# Book of Abstracts

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WORLD CONGRESS ON PARKINSON'S DISEASE AND RELATED DISORDERS

CHICAGO, USA

2023

13 – 16 May

INTERNATIONAL ASSOCIATION PARKINSONISM AND RELATED DISORDERS

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## Video Abstracts

# Grand Parade of Movement Disorders

### GP_1

### Propriospinal myoclonus and anti-IgLON5 disease: a case report

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**Background:** Anti-IgLON5 disease is a recently recognized neurodegenerative autoimmune disorder with heterogenous neurological manifestations including sleep disorders, bulbar syndrome, gait instability, cognitive impairment, dysautonomia, oculomotor abnormalities, neuropsychiatric symptoms, and movement disorders. Here we present the first case of anti-IgLON5 disease with propriospinal myoclonus.
**Methods:** Case report with video.
**Results:** A 68-year-old man with history of obstructive sleep apnea developed shoulder and axial jerks after an EMG test while being seen in the neurology clinic for two years of slowly progressive various neurological symptoms including insomnia, occipital headaches, intermittent diplopia, voice change, dysarthria, dysphagia, gait instability, urinary urgency, constipation, and short-term memory loss. Physical exam demonstrated upward vertical gaze impairment, left eye abduction impairment, bilateral fine postural tremor, and arrhythmic, distractable, position dependent propriospinal myoclonus [see video] that is present only during wakefulness and sleep transition, and more prominent with inactivity. Workup included routine laboratory testing, CSF analysis, brain and C-spine MRIs, CT of the chest, abdomen and pelvis, routine EEG, repetitive nerve stimulation, and neuropsychology evaluation that were all unremarkable. Polysomnography showed obstructive and central respiratory events, confusional arousals, and sleep-specific spontaneous tachypnea. IgLON5 antibodies were detected in the CSF with a titer of 1:128 (normal range <1:2). Immunotherapy with IV methylprednisolone pulse (1g/day for 5 days), five therapeutic plasma exchange sessions, and rituximab resulted only in mild transient improvement in speech, balance, and vision. Symptomatic treatment of the myoclonus with levetiracetam, clonazepam, zonisamide, and baclofen was ineffective.
**Conclusions:** This case highlights the variable clinical manifestations of anti-IgLON5 disease and adds a unique and rare disease to the list of propriospinal myoclonus etiologies.

### GP_2

### Hemi-myoclonus hemi-ballism in a young man

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**Background:** 23 year old male patient presented with a 3 month history of right sided violent flinging movement of the right side of the body and right half of face.
**Methods:** He was having slow myoclonus of the right side of the body with proximal flinging movement resembling a ballistic movement. There was subtle weakness of the right half of the body. His cognition was intact and so was his sensory and cerebellar functions. His MRI showed a white matter hyperintensity in the left parietal lobe.
**Results:** CSF measles antibody Index was positive and suggested intrathecal antibody response to (mutated) measles virus. EEG showed long interval periodic discharges. The patient was diagnosed to have SSPE and was started on intrathecal interferons and isoprinosine.
**Conclusions:** SSPE can have a focal demyelination on imaging. Proximal ballistic myoclonus with a slow myoclonic component with bradykinesia and weakness causing a Pallido-pyramidal syndrome is a rare presentation of the disease.

### GP_3

### Unwinding the puzzle of a banker with sleep-related movement disorder

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**Background:** This case with persistent limb movements in sleep progressing to agrypnia excitata highlights the importance of sleep-related movement disorders which are seldom discussed.
**Methods:** A 57-year-old man presented with persistent limb movements and stereotypic gestures (cycling, leg crossing, scratching and bedsheet/shirt pulling) during sleep. He had no significant medical and family history, fever or constitutional symptoms. He developed progressively worsening excessive daytime sleepiness/drowsiness, memory decline, and visual hallucinations, and became dependent to caregivers. Examination showed dysarthria, impaired vertical gaze, myoclonus, postural instability and autonomic dysfunction. He alternated between wakefulness and dream-like state, representing episodes of "*oneiric stupor*", characterized by the recurrence of stereotyped gestures mimicking daily-life activities.
**Results:** The main diagnostic considerations were autoimmune encephalitis including antibodies to IgLON-5, LGI-1, CASPR-2, NMDAR, DPPX, AMPAR or anti-Ma1/Ma2, infectious diseases and prionopathies. Electroencephalogram revealed diffuse slowing without periodic sharp wave complexes. MRI brain and CSF examination including viral PCR panel were normal. Autoimmune and paraneoplastic encephalitis antibody panel for serum and CSF were negative, as were tests for thyroid, celiac autoantibodies and tumour markers. Oesophagoduodenoscopy, colonoscopy, and full-body CT scan did not uncover any malignancies. CSF 14-3-3 protein and RT-QuIC were negative. The patient evolved into a state of "*agrypnia excitata*", characterized by severe loss of sleep and prominent motor and autonomic hyperactivation, caused by thalamo-limbic dysfunction. We proceeded with targeted gene panel testing which revealed a pathogenic p.D178N point mutation (c.532G>A) in the prion protein gene (*PRNP*) and methionine homozygosity at codon 129, confirming the diagnosis of fatal familial insomnia.
**Conclusions:** FFI is an autosomal dominant prion disease with prominent sleep disturbances, neuropsychiatric features and sympathetic hyperactivation. Ataxia, parkinsonism, and myoclonus may be present but more common in other prion diseases. Neuroimaging and electroencephalogram changes characteristic of prion disease are often absent, while CSF 14-3-3 protein and RT-QuIC have poor sensitivity in diagnosing FFI.

## GP_4

## Feasibility of the use of therapy dog with American Kennel Club Canine Good Citizen certificate to facilitate the evaluation and treatment of patients with Parkinson's disease in a rehabilitation hospital

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**Background:** Although the utilization of animal-assisted therapy generates physical, psychological, and social benefits for individuals with neurological disorders (Rodríguez-Martínez, *et al.,* 2021), there is a dearth of investigations of the use of animals to benefit people with Parkinson's Disease (PD). The utilization of an American Kennel Club Certified Therapy Dog has greatly enhanced the good will and effectiveness of a spectrum of interventions (American Kennel Club, 2022). We seek to determine if a therapy dog can be incorporated in the evaluation and treatment of PD in a rehabilitation hospital.
**Methods:** Participants will be patients with PD who require medical management with 24-hour in-patient nursing care and a spectrum of rehabilitation services. For two weeks participants will undergo routine evaluation and treatment with physical therapy (PT), occupational therapy (OT), speech and language pathology (SLP), psychology, and physiatry. Mini-Mental State Examination (Folstein, *et al*., 1975) is administered on admission. Section GG Inpatient Rehabilitation Facility Resident Assessment Instrument (IRF–PAI), Self-Care (Activities of Daily Living) and Mobility Items (American Occupational Therapy Association, 2022) and Patient Health Questionnaire-9 (PHQ-9), (Kroenke and Spitzer, 2002) will be administered on admission and weekly to identify the progress of the patient. Treatment sessions and evaluations will be enhanced by the utilization of an American Kennel Club Certified Therapy Dog to provide comfort and encouragement.
**Results:** Participants will be volunteers recruited from a rehabilitation hospital with patients with PD who meet the characteristics in Table 1. Treatment and evaluation will be accomplished by a therapy dog and their owner in Figures 1 to 3. The video illustrates the use a therapy dog along with gait training in a rehabilitation hospital.

**Conclusions:** Treatment of patients with PD utilizing therapy dog with American Kennel Club Canine Good Citizen certificate in a rehabilitation hospital is feasible.

**GP_5**

**Spasm, blink, doop or wink: a puzzle to solve!**

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**Background:** It is not uncommon to find patients coming with frequent closing of eyes for long time. There are multiple differentials of such a presentation. Blepharospasm and its mimics and chameleons need to be considered, phenomenology need to be carefully observed, before deciding treatment. We present a video case of such a patient who had diagnostic dilemma for more than 5 years before reaching a correct diagnosis and treatment.
**Methods:** A 57-year old male presented with a history of frequent closure of both the eyes, throughout the day, affecting all daily activities for 5 years. He had frequent blinking and closure of eyes. He had multiple consultations and received different diagnoses ranging from blepharospasm/ tics/ myasthenia/dry eyes/functional movement disorders. Varied treatments ranging from Pyridostigmine, prednisolone, benzodiazepam to botulinum toxin injections did not help ever. He underwent treatment as Myasthenia gravis based on false borderline positive AchRAb [ limited specificity].
**Results:** An examination video attached shows frequent eye blinking which needs careful observation. This video helps in teaching about observing phenomenology carefully and helps to understand on differentiating between blepharospasm, myasthenia, functional movement disorders by video. The phenomenology on video helps to consider Congenital myasthenia as the diagnosis. A trial of fluoxetine lead to significant improvement in symptoms. [a separate followup video demonstrating improvement is available.] His genetic testing for NGS panel for congenital myasthenic syndromes suggested homozygous mutation in DOK7 gene confirming the diagnosis of Congenital myasthenic syndrome. Sometimes, patients with congenital ocular myasthenia have frequent blinking as a compensatory mechanism to avoid eyelid drooping, which may be misinterpreted as blepharospasm.
**Conclusions:** There can be chameleons mimicking blepharospasm. Proper observation of phenomenology is important for optimal diagnosis and management and this case demonstrate this important teaching clinical pearl.

## GP_6

## Complex hyperkinetic movement disorder in neuromyelitis optica spectrum disorder exacerbation: a case report

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**Background:** Neuromyelitis Optica Spectrum Disorder (NMOSD) can present with hyperkinetic movement disorders. Occasionally, the movements are complex, posing a diagnostic and therapeutic challenge.
**Methods:** A 57-year-old woman with seronegative NMOSD of three years duration presented with involuntary, non-rhythmic, non-suppressible, purposeless movements affecting the right upper extremities.
The movements were accompanied by weakness, numbness, and impaired proprioception. The hyperkinetic movements were noted more with postural maintenance varying in speed and amplitude. The movements were complex and did not solely meet the classic definition of tremor, myoclonus, chorea, or dystonia.
**Results:** Cervical MRI showed an ill-defined hyperintense intramedullary lesion at C1-C6 compared to the previously affected at C1-C2 levels hence, relapse of her NMOSD was considered. Initial treatment with anti-epileptic medications, haloperidol, and muscle relaxants did not control symptoms. High-dose intravenous methylprednisolone was given for five days but offered partial improvement. The treatment was followed by 30-day oral fingolimod immunotherapy as the unconventional treatment for the refractory disease. After treatment, complete remission of the hyperkinetic movement disorders and the moto-sensory deficit was observed. The temporal association of the therapy and resolution of symptoms is speculative as it may have resolved over a month, as expected in an acute spinal movement disorder.
**Conclusions:** This report highlights the importance of recognizing “spinal movement disorders” associated with NMOSD that can be complex and diagnostically challenging in a setting of exacerbation. The purported mechanism includes voluntary compensation for weakness and a consequence of sensory deafferentation of the proprioceptive feedback mechanism. Limited therapeutic options lie in the underlying etiology; hence early identification leads to appropriate therapy and a better outcome.

## GP_7

## Myoclonic epilepsy of Unverricht and Lundborg in a 40-year old Filipino woman

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**Background:** Myoclonic epilepsy of Unverricht and Lundborg is a rare autosomal recessive disorder commonly caused by a mutation in CSTB gene in chromosome 21q22.3[1]. It is characterized by stimulus-sensitive myoclonus and tonic-clonic seizures (GTCS) occurring between 6-15 years old and has the potential to cause lifelong

disability. Worldwide prevalence is undocumented[1,2,3]. Currently, this is the only known genetically confirmed case in the Philippines.
**Methods:** Case study.
**Results:** A 40-year-old Filipino woman presented with a history of onset of myoclonic jerks at the age of 8, later associated with GTCS, dysarthria, intention tremors, gait disturbance, with inability to coordinate movements, often aggravated by stress, initiation of movements, and exertion. Symptoms gradually progressed and worsened, until she became fully dependent, and wheelchair bound at the age of 12. Consult was not done due to limited resources, and over the years symptoms were tolerated despite the ensuing disability. Recent financial support eventually prompted consult with a neurologist. With a consideration of progressive myoclonus epilepsy, she was started on clonazepam and levetiracetam, and genetic testing was done, confirming the diagnosis.
**Conclusions:** While low prevalence and variable accessibility to diagnostic modality contribute to diagnostic challenge, prompt and accurate recognition will allow for adequate intervention and support.

### GP_8

### Delayed-onset hemichorea post-successful reperfusion in an acute ischemic stroke and its treatment with Deutetrabenazine: a case report

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**Background:** Movement disorders are known to occur as an acute or delayed presentation of stroke. Recently, new-onset cases of hemichorea post-successful reperfusion in stroke have been noted.
**Methods:** A 68-year-old man with hypertension, diabetes mellitus, and a remote stroke with no residual deficits, presented with Broca's aphasia and right hemiparesis. The patient was diagnosed with critical stenosis of the extracranial left carotid artery and left middle cerebral artery (MCA) occlusion, and underwent left carotid angioplasty with stent placement and mechanical thrombectomy. Post-procedure, the patient experienced complete resolution of his neurologic deficits. A brain MRI 13 hours after the procedure demonstrated acute ischemia in the left prefrontal area and a punctate infarct in the left striatum. Three days after the procedure, the patient developed progressive dance-like involuntary movements of the right upper and lower extremities and was diagnosed with hemichorea. The patient was started on Haloperidol for symptomatic treatment of the chorea but due to a lack of improvement, was transitioned to Deutetrabenazine. On follow-up around 50 days after discharge, his chorea was well-controlled on a 9 mg twice daily dose of Deutetrabenazine.
**Results:** In comparison to hemichorea occurring at the time of the stroke which improves after reperfusion, hemichorea in our case developed several days after successful reperfusion despite the resolution of the initial deficits. It could thus, be argued to be a sequel of reperfusion injury. Four similar cases of post-reperfusion hemichorea in the literature resolved within 30 days after onset. Our patient had symptoms that did not self-resolve, and were not controlled with haloperidol but improved with Deutetrabenazine, a relatively new drug mainly used for the treatment of Huntigton's chorea and tardive dyskinesia.
**Conclusions:** Our case adds evidence to the theory of hemichorea developing as a sequel of reperfusion injury and illustrates the effectiveness of Deutetrabenazine for its management.

## Oral Abstracts

## Other Movement Disorders

### O_1

### Alterations of brain neurotransmitters and metabolites in a rat model of Huntington's disease

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**Background:** Huntington's disease (HD) is a neurodegenerative disorder that results from the destruction of neurons in the basal ganglia, and oxidative stress has been implicated in its pathogenesis. Neurotransmitters play a vital role in the functioning of brain. Present study aimed to investigate the changes in various neurotransmitters and their metabolites in 3-nitropropionic acid (3-NP)-induced oxidative stress in a rat model of HD and explored the mechanisms of action.
**Methods:** 48 animals of 3-NP induced HD rat model were studied. Determination of various classical neurotransmitters (dopamine, norepinephrine, acetylcholine, glutamate, serotonin, gamma-aminobutyric acid (GABA), and adenosine and neuropeptides (cholecystokinin, dynorphin, neurotensin, substance P) in was carried out using high performance liquid chromatography HPLC) (1100 series, Agilent Technologies Inc., Santa Clara,

CA, USA) with green fluorescence detection was utilized to quantify metabolite concentrations. Standards were also run after every fourth sample as controls. Concentrations were corrected for potential metabolite loss during extraction using α-ABA as an internal standard.
**Results:** The mean values of various neurotranmitter, norepinephrine, dopamine, GABA and serotonin levels in striatum and cerebral cortex of 3-NP rat HD models were significantly decreased compared to control group, which consequently, may changes motor and non-motor symptoms in HD rat models. There was a significant increased in levels of glutamate and acetylcholine in striatum and cerebral cortex of treatment group. There was a significant alternations in adenosine, cannabinoids and neuropeptides, metabolites values in treatment group compared to control.
**Conclusions:** Brain neurotransmitters play a vital role in brain functioning and also have important function in HD status. It remains to be examined the clinical efficacy of such neurotransmitters and to investigate in-depth the neural networks suggested in the extrapyramidal system. Thus, it can be concluded that restoring the neurotransmitters balance in the brain may prevent or delay the symptoms of movement disorders.

## O_2

### Perry syndrome (parkinsonism, neuropsychiatric symptoms, weight loss, hypoventilation): large new pedigree and first study on prodromal stage of the disease

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**Background:** Perry syndrome (PS) is an autosomal-dominant neurodegenerative disorder characterized by parkinsonism, neuropsychiatric symptoms, weight loss, and hypoventilation. It is caused by *DCTN1* mutations and belongs to the spectrum of TDP-43 proteinopathies. To date, little is known about the asymptomatic and prodromal stages of the disease.
**Methods:** We investigated 27 individuals from a large pedigree (n=104) from Louisiana with hereditary atypical parkinsonism. We studied clinical (neurological status, motor, and non-motor measures), genetic (next-generation and Sanger sequencing), and laboratory (plasma glial fibrillary acidic protein, pGFAP; neurofilament light, pNFL) aspects. Neuropathological examinations were performed on two patients.
**Results:** The median age at evaluation was 45 years. Health complaints were reported by 20 individuals, including sleep disorders (n=15), autonomic disturbances (n=10), loss of weight (n=8), and neuropsychiatric symptoms (n=8). Neurological evaluation revealed abnormal findings in 18, including parkinsonism in 7, tremor in 2, and isolated findings in individual cases. Cognitive and smell functions were good. Genetic workup found a novel *DCTN1* Gly67Val variant in 10 cases. The variant was in the genetic “hotspot” for PS mutations, was present in 4/4 individuals with PS phenotype, and was pathogenic according to *the in silico* computational models. Three mutation carriers were asymptomatic, and 3 showed isolated findings on neurological examination. We did not find differences in pGFAP and pNFL levels in the whole group. Neuropathological examination showed classical features of PS.
**Conclusions:** We report a new large pedigree with PS and a novel *DCTN1* mutation, which, based on history, clinical, genetic, and neuropathological findings, was proven to be pathogenic. We also draw attention to the prospect of the prodromal stage of PS in some *DCTN1* mutation carriers, which we plan to evaluate further in more detail.

## O_3

### Mutation screening of *AOPEP* variants in a large dystonia cohort

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**Background:** Recently, *AOPEP* has been identified to be a novel causative gene of autosomal recessive dystonia. However, no large cohort study has been conducted to confirm the association. We aimed to systematically evaluate the genetic associations of *AOPEP* with dystonia in a large Chinese dystonia cohort.
**Methods:** Weanalyzed rare variants of *AOPEP* in 878 dystonia patients with whole exome sequencing. The over-representation of rare variants in patients was examined with Fisher’s exact test at allele and gene levels.
**Results:** Among the 878 patients with dystonia, ten rare variantswere identified in 17 individuals, including 2 loss-of-function variants (p.M291Nfs*68 and p.R493X) and 8 missense variants.One loss-of-function variant (p.R493X)

was the same as previously reported. One patient carriedputative compound heterozygous variants (p.A212D and p.G216R) and presented withchildhood-onset segmental dystonia involving the upper limbs and craniocervical muscles accompanied by myoclonus of the dystonia affected areas. One patient carried homozygote of p.M291Nfs*68 and presented with adult-onset isolated cervical dystonia. The other 15 patients carriedheterozygous variant in *AOPEP* and nearly all of them presented with isolated dystonia with only craniocervical muscles affected, except for one patient who carried the p.R493X variant presented with segmental dystonia affecting the neck and right upper limb combined with parkinsonism. Gene-based burden analysis detected enrichment of rare variants andraredamagingvariantsof *AOPEP* in dystonia.
**Conclusions:** Our study supplemented the evidence on the role of *AOPEP* in autosomal recessive dystonia in Chinese population, andexpanded the genotypic and phenotypic spectrum of *AOPEP.*

## O_4

### Mitochondrial ATP synthase variants in dystonia, spastic paraplegia and ataxia

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**Background:** Recently, rare variants in four mitochondrial ATP synthase genes (*ATP5F1E*, *ATP5PO*, *ATP5F1A*, *ATP5MC3*) have been linked to variable neurological disorders manifesting with predominant dystonia, spastic paraplegia, or ataxia in several families. However, no replicative study has been conducted yet to confirm the role of mitochondrial ATP synthase variants in these disorders. We aimed to systematically evaluate the genetic associations of mitochondrial ATP synthase genes with dystonia, spastic paraplegia, and ataxia in a large Chinese cohort.
**Methods:** We analyzed rare variants of 17 mitochondrial ATP synthase genes in a cohort with dystonia, spastic paraplegia, or ataxia with whole exome sequencing. The over-representation of rare variants in patients was examined with Fisher's exact test at allele and gene levels.
**Results:** A total of 1262 patients (1124 with dystonia, 73 with spastic paraplegia, and 65 with ataxia) were included. Three rare variants in *ATP5MC3*, one rare variant in *ATP5MC1*, six rare variants in *ATP5F1A*, and five rare variants in *ATP5PO* were identified in 16 individuals with dystonia. One rare variant in *ATP5MC1* and one rare variant in *ATP5F1A* were identified in 2 individuals with spastic paraplegia. One rare variant in *ATP5MC3*, one rare variant in *ATP5MC1*, and one rare variant in *ATP5F1E* were identified in 3 individuals with ataxia. At allele level, c.A40G in *ATP5MC1* and c.G356A in *ATP5F1A* were associated with higher risk of spastic paraplegia; c.C323T in *ATP5MC3*, c.297-2A>C in *ATP5MC1*, and c.C19T in *ATP5F1E* were associated with higher risk of ataxia. No significant association was detected between mitochondrial ATP synthase genes and dystonia in allele or gene levels.
**Conclusions:** Our study supplemented the evidence on the role of mitochondrial ATP synthase genes in neurological disorders including spastic paraplegia and ataxia.

## O_5

### The Huntington Disease Health Index (HD-HI): measuring changes in disease burden in response to valbenazine during the KINECT-HD trial

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**Background:** The Huntington Disease Health Index (HD-HI) is a validated, disease-specific measure that was designed to evaluate patient-reported symptoms in Huntington disease (HD), but had not yet been used to assess the impact of therapeutic interventions. The HD-HI consists of 13 subscales, each measuring a distinct area of HD symptomatic burden, and a total score (score range: 0=no disease burden to 100=highest disease burden). Here we describe results of the HD-HI in KINECT-HD (NCT04102579), a Phase 3 trial evaluating 12 weeks of valbenazine versus placebo in HD.
**Methods:** The HD-HI was administered to participants throughout KINECT-HD. Mean HD-HI scores at baseline, 10 weeks, and 12 weeks were analyzed descriptively. Post hoc exploratory ANCOVA analyses evaluated changes from baseline in the HD-HI and its subscales.
**Results:** The HD-HI detected improvements in disease burden in response to valbenazine. Compared to placebo, participants receiving valbenazine had numerical improvements in mobility (Wk10: -6.3 vs -4.1; Wk12: -

4.2 vs -2.7), abnormal movements (Wk10: -12.2 vs -9.6; Wk12: -11.2 vs -4.3), and upper extremity function (Wk10: -7.2 vs -1.6; Wk12: -7.2 vs -1.4). Changes from baseline to Wk10 and Wk12 for fatigue and gastrointestinal health did not indicate any worsening in response to treatment. No changes in HD-HI total score were noted at Wk10 and Wk12. Least squares (LS) mean changes from baseline to Wk12 in the HD-HI abnormal movements subscale were -11.1 for valbenazine and -4.4 for placebo, with an LS mean difference between treatment groups of -6.7 (nominal *P*=0.0379).
**Conclusions:** KINECT-HD participants were able to utilize the HD-HI to report longitudinal changes in their symptomatic disease burden in response to valbenazine. The HD-HI provides a mechanism for individuals with HD to report clinically meaningful changes in their health in response to a therapeutic intervention, and for these changes to be quantified in the context of a clinical trial.

### O_6

### Fixing a shaky video to remotely program deep brain stimulation

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**Background:** Deep Brain Stimulation (DBS) is an increasingly used therapy to treat refractory tremor in Parkinson's Disease (PD) patients. Recurrent postoperative appointments for programming tuning are fundamental for successful outcomes. In Canada, long distances and difficult weather conditions may restrict the access to DBS-specialized clinics. Novel technologies, particularly remote programming, may overcome these issues. We aimed to describe a new strategy to assess tremor remotely during DBS programming.
**Methods:** We present the case of a 65-year-old female patient with tremor-predominant PD, only partially responsive to L-dopa. She successfully underwent bilateral subthalamic nucleus (STN) DBS surgery. As her hometown was 1500 km away from our center, the programming was carried out remotely using Neurosphere™ technology (Abbott).
**Results:** During the evaluation, the patient was asked to hold her controller in a fixed position until the rest tremor re-emerged. Once it reached the maximum amplitude and was clearly noticeable by a shaking video frame, we started optimizing the stimulation parameters until the frame was still (video). She reported a sustained benefit at follow-up.
**Conclusions:** We described an alternative way to remotely assess upper limb tremor in PD patients during remote DBS programming. A prospective cohort comparing different strategies will be needed to validate our findings.

## PD: Clinical and Neuroscience

### O_10

### Representation of Parkinson's disease in the cinema

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**Background:** The topic of Parkinson's Disease (PD) has been depicted in variety of works of art, the most prolific being the cinema. With this submission we would like to present an overview of the cinematographic work dedicated to PD.
**Methods:** We have searched the most detailed and critically acclaimed film databases such as internet movie data base(IMDb) and Rotten Tomatoes using the terms "Parkinson's disease" and posteriorly conducted detailed analysis of the selected movies.
**Results:** Altogether we identified ten films which allude to the topic of PD, four of them being fiction and another six documentaries. The most well-known example is *Awakenings* (1990) by Penny Marshall. Based on the acclaimed semi-autobiographic novel by American neurologist Olivier Sacks which presents how a life of several patients with encephalitis lethargica have been changed through an accidental discovery of efficacy of L-dopa administration. Another example constitutes a romantic comedy *Love and other drugs* (2010), in which the main female protagonist must struggle with a burden of young onset PD. *Quartet* (2012) by Dustin Hoffman is a story of

elderly musicians one of whom is suffering from the PD. Based in Alberta Canadian fiction feature *Never steady, never still* (2017) by Kathleen Hepburn is a story of a mother who must struggle with advanced PD and also support her son. *Kinetics* (2017) is a film of unusual friendship between Rose, a woman with PD and a teenager Lukas. Finally, several documentaries have shown a life of patients with PD, such as BAFTA-awarded short film *Isabella* (2015) about the interplay between dementia and PD or Emmy-nominated *Present moment* (2015) in which director Aimie Vallat tells a story of her own father who suffers from PD.
**Conclusions:** PD is displayed in variety of movies which concentrate mainly around of the topic of dealing with the disease burden.

## O_13

### The Parkinson's Disease-Health Index (PD-HI): development and validation of a novel, disease-specific, patient-reported outcome measure

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**Background:** Disease-specific patient-reported outcome (PRO) measures are an optimal way to bring the patient voice to the forefront of clinical trials and track small, clinically meaningful changes in health in response to therapeutic intervention. As clinical trials are planned and implemented for patients with Parkinson's disease (PD), there is a clear need for the research community to have access to a comprehensive, valid, and sensitive PRO. This research utilized large scale patient-reported data and published FDA guidelines to develop and validate the Parkinson's Disease-Health Index (PD-HI), a PRO designed for use in PD clinical trials.
**Methods:** We used qualitative interviews and a national cross-sectional study of individuals with PD to identify the symptoms of greatest importance to this population. Symptoms with the highest frequency and relative impact to the cross-sectional sample cohort were selected as questions in the PD-HI. Using factor analysis, we grouped symptom questions into symptomatic themes of PD health. We conducted beta interviews to assess the relevance and usability of the PD-HI. We evaluated the test-retest reliability of the PD-HI over a two-week period. We used known groups and area-under-the-curve (AUC) analyses to assess the ability of PD-HI scores to distinguish between subgroups of participants with differing disease severity.
**Results:** Twenty individuals with PD participated in qualitative interviews. Four-hundred and four individuals with PD participated in the cross-sectional study, providing over 120,000 symptom rating responses**.** Beta testing with 15 individuals with PD revealed that the PD-HI was comprehensive, relevant, and easy to use. The PD-HI demonstrated high internal consistency, test-retest reliability, and an ability to differentiate between individuals with varying disease severity. The final PD-HI consists of 13 symptomatic themes which comprehensively measure patient-reported disease burden.
**Conclusions:** The PD-HI provides researchers with a valid mechanism to quantify disease burden using the direct perspective of the patient.

## O_14

### Neurophysiological markers of motor reserve in Parkinson's disease

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**Background:** Motor reserve (MR) is defined as the resilience mechanisms of the brain coping with neurodegeneration in idiopathic Parkinson's Disease (PD). No investigation of MR focused on lateralized PD with bilateral binding reduction at dopamine transporter (DAT) imaging.
**Methods:** In this cross-sectional case-control study, we included 16 PD patients and 28 healthy control. Patients were included if their motor signs were unilateral (Hoehn and Yahr stage =1/5, two independent raters) but DAT density ([123I]-Ioflupane-SPECT, DATQUANT$^{TM}$) was significantly reduced in bilateral putamina (Putamen z-score>0.5). Subjects were extensively investigated using the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS; part-III was videorecorded), Hoehn & Yahr (H&Y)

stage.Transcranial magnetic stimulation (TMS) was performed on primary motor cortices (M1) in presymptomatic (PH) and symptomatic hemispheres (SH) for patients and on dominant hemisphere for HC. TMS measured cortical excitability, plasticity and interhemispheric-inhibition (IHI).
**Results:** TMS testing revealed asymmetries in corticospinal excitability with higher values in the PH. SH demonstrated lower M1-plasticity (compared to the asymptomatic hemisphere). Finally, we found reduced IHI from PH to SH. Interestingly, reduced putamen binding was predicted by reduced ICF in SH and by higher plasticity and reduced IHI in PH. Reduced putamen binding was predicted by enhanced plasticity and reduced IHI in PH, and by reduced ICF in SH. Putamen/caudate ratio was directly associated with corticospinal excitability in PH and inversely associated with cortical plasticity in symptomatic hemisphere. MRC distinguished PH from SH (AUC 0.9844). It was associated in SH with PAS increment, IHI and corticospinal excitability reduction.
**Conclusions:** Response to PD neurodegeneration involves a M1-putamen network, and cortico-M1 connections, responsible for excitability and plasticity changes, depending on caudate activity and becoming more effective with binding reduction in putamen. Further insight on PD MR networks is relevant for novel neuromodulation approaches, aimed at reducing motor burden in daily life.

### O_15

### Expanding the genetic basis of PD heterogeneity: genome-wide association study on PD subtypes

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**Background:** Parkinson's disease (PD) is characterized by motor and non-motor symptoms; however, there is substantial variability in the presentation between the patients. The pathophysiological basis of PD heterogeneity is not understood. Therefore present study aimed to investigate the genetic differences among the PD subtypes.
**Methods:** We included 830 patients diagnosed with PD from our clinic, who had complete clinical and genetic data, were not carriers of known pathogenic PD mutations, and were of Caucasian ethnicity. Patients were classified into tremor-dominant (TD), akinetic-rigid (AR), gait-difficulty (GD), and mixed (MX) subtypes. Genome-wide association study was performed, and after excluding patients with low call rates, significant relatedness, and non-Caucasian ancestry, a total of 799 patients were included in the further analysis.
**Results:** Most common PD subtype was TD (n=345), followed by AR (n=227), mixed (n=145), and GD (n=82). We found one genome-wide significant ($p<5x10^{-8}$) association between the *MIR3976HG* rs7504760 variant and AR subtype (OR=6.12, $p=2.57x10^{-8}$). Suggestive associations ($p<1x10^{-6}$) were observed regarding TD subtype for *RP11-497G19.3/RP11-497G19.1* rs7304254 (OR=3.33, $p=3.89x10^{-7}$), GD subtype for *HES2* rs111473931 ($p=6.85x10^{-7}$), *RP11-400D2.3/CTD-2012I17.1* rs149082205 ($p=9.08x10^{-7}$), and *RN7SL408P/SGK1* rs56161738 (OR=2.97, $p=6.19x10^{-7}$), and MX for *MMRN2* rs112991171 (OR=4.98, $p=1.02 x10^{-7}$). None of the 103 variants previously associated with PD or essential tremor (ET) were of genome-wide significance; however, 17 were nominally significant, including *CHD9* rs10221156 with MX, *RNF141* rs7938782 with AR, and *KRTCAP2* rs35749011 with TD PD subtype. Additionally, we observed divergent effects in GD vs. AR/MX/TD subtypes in 5, AR vs. GD/MX/TD in 4, TD vs. AR/GD/MX in 2, and MX vs. AR/GD/TD in 1 variant.
**Conclusions:** Sporadic PD is a clinically and genetically heterogeneous disorder with discernible differences among the AR, GD, MX, and TD subtypes. More studies on larger groups of patients are needed to better define PD subtypes' genetic architecture and pave the way toward precision medicine in PD.

## PD: Therapy

### O_20

### Connectivity profile for deep brain stimulation in early-stage Parkinson's disease

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**Background:** Subthalamic nucleus (STN) deep brain stimulation (DBS) is an effective adjunctive therapy for mid-/advanced-stage Parkinson's disease (PD); however, individual motor improvement is variable, with electrode localization being a key determinant of efficacy. While DBS symptomatic effects are well-established, it is currently unclear how DBS influences motor progression. This study's objective was to describe the relationship between stimulation location and motor progression for the DBS in early-stage PD pilot trial cohort [1].
**Methods:** To determine anatomical and network correlates associated with motor progression in the early DBS cohort (n=14), voxel-wise sweet spot mapping and normative structural connectivity analysis were carried out using the outcome of two-year motor progression [Unified Parkinson Disease Rating Scale Part-III 7-day OFF therapy (MedOFF/StimOFF); change from baseline to 24 months].
**Results:** Sweet spot mapping revealed an early-stage PD optimal location associated with slower motor progression in the dorsolateral STN (AC/PC coordinates: 11.07±0.82 mm lateral, 1.83±0.61 mm posterior, 3.53±0.38 mm inferior to the midcommissural point; MNI coordinates: +11.25, -13.56, -7.44 mm). Modulating fiber tracts originating from supplementary motor area (SMA) and primary motor cortex (M1) to the STN correlated positively with slower motor progression, whereas fiber tracts originating from pre-SMA and cerebellum were negatively associated with motor progression. Robustness of the motor progression fiber tract model was demonstrated in leave-one-patient-out (R=0.56, P=0.02), 5-fold (R=0.50, P=0.03), and 10-fold (R=0.53, P=0.03) cross-validation paradigms.
**Conclusions:** This study suggests that stimulating the dorsolateral region of the STN in early-stage PD, specifically areas receiving input from SMA and M1 while avoiding input from pre-SMA, is associated with slower motor progression. This result is hypothesis-generating and must be prospectively tested in larger prospective study.
**Reference:** [1] Charles et al., 2014; http://dx.doi.org/10.1002/mds.22603.

## O_21

### Image-guided programming in patients with Parkinson's disease with suboptimal response to deep brain stimulation

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**Background:** Deep brain stimulation (DBS) is an effective treatment for patients with Parkinson's disease (PD). However, some patients may not respond optimally to programming adjustments, reducing patient satisfaction. Besides, with the recent advances in DBS technology, programming has become more complex and time-consuming. The use of image-guided programming (IGP) could provide precise and specific targeting for DBS patients.
**Methods:** During routine follow-ups, 31 PD patients with subthalamic nucleus (STN) DBS with suboptimal response refractory to conventional programming were included. This was defined as 1. patients on high-dose dopaminergic medication, 2. refractory dyskinesias, 3. gait disturbances, 4. discrete motor improvement on the MDS-UPDRS-part III, 5. speech disturbances, and 6. mood changes. Using postoperative imaging software, we performed the volumetric reconstruction of the electrode field to establish optimal localization. We focused on targeting the dorsolateral portion of the STN, which would correlate with clinical improvement based on previous reports. Programming settings were adjusted according to the reconstruction. Clinical outcomes were assessed by motor and quality of life scales at baseline, immediately after IGP, and 3-and 6-month follow-ups.
**Results:** After IGP, 26 patients (83.9%) experienced motor and quality-of-life improvements, with 25.8% feeling much better and 38.7% feeling moderately better on the patient global impression scale. The EQ-VAS and PDQ-8 scales showed an improvement of 31.6% and 38%, respectively, after IGP. Patients also showed significant motor improvements measured by MDS-UPDRS part III in 22%. The DBS-IS global score improved by 41.5%. Five patients (16.1%) had no clinical or quality of life changes after I-GP.
**Conclusions:** Implementing IGP improves motor clinical outcomes and quality of life by optimizing patient-specific stimulation. IGP can offer significant clinical benefits, while also saving time that might otherwise be spent on trial-and-error programming methods. Given the increasing complexity of DBS programming, incorporating IGP into clinical practice should be strongly considered as a valuable tool.

## O_22

### Geographic disparities and access to device-aided therapy services for medicare beneficiaries with advanced Parkinson's disease

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**Background:** About 1 million US adults have Parkinson's disease (PD); approximately 20% with Advanced PD (APD). Despite known efficacy of surgical device-aided therapies (DAT) (deep brain stimulation [DBS]; carbidopa/levodopa enteral suspension [CLES]), use of DAT is low. The study aim was to understand APD prevalence and if DAT access is limited based on geographic location of DAT facilities relative to patient's residence.
**Methods:** The study included Medicare Fee-for-Service (100%) enrollees age≥18 years with APD, defined as ≥1 inpatient/≥2 outpatient claims with PD diagnosis 01/01/2018-12/31/2020 followed by ≥1 of the following: 30-day consecutive levodopa equivalent dose >1000 mg/day oral PD medication; ≥5 levodopa-containing pills-per-day; non-oral/rescue medication use; drug-induced dyskinesia or amantadine use. Proportion of APD patients and those who received a DAT, number of facilities (based on DAT claims), and distance between patients' residence and facility at which they received DAT are described by state.
**Results:** Of 503,245 beneficiaries with PD, 112,773 (22%) were identified with APD. Only 2.2% (2,450) received DAT (83% DBS, 17% CLES) at 413 facilities. APD patients traveled 87 miles on average for both DBS and CLES, with 33% traveling >60 miles. The largest proportion of identified APD patients resided in California (10.37%) with 2.7% having received DAT, and 27% traveling >60 miles. Texas, Florida, and New York had the next largest proportions of APD patients, 7.10%, 6.98%, and 6.40%, with 2.4%, 2.4%, and 1.6% receiving DAT, respectively. New York had the highest proportion traveling <18 miles (56%), followed by New Jersey (49%). Montana had only 0.45% of APD patients but had the highest proportion receiving DAT (4.2%) and highest proportion traveling >60 miles (80%).
**Conclusions:** DAT are utilized by a small minority of APD patients covered by Medicare. Geographic availability likely impacts access, and even states with higher utilization often require significant travel to receive care.

## O_23

## Safety of foslevodopa/foscarbidopa during optimization and maintenance treatment: post hoc analysis of a phase 3 trial

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**Background:** Continuous subcutaneous infusion with foslevodopa/foscarbidopa, a soluble formulation of levodopa/carbidopa (LD/CD) prodrugs, provides individualized, 24-hour/day therapy. This study characterizes the time course of adverse events (AEs) in patients with Parkinson's disease (PD) and motor fluctuation treated with foslevodopa/foscarbidopa.
**Methods:** Patients aged ≥30 years with idiopathic, LD-responsive PD inadequately controlled with current therapy (≥2.5 average "Off" hours/day) were enrolled in a 12-week, phase 3, randomized, double-blind study comparing foslevodopa/foscarbidopa to oral immediate release LD/CD (NCT04380142). Foslevodopa/foscarbidopa doses were titrated and individualized during the 4-week optimization period, followed by a stable dose regimen during the 8-week maintenance period. Safety was assessed in all patients who received ≥1 dose of study drug.
**Results:** A total of 74 patients received foslevodopa/foscarbidopa. Overall AEs occurred more frequently during the 4-week optimization vs the 8-week maintenance period (74.3% vs 67.9%), as did treatment discontinuations due to AEs (16.2% vs 7.1%). A greater proportion of patients experienced movement-related AEs during optimization vs maintenance, including dyskinesia (10.8% vs 0%), "On" and "Off" phenomenon (6.8% vs 1.8%), and falls (13.5% vs 8.9%). Incidence of infusion site AEs was higher during optimization vs maintenance (67.6% vs 58.9%); individual infusion site AEs generally followed a similar trend (erythema [20.3% vs 21.4%], pain [21.6% vs 8.9%], cellulitis [10.8% vs 12.5%], bruising [6.8% vs 1.8%], nodules [5.4% vs 3.6%]).
**Conclusions:** In this phase 3 trial involving patients with PD treated with foslevodopa/foscarbidopa, AEs and discontinuations were generally higher during the 4-week optimization compared with the 8-week maintenance period. Higher rates of AEs and discontinuations during optimization may have been the result of the dose titration process and acclimation to a new drug delivery system. Patient and physician training, education, and expectation setting before treatment initiation and during optimization may help reduce rates of treatment discontinuation.

