.2. At baseline in both trials, the mean EDSS score was 2.4, and 35% of participants had gadolinium-enhancing lesions.
Conclusion: GEMINI 1 and 2 trial cohorts have similar baseline characteristics, consistent with the tolebrutinib Phase 2b RMS trial (NCT03889639). These trials will provide a comprehensive assessment of tolebrutinib efficacy and safety in RMS.
Disclosure: STUDY FUNDING: Sanofi. HW: honoraria (Abbvie, Alexion, Argenx, Biogen, BMS, F Hoffmann-La Roche, Janssen, Merck, Neurodiem, Novartis, Roche, Sanofi, Teva, WebMD); consulting (Abbvie, Actelion, Argenx, Biogen, BMS, EMD Serono, Fondazione Cariplo, Gossamer Bio, Idorsia, Immunic, Immunovant, Janssen, Lundbeck, Merck, NexGen, Novartis, PSI, Roche, Sanofi,

Swiss Multiple Sclerosis Society, UCB, Worldwide Clinical Trials); research funding (German Ministry for Education & Research, Deutsche Forschungsgesellschaft, Deutsche Myasthenie Gesellschaft, Alexion, Amicus, Argenx, Biogen, CSL, F Hoffmann-La Roche, Merck, Novartis, Roche, Sanofi, UCB). JO: consulting/speaking (Biogen, BMS, EMD Serono, Novartis, Roche, Sanofi); research (Biogen, EMD Serono, Roche). MPS: fees (Biogen, Merck, Roche, Sanofi, Novartis, Geneuro, GSK); grants (Italian Multiple Sclerosis Foundation). SS, DD, PB, LP: employees of Sanofi and may hold shares and/or stock options. HJK: grant (National Research Foundation of Korea); research (Aprilbio, Eisai); consulting (Alexion, Aprilbio, Altos, Biogen, Celltrion, Daewoong, Eisai, GC Pharma, HanAll, Handok, Horizon Therapeutics, MDimune, Mitsubishi Tanabe Pharma, Merck, Novartis, Roche, Sanofi, Teva, UCB); Mult Scler J coeditor; J Clin Neurol associate editor. BACC: consulting (Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Horizon, Immunic, Neuron23, Novartis, Sandoz, Sanofi, Siemens, TG Therapeutics, Therini); research (Genentech)

EPO-665

What is the best titration protocol for dimethyl fumarate? Preliminary results of a multicenter real-world study

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Background and aims: Dimethyl fumarate (DMF), an oral medication commonly used to treat relapsing forms of multiple sclerosis (MS), is generally well tolerated, with common side effects including flushing, and gastrointestinal symptoms, particularly in the first month of the treatment. Slower titrations of DMF and dietary recommendations may reduce side effects. However, to date, there are no studies comparing titration protocols. The aim of this study is to exhibit a real-world safety profile and to compare the titration protocols.

Methods: Individuals with MS who were started on DMF treatment in thirteen tertiary MS centers were included in the study. In addition to the demographic and disease characteristics of the participants, DMF side effects and other safety data, titration protocols were recorded to an online database.

Results: A total of 825 individuals were included in the study. Mean age at the initiation of DMF treatment was 32.5±9.7 and the mean EDSS was 1.2 (0.8). In 505(61.2%) individuals, DMF was started as first-line therapy. 405(49.08%) individuals experienced flushing, 89 (11.38%) abdominal pain and 51 (6.53%) diarrheas. 694 individuals (84.12%) continued DMF treatment. The protocol increasing 120 mg weekly to 240 mg BID in the fourth week was associated with less flushing and GI side effects compared to the protocol increasing to 240 mg BID in the second week.

Conclusion: In this study, it has been shown that slower titration is associated with less flushing and fewer GI symptoms, and it has been demonstrated that appropriate patient management and supportive treatment can increase treatment adherence.

Disclosure: Nothing to disclose.

EPO-666

Acute hemorrhagic leucoencephalitis with subacute onset: a case report.

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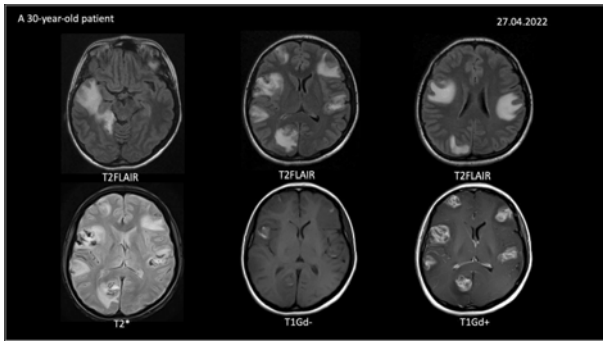
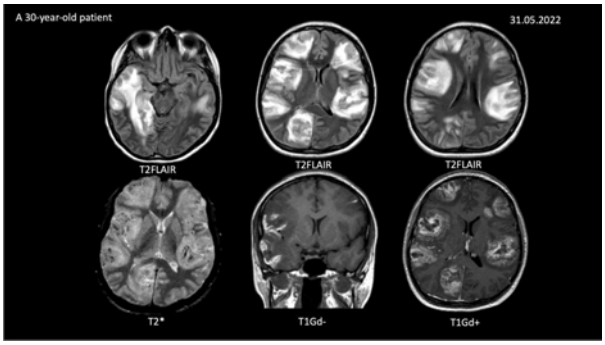
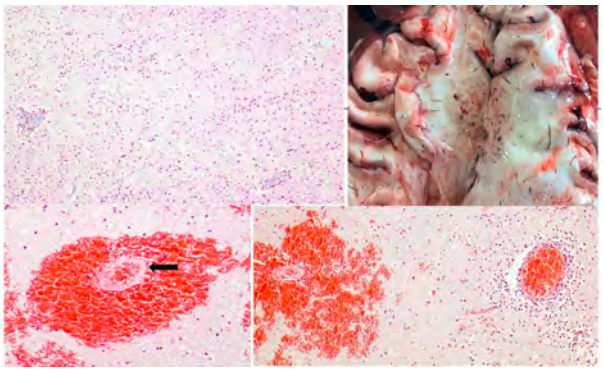
Background and aims: Acute hemorrhagic leukoencephalitis (AHLE), rare and severe form of acute disseminated encephalomyelitis, is an inflammatory fulminant CNS disorder.
Methods: We report a case of a 30-year-old patient with a rare AHLE presentation characterized by subacute onset and slow progression, her clinical, radiological, laboratorial and post-mortem histological findings.
Results: AHLE is usually characterized by an acute onset and fulminant disease course. In our case first symptoms appeared in April 2022 as a nonspecific headache. MRI demonstrated large multifocal T2 and T2-FLAIR-hyperintense brain lesions, surrounded by T2*-hypointense areas (signs of blood). Lesions heterogeneously accumulated contrast. Diagnostic search included CNS paraneoplastic processes and infectious diseases. During the following month, relatives noted only slight personality changes, like irritation and hypersomnolence. In the end of May she was admitted to our department where negativism, aggression, psychomotor agitation, sensorimotor aphasia. CSF analysis showed an increased protein (0.551 g/l) and slight pleocytosis (8 cells/mm^3). Preliminary diagnosis of AHEM was established. High-volume plasmapheresis couldn't be performed due to the patient's menarche and large hemorrhagic component in the brain foci. Therefore, methylprednisolone pulse therapy was initiated, however patient's state gradually deteriorated resulting in coma and subsequent death on the 10th day of hospitalization. Post-mortem histological analysis revealed the classic triad - white matter demyelination in cerebral hemispheres, multiple perivascular hemorrhages and inflammatory infiltrate.



MRI demonstrated large multifocal T2 and T2-FLAIR-hyperintense brain lesions, surrounded by T2*-hypointense areas (signs of blood). Lesions heterogeneously accumulated contrast



The negative dynamics in MRI of the brain



Post-mortem histological analysis revealed the classic triad - white matter demyelination in cerebral hemispheres, multiple perivascular hemorrhages and inflammatory infiltrate

Conclusion: Approximately in 30% of AHLE cases, patients survive due to early disease recognition and following aggressive immunosuppression. Unusual subacute onset and progression impede AHLE recognition and life-threatening delay in treatment, as in our case.
Disclosure: No conflict of interest.

EPO-667

Abstract withdrawn

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EPV-001

Radiological Features of Cerebral Small Vessel Disease and Determinants of their Correlation with Symptomatology

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EPV-002

Do Subclinical or Overt Seizure Activity Play a Role in Symptomatology in Cerebral Small Vessel Disease (CSVD)?

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EPV-003

A visuomotor ability-based screening tool for mild cognitive impairment – a pilot study

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EPV-004

Efficacy of Pimavanserin on Dementia-Related Psychosis: A Systematic Review and Meta-Analysis

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EPV-005

Time lag to first visit to memory clinic between different young-onset dementia groups

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EPV-006

Cerebrospinal (CSF) p-tau/t-tau ratio determines different CSF and FDG-PET findings in sporadic Frontotemporal Dementia

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EPV-007

Sociodemographic and cognitive characteristics of superagers

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EPV-008

Novel splice site GRN mutation in a patient with AD-like phenotype at onset

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EPV-009

An attempt to understand a mysterious entity – a 6-year review of patients with Transient Global Amnesia

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EPV-010

A Systematic Review of Pharmacological Treatments for Motor Symptoms in Creutzfeldt-Jakob Disease (CJD)

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EPV-011

Incident Anti-LGI1 autoimmune encephalitis during dementia with Lewy bodies: when Occam razor is a double-edged sword

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EPV-012

Features of disorders of cerebral circulation in patients with vascular dementia

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EPV-013

Sleep microstructure disruption in Parkinson's disease related dementia reflects neurodegeneration progression.

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EPV-014

Exploring modificable risk factors across the Alzheimer's Disease Continuum

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EPV-015

Quantitative EEG analysis as a possible treatment efficacy biomarker in cerebral amyloid angiopathy-related inflammation

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EPV-016

Mass-spectrometric study of changes in the blood plasma proteome associated with frontotemporal dementia

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EPV-017

Burnout among neurologists caring for patients with cognitive disorders

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EPV-018

Zinc Deficiency Its Supplementation in iAlzheimers-like Disease in Rats Are Associated with Cerebral Cortex ZIP14 Levels

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EPV-019

Impact of Omega-3 Fatty Acid on Cognitive Function Among Healthy & AD Elderly: A Systematic Review and Meta-analysis

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EPV-020

Differential clinical profile of typical and atypical phenotypes of progressive supranuclear palsy

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EPV-021

Posterior Cerebral Vasoconstriction Associated to sporadic Creutzfeldt Jakob Disease

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EPV-022

Right temporal variant frontotemporal dementia with a mutation in p62/SQSTM1.

E. Koumasopoulos[1], E. Stanitsa[1], E. Angelopoulou[1], D. Barbarousi[2], G. Velonakis[2], C. Michaletou[1], S. Alevetsovitis[1], V. Constantinides[1], C. Koros[1], A. Kyrozis[1], L. Stefanis[3], C. Kroupis[4], S. Papageorgiou[1]
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EPV-023

Behavioral variant frontotemporal dementia phenotype in a heterozygous prion gene mutation carrier.

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EPV-024

Right temporal variant frontotemporal dementia with a mutation in p62/SQSTM1.

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EPV-025

Effects of cognitive training system (CAVE) on cognitive function in patients with Alzheimer's dementia

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EPV-026

Micro-RNA in a Sample of Egyptian Patients with Incidental Cerebral Small Vessel Disease

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EPV-027

Biomarkers of cognitive decline.

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EPV-028

Functional connectivity as predictor of transformation to dementia

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EPV-029

A man with neuropsychiatric symptoms and cognitive decline

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EPV-030

CD40 activation mediates neuroinflammation in experimental epilepsy

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EPV-031

Tau pathology in hub regions is associated with higher conversion to Alzheimer's disease

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EPV-032

Association of T1W/T2W ratio and cognitive decline in Alzheimer's disease

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EPV-033

Study of psychiatric comorbidities in dementia

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EPV-034

Additional behavioral features to improve the diagnosis of semantic behavioral variant frontotemporal dementia

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EPV-035

Right temporal variant frontotemporal dementia and parkinsonism: a rare association?

