2nd Alpe Adria

Update on Movement Disorders 2025

27 – 29 November 2025

Ljubljana, Slovenia

ABSTRACTS

Update on Movement Disorders 2025

27 – 29 November 2025, Ljubljana, Slovenia

Organised by

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ABSTRACTS

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Session 1 – Parkinson's Disease (PD) and Non-Motor Symptoms (NMS)

Towards a Biological Definition of Parkinson's Disease

Poewe Werner[1]
[1]*Medical University Innsbruck, Innsbruck, Austria*

Current clinical diagnostic criteria for PD require the presence of cardinal motor features of the disease but there is ample evidence to suggest that the underlying pathological events may start many years prior to the full expression of PD motor symptoms. Initiating disease-modifying interventions at the earliest stages of the biological processes driving PD pathology would enhance chances of success but require diagnostic criteria that are anchored on reliable biomarkers of disease –potentially enabling identification of pre-clinical disease in asymptomatic subjects. The concept of a 'biological' definition of disease independent of the presence of defining clinical features has been pioneered by the Alzheimer field by developing a framework of biomarkers for Abeta- and Tau-pathology, and imaging evidence for neurodegenerative brain changes. Similar efforts are now underway also for Parkinson's disease and may have far-reaching implications not only for the planning of clinical trials but also for future implementation of PD risk screening programmes and ultimately efforts aimed at disease prevention.
Two recent proposals have for the first time conceptualized biological disease anchors that would enable a 'preclinical' diagnosis in asymptomatic individuals. Despite important differences, both the 'SynNeurGe' and the 'Neuronal Synuclein Disease Integrated Staging System (NSD-ISS)' use a framework of positive α-synuclein SAA's, imaging evidence for neurodegeneration and certain genetic mutations for their diagnostic classification. These developments have far-reaching implications for clinical research and drug development and ultimately population-based risk-screening, but also pose important ethical and research challenges.
Both frameworks have not yet been validated in prospective studies regarding their predictive value for symptomatic disease in biologically defined subjects without clinical symptoms and thus are only appropriate for research purposes at present. Once validated, however, a framework based on a biological definition of PD that enables early diagnosis would be invaluable in supporting reseach and improving the design of clinical trials

Parkinson's Disease is characterised by disturbances of movement with slowness, stiffness and trembling. These symptoms appear when at least 40% of nerve cells producing the chemical messanger called dopamine have lost their function. The underlying processes for this degeneration therfore start long before patients notice any of these motor symptoms. There are now new insights into markers of disease that can be detected before symptoms have started and can be used for much earlier diagnosis than currently possible. These 'biomarkers' include changes of a protein called α-synuclein and are now tested for their usefulness for detection of disease risk before the appearance of symptoms

Non-Motor Symptoms in Parkinson's Disease(s) – All the Light We Cannot See

Gabriela Novotni[2]

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What James Parkinson beautifully described in his Essay on the Shaking Palsy more than two centuries ago, were the motor features of what he thought to be a distinct neurological disorder, later called by his name. Though he did not provide explanation on the disease pathology or pathophysiology, he expressed a desire that further investigation might uncover the true nature of the disease and lead to effective treatments, especially if applied early in its course. His desire remains a guiding light for neurologists today, and the light he then could not "see", notably absent from his essay, is what we now recognize as non-motor symptoms (NMS) of Parkinson's disease. Non-motor symptoms in PD often impact quality of life more profoundly than motor, yet they remain underrecognized, undertreated, and under-researched.

This talk will explore and underscore the importance of NMS in PD, from hyposmia, autonomic dysfunction, REM sleep behavior disorder (RBD), to apathy, depression, hallucinations, and dementia, dissecting them through three intersecting axes:

1. NMS and pathomechanistic insights - from biological underpinnings to endophenotypes, treatment trials stratification and outcome prediction.
2. NMS and the time-window - as prodromal indicators for early detection in the era of biomarkers and biological definition of PD, opening avenues for risk stratification, prevention and early interventions through disease-modifying treatment and lifestyle interventions.
3. NMS and quality of life - the person-centered approach.

Understanding PD not only as a movement disorder, but as a complex, multifaceted, multisystem degenerative disease, brings promise to fulfill James Parkinson's desire and of those living with PD, for an early/timely diagnosis, disease modification (both pharmacological and nonpharmacological) and halting progression.

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Cardiovascular Autonomic System Dysfunction in Parkinson's Disease

Sandro Ibrulj[1], Maja Trošt[1], Alessandra Fanciulli[2]

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Autonomic nervous system dysfunction in Parkinson's disease (PD) is common and represents an important subset of non-motor features which significantly decrease patients' quality of life. Earlier presentation of autonomic failure is associated with a more rapid progression of disease and shorter survival in patients with PD.

Manifestations of autonomic dysfunction are varied in relation to affected systems and include gastrointestinal (GI), urogenital, cardiovascular, sudomotor and thermoregulatory symptoms. Orthostatic hypotension (OH), supine and nocturnal hypertension and postprandial hypotension are features of cardiovascular dysfunction in PD. While both preganglionic (baroreflex failure) and postganglionic (sympathetic denervation) lead to these, the precise pathogenesis and relationship to other PD symptoms remain unclear. OH manifests in 30% with a protean and often under-recognized symptoms of syncope, unexplained falls, lightheadedness, cognitive impairment, blurred vision, dyspnea, fatigue, shoulder, neck, or low-back pain on standing. Half of PD patients with OH have concurrent supine and nocturnal hypertension. While mostly asymptomatic, both limit the efficiency of OH treatment, increase the risk of hypertensive crises and lead to end-organ damage.

Management focuses on addressing reversible causes and implementing lifestyle and non-pharmacological measures as first-line therapy. When OH symptoms persist, stepwise pharmacological treatment with sympathomimetic agents or fludrocortisone may be required. Those with supine or nocturnal hypertension warrant regular BP monitoring. Behavioral adjustments are preferred for control, with short-acting antihypertensives prescribed for refractory cases. In advanced PD, currently available continuous dopaminergic stimulation therapies and DBS have so far been shown to have variable and inconsistent effects on cardiovascular domains and existing dysfunction.

Autonomic nervous system problems are common in Parkinson's disease and can greatly affect quality of life. These issues may appear early and signal faster disease progression. They can involve the gut, bladder, heart, and temperature control. Blood pressure problems are frequent—especially drops when standing (orthostatic hypotension) and high pressure when lying down or at night. They lead to symptoms such as dizziness, fainting, fatigue, or blurred vision and are often overlooked. Early diagnosis is key. Treatment begins with lifestyle changes and managing contributing factors; medications may be added if needed. Regular blood pressure monitoring and careful balance between low and high pressure are essential to prevent complications.

Session 2 – Other Movement Disorder Syndromes

Atypical Parkinsonisms

Iva Stanković

Dystonia

Aleksandra Tomić

Tourette Syndrome

Zvezdan Pirtošek

Paroxysmal Movement Disorders

Roberto Erro

Session 3 – Sleep and Dystonia

Sleep Disorders in Parkinson's Disease

Lea Dolenc Grošelj

Sleep Disorders in Other Movement Disorders

Cristian Falup-Pecurariu
[1]*Transilvania University, Brasov, Romania*

BACKGROUND: Sleep disorders are one of the most common non-motor symptoms in both hypo- and hyperkinetic movement disorders.

AIM: This is a review on current and emerging evidence on pathology of sleep in atypical parkinsonian syndromes like progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration; hyperkinetic disorders like Huntington's disease, essential tremor and dystonia.

METHODS: Insomnia, excessive daytime sleepiness, restless legs syndrome and REM- sleep behaviour disorder are some of the most prevalent sleep disorders. These could be aggravated by medication regime and comorbidities. In contrast to Parkinson's disease, where mechanisms of disrupted sleep have been extensively investigated, up to the present day, other movement disorders still lack sufficient research in the area. Insomnia, excessive daytime sleepiness, restless legs syndrome and REM- sleep behaviour disorder are some of the most prevalent sleep disorders.

RESULTS: These could be aggravated by medication regime and comorbidities. In contrast to Parkinson's disease, where mechanisms of disrupted sleep have been extensively investigated, up to the present day, other movement disorders still lack sufficient research in the area.

DISCUSSIONS: This presentation will focus on early clinical recognition, diagnosis and therapeutic considerations of sleep disturbances in other movement disorders than Parkinson's disease, in order to provide the best possible care and increase the quality of life of these patients.

CONCLUSIONS: By delineating sleep profiles across these conditions, we aim to inform targeted interventions and also highlight sleep as a potential biomarker and modifiable factor in disease management.
Patients with movement disorders can experience a significant impact on sleep quality. Difficulty falling asleep, daytime sleepiness, the urge to move the legs at night and acting out dreams are often symptoms linked to tremor, Huntington's disease, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration. Not only is everyday life harder when one can no longer rest, but other symptoms can worsen and the quality of life can be reduced. Recent scientific evidence suggests that by suffering from these disorders, changes in the normal circuits of the brain occur and can significantly interfere with restful sleep. This presentation explains how sleep is affected in movement disorders and how better sleep could improve overall well-being for these patients.

The New Classification of Dystonia and What It Means

Alberto Albanese

Session 4 – Treatment of PD I.

Treatment Challenges in Early PD

Carlo Colosimo[1]
[1]*Santa Maria University Hospital, Terni, Italy*

Parkinson's disease (PD) is a progressive neurodegenerative disorder mainly characterized by the loss of dopaminergic neurons in the pars compacta of the substantia nigra, leading to a constellation of motor and nonmotor symptoms. Current pharmacological treatments focus on alleviating symptoms, with levodopa (LD), together with DOPA decarboxylase enzyme inhibitors, being the gold standard for motor symptom management. Additionally, dopamine agonists, monoamine oxidase B (MAO-B) inhibitors, amantadine, and centrally acting anticholinergics are employed to modulate dopaminergic response, reducing parkinsonian symptoms and improving quality of life. These drugs can be used as monotherapy or polytherapy, and the choice is based on several factors, including symptom severity, age, sex, occupation of the patient, and presence of comorbidities. The pivotal role of physical activity is also increasingly recognized. Despite significant advances in the treatment of early PD, the long-term efficacy of existing therapies usually diminishes over time and presents with several adverse effects, necessitating the exploration of novel therapeutic approaches. There are some limitations to consider when testing these novel therapies, such as inadequate measurement tools, small sample sizes, and short follow-up periods. Indeed, the measures currently used to assess PD in clinical trials were developed for a broad spectrum of disease severity, limiting their ability to detect meaningful changes in early PD over a feasible study period. Attempts have been made to develop PD composite scales (PARCOMS) using clinical trials data, aiming at increased responsiveness to clinical decline in patients with early untreated disease: initial results have shown greater sensitivity to disease progression in patients with early PD compared to the original scales.

Treatment Principles of Middle Stage PD

Regina Katzenschlager

Best Timing and Choice for the Continuous Treatment in PD

Norbert Kovacs

Session 5– Treatment of PD II.

Common Troubles and Their Prevention/Solution in Invasive Treatment of Parkinson's Disease

Vladimira Vuletić[1]

Invasive treatments for Parkinson's disease (PD), such as Deep Brain Stimulation (DBS) and device-assisted drug therapies like pumps, can significantly improve motor and non-motor symptoms when oral medications are no longer sufficient. These treatments offer continuous, non-oral delivery of medication or neuromodulation and neurostimulation to manage severe motor and non-motor fluctuations. However, these procedures come with potential complications and side effects that require careful management. Common issues in Parkinson's Disease (PD) invasive treatments include surgical complications, device malfunction, infections and neurological side effects like increased sleepiness or psychological issues etc. To prevent and manage these troubles, careful patient selection, precise electrode placement, proper staff training and adherence to cleaning protocols, medication management, education of patients and caregivers and post-operative therapy are crucial. While solutions often require medication adjustments, device adjustments, or adding other invasive therapies. This approach to management, prevention and solution of common troubles is in a multidisciplinary way to optimize outcomes and quality of life. In this lecture, we will provide an overview of the most common problems with invasive methods in Parkinson's disease, the possibilities of prevention and solutions, and our experiences.

Non Invasive Brain Stimulation in PD: The Novelty of Ultrasound

Paolo Manganoti

Neuro-Paliative Care in Parkinsonism

Manon Auffret

Disease Modifying Treatment in PD – Where Are We?

Jaroslaw Slawek

Session 6 – Treatment of PD III.