## O_24

### Characterizing a Parkinson's disease population inadequately controlled by oral therapy: baseline characteristics of the Phase 3 clinical program for foslevodopa/foscarbidopa

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**Background:** While identification of advanced PD (aPD) continues to be a challenge, new tools have emerged to help clinicians determine if patients have reached aPD. Recently, a validated tool known as MANAGE-PD was launched to help clinicians identify suboptimal PD symptom control and categorize patients with advancing PD as either controlled, inadequately controlled possibly needing treatment optimization, or potentially eligible for device-aided therapies (DATs). The aim of this analysis was to characterize the patient populations of two pivotal clinical trials with foslevodopa/foscarbidopa (LDP/CDP, also referred to as ABBV-951), an investigational drug for Parkinson's Disease (PD).
**Methods:** This post-hoc analysis evaluated the baseline characteristics of patients enrolled in two ABBV-951 phase 3 studies (one double-blind/double-dummy, NCT04380142; and one open-label safety, NCT03781167). Additionally, in the open-label study, the MANAGE-PD criteria (section 1 and 2) was applied to the participants prospectively, which may further validate the use of the tool in identifying patients eligible for DATs.
**Results:** In the double-blind (n=141) and open-label (n=244) studies, the percentages of participants at baseline in the 55-74 age category were 66.7% and 73.4%, that had daily off time >3 hours were 97.2% and 88.1%, that had a 0-3 Hoehn and Yahr stage were 96.5% and 94.7%, and had time to occurrence of motor fluctuations as >3 years of 73.0% and 77.5%, respectively. Based on the MANAGE-PD categorization, in the open label-study all patients were considered to be inadequately controlled with the current treatment regimen, with 14.8% possibly benefitting from current treatment optimization, and 85.2% as potentially benefitting from DAT.
**Conclusions:** The vast majority of patients from the pivotal trials in the LDP/CDP clinical program were consistent with populations characterized as 'advanced' and eligible for a DAT such as ABBV-951, which was substantiated using the MANAGE-PD categorization, adding to the validation of this tool.

## O_25

### Teleprogramming results in quicker optimization of DBS in Parkinson's disease: early results from the ROAM-DBS trial

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**Background:** The optimization of deep brain stimulation (DBS) settings requires several clinical visits. Repeated programming sessions are challenging because of patient schedules and travel burden. Teleprogramming for DBS adds scheduling flexibility and eliminates the need for patient travel for programming, potentially minimizing delays in therapy optimization. ROAM-DBS evaluates the real impact of teleprogramming on the time course of improvement after DBS.
**Methods:** The ROAM-DBS study is a multicenter, prospective randomized controlled trial for Parkinson's Disease patients comparing in-clinic DBS programming only with remote DBS programming using Abbott's Neurosphere™

Virtual Clinic platform. After each programming visit, participants are asked to evaluate their symptom improvement using the Patients Global Impression of Change (PGI-C). In addition, participants are complete the PDQ-39 quality of life questionnaire monthly.
**Results:** Thus far 25 participants have completed the 3 month time point. , Participants in the teleprogramming arm reported feeling at least 1 point of improvement in the PGI-C (MCID) in less days compared to the in-clinic arm, 36.8(15.8) days vs 51.2(15.2) days ($p<.05$). Additionally, There was a higher rate of patients reporting an improvement in the teleprogramming arm compared to the in clinic arm (92% vs 75% respectively). Additionally, there was a higher improvement in quality of life in the teleprogramming arm (insert actual numbers here with p value).
**Conclusions:** Teleprogramming DBS resulted in significantly faster improvements in self-reported outcomes compared to participants treated only with in-clinic programming Additionally, there were more participants in the teleprogramming arm that reported optimization of DBS settings at 3-months. Finally, participants in the teleprogramming group also report earlier improvements in quality of life. These results suggest that the use of telemedicine in DBS care is a necessary tool to more quickly optimize programming and better manage patients' symptoms.

## Guided Poster Tour: Neuroscience

### P_07 (GPT)

### Development and validation of the Vietnamese Smell Identification Test (VSIT)

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**Background:** Smell identification tests are used widely to evaluate olfactory function in patients. However, odor identifiability is influenced by cultural factors, and tests developed in one country may not be appropriate for patients in other countries. This study aimed to develop a smell identification test suitable for Vietnamese patients and to assess its clinical validity and reliability
**Methods:** Our study included four experiments. In Experiment 1, 1,050 people in the community from three regions of Vietnam rated the familiarity of 68 odors on a Likert-type scale ranging from 1 (unfamiliar) to 5 (highly familiar). Based on these results, 18 smell items were selected for use in Experiment 2. In Experiment 2, 50 healthy participants were asked to smell the 18 items and to choose 12 odors with correct odorant identification rates based on a list of four descriptors above 70%. In Experiment 3, 60 hypo/anosmic (BSIT score < 8) patients and 120 normosmic (BSIT score ≥ 8) subjects were tested to assess the validity of the newly developed smell identification test. Validity was assessed by comparing VSIT scores of two groups using the Mann-Whitney U test. In Experiment 4, the test-retest reliability was examined in 60 healthy subjects who had participated in Experiment 3 after one month with interclass correlation.
**Results:** The mean VSIT score was significantly higher in the healthy control group than in the hyposmic group [10.28 (1.34) and 4.57 (1.76); $P < 0.001$]. Using a cutoff value of 8, the VSIT showed a sensitivity of 93.3% and specificity of 97.5% for diagnosing hyposmia in Vietnamese patients. The VSIT has a test-retest reliability of 0.72 ($P < 0.001$).
**Conclusions:** The Vietnamese Smell Identification Test (VSIT) is a 12-item smell rating scale that demonstrates favorable validity and reliability. It is an effective tool for the evaluation of hyposmia in the Vietnamese population

### P_09 (GPT)

### Role of brain renin angiotensin system in the pathophysiology of neurodegenerative disorders

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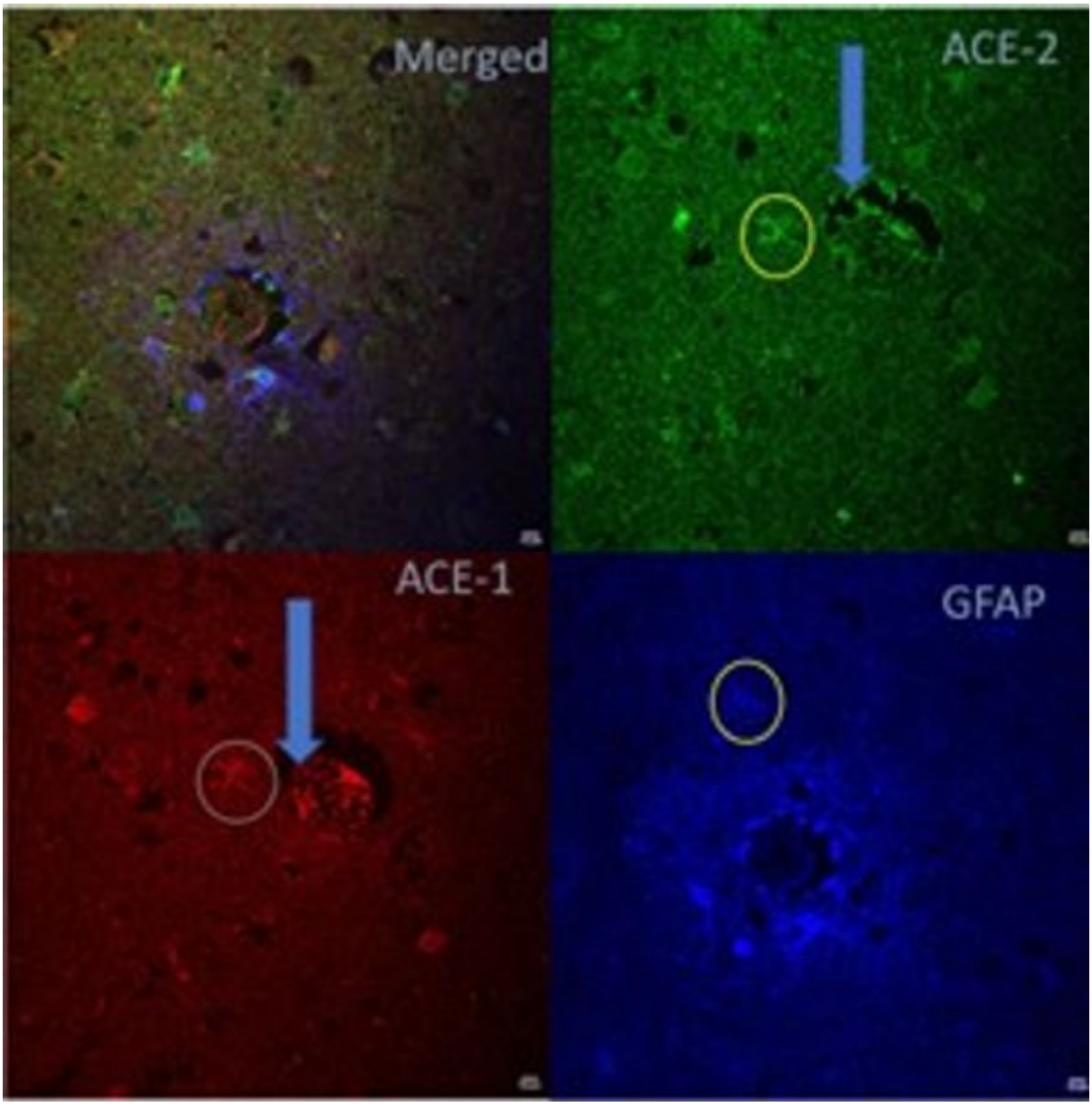
**Background:** Dementia currently affects more than 50 million globally with an expected tripling over the next 20 to 30 years. Among many theories of its underlying pathology across its various types, the vascular theory of the brain renin-angiotensin system (RAS) has got less focus among researchers.
**Aims:** This owes to several transitions from a debate over its site- characterization inside the brain up to the nature of changes in its regulators between the diseased and healthy individuals. Additionally, a controversy has raised regarding the pathological similarity among the different neurodegenerative-disease models and the

human brain tissues, as simulators to the real process. Consequently, I have tried to address these hindering gaps for the progression of the dementia research.
**Methods:** Sample size: 20 post-mortem human brain tissue samples of an acceptable post-mortem delay for both healthy and dementated individuals (Alzheimer`s or Parkinson`s disease). A non-conventional bio-imaging technique, immunofluorescence unlike the commonly used protein assays, for characterization of ACE-1 and ACE2 as main key regulators of the brain RAS. Measurement of the difference in expression of these key regulators between dementated and non-dementated individuals regarding the variation in fluorescence, using a colocalization protocol with discrete or perivascular astrocytes.
**Results:**




Blue arrows heads point to vascular distribution of ACE-1 &ACE-2 in addition to the GFAP-positive astrocytic expression for both ACE-1 &ACE-2 in yellow circle.
**Conclusions:** Astrocytic and vascular distribution of both ACE-1 and ACE-2 in both the frontal and temporal regions of the brain in both dementia and health at variable levels.

## P_10 (GPT)

## α-Synuclein induces neuroinflammation injury through the *IL6ST-AS*/STAT3/HIF-1α axis

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**Background:** The aggregation of α-synuclein (α-syn) promotes neuroinflammation and neuronal apoptosis, which eventually contribute to the pathogenesis of Parkinson's disease (PD). Our microarray analysis and experimental data indicated a significant expression difference of the long noncoding RNA *IL6ST-AS* and its anti-sense strand, *IL6ST*, in α-synuclein-induced microglia, compared with the unstimulated microglia. IL6ST is a key component of the IL6R/IL6ST complex in the microglial membrane, which recognizes extracellular inflammatory factors, such as IL6. Studies have shown that the binding of IL6 to the IL6R/IL6ST complex could activate the JAK2-STAT3 pathway and promote an excessive immune response in glia cells. Meanwhile, the phosphorylation and activation of STAT3 could increase the transcription of *HIF1A*, encoding a hypoxia-inducible factor related to cytotoxic damage. The present study aimed to find the key molecular targets in the process of microglia-neuron interaction.
**Methods:** We determined the DEGs by a microarray analysis upon PD patients and confirmed the expression change by qPCR and WB technique in α-synuclein-induced HMC3 cells. Follow, we detected the pathway associated protein expression and ROS content in HMC3 and SY-SH5Y cell co-culture system.
**Results:** Our results indicated that the overexpression of *IL6ST-AS* was associated with the downregulation of *IL6ST* and the inhibition of the JAK2-STAT3 pathway in α-synuclein-induced HMC3 cells. In addition, reduction of STAT3 resulted in transcription inhibition of *HIF1A* and the acceleration of oxidative stress injury in SH-SY5Y cells co-cultured with α-synuclein-induced HMC3 cells. Our findings indicated that *IL6ST-AS* is an important factor that regulates microglia activation and neuronal necrosis in the progression of PD. In the HMC3 and SH-SY5Y cell co-culture system, overexpression of *IL6ST-AS* led to microglial dysfunction and neurotoxicology through the *IL6ST-AS*/STAT3/HIF-1α Axis.
**Conclusions:** Our research revealed the relationships among α-synuclein, IL6ST, STAT3, and HIF-1α in the pathological process of PD and provided a new inflammation hypothesis for the pathogenesis of PD.

## P_12 (GPT)

### Experimental model of Parkinsoan diseases on the example of oxotremorine

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**Background:** To evaluate of a muscarinic agonist by using the model of tremor caused by active metabolite of oxotremorine.
**Methods:** Active metabolite of oxotremorine, specific cholinergic muscarinic agonist. Systemic administration of oxotremorine is in rats and mice called hypokinesia, generalized tremors, and muscle rigidity. When evaluating the tremor rats' oxotremorine stock solution (1 mL - 1 mg), 1 l of diluted in 20 ml of dispersion distilled water and administered intraperitoneally in an amount of 0.2 ml per 100 g of body weight animal body.
**Results:** Tremor evaluated for severity on a scale and duration, filing start and end time. Localization and tremor amplitude expressed in scores: 0 - no, 1 - local low amplitude tremor of the head, front paws, or tail, 2 - Peak-to-local tremors, 3 - generalized small- or middle --amplitude tremor of the whole body. Also, tremors recorded manifestations of rigidity, salivation, and piloerection. The test substances and reference preparations are administered for 30 min before the administration of oxotremorine. Depending on the objectives of the experiment, the introduction of the test substances after the administration of oxotremorine.
**Conclusions:** Points received in the assessment of the average value for the group. The results allow us to know about the quality of the experiment and the whole study drug.

## P_13 (GPT)

### Estrogen and progesterone influence membrane functions and glucose transporter expression in synaptosomes of different age groups of naturally menopausal rats

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**Background:** Normal brain aging is associated with progressive cellular and increased vulnerability to neurobiological diseases. The objective of this study was to determine the effect of 17 β-estradiol (E2) and progesterone (P4) on the activities of Na+ K+ ATPase, monoamine oxidase (MAO), neurotransmitters levels, glucose transporter (GLUT) expression and neurobehavioral characteristics in naturally menopausal female rats of 3 months (young), 12 months (adult) and 24 months (old) age groups.
**Methods:** The aged rats (12 and 24 months old) (n= 8 for each group) were given subcutaneous injection of E2 (0.1 µg/g body weight) daily and P4 (2.5 µg/g body weight) was injected on alternate days for one month. For the combined treatment similar concentrations of E2 and P4 were given daily. After treatment period, cortex, striatum, and hippocampus were isolated for further studies. Biochemical parameters such as pro-inflammatory cytokines, tumor necrosis factor, tyrosine hydroxylase (p-TH), brain-derived neurotrophic factor (BDNF), neurotransmitters (dopamine, acetylcholine, gamma-aminobutyric acid (GABA) and glutamate), nitrite levels, antioxidant defense enzymes and 4-hydroxynonenal (HNE) levels were measured in the experimental-treated rat brain.

**Results:** The results obtained in the present work revealed that normal aging was associated with significant increases in the activity of MAO, HNE levels, and a decrease in antioxidant status, Na+ - K+ ATPase activity, expression of (GLUT 1 & GLUT 3), BDNF expression levels, neurobehavioral functions and modulation of glutamate, dopamine, acetylcholine and GABA levels in rats. There was a significantly increased PPARγ, p-TH expression and depletion TNF-α, IL-1β in various brain areas compared with the E2, P4 and combined treatment group (E+P). Present data showed that (E+P) group, effectively brought these changes to near normalcy in aging female rats.
**Conclusions:** Hence, the combined treatment with E2, and P4 in aging rats has a beneficial effect and therapeutic potential for adjunctive therapy for age related disorder including Parkinson's disease.

## P_36 (GPT)

### pS129-α-synuclein and α-synuclein in CNS-originating extracellular vesicles improve the differential diagnosis of Parkinson's disease and multiple system atrophy

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**Background:** Differential diagnosis of Parkinson's disease (PD) and multiple system atrophy (MSA) poses a challenge for neurologists due to the overlap of early-stage parkinsonism symptoms. A minimally invasive diagnostic test is not currently available. Extracellular vesicles (EVs) contain cell-state-specific cargo and cross the blood-brain barrier into the blood, providing a window into biochemical changes in the CNS. We showed previously that the level of total α-syn was significantly higher in neuronal- and oligodendroglial EVs (nEVs and oEVs, respectively) in the order HC < PD < MSA (Dutta et al. 2021). Separation of MSA from HC or PD was high whereas between PD and HC it was moderate. The level of pS129-α-syn in normal adult brains is ~4% but is substantially higher in PD and MSA brains. Tau aggregates are found in ~50% of PD brains but are rare in MSA.
**Methods:** EVs were isolated from serum/plasma by an ExoQuick kit followed by immunoprecipitation of nEVs and oEVs separately. pS129-α-syn (32 HC, 46 PD, 30 MSA) was measured using an in-house developed electrochemiluminescence ELISA (ECLIA). Tau (54 HC, 51 PD, 41 MSA) was measured by a commercial ECLIA kit. Multinomial logistic regression with LASSO variable selection was used for ROC analysis.
**Results:** pS129-α-syn was significantly higher in the same order as total α-syn but only in oEVs. The addition of pS129-α-syn in oEVs to the discriminative formula increased the separation among all the groups, particularly between HC and PD. Total tau was significantly lower in nEVs and oEVs in MSA compared to HC and PD though did not increase the separation power.
**Conclusions:** The accuracy of an algorithm comprising total α-syn in nEVs, oEV:nEV α-syn concentration ratio, pS129-α-syn in oEVs, and total EV concentration is ~80% for discriminating HC from PD, ~99% for separating HC from MSA, and ~93% for distinguishing between PD and MSA.

## P_40 (GPT)

### The Synuclein-One study: skin biopsy detection of phosphorylated alpha-synuclein for diagnosis of the synucleinopathies

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**Background:** The Synuclein-One study is an NIH-funded 30-site multicenter trial of 426 patients with synucleinopathies including Parkinson's disease (PD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA) and pure autonomic failure (PAF). The study was designed to describe the sensitivity, specificity, accuracy and precision of skin biopsy to detect the presence of phosphorylated alpha-synuclein in patients with synucleinopathies.
**Methods:** After signing informed consent, all subjects will complete detailed neurologic examinations (MDS-UPDRS, Hoehn and Yahr scale), detailed disease history review, cognitive evaluation (MOCA), orthostatic vital signs, RBD questionnaire, orthostatic hypotension questionnaire, and Parkinson's Disease Questionnaire-39. All subjects will complete skin biopsies at the distal leg, distal thigh and proximal thigh. All clinical material will be reviewed by a blinded expert consensus panel to confirm the referring diagnosis or move to an 'indeterminate' category. Skin biopsies will be processed at 2 independent laboratories. Phosphorylated alpha-synuclein deposition will be quantified by 2 readers, blinded to referring diagnosis and results of the other reader.Enrollment closed in January 2023, with final data analysis by 3/15/2023.
**Results:** Final un-blinded results will be presented at the IAPRD 2023 annual meeting with a focus on sensitivity, specificity, accuracy and precision. In addition, synucleinopathy subgroup analysis will be performed to define unique pathological characteristics of disease (PD, MSA, DLB or PAF).
**Conclusions:** The need for a validated, well-characterized, simple, reproducible marker of synuclein pathology has never been greater. The number of individuals with neurodegenerative diseases continues to grow and misdiagnosis within and among synuclein and non-synuclein pathologies continues to occur, resulting in incorrect medication choices, iatrogenic complications, poor prognostication and patient frustration. The Synuclein-One study is the largest investigation of cutaneous phosphorylated alpha-synuclein detection across all four synucleinopathies and will advance the field of neuro-diagnostic testing in neurodegenerative disease.

## P_74 (GPT)

### Whole-exome sequencing study of Parkinson's disease in the Croatian population

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**Background:** Parkinson's disease is a multifactorial disease, and an estimated 5-10% can be contributed to monogenic causes, and identifying those patients remains a diagnostic challenge. Whole-exome sequencing presents a clear improvement on previous sequencing capabilities. Our aim was to assess the type and frequency of mutations leading to monogenic Parkinson's disease in Croatian patients.
**Methods:** Our study cohort includes patients from the Clinic of Neurology at the Clinical Hospital Centre Rijeka, referred to genetic testing during 2021 and 2022. Exome sequencing was performed at CIGM using standardized protocols in use at the time of processing. Identified variants were classified according to the ACMG and AMP 2015 joint consensus recommendation, along with ACGS recommendations where applicable.
**Results:** We have performed exome sequencing in 152 patients. Causative pathogenic mutations have been confirmed in 9 patients (9,21%, GBA n=11, PRKN n=3), while variants of uncertain significance were found in 43 patients (28,29%). Additonally, 14 patients have confirmed carriership of classically recessive genes (9,21%).
**Conclusions:** Pathogenic mutation yield of 9,21% is slightly lower compared to current findings for european populations, although in similar genes (GBA and PRKN) compared to Czech and German populations. Our findings show that whole-exome sequencing can be considered in the clinical evaluation of Parkinson's disease, as it can lead to the findings of causative pathogenic mutations and expand our knowledge by discovering novel variants of target genes.

## P_106 (GPT)

### Serum inflammatory cytokines levels and the correlation analyses in Parkinson's disease

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**Background:** Serum inflammatory cytokine levels and their correlation with the clinical symptoms of Parkinson's disease (PD) are still significantly controversial, and there is little research on the diagnostic value of cytokines.
**Methods:** Serum levels of the cytokines, including IL-6, IL-8, and TNF-α, were measured in 183 PD patients and 91 healthy controls (HCs). The motor and non-motor symptoms of PD were assessed with different assessment scales including UPDRS, H&Y stage, Hamilton Depression Scale (HAMD), Non-Motor Symptom Scale (NMSS),

Frontal Assessment Battery (FAB) and Montreal Cognitive Assessment (MoCA). The correlations of these inflammatory measures with clinical variables and diagnostic value of cytokines were analyzed in PD patients.
**Results:** Except for IL-8 factor, serum interleukin -6 (IL-6) and tumor necrosis factor-α (TNF-α) levels in PD patients were higher than HCs. In PD patients, serum IL-6 level was positively correlated with age of onset, the scores of HAMD, NMSS, UPDRS part I, UPDRS part II, UPDRS part III, FAB and MoCA. Serum TNF-α level was positively correlated with age of onset and H&Y stage in PD patients ($P = 0.037$). However, no associations were found between all the clinical variables and the serum IL-8 level. The forward binary logistic regression model revealed that serum IL-6 level was associated with scores of MoCA ($P = 0.023$) and UPDRS I ($P = 0.023$), but no associations were found with the remaining factors. The ROC curve of TNF-α for the diagnosis of PD showed the area under the curve (AUC) was 0.719 ($P < 0.05$, 95% CI: 0.655-0.784), with a diagnostic sensitivity of 76.0% and a specificity of 59.3%.
**Conclusions:** Our results found that IL-6 level was associated with non-motor symptoms and cognitive dysfunction, and we also propose that TNF-α has a good diagnostic value for PD despite its irrelevance to clinical symptoms.

## Guided Poster Tour: PD: Clinical

### P_64 (GPT)

### Working memory dysfunctions in Parkinson's disease in a sample of the Tunisian population

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**Background:** The study aimed to examine cognitive changes observed in Parkinson's disease using a cognitive theoretical framework. We used Baddeley's working memory model and its corollary, the Norman and Shallice Supervisory Attentional System model, in order to move from the simple description of the disorders to the explanation of the deficits in terms of cognitive processes.
**Methods:** 21 non-demented, non-depressed parkinsonian participants at stages 1, 2, or 3 of Hoehn & Yahr (1968) were compared to 21 controls paired for age, sex, and education. The neuropsychological assessment battery was composed of culturally adapted tasks assessing: attention and processing speed (phasic alertness and design judgment), forward and backward verbal and visuospatial span, management of attentional resources (dual tasks), planning (Tower of London), inhibition (Hayling test), and flexibility (simple and alternate verbal fluency tasks). All patients were examined one hour after the morning L-dopa intake.
**Results:** The findings showed that the deficit was not noted on the non-specific factors such as phasic alertness or processing speed and was not correlated to the severity of the motor symptomatology of depressive scores. Also, it does not appear either in the temporary storage capacity or in the functionality of the working memory (Phonological and Articulatory Loop and Visuo-Spatial Sketchpad). On the other hand, Parkinson's patients were deficient in the functionality of the central executive in its management of attentional resources functions and its executive control functions at the level of planning, cognitive inhibition of dominant responses, and reactive and spontaneous mental flexibility.
**Conclusions:** The theoretical models used have proven to be a valuable metaphor to describe and explain the observed deficits. However, these models lack specificity since the central executive deficits were also observed in other pathological conditions.

### P_79 (GPT)

### Longitudinal analysis of plasma biomarkers for freezing of gait in Parkinson’s disease

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**Background:** This study aimed to examine whether plasma biomarkers (β-amyloid 40 [Aβ40], β-amyloid 42 [Aβ42], phosphorylated tau 181 [p-tau$_{181}$], glial fibrillary acidic protein [GFAP], and neurofilament light chain [NFL]) can predict the development and progression of freezing of gait (FOG) in Parkinson’s disease (PD).
**Methods:** We enrolled 184 early PD patients to complete 5-year annually repeated clinical assessments. Plasma candidate biomarkers at baseline, 1-year, and 2-year were quantified using the ultrasensitive Simoa technology.
**Results:** Linear mixed-effect models indicated that high plasma NFL and GFAP were significantly associated with high FOG Questionnaire (FOG-Q) score over time, and high plasma NFL at baseline correlated with a faster increase in the FOG-Q score during follow-up. Combined sex, age, disease duration, motor and cognitive measurements, and plasma NFL, GFAP, and p-tau$_{181}$ could predict with 74.7% sensitivity and 75.3% specificity those patients who would and would not develop FOG during follow-up ($P$<0.05). Kaplan-Meier analysis showed a

significantly increased risk of FOG in patients with plasma NFL > 9.51 pg/mL, GFAP > 50.15 pg/mL, and p-tau$_{181}$ > 1.47 pg/mL at baseline. Multivariate Cox regression analysis adjusted for age, sex, disease duration, motor subtype, levodopa dose, Fazekas score, GFAP, and motor and cognitive scores showed that plasma NFL (HR=1.093, 95%CI=1.043-1.144, *P*<0.001) and p-tau$_{181}$ (HR=1.332, 95%CI=1.027-1.727, *P*=0.031) at baseline correlated with an increased risk of developing FOG.
**Conclusions:** Our study may suggest plasma biomarkers NFL, GFAP and p-tau$_{181}$ could correlate with the development and progression of FOG in PD, which needs to be further verified.

## P_81 (GPT)

### Observational study to investigate the relationship between stress related disorders and dysautonomic symptoms in Parkinson's disease

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**Background:** Post-traumatic stress disorders are associated with an increased risk of developing Parkinson's disease. Studies demonstrate that these disorders share physiopathological characteristics with dysautonomic symptoms of Parkinson's disease. Dysautonomic symptoms have a negative impact on disease progression, morbidity, and mortality in patients. The relationship between post-traumatic stress disorders and dysautonomic symptoms in Parkinson's disease is unknown. We aimed to find a relationship between stress disorders and dysautonomic symptoms in Parkinson's disease.
**Methods:** A cross-sectional study was designed. Patients were selected from PI's clinic from July to September 2022. Patients were excluded if presented dementia, psychosis, TBI, DBS or missing data in medical files. Non-probability convenience and consecutive sampling was applied. SCOPA-AUT scale was used to identify dysautonomic symptoms and arbitrarily categorized into two groups, predominance of dysautonomic symptoms (total score ≥ 10), and without a predominance of these symptoms (total score <10). Patients were interrogated about personal experiences of a traumatic event. The psychiatric PCL-5, ACE, ASDS scales and a structured interview were applied to explore disorders related to post-traumatic stress.
**Results:** Thirty-two patients with Parkinson's disease were included, 16 with SCOPA-AUT ≥ 10 and 16 with SCOPA-AUT < 10. We observed a significant difference in PCL5 between groups, SCOPA-AUT ≥ 10 group scored 23.06 (SD 24.5) vs SCOPA-AUT < 10 group 3.2 (SD 9.8), p = 0.007. Among those in SCOPA-AUT ≥ 10, a positive correlation was observed between PCL5 and total SCOPA-AUT score, p = 0.002, rho = 0.530. A higher prevalence of a previous traumatic event (OR 4.84, p = 0.034) or of any stress-related disorder (OR 15.4, p = 0.003) was also observed in those with in SCOPA-AUT ≥ 10 group.
**Conclusions:** The present study suggests that Parkinson's patients with stress-related disorders have a higher prevalence of dysautonomic symptoms. Further studies with better design are required to confirm our results.

## P_96 (GPT)

### A 26-week study of long-term adherence to a iPhone and Apple Watch based PROM platform: enhancing measurement and improving outcomes

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**Background:** We outline the utilization habits and resulting data from a six-month pilot of a PwP using NeuroPath Insights ™ on an iPhone and Apple Watch and digital platform in real-life.
**Methods:**

- Single male user, age 64, H&Y 1, neurologist-verified diagnosis of idiopathic Parkinson disease (June 2018)
- NeuroPath Insights™ implemented on iPhone and Apple Watch (June-December 2022)
- Multiple active and passive data entries regarding motor/non-motor symptoms and activities

**Results:** User implemented NeuroPath Insights ™ for a total of 460 entries over 146 out of 182 days, resulting in 80.2% compliance over 26 weeks. Participant used NeuroPath Insights ™ at least once per day for six days of every seven-day window, including 97 Neuro-QoL™ questionnaires entries and 146 notes.
These insights were combined with passively captured data and reported on a dashboard via iPhone and Apple Watch.
The participant tracked significant improvements in mobility, flexibility and cognitive function, which motivated him

to adhere to his medication and physical exercise regimen. On average, it took about five minutes of active tracking of symptoms per day, typically over two or three sessions.
**Conclusions:** NeuroPath Insights™ allowed for active and passive monitoring. User reported sharing the collected information which provided relevant insights to the user and his neurologist about his condition and care path.
Recognizing the limitations of a single case design, utilization and compliance above 80% provides encouraging signaling towards wider implementation.
This may be due to a combination of the motivation of the user due to the information being provided by the NeuroPath Insights™ platform in conjunction with the ease of use of the interface, which includes passive monitoring functions and a voice interface that extends to the Apple Watch.
According to the participant, "using NeuroPath Insights™ increases my **understanding** in my Parkinson's and helps me to **anticipate** and **manage** my mental and physical activities."

## P_101 (GPT)

## Feasibility of virtual measurement of sequential motor assessments for Parkinson's disease

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**Background:** To assess if multiple trained raters in different geographical locations can reliably assess sequential videotaped motor assessments of healthy adults with typical development (TD).
**Methods:** An examiner certified in the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz, *et al.,* Mov. Disord. 23 (2008) 2129–2170) videotaped the administration of a low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease (PD) (McKay, *et al.,* MethodsX 6 (2019) 169–189 https://doi.org/10.1016/j.mex.2018.12.017) to healthy men with TD aged 55 and 58 years during two complete sessions separated by a month. An investigator presented the videos on his monitor to teams of five raters viewing the shared screens on individual monitors in separate locations on three continents. Raters were required to independently score each task immediately after the video was shown.
**Results:** Percent agreements were calculated for test-retest for each item of each participant by each rater. The percentage agreements for each item for each participant were 100 (N=10), 75 (N=2), 66 (N=7), 50 (N=9), 33 (N=8), 25 (N=5), 0 (N=3) (Table 1). There was better agreement for tasks with stationery extremities.

| Age | Ht | Wt | 3.17UR | 3.17UL | 3.17UCR | 3.17UCL | 3.15R | 3.15L | 3.4R | 3.4L | 3.5R | 3.5L | 3.6R | 3.6L | 3.9U | 3.17LR | 3.17LL | 3.17LCR | 3.17LCL | 3.7R | 3.7L | 3.8R | 3.8L | 3.9L |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 58 | 71 | 215 | 100 | 100 | 75 | 100 | 50 | 50 | 66 | 50 | 75 | 25 | 33 | 50 | 50 | 100 | 100 | 100 | 100 | 100 | 66 | 50 | 33 | 66 |
| 55 | 67 | 159 | 25 | 50 | 50 | 25 | 25 | 66 | 50 | 0 | 0 | 66 | 33 | 33 | 100 | 33 | 33 | 66 | 66 | 33 | 25 | 33 | 0 | 100 |

**Table 1. Demographic and consensus scores of five independent raters of motor tasks for test and retest of two healthy male participants with typical development.**

**Age: Age in years; Ht: Height in inches; Wt: Weight in pounds; 3.17UR: 3.17 Rest tremor amplitude upper limbs right; 3.17UL: 3.17 Rest tremor amplitude upper limbs left; 3.17UCR: 3.17 Rest tremor amplitude upper limbs counting right; 3.17UCL: 3.17 Rest tremor amplitude upper limbs counting left; 3.15R: 3.15 Postural tremor of the hands right; 3.15L: 3.15 Postural tremor of the hands left; 3.4R: 3.4 Finger tapping right; 3.4L: 3.4 Finger tapping left; 3.5R: 3.5 Hand movements right; 3.5L: 3.5 Hand movements left; 3.6R: 3.6 Pronation-supination movements of the hands right; 3.6L: 3.6 Pronation-supination movements of the hands left; 3.9U: 3.9 Arising from chair upper limbs; 3.17LR: 3.17 Rest tremor amplitude lower limbs right; 3.17LL: 3.17 Rest tremor amplitude lower limbs left; 3.17LCR: 3.17 Rest tremor amplitude lower limbs counting right; 3.17LCL: 3.17 Rest tremor amplitude lower limbs counting left; 3.7R: 3.7 Toe tapping right; 3.7L: 3.7 Toe tapping left; 3.8R: 3.8 Leg agility right; 3.8L: 3.8 Leg agility left; 3.9L: 3.9 Arising from chair lower limbs**

**(McKay GN, Harrigan TP, Brasic JR. A low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease. MethodsX 2019; 6:169-189. PMID: 30733930 https://doi.org/10.1016/j.mex.2018.12.017)**

**Conclusions:** We have demonstrated the feasibility of virtual evaluations of sequential videotaped motor assessments by multiple trained raters in different geographical locations. This protocol can be utilized to apply precision medicine for virtual motor assessments of persons with possible Parkinson's disease and related conditions in vastly different locations.

## P_105 (GPT)

## Sex differences in the age at onset of Parkinson's disease in Latin American populations

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**Background:** It remains controversial if there are sex differences in the Age at Onset (AAO) of Parkinson's Disease (PD), with almost no studies including Latin American individuals. The Latin American Research Consortium on the Genetics of PD (LARGE-PD) includes participants from 13 countries in Central and South America. Our study aimed to examine the sex differences in AAO for LARGE-PD PD patients.
**Methods:** All LARGE-PD patients were diagnosed with PD based on UK Brain Bank diagnostic criteria, were 18 years or older, and were Latin American. AAO data was extracted for participants in ten Latin American countries. AAOs for males and females were calculated including overall, country-specific, and in decade-long age ranges. T-tests at 95% confidence were used to identify any statistical significance between mean AAOs for males and females for each country and in decade age ranges.
**Results:** We included 2,354 participants, 1,329 males and 1,025 females, with AAO between 7-90 years old (Table 1). Overall mean AAO for females was 55.6±13.8 compared to 55.1±13.7 in males (Table 1).
**Conclusions:** Our results show that AAO in LARGE-PD is not statistically significant between sexes, neither overall nor at any age range (Tables 1-2). Interpretation of results by site is harder due to low population sizes. Interestingly, the overall AAO in LARGE-PD compared to large studies in Europeans was almost 7 years earlier. More studies are needed to understand if earlier AAO is due to sampling bias or genetic/environmental factors in this population.

*Table 1. Country-specific means and p-values for two sample t-tests.*

| | Frequency | | Average Age at Onset (Years ± SD) | | Age Range (Years) | | P-Values |
|---|---|---|---|---|---|---|---|
| **Country** | **Male** | **Female** | **Male** | **Female** | **Male** | **Female** | |
| Argentina | 13 | 8 | 46.85 ± 6.86 | 55.88 ± 7.94 | 36-60 | 47-71 | 0.02* |
| Brazil | 184 | 119 | 50.88 ± 12.84 | 51.05 ± 13.36 | 12-84 | 21-85 | 0.91 |
| Chile | 118 | 93 | 55.61 ± 11.95 | 57.58 ± 11.22 | 20-84 | 17-86 | 0.23 |
| Colombia | 270 | 236 | 55.39 ± 14.08 | 55.28 ± 14.19 | 7-80 | 10-85 | 0.93 |
| Costa Rica | 70 | 48 | 54.30 ± 12.22 | 54.13 ± 15.56 | 28-83 | 13-76 | 0.95 |
| Honduras | 5 | 3 | 65.80 ± 6.52 | 53.67 ± 7.36 | 58-75 | 45-63 | 0.08 |
| Mexico | 169 | 109 | 57.47 ± 12.89 | 59.84 ± 11.18 | 18-89 | 27-88 | 0.12 |
| Peru | 373 | 305 | 55.81 ± 14.41 | 54.50 ± 14.98 | 13-90 | 8-90 | 0.25 |
| Puerto Rico | 38 | 26 | 55.74 ± 10.72 | 63.50 ± 10.54 | 32-78 | 40-83 | 0.01* |
| Uruguay | 89 | 78 | 55.01 ± 15.64 | 57.27 ± 11.88 | 12-83 | 30-83 | 0.30 |
| **Totals** | **1329** | **1025** | **55.05 ± 13.70** | **55.56 ±13.82** | **7-90** | **8-90** | **0.38** |

**Statistical significance at the 95% confidence level*

*Table 2. Decade age range means and p-values for two-sample t-tests.*

| | Decade Age Ranges (Years) | | | | | |
|---|---|---|---|---|---|---|
| | **≤39** | **40-49** | **50-59** | **60-69** | **70-79** | **≥80** |
| **Male Mean (N)** | 30.17 (169) | 44.79 (253) | 54.43 (357) | 64.33 (365) | 73.80 (167) | 82.94 (18) |
| **Female Mean (N)** | 30.36 (126) | 44.83 (180) | 54.60 (273) | 64.26 (302) | 73.33 (126) | 83.00 (18) |
| **P-Value*** | 0.83 | 0.89 | 0.47 | 0.75 | 0.14 | 0.95 |

## P_150 (GPT)

## Healthcare access in patients with Parkinson ’s disease – analysis of the health and retirement study

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**Background:** Previous population-based studies in patients with Parkinson’s disease (PD) have addressed disparities in diverse gender, racial, and ethnic groups. Currently, we still lack data about general healthcare access in this population. The aim of our study is to compare healthcare access among individuals with and without the diagnosis of PD.
**Methods:** Data analysis of the Health and Retirement Study (HRS) was conducted. The HRS is a longitudinal of older adults (≥ 50 years old) in the United States where participants have a biannual interviews to assess physical and mental health, family and work life, and aging. In our analysis we included only the individuals who participated in the HRS 2019 Health Survey which was administered to a sub-sample of respondents to gather information about their healthcare access. We used t-test and logistic regression modelling to compare PD patients with PD-free participants.
**Results:** Out of 5089 individuals included in this study, 54 (1%) were diagnosed with PD. In comparison with PD-free individuals, patients with PD rated their overall health as much worse (p=1.337e-12). As a probable repercussion of this, they talked more frequently to their doctor during the last year (p=0.009). Moreover, they felt less confident filling out the medical forms (p = 3.011e-06). They also reported that they felt less respected by doctors and nurses (p=0.042). Probably due to greater degree of physical disability, they used internet less frequently to communicate with medical professionals (p=3.37e-06). In addition, they reported more frequently having problems with access to the healthcare because lack of financial resources (p=0.013). As a result of all these factors, they also felt more dissatisfied with overall quality of care (p=0.04).