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EPV-036

Neurological Soft Signs usefulness in neurodegenerative dementias

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EPV-037

Time to progression through AD disease stages & associated probability of institutionalization

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EPV-038

First report of a portuguese family with frontotemporal dementia due to CHMP2B gene mutation

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EPV-039

Caudate functional connectivity network in amyloid positive mild cognitive impairment and Alzheimer's disease patients

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EPV-040

Alterations of Sleep Spindle Frequency, Duration, and Amplitude in Patients with Mild and Severe Alzheimer's Disease

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EPV-041

Correlation between blood monocytes and CSF Tau in Alzheimer's disease: the effect of gender and cognitive decline

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EPV-042

Acceptance rate of the APOE gene (APOE-ε4) study in routine clinical practice. Preliminary results

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EPV-043

The frequency of psychotropic drug use in early-onset Alzheimer's Disease

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EPV-044

Brain stimulation with MRI-guided transcranial pulse stimulation (TPS) – Improvement of cognitive deficits in AD

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EPV-045

Vascular dementia is associated with an increased risk of vascular events or death.

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EPV-046

Nasu-Hakola disease associated with early onset dementia of frontal lobe type

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EPV-047

Evaluating intangible costs for patients with mild cognitive impairment or Alzheimer's Disease in the United States

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EPV-048

Evaluating caregiver and employer indirect costs for patients with MCI or AD in the US

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EPV-049

Abstract withdrawn

EPV-050

FDG/PET as diagnostic tool in atypical case of Huntington disease

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EPV-051

Preventive, screening system for early detection of demencia

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EPV-052

Is there correlation of executive functions and brain white matter in amnestic multidomain Mild cognitive impairment?

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EPV-053

1 year follow-up after Transcranial Pulse Stimulation in Alzheimer´s patients

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EPV-054

Pharmacoepidemiology of Creutzfeldt-Jakob Disease in Austria - an exploratory retrospective analysis

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EPV-055

Abnormal dopamine transporter imaging in pure autonomic failure: A potential biomarker of CNS involvement

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EPV-056

Plasma and CSF biomarkers of neurodegeneration in multiple system atrophy

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EPV-057

Alignment and recovery of physiological signals of two asynchronous sources for MMDD protocol

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EPV-058

Trends of autonomic dysregulation in the first 24h after suffering stroke, or intracerebral hemorrhage

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EPV-059

Impact of awareness about FAST in stroke

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EPV-060

The prognostic role of eosinophil-to-monocyte ratio in patients with ischemic stroke

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EPV-061

The association between systematic inflammation response index and 3-months functional outcome in acute ischemic stroke

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EPV-062

Post-traumatic ischemic stroke: a rare complication

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EPV-063

Non-Aneurysmal subarachnoid haemorrhage: The yield of repeated angiogram

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EPV-064

Early onset cerebral amyloid angiopathy in 3 patients with recurrent hemorrhagic stroke and a history of neurosurgery.

I. Albajar, J. Equiza, P. Iruzubieta, N. Sulibarria, G. Nuñez, P. Arratibel, J. Marta, C. Gutierrez, A. De Arce, N. Diez, F. Gonzalez, M. Martinez, J. Larrea, M. Alonso, V. Gomez, P. De la Riva
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EPV-065

From the trauma operating room to the thrombectomy room. A case report.

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EPV-066

The importance of repeating transesophageal echocardiography in ESUS: unnoticed cardiac papillary fibroelastoma

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EPV-067

Beyond the limit: salvaging the posterior circulation territory via late endovascular thrombectomy

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EPV-068

Mechanical thrombectomy for ischemic stroke presenting with concomitant ipsilateral hyperacute haemorrhage,

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EPV-069

Endothelial dysfunction in patients undergoing carotid artery stenting

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EPV-070

Hemostasis and hemorheology markers in atherosclerosis and cerebrovascular disease after carotid artery stenting

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EPV-071

Visceral adipose tissue and hemostasis in patients with cerebrovascular diseases

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EPV-072

Nitrous oxide, Dangerous euphoria A Central venous thrombosis in a nitrous oxide user

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EPV-073

Quality indicators in the stroke care in the young population

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EPV-074

Stroke after COVID-19 era: is there a "stroke wave" resulting from the pandemic?

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EPV-075

Analysis of cardiovascular risk factors and their treatment in stroke patients admitted to a third level hospital

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EPV-076

Bilateral anterior cerebral artery stenosis due to fibromuscular dysplasia: an unusual cause of ischemic stroke

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EPV-077

Intravenous (IV) thrombolysis in cardioembolic and in large artery stenosis (LAS) acute ischemic stroke

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EPV-078

Direct carotid artery puncture in acute thrombectomy: a case report

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EPV-079

Border-zone infarcts due to severe chronic anemia

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EPV-080

Analysis of patients with lacunar stroke at a third-level hospital

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EPV-081

Cerebral Amyloid Angiopathy Related Inflammation (CAARI) in Down Syndrome

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EPV-082

Ischemic stroke and the knee-chest position in labor, a case report

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EPV-083

A cervicomedullary lesion with a challenging differential diagnosis

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EPV-084

An Unusual Case of Cerebrovascular Dysregulation

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EPV-085

Extra-intracranial Anastomosis In The Acute Phase Of Stroke

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EPV-086

Lyme disease-associated vasculitis with fatal course

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EPV-087

Ischemic stroke in chronic bilateral middle cerebral artery occlusion caused by acute vertebral artery occlusion

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EPV-088

CEREBROVASCULAR COMPLICATIONS IN RCVS: 2 CLINICAL CASES AND REVIEW OF LITERATURE.

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EPV-089

Panel of serum biomarkers of brain damage in acute ischemic stroke

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EPV-090

Hypersomnolence in patients in the acute period of ischemic stroke

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EPV-091

Can clinical scores substitute CT scan in rural settings for differentiating ischemic from hemorrhagic stroke?

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EPV-092

A descriptive single-centre study of adults with cerebral venous thrombosis.

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EPV-093

Multiple strokes at the time of diagnosis in a patient with giant cell arteritis.

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EPV-094

Post-stroke pneumonia – clinical features and outcome

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EPV-095

What should we do when there is air in the cerebral artery?

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EPV-096

Factors affecting functional prognosis after acute reperfusion therapy with successful recanalization

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EPV-097

Disorders in genes for thrombophilia as the only risk factor for the development of spontaneous SAH – a case report

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EPV-098

One- and- a -half syndrome due to unruptured basilar trunk artery aneurysm

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EPV-099

Unroofed coronary sinus and its relation to embolic stroke of undetermined source

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EPV-100

Added value of MRI radiomics features in acute stroke imaging – a systematic review and meta-analysis

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EPV-101

Brain symmetry index as a prognosis tool in ischemic stroke patients – a systematic review

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EPV-102

Factors Influencing Recurrent Stroke: A Case-Control Study

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EPV-103

Correlation of Neurofilament Light Chain serum concentrations with renal function in acute ischemic stroke patients

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EPV-104

Fatty-acid Binding Protein-2 (FABP2) serum concentrations and blood lipid profile in ischemic stroke patients

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EPV-105

Predictors of good outcome in Tandem Occlusion: single center experience with 12-month follow-up

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EPV-106

Paradoxical cerebral embolism secondary to pulmonary arteriovenous malformation, chance or genetics?

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EPV-107

Cerebral Amyloid Angiopathy related inflamation: amyloid biomarkers useful for diagnosis?

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EPV-108

Rapidly progressive dementia: a case of intracranial giant cell arteritis

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EPV-109

Charles - Bonnet syndrome in patient with occipital lobe stroke – a case report

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EPV-110

Isolated hand thermo- and pain anaesthesia due to midlateral medullary infarction

L. Franco Rubio, P. Abizanda Saro, N. Rodríguez Albacete, A. Aldaz Burgoa, L. López Trashorras, V. Cid Izquierdo, A. Fernández Revuelta, A. Marcos Dolado, R. Ginestal López, E. López Valdés
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EPV-111

Description, analysis and comparison of patients admitted during the year 2021 with acute cerebrovascular disease

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EPV-112

Diffuse Proliferative Cerebral Angiopathy

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EPV-113

Indicators of D-dimer as a predictor of ischemic stroke in COVID-19 in Tashkent

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EPV-114

Impact of HbA1c level on the occurrence of early epileptic seizures in the acute ischemic cerebral stroke

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EPV-115

Adult Moyamoya angiopathy related stroke: long-term follow-up and outcomes in a Tunisian population

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EPV-116

Eight and a half syndrome: A rare manifestation of brainstem stroke

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EPV-117

Intracranial arterial dissection as a cause of stroke in a middle-aged adult

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EPV-118

Atypical cervical spinal cord infarction caused by transient hypoperfusion

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EPV-119

1 patient, 2 amyloidoses: Cerebral amyloid angiopathy and light chain amyloidosis

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EPV-120

Clinical case. Multiple cerebral cortical hemorrhage associated with subarachnoid hemorrhage

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EPV-121

Carotid web: a little known cause of cryptogenic stroke in young patients. Two clinical cases

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EPV-122

Bilateral wrist drop as an infrequent stroke chameleon

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EPV-123

Bilateral carotid dissection: a rare manifestation of eagle's syndrome

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EPV-124

Mechanical thrombectomy in cerebral venous thrombosis: myth or challenge?

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EPV-125

Young stroke due to Neuroborreliosis: case report

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EPV-126

Thrombotic Thrombocytopenic Purpura and Neurological Complications

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EPV-127

Ipsilateral Weakness Caused by Ipsilateral Stroke: A Case Series

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EPV-128

Diagnostic algorithm for identifying ischemic stroke associated with cancer

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EPV-129

Pre-antibiotics use and stroke recurrence and mortality

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EPV-130

Cervical artery dissection in the elderly: does it exist?

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Abstract withdrawn

EPV-132

Blood Pressure Variability and Shifting in Clinical Outcome Amongst Stroke Patients in Uganda

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EPV-133

Postpartum reversible cerebral vasoconstriction syndrome probably associated with eclampsia: a case report

M. Lara González, M. García Ruiz, B. Hidalgo Valverde, J. Alcalá Ramírez del Puerto, V. Cid Izquierdo, C. Ribacoba Díaz, R. Ginestal López, A. Marcos Dolado, E. López Valdés, P. Mayo Rodríguez
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EPV-134

Successful vertebrobasilar dissection treatment in a stroke patient and the significance of ultrasound follow-up

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EPV-135

Unilateral basal ganglia calcification and ischaemia due to developmental venous anomaly mimicking haemorrhagic stroke

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EPV-136

Cerebral Venous trombosis secondary to lymphoproliferative neoplasm treated thrombolysis and mechanical thrombectomy

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EPV-137

When "the world is upside down" – a rarely documented manifestation of stroke

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EPV-138

Post-stroke sexual dysfunction in first stroke male patients

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EPV-139

Differences in risk factors for intracerebral hemorrhage of various localization in the Kazakh population

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EPV-140

Ischemic stroke in the posterior circulation: retrospective cohort study

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EPV-141

Decompressive craniectomy for malignant cerebral edema in patients with mechanical thrombectomy for stroke

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Carotic endarterectomy as an alternative to acute placement of carotic stent in the management of acute ischemic stroke

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EPV-143

Post stroke depression: A major determinant of quality of life amongst stroke survivors in a Cameroonian hospital

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EPV-144

Cerebral amyloid angiopathy, comorbid atrial fibrillation: management of patients with ischemic stroke. Case report

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EPV-145

Indication of decompressive craniectomy for stroke by traumatic carotid dissection

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EPV-146

Developing thrombolysis service for ischemic stroke patients in an under-developed country, our seven year wexperience.