The History and Future of Deep Brain Stimulation for PD

Elena Moro

Deep Brain Stimulation for Other Movement Disorders

Dejan Georgiev

Focused Ultrasound in Movement Disorders

Andres Lozano[1]
[1]*Alan and Susan Hudson Cornerstone, University of Toronto, Toronto, Canada*

Focused ultrasound is a new technology that may have important therapeutic implications in the field of movement disorders. There are 3 main interventions. First, high intensity ultrasound can be used to make therapeutic lesions to treat tremor and parkinsonism. Second, it is possible to modulate the activity of deep brain targets with low intensity focused ultrasound. Third, low intensity ultrasound can be used to open the blood brain barrier. These approaches are non-invasive and can be performed in an out-patient setting. There various modalities will be reviewed.
High frequency Sound waves (ultrasound) can be used to treat tremor and other symptoms. Ultrasound can also be used to increase the penetration of drugs into the brain. In addition, ultrasound can be used to activate various brain regions. The therapeutic implications of ultrasound to treat brain disorders will be discussed.

Session 7 – Imaging

Molecular Brain Imaging in Everyday Clinical Practice

Maja Trošt[2]
[1]*University Medical Centre Ljubljana, Ljubljana, Slovenia,* [2]*Medical Faculty, University of Ljubljana, Ljubljana, Slovenia*

Molecular brain imaging plays an important role in the diagnosis and differential diagnosis of parkinsonism. Dopamine transporter (DAT) imaging using SPECT (e.g., 123I-ioflupane/DaTscan) or PET (e.g., 18F-fluorodopa) assesses the integrity of the nigrostriatal dopaminergic pathway and is highly sensitive and specific for detecting presynaptic dopaminergic deficits, which are characteristic of neurodegenerative parkinsonian syndromes.
However, DAT imaging cannot differentiate between Parkinson's disease (PD) and atypical parkinsonian syndromes (multiple system atrophy - MSA, progressive supranuclear palsy - PSP, corticobasal degeneration – CBD, dementia with Lewy bodies- DLB), as all show reduced striatal uptake. To differentiate between neurodegenerative parkinsonian syndromes a metabolic brain imaging with 18F-FDG PET should be performed, as disease-specific changes of cerebral metabolism can be detected. In PD the metabolic hallmark are hyperactive basal ganglia and various degree of frontal and pariental cortical hypoactivity. In PSP the caudate and medio-frotal hypometabolism is observed. In MSA the posterior putamen and cerebellum are hypoactive and in DLB hyperactive basal ganglia and hypoactove occipital corex are seen. To improve differential diagnostic utility of metabolic brain imaging a network analyses of the 18F-FDG PET images have been apllied. Scaled subprofile model based on the principal component analysis, has been used to identify specific disease related metabolic patterns, which present a metabolic biomarker of neurodegenerative movement disorder syndromes and can be applied in everyday clinical practice to improve the acuracy of early diagnosis.

Molecular brain imaging (MBI) allows us to see brain activity at a chemical level. Unlike MRI or CT, which show structure, it uses tiny amounts of radioactive tracers that attach to specific brain molecules. These tracers emit signals detected by PET (Positron Emission Tomography) or SPECT (Single Photon Emission Computed Tomography) scanners. MBI allows us to study brain function, detect chemical changes, and identify early signs of diseases such as Parkinson's, Alzheimer's, and other neurodegenerative disorders—often before visible brain damage occurs.
In Parkinson's disease and similar movement disorders, dopamine transporter imaging shows how well dopamine pathways work. Reduced activity suggests neurodegeneration but cannot distinguish between various parkinsonian syndromes. For this, an 18F-FDG PET scan, which measures brain activity, is employed. Each disorder has its unique metabolic pattern, which can be indentified using specific networ analyzes. These patterns enable an improved early and accurate diagnosis of parkinsonisms and dementias.

Novel Applications of Metabolic Brain Networks

David Eidelberg[1]
[1]*Center for Neurosciences, The Feinstein Institutes for Medical Research, Manhasset, United States*

BACKGROUND: Brain imaging has been used extensively to identify and validate disease-specific functional networks as biomarkers in neurodegenerative disorders. Although disease networks are highly reproducible across patient populations, it is not known whether these topographies reflect pathological connectivity patterns, or beneficial adaptations.

AIM: To distinguish between these possibilities, we used graph theory to study connectivity patterns in a validated metabolic network termed the Parkinson's disease-related metabolic pattern (PDRP).

METHODS: We applied graph theory algorithms to metabolic PET scans from PD and control subjects and computed three primary (degree centrality, clustering coefficient, and characteristic path length) and two secondary (assortativity and small-worldness) network metrics for each group. We focused on assortativity, a metric that captures the tendency for connections to form between nodes with similar properties. Patterns with high assortativity are defined by homogeneity of network connections and inefficient information flow. Those with low assortativity are defined by heterogeneity of connections and relatively efficient information flow.

RESULTS: We found that PDRP assortativity increased with disease progression in multiple longitudinal imaging cohorts of PD or isolated REM sleep behavior disorder (iRBD) subjects. Compared to sporadic PD, this network metric was increased in PD-GBA, and relatively reduced in patients with slowly progressive mutations (PD-LRRK2). Divergent assortativity responses were seen in response to levodopa treatment compared to subthalamic nucleus deep brain stimulation (STN-DBS). Despite similar motor improvement, the two interventions had opposite effects on PDRP assortativity. Levodopa was associated with abnormal increases in assortativity, which declined to normal levels with DBS.

DISCUSSIONS: The findings are consistent with stereotyped changes in PD network organization in response to disease progression and treatment. Graph metrics such as assortativity provide additional insight into network-level connectivity changes beyond basic expression measures.

CONCLUSIONS: Network metrics can provide unique mechanistic information regarding new treatments for PD and related disorders.
Interest has grown in the use of functional imaging to identify and evaluate disease-specific brain networks in patients with neurological disorders. Network quantification methods are currently being used in parkinsonian disorders to assist in differential diagnosis, monitor disease progression, and evaluate new treatments. Nonetheless, little attention has been dedicated to the reorganization of networks by treatment. We will review the use of graph theory to describe changes in network configuration in preclinical disease and during conventional antiparkinsonian therapies. Likewise, we will discuss network reorganization following novel interventions such as gene therapy and in response to placebo.

Session 8 – Genetic Movement Disorders

Phenotype-Genotype Correlations in Movement Disorders

Kailash Bhatia

Genetics of PD

Maria Valente Enza

Session 9 – Neurophysiology of Movement Disorders

Neurophysiological Evaluation of Tremor

Petra Schwingenschuh

Neurophysiological Evaluation of Dystonia

Francesca Morgante

Neurophysiological Evaluation of Other Movement Disorders

Maja Kojović

Session 10 – Functional Movement Disorders

Functional Movement Disorders – Classification

Michele Tinazzi

Functional Movement Disorders- Pathophysiology

Mark Edwards

Mangement of Functional Movement Disorders

Tereza Serranová[1]
[1]*Charles University, Prague, Czech Republic*

Functional movement disorders (FMD) are a common cause of persistent and disabling symptoms in neurological practice. Management begins with a comprehensive assessment of both motor and non-motor symptoms and a rule-in diagnosis, which involves demonstrating characteristic clinical features such as inconsistency between voluntary and automatic movements. Subsequent steps include the delivery of a positive diagnosis and patient education that provides a clear rationale for treatment, fosters understanding of the condition, and encourages the development of self-management skills.
Accompanying symptoms such as psychological symptoms, pain, fatigue, and cognitive complaints are frequent and should be addressed alongside an evaluation of predisposing and precipitating factors, which inform referral and triage to specific treatment modalities.

A growing body of evidence supports the efficacy of physiotherapy with movement retraining and psychological interventions, delivered either alone or in combination. Neurologists play a key role not only in diagnosis but also in ongoing management, including the identification and treatment of modifiable comorbidities such as sleep disorders, migraine, and other coexisting conditions. Psychiatrists should assess and treat comorbid psychiatric disorders, including anxiety and depression, and assist early in treatment triage.

While the overall quality of evidence for individualized, multimodal approaches integrating physiotherapy, occupational therapy, psychological, and educational interventions remains limited, emerging results from randomized controlled studies are beginning to identify predictors of treatment response and prognosis. As research advances, expanding professional education and developing specialized multidisciplinary services will be essential to promote early and accurate diagnosis and ensure evidence-based, patient-centred care for individuals with FMD.

Functional movement disorders (FMD) cause disabling symptoms such as tremor, weakness, or walking difficulties due to abnormal functioning of the brain rather than structural damage. Effective care begins with a clear explanation of the diagnosis, helping patients understand their condition and develop self-management skills. Treatment usually combines physiotherapy focused on movement retraining with psychological support or a combination of both. Addressing symptoms such as pain, fatigue, and coexisting psychological conditions is also essential. Early recognition and coordinated multidisciplinary care can greatly improve recovery and quality of life for people living with FMD.

Parallel Session 1: Role of PD Nursing in PD: Competences, Patient Care and Lessons from Practices in Various Countries

The role of the PD nurse: good practices and competencies from the UK

Yogini Chokeepermal-Naidu

The Croatia Perspective on Holistic Patient Care in Parkinson's Disease

Romana Brnić Andrić

Experiences From Poland: The Nurse's Involvement in Care Planning

Anna Roszmann

Comparative Approaches in the Region – Key Practices and Collaboration Highlights

Robert Rajnar

Parallel Session 2

Daily Dosing, Daily Living: The Nurse's Role in Supporting Patients on LECIG

Martina Rozina Bučar, **Robert Rajnar**

Flowing Support: Nursing Care in s.c. Apomorphine Injections and Infusion Pumps

Robert Rajnar, **Marina Krivokuća**

Deep Brain Stimulation in Practice: The Expertise and Impact of PD Nurses

Denisa Sambolić, **Edin Agović**

Integrating Phisioterapy into the Treatment of Parkinson's Disease with Deep Brain Stimulation

Sabina Ajdnik

Parallel Session 3 - Comprehensive Medical Device Support Programs With Discussion

Maurizio Moroni

Posters

P1: A novel split ends homologue gene (SPEN) variant in a mother and daughter with radio-tartaglia syndrome (RTS) presenting as cervical dystonia

Matej Lokar[1],2, Lisa Buikema[1],3, Saman Vinke[3], Gaber Bergant[4], Dejan Georgiev[1],2,5

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BACKGROUND: Truncated variants in SPEN, located on chromosome 1p36.21-p36.13, have recently been associated with RTS (MIM 619312), a disorder characterised by developmental delay (DD), anxiety, aggression, attention deficit disorder, facial dysmorphism, congenital heart defects and CNS abnormalities.

AIM: We present two cases of a mother and daughter with a novel SPEN variant leading to RTS and characterised by a unique cervical dystonia and dystonic head and upper limb tremor.

METHODS: N/A

RESULTS: A 37-year-old woman with a history of DD, anxiety and delusions presented with torticollis with a mixed no-no/yes-yes dystonic head tremor and a fine, irregular postural and kinetic tremor in the upper extremities. Family history was positive for tremor/dystonia. Cognitive screening revealed MMSE score 25/30 and MoCA score 16+1/30. Brain MRI was unremarkable. Whole-exome sequencing revealed a likely-pathogenic heterozygote SPEN variant (NM_015001.3: c.2170C>T,p.Arg724*).
Her 18-year-old daughter also had DD and showed a hand tremor at primary school. The pregnancy and birth were uneventful. Examination revealed a bulbous nose, contractures of several fingers and toes, occasional dystonic head tremor and postural and kinetic tremor in all limbs. Fine motor skills were slightly impaired. Cognitive screening revealed MMSE score of 23/30 and MoCA score of 19+1/30. MRI of the brain was normal. Molecular genetic testing revealed the same likely pathogenic SPEN variant as in her mother.

DISCUSSIONS: This is the first report of cervical dystonia and dystonic tremor of the head and upper limbs in a patient with RTS. In addition, the SPEN variant c.2170C>T,p.Arg724* has not been previously described in the literature. It is thought to lead to a loss of normal protein function, a known cause of RTS, and therefore probably explains the clinical features of our patients, including dystonia.

CONCLUSIONS: This report expands the current phenotypic and genotypic spectrum of RTS. Further research is needed to improve our understanding of this disorder.

P2: Assessing the effect of taVNS on the activity of brainstem nuclei in PD patients: an fMRI study

Vesna van Midden[1], Andrej Vovk[2], Rok Berlot[1], Zvezdan Pirtošek[1], Maja Kojović[1]

[1]University Medical Centre, Ljubljana, Ljubljana, Slovenia, [2]Centre of Clinical Physiology, Medical Faculty, University of Ljubljana, Ljubljana, Slovenia

BACKGROUND: Transcutaneous auricular vagus nerve electrostimulation (taVNS) is under investigation as adjunct therapy for Parkinson's disease (PD). fMRI studies in healthy cohorts show taVNS activates the nucleus tractus solitarii (NTS) and locus coeruleus (LC). Whether this applies to PD, which features asymmetric degeneration of LC and dopaminergic circuits, is unknown.