**Conclusions:** Individuals with PD are less satisfied with their standard of care and healthcare access. Systemic interventions aiming to target these disparities should be implemented to improve this issue.

## P_157 (GPT)

### Freezing of gait detection using RGB and walkway pressure data with AFSD algorithm

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**Background:** Freezing of gait (FoG) is a common issue for patients with advanced Parkinson's disease, affecting their ability to initiate and take steps. Accurately identifying and quantifying FoG episodes remains a challenge for healthcare professionals.
**Methods:** The study used a combination of video recording and walkway pressure data to detect FoG episodes in 28 patients diagnosed with the condition. The patients underwent a standardized walking protocol using the gait analysis system (GAITRite System), where video recording and foot pressure data were collected simultaneously. The videos were then labeled by a specialist to indicate the presence of FoG. The raw RGB and optical flow data were processed using an adaptive fusion algorithm (AFSD) for temporal segmentation. The machine learning model was trained using 80% of the data and tested using 20%. Walkway pressure data were processed using Nantel's method to infer FoG episode start and end times. Performance was evaluated using MAP@IOU (Mean Average Precision at Intersection Over Union) threshold.
**Results:** The analysis of 44 videos with 203 FoG episodes showed that the AFSD algorithm performed well at higher MAP@IOU thresholds, but underperformed at lower thresholds. It tended to confuse standing phases with FoG episodes, resulting in false positive predictions. The results were presented in an online platform for physician review and correction.
**Conclusions:** The combination of video recording and walkway pressure data with machine learning algorithms shows potential in FoG detection. The online platform offers a user-friendly evaluation of FoG and could aid in clinical decision making. The AFSD algorithm and Nantel's method could improve sensitivity and precision, but further research is necessary to enhance accuracy and provide objective outcomes for patients with FoG.

## P_158 (GPT)

### Abnormalities on pareidolia testing and visual hallucinations in patients with Parkinsonism

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**Background:** Pareidolia is a type of complex visual illusion involving ambiguous forms being perceived as meaningful objects, a phenomenon analogous to visual hallucinations.
Aim: To measure pareidolic illusions using noise pareidolia test in Parkinsonism (Parkinson's disease and Atypical Parkinson's diseases) in comparison to healthy controls and to correlate it with motor and non-motor symptoms.
**Methods:** In a single-center prospective cross-sectional observational study, 30 patients with Parkinson's disease, 30 patients with Parkinson's plus/ Atypical Parkinsonism and 30 healthy subjects were enrolled. Demographic data and clinical features were noted. A Noise pareidolia test (face version with forty images) was performed to assess pareidolic illusions in all.
**Results:** Atypical Parkinson's disease (APD) patients (90%) and PD patients (73.3%) without dementia more frequently experienced pareidolias than healthy controls (13.3%). Among APD, all patients of DLBD and CBS subgroups with CDR ≤2 experienced pareidolias. MSA patients (83.3%) experienced pareidolias less often than PSP (86.7%). Dysarthria/hypophonia, micrographia, turning difficulty, dyskinesia and motor fluctuations, motor disability ( Modified H&Y scale) in PD patients, freezing episodes in APD, micrographia in PSP subgroup showed statistically significant correlation with pareidolias. Neuropsychiatric disturbances [low mood, anxiety, panic attacks and decreased concentration], cognitive dysfunction [impaired learning, memory, dysexecution and complex attention] and sleep disturbances [RBD, Insomnia, excessive daytime sleepiness] showed significant correlation with pareidolias ($P<0.05$).
Among PD and APD groups, cognitive impairment, neuropsychiatry symptoms, MOCA and CDR showed significant correlation with pareidolias in all groups except PSP.
**Conclusions:** Pareidolias are more frequent in atypical Parkinson's disease and PD group than in healthy controls. All patients of DLB and CBS experienced pareidolias while MSA patients experienced pareidolias less often than PSP. More frequent pareidolias were observed in DLB and they were observed less frequently in MSA than PD. Cognitive impairment, neuropsychiatry disturbances, sleep disturbances were significantly associated with pareidolias.

## Guided Poster Tour: Other Movement Disorders

### P_25 (GPT)

### Usefulness of dual-phase FP-CIT PET in distinguishing between corticobasal degeneration and idiopathic Parkinson's disease within 2 years of disease duration

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**Background:** Corticobasal degeneration (CBD) is a degenerative disorder characterized by asymmetric motor symptoms and cortical degeneration. In the early stage of disease, CBD and idiopathic Parkinson's disease (IPD) share clinical features of asymmetric parkinsonism, making early clinical differentiation challenging. This study aimed to delineate the usefulness of dual-phase FP-CIT PET in discriminating between IPD and CBD within 2 years of disease duration.
**Methods:** The study enrolled clinically diagnosed CBD (n=11) and IPD (n=22) patients (age, sex matched). All participants underwent dual-phase 18F-FP-CIT PET, and regional standard uptake value ratio (SUVR) was obtained by semi-quantitative analysis. The early perfusion imaging and dopamine transporter (DAT) imaging was compared between two groups.
**Results:** Early-phase FP-CIT PET showed that the CBD group exhibited more prominent asymmetry than the IPD group, particularly in the perirolandic area (asymmetry index, 11.09% vs 3.97%, p=0.007), superior frontal gyrus (8.68% vs 2.85%, p=0.047), and anterior parietal lobe (9.78% vs 4.60%, p=0.043). The regional SUVR of frontal lobe, thalamus, cingulate, and caudate were significantly lower in patients with CBD, while the SUVR of occipital lobe was lower in the IPD group. DAT imaging revealed that the caudate showed lower SUVR in the CBD group, and the putamen-to-caudate ratio (PC ratio) was significantly higher in the CBD group (1.488 vs 0.966, p<0.001). The PC ratio exhibited the most powerful discriminative power from ROC curve comparison (AUC=0.955).
**Conclusions:** This study demonstrated that the dual-phase FP-CIT PET is useful in differentiating CBD and IPD in the early stage of the disease, and an increased PC ratio of DAT imaging is highly informative for distinguishing between CBD and IPD.

### P_177 (GPT)

### Orthostatic hypotension in multiple system atrophy: related factors and disease prognosis

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**Background:** Multiple system atrophy (MSA) is a rare neurodegenerative disease characterized by Parkinson's disease, ataxia and autonomic nervous failure. Orthostatic hypotension (OH) is the main feature of central vascular autonomic failure in MSA.
**Methods:** A total of 444 patients with clinically probable MSA were enrolled. The Unified MSA Rating Scale (UMSARS), cognitive scale, and clinical milestone were recorded. Mild OH was defined as a decrease of systolic blood pressure (SBP)/diastolic blood pressure (DBP)>20/10 mmHg, and severe OH was defined as a decrease of SBP/DBP ≥ 30/15 mmHg.
**Results:** In our study, 215 patients had no OH, 88 had mild OH, and 141 had severe OH. The proportion of female patients in the severe OH subgroup was significantly lower than that in the other two groups (53/88 vs. 46/42 vs. 109/106, p=0.028), and the proportion of MSA-C in the severe OH subgroup was significantly higher than that in the no OH subgroup (95/46 vs. 113/102, p=0.021). The UMSARS I score and the frequency of supine hypertension in patients with OH was significantly higher than that of patients without OH (16.22±5.58 vs. 16.89±5.87 vs.14.60±5.46, p=0.000; 77/64 vs 29/59 vs 32/183, p=0.000). In the ordered logistic regression model, factors related to OH severity included sex (OR, 0.68; P=0.047), age of onset (OR, 0.98; P=0.030), clinical type (OR, 1.48; P=0.050) and supine hypertension (no vs. yes) (OR, 0.21; P=0.000). The survival time of patients with severe OH was significantly lower than that of patients without OH (6.79 vs. 8.13 years, p=0.001). Consistently, cox survival analysis found patients with severe OH had a significantly increased of death risk compared with patients without OH (OR, 2.32; P=0.000).
**Conclusions:** Our large cohort study of MSA provides additional evidence for the negative impact of severe OH on survival. Timely measures should be taken in patients with OH.

## P_181 (GPT)

### The perfusion of the parietal region as a feature of progressive supranuclear palsy subtypes

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**Background:** Progressive Supranuclear Palsy (PSP) is the most common atypical parkinsonism. The Hoglinger et al criteria of diagnosis systematized the examination of subtypes. Among them two subtypes are associated with up to 90% of the cases. PSP-Richardson Syndrome (PSP-RS) is the most common and affects about 60% of patients, while the second PSP-Parkinsonism Predominant (PSP-P) is present in about 30% of patients. The entities, though considered as subtypes of the same diseases, are related to different courses.
**Methods:** The examination was performed using analysis of perfusion SPECT ($^{99}$Tc-HMPAO) of 39 patients, 21 diagnosed with PSP-RS and 18 diagnosed with PSP-P. The diagnosis was based on the most contemporary criteria of diagnosis. The duration of symptoms varied from 3 to 6 years. Patients with vascular focuses over 1 mm, with neoplasms, who suffered traumatic brain injury, were not included in the study as the comorbidities could affect the results of brain perfusion evaluation.
**Results:** The highest difference between median values of absolute SPECT perfusion between PSP-P and PSP-RS patients was observed in postcentral gyrus (AAL) (L) on the left side (PSP-P = -0.75 vs PSP-RS = 0.5; p=0.0033). For the remaining regions, no statistically significant differences in perfusion were found. Additionally for postcentral gyrus (AAL) we have performed perfusion asymmetry analysis for PSP-P and PSP-RS patients. For both groups, the perfusion asymmetry was negligible with respect to the corrected p value (p=0.0042), for PSP-P patients p=0.0140 and PSP-RS patients p=0.1045.
**Conclusions:** PSP-RS and PSP-P examination could be possibly facilitated using neuroimaging. The evaluation of the role of parietal lobe in PSP requires further analysis using more specific methods.

## P_182 (GPT)

### Remote assessments using wearable sensors can differentiate Progressive Supranuclear Palsy from Parkinson's disease

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**Background:** Wearable sensors have been shown to differentiate Progressive Supranuclear Palsy (PSP) from Parkinson's Disease (PD) in laboratory settings but have not been tested in participants' homes. Remote assessments increase accessibility and can be performed more frequently, reducing biological variability.
**Methods:** Participants with probable PSP or PD with reliable caregivers still able to ambulate 10 feet unassisted were recruited at Massachusetts General Hospital and Johns Hopkins between November, 2021- November, 2022. Participants were enrolled and consented remotely and instructed by video conference to operate a custom tablet solution (BioDigit Home$^{TM}$) and to wear three inertial sensors (LEGSys$^{TM}$ and BalanSense$^{TM}$, BioSensics LLC, Newton, MA USA) while performing the Timed Up and Go, 5x sit-to-stand, and 2-minute walk tests. PSPRS and MDS-UPDRS were collected virtually or during routine clinical visits.
**Results:** As of November, 2022, 13 PSP and 12 PD participants were enrolled. Three PSP participants were unable to complete virtual assessments due to lack of caregiver support, inadequate cellular service, or difficulty with video technology. Data was uninterpretable in two PD participants. Analyzed PSP participants (n = 10, age = 67.6 ± 1.3 years, 40% female) were well-matched to PD (n = 10, age = 70.3 ± 1.8 years, 40% female) except for disease duration (14 ± 3.5 months for PSP vs 87.9 ± 16.9 months for PD). Gait parameters showed significant group differences with an effect size ranging from d = 1.0 to 2.27. Gait speed was significantly slower in PSP: 0.45 ± 0.06 m/s vs. 0.79 ± 0.06 m/s in PD (d = 1.78, p < 0.001). Sit-to-stand transition duration showed a significant group difference (d = 1.12, p = 0.031) and correlated with the PSPRS gait sub-score (R = 0.65, p = 0.043).
**Conclusions:** Our study demonstrates the feasibility of differentiating PSP from PD remotely using wearable sensors. These findings are being validated in a larger sample.

## P_205 (GPT)

## Adult-onset tics after being crushed by an air conditioner – a case report

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**Background:** Tics are sudden, repetitive, non-rhythmic movements (motor) and/or vocalizations (phonic or vocal). Generally, tics begin during childhood as a part of Tourette syndrome (TS), commonly in males, and are associated with attention-deficit/hyperactivity disorder (ADHD) and/or obsessive-compulsive disorder (OCD). They rarely have an onset in adulthood. We present here an adult male who developed multiple motor and vocal tics within a couple of weeks following a closed head injury with alteration of consciousness.
**Methods:** Retrospective chart review and literature search.
**Results:** A 30-year-old man was crushed against the wall by a 4,100 pound air-conditioning unit at work, sustaining a traumatic brain injury (TBI) with alteration of consciousness. Two weeks after the injury, he developed motor tics in a rostral-caudal pattern, followed by simple and complex vocal tics. He had no personal or family history of tics, ADHD, or OCD before the injury. The motor tics included jerks of the neck, left arm, shoulder, and leg. Vocal tics included grunts, gasps, and palilalia. He endorsed a sense of relief after the expression of the tics. At the time of his injury, head imaging was unremarkable for any acute intracranial pathology. Due to concerns of blood pressure variability with alpha-agonists, he was started on pimozide which improved both his vocal and motor tics.
**Conclusions:** Tic disorders rarely start in adulthood, but a few cases have been described of their emergence following TBI. The tics post TBI may represent an unmasking of an underlying mild tic disorder or are a result of alterations to the brain circuitry following the injury. Clinically, they tend to mirror the rostral-caudal and motor to vocal pattern as seen in TS.

## P_214 (GPT)

## Another common genetic ataxia in South Korea: spinocerebellar ataxia 36

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**Background:** Spinocerebellar ataxia (SCA) 36 is caused by a repeat expansion of the intronic GGCCTG hexanucleotide in the *NOP56* gene. Although SCA 36 is believed to be highly prevalent in South Korea, the limited availability of genetic diagnostic tools has prevented the identification of cases. We investigated the prevalence and clinical features of individuals affected by SCA36 in the ataxia population using repeat-primed PCR (RP-PCR) and long read sequencing (LRS).
**Methods:** Patients were required to have negative testing for the SCA1, SCA2, SCA3, SCA6, SCA7, SCA8 and 17 and dentatorubral-pallidoluysian atrophy. RP-PCR was used to screen for the presence of a repeat expansion in the *NOP56* gene, and diagnosis of SCA36 was confirmed by LRS.
**Results:** In this study, 75 patients from 67 families with cerebellar ataxia were screened using RP-PCR. Out of these, 10 patients were suspected of having abnormal repeat expansion, which was later confirmed through LRS. The diagnosis of SCA36 was confirmed in ten patients from eight families (13.3%). The prevalence of SCA36 in the ataxia population of South Korea was found to be higher compared to the Galicia region (6.3%), Japan (3.6%), France (1.9%), and the United States (0.7%). The mean age of onset was 52.2 years, and seven of the 10 patients was female. All 10 patients presented with ataxia as the main symptom. Hyperreflexia (9/10, 90.0%), hearing impairment (7/10, 70.0%) and cerebellar atrophy in brain MRI (9/10, 90%) were common in SCA 36. In contrast, muscle atrophy (1/8. 12.5%) and fasciculation (1/6, 16.7%) were less commonly observed in SCA36 patients.
**Conclusions:** In the present study, LRS successfully detected pathological expansion in the *NOP56*, and revealed that SCA36 is common in South Korea. The diagnostic test for SCA36 should be considered in patients with ataxia, especially who had hyperreflexia or hearing impairment.

## P_237 (GPT)

## Predictors of bone marrow transplant outcomes in *CSF1*R-related adult-onset leukoencephalopathy with axonal spheroids and pigmented glia

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**Background:** Bone marrow transplant (BMT) is currently the only available therapy for *CSF1R*-related adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (*CSF1R*-ALSP); however, the clinical profile of the best candidates for this treatment was not ascertained. Therefore, we aimed to determine the predictors of good and poor BMT outcomes in *CSF1R*-ALSP.
**Methods:** The literature search for *CSF1R*-ALSP patients treated with BMT yielded 13 cases, of whom 5 were followed up in our center. Additionally, we recruited 2 new cases. Thus, total of 15 patients were included in the study. We collected detailed information on demographics, activities of daily living (ADL), professional activity, clinical and radiological characteristics in a structured manner. The patients who improved or did not worsen following BMT in clinical symptoms or were independent in ADL or professionally active had good outcomes, whereas the others were considered to have poor outcomes.
**Results:** The median age of onset and BMT was 39 and 43 years, respectively. First symptoms included cognitive dysfunction (43%), gait difficulty (21%), and neuropsychiatric disturbances (21%). Dependence in ADL and professional inactivity was noted in 55% and 67%, respectively, at the last follow-up visit at a median of 26 months after BMT. Cognition, neuropsychiatric disturbances, extrapyramidal, pyramidal signs, gait difficulty, and seizures improved or did not worsen in 60%, 67%, 54%, 75%, 73% and 91% after BMT, respectively. Good BMT outcomes were noted in 40% of patients and were associated with difficulty as the first (p=0.041) and dominant (p=0.017) presentation. In contrast, patients with cognitive dysfunction as the initial presentation had poor outcomes (p=0.016), and their cognition continued to worsen after BMT (p=0.025).
**Conclusions:** Gait difficulty, as the first and main presentation in *CSF1*R-ALSP, is associated with good BMT outcomes. Cognitive dysfunction, as the first manifestation, is linked to poor BMT outcomes.

## P_238 (GPT)

## Differences in patient and healthcare professional perspectives on the key impacts of tardive dyskinesia

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**Background:** Physical manifestations of tardive dyskinesia (TD) impact daily activities and present a substantial psychosocial burden. This study was designed to survey differences in perception of TD impact among US-based patients and healthcare professionals (HCPs).
**Methods:** Patients (adults with TD and schizophrenia, bipolar disorder [BD], or major depressive disorder [MDD]) and unconnected HCPs (psychiatrists, neurologists, or psychiatric nurse practitioners with ≥2 years' experience treating patients with schizophrenia, BD, or MDD and ≥1 patient with TD) participated in online surveys; HCPs reported on a specific, recently seen patient. Respondents ranked domains by TD impact, and rated impact within domains from 0 (least impact) to 10 (most impact; impact score is average response within domain).
**Results:** 154 patients and 150 HCPs responded to unlinked surveys. Most patients and HCPs reported the psychological/emotional domain as most impacted (40.9%, 53.3%, respectively); nearly double the patients versus HCPs reported the physical domain as most impacted (33.1%, 16.7%; *P*<.01), while similar proportions reported social (22.1%, 26.7%) and professional (3.9%, 3.3%) domains as most impacted. Patients reported significantly higher (*P*<.001) psychological/emotional (mean score [SD], 4.1 [2.4] vs 2.6 [2.0]), physical (3.0 [1.8] vs 1.1 [1.2]), social (3.7 [2.3] vs 2.6 [2.0]), and professional (4.9 [2.9] vs 3.4 [2.9]) impact than HCPs. Specifically, there were significant differences (*P*<.001) in proportions of patients/HCPs reporting that they or their patient had ever experienced feelings of anxiety, sadness, anger, or loss of focus; physical impacts on sleeping, speaking, walking, holding onto objects, pain, or breathing; social difficulties in communication with others; and difficulties with professional interactions at work/school, work/school performance and attendance, job retention, volunteering, or pursuing further education or work promotion.
**Conclusions:** In unlinked surveys, patients reported greater TD impact across domains, especially in psychological/emotional and physical subdomains. These results highlight the need for better dialogue between HCPs and patients.

## P_239 (GPT)

## A novel *C19ORF12* mutation in two MPAN sisters treated with deferiprone

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**Background:** Mitochondrial membrane protein-associated neurodegeneration (MPAN) is a rare and devastating disease caused by pathogenic mutations in the *C19orf12* gene. MPAN is characterized by pathological iron accumulation in the brain. Less than 100 patients with MPAN have been described. Although the diagnosis of MPAN has achieved a great breakthrough with the application of the whole exome gene sequencing technology, effect of iron chelation therapy in MPAN remains controversial.
**Methods:** We reported that the proband and her sister from the same family diagnosed with MPAN had dramatically different responses to deferiprone (DFP) treatment. The diagnosis of MPAN were established based on typical clinical manifestations, brain magnetic resonance imaging (MRI) and genetic testing.
**Results:** The clinical presentations of the two patients with MPAN due to novel gene locus mutations (exon3:c.371T>G,p.Met124Arg) were similar to those previously reported. There is no other difference in basic information except that the proband had a later onset age and fertility history Compared with cases reported in the previous literature. Both the proband and her sister were treated with deferiprone (DFP), but they had dramatically different responses to the DFP treatment. The proband's condition including psychiatric symptoms and movement disorders deteriorated sharply after DFP treatment. However, the proband' sister became relatively stable after receiving DFP treatment. After four years of follow-up, the patient still denies any new symptoms of neurological deficits.
**Conclusions:** Our newly discovered mutation sites enrich the gene databaseand indicated that DFP might delay the progress of MPAN in patients without severe autonomic neuropsychiatric impairment at the early stage of the disease.

### P_242 (GPT)

### Real-world adherence to deutetrabenazine or valbenazine among patients with tardive dyskinesia

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**Background:** Data on adherence patterns of vesicular monoamine transporter type 2 (VMAT2) inhibitors, deutetrabenazine (DTBZ) and valbenazine (VBZ), are limited. This study was designed to describe real-world DTBZ and VBZ adherence among patients with tardive dyskinesia (TD).
**Methods:** Using the Symphony Health Solutions' Integrated Dataverse (May 2017–May 2019), adults with ≥1 TD diagnosis and ≥1 prescription for DTBZ or VBZ (first defined as index date), were identified. Outcomes included adherence rate (proportion of days covered [PDC] >80%), PDC, discontinuation rate, and healthcare resource utilization (HCRU) for 6 months starting 30 days after index date.
**Results:** 362 and 224 patients were identified for the DTBZ and VBZ cohorts, respectively. Adherence rates (53.3% vs 50.9%, *P*=.6098), PDCs (mean [SD]; 70.7% [29.6] vs 68.5% [30.8], *P*=.4839), and discontinuation rates (36.2% vs 40.6%; log-rank *P*=.227) were not significantly different between DTBZ and VBZ cohorts; similar results were obtained after adjusting for baseline characteristics. DTBZ adherent and non-adherent cohorts were not significantly different in comorbidity, concomitant treatment, and HCRU profiles, except for substance-related/addictive disorders (15.0% vs 24.3%), schizoaffective disorder (6.7% vs 18.3%), diarrhea (1.6% vs 6.5%), all-cause inpatient admission (8.3% vs 15.4%), and all-cause or psychiatric-related emergency department (ED) visit (17.1% vs 27.2% or 7.8% vs 18.3%, all *P*<.05). VBZ adherent and non-adherent cohorts were not significantly different except for diabetes with chronic complication (4.4% vs 11.8), depressive disorders (33.3% vs 20.0%), antidepressant agent use (67.5% vs 44.5%), and all-cause or TD-related ED visit (22.8% vs 37.3% or 2.6% vs 9.1%, all *P*<.05).
**Conclusions:** Patients with TD who were treated with DTBZ or VBZ had adherence rates, PDCs, and discontinuation rates that were not significantly different. In addition, patients in the adherent cohort were less likely to have an HCRU event compared with those who were non-adherent.

## Guided Poster Tour: Resident and Trainee I

### P_68 (GPT)

### Longitudinal cognitive changes in genetic and idiopathic Parkinson's disease: 5-year follow-up study

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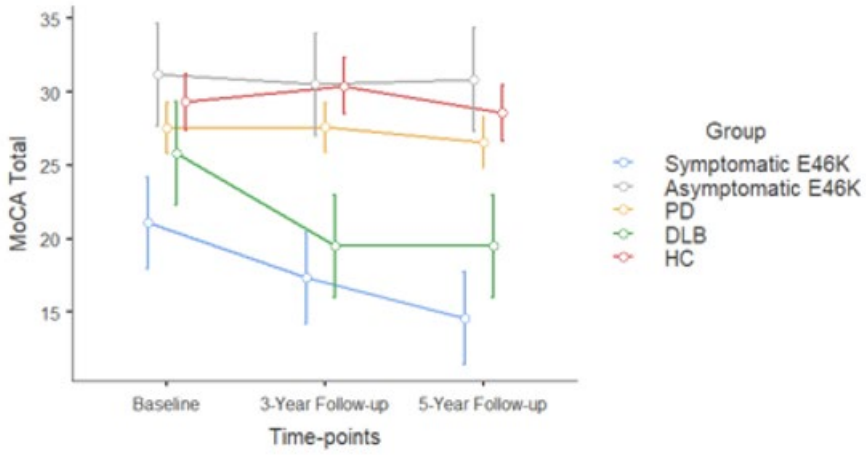
**Background:** Cognitive deficits are common in Parkinson's disease (PD), however, longitudinal studies assessing cognitive progression in idiopathic and genetic PD are lacking. This study aimed to investigate whether cognition differs in genetic or idiopathic PD compared to dementia with Lewy body (DLB) patients and controls over a 5-year period with 3 time-points.
**Methods:** Sixty-seven patients [n=7 E46K-SNCA (3 asymptomatic and 4 symptomatic carriers), n=3 DLB, n=37 idiopathic PD and 20 normal controls] underwent cognitive assessment at 3-time points (baseline, 3-year follow-up, 5-year follow-up). Cognitive assessment included the Montreal Cognitive Assessment adjusted for age (years) and years of education. Repeated measures analysis of variance (ANOVA) (3-times x 5-groups) was used to evaluate cognitive changes and post-hoc tests were acquired.
**Results:** Repeated measures ANOVA showed that there was a significant time ($F=17.11$, $p<.001$ $\eta^2_p=0.225$), group ($F=15.90$, $p<.001$ $\eta^2_p=0.518$) and time x group interaction effect ($F=5.29$, $p<.001$, $\eta^2_p=0.264$). Specifically, significant time x group interaction was found when baseline and 3-year ($t=3.73$, $p<.001$) or 5-year follow-up was compared ($t=5.77$, $p<.001$), and between 3-year and 5-year follow-up ($t=2.04$, $p=0.044$). Additionally, significant differences ($p<.001$) were found between symptomatic E46K carriers and all groups evaluated except for DLB group.




Note. E46K= E46K carriers of alpha-synuclein gene; PD=Parkinson's disease; DLB=Dementia with Lewy bodies; HC= healthy controls

**Conclusions:** These findings suggest that global cognition deteriorates over 5 years, being more marked in symptomatic-E46K and DLB patients during the first 3-years, but not in idiopathic PD or in asymptomatic E46K. For future studies it would be interesting to study cognition according to PD-MCI Level II together with motor and non-motor symptomatology to early identify the course of this heterogeneous disease.

## P_95 (GPT)

## Evidence of intrinsic vestibular deficits in Parkinson's disease correlated with brain cholinergic system integrity

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**Background:** Chronic bilateral vestibular dysfunction of older age, so-called presbyvestibulopathy (PVP), affects neurologically intact aging adults and those with Parkinson's disease (PD) alike. Clear and definite evidence of individuals with PD being more likely to have more severe vestibular system dysfunction than normal age-matched counterparts has been slow to emerge. The vestibular system is subject to frequency-dependent

reduction in function with normal aging, but it is unclear whether additional PD-specific vestibular system changes may occur simultaneously.
**Methods:** Detailed vestibular testing was performed in PD subjects (n = 14; M12/F2; mean age 70.6 ± 4.6 years) and older adult normal controls (NC) (n = 15; M6/F9; mean age 68.3 ± 5.9 years) to examine the responsiveness of the vestibular system across a broad frequency range from 0.01 to 0.32 Hz. Clinical assessments include the video head impulse test, sinusoidal harmonic acceleration (SHA), and bithermal water caloric irrigation. The patients also underwent a PET scan for the regional cerebral vesicular acetylcholine transporter (VAChT) ligand [$^{18}$F]-fluoroethoxybenzovesamicol (FEOBV).
**Results:** The mean SHA gain was higher in the NC group than in the PD group across all frequencies and differed significantly at 0.01 Hz ($p < 0.05$). This frequency also correlated with regional FEOBV binding. Significant correlation was found in left hemisphere primary and early visual associative cortices with less correlation in downstream cortices. A more even distribution was found in right hemisphere cortices.
**Conclusions:** We conclude that vestibular deficits cannot solely be explained by the presence of PVP in PD suggesting additional disease-specific changes. Evidence of abnormal vestibulo-ocular gain in PD correlates with cholinergic vulnerability in visual and wider right hemispheric coritcal reigions. The right hemisphere is dominant for vestibular functions, and our findings point to deficient visual-vestibular integration. These findings may augur novel treatment approaches, such as portable thermoneuromodulation or galvanic stimulation in PD persons with postural changes.

## P_103 (GPT)

### Effect of changes in stomach and small intestinal pH on response to levodopa in patients with Parkinson's disease

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**Background:** A relationship between levodopa response and pH throughout the stomach and small intestine in patients with Parkinson's Disease (PwPD) was explored using SmartPill wireless motility capsules. Establishing a connection will better elucidate the impact of pH on levodopa absorption.
**Methods:** The study included 10 patients with typical response to levodopa (time to "ON" within an hour) and 10 erratic responders (sudden "ON"/"OFFs", delayed time to "ON", response failure). SmartPill captured pH data from stomach and small intestine, as well as motility data. For three hours, assessment of dose response by finger tapping scores and patient reporting was obtained every 30 minutes.
**Results:** For approximate median stomach pH, most typical responders had values between 0.5 and 1.5; most erratic responders were between 0.5 and 2.5. For approximate median small intestine pH, most typical responders had values between 6.5 and 7.5; most erratic responders had values between 6 and 7. Of the typical responders, 9 reported being ON within an hour of their first dose of levodopa. Only 6 erratic responders reported being ON within one hour. At 180 minutes, 8 of the erratic responders reported being ON, though only 2 typical responders reported still feeling ON. Finger tapping scores improved for 90% of typical responders in one hour compared to only 50% of erratic responders.
**Conclusions:** Erratic responders reported more delayed time to ON than typical responders. In the stomach, erratic responders showed more spread of approximate pH values and more above 1.5. Typical responder's approximate pH values in the small intestine were slightly more alkaline. Further exploration of differences in pH throughout the stomach and small intestine can reveal differences in absorption of levodopa. Defining the ideal range of pH for levodopa absorption can provide crucial information for improving efficacy of doses and clinical outcomes for PwPD.

## P_107 (GPT)

### Touchscreen nQ application as a remote digital biomarker in Parkinson disease

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**Background:** To date, a reliable biomarker of motor severity and progression in Parkinson disease (PD) remains elusive. nQ's machine learning platform leverages touchscreen keyboard inputs from a personal computer or smartphone to produce quantitative measurements (nQiTouchPD score) passively characterizing motor state. Indeed, typing performance *in-clinic*, using the nQ platform, has been shown to distinguish early PD versus normative keystroke patterns [1]. This study extends its use as a biomarker for PD motor function in the natural home setting.

**Methods:** Participants with PD diagnosed and followed at Cleveland Clinic for <10 years and age-matched controls were recruited. The nQ keyboard application was incorporated in their personal touchscreen device. Typing performance was assessed *in-clinic* (5-minute typing task) and *at-home* (normal typing activity over three weeks). nQiTouchPD measurements *in-clinic* and *at-home* were correlated with the MDS-UPDRS Part III.
**Results:** 31 PD and 29 controls participated, with a mean MDS-UPDRS III of 27.4 (SD=10.7) and 2.6 (SD=3.7), respectively. Data from 62,632 typing sessions and 1,917,626 total keystrokes were analyzed. nQiTouchPD *in-clinic* and *at-home* directly correlated with MDS-UPDRS III (r=0.34, p<0.001, and r=0.53, p<0.001, respectively). The area under the curve was greater *at-home* than *in-clinic* (0.74 vs 0.69). In the PD cohort, nQiTouchPD correlated best with rigidity (r=0.48; p<0.05), followed by the bradykinesia (r=0.26; p=-0.18), and least with posture/gait (r=0.09; p=0.65) and tremors (r=-0.08; p=-0.68).
**Conclusions:** nQ touchscreen keyboard application used in the natural home setting can differentiate PD from controls. nQiTouchPD correlated with motor states assessed using MDS-UPDRS III, supporting its potential as a PD digital biomarker. Higher data volume used to compute *at-home* scores (weekly aggregate) compared to *in-clinic* (5-minute typing task) could explain better nQ performance in the home setting. In addition, natural home settings might capture impaired states better than controlled settings.
[1] T. Arroyo-Gallego *et al*., Detection of Motor Impairment in Parkinson's Disease Via Mobile Touchscreen Typing. *IEEE Transactions on Biomedical Engineering*, 2017; 64 (9):1994-2002. doi: 10.1109/TBME.2017.2664802.

## P_164 (GPT)

### Association between lifestyle and environmental factors with disease severity and age at onset in multi-ethnic Malaysian Parkinson's disease patients

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**Background:** Caffeine and cigarette smoke exposure are associated with reduced Parkinson's disease (PD) risk, while various toxins increase the risk of PD. However, whether these factors influence the age at onset (Aao) or severity of PD remains unclear. We explored the association between self-reported exposure to caffeine, smoking, and environmental toxins (pesticides, chemical solvents, heavy metals, other chemicals, and fumes) with Aao and severity of PD in a Malaysian cohort.
**Methods:** The Mini Environmental Risk Questionnaire for PD (MERQ-PD-B) was completed by patients. This included seven items on past (before PD diagnosis) and current exposure to caffeine and cigarette smoking. PD severity was evaluated by neurologists using the Clinical Impression of Severity Index for PD (CISI-PD), covering motor signs, disability, motor complications, and cognition. Spearman correlation was used to investigate the relationship between lifestyle/ environmental factors with Aao and severity of PD.
**Results:** Among the 686 patients (55.2% male; median age=67[11] years; 82.7% late-onset PD[LOPD] with Aao>50years), prior history of caffeine intake or smoking exposure, as well as quantity of past caffeine intake or cigarette pack-years did not correlate with Aao. Current caffeine drinking status correlated with better CISI- total score (r=-0.17, P<0.001) and sub-scores for motor signs (r=-0.13, P=0.001) and disability (r=-0.17, P<0.001). However, among current caffeine consumers, the quantity of caffeine intake did not correlate with PD severity. Heavy metal exposure correlated weakly with worse CISI-total score (r=0.08, p<0.05) and subscores for motor complications (r=0.12, p<0.05) and cognition (r=0.08, p<0.05). Chemical solvent exposure correlated weakly with motor complications (r=0.09, p<0.05). Pesticides, other chemicals, and fumes showed no significant correlation with PD severity. Meanwhile, exposure to these environmental toxins showed no correlation with Aao.
**Conclusions:** Current caffeine intake was associated with lesser, whereas heavy metals and chemical solvents with greater disease severity. We observed no association between lifestyle/environmental factors and PD Aao.

## P_165 (GPT)

### Establishing a framework for quality of inpatient care for Parkinson's disease: a study on inpatient medication administration

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**Background:** The complexity of antiparkinsonian medications makes patients vulnerable to medication deviations. Past studies focused on a deviation between inpatient medication orders and inpatient administrations. This study examines the frequency and outcomes of deviations between outpatient regimen and inpatient medication administrations in patients with Parkinson's disease (PD).
**Methods:** We included hospital admissions of patients with PD during a 12-month period at the Cleveland Clinic Main and Fairview campuses. Outpatient regimens were compared with hospital medication administration records to establish rates of deviations in terms of 1) levodopa equivalent daily dose (LEDD) difference, 2) timing deviations/omissions of time-critical medications, 3) substitution of levodopa compounds, and 4) administration of contraindicated medications. Logistic regression analyses were used to investigate associations with length of stay (LOS), readmission rates, and mortality.
**Results:** The study included 492 patients with 725 admissions. Of those on time-critical medications, 43% had a LEDD deviation and 19% had levodopa formulation substitutions. Of the admission days with known outpatient timing regimens, 47% had an average deviation of more than 30 minutes and 22% had at least one missed levodopa dose. LOS was longer with each additional day of over-dose (4%), under-dose (14%), missed dose (21%), timing deviation (15%) and substitution (19%), (all $p<0.0001$). Contraindicated medications were administered in 9.9% of admissions, with haloperidol comprising 34%, followed by olanzapine (23%) and metoclopramide (17%). Administration of contraindicated medications was associated with increased 30-day readmission/death (OR 1.85, $p=0.041$), 90-day mortality (OR 2.2, $p=0.018$), and LOS (7.6 vs. 3.8 days, $p<0.0001$). LEDD underdose was associated with 30-day readmission/death (OR 1.78, $p=0.025$) and 90-day mortality (OR 1.14, CI 1.05-1.24, $p=0.002$).
**Conclusions:** Deviations between outpatient and hospital regimens, and administration of contraindicated medications, were associated with poor outcomes.

### P_253 (GPT)

### Effects of aerobic exercise on motor and non-motor symptoms of Parkinson's disease: a systematic review and meta-analysis

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**Background:** Parkinson's disease (PD) is a motor system disorder causing tremors, stiffness, and slowness. Aerobic exercise is a non-pharmacological intervention to relieve these symptoms and improve the quality of life of people with PD, but evidence supporting its effectiveness is inconclusive. This study aims to evaluate the effects of aerobic exercise on the motor symptoms, quality of life, and cognitive function of people with PD.
**Methods:** We searched several databases, including PubMed, Scopus, and Web of Science, until December 2022 for studies investigating the effects of aerobic exercise on people with PD and reporting outcomes related to motor symptoms, quality of life, and/or cognitive function. We used R version 4.0.3 statistical computing software with metafor and meta package for statistical analysis.
**Results:** The review analyzed 20 studies with 735 participants, 382 receiving aerobic exercise and 353 as controls. The results showed that aerobic exercise had a significant positive effect on motor symptoms in people with Parkinson's disease. Specifically, there was a significant improvement in the timed up and go test (SMD: -0.49; 95% CI: -0.75 to -0.23, $p < 0.01$, $I2=29\%$), Berg Balance Scale (SMD: 1.06; 95% CI: 0.77 to 1.35, $p < 0.01$, $I2=21\%$), stride/step length (SMD: 0.32; 95% CI: 0.004 to 0.63, $p < 0.05$, $I2=0\%$), and gait velocity (SMD: 0.55; 95% CI: 0.15 to 0.96, $p < 0.01$, $I2=36\%$). Moreover, the aerobic exercise interventions significantly improved the Unified Parkinson’s Disease Rating Scale Part-III (SMD: -0.48 points; 95% CI: -0.73 to -0.23) and the 6-minute walking test (SMD: 0.41; 95% CI: 0.07 to 0.74).
**Conclusions:** Aerobic exercise effectively improves motor symptoms, gait, and balance in people with Parkinson's disease. It significantly improves people with PD's quality of life and motor function. These findings will aid in developing future interventions and recommendations for clinicians and patients.