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Epv-147

Endovascular Treatment For Anterior Cerebral Artery Occlusions

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EPV-148

The effect of the mpv on short-term prognosis in acute ischemic stroke patients

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EPV-149

Bilateral simultaneous thalamic hematomas – unusual presentation of hypertensive intracerebral hemorrhage

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EPV-150

Cerebral fat embolism combined with venous thromboembolism after bilateral total knee replacement arthroplasty

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EPV-151

Early Post-Stroke Cognitive Impairment in Young Adult Ischemic Stroke is associated with stroke subtypes and severity

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EPV-152

Room tilt illusion as the only manifestation in vertebral artery dissection

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EPV-153

Diagnostic and prognostic significance of carotid doppler ultrasonography in diabetic atherosclerosis

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EPV-154

Traumatic brain injury and glymphatic system impairment

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EPV-155

Atherosclerosis disease and increased risk of stroke associated with chronic opioid use– a distinct spell of Morpheus?

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EPV-156

PREDICTORS OF ACUTE SYMPTOMATIC SEIZURES IN CEREBRAL VENOUS THROMBOSIS

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EPV-157

miR-33a levels are associated with higher LDL cholesterol in carotid atherosclerosis

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EPV-158

Cerebral Hyperperfusion Syndrome and the stroke that never was

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EPV-159

Atypical Skull Base Osteomyelitis: a rare cause of bihemispheric strokes

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EPV-160

The prognostic role of inflammation serum markers in stroke: a retrospective observational study

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EPV-161

Aortic floating thrombi causing stroke in a young man with antiphospholipid syndrome

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EPV-162

Cervical Artery Dissection: A retrospective study of clinical features, etiology and outcomes

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EPV-163

Eagle's syndrome as a cause of stroke and its treatment in the acute phase: a case report

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EPV-164

Endovascular Treatment of Anterior Communicating Artery Aneurysms: A Retrospective Single-center Experience from Iran

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EPV-165

Sudden coma onset as a form of presentation of acute bilateral arterial occlusion.

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EPV-166

Thrombolysis in stroke-heart syndrome: an useful tool for neurocardiac wellness?

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EPV-167

The role of Neurohospitalism in a specialized Cardiovascular Hospital

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EPV-168

Encephaloduroarteriomyosinangiosis for treatment of carotid fibromuscular dysplasia

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EPV-169

Acquired Cerebral Amyloid Angiopathy following Epilepsy Surgery

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EPV-170

Recurrent embolic stroke due to endocarditis in drug-addicted patients

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EPV-171

Nonspesific white matter hyperintensities(wmh) on brain – is it always nonspesific? A case report of a rare cause of WMH

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EPV-172

Investigation of Hemorheological Parameters in Stroke Patients

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EPV-173

Persistent trigeminal artery as a rare cause of vertebrobasilar insufficiency sypmtoms

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EPV-174

Aortitis and aortic thrombosis in primary antiphospholipid syndrome: where is the link?

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EPV-175

The role of the excessive nighttime activity in the incidence of ischemic stroke

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EPV-176

Dysphasia after stroke and legal capacity

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EPV-177

Predictive value of nontraditional lipid parameters for symptomatic intracranial atherosclerosis in stroke patients

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EPV-178

Grouping signs of cerebral small vessel disease: clinical and neuroimaging features

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EPV-179

ATYPICAL CELIAC DISEASE AS A RARE CAUSE OF STROKE

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EPV-180

Treatment of deep vein thrombosis in a female patient with intracerebral hemorrhage – case report

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EPV-181

Acute intermittent porphyria: a rare challenging neuro-metabolic disease; a case study

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EPV-182

"A comparative analysis of the qualitative characteristics of the sleep among school-aged children"

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EPV-183

Serial organization of movements in children with autism spectrum disorders

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EPV-184

Changes in neuropsychological status of children with high benign focal epileptiform discharges of childhood index

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EPV-185

Prenatal dorsoventral differentiation of the human cingulate cortex during the subplate formation period

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EPV-186

Deep-layer neuron markers reveal early regional differences during initial cortical plate formation in the human brain

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EPV-187

General Movements: Predictive Tool of the Neurological Outcome in Term-Babies with HIE at 12 months of age.

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EPV-188

The dynamic clinical course of a pediatric patient with a CACNA1A mutation

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EPV-189

KIF1A-dependent disorders in a group of first Polish patients

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EPV-190

The effect of cathodal tDCS in the treatment of Levodopa-Induced Dyskinesias in PD: a preliminary report.

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EPV-191

Video-head impulse test characteristics in peripheral, central and neuromuscular disorders

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EPV-192

Expiratory CO_2 levels reduction: a misinterpreted alert of motor prognosis in IONM

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EPV-193

Extrapulmonary tuberculosis with a clinical presentation with spondylodiscitis and secondary bacterial meningitis

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EPV-194

Impact of the first Electromyography in the diagnostic delay of Amyotrophic Lateral Sclerosis

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EPV-195

Electroencephalography Findings in Rasmussen Encephalitis

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EPV-196

Sural to radial ratio lower limits of normal: systematic review of the current literature

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EPV-198

Childhood trauma and multiple sclerosis: coincidence or causality

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EPV-199

Smartphone-based cognitive dual-task cost is not influenced by mobility and cognition in independent neurologic patients

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EPV-200

Impact of Leukoaraiosis on Post-Stroke Executive Function Impairment

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EPV-201

Anatomical correlates of strategic memory: a neuropsychological study

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EPV-202

Neuropsychological evaluation and treatment adherence in adults with Atrial Fibrillation and Silent Brain Infarcts

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EPV-203

Multivariate analysis of the effects of asthma and COPD on cognition in chronic inflammatory pulmonary diseases.

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EPV-204

Discriminative value of Free and Cued Selective Reminding Test in dementias in a Tunisian cohort

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EPV-205

Mood disorders after stroke: prevalence and risk factors in a Tunisian cohort

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EPV-206

Vascular cognitive impairment with and without vascular parkinsonism from a behavioural and psychological approach

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EPV-207

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EPV-208

Functional near-infrared spectroscopy (fNIRS) for the diagnosis of schizophrenia

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EPV-209

Dressing apraxia: a long time isolated symptom in a patient with Alzheimer's disease

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EPV-210

Literacy Independent Cognitive Assessment assessing Post-stroke Cognitive Impairment: A Single-Center Experience

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EPV-211

Longitudinal Analysis of the Clock Drawing Test After Stroke

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EPV-212

Validation of the Mini-Linguistic State Examination in Post-Stroke Aphasia

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EPV-213

Optimization of AT(N) classification using clustering analysis in Cerebrospinal Fluid Biomarkers

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EPV-214

Comparative study of the cognitive profile in patients with mild cognitive impairment with and without type 2 diabetes.

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EPV-215

Cognitive function in non-relapsing myelin oligodendrocyte glycoprotein antibody-associated disease: a case series

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EPV-216

Exploring hypomimia in Alzheimer's disease

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EPV-217

Prevalence and Risk Factors Associated with the Cognitive Impairment Among Type-2 Diabetes Mellitus Patients

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EPV-218

Low Plasma Kynurenic Acid Sustains Normal Cognitive Maturation

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EPV-219

Cognitive Impairment and depression in Albanian patients with epilepsy

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EPV-220

Evaluation of the effect of the coexistence of ischemic stroke and osas on cognition in young patients

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EPV-221

Predicting long-term functional and cognitive outcome in patients emerging from a post-traumatic confusional state

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EPV-222

The Swallowing Assessment in Disorders of Consciousness (SWADOC) Validation: A Multicenter Prospective Cohort Study

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EPV-223

EEG connectivity measures have superior prognostic value to predict outcome in patients with disorders of consciousness

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EPV-224

The Comorbidities Coma Scale (CoCoS): validation study in Russia

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EPV-225

Immunity after vaccination against SARS-CoV-2 in MS patients treated with dimethyl fumarate and interferon-beta

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EPV-226

COVID-19 and its effects on the stroke management pathway in the Maltese population

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EPV-227

Post-COVID-19 syndrome in patients with Parkinson's Disease: a prospective cross-sectional study

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EPV-228

COVID-19 vaccination hesitancy among people with Parkinson's disease

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EPV-229

Investigation of the effects of the COVID-19 pandemic on epilepsy patients in Kayseri-Turkey

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EPV-230

Severe COVID-encephalopathy: from movement disorders to a surprising cognitive outcome

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EPV-231

The SARS-CoV-2-Pandemic And Its Impact On Patients With Chronic Inflammatory Neuropathies

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EPV-232

Facial Nerve Palsy a Possible Neurological Complication After SARS-CoV-2 Infection: Systematic Review and Meta-Analysis

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EPV-233

Novel mentorship program for young physicians, Neurologists, and medical students: Lessons from COVID-19 lockdown

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EPV-234

Psychological and cognitive effects in a group of COVID-19 survivors; preliminary results of a cross-sectional study

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EPV-235

Analysis of coronavirus disease 2019 and post-COVID-19 syndrome in patients with multiple sclerosis

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EPV-236

Assessment of the neurodegenerative changes of the central nervous system in patients after SARS-COV-2 infection

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EPV-237

Is telemedicine suitable for the assessment of neurological symptoms in Post-COVID-19 syndrome?

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EPV-238

Symptomatic treatment of persistent headache related to COVID-19

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EPV-239

Profile of headaches in patients with post-COVID syndrome. Experience of a Neuro-COVID Neurology consultation.

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EPV-240

Cognitive Inhibition Deficit as a Potential Sensitive Marker of Long Term Follow-up of COVID-19 Syndrome

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EPV-241

Features of Guillain-Barré syndrome (GBS) associated with COVID-19

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EPV-242

Impact of SARS-CoV-2 infection and vaccination in migraine symptoms during the COVID-19 pandemic

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EPV-243

Nonketotic Hyperglycemic–Induced Hemichorea–Hemiballismus Following COVID-19 (BNT162b2) Vaccination

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EPV-244

Sleep disturbances after COVID-19 in patients with coronary artery disease

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EPV-245

Type I interferon signalling in SARS-CoV-2 infected epithelia: a prelude to neuroinflammation

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EPV-246

Neurological post-COVID-19 symptoms in general population

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EPV-247

Neurophobia: Nigerian medical students' perception of Neurology

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EPV-248

Motivation profiles in neurological medical center: similarities and differences among medical and administrative staff

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EPV-249

Portuguese residents self-perception on skills in Stroke Medicine acquired during Neurology residency

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EPV-250

"Neurophobia" and the perception of neurology among junior doctors in a northern Spanish region

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EPV-251

Neurogame or the benefit of gamification in neurological pedagogy

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EPV-252

Assessing Motor Neurone Disease (MND) skills amongst UK trainees.

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Epv-253

Electrocorticogram [Ecog] Experience In A Tertiary Care Hospital In India

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EPV-254

New on set refractory status epilepticus (norse): a restrospective case-series

J. Bermejillo Barrera, J. Fajardo Sanchís, B. Gómez Gozálvez, J. Garcia-Carmona, T. Espinosa Oltra, I. Díaz Jiménez, D. Vidal Mena, C. Sánchez-Vizcaíno Buendía, J. Pérez Vicente, J. Sánchez Villalobos, E. Conesa García
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EPV-255

Analysis of antiepileptic treatment in patients admitted with a diagnosis of status epilepticus between 2017 and 2022

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EPV-256

Chemokine C-C motif ligand 2 (CCL2) in children with status epilepticus

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EPV-257

Cannabidiol is associated with the improvement of neuropsychiatric profile in patients with Lennox-Gastaut syndrome.