AIM: We quantified taVNS effects on LC and NTS activation in PD using fMRI, and explored gait correlates

METHODS: We enrolled 40 PD patients in our double-blind, sham-controlled, within-subject, block-design fMRI study (NCT05967598). 32 were analysed. During a single ON-medication visit, each participant received taVNS at 100 Hz (taVNS100), taVNS at 25 Hz (taVNS25), and sham, in randomised order during which functional MRI imaging was obtained. Activity of LC and NTS was analysed using LME models accounting for stimulation type, degeneration-onset side (Deg_onset_side), and UPDRS-III-tertiles. Furthermore, NTS functional connectivity was analysed. After imaging, we assessed gait using motion sensors across stimulation conditions.

RESULTS: NTS activation showed a main effect of stimulation type ($p=0.021$) and an interaction with Deg_onset_side ($p=0.011$). taVNS100 increased NTS activity relative to taVNS25 ($p=0.018$). In left-onset PD, taVNS100 exceeded both taVNS25 ($p=0.005$) and sham ($p=0.029$). No NTS differences were detected in right-onset PD. LC activity showed a main effect of stimulation type ($p=0.034$) driven by decreased LC activity during taVNS100 versus sham ($p=0.033$). UPDRS-III-tertiles did not modulate nuclei responses. LC activity was predicted by NTS activity with Deg_onset_side interaction ($p=0.007$), featuring a negative NTS–LC correlation in left-onset PD. NTS connectivity findings did not survive corrections. Stimulation had not effect on gait.

DISCUSSIONS: taVNS100 decreased LC activity and increased NTS activity selectively in patients with left Deg_onset_side, independent of motor severity. This suggests PD-specific effects on brainstem-nuclei activation, which are driven by disease asymmetry.

CONCLUSIONS: Side-tailored or bilateral protocols, combined with real-time behavioural readouts, warrant further exploration.

P3: Aubert-Fleisch phenomenon in Parkinson's disease and in healthy subjects

Eva Pipan[1], Dejan Georgiev[1]

[1]Department of Neurology, University Medical Center Ljubljana, Ljubljana, Slovenia, [2]Medical Faculty, University of Ljubljana, Ljubljana, Slovenia

BACKGROUND: The haptic Aubert-Fleischl phenomenon (AFP) describes a condition in which the perceived speed of a moving stimulus is slower when the person with the receptive organ follows the stimulus than when the receptive organ is stationary.

AIM: We aimed to investigate the presence of AFP in Parkinson's disease (PD) and in healthy controls, as well as the effect of dopaminergic medication on AFP.

METHODS: Subjects assessed the speed of movement of a rigged belt on a specially constructed device under two conditions: 1. Kinesthetic (K) - by holding the fingertip of the index finger of dominant hand fixed on the belt, allowing them to track the movement of the belt with their hand, and 2. Tactile (T) - by holding the hand still. Subjects were asked to estimate the belt speed compared to the reference speed. Each patient and each healthy subject was tested twice.

RESULTS: 33 PD patients and 35 healthy subjects were tested. ON medication, AFP was present in 17/33 PD patients (51.5%) and in 6/33 PD patients (18.2%) AFP was reversed. AFP OFF medication was present in 12/33 (36.4%), no AFP in 10/33 subjects (30.3%) and reversed AFP in 11/33 subjects (33.3%). In healthy subjects AFP was present in 22/35 subjects (62.8%) and reversed AFP was present in 6/35 (17%) od the healthy subjects.

DISCUSSIONS: AFP was less pronounced in patients with PD, especially while OFF medication. We also observed a previously undescribed phenomenon, a reversed AFP, i.e. the tactilely assessed speed of a moving stimulus was perceived as slower compared to the kinaesthetically assessed stimulus - more often OFF medication.

CONCLUSIONS: Perceptual disturbances in PD are more pronounced when dopamine levels are low. The distribution of AFP in PD patients ON medication was similar to age- and sex-matched healthy subjects.

P4: Bilateral magnetic resonance-guided focused ultrasound thalamotomy in essential tremor: real-world data up to 1 year and evidence from the literature

Fabio Paio[1], Giuseppe Kenneth Ricciardi[2], Giorgia Bulgarelli[3], Micaela Tagliamonte[2], Elisa Mantovani[1], Chiara Zucchella[4], Tommaso Bovi[4], Michele Longhi[3], Zeno Lombardi[1], Paolo Maria Polloniato[5], Emanuele Zivelonghi[5], Carlo Cavedon[5], Antonio Nicolato[3], Francesco Sala[6], Benedetto Petralia[2], Bruno Bonetti[4], Michele Tinazzi[1], Stefano Tamburin[1]

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BACKGROUND: Staged bilateral magnetic resonance–guided focused ultrasound (MRgFUS) thalamotomy is an incisionless option for medication-refractory essential tremor (ET). While efficacy and safety of unilateral MRgFUS are established, evidence for bilateral treatment remains limited.

AIM: To evaluate the safety and efficacy of staged-bilateral MRgFUS in a real-world cohort and perform a systematic review and meta-analysis.

METHODS: Consecutive ET patients undergoing second-side MRgFUS since November 2023 were prospectively assessed. The primary efficacy endpoint was the change in Clinical Rating Scale for Tremor (CRST) A+B scores for the treated hand, while safety was evaluated by collecting and grading adverse events (AEs). A systematic review identified published bilateral MRgFUS series; efficacy data were meta-analysed using random-effects meta-analysis, while AEs were reported descriptively.

RESULTS: Fifteen patients (60% men; mean age 74.1 ± 8.9 years) underwent second-side MRgFUS with a mean interval of 28.9 ± 22.5 months from first-side treatment. At the 12-month evaluation, CRST A+B decreased from 21.0 to 8.8 (–58%), CRST C from 7.3 to 1.9 (–74.2%), and QUEST from 30.5 to 9.5 (–68.7%). Head and voice tremor were reduced by 73.8% and 40.3%. AEs were predominantly mild (95.2%) and transient (88%). Cognition at 1 year was globally preserved, with a selective decline in verbal episodic memory. Meta-analysis confirmed significant improvement in tremor severity and functional outcomes

DISCUSSIONS: Staged-bilateral MRgFUS provided durable bilateral and midline tremor suppression with high acceptability and a manageable safety profile. Aggregate AE analysis showed consistent patterns across series and suggests that, when indirectly compared with other bilateral lesioning techniques, persistent dysarthria rates may be lower, though still higher than with unilateral MRgFUS. Limitations include the single-centre design and small sample in our cohort, and, from a meta-analytic perspective, heterogeneity across studies and inconsistent AEs grading.

CONCLUSIONS: These real-world findings, integrated with a literature review, support staged-bilateral MRgFUS as a therapeutic option for ET.

P5: Characteristics of dystonia in Niemann-Pick disease type C

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BACKGROUND: Niemann–Pick disease type C (NPC) is a rare inherited neurovisceral disorder characterized by vertical gaze palsy, ataxia, involuntary movements, dysphagia, dysarthria, cognitive decline, and psychiatric manifestations. Movement disorders, particularly dystonia, are among the most disabling features and strongly influence quality of life, yet their progression remains insufficiently studied.

AIM: This study aimed to determine the frequency, distribution, and progression of dystonia in patients with NPC

METHODS: We conducted a retrospective descriptive study including 20 patients diagnosed with NPC between 2010 and 2025. Data on the initial localization of dystonia were collected from medical histories. Neurological examinations at diagnosis and at the most recent follow-up provided information on dystonia distribution. Severity was assessed using the Fahn–Marsden scale.

RESULTS: At onset, dystonia most often appeared as isolated or multifocal in the arms or legs, while generalized forms were rare. During follow-up, 15 of 20 patients developed generalized dystonia, with all limb-onset cases progressing, whereas cervical dystonia largely remained restricted and was observed only in adult-onset NPC. A comparison between adult and juvenile forms showed statistically significant differences in dystonia severity in the legs (right $p = 0.040$; left $p = 0.019$) and arms (both $p = 0.024$), with more severe involvement in juvenile patients. Overall dystonia severity was also higher in the juvenile group ($p = 0.031$).

DISCUSSIONS: Dystonia emerged as a nearly universal feature in Niemann-Pick disease type C, affecting 95% of patients and generalizing in 78%, markedly exceeding prior reports. The distribution pattern, with limb-onset cases progressing to generalized forms while cervical dystonia remained largely restricted, highlights its diagnostic value and clinical relevance.

CONCLUSIONS: This study is the first to outline the pattern of dystonia progression in NPC, from its initial localization to final clinical presentation.

P6: Clinical correlates of adolescents with functional motor disorders in a neurology setting, data from the Italian registry of functional motor disorders

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BACKGROUND: Functional Motor Disorders (FMDs) represent a significant diagnostic and therapeutic challenge in pediatric neurology, particularly among adolescents.

AIM: The objectives of this study were to (1) describe the clinical manifestations of FMDs in adolescents, including nonmotor symptoms and occurrence of other functional neurological disorders (FND), and (2) compare the demographic and clinical features between adolescents and adults in a large sample of Italian FMD patients.

METHODS: In this multicenter observational study, we enrolled consecutive outpatients with a definite diagnosis of FMDs who attended 25 tertiary movement disorders centers in Italy. Each patient underwent a detailed clinical evaluation, including a definition of the phenotype and number of FMDs (isolated, combined) and an assessment of associated neurological and psychiatric symptoms. Adolescence was defined as ages 10 and 19, based on age at FMD onset, which was considered the year of the first clinical manifestation.

RESULTS: Of 847 patients with FMDs (72% females) 93 (11%) were adolescent. The most common phenotype among adolescent was weakness (52%), which, along with the other motor phenotypes, did not differ significantly from adults, except for parkinsonism, which was more common in the adults group ($p<.001$). Among adolescents, 43 (46.3% had isolated FMDs and 50 (53.7%) had combined FMD, with no significant difference compared with adults.
Compared with adults, adolescents had a significant longer FMD duration, had seen a higher number of medical doctors before the diagnosis of FMD, and showed a higher frequency of functional seizures and infections, but a lower frequency of insomnia and fatigue. Multivariate regression analysis confirmed that insomnia and fatigue were more likely in adults, whereas functional seizures and infection were more likely in adolescents.

DISCUSSIONS:

CONCLUSIONS: Our findings highlight the need for prompt, multidimensional assessments in adolescent with FMDs, given the coexistence of other FNDs.

P7: Correlation of sleep microstructure and cerebrospinal fluid biomarkers of neurodegeneration in early parkinson's disease

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BACKGROUND: Sleep alterations are frequent in Parkinson's disease (PD), but their relationship with early neurodegenerative processes remains poorly understood. Sleep microstructure, assessed through spectral EEG analysis, may provide novel biomarkers of early PD pathology.

AIM: To investigate the association between polysomnographic sleep parameters and cerebrospinal fluid (CSF) biomarkers of neurodegeneration in patients with early, drug-naïve PD

METHODS: We enrolled 22 ealry de novo PD patients from our Neurology Clinic in Verona. All underwent comprehensive neurological evaluation, overnight polysomnography, and lumbar puncture. CSF was analyzed for β-amyloid 1–42 (Aβ42), β-amyloid 1–40 (Aβ40), total tau, and phosphorylated tau (pTau181). Sleep macrostructure measures included total sleep time, sleep efficiency, and stage distribution. Microstructural features, derived from central EEG channels (C3, C4), comprised spectral power, slow-wave activity (SWA), and spectral ratios (slow-to-fast, fast-to-slow) during NREM stages (N1, N2, N3). Correlations with CSF biomarkers and their ratios (Aβ42/pTau181, Aβ42/Aβ40) were assessed with Spearman's tests and linear regression adjusting for age.

RESULTS: No significant correlations emerged between macrostructural sleep parameters and CSF biomarkers. In contrast, NREM sleep microstructure showed consistent associations. The Aβ42/pTau181 ratio correlated positively with the fast-to-slow ratio in NREM and N3 and negatively with the slow-to-fast ratio in both stages (all $p<0.05$). SWA in N2 and N1 negatively correlated with Aβ42/pTau181 ($p<0.05$). Regression confirmed the predictive role of NREM slow-to-fast ratio on Aβ42/pTau181 ($\beta = -3.7$, $p=0.031$). Similar associations were observed with Aβ42/Aβ40. No significant associations were found for individual biomarkers.