## Guided Poster Tour: Resident and Trainee II

### P_62 (GPT)

### Exploration of antipsychotic prescribing practices among movement disorders subspecialists for patients with Parkinson's disease dementia and dementia with Lewy Bodies

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**Background:** Psychosis in patients with Parkinson's Disease Dementia (PDD) and Dementia with Lewy Bodies (DLB) negatively impacts quality of life and increases healthcare resource utilization. Managing psychosis is

challenging as many antipsychotic drugs (APDs) can worsen parkinsonian symptoms. Pimavanserin has been associated with superior outcomes and fewer adverse effects than other APDs, but the prevalence of its use in practice has not been well-studied. This study explored APD prescribing practices with a focus on Pimavanserin in the PDD and DLB populations.
**Methods:** Physician members of the International Parkinson and Movement Disorder Society (MDS) were surveyed regarding management of psychosis in patients with PDD and DLB.
**Results:** 496 physicians from 85 countries completed the survey. Quetiapine was the most prescribed APD for both PDD (54.6%) and DLB (44.2%). Only 30% of all respondents had ever used Pimavanserin; of these, 65.8% reported using it only for escalation of therapy after other drugs failed. Limitations in use of Pimavanserin most cited were cost (80.4%) and availability (51.9%). Pimavanserin use was higher among U.S.-based respondents compared to the international community [PDD OR = 4.52 (CI 1.68-12.15), DLB OR = 4.19 (CI 1.79-9.82)]. Among all Pimavanserin prescribers, U.S respondents were less likely to use Pimavanserin first-line vs as escalation therapy [OR=0.37 (CI 0.16-0.86)]. Pimavanserin prescribers in the academic setting were also less likely to use Pimavanserin first-line compared to those in the community setting [OR = 0.32 (CI 0.14-0.69)].
**Conclusions:** Quetiapine is the most popular APD for both PDD and DLB. Pimavanserin use is more common overall among U.S. respondents, largely owing to its limited availability internationally; however, U.S prescribers are less likely to use Pimavanserin first-line and more likely to use it as escalation therapy. Use of Pimavanserin first-line is more common among providers in the community setting compared to the academic setting.

## P_194 (GPT)

### Adult-onset cervical dystonia with botulinum toxin resistance and approach to severe spine deformity for deep brain stimulation: a case report

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**Background:** Cervical dystonia (CD), the most common adult-onset focal dystonia, can cause abnormal postures of the head/neck and is often treated with injections of botulinum toxin. Secondary non-response/resistance can occur in patients who previously derived benefit. Cervical spine degeneration often affects upper cervical levels in CD patients. We report the management complexity of a patient with longstanding CD and severe cervical degeneration with concern for osseous fusion.
**Methods:** An 81-year-old woman with 30+ year history of CD had developed secondary resistance to both onabotulinumtoxinA and rimabotulinumtoxinB. In 2021, she developed fixed posture with severe right head tilt (ear touching shoulder), right shoulder elevation, and notable hypertrophy of right posterior neck musculature. Therefore, consideration was given to pallidal deep brain stimulation (DBS) for her CD.
**Results:** Further complicating her presentation was severe cervical spine coronal deformity with possible autofusion at multiple cervical levels, making her a difficult candidate for DBS. Attempts to reduce her deformity under general anesthesia were unsuccessful. Additional imaging sequences revealed destruction in the right-sided C2 lateral mass. She underwent cervical traction and partial reduction that ultimately allowed her to undergo successful DBS lead placement. Six months later, she has had 80% reduction in pain/spasms and improvement in neck range of motion.
**Conclusions:** The complexity of this case illustrates the importance of careful consideration of the sequence of interventions. In patients with CD, there is greater concern for spinal hardware failure given CD is an abnormality of central motor processing which can overcome any attempted spine fixation. This often results in a preference to first proceed with treatment of CD, but in cases such as this where a patient has botulinum toxin resistance to both serotype A and B, as well as multilevel cervical spine deformity such that posture appears fixed, the management pathway is more challenging.

## P_201 (GPT)

### New-onset Chorea post-SARS-CoV-2 infection: a case report

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**Background:** Although the severe acute respiratory syndrome (SARS) coronavirus (COV)-2 primarily involves the cardiovascular and respiratory systems, neurological manifestations including movement disorders have also been reported, the most common being myoclonus and ataxia. However, the occurrence of post-COVID-19 chorea is rare, and to our knowledge, there have been less than 10 cases reported in the literature.
**Methods:** Retrospective chart review and literature search.

**Results:** A 91-year-old lady presented to our movement disorder clinic for evaluation of abnormal involuntary movements. About 5 months ago, she had a bout of mild cough, and runny nose and was diagnosed with COVID-19 after testing positive for coronavirus reverse-transcription polymerase chain reaction (RT-PCR) by nasopharyngeal swab. She did not require admission and recovered in home isolation. Two weeks from the symptom onset, she developed excessive involuntary movements of the tongue, jaw, and face. Then, slowly over the next several months, she started to develop these excessive movements involving the arms, legs, and torso. There was no family history of any involuntary abnormal movements and no personal history of neuroleptics or other dopamine blockers. Neuroimaging was unremarkable. Systemic and neurological examinations were normal except for choreiform movements in the face and all four limbs, albeit left predominant and causing gait instability. Extensive diagnostic testing including a serum paraneoplastic panel was found to be unremarkable. She was started on a VMAT-2 inhibitor (tetrabenazine) with moderate relief.
**Conclusions:** Neurological complications with SARS-CoV2 occur via hypoxic brain damage and/or immune-mediated damage to the central nervous system. In the post-SARS-CoV2 setting, clinicians should be aware of chorea as a post-infectious complication that seems to be independent of the severity of the COVID-19 infection.

## P_204 (GPT)

### Persistent chorea gravidarum with an autoimmune etiology: a follow up four years later

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**Background:** Chorea gravidarum is the onset of any choreic movements occurring during pregnancy. Two-thirds of cases arise during the first trimester of pregnancy before spontaneously resolving before delivery. In the remaining one-third of cases, most will resolve after delivery, however, for a rare subset of patients, chorea can persist. For these patients, symptoms can interfere with activities of daily living, or become severe enough to lead to weight loss, self-injury, rhabdomyolysis, hyperthermia, and death.
**Methods:** A 28 year old female had severe disabling ballistic chorea with each of her three pregnancies which did not resolve spontaneously following her third pregnancy persisting thirteen years. Labs and imaging were obtained and did not provide insight into the etiology of her chorea. Standard treatment of the chorea was not well tolerated and ineffective. Hormonal therapy produced minimal reduction in the chorea. It was postulated that there may be an autoimmune etiology to her chorea given unresponsiveness to standard treatment and negative work up.
**Results:** Steroids and IVIG were tried and had the most improvement of her symptoms. She now has minimal unilateral chorea that has been maintained with IVIG therapy over the past six months.
**Conclusions:** The treatment for chorea gravidarum is largely based on the etiology of the chorea which has a broad differential diagnosis. Autoimmune mediated chorea resulting from antibodies targeting the basal ganglia is an entity gaining more attention with new biomarkers being found. Parainfectious, paraneoplastic, systemic and idiopathic diseases should be considered as possible triggers. The use of IVIG in this case is important when considering that dopamine receptor blockers are considered pregnancy category C during the first trimester and many treatment options are not at the practitioners' disposal should a severe case present. IVIG may provide a safe treatment worth trying in the case of suspected autoimmune etiology in chorea gravidarum.

## P_212 (GPT)

### Translation and argentinean adaptation of the scale for the assessment and classification of Ataxia (SARA)

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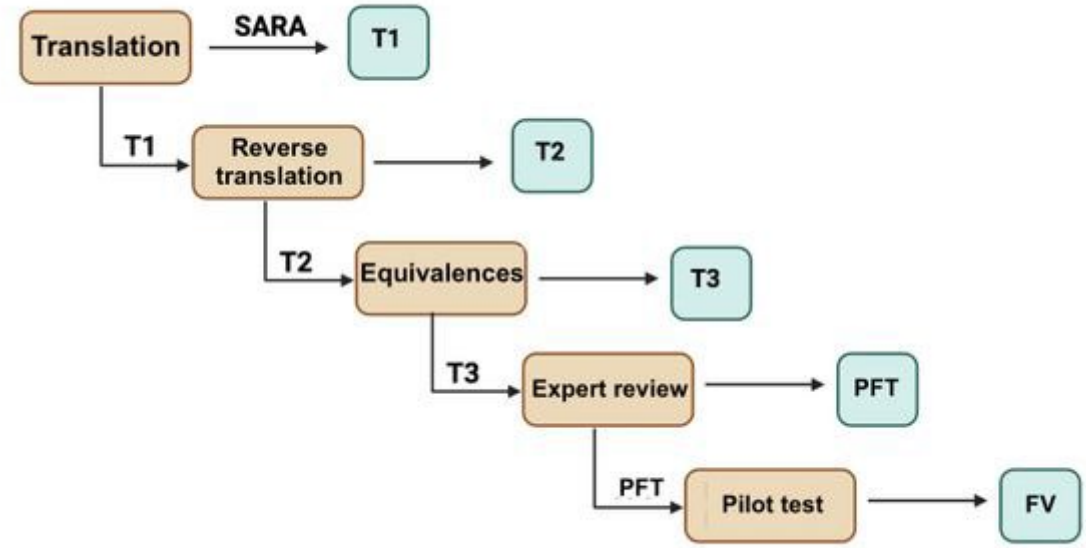
**Background:** Ataxias comprise a heterogeneous group of disorders, which may be multicausal, including genetically determined forms, immune-mediated forms, or secondary to structural damage processes (ischemic stroke, multiple sclerosis) or metabolic/toxic alterations.
There is a growing interest in the diagnosis and management of patients with hereditary ataxias, which makes relevant the need for sensitive and ideally locally validated scales.
At present there are several rating scales, one of them being the "Scale of the Assessment and Rating of Ataxia" (SARA), whose cross-cultural adaptation and validation is available in several languages, but not in Spanish.
The objective of this work is to translate and cross-culturally adapt the "Scale of the Assessment and Rating of Ataxia" (SARA) to Spanish and to carry out a pilot test for its subsequent validation in this language.
**Methods:** The SARA scale was translated and linguistically adapted to Spanish. Subsequently, the translated scale was applied in a population of 13 patients with a diagnosis of genetically established (11) or immune-

mediated (2) ataxia. Internal consistency was analyzed by Cronbach's alpha coefficient and external validity by correlations with the Barthel index, stage of disease and duration of the disease.

**Figure 1. Stages of the cross-cultural adaptation process**




SARA: Scale for the Assessment and Rating of Ataxia (English), T1: English-Spanish translation, T2: reverse translation from Spanish to English, T3: unified Spanish translation after conceptual equivalences, PFT: pre-final Spanish translation, FV: final version after pilot test observations and expert suggestions.

**Results:** The scale was translated maintaining semantic equivalence. The preliminary study showed adequate internal consistency (Cronbach's alpha=0.87). Significant associations were found between the SARA scale and the Barthel index (r=0.94, p<0.01) and stage of illness (rho=0.921, p<0.01).
**Conclusions:** A cross-culturally adapted version of the SARA scale was generated, with a pilot test with encouraging preliminary results for further validation in ataxia patients.

### P_218 (GPT)

### A case series of essential tremor featuring rest tremor of the lower extremities

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**Background:** Essential Tremor (ET) is a postural/kinetic tremor. The observation of rest tremor can present a diagnostic challenge. The literature suggests that rest tremor is limited to the upper extremities, not the lower extremities, in longstanding ET. We report three ET cases with rest tremor of legs which demonstrate the complexity of clinically differentiating from diagnoses like Parkinson's Disease (PD).
**Methods:** We are reporting a series of 3 patients, ages 60, 67, and 79, with gradually progressive onset of action tremor involving the arms, legs, head, and voice ranging from a 7-year to more than 30-year history of tremor. All of these patients developed rest tremor of the arms and legs several years after action tremor onset. To date, two of these patients have undergone (123I) ioflupane dopamine-transporter SPECT (DaTscan) which showed normal symmetric striatal uptake bilaterally.
**Results:** Among these patients, examination showed no signs of dystonic posturing or clear evidence of parkinsonism. They all had suboptimal control of tremor with medication management alone and two of these patients have pursued deep brain stimulation (DBS).
**Conclusions:** This case series presents patients with ET who manifest rest tremor in the legs with normal DaTscans. While the era of biomarker development is evolving and changing our methods for confirming a clinical diagnosis of PD, DaTscan remains an important tool in distinguishing between PD and ET. In the correct clinical context, rest tremor of the legs should not necessarily preclude a diagnosis of ET.

## Guided Poster Tour: PD: Therapy

## P_48 (GPT)

### Pallidal deep brain stimulation for Tourette's syndrome: a case series

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**Background:** Tourette syndrome (TS) is a neurodevelopmental disorder that has an onset in childhood and is characterized by multiple vocal and motor tics. It usually peaks by 12 years of age with cessation of symptoms in most patients by early adulthood. About 20% of the patients can continue to experience distressing and persistent tics throughout adulthood. Such cases are treated with conventional (pharmacological and/or cognitive behavior) therapies. In cases where the symptoms are refractory to the aforementioned measures, deep brain stimulation (DBS) can be considered an alternative option to achieve symptomatic benefit.
Disturbances in the cortico-basal ganglia-thalamo-cortical (CBGTC) circuitry have been postulated as the underlying pathophysiology of TS, while the limbic, sensorimotor, and associative circuits attribute to the comorbidities such as attention-deficit hyperactivity disorder, obsessive-compulsive disorder, or depression. Hence, the target location for TS is chosen based on the CBGTC circuitry and comorbidities, with the most common targets being the thalamic nuclei and the globus pallidus internus (GPi). We describe the outcomes of 3 cases with refractory TS who underwent GPi DBS implantation at our center.
**Methods:** Retrospective chart review and literature search.
**Results:**

| | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Age (years)/ Gender | 35 / Male | 78 / Male | 35 / Male |
| Age (Years)of onset of Tics | 4 | 8 | 8 |
| Tic Types | Oral (lip licking, biting)<br>Lingual (biting)<br>Vocal (grunting, singing) | Head twitching<br>Vocal (grunting) | -Startle (jumping up from the chair)<br>-Vocal (intermittent yelling, "barking" coprolalia).<br>-Motor tics (head jerk, extremities twitch, "squinting"). |
| Medical refractoriness prior to DBS implantation | -Quetiapine<br>-Clonazepam<br>-Clomipramine<br>-Risperidone<br>-Trazodone<br>- Clonidine | -Haloperidol<br>-Ziprasidone<br>-Pimozide<br>-Risperidone<br>-Methylphenidate<br>-Aripiprazole<br>-Benztropine<br>-Carbidopa-Levodopa<br>-Amantadine<br>-Sertraline | -Ziprasidone<br>-Clonidine<br>-Risperidone<br>-Quetiapine<br>-Gabapentin<br>-Pimozide<br>-Olanzapine<br>-Guanfacine<br>-Tetrabenazine<br>-Clonazepam<br>-Ropinirole |
| Neuropsychiatric Comorbidities | Impulse control disorder<br>Anxiety<br>Depression | Parkinson's disease (tremor predominant)<br>Obsessive compulsive disorder<br>Anxiety | Depression<br>Restless legs syndrome |
| Age (Years) at implantation / Site | 29 / GPi | 69 /GPi | 27 / Centromedian-parafascicular)<br>32 / GPi |
| Outcome | >50% improvement | ~25% improvement | <20% improvement |
| Side effects of DBS | Right foot dystonia | Left leg dystonia | Worsening headache<br>Blurry vision |
| Current medications | -Clomipramine<br>-Trazodone<br>-Clonidine<br>-Risperidone PRN | -Carbidopa-levodopa,<br>-Amantadine<br>-Ropinirole 4 mg bid | -Aripiprazole<br>-Baclofen<br>-Cannabidiol<br>Clonidine<br>-Risperidone<br>-Tetrabenazine<br>-Vortioxetine |

**Conclusions:** DBS is a clinically effective option for patients with treatment-refractory TS. Determination of the optimal target should be based on the patient's symptomatology and comorbid disorders. The reduction rates in tic symptoms will differ across patient populations, especially when additional comorbidities are in play.

## P_50 (GPT)

### The location of subthalamic nucleus neurostimulation is associated with axial motor outcomes in Parkinson's disease

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**Background:** Subthalamic nucleus (STN) deep brain stimulation (DBS) improves limb tremor, rigidity, and bradykinesia in people with Parkinson's disease (PD), but its effect on axial motor signs is less well-characterized.

The location of lead placement may differentially affect limb vs. axial motor outcomes. In this study, we investigate the effect of STN DBS on axial symptoms and the role of electrode location on axial motor scores.
**Methods:** This single institution retrospective cohort study evaluated 68 patients with advanced PD at 6- or 12-month follow-up after bilateral STN DBS. Axial scores were assessed using the MDS-UPDRS for parts 3.1 (speech), 3.3a (neck rigidity), 3.9 (arising from chair), 3.10 (gait), 3.11 (freezing of gait), 3.12 (postural stability), and 3.13 (posture). The total axial score was defined by the sum of these subscores, and scores were compared between different treatment conditions on and off medication and/or stimulation. Multiple linear regression was performed to determine the association between electrode location (defined by x, y, and z coordinates) and axial scores (OFF MED-ON STIM), controlling for LED reduction, total motor improvement, and axial scores (OFF MED-OFF STIM).
**Results:** STN DBS (OFF MED-ON STIM) improved the mean total axial score compared to the OFF MED-OFF STIM condition (6.53 ± 4.49 vs. 9.19 ± 5.48, p<0.0001). Neck rigidity, arising from chair, gait, freezing of gait, and posture, but not speech or postural stability, were improved. A more dorsal electrode location on the right was associated with increased (worse) total axial score (slope = 0.397, p=0.0116).
**Conclusions:** STN DBS improves axial signs in PD, and a more ventral electrode location in the right STN is associated with improved total axial score. Analysis of electrode location in other DBS cohorts is warranted to determine if this is the optimal stimulation location to improve axial signs.

## P_52 (GPT)

### Effectiveness of deep brain stimulation in Vietnamese patients with advanced Parkinson's disease

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**Background:** Deep brain stimulation (DBS) has been clinically effective and cost – efficient therapy for advanced Parkinson's disease (APD). This study aimed to evaluate the clinical efficacy and cost–effectiveness of DBS in the Vietnamese healthcare system.
**Methods:** This was a prospective, longitudinal study comparing two cohorts of APD patients, one group having undergone DBS (DBS-APD) and the other received best medical treatment (BMT) despite being eligible for DBS (BMT-APD). Data was collected at baseline, 3-month and 6-month visits. MDS-UPDRS part III was used to assess motor function during different states (*ON-stimulation/ OFF-medication*, *OFF-stimulation/ OFF-medication, ON-stimulation/ ON-medication* for DBS-APD and *ON-medication*, *OFF-medication* for BMT-APD). Demographic, levodopa equivalent dose (LED) and health state utilities assessed by questionnaire EQ-5D-5L were also collected. The medical expenses were determined from the perspective of health care provider. The cost-effectiveness analysis (CEA) were calculated by ICER (Incremental Cost-Effectiveness Ratio) using Generalized Estimating Equation (GEE) and life years gained adjusted by quality of life (QALYs) respectively.
**Results:** A total of 73 patients were recruited including 36 for DBS-APD and 37 for BMT-APD. The mean age was 63.1 ± 9.6 in DBS-APD and 58.2 ± 8.7 in BMT-APD (p=.027). The mean duration of disease was 14.0 ± 5.2 years in DBS-APD and 9.7 ± 5,4 years in BMT-APD (p=.001).
Regarding clinical efficacy, MDS-UPDRS part III score while ON-stimulation/ OFF-medication, at 42.2 ± 14.2, was significantly different from that while OFF-stimulation/ OFF-medication, at 64.6 ± 18.2 among DBS-APD (p<0.001). However, no statistical difference was found between the former and the MDS-UPDRS part III score of BMT-APD while OFF-medication (41.4 ± 11.0, p=0.785). LED was significantly lower in DBS-APD compared to that in BMT-APD (514.6 ± 322.7; 1218.9 ± 402.3, p<0.01).
In CEA, compare to BMT-APD, DBS-APD was more cost-effective in correlation with MDS-UPDRS-IV with the incremental utility 1.45, 1.47, 1.56 points and ICER 8.037.000, 4.124.000, 6.346.000 (VND) at each 3-month visit (p<0.05).
**Conclusions:** DBS could be a clinically efficient and cost-effective therapy for APD patients comparable to the BMT in Vietnam.

## P_71 (GPT)

### Current perspectives on the pharmacogenomics of the side effects of Parkinson's disease treatment: a systematic review

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**Background:** One of the major challenges of Parkinson's disease (PD) treatment is the differences between patients, in terms of response and side effects. Considering that PD is complex, pharmacogenomics can serve as a platform to understand these variances. There have been several efforts to identify genetic markers that allow clinicians to anticipate the possible response to standard therapies. Our aim is to assess current perspective on the field and determine the required future directions.
**Methods:** We performed a systematic review following PRISMA guidelines. Pubmed database was searched for original papers, using the MesH terms: "Parkinson's disease", "pharmacogenetics", "pharmacogenomics", "levodopa" and "polymorphism". A total of 182 articles were found. Data were extracted by two independent reviewers. Differences were solved by consensus. Study characteristics including population, sample size, outcome, evaluated genes and polymorphisms, were all reviewed.
**Results:** Seventy six articles were included. Polymorphism rs4680 in *COMT* had the higher number of concordant results, associating the low enzymatic activity of COMT with a higher risk of developing complications with the use of levodopa. Other polymorphisms showed contradictory results or no evidence. Levodopa induced dyskinesia (LID) was the most investigated side effect. The largest sample included 741 participants; 86.8% of the studies involved less than 300 participants. The majority (50.81%) of studies included participants of European ancestry, and 24.6% did not specify ethnicity.
**Conclusions:** Not surprisingly, most studies screened candidate genes based on the dopamine metabolic pathway; however, the contradictory results and lack of evidence suggest the need to investigate other genes that may explain current challenges. Moreover, the pharmacogenomics of frequent side effects besides LID should be investigated. Finally, it is important to ensure more ethnical diversity in future studies.

## P_248 (GPT)

### Pharyngeal structure and dysphagia in patients with parkinsonism

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**Background:** About 80% of patients with Parkinsonism have dysphagia. In this study, the width and the thickness of the pharynx were measured and compared in the patient and the normal control groups.
**Methods:** Lateral neck roentgenograms were acquired for both parkinsonism and control groups, and the width of the pharynx at rest (PWR) was measured using the same method as in the previous studies. The pharyngeal wall thickness (PWT) was measured at the same spine level where the PWR was measured. A video fluoroscopic swallowing study (VFSS) was performed for the parkinsonism group. The shortest width of the pharynx during forceful swallowing (PWS) was measured and the PWS/PWR ratio was calculated. We compared PWR and PWT between the parkinsonism group and the control group using the independent t-test. Spearman correlation test was done among the radiological data (PWR, PWT, and PWS/PWR ratio), the dysphagia scale (PAS and DOSS), and Hoehn and Yahr scale (HY scale).
**Results:** PWR was wider and PWT was thinner with statistical significance in the parkinsonism group ($p<0.05$). The dysphagia scale (PAS and DOSS) was correlated with the radiological data (PWT and PWS/PWR ratio) ($p<0.05$) and the HY scale ($p<0.05$).
**Conclusions:** 74% of the parkinsonism group were identified with HY scale 4 and 5, indicating that patients with severe parkinsonism tend to have dysphagia. The muscle wall atrophy and the contractile strength of the pharynx measured that were measured using the PWT and the PWS/PWR ratio were factors influencing dysphagia in Parkinsonism. Therefore, the lateral neck roentgenogram and the VFSS are valuable methods for detecting dysphagia in patients with Parkinsonism. Moreover, PWT can be an easy and simple indicator that can be measured even in patients who cannot perform the VFSS, which will help predict swallowing disorders at the bedside.

## P_252 (GPT)

### Combined physiotherapy and deep brain stimulation to improve independent community mobility in Parkinson's disease

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**Background:** Deep brain stimulation (DBS) is an established and highly effective treatment for individuals in the advanced phase of Parkinson's disease (PD). Despite overall improvements in motor function, studies have reported that DBS alone may not increase community mobility and may be associated with balance and gait instability and an increased rate of falling. Physiotherapy has been shown to effectively improve control of balance and gait, and prevent falls, among individuals with PD who are treated with medication only. The overall objective of this study was to determine if DBS combined with physiotherapy is effective for improving safe, independent mobility in the community in individuals with PD compared to patients receiving DBS only.
**Methods:** This is a single-center, single-blind non-randomized controlled study, whereby individuals receiving DBS were allocated to receive either physiotherapy 3 times/week for 8 weeks or no intervention (control group).
**Results:** There were 24 participants included in this interim analysis: 9 in the physiotherapy group and 15 in the control group. There were no differences between the two groups at baseline. At post-intervention, there were significant differences in change of scores between groups for balance (mini-BESTest: $p = 0.037$) and gait performances (gait velocity: $p = 0.042$; stride velocity: $p = 0.026$; stride length: $p = 0.041$; step length: $p = 0.048$) favouring the physiotherapy group. At the three months post-intervention follow-up, the physiotherapy group showed better performance for balance and certain gait functions compared to their pre-intervention assessment while the control groups showed a slight decline.
**Conclusions:** In conclusion, the findings from this study suggest that physiotherapy combined with DBS may be effective in improving balance and gait functions and reducing near-falls in PD compared to patients receiving DBS only. Studies involving larger sample sizes are needed to determine its effect on overall community mobility.

# Poster Exhibition

## Basic Neuroscience (excluding Genetics)

### P_01

### Role of heterozygous mutations in ‘recessive’ genes in Parkinson disease

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**Background:** Considerable percentage of patients with PD was shown to carry a single heterozygous mutation in the Parkin, DJ1 or PINK1 genes, raising the intriguing question of whether the much more frequent heterozygous mutations in ‘recessive’ genes might act as susceptibility factors for PD. Several ways lead to explore the potential role of these mutations. First, the frequency of single heterozygous mutations in ethnically matched PD cases and controls could be compared. According to recent reports, heterozygosity for Parkin mutations was similar between patients and controls, whereas heterozygous PINK1 mutations were rarer in controls. The probability that a second mutation might have been overlooked in these carriers is much lower than the probability of a mutation being missed in sporadic cases of PD.
**Methods:** There is a growing body of evidence that genetic risk factors are of major importance in PD.
**Results:** In most studies, however, healthy controls are not subjected to detailed neurological and neuroimaging examinations, leaving open the possibility that mild clinical (or preclinical) changes could have been present but were not screened for. As recently shown for Parkin and PINK1 families, subtle, but unequivocal, clinical signs of possible or probable PD can be found on careful motor examination in a considerable number of the heterozygous mutation carriers who consider themselves asymptomatic.
**Conclusions:** Last, further functional studies of the affected allele carriers would be highly valuable. Haploinsufficiency, leading to a functional loss of heterozygosity or a dominant-negative effect of some mutant alleles, could explain why a second mutation cannot (and need not) be found for some mutations in the above mentioned recessive genes. Although the role of heterozygous mutations in the development of clinical signs currently remains a matter for debate, there is growing evidence that they are associated with pre clinical changes.

### P_02

### Smek1 deficiency in PSP induces tau pathology via regulating Kif2a translocation

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**Background:** Tauopathies are a group of human neurological disorders that have hyperphosphorylated tau in neurons or glia. Hyperphosphorylation of tau destabilizes tau-microtubule interactions, leading to microtubule

instability and transport defects. Kif2a is regarded as a potential target for treatment of tauopathy due to its role in inducing microtubule disassembly. Genome-wide association study have identified the protective effect of *SMEK1* in Alzheimer's disease (AD). Moreover, Smek1 is found downregulated in PSP. However, the physiological and pathological roles of Smek1 in tauopathies are largely unclear. Herein, we investigated the neuroprotective potential of Smek1 against neurodegeneration in tauopathy.
**Methods:** Smek1 constitutive knockout mice were generated. Single-cell RNA sequencing was carried out using mice brain tissues. Phenotypic changes were studied in Smek1 knockout mice. Biological function of Smek1 was characterized using primary cultured neurons and shRNA transfected cell lines.
**Results:** Through single-cell sequencing, we identified a novel neuronal cluster possessing neurodegenerative characteristics in Smek1$^{-/-}$ mice. Loss of Smek1 resulted in neuronal loss, gliosis and tau hyperphosphorylation at major Gsk3β sites. Smek1$^{-/-}$ mice developed markedly more severe motor and cognition impairments by the age of 6 months. Depletion of Smek1 resulted in Kif2a cytosol aggregation, retarded axon outgrowth and mitochondrial axonal trafficking. Downregulation of Kif2a markedly attenuated tau hyperphosphorylation and axon outgrowth defects in shSmek1 cells.
**Conclusions:** For the first time, we demonstrate that Smek1 depletion exacerbates tau pathologies and tau-mediated neurodegeneration in an age-dependent manner. Our findings suggest that Smek1 deficiency could play an important role in the molecular pathogenesis and increased the risk of tauopathy including PSP.

## P_05

### Features of orthostatic hypotension in patients with mild cognitive impairment

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**Background:** Based on recent data, OH is associated with the formation of cognitive decline as a result of a developing neurodegenerative process or as a result of persistent ischemia of subcortical brain areas under orthostatic stressor.
**Methods:** We saw 14 patients with PD and 16 patients with CVD. All of them had OH in combination with MCI. The hypothesis of our study were:

- that the degree of blood pressure drop may have an impact on cognitive impairment;
- there may be a difference between normotensive and hypertensive patients;
- cognitive impairment may depend on the form of OH.

**Results:** A drop in SBP greater than 25 mmHg leads to a more pronounced cognitive impairment in normotensive patients.
In patients with supine hypertension, there is no correlation between the degree of SBP drop and severity of cognitive decline.
Patients with nOH were characterized by a more marked cognitive deficit.

| SBP | PD | CVD | MoCA | | | | | | | | | Corr. | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | | Visuospastial | Naming | Attention | Language | Abstraction | Delayed recall | Orientation | Education | Total score | | |
| **Normotensive (n=13)** | | | | | | | | | | | | | |
| **↓>25** | 5 | 1 | 2.6 | 3 | 2.4 | 1 | 1 | 2.8 | 5 | 0.8 | 18.6 | -0.9 | 0.0002 |
| **↓<25** | 4 | 3 | 2.8 | 3 | 4.3 | 1.5 | 1.5 | 3.6 | 5 | 0.1 | 21.5 | -0.9 | |
| **Supine hypertension (n=17)** | | | | | | | | | | | | | |
| **↓>30** | 3 | 7 | 2.7 | 3 | 3.9 | 1.3 | 1.5 | 3.3 | 5.5 | 0.5 | 21.7 | -0.4 | 0.5 |
| **↓>35** | 2 | 5 | 2.6 | 3 | 4.3 | 1.5 | 1.4 | 3.3 | 5.4 | 0.5 | 21.9 | 0.3 | |
| **ΔHR/ΔSBP** | | | | | | | | | | | | | |
| **<0.5** | 11 | 0 | 2.7 | 3 | 3.2 | 1.1 | 1.4 | 2.9 | 5.1 | 0.6 | 20 | -0.9 | 0.0006 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **>0.5** | 3 | 16 | 2.7 | 3 | 4.2 | 1.5 | 1.5 | 3.3 | 5.3 | 0.3 | 21.8 | 0.4 | |

**Conclusions:** Greater severity of cognitive decline in the nOH group may be associated with an underlying neurodegenerative process. In turn, patients with MCI, OH and supine hypertension may be exposed to persistent cerebral ischemia or be at the beginning of the neurodegenerative process with still preserved compensatory mechanisms.

## P_08

### The impact of altered sensory metacognition in Parkinson's disease

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**Background:** We recently found that when integrating vestibular and visual cues of self-motion, Parkinson's disease (PD) patients overweight their visual cues, despite degraded visual perception (Yakubovich et al., 2020). Moreover, we found that PD patients overestimate their visual perceptual performance (Halperin et al., 2021). Together, these results suggest a deficit in metacognition of perceptual function in PD. How this relates to primary (motor) symptoms in PD is unknown (Halperin et al., 2020).
**Methods:** Here we summarize and integrate these recent psychophysical results, and further investigate how altered perceptual metacognition in PD can affect motor function by simulating a dynamic model. We tested how overestimated sensory reliability, incorrect multisensory weighting and/or altered predictions of motor output (forward model) can affect motor function in PD.
**Results:** Theoretical considerations and model simulations suggest that overestimating sensory reliability, altered multisensory weighting and/or overestimating the expected sensory outcomes of one's own actions can lead to impoverished motor performance.
**Conclusions:** This suggests that altered sensory metacognition in PD can contribute to hypokinetic motor symptoms (e.g., akinesia, bradykinesia). A better understanding of this understudied aspect of PD can open up novel avenues for developing functional aids.
Halperin, O., Israeli-Korn, S., Yakubovich, S., Hassin-Baer, S., & Zaidel, A. (2020). Self-motion perception in Parkinson's disease. *European Journal of Neuroscience*. https://doi.org/10.1111/ejn.14716
Halperin, O., Karni, R., Israeli-Korn, S., Hassin-Baer, S., & Zaidel, A. (2021). Overconfidence in visual perception in parkinson's disease. *European Journal of Neuroscience*, *53*(6), 2027–2039. https://doi.org/10.1111/EJN.15093
Yakubovich, S., Israeli-Korn, S., Halperin, O., Yahalom, G., Hassin-Baer, S., & Zaidel, A. (2020). Visual self-motion cues are impaired yet overweighted during visual–vestibular integration in Parkinson's disease. *Brain Communications*, *2*(1). https://doi.org/10.1093/braincomms/fcaa035

## P_11

### Evaluation of orthostatic hypotension questionnaires

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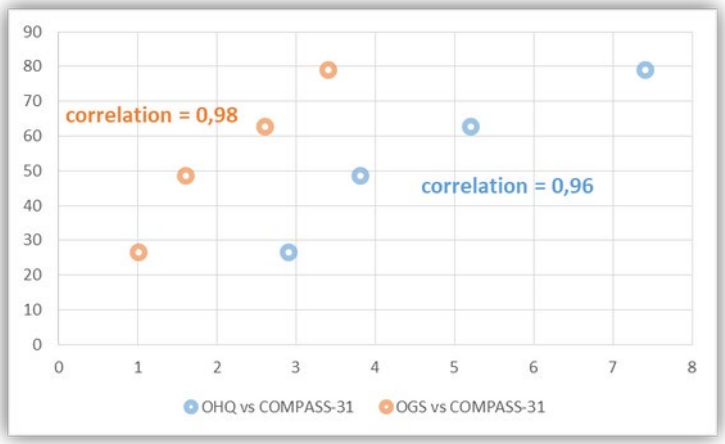
**Background:** Assessment and detection of OH is life-saving goal in elderly patients and in patients with neurodegenerative diseases. Underlying OH is autonomic insufficiency of varying severity, which may correlate with the FC of OH.
**Methods:** 20 patients with PD and 20 patients with CVD were questioned in our neurology clinic. All of them had OH. During the study, we used orthostatic test and interview with: OGS, OHQ, COMPASS-31.
**Results:** The OHQ proved to be the most sensitive and valid questionnaire due to its quantifiability, better visual presentation of symptoms and less time-consuming interview. We are revealed a difference between the prevalence of OH symptoms in PD and CVD patients.
OGS - did not provide sufficient clarity for patients and did not reveal a difference in OH symptoms.
COMPASS-31 is a more complex questionnaire, but remains a sensitive marker of autonomic insufficiency, which correlates with FC of OH.

| FC | Disease | Symptoms | OGS | OHQ | COMPASS-31 |
|---|---|---|---|---|---|

| OH | PD (n) | CVD (n) | PD | CVD | ΔOGS | p | Δt (min) | ΔOHSA | p | ΔOHDAS | p | Δt (min) | ΔCOMPASS-31 | Δt (min) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 4 | 6 | Neck Discomfort | Dizziness | 1 | 0,008 | 3,2 | 3,3 | 0,008 | 2,5 | 0,007 | 2,5 | 26,75 | 16,7 |
| 2 | 6 | 6 | Neck Discomfort, Lightheadedness, Trouble concentrating | Dizziness, Problems with vision | 1,6 | | | 5,1 | | 2,5 | | | 48,63 | |
| 3 | 6 | 6 | Weakness, Fatigue, Trouble concentrating | Weakness, Fatigue | 2,6 | | | 6,3 | | 4,1 | | | 62,82 | |
| 4 | 4 | 2 | Weakness, Fatigue, Trouble concentrating | Weakness, Fatigue, Trouble concentrating | 3,4 | | | 7,3 | | 7,5 | | | 79,14 | |




**Conclusions:** FC of OH reflects the degree of autonomic insufficiency, which can also be divided into 4 classes. The manifestation of OH in the form of nonspecific symptoms prevails in patients with PD, therefore, the use of OHQ may be more effective for differential diagnosis.

## Imaging and Biomarkers

### P_14

### Biochemical markers in Parkinson's disease

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**Background:** Parkinson's disease (PD) is a chronic neurodegenerative disease, accompanied by a progressive increase in extrapyramidal disorders and causing more than 1% of the population over 65 years of age. For this reason, modern research is mainly devoted to identification potential markers of the early stages of PD, on which dopaminergic neurons are still relatively preserved and therefore neuroprotective therapy can be potentially effective. Thus, the identification of the premotor stage of PD through the identification of a number of non-motor symptoms, such as impaired smell, constipation, impaired REM-stage sleep, increased daytime sleepiness or depression.Another current direction of early diagnosis of PD is the identification of biological laboratory markers that could help in identifying high-risk groups or monitoring the progression of the disease and its response to various methods of therapy.

**Methods:** Thesis was conducted pertaining to objective biomarkers for PD. thesis was selected based on relevance and methodology; where available, meta-analyses, systematic reviews, and comprehensive qualitative review thesis was preferentially referenced.
**Results:** Estimate the actual internal dose of progression of PD. Improves precision in the measurement of any risk factor by adding both internal and external validity when examining the effect of the exposure on the outcome.
**Conclusions:** The development of biomarkers that will predict, diagnose, evaluate, andprognosticate PD is essentialfor patient's health care and research. In addition,unbiased discovery isunderway using techniques including metabolomics, proteomics, andtranscriptomics (geneprofiling). Recently, it was also suggested that post-transcriptional regulation has important role in molecular mechanisms for PD. Severalpotential biomarkers identified in other diseases or in other types of biologicalfluids are investigated as blood-based biomarkers for the PD.

## P_15

### Biomarkers of vascular cognitive dysfunction.Identification of early markers of cognitive impairment before the development of dementia

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**Background:** Currently, there is no approved list of biomarkers for diagnosing vascular cognitive dysfunction. The main problem for the practitioner in identifying cognitive impairment in patients is the differential diagnosis of Alzheimer's disease, vascular cognitive dysfunction and other types of cognitive impairment, which are much less common. Vascular cognitive dysfunction includes post-stroke dementia, cognitive dysfunction in cardiovascular and cerebrovascular diseases. Without determining the etiology of the disease, it is impossible to prescribe adequate treatment.
**Methods:** Retrospective analysis.
**Results:** Lipocalin-2 (lipocalin 2 - LCN2) is an acute phase protein that is synthesized and secreted as an inducible factor from reactive astrocytes, activated microglia, neurons, and endothelial cells in response to infectious, inflammatory, or damaging effects. Lipocalin-2 modulates several biobehavioral responses such as emotional behavior, hypersensitivity to pain, CD, depression, neuronal excitability, and anxiety. In a study by Llorens F, et al. (2020) found that the level of lipocalin-2 in the cerebrospinal fluid is significantly increased in DM compared with healthy volunteers and patients with BA. A study by Naude PJW, et al. (2012) showed that the level of lipocalin-2 in the cerebrospinal fluid is reduced in patients with BA and in patients with UKD. Thus, lipocalin 2 can act as a biomarker for DM and allows differential diagnosis between DM and AD. Liguori C, et al. (2015) found that the level of lactate in the cerebrospinal fluid is significantly increased in patients with BA compared with patients with DM and the control group.
**Conclusions:** These biomarkers will make it possible to carry out differential diagnostics between vascular CD and AD, which will allow choosing a more effective treatment aimed at the etiology and pathogenetic links of the disease.