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EPV-258

Diagnosis and treatment of late onset myoclonic epilepsy in Down Syndrome (LOMEDS): a systematic review

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EPV-259

Predictors of psychogenic non-epileptic seizures in patients admitted to emergency service

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EPV-260

Refractory epilepsy with a good response to clobazam

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EPV-261

Effectiveness of Cannabidiol in epileptic syndromes besides Dravet and Lennox-Gastaut

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EPV-262

Risk factors for drug-resistant epilepsy among pediatric patients in Philippine Children's Medical Center

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EPV-263

Heart rate variability (HRV) as predictive factor of SUDEP: A systematic review and meta-analysis

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EPV-264

Epilepsy and music; reflex seizures and seizures with music production

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EPV-265

Epileptic and structural variability in a family with familiar focal epilepsy with variable foci

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EPV-266

Nonconvulsive status epilepticus as a presenting form of diabetic ketoacidosis in patient with Type 1 Diabetes Mellitus

L. Fernández Pérez, I. Sánchez-Miranda Román, R. Amela Peris, A. Ruano Hernández, A. Díaz Díaz, L. Pérez Navarro, D. Cardona Reyes, A. Hernández Concepción, M. Pinar Sedeño
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EPV-267

Outcomes and retention rate of lamotrigine and levetiracetam double therapy: a peak ten years into the future

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EPV-268

Late-onset epilepsy and subclinical cerebrovascular disease

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EPV-269

Dissociative disorders in patients with epilepsy

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EPV-270

Nodding Syndrome

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EPV-271

Serum concentrations of cenobamate in seizure-free and in unsuccessfully treated patients

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EPV-272

Electroclinical description of glutaric aciduria type 1 associated epilepsy

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EPV-273

Epileptiform discharges in the anterior thalamus of epilepsy patients

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EPV-274

Headache is a common aura in patients with generalized seizures

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EPV-275

Ten patients with MRI verified hippocampal lesions and epileptiform discharges in EEG

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EPV-276

Screening for comorbid depression in epilepsy with NDDI-E for neurologists

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EPV-277

Structural heterogeneity of epileptic focus in neurosurgical patients

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EPV-278

Absence status epilepticus as a debut of idiopathic generalized epilepsy in adulthood: a case report

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EPV-279

Epilepsy in Alzheimer's Disease Patients

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EPV-280

Epilepsy in infancy with migrating focal seizures: the second reported de novo KCNT1 mutation c.1438G>A (p.Asp480Asn)

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EPV-281

Quality of sleep and daytime sleepiness in patients with Lennox-Gastaut syndrome treated with cannabidiol

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EPV-282

Epilepsy surgery in patients 50 years or older

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EPV-283

Clinical characteristics of new-onset epilepsy during pregnancy.

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EPV-284

Similarities in long-term memory function among patients with temporal and genetic generalized epilepsy

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EPV-285

The knowledge and awareness of epilepsy among medical students in Poland ,

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EPV-286

Subacute Encephalopathy With Seizures in Alcoholics Syndrome – an underdiagnosed disorder in chronic alcoholism

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EPV-287

New-Onset Refractory Status Epilepticus (NORSE) responsive to ketogenic diet in an adult patient

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EPV-288

Frequency of menstrual abnormalities and their associated neuroimaging findings in women with focal refractory epilepsy

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EPV-289

Diffusion Tensor Imaging in Posttraumatic Epilepsy & Poststroke Epilepsy

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EPV-290

Fetal Outcomes of Anti-epileptic Drugs Used as Polytherapy during Pregnancy: Teratologic Approach

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EPV-291

Clinical approaches in patients with epileptic encephalopathy and continued spike-wave activity during sleep

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EPV-292

Neuroimaging changes in epilepsy patients with suicidal intentions

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EPV-293

Bone mineral density in patients with long-term history of antiepileptic therapy: preliminary study results

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EPV-294

Telemedicine with mobile internet devices for innovative care of patients with epilepsy (TELE-EPIC_RCT)

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EPV-295

Abstract withdrawn

EPV-296

Pulvinar involvement in a patient with ictal paresis mimicking a stroke: a case report.

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EPV-297

Epilepsy with auditory features. A clinical and genetic family case characterization.

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EPV-298

Patterns of cerebral perfusion alteration in epileptic seizures attended at Emergency Department

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EPV-299

Employment outcomes after epilepsy surgery

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EPV-300

Outcomes of epilepsy surgery from a tertiary epilepsy center

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EPV-301

NEXMIF encephalopathy: Undescribed variant of the NEXMIF gen

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EPV-302

Cannabidiol as add-on treatment in drug resistant epilepsy: real-life experience in a tertiary centre

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EPV-303

Risk factors associated with uncontrolled seizures in mexican women with epilepsy during pregnancy: case- control study

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EPV-304

New onset seizures and seizure worsening in the course of COVID-19 infection

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EPV-305

Bone metabolic disorders in young men suffering from epilepsy

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EPV-306

BRAIN AREAS PREDISPOSING TO THE STROKE-RELATED EPILEPSY DEVELOPMENT

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EPV-307

Clinical approach of epileptic patients at OSAS comorbiditiy

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EPV-308

Relationship of blood cytokine profile levels and epileptic activity index

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EPV-309

The results of the study of the content of cytokines in the blood serum of an adult patients with epilepsy

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EPV-310

Peri-ictal neuroimaging of Status Epilepticus: preliminary results of a prospective study

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EPV-311

A SWOT analysis of the Berdzor (Lachin) corridor blockage in Artsakh (Nagorno-Karabagh): a neurological perspective

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EPV-312

Bioethical considerations in Drug-Resistant Epilepsy (DRE)

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EPV-313

Efficacy and safety of Fremanezumab in the treatment of migraine: Russian real-life study

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EPV-314

Autoinmune complications of CGRP inhibitors: a case series

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EPV-315

Impact of daith piercing as a preventive migraine treatment

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EPV-316

Quality of life and disability in hemiplegic migraine

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EPV-317

Hemicrania Continua revealing a carotid artery paraganglioma

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EPV-318

Anti-CGRP in cluster headache therapy: a retrospective case series study

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EPV-319

Average steps per day as marker of treatment response in adults with chronic migraine: a cross-sectional study

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EPV-320

A real-world study of fremanezumab at 3,6 and 12 months in refractory migraine in a tertiary Portuguese hospital

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EPV-321

"A two-hit headache": when late diagnosis could be easy and harmful

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EPV-322

Beneficial effect of the correction of vitamin D deficiency on migraine course: an observational study.

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EPV-323

The impact of anti-CGRP monoclonal antibodies therapy in anxiety and depression scales in migraine

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EPV-324

Erenumab effect on Hemiplegic Migraine

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EPV-325

Comorbidities in egyptian patients with migraine: a cross-sectional, population-based study

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EPV-326

Real-world evidence on 24 months of erenumab treatment of migraine patients in Switzerland: Long-term data from SQUARE

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EPV-327

Pituitary apoplexy during pregnancy, a potentially dangerous headache

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EPV-328

Evaluation of concomitant preventive treatments in patients with migraine with anti-CGRP therapies: the PREVENAC study

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EPV-329

GENDER DIFFERENCES OF BDNF DURING CLINICAL COURSE OF MIGRAINE

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EPV-330

Influencing factors of the quality of life among migraine patients in Szeged, Hungary

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EPV-331

Management of Migraine Without Aura in Adolescents: The Efficacy of Flunarizine in a Turkish Cohort

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EPV-332

Females are 6 times more prevalent among patients with medication overuse headache in a tertiary headache centre

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EPV-333

The Impact of the COVID-19 Pandemic on the Migraine Patients

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EPV-334

Abstract withdrawn

EPV-335

Gender-dependent differences in patients with migraine treated with anti-cgrp monoclonal: a real-life pilot study

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EPV-336

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EPV-337

Headache in acute stroke: a cross-sectional study in Bishkek, Kyrgyzstan

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EPV-338

The Comparison of Visual Evoked Potential Abnormalities in Migraineurs with and without aura and healthy population

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EPV-339

Does chronic migraine influence the food frequency of patients? – a case-control study

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EPV-340

Intracranial Hypotension and Brain Sagging Dementia secondary to spinal leak: a case of hide and seek.

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EPV-341

Course and predictors of poor outcome in patients with idiopathic intracranial hypertension

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EPV-342

Study of clinical characteristics associated to refractoriness in a cohort of chronic cluster headache patients

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EPV-343

Home-withdrawal program with behavioural approach in Chronic Migraine and Medication Overuse: 1 year's follow up

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EPV-344

Sleep quality in high frequency and chronic migraine patients treated with anti-CGRP monoclonal antibodies

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EPV-345

3 cases about recurrent HaNDL syndrome

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EPV-346

Impact of concomitant symptoms on the quality of life of migraine patients

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EPV-347

Failure of two anti-GCRP monoclonal antibodies in migraine prevention: will a third antibody work?

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EPV-348

Spontaneous spinal cerebrospinal fluid leak causing bilateral subdural hematoma: a not so benign entity.

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EPV-349

Diagnostic Clues and Challenging Features of Persistent Idiopathic Facial Pain

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EPV-350

Post-lumbar puncture headache from patients' perspective: the importance of using an atraumatic needle

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EPV-351

Efficacy of Greater Occipital Nerve Block as a Bridging Therapy in Chronic Migraine with Medication-Overuse Headache

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EPV-352

Evaluation of Patients with a Pre-Diagnosis of Multiple Sclerosis and Diagnosed with Migraine-Related NWML

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EPV-353

Migraine Epidemiology in Israel: Real-World Retrospective Database Study from a Nationwide Israeli Healthcare Provider

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EPV-354

Treatment And Outcome Of Patients With Idiopathic Intracranial Hypertension

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EPV-355

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EPV-356

Migraine in menopause – a hormonal rollercoaster?

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EPV-357

Non-invasive Vagal Nerve Stimulation: technical discussion of dosing

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EPV-358

Virtual and augmented reality in the treatment of headaches: a review and cost-aware discussion

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EPV-359

Olfactory hallucinations could be a migraine aura? A case series.

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EPV-360

Efficacy of Transcranial direct current stimulation on Functional connectivity and Motor Learning in Ischemic Stroke

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EPV-361

Effect of hypnotizability and hypnosis on the heartbeat evoked cortical potential and heart rate variability

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EPV-362

Diagnostic Test of TADIR (Tes Afasia, Diagnosis, Informasi dan Rehabilitasi) for Aphasia

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EPV-363

How big is the motor cortex of a surgeon? – A case report assessing the size of the motor area of a surgeon through TMS

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EPV-364

Santiago Ramón y Cajal's developmental laws on ontogeny and phylogeny

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EPV-365

The diagnostic challenge of Cryptococcal meningoencephalitis in the immunocompromised SLE patient: case study

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EPV-366

Virulent EBV encephalitis in a young patient as a trigger for para-infectious MOG-related ADEM: a case report.

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EPV-367

Hamburger disease mimicking stroke

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EPV-368

Varicella zoster virus: a rare cause of radiculoplexopathy

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EPV-369

Intraventricular Colistin In The Treatment Of Healthcare-Associated Ventriculitis Acinetobacter Baumannii In An Infant

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EPV-370

Topical antibiotics in brain surgery - systematic review

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EPV-371

Subarachnoid neurocysticercosis, an unusual challenge

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EPV-372

Central nervous system tuberculosis a challenging diagnosis in neurology

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EPV-373

Fluid-fluid levels in the lateral ventricle in patients with bacterial meningitis

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EPV-374

Human Rabies: a fatal neuroinfection - a review of the literature

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EPV-375

Visceral Leishmaniasis and its neurological manifestations: a brief review of the current literature

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EPV-376

Central nervous system vasculitis and other severe complications of pneumococcal meningitis

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EPV-377

Abstract withdrawn

EPV-378

Infectious longitudinally extensive transverse myelitis: an uncommon severe form of varicella-zoster virus reactivation.

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EPV-379

Longitudinal extensive transverse myelitis after infection with Campylobacter jejuni

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EPV-380

Predictors of duration of clearance of meningeal symptoms in tuberculous meningitis and its impact on outcome

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EPV-381

Miliary Tuberculosis with Central Nervous System Dissemination

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EPV-382

Review of the Stroke Presentation of Aspergillosis of the Central Nervous System (CNS) in Immunocompromised Patients.

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EPV-383

Super-additive effects of age and oxygen saturation on cognitive performance In COVID-19 survivors

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EPV-384

Idiopathic Hypertrophic Pachymeningitis can present with psychosis and a new-onset seizure.

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EPV-385

Clinical characteristics and outcomes of bacterial meningitis: a retrospective study from Lithuania

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EPV-386

Familial ALS with novel mutation in stalk domain of KIF5A gene

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EPV-387

Assessment of a comprehensive digital health solution to improve the independence of people with spinal muscular atrophy

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EPV-388

Limited utility of Nfs for diagnosis of restricted MND phenotypes and differentiation from compressive radiculopathies.