DISCUSSIONS: Spectral imbalances in NREM sleep, particularly a dominance of lower frequencies, are linked to unfavorable CSF profiles. This may reflect early thalamo-cortical dysfunction and impaired glymphatic clearance in PD.

CONCLUSIONS: NREM sleep microstructure represents a promising electrophysiological marker of early neurodegeneration in PD. Longitudinal studies are warranted to validate its role in disease progression and phenotypic stratification.

P8: Correlations between the development of axial postural abnormalities and genetically determined parkinson's disease

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BACKGROUND: Axial postural abnormalities (PA) can complicate Parkinson's disease (PD) in advanced stages, determining quality-of-life impairment. Age and motor symptoms severity are predictors of PA development, but a genetic involvement remains underexplored.

AIM: To assess the influence of genetic variants in GBA, LRRK2 and SNCA on PA development in PD.

METHODS: We analysed 429 patients from Parkinson's Progression Markers Initiative (PPMI), a multicentric longitudinal cohort study about PD, including GBA (37), LRRK2 (71), or SNCA (12) pathogenic variants carriers. PA were assessed at baseline and after 4 years using MDS-UPDRS-III item 3.13 with cut-off ≥ 2 in OFF-medication. PA prevalence, cumulative incidence and incidence rates were compared between genetic subgroups. PA risk factors were analysed with Cox-regression.

RESULTS: General PA prevalence was 11.2% at baseline and 32% at 4 years. Prevalence was highest among SNCA-PD (16.7% at baseline, 41.7% after 4 years), followed by GBA-PD (16.2%, 40.5%), idiopathic-PD (10.7%, 32%) and LLRK2-PD (9.9%, 25.3%). PA incidence over 4 years was 22.5% overall, highest in SNCA-PD (30%) followed by GBA-PD (25.8%), idiopathic-PD (23%) and LRRK2-PD (17.2%). No significant differences were found at any time in PA prevalence ($p=0.680$, $p=0.362$) and cumulative incidence ($p=0.328$). Genetic status was not a significant predictor for PA development ($p=0.742$), in contrast to age and UPDRS-III ($p<0.001$).

DISCUSSIONS: Although not significantly different, trends suggest that GBA and SNCA mutations may be associated with greater levels of PA in early stages. The highest incidence of PA in SNCA-PD despite the youngest average onset age, and the lowest in LRRK2-PD despite the oldest medium age, could suggest a genetic role in PA early development, independently of age. The lowest tendency to develop PA in LRRK2-PD could be related to its slow progression.

CONCLUSIONS: Genetic variants might play a role in PA development, but larger studies are needed, possibly including also other gene mutations.

P9: Domain-based LRRK2 burden analysis in Parkinson's disease across diverse ancestries

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BACKGROUND: LRRK2 variants contribute to Parkinson's disease (PD), with domain-specific effects on kinase activity, GTPase function, and microtubule binding. These might be obscured in gene-wide analyses.

AIM: To identify domain-level contributions of LRRK2 variants to PD risk across ancestries.

METHODS: Using GP2 Release10 imputed genotyping and WGS data, and the EUR AMP-PD WGS dataset, we extracted coding variants across eight LRRK2 domains (ARM, ANK, LRR, ROC, COR, KIN, WD40, CH). We performed domain-based SKAT-o analyses, followed by single-variant analyses in nominally associated domains. Genotyped data were analyzed in four ancestries: European (EUR 22,908 cases vs.9146 controls), East Asian (EAS; 2,285 vs. 1,946), Ashkenazi Jewish (AJ; 1317 vs. 367), and Latino/Indigenous American (AMR; 1,866 vs. 1,394). WGS data included only EUR (GP2 Rel10: 6,751 vs. 1,309; AMP-PD Rel3: 1571 vs. 2,606).

RESULTS: In WGS Rel10, the KIN domain was significantly associated with PD (p=0,013), while in the AMPPD data ARM, LRR, ROC, and KIN were significantly associated (p of <0.001, 0,023, <0.001, and 0.024, respectively). In genotyped EUR data, KIN and COR were significantly associated with PD (p<0.001, p=0.014). In EAS, nominal associations were observed in the ARM, LRR, and WD40. In AJ, the KIN domain showed a significant association (p<0.001), primarily driven by p.G2019S. No associations were found in AMR.
Single-variant analysis in EUR WGS data nominated the following variants as significantly associated with PD: p.N2081D and p.G2019S in GP2 data, and p.N551K, p.R1398H and p.G2019S in AMPPD data. In genotyped data we nominated p.G2019S in the EUR ancestry, p.A419V, p.N551K and p.G2385R in EAS ancestry, and p.G2019S in AJ ancestry.

DISCUSSIONS: Large differences between datasets likely reflect 1) insufficient power, 2) limited resolution of imputed data, and 3) an unbalanced number of cases vs controls.

CONCLUSIONS: Domain-level analyses can reveal ancestry-specific signals, though larger WGS datasets are needed to resolve inconsistencies.

P10: Effect of group size and image resolution of the FDG-PET scans on the diagnostic performance of Parkinson's disease related pattern

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BACKGROUND: Due to overlapping of early symptoms between Parkinson's disease (PD) and other neurological syndromes, an objective biomarker is essential. The Parkinson's Disease-Related Pattern (PDRP), derived from [18F]FDG-PET via spatial covariance analysis (SSM/PCA), shows promise. However, its clinical application depends on the understanding how technical factors like image resolution and identification cohort size affect its reliability and diagnostic value.

AIM: This study aimed to investigate how the size of the group used for pattern identification and the spatial resolution of [18F]FDG-PET images affect the reproducibility and clinical performance of the PDRP.

METHODS: [18F]FDG-PET images from 186 PD patients and 201 cognitive normal (CN) subjects were collected from University Medical Centre Ljubljana, Feinstein Institutes for Medical Research and ADNI. PDRPs were identified 750 times using varying group sizes (20–80 PD/CN) and resolutions (6–20 mm FWHM). Each was validated on an independent set (20 PD/20 CN) at various resolutions. Diagnostic performance was assessed using ROC analysis.

RESULTS: All identified PDRPs significantly distinguished PD from CN ($p < 0.001$). Metabolic topographies consistently showed increased activity in the basal ganglia, thalamus, cerebellum, and motor cortex, alongside reductions in prefrontal and parietal regions. Larger identification groups led to more stable and accurate PDRPs. Diagnostic performance improved when identification was done at 6–10 mm resolution and validation at 8–15 mm.

DISCUSSION: Larger identification cohorts improve pattern stability. Higher image resolution during identification further enhances robustness. During validation, medium resolution generally improves results; perhaps by reducing noise and misalignment effects. Both factors influence PDRP stability and diagnostic accuracy.

CONCLUSION: For reliable PDRP identification, at least 30 PD/30 CN subjects should be used, with image resolution between 6–10 mm. Validation performs best at 8-15 mm. SSM/PCA-based network patterns are robust across scanners and resolutions, but optimal settings enhance diagnostic consistency.

P11: Expanding the differential diagnosis of multiple system atrophy: a systematic review on dysautonomia in genetic movement disorders

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BACKGROUND: Adult-onset genetic movement disorders may manifest with autonomic failure alongside parkinsonism, ataxia, and a variety of other movement disorders. Autonomic dysfunction, a common reason for misdiagnosis of multiple system atrophy (MSA), has not been systematically evaluated in genetic movement disorders.

AIM: To systematically characterize dysautonomia in adult-onset genetic movement disorders.

METHODS: A PubMed search using predefined search terms was performed. Original research articles published in English were evaluated. Out of 313 papers retrieved on September 8th, 2025, 82 papers were considered relevant (61 original papers, 5 case series and 16 case reports). Seven review papers, 12 chapters, 206 articles unrelated to the subject matter, and 6 papers written in a language other than English were excluded. Study population, age at onset, mode of inheritance and mutation, presence of control group, clinical presentation including type of movement disorders, methodology for autonomic dysfunction assessment and main findings related to autonomic dysfunction were summarized in a table of evidence.

RESULTS and DISCUSSIONS: A total of 34 adult-onset genetic movement disorders, caused by mutations in 52 genes, manifesting with autonomic failure associated with ataxia, parkinsonism, dystonia, spastic paraplegia, chorea or a complex phenotype were identified. Among these, spinocerebellar ataxias, hereditary spastic paraplegias, some forms of genetic parkinsonism, fragile X tremor-ataxia syndrome, LMNB1-related autosomal dominant leukodystrophy, and RFC1 disease represent MSA mimics. Dysautonomia phenotype varies across the disorders.

CONCLUSIONS: A number of adult-onset genetic movement disorders may resemble MSA posing a differential diagnostic challenge. Autonomic dysfunction is an important, yet commonly overlooked feature of various adult-onset genetic movement disorders which should be considered in the differential diagnosis of MSA. A detailed history and autonomic function testing should be performed to better characterize autonomic dysfunction in these disorders. Genetic testing should be ordered in selected cases to exclude common mimics and improve diagnostic accuracy of MSA.

P12: Functional motor disorder associated with focal brain lesion: a case series

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BACKGROUND: Functional motor disorders (FMD) are characterised by internal inconsistency, with diagnosis relying on positive clinical signs. While functional brain network alterations underlie FMD, cases where functional symptoms are precipitated by structural lesions challenge the traditional dichotomy between functional and structural neurological disorders.

AIM: To present a case series linking focal brain lesions to FMD and examine their role in the pathophysiology of functional symptoms.

METHODS: We retrospectively reviewed patients diagnosed with FMD in whom neuroimaging revealed focal abnormalities, focusing on clinical features and lesion locations.

RESULTS: Eight patients were included. Ischemic lesions involved the pre/-postcentral cortex, parietal lobe, caudate/lentiform nuclei, thalamus and anterior parafalcine region. Additional cases involved a parietal toxoplasma abscess, a thalamic neoplasm and focal hypometabolism in the postcentral gyrus and basal ganglia in early Creutzfeldt–Jakob disease. Presentations included hand tremor (n=5), hemiparesis (n=1), leg weakness (n=1), and clonic leg jerks (n=1), all compatible with a FMD based on clear positive signs of inconsistency, including Hoover's sign, entrainment and distractibility.

DISCUSSIONS: This series illustrates that clinical hallmarks of FMD can emerge in the context of structural lesions. Mechanistic parallels with FMD include reduced proprioceptive precision and altered sense of agency in parietal lesions, altered somatosensory processing due to thalamic involvement and abnormal motor processing linked to supplementary motor area, anterior cingulate cortex or basal ganglia dysfunction.

CONCLUSIONS: Focal lesions can disrupt neural circuits and give rise to symptoms with functional phenomenology through distinct mechanisms. Our findings support the view that altered distributed network activity underlies FMD and highlight the potential of targeted approaches to modulate network function in these patients.

P13: High prevalence of et-plus signs in prospectively assessed essential tremor patients: clinical correlates and implications for disease stratification

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BACKGROUND: Essential tremor (ET) has been recognized a heterogenous syndrome. Potential subtypes might be defined by the presence or absence of additional neurological soft signs (pure-ET vs. ET-plus).

AIM: To prospectively assess a large number of ET-patients for the presence of additional neurological signs.

METHODS: We prospectively enrolled 79 ET-patients (38.0% female), undergoing clinical assessment focused on identification of potential signs of ET-plus. Soft signs considered were resting tremor, impaired tandem gait, questionable dystonia, questionable bradykinesia, other mild parkinsonian signs (hypomimia, reduced arm swing) and marked asymmetry of action tremor. Tremor severity was assessed with TETRAS.

RESULTS: 70/79 patients (88.6%) were classified as ET-plus, while the remaining 9 (11.4%) were diagnosed as pure-ET. ET-plus-patients were older at baseline than pure-ET-patients (median age 64.0 vs. 41.3 years, p=0.013), but they did not differ either in age at tremor onset (median age 28.7 vs. 19.3 years, p=0.099), disease duration (median disease duration 19.4 vs. 22.4 years, p=0.655), sex distribution (35.7% vs. 55.6% female, p=0.248), family history (85.7% vs. 66.7% positive, p=0.147) nor alcohol responsivity (58.0% vs. 75.0%, p=0.506). 49/70 (70%) of ET-plus-patients had more than one soft sign. Resting tremor was present in 91.4% of ET-plus-patients, followed by questionable dystonia (47.1%), impaired tandem gait (31.4%), questionable bradykinesia (27.1%), mild parkinsonian signs (27.1%) and marked action tremor asymmetry (14.3%). Tremor tended to be worse in ET-plus-patients (median TETRAS score 17.5 vs. 11.5, p=0.085).

DISCUSSIONS: Additional neurological signs like resting tremor or questionable dystonia are a frequent finding in prospectively evaluated ET-patients. ET-plus and pure-ET-patients do not differ in important clinical aspects of ET like family history or alcohol responsiveness, yet ET-plus-patients tend to be older and more severely affected by tremor.