## P_19

### The variability in clinical manifestations of brain iron deposition

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**Background:** Neurodegeneration with brain iron accumulation (NBIA) involve a spectrum of heterogenous diseases with variable presentations. We present a set of patients with MRI findings typical for NBIA but whom are seronegative with atypical presentations.
**Methods:** Retrospective chart review of patients with similar MRI findings.
**Results:** A 58 year-old male with a 30-year history of methamphetamine abuse (abstinent for the past 4-5 years) presented with 9 months of abnormal movements of the face and hands. MRI demonstrated prominent SWI hypointensity in the bilateral globus pallidi, substantia nigra, red nuclei, and dentate nuclei.
A 19 year-old male with a history of schizophrenia and polysubstance abuse presented with bradykinesia in addition to intermittent confusion, paranoia, and poor oral intake. MRI revealed nonspecific mineralization of the globus pallidi and reduced NAA production in the bilateral basal ganglia.
A 71 year-old female presented with a right-handed tremor and was diagnosed with Parkinson's disease. Although MRI revealed 'Eye of the Tiger' sign (T2 hypointensity in the bilateral globus pallidi with central circumscribed T2 hyperintensity), presentation was atypical for PKAN and gene testing negative.
An 81 year-old male presented with a 20-year history of gait difficulty and unexplained macrocytic anemia attributed to vitamin B12 deficiency. Despite replacement his symptoms progressed to involve characteristic

features of Parkinsonism. MRI brain revealed iron deposition in the basal ganglia in a pattern consistent with aceruloplasminemia (ACP). Despite low serum copper and ceruloplasmin, DNA sequencing did not demonstrate any associated mutations for ACP.
**Conclusions:** These cases demonstrate the importance of further characterizing the clinical spectrum of NBIA. Imaging alone may not be sufficient to categorize patients presenting outside of hallmark progressive movement disorders, as these may not be the only manifestation. As such, we propose that atypical presentations in the context of NBIA findings should prompt investigation into alternative etiologies for brain iron accumulation.

## P_20

### Cerebrospinal fluid analysis in amyotrophic lateral sclerosis

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**Background:** Amyotrophic lateral sclerosis (ALS) is a fatal disease characterized by degenerative changes in the central and peripheral motor neurons. There is currently no definitive diagnostic test or marker for ALS. The discovery of new biomarkers is important for diagnosing and monitoring the progression of ALS. In our study, we focused on the clusterin, tau protein, beta-amyloid$_{1–42}$ cerebrospinal fluid (CSF) levels in patients with ALS.
**Methods:** Biomarker levels were examined by ELISA. The study included 54 patients with a diagnosis of ALS and 58 control subjects. The control group consisted of patients diagnosed with back pain, vertigo, etc. The observed groups were homogeneous in terms of age and gender.
**Results:** Significantly higher clusterin levels (2,148 µg/l vs 1,987.5 µg/l; $p = 0.038$), tau protein levels (323.5 ng/l vs 177.5 ng/l; $p < 0.0001$) and index tau-protein/beta-amyloid$_{1–42}$ (0.340 vs 0.224; $p = 0.0002$) were observed in the patients diagnosed with ALS than in the control group. No significant difference was detected for beta-amyloid$_{1–42}$.
**Conclusions:** Finding a specific marker could help diagnose the disease and better understand its often unpredictable progression.
**Supported by:** the European Regional Development Fund - Project ENOCH (No. Z.02.1.01/0.0/0.0/16_019/0000868)

## P_21

### Clinical improvement with normalization of dopamine transporter imaging in a patient with bupropion-induced Parkinsonism

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**Background:** Dopamine transporter (DAT) imaging is valuable in the differential diagnosis of neurodegenerative parkinsonism from essential tremor, vascular parkinsonism, and drug-induced parkinsonism. [18F]PR04.MZ is a positron emission tomography (PET) tracer for DAT with very high affinity, selectivity, and specific uptake in the striatum and midbrain, which permits assessing the integrity of the nigrostriatal pathway. In Parkinson disease, a decreased uptake with a rostral-caudal gradient is expected. The Test-Retest variability of [18F]PR04.MZ PET has been estimated at 6-9% in the putamen, 10-11% in the caudate, and 2-7% in the substantia nigra. Several drugs (e.g., cocaine, amphetamines, opioids, phentermine, methylphenidate, bupropion, and some anesthetics) can decrease the striatal availability of DAT. Bupropion has been shown to reduce striatal DAT by 14 to 26%, influencing PET analysis.
**Methods:** Herein, we present a drug-induced parkinsonism case with clinical and PET normalization after a two-year follow-up.
**Results:** A 58-year-old woman, with a history of depression, on lamotrigine 100 mg per day and bupropion 300 mg per day, presented with decreased right arm swing and asymmetrical upper-limbs postural and intention tremors. Transcranial ultrasound revealed an increased echogenicity in the substantia nigra, and her [18F]PR04.MZ PET demonstrates a symmetrical decrease in DAT without a rostral-caudal gradient (i.e., a loss of 41% and 33-40% in the anterior and posterior putamen, respectively, and a 29% and 35% loss in the caudate and substantia nigra, respectively). After suspending her medications, in a two-year follow-up, the patient´s parkinsonism improved. [18F]PR04.MZ PET was repeated, showing normal values.
**Conclusions:** The patient´s bupropion-related parkinsonism and DAT abnormalities seem more significant than previously described in the literature for this drug. The test-retest reliability, abnormal cutoff values, and technical aspects in the analysis of [18F]PR04.MZ PET should be considered when interpreting these changes.

## P_22

### Pilot investigation of MRI-derived perfusion measures in cognitively impaired patients with Parkinson's disease

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**Background:** Mild cognitive impairment (MCI) is observed in approximately 33% of early stages of Parkinson's disease (PD). Several attempts from various MRI techniques have been utilized to identify and understand brain correlates of the neuropsychological scores used to diagnose PD-MCI clinically. However, a consensus MRI-based biomarker is still elusive. Recent investigations have revealed that patients with PD-MCI have a lower cerebral blood flow (CBF) in the frontal and parietal brain regions in early-stage PD. In this pilot analysis, we attempted to replicate these findings in late-stage patients with PD-MCI with a multi-delay 3D pseudo-continuous arterial spin labeling (pCASL) acquisition.
**Methods:** Ten patients with PD-MCI, 4 cognitively normal patients with PD, and 15 healthy controls (HC) were recruited at our center. 3D pCASL MRI was acquired on a 3T Skyra scanner with the following parameters: field of view (FOV) = 224 × 224 mm2, matrix = 64 × 64, 44 axial slices, thickness = 3.5 mm, TR/TE = 4130/39 msec, labeling duration = 1.8 seconds, multiple post labeling delays (PLD) = [0.5, 1.0, 1.5, 2.0, 2.5] seconds. CBF maps were generated from the pCASL MRI images using Johns Hopkins University's cloud-based ASL analysis software, ASL-MRICloud (https://braingps.mricloud.org/asl).
**Results:** Our pilot analysis revealed that HC has significantly (p-uncorrected < 0.005, extent cluster threshold: 350 voxels) higher arterial transit time (ATT) and lower relative CBF (rCBF) in the cerebellum compared to PD-MCI. Furthermore, rCBF was higher in HC as compared to PD-MCI in the frontal and parietal regions but there was no significant difference in ATT in those regions.
**Conclusions:** Our pilot analysis confirmed that CBF and ATT are affected in the PD-MCI. However, the data quality was significantly worse in the cerebellum regions dampening the findings of this study. Future analysis with good-quality data and correlation with neuropsychological scores is currently underway.

## P_23

### Hyperhomocysteninemia in Parkinson's disease

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**Background:** The significance of hyperhomocysteinemia is a significant factor leading to the development of cerebrovascular pathology and cognitive impairment. A number of data on the impact of elevated levels of homocysteine on cognitive and emotional disorders are contradictory.
**Methods:** 110 patients with varying degrees of cognitive impairment from moderate cognitive impairment to severe dementia in Parkinson's disease were examined.All patients underwent homocysteine level in blood plasma.All patients underwent comprehensive clinical and neuropsychological examination.
**Results:** Homocysteine level in blood plasma was considered to be a normal value below 15 μmol/l in both men and women.In Parkinson's disease homocysteine concentration was somewhat higher, nevertheless it was within the limits of usual normative values and was 14,89 ±3,86 μmol/l, which was different from control (p<0,01), having similar disease genesis.
**Conclusions:** Hyperhomocysteinemia as a metabolic complication of Parkinson's disease is currently the most important clinical problem, the solution of which requires further research. It has been established that hyperhomocysteinemia influences the systemic process of neurodegeneration through the trigger of glutamate-calcium cascade: oxidative stress, mitochondrial dysfunction, excitotoxicity and deficiency of neurotrophic factors.

## P_26

### The role of inflammation in the pathophysiology of primary tauopathies

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**Background:** Primary tauopathies such as progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) are neurodegenerative diseases (NDD) characterized by aggregation of abnormal tau protein and neuroinflammation. There is increasing evidence that chronic inflammation contributes to the progression of NDD; however, the precise mechanisms by which neuroinflammation participates in the pathogenesis of tauopathies are still a subject of investigation. Identifying sensitive neuroinflammation biomarkers would be a critical step to understanding the involvement of neuroinflammation in tauopathies and could mean a valuable contribution to early diagnosis and monitoring of the progression of the disease. This study aimed to evaluate whether there is a significant difference in levels of cerebrospinal fluid (CSF) and blood serum (BS) inflammation markers between patients suffering from tauopathies and controls.
**Methods:** Samples of CSF and BS were obtained from 31 patients suffering from PSP (n=24) or CBD (n=7) and 90 patients for differentially diagnostic reasons used as the control group (CG). Levels of biomarkers, including β-2 microglobulin, CRP, C3, C4, haptoglobin, transferrin and orosomucoid, were quantitatively determined using ELISA. Statistical analysis was done using The Mann Whitney-U and Bonferroni correction to determine the difference between biomarker levels of patients with primary tauopathies and CG.
**Results:** There was no significant difference in CSF and BS levels of the analysed inflammatory biomarkers between patients with PSP or CBD and CG.
**Conclusions:** Neuroinflammation is one of the main pathological hallmarks of NDD, including PSP and CBD. In the future, other potential CSF or BS biomarkers of neuroinflammation, such as interleukins, need to be investigated in the context of PSP and CBD.
Supported by the European Regional Development Fund - Project ENOCH (No. Z.02.1.01/0.0/0.0/16_019/0000868).

## P_27

## Characterization of the findings of the optical coherence tomography in patients with Parkinson's disease

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**Background:** PD occurs with apoptosis of dopaminergic neurons, predominantly in the basal ganglia, which explain classic motor symptoms but also occurs in the dopaminergic amacrine cells in the retina, that explain the alteration of the functions such as contrast, color, and foveal vision. The optical coherence tomography (OCT) allows obtaining in-vivo images of retina, providing structural evidence for dopaminergic loss, resulting in thinning layers of the retina.
**Methods:** An observational, analytical, retrospective study of cases and controls in PD patients was carried out. Demographic characteristics, clinical examination, and OCT evaluation of the retina and optic nerve was compared.
**Results:** Data were collected from 30 PD patients and 30 matched controls (table-1). In characterization of OCT, there was a significant difference with decrease in nerve fiber layer (RNFL) (p 0.015), cup-disc ratio (p 0.003) and disc area (p 0.008), in the group of case. In the correlation analysis, we found a weak negative correlation in the thickness of RNFL in relation to UPDRS III and equivalent dose of levodopa but also in the correlation for CCG thickness of PD patients under treatment with DBS which diminish dose of levodopa equivalent dosage.

Table 1.

| | | Age (y) | | Sex | | Hoehn and Yahr stages | | | | | Disease duration (y) | Levodopa Equivalent Dose (mg) | UPDRS III (points) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | M | F | 1 | 2 | 3 | 4 | 5 | | | |
| Cases (n=30) | Mean | 62,7 | # | 12 | 18 | 1 | 17 | 11 | 0 | 1 | 7,8 | 800,0 | 32,1 |
| | SD | 7,4 | % | 40 | 60 | 3,3 | 56,7 | 36,7 | 0 | 3,3 | 5,1 | 332,3 | 12,8 |
| Controls (n=30) | Mean | 62,2 | # | 12 | 18 | | | | | | | | |
| | SD | 7,4 | % | 40 | 60 | | | | | | | | |

**Conclusions:** OCT is a fast and non-invasive tool that generates in-vivo images of the retina, which in patients with PD could play a role as a biological marker. In this study there was a negative correlation with motor symptoms and levodopa equivalent dose and a positive correlation with the use of DBS. DBS could be a protective factor by preventing nerve fiber layer deteriorate.

## P_29

## MRI-based machine learning approach to predict the motor symptom severity in patients with Parkinson's disease

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**Background:** There is still a need for a clinically valid biomarker that can predict the severity of motor symptoms in the early stages of Parkinson's disease (PD). Application of machine learning methods to make predictions at the individual patient level using structural brain imaging might be a promising approach. In this proof-of-concept study, a patient-specific imaging marker derived from structural magnetic resonance imaging (MRI) was assessed for its potential to identify the severity of motor symptoms using machine learning in *de novo* patients with PD.
**Methods:** T1-weighted MRI, demographics at baseline (BL), and clinical motor scores (MDS-UPDRS-III; OFF medication) at BL and 48 months (48M) were obtained from the Parkinson's Progression Markers Initiative database (www.ppmi-info.org/data) for 88 patients with *de novo* PD and 120 controls. A patient-specific imaging marker indicating the gray matter volumetric atrophy in the motor-specific brain regions was calculated from the control data using a multivariate method, Mahalanobis distance ($M_{GMV}$). To build a machine learning model, the patients were categorized as "slow progressors" and "fast progressors" based on the median value of $\Delta$ MDS-UPDRS-III (MDS-UPDRS-$III_{48M}$ - MDS-UPDRS-$III_{BL}$). A support vector machine (SVM) classifier was trained using $M_{GMV}$ in combination with clinical (baseline UPDRS-III) and demographic (age, sex) data to predict the severity of motor symptoms. The performance of the classifier was evaluated using accuracy, sensitivity, specificity, and area under the curve (AUC).
**Results:** The patient data consisted of 46 slow progressors and 42 fast progressors. The accuracy, sensitivity, specificity, and AUC of the SVM classifier were 89.00%, 87.50%, 90.91%, and 0.85, respectively.
**Conclusions:** Our study indicates that our proposed machine learning method can effectively classify patients based on their motor symptom severity. Future research is required to determine whether this approach can be extended to positively impact clinical decision making.

## P_30

## Role of neuroinflammation on biomarker levels in the cerebrospinal fluid and blood serum of multiple system atrophy patients and controls

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**Background:** Neuroinflammation in neurodegeneration has been investigated for many years, with increasing evidence that neuroinflammation may be a major contributing factor in the development and/or progression of neurodegeneration. However, some details are contested, and further research is required to answer such questions as: how neuroinflammation occurs, what molecules are involved, and what biomarkers can be used for diagnosis/prognosis. Multiple system atrophy (MSA) is a synucleinopathy, characterised pathologically by glial cytoplasmic inclusions. There is a lack of reliable biomarkers for the diagnosis/prognosis of MSA, therefore the objective of this study was to identify differences in biomarkers between MSA patients and controls.
**Methods:** Cerebrospinal fluid (CSF) and blood serum (BS) samples were taken from MSA patients (n = 24) and controls (n = 90). The CSF and BS were biochemically analysed using ELISA to quantify the levels of different biomarkers, including: CRP, C3, C4, haptoglobin, transferrin, orosomucoid and β-2 microglobulin. Mann-Whitney U tests with Bonferroni's significance corrections were then performed to determine any significant difference between MSA and controls. Significance levels were set at 0.05.
**Results:** The CSF levels of transferrin (p=0.007), C3 (p=0.003) and orosomucoid (p=0.014) were significantly lower in MSA patients compared to controls. All BS biomarkers and the remaining CSF biomarkers were found to be non-significant.
**Conclusions:** These results suggest that there are some biochemical differences in the CSF between MSA patients and controls, with further investigations required to understand why these biomarkers are lower in MSA than controls. Nonetheless, this indicates that these biomarkers could possibly be adapted for use as diagnostic markers following further validation. The identification of possible biomarkers for the diagnosis/prognosis of MSA is an important finding. Additional research with more subjects and biomarkers will be essential in the search for biomarkers for the diagnosis and prognosis of MSA. Supported by: European Regional Development Fund - Project ENOCH (No.Z.02.1.01/0.0/0.0/16_019/0000868).

## P_31

## The role of inflammatory biomarkers in the LBD neurodegenerative process

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**Background:** The inflammatory process is increasingly considered to be a part of the pathology of neurodegenerative diseases. However, our knowledge of the importance of inflammation in Lewy body diseases (LBD) is not well established. Definition of the LBD inflammatory profile may help to understand the pathogenesis of the diseases, including whether they differ from other neurodegenerative diseases. This study aimed to determine whether levels of inflammatory biomarkers in cerebrospinal fluid (CSF) or blood serum (BS) differ between patients with LBD (i.e., Parkinson's disease (PD), Parkinson´s disease dementia (PDD) and dementia with Lewy bodies (DLB)) and control group (CG).
**Methods:** CSF and BS levels of inflammatory biomarkers were compared between groups of patients suffering from LBD (n=83) and CG (n=90). The biomarker concentrations were measured by sandwich ELISA (CE-IVD). Mann-Whitney U test with Bonferroni significance correction for multiple comparisons was used to compare the observed quantitative parameters; normality of the data was tested using the Shapiro-Wilk test; tests were performed at a significance level of 0.05.
**Results:** A significantly lower CSF levels of CRP (p=0.024), transferrin (p=0.04), and C3 complement (p=0.03) were presented when compared with HC. Significantly lower BS levels of orosomucoid (p=0.0003), C3 complement (p=0.05), and C4 complement (p=0.048) were found in the LBD group when compared to CG.
**Conclusions:** Many recent findings suggest, that the inflammatory process may have crucial consequences on neurodegeneration. During the last decades, inflammation was support also in the pathogenesis of LBD. Our results reveal a possible dynamic role of inflammation in this disease group. Nevertheless, our results also indicate that the inflammatory process may be reflected in BS. We, therefore suggest that inflammation may contribute to the LBD process.
**Supported by:** the European Regional Development Fund - Project ENOCH (No. Z.02.1.01/0.0/0.0/16_019/0000868).

## p_32

## Neurofilament light predicts weight loss in patients with Parkinson's disease: a prospective study

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**Background:** Weight loss is relatively common in patients with Parkinson's disease (PD) with unclear pathophysiology, which impacts on the quality of life of patients. However, there are lack of studies on the predictive biomarker of weight loss in PD. Peripheral blood neurofilament light chain (NfL) has been considered as a potential biomarker on the diagnosis, progression, and prognosis of neurodegenerative diseases. This prospective study aims to investigate the predictive value of blood NfL for the risk of weight loss in early PD patients.
**Methods:** A total of 185 PD patients were prospectively monitored for two years. Demographic and clinical data were collected. A linear mixed model was performed to detect the correlation between NfL and body mass index (BMI) in PD patients. A cox proportional hazards model was conducted to discriminate the predictive value of NfL on future weight loss in PD patients.
**Results:** Overall, weight loss was observed in 61 patients (33.0%) during the study period. At baseline, PD patients with weight loss had a higher level of NfL when compared with patients without weight loss ($p$ = 0.047) after adjusted for sex and age. The NfL was negatively correlated with BMI at baseline and each follow-up visits ($p$ = 0.031). The blood NfL level at baseline was able to predict the weight loss in the future in PD patients (HR = 1.064, $p$ = 0.012).
**Conclusions:** PD patients with high concentration of blood NfL at baseline are at higher risk of weight loss in the future.

## P_34

## Longitudinal analysis of oligomeric alpha-synuclein in Parkinson’s disease tears

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**Background:** We previously demonstrated that Parkinson's disease (PD) tears have significantly higher levels of oligomeric a-synuclein than tears of age-matched, healthy controls (HC). Analyses of hundreds of subjects (N=418) whose tears were collected from a single visit demonstrated this biomarker predicted PD diagnosis, irrespective of disease duration (AUROC=0.76). We report oligomeric a-synuclein levels longitudinally in the same cohort.
**Methods:** PD and HCs donated tears at multiple visits. Schirmer Tear Strips were used to collect tears, then frozen at -80°C. Tear proteins were eluted in PBS and immediately evaluated for oligomeric a-synuclein by ELISA, and were normalized to total soluble protein levels quantified by BCA assay. Repeat measures included 216 subjects (PD=143; HC=73) with at least 2 visits; a subset of these subjects (PD=72; HC=29) had 3 clinic visits. Oligomeric a-synuclein levels were compared across visits as a categorical variable, and in a longitudinal analysis of "months since Visit 1". Statistical analyses included all subjects correcting for age, sex and diagnosis, and within diagnostic groups (PD and HC) and biological sex (male and female).
**Results:** The average and standard deviation between Visit 1 and Visit 2 tear collections was 10.4±8.1 months; between Visit 1 and Visit 3 tear collections this was 18.2±8.7 months. Longitudinal analysis of both Visit # and "months since Visit 1" demonstrated a significant increase in oligomeric a-synuclein levels, specifically and exclusively in tears of male PD subjects. This increase in protein was observed statistically with inclusion of Visit 3, suggesting it takes approximately 18 months to detect this increase.
**Conclusions:** Male PD tears show an increase in oligomeric a-synuclein over time and may predict disease progression. This, along with our previous observation of higher levels of a-synuclein in male PD subjects, suggests intrinsic differences in tear proteins and/or oligomeric a-synuclein levels based on biological sex.

## P_35

### A proof of concept: digital diary using 24-hour monitoring using wearable device for patients with Parkinson's disease in nursing home

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**Background:** Motor complications such as wear-off and dyskinesia are problematic in the advanced stage of Parkinson's disease (PD), and it varies from day to day. Precise monitoring of these symptoms is mandatory to manage adequate care for patients with advanced PD. We have therefore explored appropriate biomarkers 24 hours for motor symptoms by using wearable device measuring multiple biomarkers in patients with PD residing in the facilities and combining them with lifestyle and clinical assessments.
**Methods:** Residents living in an elderly care facility specializing in PD care (PD houses, Sunwels, LTD, Tokyo) were enrolled in the study from April 2022 to May 2022 and wore a wearable device (iAide2, TOKAI, Gihu) on their arm to measure pulse rate (PR) and activity index (AI) over 30 days. Activity index was expressed in metabolic equivalents (METs). The PR when they sleep was also measured by a sensor in bed (Nemuri-SCAN, Paramount Bed, Tokyo). Subjective symptom data were recorded in the symptom diary.
**Results:** The data were collected for 12 patients. PR and AI were analyzed for six PD patients who showed wearing-off and/or dyskinesia. In all six patients, PR was significantly high, AI was low, and PR/AI was high during off compared to during dyskinesia (Welch's *t*-test, $p < 0.001$). The coefficient variance of PR was not significantly different between during dyskinesia and off (Welch's *t*-test, $p = 0.27$). The PR measured by the wearable device and sensor bed had a significant correlation (Pearson product-moment correlation coefficient, $r = 0.51$, $p < 0.001$).
**Conclusions:** The present results indicate that the combining of PR and AI may be a valuable indicator of wearing off and dyskinesia, and that biometric information from wearable devices may be applicable for use as a digital diary. Further accumulation of cases and collection of more data are desirable.

## P_38

### Correlates of cholinergic system vulnerability and resiliency in visual hallucinations in Lewy Body dementia

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**Background:** Visual hallucinations are a common feature of Lewy Body dementia (LBD), but the underlying mechanism remains unclear. Clinical evidence of anti-psychotic efficacy of cholinesterase inhibitors suggests a

cholinergic mechanism of hallucinations. The purpose of the study was to apply [$^{18}$F]-FEOBV vesicular acetylcholine transporter (VAChT) PET in LBD patients with hallucinations.
**Methods:** Six patients with clinically confirmed LBD and ten with suspected LBD (total, n=16; males, n=15; females, n=1; mean age=72.56 (SD=8.15)) underwent FEOBV PET imaging. Patients were defined as hallucinators or non-hallucinators based on responses to the MDS-UPDRS question 1.2. Voxel-wise *t*-test comparison was performed between the two groups and cluster-level false discovery rate (FDR) correction was applied to resulting *p*-values.
**Results:** Of the sixteen participants, seven reported recent significant history of hallucinations and nine did not. Voxel-wise *t*-test between the two groups showed cholinergic vulnerability in the primary and associative visual cortices, along with the left precuneus and left angular gyrus in those with vs. without hallucinations (FDR-corrected at 0.05). Cholinergic resilience was present in the right caudate nucleus, right basal forebrain, right tip of the temporal lobe, left posterior putamen and pons. Mixed changes in the cerebellum were also present.
**Conclusions:** Presence of hallucinations was associated with cholinergic vulnerability in posterior cortical regions, notably in visual and multimodal information processing areas, in the setting of cholinergic resilience in subcortical and right temporofrontal regions. Findings may be explained by uncoupling between posterior cortical vs. subcortical and anterior brain networks. Mixed cerebellar findings also suggest a complex role of the cerebellum in Lewy Body hallucinations.

## P_39

### Topography of cholinergic nerve terminal vulnerability and mobility self-efficacy in Parkinson's disease

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**Background:** People with Parkinson's Disease (PD) often develop postural instability and gait difficulties (PIGD), marked by slow walking, freezing of gait, imbalance, and falls. Fear of falls (FoF) leading to poorer mobility self-efficacy conceivably results in lower quality of life (QoL). Furthermore, decreases in executive functioning and attention due to reduced acetylcholine (ACh) availability in PD also potentially contribute to lower mobility self-efficacy. Exploration of decreased ACh in cortico-limbic regions of the brain and mobility self-efficacy in PD is necessary to understand these systems.
**Methods:** 56 subjects with PD underwent [$^{18}$F]fluoroethoxybenzovesamicol ([$^{18}$F]FEOBV) positron emission tomography (PET) imaging to assess ACh in the brain and completed the Short Falls Efficacy Scale (sFES) to assess FoF. [$^{18}$F]FEOBV PET data were processed using Volume of Interest (VOI) analysis for regions indicated on voxel modeling. Subjects were sorted into low, moderate, and high concern for FoF on the sFES based on sFES scoring criteria. One-way ANOVA was used to determine[$^{18}$F]FEOBV binding between sFES groups.
**Results:** The analysis found significant correlations between [$^{18}$F]FEOBV binding and the high concern group sFES scores in three brain regions: orbitofrontal cortex (β= -0.82, p= 0.041), right medial orbitofrontal (β= -0.93, p= 0.020), and parahippocampus (β= -0.09, p= 0.032). Additionally, the hippocampus (β= -0.11, p= 0.086) and the right hippocampus (β= -0.12, p= 0.064) both approached significances.
**Conclusions:** Subjects in the high concern group had decreased [$^{18}$F]FEOBV binding in the orbitofrontal cortex, right medial orbitofrontal, and parahippocampus indicating that ACh in these areas may play a role in mobility self-efficacy. Emotional processing is influenced by the orbitofrontal cortex and may be relevant for FoF. Overall findings suggests that increased ACh in the indicated regions may act as a protective factor against FoF and diminished mobility self-efficacy. Better understanding of these areas may augur novel treatments to address impaired mobility self-efficacy in PD.

## P_41

### Topographic analysis of cerebral $GABA_A$ receptor availability and functional mobility in Parkinson's disease

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**Background:** Gait changes are among the motor impairments in Parkinson's Disease (PD) that have partial responsiveness to dopaminergic drugs with advancing disease. There is a need to explore non-dopaminergic correlates of mobility in PD. γ-Aminobutyric acid (GABA) plays an important role in striatal-cortical motor circuitry. Therefore, functional GABA levels in certain brain regions could be an indicator for motor impairment in PD.

**Methods:** [$^{11}$C]Flumazenil ([$^{11}$C]FMZ) positron emission tomography (PET) studies were conducted to assess cerebral $GABA_A$ receptor availability in 26 patients with PD. These patients also underwent motor testing which included a 3-meter Timed Up and Go (TUG) test to assess functional mobility. [$^{11}$C]FMZ data were processed using Volume of Interest (VOI) analysis and applied to a linear regression model with TUG completion time as the outcome measure.
**Results:** Our analysis found that increased [$^{11}$C]FMZ binding in certain regions of the brain predicted decreased TUG completion time. This relationship was significant in the caudate (β=-0.42, p=0.035), left nucleus accumbens (β =-0.39, p=0.047), and left rostral anterior cingulate cortex (β =-0.51, p=0.007).
**Conclusions:** A significant relationship between [$^{11}$C]FMZ binding and TUG performance suggests that $GABA_A$ receptor availability may play a role in functional mobility impairments in PD. Participants with higher [$^{11}$C]FMZ binding in the caudate had better performance on the TUG, suggesting that preserved GABAergic activity in the that region could be related preserved functional mobility. Similar relationships in the nucleus accumbens and anterior cingulate cortex suggest that subcortical and limbofrontal GABA could play a significant role in functional mobility impairments in PD pathology and may augur novel non-dopaminergic therapeutic avenues.

## Neurosurgery (including Deep Brain Stimulation)

### P_42

### Gait and speech improvement in one patient with 3-month adaptive STN-DBS therapy

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**Background:** Adaptive DBS (aDBS) of the subthalamic nucleus (STN) in Parkinson's disease (PD) holds promise for the improvement of neuromodulation therapy by increasing efficacy and avoiding stimulation-related side effects such as speech and gait disturbances. While conventional DBS (cDBS) provides stimulation with constant parameters, current aDBS paradigms adapt the stimulation amplitude based on subthalamic beta power dynamics. The efficacy of long-term aDBS paradigms is currently under study.
**Methods:** One patient (male, 74 years old) with PD for 27 years and cDBS (Activa PC neurostimulator and 3389 leads, Medtronic) for 10 years started aDBS upon receiving the AlphaDBS neurostimulator (Newronika) at battery replacement. We collected clinical outcomes in chronic cDBS and after three months of aDBS. In both conditions the patient was evaluated in the morning with the same medical treatment. Oral medications were kept constant and consisted of levodopa/carbidopa 50/12.5 mg four times a day, pramipexole 0.52 mg and rasagiline 1 mg in the morning. Stimulation parameters for cDBS were: STN-right: C+0-, 70Hz, 60µs, 3.5mA and STN-left: C+3-, 70Hz, 60µs, 4.0mA. The aDBS stimulation ranged between 2.8 and 3.8mA for STN-right and between 3.0 and 4.0mA for the STN-left. Stimulation was delivered in response to beta power changes in the range 12-19Hz recorded with bipolar configuration (contact pair 1-2) in the STN-right.
**Results:** In cDBS and aDBS respectively, the UPDRS part III was 11 and 4; the Voice Handicap Index was 53 and 2; the Gait and Falls Questionnaire was 34 and 15; the Parkinson's Disease Questionnaire-39 was 33 and 6. At both evaluations, the Beck Depression Inventory and Montreal Cognitive Assessment showed absence of depressive and cognitive symptoms.
**Conclusions:** Although preliminary and of a single patient, our results are encouraging and suggest better control over DBS-related side-effects with aDBS.

### P_43

### The added value of accelerometric monitoring during thalamotomy

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**Background:** Thalamotomy, involving radiofrequency (RF) ablation of the thalamic ventral intermediate nucleus (VIM), alleviates medication-refractory tremor in patients with movement disorders such as Parkinson's Disease (PD), Essential tremor (ET) and Holmes tremor (HT). However, limited data is available on tremor intensity during different thalamotomy stages. Also, the predictive value of intraoperative tremor status for treatment outcome remains unclear. The aim of this study is to quantify the clinical changes in tremor during the different stages of thalamotomy, and to investigate the relationship between intraoperative findings and clinical outcome.
**Methods:** Data were gathered between January 2020 and May 2022 during consecutive unilateral VIM RF-thalamotomy procedures in patients with PD (n=11), ET (n=6) and HT (n=3). MDS-UPDRS scores and tri-axial accelerometry data were obtained during rest, postural, and intention tremor tests. Measurements were performed intraoperatively (1) before lesioning-probe insertion, (2) directly after lesioning-probe insertion, (3) during coagulation, (4) directly after coagulation, and (5) 4-6 months post-surgery. Accelerometric data were recorded continuously during the coagulation process. Outcome measures included MDS-UPDRS tremor scores and accelerometric parameters (peak-frequency, tremor amplitude, and area-under-the-curve of power (AUCP)). Tremor intensity was assessed for the insertion effect (1-2), during coagulation (3), post-coagulation effect (1-4), and postoperative effect (1-5).
**Results:** Following insertion and coagulation, tremor intensity improved significantly compared to baseline ($p<0.001$). The post-insertion effect clearly correlated with the postoperative effect ($\rho=0.908$, $p<0.001$). This was also the case for the post-coagulation effect ($\rho=0.932$, $p<0.001$). Both tremor amplitude and AUCP declined gradually during coagulation. Peak frequency did not change significantly intraoperatively. Accelerometric amplitude and AUCP both correlated significantly with MDS-UPDRS ratings ($\rho\geq0.688$, $p<0.001$).
**Conclusions:** This study shows that both the post-insertion effect and the post-coagulation effect are good predictors for thalamotomy outcome. Accelerometric monitoring of tremor allows the objective quantification of these intraoperative parameters, reducing the dependency on experienced raters for reliable clinical assessments.

## P_44

## Deep brain stimulation practices for Parkinson´s disease in Chile

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**Background:** Thalamic deep brain stimulation (DBS) for tremors and subthalamic (STN) or globus-pallidus-internus (GPi)-DBS for advanced- Parkinson disease (PD) are FDA-approved indications. Worldwide, DBS approaches are variable. Available in Chile since 2009, provider centers and patients accessing DBS have increased despite access barriers. Therefore, we aimed to assess DBS-practice variability in Chile.
**Methods:** A structured web survey was sent to neurologists or neurosurgeons representing the DBS centers in Chile.
**Results:** Nine centers (5 metropolitan and four regional centers) participated. The average center`s experience was six years (range:1-22). The mean number of pre-surgical evaluations and DBS surgeries per center were: five (range: <1 to 10) and 1.8 (range:<1 to 4) per trimester, respectively. Three centers use a decision-making screening tool for suitable candidates. A movement disorders neurologist pre-operative assessment is required in all centers. Most centers require more than 90% certainty in PD diagnosis. All responders specified that levodopa treatment is mandatory before surgery; opinions on dopamine agonists and amantadine before surgery are dissimilar. Most consider DBS if fluctuations occur despite dosing levodopa 5–6 times daily. All centers command an ON-OFF levodopa challenge, defining 33% as the cutoff value. A neuropsychological assessment is mandatory universally. Other providers rarely participate in preoperative evaluations. Setting up DBS committees is not unanimous. Near half centers predefine a DBS target. Most procedures are completed in one stage. All centers use microelectrode recording guidance. STN is the most targeted nucleus. Post-operative CT images are obtained within 24 hours. Neurologists program patients during follow-up. Post-surgery rehabilitation is not a standard of care. Follow-up timelines are variable.
**Conclusions:** Possibly DBS is underutilized in Chile, according to the low reference rate and surgical volume reported. Furthermore, the approaches are heterogeneous among Chilean DBS centers. Therefore, a local expert consensus is suggested to promote the proper development of this therapy in Chile.

## P_45

## Long-term outcome of globus pallidus interna deep brain stimulation for Parkinson's disease patients: five-year follow-up

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**Background:** Deep brain stimulation (DBS) of globus pallidus interna (GPi) is an established treatment for advanced Parkinson's disease (PD). However, in contrast to subthalamic nucleus (STN)-DBS, long-term outcomes of GPi-DBS have rarely been studied.
**Methods:** We retrospectively analyzed the clinical data for PD patients who underwent GPi-DBS. Longitudinal changes of UPDRS scores from baseline to 5 years after surgery were assessed.
**Results:** Forty PD patients with a mean age of 59.5 ± 7.9 years at DBS surgery (mean duration of PD: 11.4 ± 3.4 years) were included at baseline and 25 patients were included in 5-year evaluation after DBS. Compared to baseline, sub-scores for tremor, levodopa-induced dyskinesia (LID), and motor fluctuation indicated improved states up to 5 years after surgery ($p < 0.001$). However, UPDRS Part 3 total score and sub-score for postural instability and gait disturbance (PIGD) gradually worsened over time until 5 years after surgery ($p > 0.017$ after Bonferroni correction). In a logistic regression model, only preoperative levodopa response was associated with the long-term benefits on UPDRS Part 3 total score and PIGD sub-score (OR = 1.20; 95% CI = 1.04 - 1.39; $p = 0.015$ and OR = 4.99; 95% CI = 1.39 - 17.89; $p = 0.014$, respectively).
**Conclusions:** GPi-DBS provides long-term beneficial effects against tremor, motor fluctuation and LID, but PIGD symptoms gradually worsen. This selective long-term benefit has implications for the optimal application of DBS in PD patients.

## P_46

## AutoloGous UncondItioneD pEripheral nerve tissue delivery to the substantia nigra (GUIDE) in patients with Parkinson's disease undergoing DBS surgery

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**Background:** We have been investigating the direct delivery of autologous peripheral nerve tissue (APNT) as cell therapy in Parkinson's disease for the purpose of disease modification. In a previous study, PNT was harvested and implanted in participants two weeks following nerve transection. Recent evidence suggests that similar results could be obtained from freshly harvested, naïve, PNT without the 2-week delay. The objective of this pilot study is to trial the direct delivery of naïve PTN in PD participants at the time of DBS surgery. If successful, the data collected from this pilot will be used to guide and formulate our next generation of cell therapy trials and would represent a streamlining of our surgical protocol with potentially less risk to participants.
**Methods:** This study was approved by the University of Kentucky IRB and covered under the FDA's Same Surgical Procedure Exception. Ten participants will have sural APNT harvested and deployed bilaterally to the SN directly following standard-of-care DBS surgery utilizing frame-based stereotaxy for trajectories. Feasibility measures will include technical measures of the grafting procedures and percent of participants successfully receiving bilateral PNT delivery. Safety measures include continuous adverse event monitoring. Clinical assessments will be performed to follow secondary and exploratory clinical endpoints over the course of 12 months postoperatively.
**Results:** To date, we have consented three participants and one has undergone surgery. The participant successfully received bilateral DBS electrodes and bilateral delivery of APNT and is awaiting follow-up visits at 6-months and 12-months. The only study related adverse event was transient pain in the area surrounding the sural nerve biopsy.
**Conclusions:** After implanting pre-injured peripheral nerve tissue to the SN of 68 participants in previous trials, we have designed a study to assess the feasibility of using naïve peripheral nerve tissue as we trial this investigational approach.

## P_47

## Preliminary results from the Engage-PD study: enhancing gait using alternating-frequency DBS in Parkinson's disease

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**Background:** Gait impairment is a crucial unmet need in Parkinson Disease (PD) treatment. High frequency (HF) ~130Hz deep brain stimulation (DBS) treats bradykinesia, tremor, and rigidity, but can worsen gait. Low frequency (LF) ~60Hz DBS improves gait, at least transiently, but may not adequately control other symptoms. A promising approach that alternates LF and HF may simultaneously control all motor symptoms. We developed a paradigm to deliver and evaluate an alternating-frequency paradigm, and report preliminary findings concerning its effect on gait.
**Methods:** Body kinematics were assessed as individuals with subthalamic nucleus DBS navigated an augmented-reality obstacle course. The course was repeated under six DBS conditions: constant HF (control), constant LF, and alterna ting-frequency DBS with four different frequency switching intervals, 10s-HF/10s-LF, 50s-HF/50s-LF, 10s-HF/50s-LF, and 50s-HF/10s-LF. Participants were blinded to the active DBS condition, which were presented in random order. Conditions were performed OFF and ON medications.
**Results:** The gait stride time coefficient of variation (median across laps) was used to rank each condition from 1 (best) to 6 (worst). Ranks were then averaged across participants. OFF-meds, HF performed worst (mean rank 4.8) and LF performed best (mean rank 2.4). Alternating-frequency conditions 50H-10L, 10H-50L, 10H-10L, and 50H-50L had mean ranks 3.6, 3.8, 2.8, and 3.6, respectively. ON-meds, HF tied LF for best performance (mean rank 2.8), while alternating-frequency conditions 50H-10L, 10H-50L, 10H-10L, and 50H-50L had mean ranks 3.8, 3.6, 3.6, and 4.2 respectively.
**Conclusions:** Despite confounders like electrode location, and heterogeneity in disease duration and medication burden, results are consistent with the notion that, for gait in the OFF-med state, LF DBS is best, HF DBS is worst, and alternating-frequency DBS has intermediate performance. ON-meds, for gait, constant HF and LF DBS both outperform alternating-frequency DBS. Future analyses will investigate whether alternating frequencies provide a compromise between gait and tremor control that effectively treats both.