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EPV-389

Clinical characterization of genetic ALS patients in a Large Center for Motor Neuron Disease of Central Italy

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EPV-390

Oculometric Measures Use in Clinical Assessment of ALS Patients participating in a Phase IIb drug clinical trial

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EPV-391

Genotype-phenotype correlation in a cohort of fus-related als patients: the importance of a multidisciplinar approach

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EPV-392

Type 2 and 3 spinal muscular atrophy patients under treatment with Risdiplam: a small experience from a tertiary centre

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EPV-393

CuidAME: Spanish longitudinal data collection of SMA patients

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EPV-394

Gold Coast criteria in als patients: a clinical practice single-center experience

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EPV-395

Expanding the phenotype of OPTN gene among Tunisian ALS families

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EPV-396

Longitudinal follow-up of SMA patients treated with nusinersen in two Hungarian centers

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EPV-397

Salivary acetylcholinesterase activity is altered in patients with amyotrophic lateral sclerosis.

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EPV-398

Serum troponin t as a biomarker for amyotrophic lateral sclerosis

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EPV-399

Radiotherapy for sialorrhea management in MND patients- 7 year experience at a Tertiary Care Centre

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EPV-400

Genetic testing in ALS in the United Kingdom and Republic of Ireland: implications for future planning

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EPV-401

Digital solution (Dr. BetMen) serving the multidisciplinary care of SMA patients

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EPV-402

Prognostic usefulness of Motor Unit Number Index (MUNIX) in patients affected by Amyotrophic Lateral Sclerosis (ALS)

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EPV-403

Abstract withdrawn

EPV-404

Cognitive impairment is associated to gait variability and fall risk in Amyotrophic Lateral Sclerosis

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EPV-405

Nusinersen treatment in adult type 3 spinal muscular atrophy: data on motor and respiratory function at 22 and 42 months

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EPV-406

Faculty Development in a Multidisciplinary ALS Clinic

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EPV-407

A possible distinct genetic spectrum of late-onset amyotrophic lateral sclerosis

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EPV-408

Analysis of predictors of mortality at the diagnostic phase of amyotrophic lateral sclerosis

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EPV-409

Clinical phenotype of amyotrophic lateral sclerosis with C9ORF72 repeat expansion in Serbia

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EPV-410

Risdiplam in type 2 and 3 Spinal Muscular Atrophy: results of a cohort of adult Italian patients

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EPV-411

Effects of constraint induced movement therapy in patients with multiple sclerosis: A Systematic Review

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EPV-412

Early neurological deterioration in Wilson's disease: a systematic literature review and meta-analysis

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EPV-413

CORRELATION OF MINERAL MASS DISORDERS WITH COGNITIVE DEFICITS IN VASCULAR PARKINSONISM

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EPV-414

Vertical gaze disorder in patients with long-term Parkinson's disease: clinical and neuroimaging features

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EPV-415

A case of corticobasal syndrome associated with anti-Yo antibodies

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EPV-416

The prevalence of autonomic dysfunction in Parkison's disease patients in P.Stradinš Clinical university hospital

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EPV-417

Skin Conductance assessment in PD patient: a sistematic review

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EPV-418

Perampanel as a novel treatment for myoclonus in myoclonus-dystonia syndrome

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EPV-419

Dopamine striatal availability in brain and body first parkinson's disease patients

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EPV-420

PSP-PFG cohort with unusual clinical features related to dopaminergic therapy.

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EPV-421

Design of a Long-term Effectiveness Study of Foslevodopa/Foscarbidopa in Patients With Advanced Parkinson's Disease

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EPV-422

Incidence of orthostatic hypotension in Parkinson´s Disease patients starting antiparkinsonian treatment

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EPV-423

Interest of botulinum toxin in the treatment of facial hemispasm secondary to vasculo-nervous conflict,

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EPV-424

Accuracy of a commercial smartwatch in step counting in PD patients and association with spatiotemporal gait parameters

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EPV-425

Evaluation of Opicapone effects in patients with Parkinson´s Disease using inertial portable devices

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EPV-426

Rationale and design of SUCCESS trial.

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EPV-427

Vulnerability after imminent threat: Lance-Adams syndrome

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EPV-428

Effects of Opicapone on Motor Fluctuations-Related Pain in Parkinson's Disease: Status Update of the OCEAN Trial

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EPV-429

The repeated courses of the autologous stem cell therapy: effectiveness for Parkinson's disease.

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EPV-430

Efficacy of 18F-DOFA positron emission tomography for the diagnosis of Parkinson's disease

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EPV-431

Post-stroke Holmes tremor: Analysis of semiology, clinico-radiological correlation and therapeutic response

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EPV-432

Acute movement disorder with atypical topography. Acute hemichorea secondary to cortical stroke

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EPV-433

A case of late-onset Fahr' s syndrome mimicking progressive supranuclear palsy

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EPV-434

Clinico-Radiogic Evaluation Of Huntington's Disease: Neuro-Psychiatric Analysis Beyond Motor Findings

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EPV-435

Paroxysmal Autonomic Instability with Dystonia Syndrome: a rare complication of tuberculous meningitis: A Case Report

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EPV-436

Experience with levodopa–entacapone–carbidopa intestinal gel for advanced Parkinson's – data from a Romanian centre

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EPV-437

The Role of Probiotics in Relieving Parkinson's Disease-Related Constipation: A Systematic Review and Meta-Analysis

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EPV-438

Interoceptive and emotional disturbances in patients with functional movement disorders

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EPV-439

Camptocormia in Primary Progressive Freezing of Gait

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EPV-440

Ultrasound-guided administration of abobotulinum toxin on belly dancer dyskinesia- case report.

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EPV-441

What is the role of botulinum toxin in lingual dystonia?

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EPV-442

Update on the ADOPTION Study: Randomised, Open-Label Exploratory Trial of Opicapone in Parkinson's Disease

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EPV-443

Botulinum Toxin Injection: A treatment option worth trying in patients with multiple sclerosis related tremor.

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EPV-444

Discrepancies between general health-related quality of life and disease specific aspects in Parkinson's Disease

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EPV-445

The Knowledge Of The Neurologysts In The Management Of The Patient With Parkinson's Disease In The Republic Of Moldova

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EPV-446

Paroxysmal dystonia: organic versus functional.

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EPV-447

Parkinsonism-hyperpyrexia syndrome after initiation of intestinal perfusion of levodopa/carbidopa

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EPV-448

Comparative analysis of the occurrence of nonmotor disorders in Parkinson's disease and vascular parkinsonism

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EPV-449

Head Tremor in essential tremor patients: more than a marker of tremor's severity

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EPV-450

Difficulties in diagnosis of PSP

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EPV-451

Regulation of autophagy and neuroinflammation by Niclosamide in MPTP Induced-Parkinson's disease model

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EPV-452

HF-rTMS over primary motor cortex in patients with progressive supranuclear palsy alleviates disease symptoms

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EPV-453

4 mA tDCS improves walking ability in PSP: A pilot study of two cases

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EPV-454

Peripheral Blood Inflammatory Markers In Parkinson's Disease

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EPV-455

Efficacy of Safinamide as adjuvant treatment in patients with Parkinson's disease (PD) and Duodopa pump therapy.

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EPV-456

An adult-onset corticobasal syndrome due to mucopolysaccharidosis type IIIB

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EPV-457

Opicapone's effect on the 9-Symptom Wearing-off Questionnaire in Parkinson's Disease: Real-World Study OPTIPARK

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EPV-458

To evaluate role of Methylphenidate in treatment of Progressive Supranuclear Palsy [PSP]

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EPV-459

Brain-Gut Axis In The Pathogenesis Of Gba-Related Parkinson's Disease: Preliminary Data On The Italian GBA Cohort

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EPV-460

Study of the effect o safinamide as adjuvant therapy for Parkinson's disease

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EPV-461

Spanish translation and trans-culturally adaptation of the King's Parkinson Disease Pain Scale (KPPS)

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EPV-462

Can the Ohm's law predict the amplitude of neurostimulation when adapting systems in deep brain stimulation?

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EPV-463

Distinctive course characteristics of depression and anxiety disorders in Parkinson's disease

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EPV-464

Encouraging results of focused ultrasound thalamotomy for tremor in Diffuse Lewy Body Disease patients

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EPV-465

The study of the causes and stress dependence of hand tremor in military

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EPV-466

Stress in Parkinson's disease – a prospective cohort study

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EPV-467

Development of South Indian Pen based Smell test for detection, discrimination and identification of odours

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EPV-468

Movement disorders secondary to osmotic demyelination syndrome associated to glycemic alterations

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EPV-469

Assessment of retinal structure and microvascular impairment in Parkinson's Disease

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EPV-470

Evaluation of a clinically validated digital platform to provide Diffusion MRI biomarkers in Parkinsonian syndromes

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EPV-471

Applicability of imaging-guided programming during initiating deep brain stimulation for Parkinson's disease

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EPV-472

Leg restlessness and hyperparathyroidism in Parkinson's disease, a further clue to RLS pathogenesis?

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EPV-473

Fall risk and quality of life in Parkinson's disease patients

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EPV-474

Complex patterns of dystonia in two parkinsonian patients treated with continuous dopaminergic stimulation (CDS)

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EPV-475

Deep Brain Stimulation In Parkinson's Disease:the Role Of Brainsense Technology

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EPV-476

The Barriers In The Management Of Patients With Parkinson's Disease In The Republic Of Moldova

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EPV-477

The 'Gump sign' : a symptom or a complication of Normal Pressure Hydrocephalus?

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EPV-478

An Atypical Onset Of Primary Familial Brain Calcification: A Case Report

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EPV-479

Sydenham's Chorea with Onset in Childhood and Recurrence in Adulthood: Case Report and Literature Review

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EPV-480

Epidemiology of cancer in sporadic and monogenic Parkinson's disease: a cohort from Spain

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EPV-481

Abstract withdrawn

EPV-482

Prevalence of Extra-Cerebellar Symptoms in Adults with Neurodegenerative Cerebellar Ataxias

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EPV-483

Headache as the first symptom of multiple sclerosis

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EPV-484

Breaking Barriers: Improving Multiple Sclerosis Care and Management in Africa

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EPV-485

Profile of patients with Multiple Sclerosis starting diroximel fumarate in Madrid (Spain)

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EPV-486

The evaluation of MS patients treated with immunomodulatory agents in terms of fatigue, anxiety and depression frequency

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EPV-487

Early prognostic factors in multiple sclerosis

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EPV-488

For the assessment of neurological impairment in progressive MS patients after stabilometric training with rTMS

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EPV-489

Silent active brain lesion - An exceedingly rare finding in a case of neuromyelitis optica spectrum disorder

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EPV-490

Possible biological rol of HER2 in pathogenesis of Neuromyelitis Optica Spectrum Disorders. Case report.

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EPV-491

The role of RIM lesions in predicting longitudinal brain and retinal atrophy

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EPV-492

Multiple sclerosis in Ukraine

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EPV-493

Tapping Speed In Smartphone Is Useful For Disability Monitoring In Multiple Sclerosis

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EPV-494

The role of PAI mutation in differential diagnosis in multiple sclerosis

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EPV-495

A Prospective Study of the Clinical Profile of Multiple Sclerosis Patients and Correlation with Radiologic Progression

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EPV-496

Development of a self-assessment tool for the autonomy of patients with multiple sclerosis (MS)

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EPV-497

Obesity in Multiple Sclerosis: does it affect the disease prognosis?