CONCLUSIONS: ET-plus might just be the representation of a later disease stage. Stratification by specific soft signs or by age at disease onset might be more promising approaches.

P14: Impact of GBA mutations on pragmatic abilities in Parkinson's disease: an exploratory study

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BACKGROUND: Variants in the GBA gene represent the most common genetic risk factor for Parkinson's disease (PD), with a prevalence that varies across populations. GBA mutation carriers typically present with earlier onset of motor symptoms, faster disease progression, and more frequent and severe non-motor manifestations, including greater psychiatric burden, cognitive vulnerability, and language impairment.

AIM: This study aimed to assess the extent of pragmatic abilities impairment among GBA-positive patients at an early disease stage, to evaluate the potential benefit of earlier speech therapy intervention.

METHODS: In this study, we enrolled 10 early-stage PD patients: 5 GBA mutation carriers and 5 non-carriers. All participants underwent a comprehensive clinical and neuropsychological assessment, including the Montreal Cognitive Assessment (MoCA) and the Unified Parkinson's Disease Rating Scale (UPDRS, all subscales), followed by the Assessment of Pragmatic Abilities and Cognitive Substrates (APACS) test. Inclusion criteria were a diagnosis of idiopathic PD under good pharmacological control, MoCA score ≥ 26, absence of major comorbidities that could limit patient autonomy and the availability of genetic testing for known GBA mutations.

RESULTS: No significant differences in MoCA scores were found between the two groups of patients; GBA-positive patients showed significantly lower scores on APACS tasks assessing pragmatic production, while pragmatic comprehension scores did not differ substantially.

DISCUSSIONS: Language impairment in GBA-PD mainly manifests as reduced semantic and phonemic fluency, lexical processing and naming difficulties, and may extend to deficits in comprehension and production in advanced stage. Our results suggest that pragmatic abilities—encompassing the interaction between language, context, and general communicative principles—may also be compromised, with production aspects being affected earlier than comprehension.

CONCLUSIONS: If confirmed by further studies, these preliminary findings may suggest that speech therapy could be beneficial from the early stages of GBA-positive disease, even before overt cognitive involvement becomes detectable.

P15: Impulse control disorder and other psychiatric symptoms in Wilson's disease

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BACKGROUND: Wilson's disease is a rare hereditary disorder caused by impaired copper excretion, leading to its accumulation primarily in the liver and brain. The clinical presentation includes hepatic, neurological, and psychiatric symptoms. Neurological manifestations are commonly classified into Parkinson-like, dystonic, cerebellar, and mixed forms.

AIM: To evaluate the clinical characteristics and frequency of impulse control disorders (ICDs) and other psychiatric symptoms in patients with Wilson's disease.

METHODS: This observational study included consecutive patients treated at the Clinic for Neurology, University Clinical Center of Serbia, Belgrade. All participants were assessed using the following instruments: Questionnaire for Impulsive-Compulsive Disorders (QUIP-RS), Beck Depression Inventory, Hamilton Anxiety Scale, Apathy Evaluation Scale, Barratt Impulsiveness Scale, Obsessive-Compulsive Symptoms Questionnaire, and the Unified Wilson's Disease Rating Scale. Based on QUIP-RS results, patients were divided into two groups: WD-ICD+ (with ICDs) and WD-ICD– (without ICDs).

RESULTS: Of 41 patients, 9 (22%) were WD-ICD+. Compared to WD-ICD– patients, they had significantly more severe neurological symptoms, higher impulsivity on the Barratt Impulsiveness Scale, and higher QUIP-RS scores across all domains. No significant differences were observed in other psychiatric or cognitive measures. Logistic regression analysis was significant, correctly classifying 84% of patients. Higher scores on the Barratt Impulsiveness Scale and the dystonic form of the disease emerged as significant predictors.

DISCUSSIONS: In our study, impulse control disorders (ICDs) were present in 22% of patients with Wilson's disease (WD), a prevalence similar to untreated Parkinson's disease, suggesting that basal ganglia pathology may contribute to their development. Impulsivity and dystonic form of WD emerged as predictors of ICDs.

CONCLUSIONS: Impulse control disorders occur in approximately one-quarter of patients with Wilson's disease. Greater impulsivity and dystonic features increase the likelihood of developing ICDs. Recognition of these risk factors is essential for timely diagnosis and management of psychiatric comorbidities in Wilson's disease

P16: Initiating foslevodopa infusion in Parkinson disease: a pragmatic study

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BACKGROUND: Subcutaneous foslevodopa (fLD) infusions are a new therapeutic option for treating complicated Parkinson's disease (PD).

OBJECTIVES: To assess the initial period of fLD infusion as replacement of oral medications in PD.

METHODS: Twenty-three PD patients were recruited sequentially and started infusion treatment according to recommended practice. Efficacy was assessed using the MDS-UPDRS motor examination and motor complications scores in the ON condition at baseline and after 20 weeks. Safety and fLD doses were assessed on a weekly basis. The 20-week observation period was compared to baseline.

RESULTS: The MDS-UPDRS motor examination score on week 20 was unchanged, whereas the motor complications score had improved, indicating increased ON time without troublesome dyskinesias and reduced OFF time. The initial fLD dosage was gradually increased in all patients, on average by 37% on week 20. Treatment optimization was achieved at a median of 12 weeks; patients with higher body mass index required a longer titration period. The levodopa equivalent daily dose of fLD on week 20 was 0.57 mg to 1 mg. Adverse events occurred in 87% of patients, primarily consisting of skin reactions at the infusion sites that occasionally required treatment.

DISSCUSION: fLD infusion reduced motor fluctuations while maintaining stable ON motor performance. The infusion dose was increased progressively across the initial 20 weeks of treatment. The time needed for treatment stabilization was longer than previously reported and delayed in patients with higher body mass index. The treatment was generally well tolerated, neuropsychiatric effects were more common than previously reported.

P17: Integrating psysiotherapy into the treatment of Parkinson's disease with deep brain stimulation (DBS)

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BACKGROUND: Physical therapy has an important role adressing patients with ekstrapiramidal syndroms and diseases.
AIM: Parkinson Disease (PD) can be optionaly treated with Deep Brain Stimulation (DBS) and physical therapy.

METHODS:

RESULTS: Physiotherapeutic approch to patients with DBS is similar to those without DBS as regard to exercise, balance training, and compenstory strategies. Where they differ are the restrictions imposed to preserve the DBS components and secondarily to avoid harm to the patient.
Medtronic has established guidelines for various modalities of treatments commonly performed by physiotherapists. Modalities such as transcranial magnetic stimulation, shortwave diathermy, microwave diathermy, or ultra sound anywhere in the body are contrainiciated for any patient with an implanted system and cause tissue damage at the location of the implanted electrodes, resulting in sever injury and death.

DISCUSSIONS: When working with PD patient it is assesed posture, abnormal tone or movements, strenght deficits, ROM, bed mobility, chair transfers, gait, balance and falls. In physitherapy intervention patients recive movment strategy training, training with auditory, visual and proprioceptive stimulation, training gait on tredmill, dance, thai chi, boxing, yoga, traning to overcome fear of falling and overcome freezing of gait. Conventional physiotherapy includes all supervised active exercise which are focused to improve gait and overcome posture abnormality Includes exercise to improve dynamic and static balance, transfers and mobility in bed.
Sometimes, after inserted DBS in patients with PD, it can be observed strange movment like walking on toes, unstable walking and weird pathology pattern of walking. This could be treated with motor learning, to reeducate patient pattern of gait.

CONCLUSIONS: The overall goal of PD patients is to optimise actitivities, participation and quality of life by considering functioning, personal and enviromental factors. Physiotherapist work multidisciplinary as a member of the exstrapyramidal team, and contributes that patient`s condition gets better.
Physical therapy, Parkinson`s Disease, Deep Brain Stimulation

P18: Is GBA1 mutation status a game-changer for impulse control behaviour in Parkinson's disease?

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BACKGROUND: The GBA1 related Parkinson's disease (PD) is associated with more severe non-motor symptoms. To date, studies of the role of GBA1 mutations in the occurrence of impulse control behaviours (ICBs) in PD have yielded controversial results.

AIM: Our aim was to investigate the frequency and characteristics of ICBs in PD patients with GBA1 mutations.

METHODS: 213 consecutive PD patients were included. Clinical data were gathered via interviews and using the standard set of questionnaires. Genetic analysis of exons 8–11 of the GBA1 gene was performed for all participants.

RESULTS and DISCUSSIONS: GBA1 variants were detected in 32 out of 213 patients (GBA-PD). ICBs were more frequent in GBA-PD (31.2%) than in non-mutated PD (nmPD) group (25.9%), though not significantly. Among patients with ICBs and GBA1 variants female sex predominance was observed (60%, p = 0.022). GBA-PD patients with ICBs had a significantly shorter disease and therapy duration, lower total LEDD and QUIP when comparing to nmPD with ICBs. Binary logistic regression showed that age, BDI score, LEDD, and male sex significantly predicted ICBs in the whole sample. In the GBA-PD group, only dopamine agonist use, and a lower UPDRS Part I score were significant predictors.

CONCLUSIONS: Dopaminergic treatment is a significant risk factor for ICBs, irrespective of GBA1 mutation status. GBA1 mutations may increase susceptibility to dopaminergic dose-related ICBs adverse effects, particularly in PD patients with fewer non-motor symptoms, and may affect the sex distribution in PD patients with ICBs, potentially attenuating the male predominance.

P19: Low-frequency GPi deep brain stimulation for dystonia: a double blind, crossover study

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BACKGROUND: Globus pallidus internus deep brain stimulation (GPi-DBS) is an effective treatment for severe focal dystonia. High-frequency stimulation (≥100Hz), while effective, may induce parkinsonian motor side-effects.

AIM: The aim of this study was to compare low- and high-frequency GPi-DBS in its effects on dystonic symptoms and parkinsonian side effects in patients with focal dystonia.

METHODS: This double-blinded randomized crossover trial included patients with focal dystonia (N=10), each undergoing three stimulation conditions: OFF, 80Hz, and 130Hz. After initial baseline measurements, the stimulation was switched off, followed by a 1h washout period before the evaluation OFF stimulation. Participants were then randomized to receive either 80Hz or 130Hz GPi-DBS, with 1h washout period before assessment. Subsequently, they were switched to the alternate stimulation, followed by another 1h washout before their final evaluation. Each evaluation assessed dystonic motor symptoms, gait and parkinsonian motor symptoms.

RESULTS: Dystonic motor symptoms significantly improved with both frequencies of GPi-DBS, as reflected in the motor subscales of the BFMDRS and the TWSTR .Gait speed also improved with frequencies , as did step length. There were no significant differences between low- and high-frequency stimulation for dystonic motor symptoms, gait speed, and step length. Only the bradykinesia subscore of the MDS-UPDRS-III decreased OFF stimulation ($p=0.040$), with a significant difference observed compared to high-frequency stimulation ($p=0.020$) but not compared to low-frequency stimulation ($p=0.064$). There was no effect of frequency of stimulation on bradykinesia ($p=0.140$), or on other parkinsonian signs (all $p>0.05$).

DISCUSSIONS: Both frequencies GPi-DBS effectively improved dystonic symptoms and gait. Bradykinesia improved OFF stimulation and there was no effect of frequency of stimulation on bradykinesia and the other parkinsonian signs. Further large-scale studies exploring the acute and chronic effect of parameter changes are needed to optimize DBS in dystonia.

CONCLUSIONS: Lowering stimulation frequency did not consistently reduce parkinsonism, though some patients showed clinically relevant improvement in bradykinesia.

P20: Metabolic brain imaging of normal and disease-related networks in common neurodegenerative disorders: do they overlap?

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BACKGROUND: Metabolic network imaging has demonstrated that neurodegenerative disorders, including those primarily affecting motor function, are associated with distinct disease-specific metabolic networks that emerge early in the disease course.

AIM: This study aimed to investigate whether the topographical similarity between disease-specific metabolic networks and the default mode network (DMN) can provide a network-based framework for classifying common neurodegenerative disorders, such as for example Parkinson disease-related pattern (PDRP).

METHODS: We analyzed pooled multicenter imaging data from 1,207 patients diagnosed with various neurodegenerative disorders—Parkinson disease (PD), Alzheimer disease (AD), dementia with Lewy bodies (DLB) and its prodromal forms, multiple system atrophy (MSA), progressive supranuclear palsy (PSP), behavioral variant frontotemporal dementia (bvFTD), and corticobasal syndrome (CBS). Comparative data from 499 healthy controls were included. We first assessed the topographic similarity between disease-specific networks and the DMN, and then calculated individual subject scores within each cohort. Correlations between the scores were subsequently analyzed and compared across groups.