## P_49

### Right subthalamic nucleus active electrode location influences weight gain after deep brain stimulation

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**Background:** Weight gain (WG) is a well-recognized side effect of deep brain stimulation (DBS), and its etiology is poorly understood. The aim of our study was to determine whether there is a relationship between active electrode location in the subthalamic nucleus (STN) and post-DBS WG.
**Methods:** This was a single center retrospective study of 83 patients who underwent STN DBS. Two weeks after surgery, a head CT was obtained and co-registered to the patient's preoperative 3T MRI. The STN midpoint was identified, and the location of the active electrode was defined with respect to the STN midpoint in Talairach space. An ordinary least squares regression model and K-means clustering were applied to evaluate the role of active electrode location on WG measured between 6 to 12 months of follow-up compared to baseline.
**Results:** The mean weight at baseline was 175.9 ± 42.9 pounds and after STN DBS was 188.3 ± 43.1, with a mean increase of 12.4 pounds ($p$<0.001). Active electrode location in the left STN was not associated with WG. In the right STN, the X-axis was correlated with WG (coeff=2.18, p=0.03) with greater WG when moving from medial to lateral STN. The cohort was then divided into 4 clusters in the left STN and 5 clusters in the right STN based on electrode location. No clusters in the left STN were associated with changes in weight. In the right STN, patients in the most anteromedial cluster had 17 pounds less WG at follow-up compared with the most lateral cluster (coeff=-17, p-value=0.012).
**Conclusions:** Our findings suggest that there is less WG after STN DBS when the active electrode is located more medially in the right STN. This finding will need to be confirmed by analyzing active electrode location in other DBS cohorts.

## P_51

### Acceptability of adaptive deep brain stimulation for Parkinson's disease

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**Background:** Adaptive Deep Brain Stimulation (aDBS) for Parkinson's Disease (PD) consists in adjusting stimulation amplitude based on local field potential (LFP) power. aDBS was released in Japan with two modes: dual-threshold mode, which adapts stimulation amplitude to maintain the LFP power between an upper and a lower threshold; and single-threshold mode, which adapts stimulation amplitude when the LFP power exceeds one threshold. The aim of the Early Adapter Part 1 (EA1) study was to characterize the proportion of subjects for whom at least one aDBS mode was acceptable to the subject.
**Methods:** EA1 was a prospective, open-label, observational, dual-center, post-market cohort study. Inclusion criteria included diagnosis of PD with motor impairment, implantation with Percept™ PC neurostimulator (Medtronic), stable continuous bilateral stimulation (cDBS) in the subthalamic nucleus and stable medications. Acceptability of an aDBS mode was determined using the Global Impression of Change (GIC) score and defined as aDBS efficacy greater than or equal to cDBS efficacy with minimal side effects.
**Results:** Twelve PD subjects (mean [sd]: 66.8 [7.36]yo, years with PD 12.5 [4.21], 5 women) were enrolled. All had at least one aDBS mode that was acceptable. Dual-threshold was acceptable in 12/12 (100%) subjects, single-threshold was acceptable in 10/10 (100%) subjects (2 subjects failed to set-up single-threshold). Compared to single-threshold mode, dual-threshold mode was preferred by a majority of subjects (9/12, 75%), perceived as best controlling disease-related symptoms (8/12, 66.7%) and resulting in the least number of side effects (8/12, 66.7%). There were no serious adverse events, and one adverse event of dyskinesia. Further analysis of clinical outcomes will be presented.
**Conclusions:** All subjects tolerated at least one mode of aDBS, most tolerated both, with a preference towards dual-threshold. Further research is ongoing to characterize the patients with PD who will benefit most from aDBS.

## P_53

### Long-term safety of magnetic resonance-guided high-intensity focused ultrasound in movement disorders: a systematic review and meta-analysis

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**Background:** Magnetic resonance-guided high-intensity focused ultrasound (MRgFUS) has emerged as a promising novel modality in the treatment of various movement disorders. Both frame- and lesion-related adverse events are reportedly transient. The aim of this study is to compare long term safety profiles in Essential Tremor (ET), Parkinson's Disease (PD), and dystonia.
**Methods:** A systematic review and meta-analysis were conducted by database search in MEDLINE and EMBASE. Studies of unilateral MRgFUS lesioning until December 2021 were included. The primary outcome measure was the rate of long-term lesion-related adverse events (defined as events reported to persist between 3 and up to 12 months). Adverse events were classified as bulbar, sensory, motor, and cerebellar. Multiple variables were correlated with reported outcomes.
**Results:** Total number of included studies was 39 for ET with 1,001 patients, 10 for PD with 90 patients and 3 for dystonia with 14 patients. The ventral intermediate nucleus of the thalamus was the main target in 40 studies, followed by the cerebellothalamic tract in 6. Ataxia (axial/appendicular) persisted up to 12 months in 59 ET patients (5.8%), whereas only 2 PD (2.2%) and none of the patients with dystonia had persisting ataxia. The percentage of ataxia across all studies did not correlate with the mean values of disease duration, skull density ratio or number of sonications. Sensory symptoms (numbness or paresthesia) were the most reported events in dystonia (2 patients; 13.3%) and in PD (8 patients; 8.8%), followed by 45 (4.4%) in ET. No report of complete sensory loss in all studies. Compared to ET, other movement disorders showed a significantly higher frequency of sensory symptoms (chi-squared = 5.22, p = 0.002).
**Conclusions:** On long-term follow-up, MRgFUS therapy is associated with low and comparable frequency of persistent ataxia across all movement disorders. Sensory symptoms are more frequently reported in PD and dystonia.

## P_54

### Reconstructing time-domain data from discontinuous Percept™ output using external data acquisition and linear filtering

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**Background:** Deep brain stimulation (DBS) devices with recording capability enable a new era of electrophysiological research in movement and other neurological disorders. However, a popular device (Medtronic Percept™) has a key limitation: changing certain stimulation parameters introduce discontinuities of *unclear duration* into the recorded time-domain signals, making precise synchronization with external behavioral events, difficult. We focus on discontinuities introduced by stimulation frequency changes. Fortunately, the Percept™ records its own stimulation artifact, often including moments when stimulation frequencies change. We present a method that exploits this phenomenon to reconstruct accurate time-domain signals from the Percept™.
**Methods:** The stimulation frequency (55Hz or 125Hz) of an ex-vivo Percept™ was switched, every 10-30 seconds for 40 minutes, while recording in Brainsense Streaming mode from two leads. Stimulation artifacts from one of the leads were also recorded at 24kHz via an external data acquisition system (RZ2™ Bioamp, Tucker Davis Technologies, USA). Simultaneously, a 0.5Hz impulse train was applied to the other DBS lead and also recorded via the RZ2™ for use as a reference to calculate time errors.
Linear filters were separately applied to both the RZ2™ and Percept™-recorded versions of the DBS stimulation artifact in order to identify moments of stimulation frequency change. Then, using the RZ2™ recordings as the "gold standard," each discontinuous segment of Percept™ data was time-shifted so the frequency changes from both devices matched.
**Results:** The median time error between the discontinuous Percept™ segments and the RZ2™ recordings was 0.6276s (IQR 0.3665s) before and 0.0096s (IQR 0.0359s) after reconstruction.
**Conclusions:** Most Percept™ data segments were re-aligned with gold-standard external RZ2™ recordings. In vivo, an ambulatory electroencephalography device could serve the same purpose as the RZ2™. This method will reduce time errors enough to allow practical electrophysiology applications such as studies of neural correlates of gait and other motor phenomena.

## Behavior, Cognition,Psychiatry

### P_55

### HIV associated dementia, a clinical case report

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**Background:** HIV damages the nervous system demonstrating different clinical symptoms, where neuropsychological disorders are the most common. HIV-associated dementia (HAD) is the main cause of dementia for people less than 40 years old.
**Methods:** A 41 years old male patient with HIV is presented at the neurology department of Tashkent Medical Academy, diagnosed with Dementia Syndrome by several neuropsychological tests, CT-scan and SPECT changes with brain atrophy and HAD.
Flow cytometry with single platform (SP) and dual platform (DP) methods has been used to identify CD4 count which is the major indicator of HIV-positive individuals for the assessment of their prognosis, immune deficiency status and response to therapy.
**Results:** A 41-year-old, taxi driver, started in 2014 with control at the Hospital of HIV/AIDS Center with a $TCD4^+$ cell count of 589 cells/$mm^3$ and was determined as having an asymptomatic HIV infection.
Next biannual controls through July 2018, did not show significant clinical changes. Patient had no history of sexually transmitted diseases. In September 2022 he complained of mild recent memory loss and resting hand tremor. The brain CT scan showed moderate diffuse subcortical brain atrophy, without space-occupying lesions. The $TCD4^+$ cell count at that time was 595 cells/$mm^3$. Folic acid and B12 vitamin levels were normal. A neuropsychological assessment showed significant neuropsychological alterations in attention and concentration functions, as in verbal and visuospatial memory, compatible with dementia. The patient was proposed to start antiretroviral therapy (HAART), which he rejected.
**Conclusions:** CNS HIV infection is a chronic neurodegenerative disorder, presented with cognitive, motor and behavior abnormalities, including concentration, memory, learning and psychomotor speed deficits. Management of HAD, besides pharmacologic treatment, should include an interdisciplinary team with a psychiatrist, a psychologist and a social worker with an effective participation.

### P_56

### The impact of COVID-19 on depression in patients in Uzbekistan

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**Background:** Symptoms of depression and other mental diseases are experienced by people all over the world. The aim of the study is to investigate the mental health of COVID-19 patients using the Patients Health Questionnaire -9 (PHQ-9), comprised of 9 questions and whether each sub-factor and depression detected on the first days of the COVID-19 disease may impact the COVID-19 outcomes (hospitalization, ICU admission, mortality).
**Methods:** The study was conducted as a multi-centre observational cohort. The consecutive 731 SARS-CoV-2 PCR-positive patients aged over 18 years old (mean age 56,29 ± 16.92 years, 46.1% male and 53.6% female). Data was collected in the Republican Specialized Zangiota hospital – 1 in Tashkent, Uzbekistan; PHQ-9 was assessed at the first medical examination due to COVID-19.
**Results:** Among 731 patients no depression only 7 (1%) patients did not have depression (0-4 points), 5-9 points (mild depression) was in 123 (16.8%) patients, 10-14 points (moderate depression) was in 167 (22.9%) patients, and severe depression (15+points) was in 128(17,5%) patients. All-cause mortality was 116 out of 731 patients (16.0 %) with PHQ-9 determined depression.

**Results**

| | n | % |
|---|---|---|
| | | |
| **Age (years), mean ± SD** | 56,29 ± 16.92 | |
| **Sex, n (%)** | 731 | 100% |
| Male | 337 | 46.1% |
| Female | 392 | 53.6% |
| **Course of COVID-19 disease** | 731 | 100% |
| No depression (0-4) points | 7 | 1% |
| Mild depression (5-9) points | 123 | 16.8% |
| Moderate depression (10-14 points) | 167 | 22.9% |
| Severe depression | 128 | 17,5% |
| Severe (hospitalization) | 344 | 47.1% |
| Critical (ICU admission) | 387 | 52.9% |
| **Mortality** | 116 | 16.0 % |

**Table. Baseline characteristics of patients with confirmed Sars-COV-2 infection required hospitalization in the COVID-19 hospital (n=731).**

**Conclusions:** In our study, we found that COVID-19 not only causes physical health problems, but it also has the potential to induce a variety of psychiatric issues. We identified that 724 patients had depression and 116 suicidal ideation which directly increased all-cause mortality.

**P_59**

## Clinical and neuropsychological characterization of patients with primary progressive aphasia in the DESCRIBE-FTD-study

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**Background:** Patients with three PPA variants: logopenic (LPA), non-fluent/agrammatic (PNFA) and semantic (SemD) were enrolled in the DESCRIBE-FTD-study, a clinical multicenter registry study at the German Center for Neurodegenerative Diseases.
**Methods:** Anamnestic, neurological and neuropsychological (CERAD-plus Neuropsychological Assessment Battery (CERAD-plus-NAB)) data from 117 patients with three PPA variants and 61 healthy controls were analyzed.
For the neuropsychological variables, corrected norm values were calculated for age, education and sex. Statistical analysis included single factor variance analyses and the Bonferroni and Tukey tests.
**Results:** 30 patients with SemD (16 females (F) and 14 males (M)), 59 with PNFA (30 F, 29 M) and 28 with LPA (13 F, 15 M) were compared with 61 healthy subjects (31 F, 30 M). The mean age at inclusion in the study was 62 ± 14 years in the controls, 68 ± 7 years in SemD, 69 ± 9 years in PNFA, and 69 ± 8 years in LPA. The disease duration was approximately 3 years in all three PPA subgroups. PNFA was the least cognitively impaired. Compared to SemD, it scored better in semantic fluency, confrontational naming and verbal memory. PNFA was also better in confrontational naming and verbal learning compared to LPA. Visual constructive skills were impaired only in LPA. SemD showed the most marked cognitive impairments. The results of the Mini Mental Status Examination (MMSE) did not differ between the three PPA variants.
**Conclusions:** PNFA is the most frequent PPA variant in this study.
PPA is mainly seen in patients older than 65 years and affects equally men and women.
CERAD-plus-NAB is a suitable tool to evaluate neuropsychological impairments of PPA patients compared to controls.
In CERAD-plus-NAB the most marked cognitive deficits were seen in SemD, whereas PNFA showed the least severe cognitive impairments.
Only LPA revealed visuo-spatial deficits.
MMSE is not appropriate to differentiate the PPA variants.

## P_60

## Distinctive course characteristics of depression and anxiety disorders in Parkinson's disease

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**Background:** Depression is considered the most important variant of affective disorders and is included in the non-motor disorders of Parkinson's disease (PD).
The purpose of the study. Analysis of levels of depressive disorders in the course of PD.
**Methods:** 56 patients with PD (30 men and 26 women) were enrolled for the study. The average age of patients is 32-67, 44.5±3.6 years. The duration of the disease is 4-9 years, on average 6.5±2.8 years. The control group consisted of 20 age- and sex-matched patients without PD. Diagnosis was based on the UK PD Association brain bank criteria. Stages of the disease were determined according to the Hen and Yar criteria. Levels of depressive and anxiety disorders were assessed using the HADS scale.
**Results:** The results of the examination show that 36 patients (64%) had various levels of depression and anxiety, and the average HADS score was 12.6±3.4 points. In the patients of the control group, this indicator was 4.5±2.9 points. When examined according to the duration of the disease, the depression and anxiety levels were higher than 13 points in long-term patients and amounted to 15.4±3.7 points. When comparing the clinical forms of the disease, subclinical depression and anxiety predominated in the akinetic-rigid and tremor forms (11.8±4.4), and depression and anxiety were clearly expressed in the mixed form of the disease. When analyzing the stages of the disease, subclinical and moderately expressed depression (11.1±3.8) predominated in stages I and II, while moderate and high levels of depression and anxiety were observed in stage III of the disease.
**Conclusions:** Depression and anxiety disorders in PK have a specific course and are inextricably linked to the duration of the disease, clinical forms and stages of the disease.

## P_61

## Some aspects of prediction dementia in patients with Parkinson's disease

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**Background:** Predisposition to the development of Parkinson's disease dementia (PDD) is determined in the presence of early signs of cognitive deficit. Objectivization of methods for assessing cognitive deficits in patients with PD, in our opinion, will allow us to develop methods for predicting the development of dementia in patients with PD. The purpose of the study was to conduct a comparative assessment of the sensitivity and specificity of various known methods for screening and assessing possible dementia in patients with cognitive impairment associated with PD.
**Methods:** 48 patients with PD underwent neuropsychological screening to assess their cognitive state. The screening methods PD-CRS (Parkinson's disease cognitive rating scale), MMSE (mini-mental state examination), and PANDA (Parkinson neuropsychometric dementia assessment) were used. The degree of deviation from the norm, when assessing cognitive impairment, was determined on the basis of the gradation distribution of the results obtained, according to standard scales.
**Results:** The diagnostic sensitivity of the scales for predicting dementia in patients with PD was differentiated. Thus, the sensitivity of PANDA in assessing cognitive impairment was 42.9%. The PD-CRS (24.1%) and MMSE (2.5%) methods were less sensitive. The correlation between assessment methods, age and disease duration was only R=0.389±0.029 ($p<0.05$). Meanwhile, the specificity of tests in assessing cognitive impairment was significantly higher (64.9%, 51.7% and 23.9%, respectively; $p<0.05$). When diagnosing dementia in patients with PD, PANDA revealed dementia in 32.5%, PD-CRS in 8.4% and MMSE in 1% of patients. The correlation between PANDA and PD-CRS was R=0.425±0.025, PANDA and MMSE – R=0.118±0.012 and PD-CRS and MMSE – R=0.312±0.017
**Conclusions:** In the diagnosis of cognitive impairment in Parkinson's disease, PANDA and PD-CRS are more sensitive than MMSE. At the same time, the PANDA method is the most reliable for diagnosing and predicting the development of dementia in patients with PD.

## P_67

## Evaluation of voice intensity and speech loudness perception in Parkinson's disease

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**Background:** Voice in patients with Parkinson's Disease (PD) is characterized by a quiet speech (hypophonia). Nevertheless, the underlying mechanisms are not well understood. To identify potential perceptual deficits in hypophonia, this study analyzed voice intensity and speech loudness perception in PD.
**Methods:** Fifteen PD patients and fifteen age and sex-matched healthy controls participated in this study. Voice intensity was evaluated using the *Consensus Auditory-Perceptual Evaluation of Voice* (CAPE-V). Three speech loudness perception tasks included a magnitude estimation, an imitation task and a magnitude production procedure. The magnitude estimation and the imitation task were performed using an external voice at 60, 65, 70, 75 and 80 dB. For magnitude production procedure the participants were asked to repeat a sentence both quieter and louder than their own voice at an habitual volume.
**Results:** The participants with PD produced an impression of lesser voice intensity attribute of CAPE-V ($p$ = 0.035). Loudness in magnitude production task of PD patients was statistically significant lower than did the controls subjects when they asked to repeat a sentence two ($p$ = 0.003) and four times ($p$ = 0.000) louder than a previous one spoken by themselves.

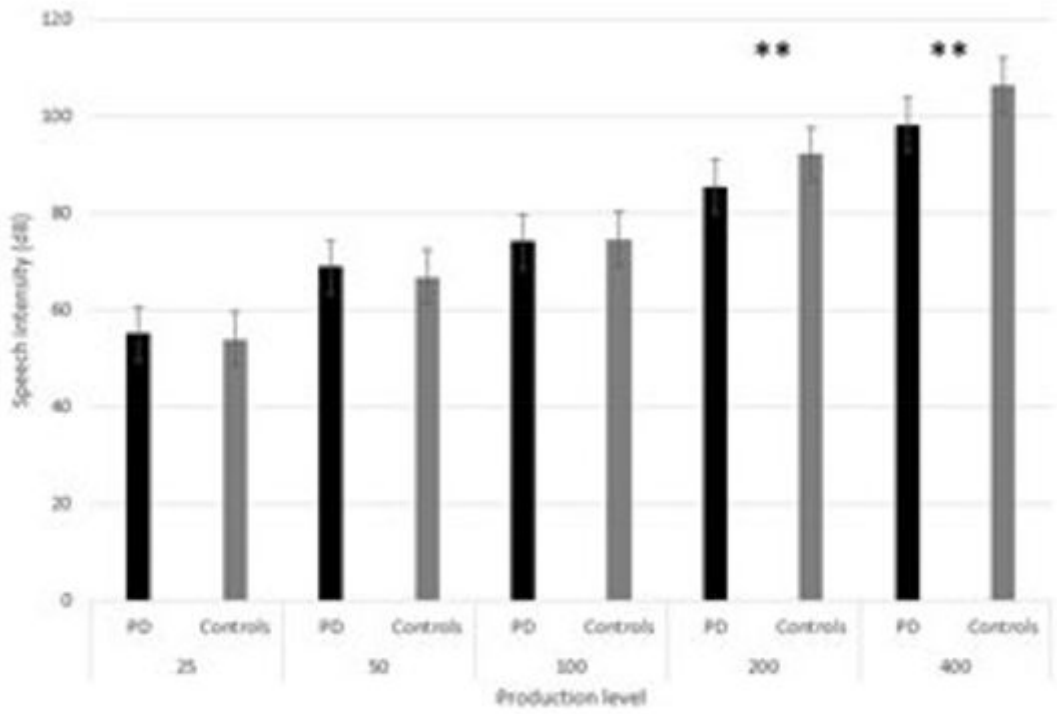


**Fig 1.** Average speech intensity produced by the Parkinson Disease (PD) and controls for the five intended loudness levels during the magnitude production task. Error bars indicate the standard deviation.
** $p \leq 0.01$

No differences were found between PD individuals and healthy controls neither when they asked to repeat the sentence two and four times quieter than their own voice nor in magnitude estimation and imitation tasks.
**Conclusions:** The findings support that hypophonia in PD patients might be driven by an impaired perception of their own speech loudness.

## P_72

### Factors predicting amantadine response among patients with Parkinson's disease

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**Background:** Amantadine is the only commercially available medication to alleviate levodopa-related dyskinesias (LRD) in Parkinson disease (PD). Amantadine response is variable and currently, there is no data to predict patients' response. We aimed to identify demographic, clinical and genetic factors that correlate with efficacy and tolerability of amantadine to predict therapeutic outcomes.
**Methods:** Patients with confirmed diagnosis of idiopathic PD and amantadine exposure (n=53) were identified and classified as responders (group 1), non-responders (group 2), and unable to tolerate due to side effects (group 3). Demographic and clinical data were collected and a biological sample (blood/saliva) for genetic testing was taken for 28 patients to date. Associations of amantadine response with clinical and demographic factors were assessed using univariate analysis. Polygenic risk scores will be calculated using the latest genome wide association data to correlate with therapeutic response.
**Results:** At present, 53 (group 1: n=17, group 2: n=14, group 3: n=22) patients have been identified. The mean age was 68.1 years and 53% (n=28) were male. Mean duration of PD was 11.2, 9.5, and 11.8 years and mean duration of formal PD diagnosis to initiation of amantadine was 8, 5 and 3 years respectively ($p$=0.049). Median levodopa equivalent daily dose was significantly lower in group 3 (group 1: 1040mg, 2: 928.5mg, 3: 690mg; $p$=0.007) with 50% (n=11) of group 3 participants having undergone deep brain stimulation. The most common side effect was leg edema (n=10; 18.9%) followed by visual hallucinations (n=8, 16.2%). Genetic analysis is ongoing.

**Conclusions:** Our cohort underscores the heterogeneity in amantadine response and tolerability. We hope that pharmacogenomic data can shed light into this variability. Results are still being analyzed and will be shared at the Congress.

## P_76

### A study of genetic variation associated with rates of motor and nonmotor progression in early Parkinson's disease

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**Background:** Genetic variation among people with Parkinson's disease (PD) has been associated with differential rates of motor and nonmotor progression. Further study of these associations may facilitate patient-specific prediction or elucidate disease mechanisms.
**Methods:** We used whole exome sequences and clinical data of participants from three studies of *de-novo* PD (PPMI, NCT01141023, n = 415; SURE-PD3, NCT02642393, n = 259; STEADY-PD III, NCT02168842, n = 289) to test for associations between pre-specified genetic variants and motor (MDS-UPDRS Part 3) and non-motor (MoCA) progression over 48 months. For each variant, we categorized participants as homozygote or heterozygote carriers. We analyzed progression using random-slope mixed models, adjusting for age at baseline, biological sex, years of education, baseline Schwab and England Activities of Daily Living, and their interactions with time. We adjusted for population structure using ten principal components. In analyses of motor progression, we excluded data after initiation of antiparkinsonian medications except for baseline use of MAO-B inhibitors, amantadine, and anticholinergics to avoid confounding by symptomatic effects.
**Results:** 19 genetic variants across 13 known genes and 5 unknown genes were identified in the literature, including 15 associated with motor progression and 4 associated with nonmotor progression. SNP variant rs12497850 in the *IP6K2* gene was associated with faster motor progression ($p < 0.05$), and no variants were associated with motor or cognitive progression after adjusting for multiple comparisons. Some confidence intervals excluded associations of the magnitudes previously reported, while others did not.
**Conclusions:** We failed to observe significant associations between the 19 pre-specified PD SNP progression variants and both motor and nonmotor progression over 48 months. Possible explanations for our negative results include a lack of power due to our smaller sample size and application of different statistical models. Future work includes validation of the previously reported SNP-progression associations by replicating the prior reported statistical models.

## P_77

### Parkinson's disease genetic results from a large midwest cohort: the Gary A Smith PD GENEration site

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**Background:** The Parkinson's Foundation PD GENEration initiative provides genetic testing and counseling at no charge, to anyone with Parkinson's disease (PD). PD GENE tests for seven genes: LRRK2, GBA, SNCA, PRKN, PINK1, PARK7, and VSP35. The goals of the initiative are to provide genetic information to patients and clinicians, advance research and clinical care, and facilitate PD genetic-based clinical trials (pdgeneration.org). To date, over 7,500 patients have been tested nationally, with 14% of patients testing positive for one of more of these genes.
**Methods:** The University of Kansas Medical Center, the Gary A Smith PD GENEration Site, offers genetic testing to anyone with PD in the Midwest. Testing is done in person with a blood sample or virtually through a buccal swab for persons unable to travel to the center.
**Results:** Genetic testing results through PD GENEration are available for 483 patients with PD who were tested between October 2020 and January 2023. In this sample, 51 patients (10.6%) are positive for at least one of these genes. More specifically, 32 have a GBA gene, 10 have a PRKN gene, and five have a LRRK2 gene. Interestingly, four (7.8%) patients testing positive have two genes of interest; two have one GBA and one PRKN gene, one has two PRKN genes and one has two GBA genes.
**Conclusions:** To date, the GBA gene is the most common gene found in a large cohort of persons with PD in the Midwest, representing 69% of those testing positive for at least one of the seven genes.

## Subtypes, natural course

### P_78

### Relationship between peripheral adaptive immune markers and Parkinson's disease progression

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**Background:** 发现适应性免疫系统与帕金森病（PD）的发病有关。在这里，我们探讨了外周血适应性免疫标记物在预测疾病进展中的价值。

**Methods:** 疾病持续时间少于 3 年的 PD 患者被纳入并每年进行评估。在基线时评估外周血适应性免疫标志物（CD3+、CD4+、CD8+ T 细胞亚群、CD4+:CD8+ 比率、IgG、IgM、IgA、C3、C4）。

**Results:** A total of 152 patients were included. Peripheral blood immune markers were not correlated with baseline scores of Montreal Cognitive Assessment (MoCA) and Unified Parkinson's Disease Rating Scale part Ⅲ. Multiple linear mixed effects regression model found that patients with higher baseline CD3+ T lymphocyte subsets had a mild rate of decline in MoCA scores.

**Conclusions:** Our results indicated that the adaptive immune system may play an important role in the cognitive decline of PD patients at the early stage.

### P_82

### The impact of type 2 diabetes mellitus drugs on the onset of Parkinson's disease

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**Background:** Multiple epidemiological studies have linked Parkinson's disease (PD) and type II diabetes (T2D); however, the relationship between the two and the impact of specific treatments remain unclear.

**Methods:** We assessed the age of onset of PD and estimated the prevalence of T2D in PD compared with individuals with essential tremor (ET) and the general Italian population. Age at onset was compared between patients without T2D (PD-noT2D), patients who developed T2D before PD onset (PD-preT2D) and patients who developed T2D after PD onset (PD-postT2D).

**Results:** The T2D standardized ratio of PD (N=8380) and ET (N=1032) patients was 3.8% and 6.1%, respectively, while the overall prevalence in the Italian general population was 5.3%. In PD-preT2D patients on antidiabetic treatment, PD onset was associated with a delay of +6.2 years ($p<0.001$), while no difference was noted in PD-postT2D. The onset of PD in patients with T2D of 7 years or less was delayed by an average of 4.8 years, while patients with T2D of more than 7 years had an average delay of 5.7 years compared with patients without T2D before the onset of PD. These differences remained after adjustment for gender, coffee consumption, and smoking. We specifically examined the effect that metformin treatment on the age of PD onset compared with other antidiabetic treatments, but found no difference ($p = 0.525$).

**Conclusions:** T2D treated with antidiabetic therapy is associated with delayed onset of PD. These findings prompt further study of antidiabetic drugs as relevant options for disease modification of PD.

### P_83

### Relationship between postural instability and gait difficulties, visuo-cognition and vision in Parkinson’s disease

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**Background:** Postural instability and gait difficulties (PIGD) are prominent features in people with Parkinson's Disease (PwP). The presence of PIGD has been associated with rapid disease progression and is a major contributor to falls, causing significant disability and decreased quality of life (QoL) in PwP. The major factors that contribute to falling are not limited to motor symptoms, but also include non-motor symptoms, such as impaired vision. Previous studies have identified a relationship between visual deficits and postural control but did not emphasize PIGD severity. Therefore, this study aims to examine the relationship between vision, visuo-cognition, and the severity of the PIGD motor subtype.
**Methods:** Twenty-seven PwP (twenty-one males, six females) underwent vision, visuo-cognition, and mobility testing. The average age was 65.0 ± 7.9 years, with a disease duration of 6.9 ± 6.3 years, and a median Hoehn and Yahr score of 2. Nine people were in the PIGD subgroup, sixteen were in the Tremor (TD) subgroup, and two were undetermined. Vision was measured by assessing visual contrast and acuity of both eyes. Visuo-cognition was measured using visuo-perception (object identification), visuo-construction (copying a figure), and visuo-spatial (judging location of object) abilities. Additionally, motor symptoms, general cognition, and attention were evaluated. A multiple linear forward stepwise regression was used to identify the determinants for the severity of the PIGD subtype based on MDS-UPDRS scores.
**Results:** Results showed that visual acuity and visuo-perception were two determinants of the severity of PIGD subtype. More impaired visual acuity (OR=0.935, 95% CI = 0.069-1.801, p=0.036) and visuo-perceptive abilities (OR= -0.405, 95% CI = -0.659 – (-0.151), p=0.004) were associated with more severe PIGD scores. No other measures were statistically significant.
**Conclusions:** Visual acuity and perception are associated with postural instability and gait disturbances, expanding the list of non-motor contributors to balance and gait disturbances in PwP.

### P_84

### Postural control subtypes in Parkinson's disease and older adults

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**Background:** Considerable evidence points towards changes in postural control among individuals with Parkinson's disease (PD). Many existing studies, however, focus on individual features of postural control, which limits insight into global patterns that can be discerned from center of pressure (COP) plots with the naked eye. Consequently, an unsupervised clustering approach is required to shed greater light on staging of progressive postural control changes.
**Methods:** Data from COP timeseries of 212 participants (PD=135) during balance on a sway-referenced platform was processed to yield 72 features of postural control. Varimax-rotated PCA, nearest neighbor graph, and Louvain graph clustering procedures were subsequently applied to these features to yield postural control subtypes. Differences between these clusters were further examined using $\chi^2$ test, one-way ANOVA, and mixed linear models.
**Results:** Our unsupervised clustering procedure yielded three quantitatively and qualitatively distinct postural control subtypes: normal (N=104), large (N=84), and high-frequency sway (N=24). PD participants made up 91.7% of the high-frequency subtype ($\chi^2$=9.37, $p$=0.0091), and about 60% of both other subtypes. 14.3% of participants in the large sway subtype exhibited a fall when relying on vestibular cues for balance ($\chi^2$=13.64, $p$=0.001), as compared to 4.2% of the high-frequency and 0.9% of the normal sway subtype. Post-hoc spectral band-power analyses revealed that distinctive 4-6 Hz oscillations observed in high-frequency sway subtype are attenuated when they have to rely on vestibular cues for balance (β=-0.738 [-1.302,-0.175], $p$=0.01).
**Conclusions:** Our unsupervised graph clustering analysis revealed a distinct PD-specific subtype of postural sway characterized by relatively spared overall postural stability and the presence of high-frequency COP oscillations that vary as a function of available sensory information. Future studies should utilize inertial sensors and recordings of electrical activity in brain and muscle to better explain how postural oscillations emerge from brain-body interactions.

## Clinical assessment

## P_85

### Evaluation of the clinical outcomes and disease burden in advanced Parkinson's disease patients: PROSPECT study preliminary results

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**Background:** There is limited prospective, real-world data describing the changing clinical outcomes and disease burden for patients with PD. This study describes the long-term clinical outcomes and disease burden of Parkinson's disease (PD) in patients with motor fluctuations inadequately controlled by current medications.
**Methods:** PROSPECT is a 24-month prospective, observational, international study evaluating the progression and disease burden of patients with PD inadequately controlled by oral conventional therapy (and potentially eligible for device-aided treatments). Key eligibility criteria include patients aged ≥ 30 years inadequately controlled after optimization efforts with available oral medication, and ≥ 2.5 hours of "Off" time/day. The primary endpoint is change in "Off" time from baseline to 24 months assessed by the patients' PD diary. Other assessments include disease severity (H&Y "On" state), changes in non-motor symptoms (NMS scale [NMSS] and PD Sleep Scale-2 [PDSS-2]), activities of daily living (UPDRS II), quality of life (PD Questionnaire-39 [PDQ-39] and EQ-5D-5L), cognitive function (Mini-Mental State Evaluation), health care resource utilization, caregiver burden (Modified Caregiver Strain Index), treatment satisfaction (TSQM-9) and patient global impression of change in severity (PGIC-S).
**Results:** This analysis of baseline demographics and disease characteristics included 232 patients from 7 countries including the US (52.6% male, 72% white, mean age of 67.9 ± 9.4 years, and PD duration of 9.1 ± 5.5 years). At baseline, the mean ± SD Off time (hours/day), H&Y stage, NMSS total score, and PDQ-39 summary index were 5 ± 2.5, 2.2 ± 0.8, 43.4 ± 30.6, and 23.7 ± 14.3, respectively.
**Conclusions:** The study is ongoing, and results will provide real-world, long-term prospective insights on the progression of disease burden, clinical outcomes, and treatment patterns in patients with PD.

## P_86

### Technology for virtual assessment of the quality of rhythmic movements in the extremities

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**Background:** A low-cost quantitative continuous measurement of movement in the extremities was developed to optimize visual observation of structured motor assessments in person and on video as well as accelerometry signals from the extremities (McKay, *et al.,* MethodsX 6 (2019) 169–189 https://doi.org/10.1016/j.mex.2018.12.017) (Figure 1). Since in person studies have been published (Harrigan, *et al.,*Data Brief 31 (2020) 105876. https://doi.org/10.1016/j.dib.2020.105876), we sought to test the feasibility of online assessment of videos of the protocol conducted in person.

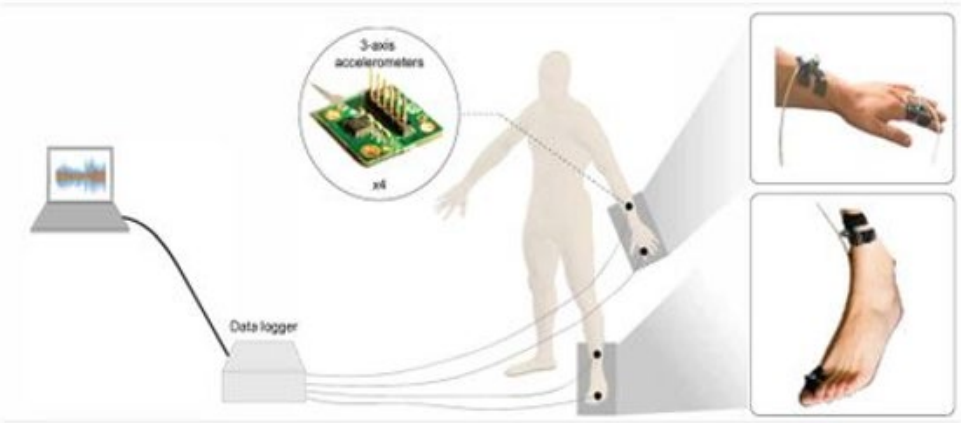


Figure 1. Schematic diagram of procedure to generate output from accelerometers on the extremities to record on a data logger to connect to a laptop computer for conversion to signals for further analysis (McKay, *et al.*, MethodsX 6 (2019) 169-189) (Courtesy of Jenny-Ann Phan, MD, PhD).

**Methods:** The protocol was administered to participants PD (N=2) as well as age-matched healthy participants with typical development (TD) (N=3). The coordinator shared the screen of his monitor to display videos edited to individually display each of the 12 tasks of the protocolr to a team of six trained raters in different locations. After viewing each individual task once, raters independently rated items. After rating all 12 items, raters sent their scores to the coordinator who then conducted a consensus to agree an a single score for each task. After the process was completed for one participant, the procedure was repeated for the next participant.
**Results:** Raters demonstrated better agreement for tasks with stationary extremities.

| Age | PD | Male | Ht | Wt | 3.17UR | 3.17UL | 3.17UCR | 3.17UCL | 3.15R | 3.15L | 3.4R | 3.4L | 3.5R | 3.5L | 3.6R | 3.6L | 3.9U |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 76 | 1 | 1 | 72 | 178 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| 70 | 0 | 1 | 61 | 122 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 72 | 1 | 0 | 64 | 177 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 3 | 0 | 0 | 0 | 0 | 0 |
| 58 | 0 | 1 | 71 | 215 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 3 | 3 | 3 | 3 | 0 |
| 55 | 0 | 1 | 67 | 159 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 |

| Age | 3.17LR | 3.17LL | 3.17LCR | 3.17LCL | 3.7R | 3.7L | 3.8R | 3.8L | 3.9L |
|---|---|---|---|---|---|---|---|---|---|
| 76 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| 70 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 |
| 72 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 58 | 0 | 0 | 0 | 0 | 3 | 3 | 0 | 0 | 0 |
| 55 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Table 1. Demographic traits and consensus scores of six independent raters of videos of motor tasks of five participants.

Age: Age in years; PD: Parkinson's disease 1 = present, 0 = absent (healthy control with typical development); Male: Male 1 = present, 0 = absent (female); Ht: Height in inches; Wt: Weight in pounds; 3.17UR: 3.17 Rest tremor amplitude upper limbs right; 3.17UL: 3.17 Rest tremor amplitude upper limbs left; 3.17URC: 3.17 Rest tremor amplitude upper limbs right counting; 3.17ULC: 3.17 Rest tremor amplitude upper limbs left counting; 3.15R: 3.15 Postural tremor of the hands right; 3.15L: 3.15 Postural tremor of the hands left; 3.4R: 3.4 Finger tapping right; 3.4L: 3.4 Finger tapping left; 3.5R: 3.5 Hand movements right; 3.5L: 3.5 Hand movements left; 3.6R: 3.6 Pronation-supination movements of the hands right; 3.6L: 3.6 Pronation-supination movements of the hands left; 3.9U: 3.9 Arising from chair upper limbs; 3.17LR: 3.17 Rest tremor amplitude lower limbs right; 3.17LL: 3.17 Rest tremor amplitude lower limbs left; 3.17LRC: 3.17 Rest tremor amplitude lower limbs right counting; 3.17LLC: 3.17 Rest tremor amplitude lower limbs left counting; 3.7R: 3.7 Toe tapping right; 3.7L: 3.7 Toe tapping left; 3.8R: 3.8 Leg agility right; 3.8L: 3.8 Leg agility left; 3.9L: 3.9 Arising from chair lower limbs (McKay GN, Harrigan TP, Brasic JR. A low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease. MethodsX 2019; 6:169-189. https://doi.org/10.1016/j.mex.2018.12.017).

**Conclusions:** Virtual rating of protocol videos by examiners in different locations is feasible.

## P_87

### Community-academic initiative to measure and improve underrepresented group participation in Parkinson's disease research

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**Background:** PD clinical trial participants are disproportionately non-Hispanic Caucasian, creating limited generalizability of research findings. It is unclear why there is incommensurate rates of underrepresented group (URG) research participation; lower health literacy and lack of trust have been suggested as contributors. Community engagement through education on PD and associated studies has the potential to improve awareness and understanding of research, and in turn increase participation rates.
**Methods:** Four educational workshops with a total of 92 participants were held at community centers in URG-predominant Chicago neighborhoods. Pre- and post- workshop surveys qualitatively assessed participants' knowledge of PD symptoms and signs, trust in medical researchers, and willingness to participate in clinical trials.
**Results:** The majority of participants identified as either African American (35.9%) or Asian (37%). Survey results indicated that on the whole, community members were trustful of clinical researchers and had positive feelings towards research and researchers' intentions. Participants were most open to participate in studies that could be done within their homes or offered financial compensation, and were least open to participate in studies that involved obtaining biological samples. Very few respondents had ever been asked to participate in a PD clinical trial before (8.1%). Respondents had a basic baseline understanding of PD, and tremor was the symptom most commonly identified as an early sign of PD (32.6%).
**Conclusions:** Surveying predominantly AA and Asian community members of URG-rich Chicago communities revealed moderate to high levels of trust of researchers in these groups, and a willingness to participate in patient-centered clinical trials that mitigate barriers and include facilitators.