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EPV-498

Ofatumumab and early immunological cells subset characterization in naïve Relapsing Multiple Sclerosis patients

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EPV-499

A real life observational prospective study about efficacy and safety of siponimod in a monocentric population of SMSP

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EPV-500

Single-attack Progressive Multiple Sclerosis in a cohort of patients

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EPV-501

Distribution of the course of familial multiple sclerosis among sibling pairs: case series

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EPV-502

Neurological manifestations of Behçet's disease

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EPV-503

VASCULAR FACTORS ARE ASSOCIATED WITH BRAIN ATROPHY AND COGNITIVE IMPAIRMENT IN MULTIPLE SCLEROSIS: A MULTIMODAL STUDY

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EPV-504

Cost-analysis of the tolerability, adherence and persistence to treatment of diroximel fumarate versus dimethyl fumarate

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EPV-505

Understanding Neurologists' Preferences For Treatment Attributes In Neuromyelitis Optica Spectrum Disorder

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EPV-506

Multiple Sclerosis and reproductive milestones in women: findings from a Tunisian study

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EPV-507

Evaluation of Fampridine Treatment Response by Triple Stimulation Technique

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EPV-508

MAGNON – final results: quantitative MRI-Analysis for daily clinical routine of MS patients

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EPV-509

The prevalence and prognostic value of prodromal symptoms in relapsing-remitting multiple sclerosis

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EPV-510

Comorbid autoimmune disorders in people with multiple sclerosis: a retrospective cohort study

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EPV-511

Interferon β1a treatment does not influence serum Epstein-Barr virus antibodies in patients with multiple sclerosis

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EPV-512

Real world data on natalizumab (Biogen) S.C. and I.V. – preliminary analysis

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EPV-513

Natalizumab reverts fatigue induced abnormal modulation of cortical network efficiency in Multiple Sclerosis

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EPV-514

How are we prescribing antidepressants to Multiple Sclerosis patients?

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EPV-515

Cognitive impairment in multiple sclerosis-information processing speed and visuospatial/visuoconstructional disfunction

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EPV-516

Potential risk of severe MS rebound after fingolimod cessation and a possible bridging exit strategy

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EPV-517

Experience with cladribine in multiple sclerosis patients in the third and fourth year of treatment

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EPV-518

Interleukins and proinflammatory factors in CSF among de novo diagnosed patients with RRMS

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EPV-519

Ofatumumab, interferon ß1 and glatiramer acetate as first-line treatment in everyday practice: the AIOLOS study

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EPV-520

Meningoencephalomyelitis and bilateral optic disc edema associated with anti-GFAP antibodies.

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EPV-521

Could the determination of the visual field be useful to detect the visual defects in Multiple Sclerosis patients?

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EPV-522

Myokymias as initial presentation of MOG antibody disease

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EPV-523

Ponesimod Pregnancy Outcomes Enhanced Monitoring (POEM) program to evaluate reproductive and embryofetal toxicity

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EPV-524

Serum amino acid profiling in patients with multiple sclerosis.

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EPV-525

Pseudotumoral forms of Multiple Sclerosis: clinical presentation and prognosis.

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EPV-526

An aggressive form of MOGAD effectively treated with aHSCT: a case report

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EPV-527

Disease exhacerbation after withdrawal of 6-months-duration siponimod therapy in SP MS: a first case report worldwide

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EPV-528

Evaluation of caregivers burden in multiple sclerosis

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EPV-529

Subacute Combined Degeneration and Multiple Sclerosis: two common conditions making a rare presentation

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EPV-530

Vitamin D in patients with multiple sclerosis and screening of polymorphisms of the CYP27B1 gene

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EPV-531

Efficacy And Safety Analysis Of Ocrelizumab In Primary Progressive Multiple Sclerosis Patients.

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EPV-532

Clinical significance and Prognostic Value of Multiple Sclerosis Differantial Diagnosis Workup: Serum Autoantibody Tests

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EPV-533

Journey of MS Patients in Turkey; a questionnaire based Covid-19 survey

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EPV-534

Neuropathic Extremity Pain in Patients With Multiple Sclerosis

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EPV-535

Validity And Reliability of The Turkish Version of Patient-Reported Impact of Spasticity Measure in Multiple Sclerosis

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EPV-536

BRISA App: correlation and analysis of PRO scores vs. Likert-Rating of MS symptoms in a real world cohort

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EPV-537

An asymmetric limb-girdle myopathy associated with LDB3 variant

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EPV-538

Neuromuscular side effects of Immune Checkpoint Inhibitors

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EPV-539

Patients review with McArdle's disease in the northern area of Tenerife

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EPV-540

The economic burden of generalised myasthenia gravis in Europe, Middle East and Africa: A systematic review

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EPV-541

Transcranial sonography findings in myotonic dystrophies

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EPV-542

Efgartigimod for Generalised Myasthenia Gravis: Review of Economic Models and an Adapted UK Perspective Economic Model

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EPV-543

ACHIEVE, a Randomized, Placebo-Controlled, Multiple Ascending Dose Study of DYNE-101 in Individuals with DM1

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EPV-544

Madelung's disease in a patient with mitochondrial myopathy: an association to take into account.

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EPV-545

The prognostic value of the C5b-9's immunohistochemical deposition in immunomediated necrotizing myopathy patients

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EPV-546

Severe muscle atrophy as the isolated initial manifestation of anti-Jo1 syndrome: a novel phenotype?

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EPV-547

Quantitative voice analysis in Patients with Myotonic Dystrophy type 1

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EPV-548

Evaluation of eye movement abnormalities in SMA patients with videonystagmography

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EPV-549

Perspectives on symptoms and treatments for Myasthenia Gravis: a real-world voice analysis of open social media

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EPV-550

Juvenile dermatomyositis: demographic, clinical, paraclinical and evolutionary aspects of a Tunisian series

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EPV-551

Assessing the extent of symptom control provided by ravulizumab or efgartigimod in generalised myasthenia gravis (gMG)

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EPV-552

Possibilities of Ultrasound (US) of Respiratory Muscles (RMs) in Myasthenia Gravis (MG)

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EPV-553

Recurrent myasthenic crisis do not significantly predict mechanical ventilation (MV) need

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EPV-554

Distal myopathy with anterior tibial onset: A rarer phenotype of dysferlinopathy in a Tunisian population

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EPV-555

Myasthenia Gravis Crisis and Severity in an Unselected Turkish Patient Cohort

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EPV-556

The Burden of MG Patients In Terms Of Utilities And Health Care Utilization: Comparison To The General Population

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EPV-557

Evidence of Intellectual Impairment in Children with Duchenne Muscular Dystrophy: A Systematic Review and Meta-Analysis

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EPV-558

Clinical evaluation of rituximab treatment experience in myathenia gravis.

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EPV-559

Thyrotoxic periodic paralysis as a differential diagnosis of acute weakness. A case report.

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EPV-560

Myasthenia Gravis (MG) with anti-MuSK antibodies developed after COVID-19 infection

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EPV-561

Immune-mediated rippling muscle disease (RMD) secondary to a renal carcinoma

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EPV-562

Nusinersen treatment in a type 3 spinal muscular atrophy patient during early pregnancy

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EPV-563

TRANSIENT THYMIC HYPERPLASIA RELATED TO COVID–19 IN A THYMECTOMIZED MYASTHENIC PATIENT

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EPV-564

Comparison of Different Repetitive Nerve Stimulation Techniques and Single-Fiber Electromyography in Myasthenia Gravis

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EPV-565

The Efficacy and Safety of Rituximab in Acetylcholine Receptor Antibody Positive Myasthenia Gravis

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EPV-566

Deflazacort treatment in LMNA-related congenital muscular dystrophy: an ongoing Italian cohort pilot study

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EPV-567

Progressive external ophthalmoplegia: not always a mitochondrial syndrome

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EPV-568

The effect of statins on Lipid-lowering treatment in myasthenia gravis among elderly patients

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EPV-569

A retrospective study on non-benzodiazepine hypnotics in the treatment of myasthenia gravis patients with insomnia

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EPV-570

Frequency of stroke in patients with myotonic dystrophy type 1

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EPV-571

Multicentric study for critical cerebral venous thrombosis prediction: VENTISCA score.

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EPV-572

Hypoxic-Ischemic Encephalopathy after cardiac arrest: Prognostic factors

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EPV-573

Cerebral infrared spectroscopy for monitoring cerebral oxygenation

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EPV-574

Predictors of unfavorable outcome of disease in the neurological intensive care unit – retrospective unicentric study

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EPV-575

Predicting the Mortality in Hemorrhagic Stroke

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EPV-576

Recent Management of Elevated Intracranial Pressure in Intracerebral Hemorrhage: A Systematic Review

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EPV-577

CORMORAN. Hormonal contraceptive-associated cerebral venous thrombosis: a multi-centre case-control study.

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EPV-578

Muscle biopsy in the Intensive Care Unit setting: experience from a tertiary laboratory of Neuropathology

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EPV-579

Analysis of the organization of medical care for patients with stroke in the period from 2019 to 2022

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EPV-580

Remnant and non-HDL cholesterol in a Myotonic Dystrophy Type 1 cohort

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EPV-581

Descriptive analysis of lipid profile in patients with previous stroke and carotid revascularization

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EPV-582

Guillain-Barré Syndrome (GBS) prevalence in the last 4 years:

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EPV-583

Hospital Admissions after Falls in Slovakia

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EPV-584

Prevalence and return-to-play procedures after potential concussion events in the Spanish professional soccer league

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EPV-585

How many stroke survivors develop problematic spasticity requiring pharmacologic therapy? Observational study protocol

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EPV-586

Prevalence of migraine headache in patients with multiple sclerosis

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EPV-587

Genetic epilepsy. New KCNA2 gene mutation as a cause of epilepsy and ataxia: a case report

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EPV-588

L-2-Hydroxyglutaric Aciduria: A Report of Clinical, Radiological, And Genetic Characteristics of Two Siblings from Egypt

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EPV-589

Rare case of slowly progressive genetic prionopathy with immunotherapy response and lesions mimicking autoimmune disease

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EPV-590

Acute worsening after minor head trauma in Alexander disease: case report

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EPV-591

A different phenotype of neurodevelopmental encephalopathy without epilepsy associated with a novel EEF1A2 mutation.

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PV-592

Relative frequency and phenotype spectrum of adult leukodystrophies: a single center experience from Hungary

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EPV-593

A novel GRN mutation in an Italian patient with non-fluent variant of primary progressive aphasia at onset

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EPV-594

SMN1 Gene Duplications and Their Link to Neurodegenerative Disorders: A Case Study

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EPV-595

Severe atypical phenotype of leukoencephalopathy with ataxia

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EPV-596

miR-191 expression in amyloid beta oligomer induced toxicity

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EPV-597

Genetic landscape of ataxia in childhood: About Tunisian cases

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EPV-598

CLCN2-related leukoencephalopathy, the relevance of a new variant of uncertain clinical significance.