RESULTS: Significant topographic overlap with the DMN was observed in bvFTD, PSP, and CBS, accompanied by strong inverse correlations between subject scores ($R^2 > 0.65$). In contrast, AD, PD, and DLB showed lesser topographic overlap and weak score correlations ($R^2 < 0.21$). Prodromal forms mirrored these trends. No evidence of DMN overlap was found in MSA.

DISCUSSIONS: Our findings categorize common neurodegenerative disorders into three distinct groups based on the degree of topographic overlap between disease-specific metabolic patterns and the DMN.

CONCLUSIONS: This novel framework offers a network-based perspective on neurodegenerative disorders. Utilizing metabolic brain imaging to classify individual patients based on pattern expression may enhance diagnostic accuracy and support personalized treatment strategies.

P21: Microbial diversity in drug naïve Parkinson's disease patients

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BACKGROUND: Parkinson's disease (PD) is a neurodegenerative disorder with a multifactorial origin, where the gut microbiota has recently been implicated as a potential modifier of disease onset and progression. Despite growing interest, few prospective investigations have assessed the gut microbiome prior to treatment initiation, particularly in relation to disease severity and microbial dynamics over time.

AIM: This study aimed to profile the gut microbiome of untreated PD patients from the Croatian GiOPARK cohort, establishing a valuable baseline for future longitudinal and intervention-based research.

METHODS: A total of 49 drug-naïve PD patients and 34 matched healthy controls were enrolled. Stool samples were subjected to 16S rRNA gene sequencing targeting the V3–V4 hypervariable region. Microbial composition and diversity were analyzed and compared between the two groups to identify potential disease-associated taxa prior to any pharmacological influence.

RESULTS: No significant differences were observed in alpha diversity indices between PD patients and healthy controls, suggesting comparable overall microbial richness. However, taxonomic composition varied. Increased relative abundance was observed in PD patients for members of the Bacteroidetes and Bacillota phyla, including Bacteroides fluxus, B. intestinalis, and B. eggerthii and Dielma fastidiosa. In contrast, reduced levels were noted for genera such as Alistipes, Barnesiella, Dialister, and Prevotella_9.

DISCUSSIONS: While global microbial diversity remained unchanged, these taxonomic shifts may reflect early gut dysbiosis preceding pharmacological intervention. These findings highlight the potential influence of prodromal factors and disease-specific gut changes, reinforcing the value of drug-naïve cohorts as a baseline for longitudinal microbiome research in PD.

CONCLUSIONS: As one of the few studies focused exclusively on drug-naïve individuals and the first in the Croatian population, our findings provide a critical microbiome baseline for evaluating PD progression and therapeutic effects in future research.

P22: Movement disorders and clinical outcomes in autoimmune encephalitis with neuronal surface antibodies: a registry-based study

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BACKGROUND: Autoimmune encephalitis (AE) frequently presents with movement disorders (MDs), either in isolation or as a part of a complex syndrome involving multiple MDs and other neurological symptoms.

AIM: This study aimed to determine the frequency and spectrum of MDs in AE, the associated antibodies, and the clinical outcomes of adult patients.

METHODS: Data was obtained from an ongoing prospective AE registry. Treating physicians of the enrolled patients were retrospectively contacted to complete a structured questionnaire to collect detailed information on MDs.

RESULTS: 34 patients were included, of whom 19 presented with MDs and 15 did not. 12 patients presented with more than one MD, and MDs were classified as severe in seven cases. The most common MDs were gait disorders (n = 8) and myoclonus (n = 7). Greater MD severity was associated with worse functional outcome at 3 months (p = 0.009, corrected: p = 0.027) and 6 months (p = 0.016, corrected: p = 0.048). Patients with severe MDs were more frequently treated at the ICU, more often required second line treatment, and were more commonly diagnosed with an underlying tumor, although these findings did not reach statistical significance. Anti-LGI1-Ab were the most frequent antibodies, with faciobrachial dystonic seizures (FBDS) occurring in 33.3% of the patients. The second most frequent antibodies were anti-NMDAR-Ab, with 60% of patients developing a variety of MDs.

DISCUSSIONS: Our study identified a statistically significant correlation between MD severity and mRS scores. All patients with severe MDs presented with multiple MDs and had poorer functional outcomes compared to those with moderate and mild MDs. Although gait disturbance and stiffness were the most frequent severe MDs, no single MD was independently associated with worse clinical outcomes.

CONCLUSIONS: Greater MD severity was associated with a more severe disease course and worse clinical outcome, underscoring the prognostic relavance of MDs in AE.

P23: Multidomain Feature Extraction for Discriminating Parkinson's Disease

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BACKGROUND: Parkinson's Disease (PD) is a neurodegenerative disorder whose effective management relies on early and accurate diagnosis. While observable motor signs like slowness of movement and tremor are key indicators, they can be subtle and subjective to assess clinically.
The Parkinsons Disease Smartwatch dataset (PADS) addresses this by providing objective movement records from various neurologically valuable tasks.

AIM: The main aim of the research is to distinguish PD patients from healthy controls (HC) and individuals with differential diagnoses (DD) based on the PADS dataset. The second aim is to provide interpretability of the decision model.
Methods: It this study, we propose a robust machine learning framework to distinguish individuals with PD from HC and DD. We first performed a comprehensive multidomain feature extraction. We then derived an extensive set of features capturing not only statistical properties but also nonlinear dynamics, complexity, and fractal characteristics of the records. The classification was performed using a 10-fold cross-validation scheme. We evaluated several classifiers, including XGBoost, K-Nearest Neighbours (K-NN), and Logistic Regression. We addressed class imbalance through oversampling techniques.

RESULTS: The balanced accuracy for the distinction between PD and HC for the K-NN classifier with RandomOverSampler was 92.03 %. The balanced accuracy for the distinction between PD and DD was 77.54 % (XGBoost with BorderlineSMOTE), whereas multiclass classification differentiated the three groups with 75.05 % balanced accuracy (XGBoost with ADASYN). The best task turned out to be StretchHold with 87.06 % balanced accuracy. This exercise is: extend both arms and maintain the position to assess flexibility and muscular endurance.

DISCUSSION: Our results show that this multifaceted methodology effectively leverages rich information to create a discriminative model.
Conclusion: This work underscores the potential of computational approaches built on comprehensive feature engineering and rigorous validation to provide a non-invasive, scalable, and viable solution for the digital assessment of PD.

P24: Multimodal approach to device-aided management of advanced Parkinson's disease: insights from two cases

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BACKGROUND: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms such as tremor, rigidity, bradykinesia and postural instability, as well as diverse non-motor complications. In advanced stages, device-aided therapies are standard of care, with deep-brain stimulation (DBS) preferred in patients without psychiatric or cognitive contraindications. However, disease progression frequently necessitates adjunctive strategies for sustained symptom control.

AIM: To illustrate the benefits of a multimodal therapeutic approach in advanced PD through two complex patient cases.

METHODS: We present two patients with advanced PD who underwent device-aided interventions following the reemergence of motor and non-motor complications despite initial response to DBS. Clinical outcomes were assessed through motor function, non-motor features, and quality of life (QoL) improvements.

RESULTS: A 71-year-old man, diagnosed at 52, underwent bilateral subthalamic nucleus (STN) DBS in 2015 after initial oral therapy. Following six years of stability, he reported a reemergence of motor fluctuations, dyskinesias, gait impairment, and cognitive decline despite programming adjustments. Subcutaneous foslevodopa/foscarbidopa infusion was initiated in 2024, leading to a 38% improvement in MDS-UPDRS scores and significant QoL benefit.
A 73-year-old woman, diagnosed at 45, underwent pallidotomy at 49 and later bilateral STN DBS in 2013. Initial outcomes included reduced fluctuations and medication-related dyskinesias. However, within one year, she experienced progressive motor and psychological decline, compounded by inadequate home support, necessitating device removal in 2014. Following reassessment and introduction of levodopa/carbidopa intestinal gel infusion in 2017, she reported sustained motor improvement and improved QoL.

DISCUSSIONS: These cases highlight the need for flexibility in advanced PD management. Combined device-aided therapies may address evolving motor and non-motor challenges where single modalities prove insufficient.

CONCLUSIONS: A multimodal, patient-centered approach is essential in advanced PD as disease trajectories evolve. Integrating invasive and minimally invasive strategies can mitigate symptom burden, prolong therapeutic benefit, and improve long-term outcomes in complex PD.

P25: Neurophysiological signature of cognitive–motor interaction during dual-task balance in early Parkinson's disease

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BACKGROUND: People with Parkinson's disease (PD) often depend on conscious attention to compensate for impaired automatic balance regulation. As PD progresses, cognitive decline may further compromise postural control. However, the interaction between cognitive and motor systems in early PD remains insufficiently understood.

AIM: This study aimed to identify behavioral and neural alterations in early-stage PD to clarify subtle distinctions from healthy motor–cognitive functioning.

METHODS: Eighteen individuals with PD (mean age: 62.9 ± 6.6 years) and eighteen sex- and age-matched healthy controls (mean age: 62.9 ± 6.4 years) performed three conditions: (1) a balance-only semi-tandem stance task (ST-balance), (2) a Stroop-based visual oddball task with color–word stimuli (ST-cognitive), and (3) a dual-task (DT) combining both. Postural sway was measured via center-of-pressure displacement on a force plate, and brain activity was recorded using 128-channel EEG.

RESULTS: Compared with controls, PD participants exhibited smaller ($p = .009$) and slower ($p = .008$) sway amplitudes. Across groups, DT performance resulted in reduced sway compared to ST-balance ($p < .001$). EEG analyses revealed that central low-frequency (delta, theta) power increased with cognitive demand ($p < .012$), centroparietal beta desynchronization strengthened during motor activity ($p < .050$), and parietal alpha desynchronization was greater in DT ($p = .025$). PD participants also showed delayed P300 responses ($p = .034$), suggesting slowed conflict resolution or compensatory neural processing.

DISCUSSIONS: Reduced sway in PD may reflect rigidity and increased tonic muscle activity, while decreased movement in DT could indicate more automatic postural control under divided attention. Despite comparable cortical power spectra between groups, altered event-related potentials point to early attentional vulnerabilities in PD.

CONCLUSIONS: Early-stage PD involves subtle yet distinct disruptions in cognitive–motor integration. Event-related potentials may serve as sensitive neural markers for detecting early cortical changes before overt motor decline becomes evident.

P26: Not All Pretrained Gene Expression Transformers Encode Parkinson's Disease Information

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BACKGROUND: Pretrained models such as GeneFormer (Theodoris et al., 2023) and scGPT (Chen & Zou, 2024) have shown promise in representing gene expression data. However, their embeddings are often applied to new biological tasks without fine-tuning, under the assumption that the rich representations they capture will generalize. Our analysis suggests that open-source model embeddings do not predict the Parkinson's disease (PD) target in their pretrained form, but their openly available weights make them valuable starting points for task-specific fine-tuning.

AIM: Investigate how fine-tuning pretrained gene expression encoders can yield statistically significant representations for Parkinson's disease (PD) prediction.

METHODS: We evaluated GeneFormer's pretrained embeddings against PD status using permutation tests to assess whether observed correlations could arise by chance. We compared three input types: (1) raw gene expression, (2) PD-related genes (Lange et al., 2025), and (3) pretrained embeddings.

RESULTS: These representations correlate similarly with the PD target, exhibiting maximum Pearson correlations of 0.16, 0.13, and 0.08 for raw genes, pretrained embeddings, and PD-related genes, respectively. However, the permutation test tells another story, reporting p-values of 0.983 for GeneFormer embeddings, 0.071 for raw genes, and 0.054 for curated PD-related genes. These findings indicate that non–fine-tuned embeddings are random with respect to the PD label, while biologically curated features approach significance.

DISCUSSION: Recent benchmarking work (Zhong et al., 2025) compared closed-source versus open-source models without fine tuning the latter. Consequently, while GenePT (Chen & Zou, 2025) achieves strong performance, GeneFormer and scGPT performed poorly. This together with our results, suggests that fine tuning open-source models is both an option and essential for a fair comparison.

CONCLUSION: Our findings suggest pretrained embeddings from open-source models such as GeneFormer, should not be used directly for disease prediction tasks. Instead, they may require fine-tuning to yield statistically meaningful representations that could surpass closed-source baselines.