## P_89

### Wearables for advanced Parkinson's therapy screening and management

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**Background:** Advanced therapies (AT) such as deep brain stimulation (DBS) and levodopa-carbidopa intestinal gel (LCIG) can meaningfully lessen advanced Parkinson's disease (PD) motor symptoms and improve quality of life. However, determining who should be referred for AT and when a recipient needs therapy adjustment remain a challenge.
**Methods:** Adults clinically diagnosed with PD and primary complaints of motor fluctuations including peak dose dyskinesia, off-period tremor, and/or off-period akinesia/bradykinesia who are potential candidates for AT were recruited. For eight months, participants were instructed to wear a smartwatch-based monitoring system at least four days per month to passively monitor tremor, slowness, and dyskinesia. We compared frequency of dyskinesia and tremor episodes to identify differences in participants who were recommended for AT before and after intervention, as well as between participants who were and were not referred for AT.
**Results:** To date, ten participants enrolled and two withdrew (5F/3M, age 68±9 years, disease duration 7±3 years, HY 2.3±0.5). Two received DBS implants two months into the study and none received LCIG. At baseline, tremor and dyskinesia were present more frequently in participants who later received DBS than in those who did not (tremor: 52% vs 12%; dyskinesia: 2.9% vs 0.9%). In one participant, DBS was recommended due to dyskinesia. Their dyskinesia frequency was reduced by 96% compared to before surgery (6% vs 0.2%), while tremor frequency was reduced by 70% (30% vs 9%). DBS was recommended for another participant due to tremor, which was present 74% of the time as measured by the wearable system.
**Conclusions:** The smartwatch system detected differences in symptoms before and after DBS and between patients who did and did not receive DBS. As more data is collected, we will investigate using wearables to develop predictive models to identify appropriate candidates for AT and when AT recipients need therapy adjustment.

## P_90

### Actigraphy shows feasibility as a biomarker of dopaminergic medication use and motor fluctuations in Parkinson's disease

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**Background:** We evaluated the feasibility of using real-world mobility from actigraphy to track dopaminergic medication use and complications, like motor fluctuations, in Parkinson's disease (PD). PD dopaminergic medication use commonly causes motor complications, worsening PD disability and quality of life. Clinical care is limited by biased self-reporting, heterogenous disease courses, and reliability and subjectivity of clinical evaluations to assess fluctuations. Objective tracking of medication use and complications can improve PD clinical care and early identification of worsening PD. We tested the hypothesis that real-world mobility data could track PD patient mobility response to dopaminergic medication use.
**Methods:** Twenty-nine, idiopathic PD patients (mean age = 66, 22 males, median Hoehn & Yahr = 2) using dopaminergic medications participated. Demographics and medication prescription were self-reported (mean Levodopa Equivalent Dose = 574mg). Real-world mobility was monitored using wrist-worn actigraphy for 4 weeks (N = 793 days, 91% wear compliance) with concurrent dopaminergic medication usage logs (80% compliance). Steps were counted in 1-hr bins from time of medication use to 5-hrs post and evaluated with multivariate linear regression, adjusting for age, gender, and employment and accounting for subject- and day-level variance.
**Results:** PD step counts showed no significant change until 3 hrs post-dopaminergic medication usage. Consistent with hypothesis, step counts significantly decreased after 3-4 hrs ($b$ = -0.09, $p$ = 0.005) and continued to decrease for 4-5 hrs from medication usage ($b$ = -0.19, $p$ < 0.001).
**Conclusions:** This pilot analysis shows feasibility to use real-world mobility data to index PD dopaminergic medication usage and complications. Further research may assess larger sample sizes to determine the relationship of real-world motor complications to clinical data on motor complications and PD severity. Results underscore the feasibility to use real-world digital data to improve clinical care and early identification of disease complications in PD and related disorders.

## P_91

### Is there a white coat effect in Parkinson disease?

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**Background:** The objective of this study is to determine among Parkinson disease (PD) patients if motor performance in the clinical office setting is representative of motor performance in the home environment. Discrepancies may exist in PD patients' situational motor function, analogous to the "white coat effect" of blood pressure, in which function at home differs from formal evaluation in the clinic. Exposing this discrepancy in PD is challenging using conventional methods. However, new technologies, such as wearable kinematic devices, enable remote and objective measurements of motor function which can be compared to in-clinic assessment. Certain populations of PD patients may be more vulnerable to this effect than others. Apathy is common in PD, and we suspect those with greater apathy may have less of a "white coat effect," while those with greater fear of negative evaluation or anxiety will have a greater "white coat effect."
**Methods:** Non-fluctuating PD participants were provided with a wearable a kinematic device (Kinesia U™, Great Lakes Neurotechnology, Cleveland, Ohio). Participants completed a motor assessment task both during a regularly-scheduled movement disorders visit and subsequently at home daily for the following seven days. Demographic profiles, MDS-UPDRS II and III, and clinical scales of anxiety, depression, fear of negative evaluation, apathy were collected for correlation with kinematic motor assessments.
**Results:** A majority of the intended 40 participants with non-fluctuating PD have completed the study with further data collection currently ongoing. Formal analysis and presentation of these data are pending imminent study completion.
**Conclusions:** This study attempts to address ecological validity of PD motor assessments and identifying those who may be vulnerable to a "white coat" phenomenon. Novel methods with remote kinematic devices are advantageous to address new and previously undescribed phenomena in PD.

## P_93

### Clinical and motor fluctuation assessment with a mobile app and electronic diary

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**Background:** Parkinson`s disease (PD) is a progressive neurodegenerative disorder. The progression of the disease is linked with a lower response to antidopaminergic medication, therefore a poor symptomatic control and the advent of motor complications. A mobile app could provide an adequate monitorization of the patient`s symptoms, which would lead to an improvement of therapeutic interventions focused on the individual needs
**Methods:** We developed a free, open-access mobile app in Spanish language, suitable for Android with an electronic diary, non-motor symptoms questionaries, medication section with adjustable intervals and dose, to evaluate and monitor motor fluctuations in Parkinson`s disease patients. Prospective evaluation included a 4-week period pilot trial at home to register ON-OFF periods, dyskinesia, and fill out the questionaries, prior explanation of the app`s features.
**Results:** 17 patients were recruited for the study, of which 2 patients withdrew informed consent and 5 patients were lost in follow-up. A total of 10 patients completed the 4-week trial period. We observed a fluctuation both in motor and non-motor symptoms, being restless leg syndrome the most prevalent non-motor symptom. There was an increase in the percentage of good ON time comparing the first week of use of the app to the fourth week of usage, and a decrease in the percentage of dyskinesia. This difference was non-significant.

| | |
|---|---|
| N | 10 |
| Gender | Female 60%; Male 40% |
| Age (SD) | 57.2 (10.3) |
| Most prevalent non motor symptom in T1 | Restless legs syndrome (60%) |
| Most prevalent non motor symptom in T4 | Restless legs syndrome and pain (40%) |

**Conclusions:** The preliminary results show a high percentage of acceptance towards the mobile app. We observed an increase in the percentage of good ON time and a decrease in the percentage of dyskinesia, although this difference was non-significant.

## P_99

## Acceptability of movement-prompting rehabilitation device to increase non-exercise physical activity levels in people with Parkinson's disease

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**Background:** Physical therapy (PT) is often recommended to people with Parkinson's disease (PwPD) to improve quality of life, however, PT imposes limitations such as little sustained adherence to post-PT instructions. Therefore, recognizing the importance of post-PT interventions with the potential for long-term benefits is essential. This study seeks to test the acceptability of a movement-prompting rehabilitation device (MPRD) prototype to address these shortcomings and increase physical activity in PwPD.
**Methods:** Eighteen PwPD (14M/4F, Hoehn and Yahr (HY) score = 2.33 ± 0.42) underwent motor testing and self-reported activity levels. Participants completed two sessions standing behind a height adjustable table receiving cues from the MPRD to induce stepping. Each session, the User Acceptance Questionnaire (UAQ) was completed; part one addresses usage difficulties and part two addresses participant preference. Acceptability was analyzed according to disease severity with correlation and linear regression. Total standing time was also recorded, with the goal of 80% or more of participants standing for sixty minutes during the second session.
**Results:** For participants with mild PD (HY≤2), greater independence levels were associated with a stronger preference for using the MPRD (OR=3.412, 95% CI = 1.329 - 5.494, p=0.005). For participants with moderate PD (HY>2), a longer Timed Up and Go correlated with more concerns using the device (OR=1.354, 95% CI = 0.046 - 2.663, p=0.045). During the second session, 83% of participants stood for sixty minutes without breaks and 100% with breaks.
**Conclusions:** Results indicate that preference to use the MPRD is greater in participants with mild PD while ease-of-use concerns increase with PD progression. Over 80% of participants used the device for sixty minutes, indicating feasibility in PwPD. Clinical applications in frailer PwPD will require a careful titration protocol to guide the physical standing conditioning process, best supervised by a physical therapist.

## P_100

## Composite measures of motor performance and self-efficacy are better determinants of postural instability and gait difficulties than individual clinical measures in Parkinson's disease

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**Background:** Postural instability and gait difficulties (PIGD) are a significant cause of lower quality of life (QoL) in Parkinson's Disease (PD). Most research on clinical predictors of PIGD measures have focused on individual clinical motor performance variables, However, PIGD motor features often result in fear of falling (FoF) lowering a patient's self-efficacy. We assessed composite measures of motor and self-efficacy of PIGD motor features in PD and compare these to analysis of individual clinical metrics.
**Methods:** 75 PD participants underwent detailed motor and non-motor test batteries. Principal component analysis (PCA) was used to identify clusters of covarying correlates of slow walking, imbalance, falls, freezing of gait (FoG). Traditional univariate analyses were also performed.
**Results:** A single PCA-derived measure of motor performance and self-efficacy of mobility was the most robust determinant of all PIGD motor features except for falls. Univariate logistic regression with adaptive Holm adjustment for multiple testing identified motor performance and self-efficacy of mobility as a determinant of imbalance ($\chi2$=9.237, OR=1.71, 95% CI = 1.21-2.416, p=0.002), slow walking ($\chi2$=12.275, OR=1.678, 95% CI = 1.256-2.241, p=0.0005), and FoG ($\chi2$=10.44, OR=1.579, 95% CI = 1.197-2.082, p=0.001). In addition, postural and balance control components ($\chi2$=3.286, OR=0.631, 95% CI = 0.383-1.038, p=0.007) also associated with FoG. In contrast, analysis of the individual clinical variables showed more limited and diverging findings, including evidence of better cognitive performance but more severe motor parkinsonian ratings in the falls group.
**Conclusions:** Composite measures of motor performance and self-efficacy of mobility are robust determinants of all PIGD motor features except for falls. Univariate analysis of individual clinical measures showed limited correlation with PIGD motor features. Patient's own perception of motor performance, FoF, and QoL deserve more attention as PIGD therapeutic targets in PD.

## P_102

## The effect of 4-month exercise programme on timed up and go test in patients with Parkinsons disease – interim analysis

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**Background:** The timed up and go test (TUG) is a simple performance-based measure of functional mobility and balance in elderly people. It involves timing how long it takes a person to stand up from a chair, walk 3 meters, turn around, walk back and sit down. The objective was to assess the effectiveness of a multimodal exercise training program in patients with Parkinson's disease (PD) using instrumentalized TUG test.
**Methods:** A group of 9 patients with mild to moderate PD (mean age 63.9 ±6.25 years, 6 men) participated in a 4-month exercise program consisting of aerobic-strength training 2x1h/week and coordination training 1h/week. The TUG test was recorded pre- and post-intervention using Microsoft Azure Kinect DK camera during both the ON and OFF state.
**Results:**

| | ON STATE | | | OFF STATE | | |
|---|---|---|---|---|---|---|
| | Baseline | Post-intervention | P-value | Baseline | Post-intervention | P-value |
| Total time (s) | 9±1.74 | 9,9±0,8 | 0,26 | 9,86±2,38 | 9,59±1,459 | 0,91 |
| Standing time (s) | 1,25±0,27 | 1,4±0,23 | 0,09 | 1,41±0,27 | 1,51±0,49 | 0,26 |
| Sitting time (s) | 1,68±0,6 | 1,511±0,53 | 0,55 | 1,514±0,49 | 1,635±0,40 | 0,65 |
| Turning time(s) | 1,28±0,32 | 1,547±0,25 | 0,1 | 1,47±0,43 | 1,36±0,39 | 0,73 |
| Forward_walk time (s) | 2,053±0,38 | 1,973±0,21 | 0,99 | 2,2±0,6 | 1,987±0,32 | 0,36 |
| Backward_walk time(s) | 1,96±0,36 | 1,94±0,21 | 0,82 | 2,068±0,49 | 2,123±0,36 | 0,65 |
| Walking speed (m/s) | 5,05±0,85 | 4,93±0,72 | 0,73 | 4,9±1,05 | 4,666±0,58 | 0,2 |
| Mean step length (cm) | 54,5±12,93 | 51,29±11,1 | 0,164 | 48±11,6 | 49,5±11,2 | 0,65 |

**Conclusions:** We did not observe a significant improvement. This can be due to the low sensitivity of the test metrics in mild to moderate PD patients, the small study population, and lower adherence to training in some of the patients. The study is still ongoing, and the bigger study population may allow us to assess the impact of training with greater accuracy.
**Grant support:** APVV 20-0466, VEGA 2/0076/22, COST DEPASS

## P_104

### Impact of Covid-19 infection on the course of Parkinson's disease

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**Background:** The complete information about the relationship between the infection of Covid-19 and Parkinson's disease is not known. Patients with Covid-19 have been shown to have non-motor cognitive impairments, and worsening levels of depression and anxiety.
**The purpose of the study:** To study the investigating the impact of Covid-19 infection on non-motor impairment in Parkinson's disease.
**Methods:** 34 patients with PD (17 men and 17 women) were enrolled for the study. The average age of the patients was 56-78 years, with an average of 67,0±6.4 years. The average duration of the disease is 5.6±3.6 years. Special neuropsychological tests were conducted. All of these patients were screned before and after Covid-19 infection. Neuropsychological indicators were compared in the dynamics of the period after the transfer of Covid-19 infection.
**Results:** In 34 patients, 61.7% had depression and 64.7% had anxiety before Covid-19 infection. When analyzing the level of cognitive impairment, 82.3% of patients had cognitive impairment, 78.5% of patients had pre-dementia cognitive impairment, and 21.5% of patients had mild dementia symptoms. When 34 patients were re-examined after Covid-19 infection, 91.1% had depression and 94.1% had anxiety. 97% of patients had cognitive impairment, 61.7% had pre-dementia cognitive impairment, and 38.3% had dementia symptoms. Constipation was observed in 52.9% of patients before infection and in 76.4% of patients after Covid-19 infection. 91.1% of the above disorders were strongly manifested in patients aged 60-78 years. When compared with the post-Covid-19 infection period, depression and anxiety predominated in the early stages, while cognitive impairment and constipation deepened over time.
**Conclusions:** Covid-19 infection strongly affects non-motor disorders in Parkinson's disease, increases depression and anxiety scores, deepens cognitive impairment, and accelerates the development of constipation.

## P_109

### Visualization of the MDS-UPDRS results

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**Background:** The MDS-UPDRS is the most widely used assessment for Parkinson’s disease. It captures disease symptom severity with 65 individually scored items divided into four parts. Each part produces a subtotal score; the full scale has a total score. Comparing scores for individual symptoms within a given patient can be cumbersome and challenging.
**Methods:** UPDRS scores obtained from routine clinical evaluations were entered into spreadsheet software that had been formatted to visually depict symptoms and their severity. Parts I, II, and IV of the assessment were illustrated as three individual inline columns maintaining the item arrangement for each part. The motor symptoms in Part III were grouped by anatomical location (i.e. right arm), and secondarily by symptom type (i.e. tremor), resulting in a Vitruvian Man-style figure. The scoring system of the UPDRS was maintained with each number 0-4 being color coded to further facilitate interpretation of symptom severity.
**Results:** Three identical Part III visualizations are present. Two depict two clinical states (i.e. OFF or ON medication) while a third illustrates changes observed between the two clinical states. The utility of this visualization allows for a detailed picture of the individuality of experienced symptoms associated with PD. We have routinely used it in our clinic over the last three years in over 200 patients to aid in communication among the clinical care team and to communicate with patients and caregivers. It does currently require manual entry of the data into the spreadsheet and manual transfer to the electronic medical record.
**Conclusions:** This visualization tool for MDS-UPDRS data is amenable to use in the clinic and maintains the integrity and validity of the data and exam. The tool has proved to be clinically useful in identifying the most bothersome symptoms and enabling concise interpretation with patients, families, and clinical providers.
Disclosure, CVH, JH, JEQ have a financial interest in the development of the visualization tool. Other authors declare no competing interests.

## P_110

### Smartphone app-based tapping test characteristics in a longitudinal cohort of Parkinson's disease patients

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**Background:** Smartphone applications are inexpensive, widely-available tools that could aid in the clinical assessment of patients with movement disorders. In this longitudinal study we aim to describe the features of a tapping test in Parkinson's disease (PD) patients compared to healthy controls (HC).
**Methods:** Data was prospectively collected from participants enrolled in our population-based Cincinnati Cohort Biomarker Program (CCBP) cohort study at the University of Cincinnati Gardner Center from January 1st, 2019, to December 31st, 2022. This study included (i) participants with a diagnosis of Parkinson's disease (PD) and (ii) age- and sex- matched healthy controls (HC). All participants had demographic, clinical, and technology-based assessments at baseline and one year later. The technology-based assessments included a 20-second tapping test performed using the validated customized smartphone "MJFF sensors 0.2.1" application. Tapping variables included inter-tap intervals, taps-per-second, and inter-tap variability using a coefficient of variation (CV).
**Results:** We included 321 PD patients (untreated, 54; levodopa-treated, 267) and 35 HC. At baseline, there was no difference in inter-tap interval and taps-per-second ($p>0.05$). The untreated PD group showed higher variability with a CV of 0.44 (range 0.22-0.66) than the levodopa-treated PD (0.33; range, 0.19-0.53) and the HC group (0.23; range 0.08-0.32) ($p = 0.002$). One hundred and thirty-nine PD patients (untreated, 25; levodopa-treated, 114) and 10 HC had a follow-up assessment one year later. There were no differences in inter-tap interval and taps-per-second between baseline and follow-up data in both PD groups, although they showed increased inter-tap variability compared to HC ($p=0.02$).
**Conclusions:** The tapping test performance showed higher variability in PD patients compared to controls. This variation was worse in the drug-naïve state and increased after at least one year of follow-up.

## P_111

### Levodopa–entacapone–carbidopa intestinal gel (LECIG) for advanced Parkinson's – single centre experience from Romania

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**Background:** Levodopa–entacapone–carbidopa intestinal gel infusion (LECIG) is a device-aided therapy for advanced Parkinson disease (PD) approved in Romania in 2021. We aimed to assess clinical experience of treating advanced PD patients with LECIG at a single centre in Romania with a mean follow-up of 8 months.
**Methods:** We undertook a retrospective, observational analysis of advanced PD patients initiated on treatment with LECIG. The efficacy of LECIG in reducing daily hours of *off* time and on the occurrence of motor fluctuations (morning akinesia, delayed *on*, no *on*), and type and severity of dyskinesias was assessed. Any PEG-J system issues, device complications or adverse events after starting LECIG treatment were noted.
**Results:** Fourteen 'de novo' patients were included in the analysis. Mean disease duration was 11.2 years and overall mean age was 66.6 years. LECIG treatment was found to significantly reduce daily hours of *off* time compared with baseline pre-treatment values from a mean of 4.9 hours/day to a mean of 1.5 hours per day ($p<0.01$). All types of dyskinesia were also improved. Mean optimised morning dose of LECIG was 5.9 ml and the mean optimised continuous infusion dose was 2.8 ml/hour. Adverse events reported were pain and discomfort related to PEG-J insertion for up to two weeks after the procedure. Caregivers and patients reported that the pump was light and easy to use.
**Conclusions:** Our data show that LECIG treatment was well tolerated by patients and resulted in significant improvements in motor symptoms of PD, and reduced motor fluctuations.

## P_112

## Clinical and sensor-based motor outcome parameters as predictors of freezing of gait in Parkinson's disease

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**Background:** Postural instability and gait difficulties (PIGD) especially Freezing of gait (FOG) are significant causes of loss of quality of life (QoL) in Parkinson's Disease (PD). Reliable, validated, and objective metrics to assess and/or predict FOG progression -in a research as well as clinical setting- are a critical gap in our knowledge. Filling this gap, and predicting FOG progression throughout the duration of the disease could benefit the clinical management of FOG with the ultimate goal of improving QoL for persons with PD.
**Methods:** 82 PD participants underwent clinical motor and sensor-based gait assessments at baseline and at 2-year follow-up with 6 PD participants converting from no FOG to FOG at follow-up as determined by the MDS-UPDRS III item 3.11. Principal component analysis (PCA), and multivariate logistic stepwise regression were used to find outcome parameters to predict FOG.
**Results:** 14 components were obtained from the (PCA). When adjusted for age, gender, disease duration, and LEDD in multivariate logistic stepwise regression, PCA component 2 consisted of the MDS-UPDRS PIGD score, MDS-UPDRS II & III, Bradykinesia score, the Timed Up and Go test (TUG) , The Mini-Balance Evaluation Systems Test (Mini-BESTest), 8.5 meters walking time, turn duration and turn velocity as the most robust composite predictors of FOG (OR=1.386, 95% CI = 1.071 – 1.795, p=0.013).
**Conclusions:** Although the MDS-UPDRS is the gold standard for assessing motor impairments in PD, there is a lack of reliable predictor variables for incident FOG development. We found that composite motor measures UPDRS non-FOG motor items, dynamic balance, and spatiotemporal gait measures reliably predicted 2-yr conversion to FOG.

## P_114

## Quantitative analysis of static postural balance between faller and non-faller in patients with Parkinson's disease

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**Background:** Static postural instability has been identified as important risk factor for falling with a significant impact on the quality of life in patients with Parkinson's disease (PD). The aim of this study was to compare the center of pressure (COP) between faller and non-faller patients with PD during static standing.
**Methods:** Thirty-two faller patients and 32 non-faller patients with PD participated in this study. All patients performed the static balance test on a force plate. COP data were recorded during quiet standing. Mean distance, sway area, mean velocity, mean frequency, and peak power were derived from the COP data. Statistical analysis was performed using independent t-tests to compare faller and non-faller patients.
**Results:** Fallers presented a greater average distance, wider sway area, faster average speed, and greater peak power than non-fallers ($p < 0.05$). In contrast, no significant group differences were observed in peak frequency and mean frequency ($p > 0.05$).
**Conclusions:** Although falls occur during dynamic activities, our study demonstrated that even a safe and simple static postural balance test could significantly differentiate between faller and non-faller patients. Thus, these results suggest that quantitatively assessed static postural sway variables would be useful for distinguishing prospective fallers among PD patients.

## P_115

## Change of gait in Parkinson´s disease patients according to electrode localisation in subthalamic nucleus

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**Background:** Deep brain stimulation (DBS) impacts both motor and non-motor symptoms in patients with Parkinson's disease. Subthalamic nucleus (STN), common DBS target, has its own somatotopic organization. Position of DBS electrode active contact in different parts of STN provides different results on Parkinson's disease symptoms. The aim of our study is to evaluate the impact of the DBS electrode position within the STN on gait in patients suffering from Parkinson's disease.
**Methods:** Our study is based on the results of the study of Navratilova et al [1]. Their results suggested positive effect of DBS on some gait parameters in patient with Parkinson's disease. In our study the coordinates of the DBS active electrode were localised and then the correlation between the location and the change of gait parameters before DBS, after the start of neurostimulation, and 3 months after neurostimulator activation, were calculated. Parameters step length and stance phase duration in different speed were assessed.
**Results:** Data from 20 patients were obtained. Location of DBS electrode active contact had no statistically significant impact on the parameter step length. After start of the stimulation more dorsal stimulation position (Z-axis) was associated with increased stance phase duration in various speeds. Al so more medial stimulation (X-axis) was associated with increased stance phase duration. After 3 months more dorsal, medial and anterior (Y-axis) stimulation was associated with increased stance phase duration.
**Conclusions:** Position of the DBS electrode in STN has impact on change of some gait parameters in patients with Parkinson's disease.
Supported by MH CZ – DRO (FNOl, 00098892).

## Therapy (including surgical, physical)

### P_116

### Enrollment characteristics for patients entering a phase 3 study of subcutaneous levodopa/carbidopa infusion with ND0612

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**Background:** The BouNDless study (NCT04006210) compared the efficacy, safety, and tolerability of subcutaneous levodopa/carbidopa (LD/CD) as an investigational 24-hour infusion with ND0612 versus oral immediate-release (IR)-LD/CD in people with Parkinson's disease (PwP) experiencing motor fluctuations. Here we report patient enrollment characteristics; primary results will be available in 2023.
**Methods:** Following screening, PwP on ≥4 doses/day of oral LD/dopa-decarboxylase inhibitor (LD ≥400mg/day) and experiencing ≥2.5h daily OFF-time were consented and enrolled. They entered a 4-6 week open-label adjustment period during which oral LD formulations and COMT inhibitor doses were converted to equivalent doses of IR-LD/CD and then adjusted to optimal clinical effect. Patients then entered an 4-6 week open-label ND0612 conversion period in which IR-LD/CD was replaced by ND0612 (LD/CD dose up to 720/90mg/day) with adjunct IR-LD/CD, as required, and adjusted until this combination regimen was optimal. Patients then entered a 12-week, double-blind, double-dummy period, during which they were randomized (1:1) either to their optimized regimen of ND0612 infusion (plus IR-LD/CD), or to the optimized IR-LD/CD-only regimen.
**Results:** Enrollment characteristics of randomized patients (N=259) were similar to other clinical trials in PwP experiencing refractory motor fluctuations. Mean (± SD) age of subjects was 63.5 ± 9.0 years; 63.7% male; diagnosed with PD 9.6 ± 4.3 years earlier; motor fluctuations present for 4.5 ± 3.3 years, mean OFF time 6.1 ± 1.7 hours. Levodopa equivalent daily doses at enrollment were 1029 mg; 86% of patients were receiving adjunct Parkinson's medications, mainly dopamine agonists (63%).
**Conclusions:** Enrollment characteristics of patients randomized in the BouNDless trial are consistent with those observed in other clinical studies in PwP experiencing motor fluctuations.

### P_117

## Rationale for a potentially pivotal study of NE3107 in Parkinson's disease

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**Background:** Levodopa provides pro-motoric relief in Parkinson's disease (PD) but lacks disease-modifying potential and can cause motor complications, including levodopa-induced dyskinesia. Central oxidative stress and inflammation drive neurodegeneration in PD and may contribute to motor symptoms. NE3107 is an oral, blood-brain barrier–permeable small molecule that binds extracellular signal–regulated kinase (ERK) and inhibits pro-inflammatory pathways without affecting homeostatic functions.
NM201 (NCT05083260), an exploratory, phase 2, double-blind, placebo-controlled study, assessed the safety, tolerability, and efficacy of NE3107 or placebo in combination with levodopa/carbidopa in patients with PD over 27 days. At study completion, using descriptive statistics, the MDS-UPDRS Part III score changed 3+ points (i.e., fewer symptoms) from Day 0 to Day 28 in those treated with NE3107 plus levodopa/carbidopa compared to those administered placebo plus levodopa/carbidopa 2 and 3 hours after levodopa administration. Changes of 6+ points among patients <70 years old were observed. A larger proportion of patients treated with NE3107 showed >30% descriptive improvement in motor control. A potentially pivotal confirmatory study is planned.
**Methods:** In the potentially pivotal confirmatory study, patients will be randomized 1:1 to receive 20 mg oral NE3107 twice daily or placebo for approximately 40 weeks. Patients with a diagnosis of PD and history of motor fluctuations with significant morning bradykinesia who have also demonstrated good response to levodopa may be eligible to participate. Safety and tolerability will be assessed. Efficacy endpoints will include change in the MDS-UPDRS and other clinical measures.
**Results:** Outcomes of the efficacy, safety, and tolerability of the NM201 study will be summarized, and how these outcomes may inform the design and interpretation of a potential confirmatory study will be presented at the conference.
**Conclusions:** Using safety, tolerability, and efficacy analyses, studies of the potential therapeutic benefits of NE3107 in levodopa/carbidopa-treated patients with PD will be described and extended.

## P_118

## Rapid onset of good ON time and improvement in motor-state stability in aPD patients after treatment with continuous subcutaneous foslevodopa/foscarbidopa

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**Background:** 24-hr subcutaneous infusion of foslevodopa/foscarbidopa (LDP/CDP) aims to enable continuous dopaminergic stimulation and stable plasma levodopa concentrations. Temporal patterns of motor-symptom improvements throughout the day have not been established for LDP/CDP. This study evaluates time to ON without troublesome dyskinesia ('good ON') and patterns of motor-state stability throughout the day in patients with advanced Parkinson's disease (aPD) treated with LDP/CDP vs oral levodopa/carbidopa (LD/CD).
**Methods:** Diary data collecting motor-states (OFF, good ON, ON with troublesome dyskinesia, asleep)at 30-min intervals over 3 days (normalized to 16-hr waking days) were collected from a 12-week (W), controlled Phase 3 trial of LDP/CDP vs LD/CD in aPD patients(NCT04380142). Adjusted linear regression models assessed changes at W12 relative to baseline and between treatment groups for time to good ON after waking, motor states throughout the day at 30-min and 4-hr intervals, and average number of daily motor fluctuations.
**Results:** Complete baseline and W12 diary data were available for 46 LDP/CDP and 60 LD/CD patients. At W12, LDP/CDP patients reached good ON faster (means: 28.9 vs 82.9 min; p=0.004) and twice as frequently within 30 min after waking (84.7% vs 47.6%; p<0.001) vs LD/CD. OFF was reduced throughout the day for LDP/CDP patients with only 13.8% (vs 57.8%; p<0.001) reporting OFF within 30 min after waking vs LD/CD. Analysis of 4-hr intervals showed LDP/CDP patients had increases in good ON and reductions in OFF at W12 relative to baseline, which was sustained through the day. Daily motor fluctuations was comparable at baseline (means: 12.6 vs 11.1; p=0.178). At study end, LDP/CDP patients reported fewer daily fluctuations (means: 4.7 vs 7.2; p<0.001) with 64.5% reporting ≤6 fluctuations/day vs 38.6% in LD/CD.

**Conclusions:** Patients on LDP/CDP reported good ON after awakening, greater stability of good ON time throughout the day, and fewermotor fluctuations compared to LD/CD patients.

## P_119

### Use of glutathione in Parkinson's disease at earlier stages of the disease and the prognosis of delaying its progression

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**Background:** Parkinson's disease, the second most common chronic neurodegenerative disease, which is characterized by the loss of dopaminergic neurons in the substantia nigra with the presence of corpuscles Levi in the form of intraneuronal inclusions. Redox dysfunction and neurooxidative stress play an important role in the pathophysiology and progression of Parkinson's disease.Glutathione is an endogenously synthesized tripeptide whose depletion occurs in the early stages of Parkinson's disease, and an increase in glutathione has been proposed as a therapeutic strategy.
**Methods:** We conducted a double-blind, placebo-controlled study in 45 patients with Parkinson's Disease of Hoehn and Yahr stages 1-3. The placebo group was a control group of 20 patients who received placebo (saline) and levodopa and the main group of 25 patients who received levodopa and glutathione 600mg (intravenous drip) per day for 60 days.
**Results:** Improvement was seen in the UPDRS (-4,6(4,7),P=0,0025) and UPDRS motor subscale (-2,2(3,8),P=0,00485) scores. Depending on the severity of the disease the statistical analysis showed that despite the overall positive effect of the drug the best effect was observed in the group of patients with initial stages of the disease (1 - 2 stage according to the Hoehn and Yahr scale), statistical analysis performed on the UPDRS scale showed a 16.3% decrease in the total score (P<0.05).
**Conclusions:** In our study,there was improvement of general and motor scores of PD (UPDRS) in both control and main groups.Use of glutathione preparations as additional therapy in patients with Parkinson's disease in the main group showed more appreciable improvement in the earlier period of the disease compared to the control group. This study shows that the long-term use of glutathione over 2 months should be studied.

## P_120

### Impact of physical activity to expand serum a klotho levels amidst people with Parkinson disease

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**Background:** Parkinson disease is a progressive neurodegenerative that affects movement. The pathogenesis of Parkinson’s disease is mediated by different inflammatory mediators such as TNfa, IL-1β, and IL-6. In addition, the brain and kidneys are produced transmembrane mole-ecules called Klotho. Several lines of evidence revealed that loss of Klotho may negatively impact the aging process, neural degeneration, and cognitive impairment in people with Parkinson’s disease. Indeed, Klotho molecules are playing an important role as anti-inflammation and provide a protective effect against age- related diseases such as Parkinson disease. Different lines of evidence suggests that physical activity may exert cura-tive effects in Parkinson’s disease, slowing the underlying neu-rodegeneration and improving related disability symptoms.
**Methods:** A comprehensive computer-based literature search was performed through MEDLINE database.
**Results:** The regular physical activity plays a key role in the secreted form of the a Klotho gene (S-Klotho) in animal models as well as in healthy humans. However, the current literature lacks clinical studies in investing the impact of physical activity on serum a-Klotho levels in people with Parkinson’s disease. Despite that, previous clinical studies in healthy people and animal models showed a promising result in favour of physical activity.
**Conclusions:** Physical activity is a highly effective way of treating and preventing the main causes of morbidity and mortality. Most of which are associated with aging. The absence of effective treatments for Parkinson’s disease highlights the need for preventive strategies such as physical activity. Future clinical studies are required to investigate the impact of physical activity on serum a-Klotho levels in people with Parkinson’s disease.

## P_121

### The Phase 2, randomized, placebo-controlled PRECEDENT trial of SAGE-718 in patients with

## Parkinson's disease cognitive impairment: clinical trial in progress

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**Background:** Parkinson's disease (PD) is a multisystem disorder with diverse clinical features, including neuropsychiatric symptoms and non-motor manifestations alongside motor symptomatology. Cognitive impairment, a common non-motor symptom of PD, contributes to poor functional outcomes, loss of independence, and increased risk of dementia. Significant unmet needs exist for effective and well-tolerated pharmacotherapies that address cognitive impairment due to PD. NMDA receptor hypofunction may be a common mechanism of cognitive impairment associated with neurodegenerative disorders, and positive modulation of NMDA receptors is a novel therapeutic strategy for the treatment of cognitive impairment due to PD and other neurodegenerative diseases. SAGE-718 is an investigational NMDA receptor positive allosteric modulator that has been associated with improved cognitive performance in patients with PD, Alzheimer's disease, and Huntington's disease. The randomized, placebo-controlled PRECEDENT Study is designed to evaluate the efficacy, safety, and tolerability of SAGE-718 as a potential treatment for cognitive impairment due to PD.
**Methods:** PRECEDENT (NCT05318937) is a Phase 2, randomized, double-blind, placebo-controlled trial. Approximately 76 patients aged 50–75 years meeting Movement Disorder Society Task Force Criteria for PD Mild Cognitive Impairment with mild-to-moderate motor involvement will be randomized 1:1 to receive SAGE-718 daily oral dosing or placebo for up to 42 days. The primary endpoint is change from baseline in the Wechsler Adult Intelligence Scale-IV Coding score at Day 42. Secondary endpoints include the proportion of patients with treatment-emergent adverse events (TEAEs), TEAE severity, and number of patients who withdraw due to AEs. Other endpoints include additional assessments of safety/tolerability, motor symptoms, cognitive performance, and functioning.
**Results:** PRECEDENT is currently enrolling at sites in the United States.
**Conclusions:** PRECEDENT is designed to evaluate the efficacy, safety, and tolerability of SAGE-718 in patients with PD cognitive impairment.

## P_122

## Protocol to help neurologists manage subcutaneous apomorphine therapy skin nodules: expert roundtable recommendations

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**Background:** Infusion site reactions (ISRs), including subdermal nodules, cutaneous erythema, and pruritus/pain, are a common occurrence in patients with Parkinson disease (PD) who are treated with continuous subcutaneous apomorphine infusion (CSAI). We aimed to develop a structured algorithm for the routine clinical evaluation and management of ISRs in patients with PD treated with CSAI.
**Methods:** An expert roundtable consisting of US movement disorder neurologists with CSAI experience and dermatologists with expertise in inflammatory-mediated skin disorders was convened to review current knowledge of CSAI-related ISRs and to develop recommendations regarding clinical evaluation and management of ISRs that develop during CSAI treatment.
**Results:** Experts reviewed proposed steps to minimize the development of ISRs, including patient education of proper insertion technique, site rotation, skin hygiene, sterile procedure, and avoidance of problem skin areas. Some patients may be at higher risk of ISRs despite these methods. Experts suggested that a clearer classification system of CSAI-related ISRs be developed, and proposed presence of symptoms, timing, size, erythema, and fluctuance/drainage as factors to include. Based on classification, management would be determined. Most nodules can be managed conservatively. Because infections are uncommon, empiric antibiotics were not felt to be necessary in most circumstances. Patients should be instructed to report ISRs that are not improving, expanding, or associated with systemic symptoms to their healthcare provider.
**Conclusions:** ISRs are common with CSAI therapy, and probably reflect an inflammatory reaction in sensitized patients. Most ISRs resolve spontaneously, but some require evaluation to exclude infection. Simple steps to try to minimize ISRs are proposed. Although further research will help elucidate the underlying causes of ISRs, experts agreed that most CSAI-related ISRs are self-limited, resolve spontaneously, can be managed by a treating neurologist without dermatologic/medical referral, and do not limit successful continuation of treatment.

## P_123

### Targeting the gut-brain axis in Parkinson's disease: preliminary findings from butyric acid supplementation in Parkinson's disease

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**Background:** There is emerging evidence that dysfunction in the so-called gut-brain axis (GBA) plays an important role in the pathophysiology of Parkinson's disease (PD). Prior research suggests that short-chain fatty acids (SCFAs) may provide symptomatic and disease-modifying benefits to people with Parkinson's disease (PwP) through modulating inflammatory, oxidative, and transcriptional regulatory epigenetic and GBA-mediated mitochondrial bio-energetic processes. Therefore, SCFA supplementation may provide a possible therapeutic intervention for PwP. A key SCFA that is naturally produced in the colon is butyric acid. We tested whether supplementation with the post-biotic tributyrin (the triglyceride of butyric acid, a compound naturally present in butter) may benefit PwP clinically and on disease biomarkers.
**Methods:** Our open label clinical trial is in progress. Three PwP (one male, two females) were enrolled in a 30-day trial of tributyrin. Subjects completed baseline and post-intervention follow-up clinical assessments including UPDRS-III, sleep tracking, and blood inflammatory markers via high-sensitivity C-reactive protein (hs-CRP). Within-subject random-intercept mixed-linear models were performed for each variable to assess the viability of tributyrin as a treatment for PD-related symptoms.
**Results:** Among PwP, UPDRS-III scores significantly improved following the tributyrin supplement trial [mean decrease of 5 points, $p<0.001$]. Heart rate variability during sleep also significantly improved following the supplement trial [$p<0.001$]. Lastly, there was a significant interaction between blood inflammatory marker levels and treatment on UPDRS-III scores, such that smaller hs-CRP values were associated with greater motor improvements at follow-up [$p<0.001$].
**Conclusions:** The ongoing positive results from this early trial suggest that tributyrin may help improve PD across a range of symptoms and mechanisms. Conf irmation of these preliminary findings in our Phase 1B pilot may warrant a phase 2 randomized placebo-controlled clinical trial.
Funding: Study supported by the Farmer Family Foundation.