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EPV-599

Double trouble: clinical and neuroimaging features in a case of FTD with C9orf72 expansion and progranulin mutation

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EPV-600

A homozygous mutation of alanyl-transfer RNA synthetase 2 in a patient of adult-onset leukodystrophy and ovarian failure

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EPV-601

Impact of LRRK2-G2019S mutation on response to dopaminergic treatments in Parkinson's disease

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EPV-602

Novel mutations in BTD gene causing biotinidase deficiency

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EPV-603

FMR1 mutation related disorders in a Tunisian family

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EPV-604

Hereditary spastic paraplegia 10 due to a novel mutation in the KIF5A gene with a newly described gluteal clonus

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EPV-605

Mutations in LRP10: a new phenotype

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EPV-606

Familial case of ALS with mutation in SOD1 gene

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EPV-607

Own clinical observation of very long-chain acyl-coenzyme A dehydrogenase deficiency (VLCAD)

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EPV-608

SCA 50/ATX-FGF-14: a case report on a novel repeat expansion disorder causing adult-onset progressive cerebellar ataxia

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EPV-609

SPINOCEREBELLAR ATAXIA TYPE 35 (SCA 35): A NOVEL MUTATION IN TGM6 GENE

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EPV-610

Factor V Leiden Mutation and Prothrombin G20210A Mutation in Cerebral Venous Thrombosis In An Egyptian Sample

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EPV-611

ABCA7 deletion (rs142076058) is not associated to Alzheimer Disease in Tunisian population

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EPV-612

The results of copper-eliminating therapy of Wilson disease in Belarus

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EPV-613

Neuroimaging Profile in 20 Brazilian Patients with Cadasil

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EPV-614

Atypical presentation of CADASIL: Pseudobulbar Syndrome

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EPV-615

A case of Hereditary Spastic Paraplegia type 15

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EPV-616

An elusive diagnosis of a vanishing disease

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EPV-617

10-years after Deep Brain Stimulation (DBS) for Adenylate Cyclase 5 (ADCY5)-related dyskinesia

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EPV-618

Role of skin biopsy in diagnosis of neuronal ceroid lipofuscinosis (NCL)

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EPV-619

A simple case of peripheral neuropathy: phenotypic variability and diagnostic pitfalls in MERRF syndrome

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EPV-620

A novel EIF2B3 variant associated with late-onset vanishing white matter disease

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EPV-621

L-2 glutaric hydroxy aciduria: Familial presentation discovered in adulthood

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EPV-622

Some Genes Involved in Folic Acid Synthesis in Mothers of Children with Congenital Malformations of the Brain

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EPV-623

CONDSIAS - the long road to diagnosis

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EPV-624

PNKP disorders: Ataxia with Oculomotor Apraxia Type 4 and microcephaly, seizures, development delay overlapping syndrome

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EPV-625

Features of genetic mutations in the Ukrainian population of patients with Wilson's disease

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EPV-626

Broad phenotypic spectrum of biallelic CAPN3 mutations among 3 sisters

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EPV-627

GNAO1 Exon 1-2 Deletion in a 19-year-old female: A novel GNAO1 variant associated with a mild phenotype

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EPV-628

CT perfusion imaging as a key initial test for isolated acute aphasia in the emergency department

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EPV-629

DaTScan in differential diagnostic between CANVAS and MSA-C

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EPV-630

Ultrasound features of carotid web

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EPV-631

Digital subtraction angiography for brain death determination and its effect on number of donated organs

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EPV-632

Neuromelanin distribution in patients with Parkinson's disease

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EPV-633

Transorbital ultrasound in acute optic neuritis.

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EPV-634

Machine learning-based classification of acute intracranial hemorrhages

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EPV-635

Assessing the Impact of White Matter Hyperintensities on cognitive dysfunction: a Whole-Brain Modeling Study

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EPV-636

A fully-automatic method to segment choroid plexus in multiple sclerosis using conventional MRI sequences

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EPV-637

Comparison of findings on brain magnetic resonance imaging and transcranial sonography in Parkinson's disease.

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EPV-638

No-reflow phenomenon in stroke patients: a systematic literature review and meta-analysis of clinical data

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EPV-639

Resting state functional connectivity in mild cognitive impairment with Lewy bodies

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EPV-640

Bilateral delayed non-ischemic enhancing brain lesions after endovascular treatment for unruptured intracranial aneurysm

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EPV-641

Automated differential diagnosis of parkinsonian syndromes using FDG PET and machine learning

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EPV-642

Lingual dystonia following thalamic stroke

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EPV-643

Is thalamic volume loss associated with disability worsening in multiple sclerosis?

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EPV-644

Automated CT perfusion software in stroke mimics diagnosis

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EPV-645

In-vivo measurement of tau depositions and cerebral perfusion in anti-IgLON5 disease using 18F-PI-2620 PET

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EPV-646

Altered thalamocortical connectivity in the motor network of stroke patients with sleep related breathing disorders

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EPV-647

Evaluation of Glymphatic System Activity by Diffusion Tensor Image in Mild Traumatic Brain Injury

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EPV-648

Visualisation of unconjugated bilirubin in the brain based on CEST magnetic resonance imaging

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EPV-649

Case series of MOG antibody disease in our area

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EPV-650

Pseudotumoral multiple sclerosis: an aggressive form of multiple sclerosis?

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EPV-651

NEUROLOGICAL MANIFESTATIONS IN THE DISEASE RELATED TO IGG4: TWO CLINICAL CASES.

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EPV-652

Immunological study of endothelium dysfunction on Parkinson dise3

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EPV-653

Impact of Oxidative stress in multiple sclerosis: a Tunisian case-control study

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EPV-654

Atypical Stiff Person Syndrome with anti-glycine receptor and anti-IgLON5 antibodies: a case report.

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EPV-655

MOG antibody associated disease (MOGAD): Case report in an adult whit ADEM-LIKE presentation

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EPV-656

GFAP-Abs coexpression in autoimmune encephalitis and atypical demyelinating diseases

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EPV-657

Polyautoimmunity and mesial temporal epilepsy with serum-only anti-GAD65 antibodies

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EPV-658

Bad things come in threes: keep alert for Guillain-Barré syndrome

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EPV-659

Immunological features of Guillain-Barré syndrome

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EPV-660

Autoimmune encephalitis suspicion and factors associated with diagnosis

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EPV-661

Subacute myelitis of possible vasculitic origin after SARS-CoV2 and VZV infections: a case report

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EPV-662

Vitamin D metabolism in relation with the innate and adaptive immune response during Multiple sclerosis

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EPV-663

A cost analysis for neuronal antibody testing in suspected immune-mediated neurological disorders.

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EPV-664

Frontal lobe involvement in patients treated with CAR T-cells developing ICANS

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EPV-665

Morvan syndrome superimposed on myasthenia gravis: a case report and review of the literature

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EPV-666

A novel use and dramatic efficacy of ofatumumab for treatment of anti-N-methyl-D-aspartate receptor encephalitis

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EPV-667

Rapidly progressive dementia: an atypical paraneoplastic syndrome associated to lung cancer

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EPV-668

Anti IgLON5 antibody encephalitis – Paying attention to the hypothalamus.

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EPV-669

Acute hemorrhagic leukoencephalitis: report of clinical case

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EPV-670

MOG-Ig G Antibody Positivity in Multiple Sclerosis: A Single Center Cohort

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EPV-671

Autoimmune encephalitis with mGluR5 antibodies: a case series from China and review of the literature

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EPV-672

Ondine's Curse syndrome as an unusual presentation of the recurrent autoimmune brainstem encephalitis

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EPV-673

Hypertrophic pachymeningitis, IgG4-related: case report.

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EPV-674

Cerebral amyloid angiopathy-related inflammation (CAA-rI): three heterogeneous case reports and literature review

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EPV-675

Highly active Multiple Sclerosis triggered by SARS-CoV-2 infection

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EPV-676

Comparative study of paraneoplastic and non-paraneoplastic autoimmune encephalitis with GABABR-Abs.

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EPV-677

Rituximab for Myasthenia Gravis patients: who and when?

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EPV-678

Skull-derived neutrophils facilitate neurological recovery after traumatic brain injury

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EPV-679

The influence of SSRIs on macrophages-induced Th17-immune response in multiple sclerosis.

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EPV-680

Anti-CASPR2 antibody mediated encephalitis with underlying prostatic neoplasia and atypical MRI findings.

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EPV-681

Anti-Sox1 antibodies in adult-onset Rasmussen encephalitis: a case report

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EPV-682

Gastro-intestinal dysfunction as first symptom of fatal double positive (Sox1, Hu) encephalitis

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EPV-683

Retrograde amnesia in a patient with anti-CASPR2 encephalitis: A Case Report and Literature Review

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EPV-684

The vascular smooth muscle cells and immune responses in ischemic stroke on atherosclerosis background

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EPV-685

Rapidly Progressive Dementia with axonal polyneuropathy in a female patient due to anti-GAD antibodies.

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EPV-686

Seropositive neuromyelitis optica spectrum disorder associated with myasthenia gravis

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EPV-687

Antibody-negative autoimmune encephalitis: clinical characteristics

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EPV-688

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy, a case series from a tertiary hospital

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EPV-689

NMDA encephalitis: an unexpected diagnosis in a chronically immunosuppressed patient with suspected dementia

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EPV-690

Limbic encephalitis mediated by anti-CV2/CRMP5, ZiC4 and GABAb antibodies and atypical neuroimaging finding

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EPV-691

Seronegative NMOSD: an intriguing case of B-cell inflammatory CNS syndrome

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EPV-692

Prognostic Value of Natural Neurotropic Autoantibodies in Covid-19 Associated Ischemic Strokes

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EPV-693

TCD20+ kinetics in patients switching to ocrelizumab therapy from fingolimod versus dimethyl fumarate

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EPV-694

Neurosarcoidosis : emphasizing the importance of the right approach at the right time

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EPV-695

The other side of the coin: an aggressive form of IgG4-RD presenting with acute bilateral SUNCT-like headache-crisis

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EPV-696

Slow progression of anti-LGI-1 autoimmune encephalitis leads to misdiagnosis: a case report

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PV-697

Treatment with Ocrelizumab in patients with Multiple Sclerosis:experience of immunological monitoring as safety protocol

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EPV-698

The Role and Significance of Complement C3 in the Development of Diabetic Polyneuropathies

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EPV-699

The case report of AQP4 and MOG IgG double positive NMOSD treated with subcutaneous Ofatumumab

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EPV-700

Neurological complications of immune checkpoint inhibitors therapy

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EPV-701

«MSteps : development and feasibility of a pre-consultation application for patients with Multiple Sclerosis».

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EPV-702

The use of artificial intelligence in neurosurgery today

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EPV-703

Brain health topics in Reddit's r/science, the largest online science forum

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EPV-704

A rare stroke mimic – thrombotic thrombocytopenic purpura

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EPV-705

Cerebrospinal fluid findings in COVID-19 patients with persisting neurological symptoms

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EPV-706

Severe hypomagnesemia mimicking acute stroke: a case series report and literature review

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EPV-707

Thrombotic Thrombocytopenic Purpura presenting as a stroke mimic

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EPV-708

Exclusive CNS hemophagocytic syndrome

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EPV-709

Tafamidis 61 mg delayed polyneuropathy progression in ATTR-CM patients in Spain. TRAMA Study

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EPV-710

Infiltrative Bing Neel syndrome presenting with focal onset seizure with impaired awareness

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EPV-711

BIOTINIDASE DEFICIENCY: AN UNDERDIAGNOSED DISEASE KEY FOR A WHOLE FAMILY.

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EPV-712

Secondary Hypokalemic Periodic Paralysis

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EPV-713

Hypomagnesemia-induced cerebellar syndrome: an underdiagnosed and treatable disease

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EPV-714

Apparently isolated CNS involvement in Erdheim Chester disease: case report

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EPV-715

Dry beriberi due to pyloric ulcer mimicking Miller Fisher's syndrome

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EPV-716

A rare cause for headaches: Brainstem infiltration by Langerhans cell histiocytosis (LCH) mimicking CLIPPERS

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EPV-717

SEZ6l2-associated encephalitis in a patient with small-cell lung cancer

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EPV-718

CAR T cells, a case of neurotoxicity

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EPV-719

Mixed papillary ependimoma presenting as superficial hemosiderosis of the Central Nervous System: A Case Report.

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EPV-720

INTRAVASCULAR LYMPHOMA RESTRICTED TO CENTRAL NERVOUS SYSTEM: A DIAGNOSTIC CHALLENGE

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EPV-721

Primary central nervous system lymphoma disguising as rhombencephalitis: a clinical and imagiological challenge

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EPV-722

Neurological complications following the use of checkpoint inhibitors. An emerging entity to know.

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EPV-723

Retrospective review of prophylactic AEDs and epilepsy outcome among adult patients with GBM treated in our institution

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EPV-724

Neurological Manifestations in a Series of 101 Non-Metastatic Cardiac Tumours

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EPV-725

High-grade glioma and bevacizumab therapy: a diffusion tensor MRI study

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EPV-726

Awake neurosurgery for brain tumors in polyglot patients: Do languages share the same brain regions?

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EPV-727

Frontal leukoencephalopathy in a patient with IgLON-5 antibodies: Case report.

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EPV-728

Efficacy of BRAF/MEK inhibitors in BRAF mutated leptomeningeal metastases from epithelioid glioblastoma: a case-report

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EPV-729

Myasthenic Syndrome induced by Atezolizumab in a patient with lung adenocarcinoma: Case report and literature review

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EPV-730

Frequency and prognostic value of contrast enhancement in high-grade IDH-mutant gliomas – a POLA network study

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EPV-731

Retrospective analysis of a cohort of patients with Glioma who underwent genetic testing.