P27: Paradoxical tremor amplification and impaired arithmetic performance during cognitive load in functional tremor

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BACKGROUND: Functional tremor (FT) is thought to involve abnormal attentional focus and a disturbed sense of agency. Typically, cognitive distraction (e.g. serial subtraction) reduces FT amplitude, likely because attention shifts away from the tremor and toward the cognitive task. However, in a subset of FT patients, amplitude paradoxically increases under cognitive load, which may reflect sustained attention toward the tremor itself.

AIM: To determine whether, under cognitive load, patients with paradoxical tremor increase manifest impaired subtraction performance.

METHODS: Twenty-two patients with clinically definite FT had tremor recorded by accelerometry and surface EMG. In a cognitive-load task (serial subtraction of 7 from 100, 13 steps), tremor amplitude and subtraction errors were recorded. An "amplitude-increase" subgroup was defined by >123% tremor increase (threshold = median + 2×MAD). Error counts were compared between groups using the Mann–Whitney U test. Proportions of inaccurate subtraction (>1 error) were compared across groups using Fisher's exact test.

RESULTS: Patients with amplitude increase above the 123% cut-off (N= 5) committed significantly more subtraction errors than those below (p=0.002, Mann–Whitney U). Fisher's exact test also showed a significant group difference (p=0.006).

DISCUSSIONS: FT patients with paradoxical tremor amplification may fail to shift attention away from tremor during cognitive tasks, as evidenced by increased calculation errors. Unlike the typical distractible group, this subgroup of patients exhibits an inverse "trade-off" during task that requires divided attention. Additionally, heightened stress or arousal (noradrenergic activation) during mental load could amplify tremor and impair arithmetic performance. The susceptibility of FT to modulation by diffuse stress-related neuromodulatory systems highlights the complexity of its pathophysiology, supporting the view of FT as a chronic network disorder that operates independently of patient awareness.

CONCLUSIONS: FT depends on complex interaction between attentional networks and diffuse neuromodulatory systems, resulting in between-patient variability in tremor distractibility with cognitive load.

P28: Prevalence of Cerebral Amyloid Angiopathy in Patients With Alzheimer's Disease and Dementia With Lewy Bodies

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BACKGROUND: In neurodegenerative diseases various pathologies often coexist, contributing to accelerated cognitive decline. Dementia with Lewy bodies (DLB) is primarily associated with alpha-synuclein pathology, but Alzheimer's disease (AD)–related changes, including amyloid-beta (Aβ) plaques and tau deposits, are also frequently present. The coexistence of cerebral amyloid angiopathy (CAA) in which Aβ accumulates in the walls of small cortical arteries, capillaries, and leptomeningeal vessels is not yet well studied.

AIM: To evaluate the prevalence of CAA in patients with DLB, AD, and age-matched healthy controls using the Boston Criteria v2.0. This represents an interim analysis based on partial data collection.

METHODS: We retrospectively analyzed MRI scans from consecutive dementia patients from the University Medical Centre Ljubljana database. CAA diagnosis was established according to the Boston Criteria v2.0. Statistical analyses were performed using Fisher's Exact Test and Pearson's Chi-Square Test.

RESULTS: A total of 147 participants were included: 62 patients with DLB (mean age 76 years; 27% female), 27 with AD (mean age 74 years; 67% female), and 58 controls (mean age 76 years; 64% female). CAA (probable + possible) was observed in 44% of DLB patients, 37% of AD patients, and 50% of controls, with no statistically significant group differences. Probable CAA was more frequent (nonsignificant) in AD (11%) and DLB (10%) compared to controls (5%).

DISCUSSIONS: Neuropathological studies have reported higher CAA prevalence in AD (96%) and DLB (70%), similarly however neuroimaging study suggested a lower prevalence of CAA in demented patients than previously reported.

CONCLUSIONS: CAA prevalence was similar in DLB, AD, and controls using MRI-based criteria. A larger cohort needs to be studied to clarify the coexistence of CAA neurodegenerative diseases.

P29: Six-month comparison of DBS-STN, LCIG, CSCI and LECIG in advanced Parkinson's disease patients

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BACKGROUND: Parkinson's disease (PD) is a progressive neurodegenerative disorder with disabling motor and non-motor symptoms. In advanced stages of the disease invasive treatment methods play a crucial role because oral dopaminergic therapy often fails to adequately control motor fluctuations and dyskinesias. Some of the available options, which we mention in this paper, include deep brain stimulation of the subthalamic nucleus (DBS-STN), levodopa/carbidopa intestinal gel (LCIG), levodopa/entacapone/carbidopa intestinal gel (LECIG), and the less invasive continuous subcutaneous infusion (CSCI) with foslevodopa/foscarbidopa.

AIM: To compare the short-term efficacy of DBS-STN, LCIG, LECIG, and CSCI in improving motor symptoms and complications in advanced PD.

METHODS: This prospective study included 51 patients with advanced PD treated at the Clinic of Neurology, Clinical Hospital Center Rijeka between 2022 and 2024. Patients underwent baseline and six-month evaluations after initiating one of the four invasive therapies. Clinical assessments included the Unified Parkinson's Disease Rating Scale (UPDRS) part III (motor, OFF state) and part IV (motor complications). Patients will continue to be followed longitudinally without a fixed study endpoint.

RESULTS: After six months, DBS-STN achieved the greatest efficacy, with a 51% reduction in UPDRS III and 53% in UPDRS IV scores. Both CSCI and LCIG produced 30% improvements in UPDRS III and IV, while LECIG improved UPDRS III by 29% and UPDRS IV by 22%.

DISCUSSIONS: These results confirm DBS-STN as the most effective option for short-term motor control and complication reduction in advanced PD. However, infusion therapies, particularly CSCI as a less invasive alternative, also provided clinically meaningful benefits. The differences observed may guide individualized treatment selection, balancing efficacy, invasiveness, and patient preference.

CONCLUSIONS: DBS-STN showed the greatest six-month improvement in motor outcomes and complication management. CSCI and LCIG provided comparable benefits, while LECIG showed slightly lower efficacy. Long-term prospective follow-up is needed to confirm durability and safety across modalities.

P30: Sleep as a biomarker of motor and non-motor symptom severity in parkinson's disease

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BACKGROUND: Sleep disturbances are highly prevalent and disabling in Parkinson's disease (PD). They may not only reflect underlying neurodegenerative processes but also contribute to disease severity.

AIM: To investigate the correlation between sleep macrostructure and motor/non-motor symptoms in early or de novo PD.

METHODS: Thirty-two patients with early or de novo PD underwent comprehensive clinical evaluation, including the MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Non-Motor Symptoms Scale (NMSS) and scales for fatigue, apathy, depression and anxiety. Polysomnography (PSG) was performed to assess among others the percentage of N2, N3, and REM sleep. Correlation analyses (Spearman's tests) were used to evaluate sleep parameters as predictors.

RESULTS: No significant correlation was observed between UPDRS part-III and sleep parameters ($p > 0.05$). In contrast, UPDRS part II scores correlated inversely with N3% ($\rho = -0.45$, $p = 0.012$) and positively with REM sleep without atonia (RWA%, $\rho = 0.47$, $p = 0.007$). NMSS total scores correlated inversely with N3% ($\rho = -0.44$, $p = 0.012$), as did several NMSS subdomains (gastrointestinal, urinary, sexual; all $\rho = -0.39$ to -0.50, $p < 0.01$). RWA% correlated positively with Fatigue Severity Scale scores ($\rho = 0.48$, $p < 0.01$) and negatively with the Apathy Evaluation Scale ($\rho = -0.40$, $p < 0.01$). HADS anxiety and depression did not correlate with sleep macrostructure.

DISCUSSIONS: Altered sleep architecture was associated with greater motor/non-motor symptom burden in early PD. Reduced deep sleep related to worse self-reported motor functioning and higher non-motor burden, particularly dysautonomia. Increased RWA% correlated with greater fatigue and apathy

CONCLUSIONS: These findings suggest that sleep macrostructure may represent a potential biomarker of disease severity and phenotypic expression in de novo PD. Given the exploratory design and multiple comparisons, results should be considered hypothesis-generating rather than confirmatory.

P31: Stiff person syndrome as a mimic of functional neurological disorder

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BACKGROUND: Stiff person spectrum disorder (SPSD) is a rare autoimmune mediated neurological disorder that may phenotypically mimic functional neurological disorder (FND), especially in early stages, due to atypical and inconsistent clinical features.

AIM: Our aim is to illustrate key clinical similarities and differences between SPSD and FND through a case series of patients who were initially considered to have functional movement disorders.

METHODS: We analyzed six patients (5 female, 1 male) referred to our center between 2019–2025 with a prior consideration of FND. Detailed clinical evaluation, neuroimaging, EMG, CSF analysis (including anti-GAD65 antibodies), and video documentation were reviewed. All patients were eventually diagnosed with SPSD.

RESULTS AND DISCUSSIONS: Five of six patients were initially diagnosed with functional gait disorder (FGD), and one with functional (fixed) dystonia (FDy). At the earliest stage, all six patients exhibited signs of clinical inconsistency, including symptom variability (in 3 patients), spontaneous remission or exacerbation (in 4 patients), objective-subjective disagreement (in 3 patients), and sudden onset (in 2 patients). However, regarding incongruence, our patients did not display features typically associated with incongruent neurological presentations, nor typical signs associated with FND. Specifically, the patient with FDy showed fixed dystonia involving proximal upper limb muscles with sparing of hand finger function, a distribution atypical for functional dystonia, raising a red flag and prompting further diagnostic evaluation. Patients with FGD demonstrated markedly slowed, broad-based gait with start hesitation and difficulty continuing, which did not fit clearly into established phenotypic subgroups of FGD. All patients showed significant clinical improvement following the initiation of immunotherapy.

CONCLUSIONS: Rare organic conditions such as SPSD may be misdiagnosed as FND, but a previously presented phenotype specific and sign based diagnostic approach focused on identifying clinical inconsistencies and incongruencies can significantly reduce this risk.

P32: The comparison of the effects of levodopa/carbidopa pump and Foslevodopa/Foscarbidopa pump on the quality of life and sleep in Parkinson's disease patients

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BACKGROUND: In advanced stages of Parkinson's disease, oral levodopa often leads to motor fluctuations and dyskinesias due to unstable drug levels. Continuous levodopa/carbidopa intestinal gel infusion and subcutaneous foslevodopa/foscarbidopa administration aim to provide more stable dopaminergic stimulation, improving both motor and non-motor symptoms as well as overall quality of life.

AIM: This study aimed to assess and compare the effects of continuous levodopa/carbidopa intestinal gel infusion and subcutaneous foslevodopa/foscarbidopa administration on quality of life and sleep in patients with Parkinson's disease (PD).

METHODS: A total of 28 adult PD patients treated at the Clinic for Neurology, Clinical Hospital Center Rijeka, were prospectively enrolled between January 2022 and November 2024. Participants were divided into two groups based on treatment modality. Quality of life was measured using the Parkinson's Disease Questionnaire-39 (PDQ-39), and sleep quality was evaluated with the Parkinson's Disease Sleep Scale-2 (PDSS-2), administered at baseline and after three months.

RESULTS: Both treatment groups demonstrated significant improvement in PDQ-39 and PDSS-2 scores from baseline to three months. However, no statistically significant differences were observed between the two groups at either time point.

DISCUSSIONS: Both LCIG and foscarbidopa/levodopa provide continuous dopaminergic stimulation and improve symptom fluctuations and quality of life when looked at individually. LCIG requires an intestinal procedure, whereas Produodopa offers a less invasive subcutaneous route, however, not without its own drawbacks. Their comparative efficacy and side-effect profiles are still under study, with growing attention on quality of life and non-motor symptoms.

CONCLUSIONS: Both infusion therapies yielded comparable short-term improvements in quality of life and sleep among PD patients. Continued follow-up is needed to determine whether these effects persist and to explore potential long-term differences between treatment modalities.

P33: The development of a new positive sign (Lovato's sign) for detecting lower limb functional weakness in patients with functional motor disorders.

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BACKGROUND: Functional weakness is a common clinical presentation in neurology setting, yet its diagnosis remains challenging due to the limited number of specific and validated clinical signs. Early and accurate identification of functional weakness is crucial to avoid unnecessary investigations and facilitate appropriate management.

AIM: To develop a new positive sign for detecting lower limb functional weakness and validate it through dynamometer measurements.

METHODS: We enrolled consecutive patients with a definite diagnosis of Functional Movement Disorder (FMD) attending the movement disorder clinic at University of Verona. Patients exhibited lower limb weakness due to FMD and were independently assessed by three neurologists using Lovato's sign. The test involved the evaluation of power of hip flexion with patient tested in two different body positions: supine and prone. The sign was considered positive when weakness was present only in the supine position, reflecting an incongruent patter of muscle activation and therefore suggesting a functional etiology. The same evaluations were repeated using dynamometer measurements to assess the validity of the sign, in terms of consistency between the clinicians' judgments and objective strength measurements. We also analyzed the interobserver reliability between three raters.

RESULTS: We enrolled 6 with lower limb functional weakness. Lovato's sign was positive—both clinically and confirmed by dynamometer—in 5 of 6 functional cases (sensitivity 83.3%). Measurements between three raters were consistent among all patients.

DISCUSSIONS: Preliminary findings suggest that Lovato's sign is a simple bedside test with a good sensitivity for detecting lower limb functional weakness. A large sample size along with the data from organic neurological diseases are needed to establish the test specificity.

CONCLUSIONS: Lovato's sign is a useful clinical tool for identifying lower limb functional weakness.

P34: The movement disorders game - A Gamified Card-Based Tool to Teach Diagnostic Reasoning in Movement Disorders

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BACKGROUND: Movement disorders encompass a broad spectrum, and a construction of a comprehensive differential diagnosis is crucial to obtain an accurate diagnosis. This process requires clinicians to integrate age of onset, phenotype, and “red flags” while weighing probability against rarity. This reasoning process is typically acquired gradually through clinical experience, yet it can also be trained using structured educational tools.

AIM: To design a gamified card-based learning tool, supported by a searchable database, that reinforces diagnostic reasoning in movement disorders.

METHODS: We created a deck of cards representing three diagnostic dimensions: age of onset, seven basic phenotypes, and eighteen red flag features. Learners select cards from each dimension to generate differential diagnoses, with bonus points for identifying reversible causes. To provide feedback, we are building a database of more than 600 movement disorder diagnoses. Each disorder is categorized using the card framework: basic phenotypes are coded 0-2 (0=absence, 1=presence, and 2 =typical presentation), red flags are coded 0 and 1, and age of onset is coded continuously. To reflect clinical likelihood, each diagnosis is also assigned an incidence weighting, allowing conditions to be ranked by relative rarity.

RESULTS: Pilot sessions with neurology trainees demonstrated strong engagement and improved confidence in structuring differential diagnoses. Learners reported that the tool helped them identify knowledge gaps and increased their motivation to explore specific disorders, in contrast to traditional disease-based learning.

DISCUSSIONS:
This approach provides a novel way to teach clinicians how to build comprehensive but prioritized differential diagnoses. By generating combinations of age of onset, phenotype, and diagnostic red flags, it allows learners to practice reasoning even in settings where complex movement disorders are rarely encountered. In this way, learners can practice a reasoning process traditionally gained mainly through long clinical experience, democratizing access to diagnostic reasoning skills for clinicians worldwide.

CONCLUSIONS:

P35: The role of image co-registration in deep brain stimulation (DBS) surgery of the subthalamic nucleus (STN) for Parkinson's disease (PD)

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BACKGROUND: In STN-DBS for the treatment of Parkinson's disease (PD), image co-registration is usually performed. While this has proven to be feasible in various clinical scenarios, the co-registration process leads to varying degrees of co-registration errors.

AIM: To quantify the co-registration error in two typical clinical scenarios in STN-DBS for PD.

METHODS: Brainlab Elements Stereotaxy was used to co-register postoperative CT images with preoperative MR images (CT-to-MR) and preoperative MR images with postoperative CT images (MR-to-CT). Euclidean distances (ED) and coordinate differences between the co-registered and non-registered images were calculated. In addition, CT-to-MR was evaluated with respect to the intended target by calculating the perpendicular errors and their spatial axis decomposed values.

RESULTS: Sixty-six PD STN-DBS patients were enrolled in the study. The median (IQR) ED was 0.50 (0.31) mm for CT-to-MR and 0.51 (0.24) mm for MR-to-CT. The vector coordinate differences showed similar values when comparing CT-to-MR and MR-to-CT, but in the opposite direction. In addition, co-registration error was predominant in the x-axis ($p < 0.001$). Finally, the median (IQR) differences in decomposed perpendicular errors for CT-to-MR were 0.31 (0.29), 0.14 (0.20), and 0.12 (0.15) mm for the x-, y-, and z-axis, respectively. No systematic skew was observed with respect to the intended target ($p = 0.223$, left hemisphere; $p = 0.908$, right hemisphere).

DISCUSSIONS: As far as we know, this is the largest study directly investigating co-registration error in STN-DBS PD patients. Because we excluded the manual steps in determining the error, our EDs are smaller than those reported in the literature. The largest error in the phase encoding X-axis could be attributed to MR distortion.

CONCLUSIONS: In STN-DBS for PD, image co-registration leads to an error of about 0.50 mm. Future studies should quantify the contribution of MR distortion and algorithm-specific features to the co-registration error.

P36: The role of medical device support programme in Parkinson's disease patients treated with continuous subcutaneous Foslevodopa/Foscarbidopa infusion

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BACKGROUND: Advanced Parkinson's disease (PD) often manifests with motor fluctuations and dyskinesia that are inadequately controlled with oral levodopa/carbidopa treatment. Continuous subcutaneous infusion of foslevodopa/foscarbidopa (SIFF) provides steadier dopaminergic delivery and improved symptom control. However, managing and handling the infusion system is challenging for PD patients and their caregivers.

AIM: To observe the role and patients' needs for the Medical Device Support Programme (MDSP) run by specialised PD nurses within the 1st year of SIFF treatment.

METHODS: Data were analysed from patients who initiated SIFF treatment since May 2024. The analysis included the number and frequency of nurse–patient contacts (calls or visits) per month during the first 12 months, as well as the most common patient- and caregiver-reported issues such as technical difficulties, dosing questions, and anxiety.

RESULTS: Of 78 patients, 67 (85.9%) continued treatment after initiation. The average number of nurse contacts per patient was 10 in the first month, decreasing to 5 in the second month, and stabilising at around 2 calls per month after the third month. During the first month, 62% of calls concerned pump handling or cannula changes, 28% anxiety or reassurance needs, and 10% dosing queries.

DISCUSSIONS: The decreasing number of nurse–patient contacts over time suggests increasing patient independence and adaptation to the SIFF system. The shift from technical to dosing-related questions reflects patients' growing familiarity and confidence in managing treatment, highlighting the importance of structured early-phase support.

CONCLUSIONS: Structured, ongoing nursing support through the MDSP is essential for safe initiation, continuity, and long-term success of SIFF therapy in real-world practice.

P37: Tremor in multiple system atrophy: a systematic literature review

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BACKGROUND: Tremor in multiple system atrophy (MSA) has growing diagnostic relevance, particularly for distinction from Parkinson's disease (PD). Since the last comprehensive reviews, updates on tremor classification guidelines and revised MSA diagnostic criteria emphasized its importance.

AIM: This systematic review aimed to assess prevalence, phenomenology, and treatment response of tremor in MSA.

METHODS: Following PRISMA guidelines, PubMed was searched for English-language studies (2013–2025) reporting tremor type, activation condition, frequency, or prevalence.

RESULTS: Of 136 records, 26 studies from 12 countries met inclusion criteria, encompassing 1020 patients (542 MSA-P, 453 MSA-C, 25 unspecified). Overall, tremor was reported in 56.5%. In MSA-P, rest tremor occurred in 26.8% and action tremor in 41.5%, in MSA-C, rest tremor in 19.8% and action tremor in 60.9%. Polymyoclonus was present in 16.5% of MSA-P and 10.5% of MSA-C. Three-hertz pseudoorthostatic tremor was more frequent in MSA-C (76.3%) versus MSA-P (38.3%). Vocal tremor was described in 36 patients.
Neurophysiologically, MSA-C exhibited low-frequency (~3 Hz) postural and orthostatic tremor, while MSA-P showed higher-frequency (7–8 Hz) postural tremor and less frequent rest tremor (~5–6 Hz). Levodopa improved tremor in 11.8–92% of cases, with sustained benefit in ~64%, more often in MSA-P. Improvement was greater for action (37%) than rest tremor (20%).

DISCUSSIONS: Compared with earlier reports, tremor prevalence shows greater variability, lower rates in MSA-P but higher tremor rates in MSA-C, especially action tremor. Furthermore, we identified orthostatic and vocal tremors as more common than previously recognized. Tremor in MSA occurs at higher frequencies than in PD. While Levodopa responsiveness is variable, only one third to one half sustain improvement. Limited, preliminary reports indicate benefit of clonazepam, botulinum toxin, and focused ultrasound.

CONCLUSIONS: Tremor in MSA is common, phenotypically diverse, and different from PD. However, recent studies show variable prevalence and treatment-responses, and documentation is often vague.

P38: Tremor progression of patients with Parkinson's disease over 4.22 years: clinical and fMRI neuroimaging correlates

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BACKGROUND: The longitudinal course of tremor in Parkinson's disease (PD) remains debated, with studies reporting stability, improvement, or progression. Clarifying tremor trajectories and their neural correlates may refine clinical management.

AIM: To characterize long-term clinical change in tremor and other motor features and to test whether resting-state fMRI activity/connectivity within the cerebello-thalamo-cortical (CTC) network relates to tremor severity over time.

METHODS: 113 PD patients from the PROMOVE registry (mean DD 3.64 y) with up to five visits over 4.22 y were analysed. Linear mixed-effects models (time, sex, baseline DD) tested clinical change; longitudinal modelling included only patients with tremor at baseline (n=96), while tremor-free patients (n=17) were analyzed descriptively. A fMRI subset (n=32 tremor-positive; mean interval 3.35 y) was analysed using a priori ROIs: cerebellar lobules V/VI, thalamic VLp, and M1 upper limb. ROI mean activity and pairwise connectivity were compared across time and correlated with clinical scores.

RESULTS: Bradykinesia and rigidity progressed with time, FTM scores decreased. Postural/action tremor declined while resting tremor remained stable. fMRI showed bilateral reductions of cerebellar activity over time. At baseline, tremor severity (overall/postural/kinetic) correlated negatively with activity across cerebellum, thalamus, and M1; at follow-up these associations disappeared. Connectivity changes were modest: right cerebellum–left thalamus coupling decreased over time, and at baseline stronger right cerebellum–left M1 connectivity related to lower rigidity/bradykinesia.

DISCUSSIONS: Our data suggest that PD tremor follows a nonlinear, subtype-dependent trajectory distinct from other motor symptoms; variability across studies likely reflects differences in inclusion criteria and baseline disease duration. We further speculate that declining cerebellar activity attenuated CTC-mediated tremor, improving action/postural tremor but not bradykinesia/rigidity or resting tremor and decoupled regional activity from tremor severity, conceptually echoing DBS mechanisms that inhibit thalamic relay and disrupt CTC oscillations.

CONCLUSIONS: Tremor progression in PD appears dissociable from other motor features and may involve dynamic changes within the CTC network.

P39: Why Patients Stop: Factors Behind Continous Subcutaneous Foslevodopa -Foscarbidopa Infusion Discontinuation

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BACKGROUND:Selecting the appropriate continuous therapy for advanced Parkinson's disease (PD) can be challenging. In the past year, continuous subcutaneous infusion of foslevodopa/foscarbidopa (FFCI) has been introduced in Europe and the United States. While levodopa is a well-established therapeutic agent, the novel prodrug formulation and subcutaneous route of administration introduce specific side effect profiles. The optimal patient for FFCI suitability remains unclear. This study aimed to identify characteristics of patients who discontinue FFCI treatment and evaluate the contributing factors.

METHODS: We retrospectively analyzed 74 patients with advanced PD who received subcutaneous FFCI between May 2024 and October 2025 at the UMC Ljubljana (32 females; mean age: 71.0±9.4 years; disease duration: 12.7±5.8 years; MMSE: 26.0±4.3; 27 with cognitive impairment). Patients were followed monthly. We recorded adverse effects and assessed treatment discontinuation rates using Kaplan–Meier analysis. Cox regression was employed to examine potential predictors of discontinuation, including cognitive impairment, hallucinations, gender, age, and disease duration.

RESULTS: A total of 179 adverse effects were recorded in 63 of 74 patients (85%). Excluding those who discontinued treatment during the initial 7-day testing phase, the overall discontinuation rate was 34%. Kaplan–Meier analysis of all patients who initiated FFCI, including those in the 7-day testing phase, revealed a 48% treatment discontinuation rate within the first 12 months. Older age and cognitive impairment were significantly associated with treatment discontinuation, whereas disease duration, sex, and a history of hallucinations were not significant predictors.

CONCLUSION: Subcutaneous FFCI is an effective treatment for advanced PD, but a substantial proportion of patients experience side effects, and discontinuation rates are considerable. Careful patient selection is essential to ensure treatment continuation.

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