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EPV-732

Paraneoplastic cerebellar degeneration and antibodies to TRIM 9 and 67 secondary to melanoma.

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EPV-733

UNILATERAL ACCOMODATIVE SPASM MAY BE CONSIDERED IN THE DIFFERENTIAL DIAGNOSIS OF ATYPICAL OPTIC NEURITIS

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EPV-734

Phenotype, genotype and radiological features of congenital fibrosis of extraocular muscles type 1 in a Spanish family

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EPV-735

Optic neuropathy and platinum derivatives, an association to take into account.

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EPV-736

Bilateral Ischemic optic neuropathy (ION) in patients undergoing prone ventilation

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EPV-737

Chronic relapsing inflammatory optic neuropathy (CRION) with subtle white matter lesions

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EPV-738

Delayed Oculomotor Nerve Palsy after Coil Embolization of Carotid Cavernous Fistula

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EPV-739

Sudden onset complete ptosis and painful ophthalmoplegia as the initial manifestation of pituitary apoplexy

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EPV-740

Study of saccadic profile in autosomal recessive hereditary spastic paraplegia: a pilot study

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EPV-741

Combined Oculopalatal And Convergence Retraction Nystagmus Following Ventriculoperitoneal Shunting

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EPV-742

Isolated ptosis as the only manifestation of anti-MOG syndrome

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EPV-743

Benign Paroxysmal Positional Vertigo During a Multiple Sclerosis Ocular Motor Relapse

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EPV-744

Adie's tonic pupil in migrainous patients : Two case reports

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EPV-745

Long-term course of Presbyvestibulopathy versus Bilateral Vestibulopathy – a retrospective longitudinal registry study

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EPV-746

Role of videonystagmography (VNG)in vestibular migraine

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EPV-747

Ischemic optic neuropathy associated with SARS-CoV-2 infection

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EPV-748

Algorithm for assessing the state of the hearing organ in patients with vestibular dysfunction

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EPV-749

Ocular manifestations in patients with multiple sclerosis

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EPV-750

The usefulness of optical coherence tomography thresholds in treatment-naïve multiple sclerosis patients.

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EPV-751

Recurrent neuroretinitis with glial fibrillary acidic protein (GFAP) autoantibodies: a case report.

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EPV-752

Partial third nerve palsy and Horner's syndrome as a manifestation of infiltrative superior orbital fissure disease

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EPV-753

Detecting Neurodegeneration on Optic Nerve and Cornea in Multiple Sclerosis And Neuromyelitis Optica Spectrum Disorder

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EPV-754

CRION- An experience from the Indian subcontinent

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EPV-755

Optic Perineuritis: Two Case Reports

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EPV-756

Postural Bias in Acute Unilateral Vestibulopathy: Interpretation with the Velocity-Storage Function

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EPV-757

Bell mimics VIPs – a proof-of-principle study on the merits of artificial intelligence in diagnosing facial palsy

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EPV-758

An unusual cause of chest pain, anaemia and tingly toes

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EPV-759

Ultrasonography of the vagus nerve in small fiber neuropathy

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EPV-760

Anti-Contactin 1 (CNTN1) autoimmune nodopathy: current treatment and pitfalls

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EPV-761

Cytokines in chronic immune-mediated neuropathies: a systematic review.

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EPV-762

Neuropathy related to RAF/MEK inhibitors: a case series

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EPV-763

Erythrocyte Sedimentation Rate as An Inflammatory Biomarker for Prediction of Prognosis of Guillain-Barre Syndrome

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EPV-764

Post-vaccination Guillain-Barré syndrome in a patient taking beta-glucan

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EPV-765

Multifocal Motor Neuropathy–Clinical, laboratory and electrophysiological characterization of a cohort of ten patients

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EPV-766

Trigeminal neuralgia secondary to meningioma. A series of cases.

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EPV-767

Transient focal neurological episodes – a central feature of a predominantly peripheral disease

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EPV-768

Characteristics and evolution of the Charcot-Marie-Tooth hand: an observational study over 2 years

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EPV-769

Axonal Peripheral Neuropathy (PN) induced by isolated pyridoxine-deficiency

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EPV-770

Recurrent painful ophthalmoplegic neuropathy: a rare and mysterious entity

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EPV-771

Serum NfL as a biomarker in chronic inflammatory demyelinating polyneuropathy: all that glitters is not gold.

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EPV-772

The Efficacy of Vestibular Rehabilitation Therapy for Mild Traumatic Brain Injury: A Systematic Review and Meta-analysis

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EPV-773

Transcutaneous electroneurostimulation of pudendal nerve in treatment of COVID-19-Induced erectile dysfunction

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EPV-774

High effective of percutaneous electrical neurostimulation of PSIS in treatment of piriformis syndrome

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EPV-775

The duration of Intrathecal Baclofen Therapy in MS patients – more than 20 years follow up

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EPV-776

Improving functional outcomes after acquired brain injury: a randomised clinical trial using Telerehabilitation

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EPV-777

Instrumental evaluation of postural control in patients with paraproteinemic neuropathies.

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EPV-778

Effectiveness of Pharmacophysiotherapy in the Rehabilitation of the Patients with Carpal Tunnel Syndrome

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EPV-779

Hybrid functional electrical stimulation for spinal cord injury rehabilitation: A systematic review

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EPV-780

ALAMEDA- THE ROAD TO BETTER NEUROLOGIC REHABILITATION OPORTUNITIES IN THE DIGITAL ERA

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EPV-781

Caregiver Burden in Parkinson's Disease And Atypical Parkinsonian Syndromes With consideration of Non-Motor Symptoms

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EPV-782

Long-term outcome of motor functional neurological disorder

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EPV-783

Screening tools for sarcopenia in neurologic patients – a clinical challenge

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EPV-784

A novel approach for the treatment of neurogenic dysphagia: neurophysiological outcome

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EPV-785

EFFECTS OF MOTOR IMAGERY WITH NEUROFEEDBACK AFTER BILATERAL STIMULATION WITH rTMS ON UPPER LIMB RECOVERY AFTER STROKE

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EPV-786

Effects of AR-based dual-task proprioception training on balance, positioning sensation, and cognition

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EPV-787

Venous transcranial ultrasound: present utility and future potential - a systematic review -

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EPV-788

Ultrasound diagnosis of carpal tunnel syndrome. A validation study in a high resolution neurosonology unit.

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EPV-789

Usefulness of optic nerve ultrasound to predict drug efficacy in multiple sclerosis

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EPV-790

CHASING THE DRAGON

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EPV-791

An uncommon case of normotensive hydrocephalus probably induced by Docetaxel

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EPV-792

Lithium neurotoxicity: a urge to dose life!

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EPV-793

Generalized periodic discharges with triphasic morphology associated with medication

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EPV-794

Illicit drug use and movement disorders – a secondary cause not to be missed

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EPV-795

Transient neurological symptoms after spinal anesthesia

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A case of severe methotrexate neurotoxicity in a 5-year-old child with acute lymphoblastic leukaemia

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When the hypoxia is not the only mechanism involved in delayed post-hypoxic leukoencephalopathy: a report of two cases.

J. Villamor Rodríguez, D. Barbero Jiménez, M. Hernández Ramírez, M. González Goméz, J. Celi Celi, M. Sánchez Palomo
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Cefepime neurotoxicity and chronic kidney disease: A case series on an unholy alliance

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Change in the level of expression of CD2-receptors in patients with post-traumatic gunshot neuropathies and plexopathies

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EPV-800

The consequences of traumatic brain injury in Kyrgyzstan.

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EPV-801

Analysis of combat peripheral nerve injury during the Russian-Ukrainian war in the evacuation city of Vinnytsia, Ukraine

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EPV-802

Brainstem Auditory Evoked Potentials and Neuropsychological Battery for Evaluation of the Risk After Mild TBI.

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EPV-803

Cognitive evoked potentials P300 in avaluation of maladaptive neuroplasticity in recurrent low back pain

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EPV-804

Physician's attitude to chronic pain patients in the Republic of Moldova health system

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EPV-805

Spasmophilia: phenotypic profile and clustering analysis of a misunderstood condition, a monocentric retrospective study

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EPV-806

A complex screen for biomarkers with possible role in acute low back pain

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EPV-807

Specificity of pain, anxiety and depression assessment in patients with low and high levels of alexithymia

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EPV-808

Postoperative opioid use in elective spine surgery and chronic use

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EPV-809

Monotherapy Versus Combination Therapy For Painful Diabetic Neuropathy: A Systematic Review And Meta-analysis

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EPV-810

Therapeutic and Diagnostic Sequence Using Acupressure and APP Therapy for the Relief of Myofascial Facial Pain.

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EPV-811

Abstract withdrawn

EPV-812

Evaluation of trigeminal sensorial evoked potentials and trigeminal reflexes in trigeminal neuralgia/neuropathy patients

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EPV-813

Changes in the intestinal microbiota in post-stroke pain syndrome

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EPV-814

Characteristics of the pain syndrome in patients with multiple myeloma

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EPV-815

The Fibromyalgia Rapid Screening Tool (FiRST): reliability and validity in Russian-speaking neuropsychiatric patients

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EPV-816

How early is early for Nerve conduction study (NCS) to diagnose Guillain Barre Syndrome (GBS):An interesting case report

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EPV-817

A case of Familial Amyloid Polyneuropathy with uncommon bulbar presentation and cranial nerve involvement

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EPV-818

Epidemiological, clinical and neurophysiological characteristics of Guillain-Barré syndrome in a secondary hospital

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EPV-819

A defying case of Miller Fisher Syndrome as a stroke mimic

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EPV-820

Brentuximab-vedotin induced nodo/paranodopathy

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EPV-821

Clinical presentation and treatment of a rare case of Miller Fisher Syndrome.

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EPV-822

Chronic inflammatory demyelinating polyradiculoneuropathy in patient with MOGAD

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EPV-823

Unusual signs for PMP22 duplication.

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EPV-824

Effects of drugs used in Ovarian Cancer Chemotherapy on the peripheral nervous system

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EPV-825

The spray can sign

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EPV-826

Post-COVID-19 chronic pain due to small fiber neuropathy

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EPV-827

Comorbid Psychiatric Diagnosis in Central Disorders of Hypersomnolence: "Is There a Vicious Circle in Hypersomnolence"

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EPV-828

Relapse of Kleine-Levin syndrome and COVID-19 vaccine – cause or coincidence?

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EPV-829

Parasomnias in different age- and sex groups manifest specific behavior phenotypes. An internet-based video research

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EPV-830

Relationship of sleep quality with academic performance, mental health and physical activity in high school students.

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EPV-832

A remarkable paediatric case of head rolling: example of the effectiveness of melatonin as the first therapeutic line

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EPV-833

Narcolepsy and Tourette's syndrome: Common pathways of a diverse clinical entity.

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EPV-834

Treatment of Narcolepsy with Orexin – A Systematic Review

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EPV-835

Augmentation: pitfalls in the treatment of Restless Legs Syndrome (RLS) patients

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EPV-836

A cursed sleep: the woman who forgot how to breathe

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EPV-837

Infratentorial superficial siderosis and an atypical finding: a case report

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EPV-838

Cauda Equine-Like Syndrome

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EPV-839

Severe arm hypotrophy as presenting symptom of Anterior Spinal Artery Syndrome (ASAS)

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EPV-840

Intraspinal dural arteriovenus malformations : A case series

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EPV-841

Longitudinally- extensive medullary infarct after fibrocartilaginous embolism due to herniated disc.

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EPV-842

Intrathecal hyaluronidase: rescue medication in patient of secondary syrinx with non-infective spinal arachnoiditis

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EPV-843

Cerebrospinal fluid drainage as therapy for delayed spinal cord ischemia after thoracic endovascular aortic repair

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EPV-844

Spinal cord infarction: an undesirable consequence after bronchial artery embolization

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EPV-845

Early diagnostic criteria of the resorption herniated intervertebral disc

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