## P_125

### Dysphagia and mortality in people with Parkinson's disease treated with Levodopa-Carbidopa Intestinal Gel

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**Background:** To analyze the impact of the occurrence of dysphagia in advanced Parkinson's disease (PD) patients treated with levodopa-carbidopa intestinal gel (LCIG), comparing clinical factors, disability, and mortality between those developing and those not developing dysphagia. Our primary endpoint was the mortality rate difference between patients with and without dysphagia. Secondary endpoints were the difference between the two groups regarding the presence of hallucinations, dementia, and complete loss of autonomy.
**Methods:** We performed a retrospective observational study including data from PD patients treated with LCIG in Turin and Rome between 2012 to 2022. The presence of dysphagia was identified by a score of MDS-UPDRS item 2.3 > 1. According to the development of dysphagia during follow-up, patients were divided into 2 groups: those who developed dysphagia (PD-Dys) and those who did not (PD-NDys).
**Results:** A total of 86 patients were included in the analysis according to the inclusion/exclusion criteria (Table 1). The survival analysis showed a higher mortality rate in the Dys group ($p < 0.001$) (Fig 1). According to the Cox regression analysis dysphagia was the only variable significantly associated with mortality (Table 2, Fig 1). Univariate regression analyses showed a significant correlation between dysphagia and dementia, hallucination and H&Y score at the last evaluation.
**Conclusions:** We explored for the first time the impact of dysphagia on mortality in a large cohort of advanced PD patients treated with LCIG, confirming its pivotal role as a risk factor for death suggesting the importance of prioritizing its management in the advanced PD stages.

## P_126

## Subgroup analyses of effect of treatment with levodopa inhalation powder (CVT-301) 84 mg by severity of OFF symptoms in people with Parkinson's disease, as assessed by the unified Parkinson's Disease Rating Scale Part III (UPDRS-III)

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**Background:** SPAN-PD was an efficacy and safety study of CVT-301 in patients on stable levodopa/dopa-decarboxylase inhibitor regimens experiencing ≥2h daily OFF time. Patients were randomized to placebo/CVT-301 for OFF symptom treatment as needed ≤5 times/day. CVT-301 84mg significantly improved motor function at week 12, 30 min post-dose, as measured by lower UPDRS-III scores, with improvement recorded as early as 10min post-dose. Proportion of patients achieving an ON state at week 12 also demonstrated significant superiority of CVT-301 over placebo (58% of CVT-301 84mg patients turned ON and remained ON at 60 min post-dose, vs 36% of placebo). This is an analysis of the proportion of patients who turned ON after CVT-301 84mg treatment vs placebo, compared across patient subgroups with different baseline UPDRS-III scores when experiencing an OFF period in the SPAN-PD study.
**Methods:** Analysis compared patients with differing examiner-rated OFF UPDRS-III scores at screening (median UPDRS-III scores ≤33 "low" [range 8-33] vs >33 "high" [range 34-75]). Treatment differences were calculated between CVT-301 84mg and placebo for the proportion of patients who turned ON and remained ON at 60min post-dose at week 12 (stratified by Hoehn & Yahr stage, and screening spirometry).
**Results:** In the low UPDRS-III group (≤33, n=104) at week 12, 30 (50.0%) CVT-301 patients turned ON post-dose and remained ON at 60 min compared with 11 (25.0%) placebo patients (odds ratio [OR] 3.0, *P*=0.011). In the high UPDRS group (>33, n=90) at week 12, 26 (70.3%) CVT-301 patients turned ON post-dose vs 24 (45.3%) on placebo (OR 2.8, *P*=0.026).
**Conclusions:** In SPAN-PD, CVT-301 84mg was significantly more effective than placebo in turning patients ON at week 12 in both PD patient subpopulations experiencing, respectively, more or less severe OFF periods at screening. No substantive difference in drug response was observed between the more and less severe groups.

## P_127

## A population pharmacokinetic comparison of three amantadine formulations

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**Background:** Three amantadine products are available in the U.S., with different indications and dosing regimens: the original immediate-release (AMT-IR) form, and two extended-release (ER) products, one with an IR component [AMT-IR/ER; Osmolex® ER] and one with delayed-release (DR) technology [AMT-DR/ER; Gocovri®]. Only AMT-DR/ER is approved for levodopa-related motor complications (dyskinesia and OFF episodes) in Parkinson disease; however, there are no population pharmacokinetic (PK) data directly comparing these formulations.
**Methods:** Data from 3 crossover studies evaluating AMT-IR/ER (2 studies; N=47) or AMT-DR/ER (1 study; N=23) against an AMT-IR formulation (3 studies; N=70) in healthy subjects (56 male;14 female) were used to develop a population PK model. Concentration-time profiles were generated to compare products across recommended maintenance doses.
**Results:** A PK model was developed using the same disposition process (one-compartment model with first-order elimination) for formulation specific drug absorption processes. Steady-state Cmax for recommended maintenance doses of AMT-IR 100 mg twice or three times daily, AMT-IR/ER 193mg and AMT-IR/ER 258 mg each morning, or AMT-DR/ER 274 mg each nighttime were: 576 ng/mL, 837 ng/ml, 645 ng/ml, 860 ng/ml, and 995 ng/ml, respectively; AUC 0-24 were 11640 ng/mL*hr, 18241 ng/mL*hr, 11652 ng/mL*hr, 15100 ng/mL*hr, and 20069 ng/mL*hr, respectively. Morning concentrations were higher for AMT-DR/ER than other formulations. In contrast to IR-containing formulations, AMT-DR/ER also showed low concentrations in the hours following nighttime dosing.
**Conclusions:** The population PK model predicted AMT plasma concentrations for the amantadine formulations. Comparative plasma-concentration time-profiles generated from the model confirm lack of product interchangeability reported in drug labeling, consistent with their different maintenance dosage and release technology. In contrast to AMT-IR and AMT-IR/ER, clinically used doses of AMT-DR/ER produced higher plasma concentrations in the morning and first half of the day, consistent with its intended use for levodopa-induced dyskinesia, which typically manifests with levodopa dosing in the morning and throughout the day.

## P_128

### Predictability of GOOD ON time during the waking day with amantadine extended-release capsules: a post-hoc analysis of pooled pivotal trials

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**Background:** The emergence of unpredictable levodopa-related motor complications adds extra burden to people with Parkinson disease (PwP), making it difficult to plan daily activities. A once-daily, bedtime-administered, amantadine product with delayed- and extended-release technology (AMT-DR/ER; Gocovri®) is the only antiparkinsonian medication proven to reduce both dyskinesia and OFF episodes in PwP taking levodopa. We hypothesized that treatment with AMT-DR/ER increases the predictability of GOOD ON time (ON without troublesome dyskinesia) over the waking day for PwP with motor complications.
**Methods:** This was a *post-hoc* analysis of pooled data from two similarly designed Phase 3 trials. Patients recorded their predominant motor state in diaries (30-min intervals) over 2 consecutive days. The percentage of predictable GOOD ON time over the waking day was calculated for each visit as follows: For each patient, the percentage of matched diary intervals (meaning at the same time each day) that were concordant for GOOD ON time were tallied and divided by the number of matched intervals where neither interval was recorded as 'asleep'.
**Results:** At Baseline, the percentage of the waking day that was concordant for GOOD ON time was similar for patients randomized to AMT-DR/ER (31.0%[n=98]) and placebo (31.5%[n=96]). Over 12 weeks of treatment, the mean percentage of concordant GOOD ON time improved to a greater extent for patients taking AMT-DR/ER compared to placebo at all timepoints (Week 2: 55.5%[n=93] vs 40.0%[n=91], Week 8: 60.1%[n=80] vs. 43.7%[n=87], and Week 12: 61.1%[n=79] vs 42.7%[n=85], respectively). Assessment of concordance at a stricter threshold (entries should match over all 4 diary days at Weeks 8 + 12) also showed larger improvements for AMT-DR/ER compared to placebo (44.4%[n=84] vs 25.6%[n=76]).
**Conclusions:** This post-hoc analysis of patient diary data suggests that in addition to reducing dyskinesia and OFF episodes, AMT-DR/ER may increase the predictability of GOOD ON time during the waking day.

## P_130

### L-dopa with entacapone as a rescue therapy after a failed attempt to start Duodopa - a case report

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**Background:** Entacapone is a COMT inhibitor that has been used in the treatment of Parkinson's disease. This drug increases the total concentration of L-dopa and decreases the concentration of 3-OMD. As a result, it shortens the duration of the OFF phase, extends the ON phase and improves the clinical condition in the range of motion.
**Methods:** The patient's treatment regimen was modified by discontinuing Duodopa, reducing levodopa and dopamine agonist doses, and adding entacapone, midodrine, and clozapine.
**Results:** A 66-year-old man suffering from Parkinson's disease for 10 years. For 2 years, he experienced disease progression by ON-OFF and OFF states for over 50% of daily activity. Additionally, he had anxiety-depressive states and hallucinations, which were a contraindication to deep brain stimulation (DBS). Anti-Parkinson drugs daily: levodopa 1200 mg, dopamine agonist 16 mg, amantadine 200 mg. ACE III 68/100 pts. Qualified for Duodopa treatment. On day 3 of Duodopa administration, hallucinosis and hypotonia occurred. Despite symptomatic treatment, the symptoms persisted. On day 10, Duodopa was discontinued, and oral medications were restarted at different doses, with entacapone added to the treatment regimen. After 5 months, there was an improvement. Finally, levodopa was reduced by 20%, entacapone 600 mg daily was added, the agonist was reduced to 4 mg daily, midodrine 2.5 mg daily was maintained, and the antipsychotic drug clozapol was added at night.
**Conclusions:** Entacapone may be a good pharmacological rescue therapy in patients with advanced Parkinson's disease in whom other advanced therapies are contraindicated or intolerant.

## P_132

### Real-world utilization of istradefylline among patients with Parkinson's disease

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**Background:** Istradefylline is indicated as adjunctive therapy to carbidopa/levodopa in patients with Parkinson's disease (PD) experiencing "OFF" episodes. Research regarding the real-world use of istradefylline in the US is limited since its 2019 approval. This study examined real-world utilization of istradefylline and other PD-related medications before and after istradefylline initiation.
**Methods:** In this retrospective cohort study, patients who initiated istradefylline (1st filled prescription = index) 9/1/2019-6/30/2020 were identified from the 2019-2020 US Medicare Fee-for-Service 100% sample. They were required to have ≥1 PD diagnosis in the 6-month pre-index period and continuous enrollment during the 6-month pre- and post-index periods. Patient demographics, comorbid medical conditions, istradefylline prescriptions filled, starting dosage, dose change, and concomitant PD-related medications were examined. Levodopa equivalent daily dose (LEDD) and PD-related medications were compared in the 6-month pre- and post-index periods.
**Results:** This study included 734 patients (mean age: 74.0 years; female: 41.0%; White: 86.4%). PD-related comorbid medical conditions were prevalent, including pain (65.1%), gait abnormalities (34.5%), sleep disorders (33.7%), fatigue (31.2%), falls (12.5%), fractures (9.5%), and tremor (8.2%). Overall, 78.8% of the istradefylline patients initiated with a 20mg dose. Among patients with a second istradefylline prescription filled, 89.8% had no dose change. The most common concomitant treatment was carbidopa-levodopa (28.9%) alone. The LEDD significantly decreased statistically in the 6-month post-index period vs. the 6-month pre-index period (median [interquartile range]: 430.4 [298.3-637.4] vs. 285.7 [172.5-416.7] mg/day; p <0.001). Fewer prescriptions filled per patient were also observed in the post-index period across several PD-related drug classes: dopamine precursors (4.7 vs. 4.5, p=0.036), dopamine agonists (1.5 vs. 1.3, p<0.001), catechol-o-methyl transferase (COMT) inhibitors (0.4 vs. 0.3, p=0.039), and monoamine oxidase-B (MAO-B) inhibitors (1.0 vs. 0.9, p=0.041).
**Conclusions:** In this real-world study, patients treated with istradefylline demonstrated reduced utilization of dopamine precursors, dopamine agonists, COMT inhibitors, and MAO-B inhibitors.

## P_133

### Apomorphine hydrochloride injection (Apokyn®) treatment initiations in the presence and absence of an antiemetic in people with Parkinson disease

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**Background:** Subcutaneous injection of apomorphine hydrochloride (APO) is a therapy used in the acute treatment of OFF episodes in People with Parkinson Disease (PwP). In the US, pre-treatment with trimethobenzamide (Tigan) has been recommended to mitigate the risk of nausea and vomiting during APO initiation. However, trimethobenzamide supplies have depleted since 2021 due to cessation in manufacturing. We reviewed real-world experience initiating APO with or without trimethobenzamide pre-treatment from the company sponsored, Clinical Educator Program (CEP) that works to support PwP who are prescribed APO.
**Methods:** The CEP protocol calls for scheduled visits with each patient, prior to and upon APO initiation, titration, and maintenance. Data from the CEP database, including trimethobenzamide use, initial APO dose, and patient outcomes, were reviewed from 2019 to 2021.
**Results:** Data were available for 1910 unique PwP. Among new patient starts, 32% were initiated on APO without trimethobenzamide in 2019 and 2020, increasing to over 80% by October 2021. Despite lack of trimethobenzamide availability, the APO initiation dose did not substantially change across 2019, 2020 and 2021, with 34%, 34%, and 40% of PwP prescribed a 0.1 mg [0.1 mL] starting dose, and 59%, 61%, and 58% prescribed a 0.2 mg [0.2 mL] starting dose, respectively (the remainders initiated at other doses). Lack of trimethobenzamide pre-treatment did not appear to affect the percentage of PwP who discontinued therapy (for any reason) before completing 3 months of treatment (26%, 23%, and 23% in 2019, 2020, and 2021, respectively).
**Conclusions:** These real-world data suggest patients can successfully initiate APO without antiemetic pre-treatment using a flexible initiation dose, based on tolerability, and backed by a comprehensive support network such as the CEP. These data supported a change in the Apokyn prescribing information, which now includes this flexible titration strategy.

## P_134

### Non-invasive transcutaneous afferent patterned stimulation therapy offers action tremor relief in Parkinson's disease

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**Background:** Transcutaneous afferent patterned stimulation (TAPS) of median and radial nerves has been shown to relieve essential tremor, possibly by modulating the ventral intermediate nucleus (VIM) activity within the central tremor network. Many patients with Parkinson's disease (PD) have similar action tremor (postural and kinetic) that responds to deep brain stimulation at the VIM, and may respond to TAPS therapy. This study evaluated efficacy and safety of TAPS to reduce action tremors in PD patients.
**Methods:** Forty PD patients with postural tremor were enrolled in a remote, prospective, single-arm, open-label study with 4 weeks of TAPS therapy between 2 telemedicine appointments. Improvements were calculated in (1) tremor power (2) 6 clinician-rated tasks from Movement Disorder Society Unified PD Rating Scale (MDS-UPDRS) Part III, (3) 8 patient-rated tasks from Bain and Findley Activities of Daily Living (BF-ADL) scale, and (4) clinical and patient global impressions of improvement (CGI-I, PGI-I).
**Results:** TAPS reduced postural tremor power by 66% (54%-79%) (median, interquartile range, $p<0.01$, N=35, primary). MDS-UPDRS and BF-ADL scores improved acutely by 0.5±0.4 and 0.5±0.5, per-task, respectively (mean ± standard deviation, $p<0.01$, secondary). Thirty-eight to seventy percent of patients with bradykinesia, 64% with postural tremor, 58% with kinetic tremor, and 39% with rest tremor (rated at least 'mild' before stimulation) improved by at least 1 point in that task (exploratory). At study exit, clinicians reported improvement in 83% of patients (CGI-I), and 81% of patients reported improvement (PGI-I) (exploratory). Adverse events (AEs) were similar in frequency and type (e.g., skin irritation, discomfort) to previous TAPS studies in ET, with no serious device-related AEs.
**Conclusions:** Objective, clinician-rated, and patient-rated outcomes demonstrated that TAPS improved action tremor in PD patients. Further studies are needed to advance knowledge in this field, about the efficacy of TAPS in PD.

## P_135

### Optimizing augmented reality cueing strategies for freezing of gait in Parkinson disease: the ELIMINATE FoG study

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**Background:** Freezing of gait (FoG) is a symptom of Parkinson Disease (PD) that can interrupt daily living and cause devastating falls. Previous research has demonstrated benefits of cueing on FoG. However, many cue modalities are not ideal for real-world applications, affecting social interaction or requiring adherence to cadences. Non-rhythmic, spatial augmented reality (AR) cues are promising in their versatility and user-friendliness but have not proven effective in reducing FoG, possibly due to field-of-view (FOV) limitations of AR headsets or suboptimal control of how cues are displayed. We designed a clinical trial and a novel cue to study how to best utilize non-rhythmic spatial AR cues to treat FoG.
**Methods:** In this single-center, crossover, unblinded study, 36 PD patients will complete walking tasks in an AR environment projected by the Magic Leap 2 (ML2), a recently released AR headset with a larger FOV than prior models. An AR cue consisting of two concentric circles (designed for use when walking straight or turning) with radii based on stride length will be presented in several randomized variations: constant, user hand-triggered as-needed, user eye-triggered as-needed, examiner-triggered as-needed. AR strategies will be compared to a proven physical cue and a control (no cue) condition. FoG and gait parameters will be compared between the test arms.
**Results:** To date, twelve participants (seven male, five female, mean age 68.8) have completed the trials. One hundred percent reported that the AR cue alleviated freezing during turning (a weak point of past studies). A majority of the cohort preferred self-controlled cues activated in anticipation of FoG. The no-cue condition was most frequently selected as the most difficult. Further data analysis is ongoing.
**Conclusions:** Initial feedback on novel methods of AR cueing as effective FoG therapies is positive. The ML2 headset is well-tolerated as a therapeutic device in a cohort with neurodegenerative disease.

## P_136

### Quality of life with continuous subcutaneous levodopa/carbidopa infusion: exploratory findings from the ND0612 BeyoND study

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**Background:** ND0612 is in development as a 24-hour subcutaneous infusion of liquid levodopa/carbidopa offering people with Parkinson's disease (PwP) the efficacy of continuous levodopa via a minimally invasive delivery system. Primary data from the BeyoND study showed that ND0612 has a favorable safety profile and is well tolerated up to 1 year of treatment (Poewe et al, Mov Disord; 2021).
**Methods:** The BeyoND study is an ongoing open-label study (NCT02726386) of ND0612 treatment conducted in PwP with Hoehn & Yahr score of ≤3 during ON experiencing ≥2 hours daily OFF-time. Exploratory evaluations of efficacy included the PDQ-39, EQ-5D-5L, and Subject Global impression of Improvement (SGI-I). Patient reported outcomes are presented here for 1-year completers (16h and 24h regimens combined).
**Results:** 120 of the 214 enrolled patients completed the first year of treatment. At one year, quality of life as assessed by PDQ-39 summary index changed (improved) by -5.8 points vs baseline with the most substantial improvements in the domains of mobility (-9.0), bodily discomfort (-8.4), stigma (-7.9) and activities of daily living (-6.5). A similar pattern of improvement was seen on the EQ-5D-5L Visual Analogue Scale (VAS) score which improved by 8.4 points vs baseline. A high proportion of patients reported improvement on SGI-I, with 74.7% reporting improvement at Month 12.
**Conclusions:** This open-label study provides preliminary support for the 12-month efficacy of treatment with ND0612 in improving quality of life and global clinical status in PwP experiencing motor fluctuations.

## P_137

### Impact of the highly selective D1/D5 partial dopamine agonist tavapadon on daytime sleepiness: evidence from a phase 2 clinical trial

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**Background:** D2-like receptors are expressed in sleep-regulating dopaminergic pathways, and dopamine agonists (DAs) targeting D2/D3 receptors (eg, pramipexole, ropinirole, rotigotine) can be associated with increased somnolence, excessive daytime sleepiness, and sudden-onset sleep, presenting challenges for daytime activities, including driving (Ondo et al. *Neurology*. 2001;57:1392-1396). For example, in 2 previous clinical trials in early Parkinson's disease (PD), pramipexole monotherapy was associated with Epworth Sleepiness Scale (ESS) score increases from baseline of 1.2 to 1.8 points compared with -0.6 and 0.3-point changes from baseline for placebo, respectively (Hauser et al. *Mov Disord*. 2010;25:2542-2549; Poewe et al. *Neurology*. 2011;77:759-766). Tavapadon, a new, highly selective partial agonist for D1/D5 receptors in development for PD, may ameliorate daytime sleepiness effects and sudden-onset sleep by avoiding D2/D3 receptor agonism. Herein, we report daytime sleepiness data from a phase 2 proof-of-concept trial investigating tavapadon in early-stage PD.
**Methods:** This randomized, double-blind, placebo-controlled phase 2 trial of tavapadon monotherapy flexible dosing up to 15 mg once daily enrolled participants with early-stage PD (Hoen and Yahr Stage I-III) who were treatment naïve or had received dopaminergic agents for ≤28 days (NCT02847650). The change from baseline in daytime sleepiness was investigated as an exploratory endpoint using the ESS (range, 0-24).
**Results:** Mean (SD) baseline ESS scores were 5.1 (3.02) and 4.3 (2.95) for tavapadon (flexible dosing up to 15 mg; n=26) and placebo (n=22), respectively. The mean change from baseline (SD) ESS score at Week 15 was -1.1 (3.01) for tavapadon flexible dosing and 0.3 (2.71) for placebo.
**Conclusions:** Preliminary results indicate that unlike D2/D3 DAs, the unique mechanism of action of tavapadon may impart avoidance of increase in daytime sleepiness effects. Larger ongoing phase 3 trials will further characterize daytime sleepiness with tavapadon.

## P_138

### Continuous, Subcutaneous Apomorphine Infusion for persistent motor fluctuations in Parkinson's disease: full results of the AP2-3000 open-label study

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**Background:** Continuous subcutaneous apomorphine infusion (CSAI) delivered using a wearable pump has been used worldwide to treat motor fluctuations in Parkinson's disease (PD) patients, but there are few prospective evidence-based trials performed. The objective was to evaluate long-term safety and efficacy of CSAI for motor fluctuations in PD patients treated in United States (US) settings.
**Methods:** This open-label study (clinicaltrials.gov NCT02339064) enrolled PD patients with ≥3 hours daily OFF time despite optimized antiparkinsonian therapy (levodopa plus ≥1 additional PD medication). Patients were titrated to optimal CSAI rates for best efficacy and minimal adverse events (AEs) before entering a 52-week maintenance period.
**Results:** Of the 99 patients enrolled, 85 entered maintenance, 69 completed 12 weeks, and 48 completed 52-week maintenance treatment. The mean ± Standard Deviation (SD) daily dose through Week 52 was 45.2 ± 23.1mg. Treatment-related AEs included infusion site nodules (77.8%), dyskinesia (38.4%), nausea (29.3 %), infusion site erythema (27.3%), and somnolence (25.3%), all of which occurred more frequently during the dose titration and optimization period. At Maintenance Week 12, daily OFF time decreased by a mean ± SD -3.0 ± 3.2 hours from baseline (primary efficacy endpoint), and ON time without troublesome dyskinesia increased by 3.1 ± 3.4 hours. Overall, 68.0% of patients rated themselves "much/very much" improved and mean daily levodopa and levodopa equivalent doses decreased by -198mg and -283mg, respectively. Responder analysis at Maintenance Week 12 showed that 62.1% of patients achieved ≥2 hours improvement in daily OFF from Baseline. Endpoints at Week 52 were consistent with Week 12 improvements.
**Conclusions:** CSAI reduced OFF time, increased ON time without troublesome dyskinesia, and allowed for oral PD medication reduction in patients inadequately controlled by optimized levodopa therapy. AEs were consistent with prior studies of CSAI in the PD population.

## P_139

## The complexity of Parkinson disease medication regimens may factor into treatment decisions: results of a PMD Alliance survey

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**Background:** The ongoing management of Parkinson disease (PD) requires clear and open communication between people with Parkinson disease (PwP), care partners and HCPs.
**Methods:** This online survey, conducted with members of the Parkinson Disease and Movement Disorder (PMD) Alliance, evaluated PwP and care partner perceptions about PD and its treatment, as well as the presence of motor complications (dyskinesia and OFF episodes), and communication with HCPs about these symptoms.
**Results:** Of 562 respondents, 440 (78%) were PwP and 122 (22%) were care partners. Most PwP had PD ≥5 years (69%) and took PD medications ≥4 times daily (67%). Most respondents had experienced motor complications: 82% experienced occasional OFF episodes (39% daily), 50% experienced occasional dyskinesia (19% daily), and 28% said they had delayed starting/avoided increasing medications because of dyskinesia or fear of developing it. Despite widespread acknowledgement of these motor complications, 72% felt their symptoms were well-controlled by current medications. Overall, respondents perceived themselves as well-informed about PD and its treatment. Although 72% of PwP said they discussed motor complications with their HCP on most visits; common barriers to these discussions included not wanting to take more medication (35%), difficulty describing symptoms (25%) and not remembering what they wanted to discuss with the doctor (18%). Additionally, care partners often noted that their loved ones want the HCP to think they are doing well, making it difficult for the care partner to raise concerns with the HCP in the presence of the person with PD.
**Conclusions:** Members of the PMD Alliance generally feel comfortable discussing PD symptoms and medications with their HCPs. However, even when PwP and care partners are well-informed, HCPs should be aware of potential barriers to open communication. The level of communication support needed may be even greater for individuals less well-informed about PD.

## P_140

## A blind computerized analysis. Effect of subthalamic deep brain stimulation on posture in Parkinson disease

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**Background:** We sought to assess the effect of subthalamic deep brain stimulation (STN DBS) on Parkinson's disease (PD)-associated postural abnormalities.
**Methods:** A computerized analysis of posture was used to quantify the thoracolumbar, thoracic, and cervical-occipital ventral angles, as well as the thoracolumbar and cervical-occipital lateral angles from the video-repository of three specialized movement disorder centers (n = 158 patients). Data was extracted from frames from video-recordings in the pre-surgical medication-ON (dopaminergic therapy) and post-surgical stimulation-ON/medication-ON states (STN DBS plus dopaminergic therapy). The sum of the five postural angles (global postural angle) was used to compare pre-vs. post-surgical trunk posture alterations. A multivariate analysis was used to examine the association between changes in the postural angles and demographic or clinical variables.
**Results:** There was a 6.7% amelioration in the global postural angle between the pre- and post-surgical assessments (p = 0.031). Motor response to and pre-surgical dosage of levodopa, male gender, and shorter PD duration were identified as predictors for posture improvement after STN DBS. Cases meeting criteria for lower (n = 2) or upper (n = 1) camptocormia respectively improved by 48.1% in the ventral thoracolumbar angle (from 36.4 ± 0.0° to 18.9 ± 4.2°) and 13.8% in the ventral thoracic angle (from 49.1° to 42.3°). Cases meeting criteria for Pisa syndrome (n = 2) improved by 67.5% in the lateral thoracolumbar angle (from 16.9 ± 2.0° to 5.5 ± 4.7°).
**Conclusions:** STN DBS has a relatively small but significant effect on PD-associated postural abnormalities, potentially enhancing the effect of dopaminergic medications alone.

## Parkinson disease: Other Topic

### P_141

### The importance of drug therapy and deep brain stimulation (DBS) in the treatment of Parkinson’s disease

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**Background:** Differentiating two methods of Parkinson’s disease treatment and make a conclusion on the most effective option being used nowadays. DBS has shown denoting effect in tremor form, whilst drug therapy has been practical in the form of trembling-rigid. Despite its efficacy in the early motor complications, it did not lose theraupetic value as the years passed by. Accepted treatments are DBS of the globus pallidus interna (GPi) or subthalamic nucleus (STN), when symptoms are no longer managed adequately with medications. Available drugs have a good symptomatic effect, but none has yet been shown to slow the progression of the disease in humans. In patients with frequent and irregular use of levadopa drugs causes the development of the on-off phenomenon.
**Methods:** For the investigation, 56 patients with a physician confirmed diagnosis of Parkinson’s disease were involved in the inclusion criteria included studies. Patients randomly assigned to GPi (n = 31) or STN DBS (n = 25) were followed for 36 months in the deep brain stimulation testing. The primary outcome was motor function on stimulation/off medication using the Unified Parkinson's Disease Rating Scale motor subscale.
**Results:** Motor function improved between baseline and 36 months with 95% confidence interval and the same number for STN. Health-related quality of life improved at 6 months on all subscales, but improvement diminished over time. The PLCS analysis revealed a major effect of PD but not of medication on the rs-FC strength orofacial primary sensorimotor cortex and the right caudate head. In the PD group, changes in the speech prosody were related to levodopa-induced changes in the CN and OF-SM1 connectivity strength.
**Conclusions:** The research has shown that DBS has more privileges in comparison with levodopa therapy. Despite it has significant impact on each form of PD, the examination proved that frequency of tremors were decreasing gradually.

### P_142

### Parkinson disease psychosis: a case report

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**Background:** Parkinson's disease frequently associates psychiatric manifestations, especially mood disorders such as depression and anxiety. psychosis has rarely been described in this context.
**Methods:** We report a case of a 54-year-old patient followed for Parkinson's disease for 10 years and who is treated with the Levodopa associated with a dopaminergic agonist (Pramipexole) and with the amantadine. He

consulted for a subacute clinical manifestations made of visual hallucinations and a Jealous Delusion as well as hetero-aggressive behavior disorder. On clinical examination, he had an akinetic rigid extrapyramidal syndrome. The UPDRS motor score was 34 and the MMSE score was 28.
The neuroimaging as well as the blood tests were normal and the toxicology screen was negative. The main therapeutic approach was to adjust the treatment (stopping the amantadine) and to introduce clozapine gradually up to a dose of 100mg/day. The evolution was marked by a clinical improvement and a good tolerance of clozapine.
**Results:** Parkinson psychosis is not exceptional. Its pathophysiology is poorly understood. It is probably due to a deposit of alpha synuclein in the cortex. It also behaves as a side effect of dopaminergic drugs. It is revealed by hallucinations (notably visual, but sometimes auditory or kinesthetic) and delusional disorder, mainly paranoid delusions. Management consists of a reduction or stopping this treatement in the following order: anticholinergics, amantadine, dopaminergic agonists then the administration of an atypical antipsychotic: the clozapine.
**Conclusions:** Parkinson psychosis usually appears at an advanced stage of Parkinson's disease. We must think about it before any 1st psychotic episode in a Parkinsonian patient in order to adopt specific and early management.

## P_144

## Psycho-emotional disorders in Parkinson's disease

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**Background:** Evaluation of psychological state (anxiety and depression) of patients who suffer from Parkinson’s disease.
Mental health is often spoken about these days in the popular press and is particularly important to understand as it relates to someone with Parkinson’s disease (PD). It is observed that majority patients mainly face up with anxiety and depression. Everyone involved in recovery needs to be aware of the survivor’s depression — and ready to respond to it. The right kind of treatment and support can help ease the pain and move the survivor down the road to recovery.
**Methods:** To rate the difference between psychological states of patients Hospital Anxiety and Depression Scale (HADS) and Spillberher-Hanin scale were used. 50 patients were divided into 2 groups by age and gender males (n=26, 52%) and females (n=24, 48%) took part in the survey, at the age ranging from 45-65 in both genders (average 53.6 and 57.6 years old respectively).
**Results:** Due to results, rate for anxiety showed greater number compared to depression in males. Average depression rate is 6.26, registering 6.2 in women and 7.2 in men, while numbers for anxiety were slightly higher 7.92 (7.2 and 8.7 in females and males respectively).
**Conclusions:** According to survey results, it can be boldly stated that patients who survived stroke are vulnerable to feel anxiety. Moreover, men are more prone to feel depression and anxiety in comparison to opposite gender.

## P_145

## Kampavata AKA Parkinson's disease in Ayurveda, it's etiology and therapy

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**Background:** Parkinson's disease diagnosis is not yet conceived until half of Dopaminergic neuron degenerated, resulting in inrepairable damage.
We now that pakinson's disease is 90% sporadic, yet unknown clear aetiopathogenesis.
**Methods:** We have drawn parallel between modern medical understanding of PD and Ayurvedic view of PD.
**Results:** In ayurveda, the classic indian medicine system, Parkinson disease like symptoms i.e. parkinsonism was defined as vepathu in which tridoshas are imbalanced and suggests various methods of treatment. tridoshas imbalance is unique to the body type which makes it a personalized medical treatment besides it gives an elemental understanding of the disease at it's root.
**Conclusions:** The theory of **etiology** of PD helps **customise** a working **drug** for the patient.

## P_148

## Novel characteristics of the temporal transition to maximum tongue pressure in Parkinson’s

## disease: a pilot study

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**Background:** The reason why maximum tongue pressure (MTP) decreases in patients with Parkinson's disease (PD) remains unclear. Repeated measurements of isometric force and MTP may be useful for analyzing muscle wasting and force generation. The purpose of this pilot study was to evaluate the clinical characteristics and temporal transition of MTP in PD and normal control (NC) groups.
**Methods:** There were 18 participants in this study: 10 with PD and 8 NCs. The MTP was measured 20 times at regular intervals. The area under the curve of MTP temporal transitions, time to reach MTP, and total transition time of the tongue pressure (time to return to baseline) were compared between the groups.
**Results:** MTP decreased from baseline in PD subjects. Unlike NCs, PD subjects showed diverse and inconsistent temporal transitions. The decrease in MTP and delays in time to reach MTP and time to return to baseline were significantly greater in PD subjects ($p < 0.05$), while there was no group difference in area under the curve values. According to repeated-measures ANOVA, MTP was not different over time between PD subjects and NCs.
**Conclusions:** In this study, muscle fatigue did not affect the decrease in MTP seen in PD subjects, or the diversity and inconsistency of the temporal transition in MTP in that group. These findings indicate that the motor control needed for the repeated, identical movements associated with MTP generation may be impaired in PD patients.

## P_152

## Risk disclosure in prodromal Parkinson's disease – a survey of neurologists

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**Background:** In the absence of a disease-modifying treatment and prognostic uncertainty, ethics of risk disclosure in prodromal Parkinson's disease (PD) is challenging. Previous studies highlighted several facets of these challenges from the perspective of involved parties. However, to date, the view of neurologists who may encounter individuals with prodromal PD remained unrepresented. Moreover, cross-cultural differences intrinsic to the ethics of risk disclosure are yet to be elucidated. Therefore, we investigated the attitude of neurologists toward risk disclosure in prodromal PD.
**Methods:** Turkish neurologists were invited to fill out a questionnaire investigating their approach to disclosing the risk of future PD to an individual with polysomnography-confirmed rapid eye movement sleep behavior disorder.
**Results:** Data from 222 neurologists were evaluated. 61.3% of neurologists stated that they did not attend any lectures on medical ethics. 93.7% of the participants were aware that PD has a prodromal stage. While 15.3% stated that the risk should be disclosed in any case, 6.8% chose no disclosure. The remaining 77.9% favored disclosure only under certain circumstances, the plurality of which was the individual's consent to know about the risk. After reminding the potential neuroprotective effects of exercise and diet, neurologists who chose the option of "no disclosure" decreased to 3.2% (McNemar's test $p= 0.008$). Also, most of the participants stated that it is necessary to detect PD in the prodromal stage (median= 7.5 on a scale of 1-10 ). 92.3% of the participants favored that individuals should be advised about lifestyle changes. No significant differences among the neurologists were found regarding sex, academic title, or field of interest.
**Conclusions:** The majority of the neurologists found it appropriate to disclose the risk of future PD only if the individual expresses a desire to know. Also, recognition of the impact of lifestyle factors on PD is important in prognostic counseling.

## P_153

## The diagnosis value of dopaminergic responsiveness of Parkinson's disease: a systematic review and meta-analysis

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**Background:** Clinical symptoms of early idiopathic Parkinson's disease (iPD) and other parkinsonism can overlap, resulting in a high rate of clinical misdiagnosis. We aimed to confirm the diagnostic value/accuracy of

levodopa and/or apomorphine challenge test in parkinsonian syndromes (PDS) to assess their value in the diagnosis of iPD.
**Methods:** The PubMed, Embase, Web of Science and Cochrane Library databases were searched for articles published up to 14 February 2023. Studies reporting levodopa and/or apomorphine challenge test in PDS were included. UPDRS scores improvement rates, values after the acute levodopa challenge tests (LCTs), pooled sensitivity, specificity, diagnostic odds ratio (DOR) and area under curve (AUC)were calculated.
**Results:** We ultimately included 50 studies. Pooled sensitivity and specificity (95% CI) were 0.82 (0.76-0.87) and 0.77 (0.69-0.836) for acute LCT, 0.76 (0.60-0.89) and 0.90 (0.74-0.96) for chronic levodopa therapy and 0.92 (0.83-0.96) and 0.74 (0.63-0.83) for acute apomorphine challenge test. Pooled DOR (95% confidence interval) were 14.11 (8.7-22.8) for acute LCT, 14.88 (4.22-52.39) for chronic levodopa therapy and 31.8 (10.27-94.08) for acute apomorphine challenge test. The AUC were 0.835 for acute LCT, 0.692 for chronic levodopa therapy and 0.834 for acute apomorphine challenge test. The UPDRS score improvement rate was 32.65%, (95% CI 28.33–36.96), and the UPDRS score improved by 13.97, (95% CI 10.31–17.63) in PD after the acute LCT. While the scores improvement rate was 12.45%, (95% CI 5.42–19.48), and the UPDRS score improved by 3.63, (95% CI 1.12–6.14) in other PDS.
**Conclusions:** There are significant differences in UPDRS scores improvement rates and improvement values between PD and other PDS after the acute LCTs. Acute LCT, chronic levodopa therapy and acute apomorphine challenge test are all effective in diagnosing idiopathic Parkinson's disease. Acute LCT had the highest diagnostic potency of the three groups.

## P_154

## Pharmacokinetic differences of caffeine between LRRK2 G2019s knock-in and wild-type mice

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**Background:** In metabolomic studies, plasma concentrations of caffeine have been found to be lower in Parkinson's Disease (PD) patients than in healthy controls, more so among carriers of pathogenic LRRK2 variants than non-carriers. This supports the interpretation that caffeine may be a marker of PD resistance. LRRK2 Knock-In (KI) murine models have since been used to explore the potential neuroprotective effects of caffeine in these mice, prompting consideration of any direct effect on its pharmacokinetics. The focus of this exploratory experiment was to examine possible pharmacokinetic differences of caffeine between Wild-Type (WT) and LRRK2 G2019S KI mice.
**Methods:** Single intraperitoneal injections of 20 mg/kg caffeine were administered to 20 WT and 20 G2019 KI mice. The mice were sacrificed and perfused at five separate time points post-injection, with whole brains dissected and prepared for quantification of caffeine by HPLC-UV analysis. Two-tailed t-tests were performed to assess statistical significance.
**Results:** Caffeine concentrations were highest 10 minutes post-injection and subsequently decreased with no significant difference between WT and LRRK2 KI mice. (See Table 1)

| Timepoint (Minutes Post-Injection) | Caffeine Concentration (SD) in go/g | | P-Value |
|---|---|---|---|
| | WT | LRRK2 KI | |
| 10 | 1.05 (0.25) | 1.04 (0.18) | 0.92 |
| 20 | 0.92 (0.24) | 0.92 (0.23) | 0.98 |
| 60 | 0.86 (0.24) | 0.64 (0.21) | 0.20 |
| 120 | 0.47 (0.23) | 0.57 (0.19) | 0.51 |
| 240 | 0.27 (0.17) | 0.23 (0.19) | 0.80 |

**Table 1: Wild-Type and LRRK2 Knock-In Whole Brain Caffeine Concentrations Post-Injection**

**Conclusions:** We found no significant difference in the pharmacokinetics of caffeine between WT and KI mice through 240 minutes post-injection. The findings argue against altered caffeine bioavailability as the basis for a greater association between caffeine use and PD resistance among pathogenic LRRK carriers. Studies of LRRK2 KI modulation of a caffeine protective effect in murine models of PD are unlikely to be confounded by altered pharmacokinetics.

## P_156

## The prevalence of Restless legs syndrome in Parkinson's disease in Colombia

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**Background:** Restless legs syndrome (RLS) is a primary sensory neurological disorder with a clinical variety in the presentation of symptoms. It is characterized by an urge to move the extremities, usually, the legs, accompanied by uncomfortable and unpleasant sensations, which predominate during rest or inactivity. Movement can generate partial or totally relieved of symptoms, being one of its main etiologies idiopathic, but it is frequently described in comorbidity with other pathological entities such as polyneuropathy, iron deficiency anemia, multiple sclerosis, and cardiovascular diseases. An association between RLS and PD has been described in the scientific literature.
**Methods:** This descriptive, retrospective, cross-sectional study, included 353 patients with a mean age of 69.2 SD with a diagnosis of Parkinson's disease, who were attended in two centers by movement disorders specialists, between January 2012 and December 2020.
The data were obtained through a telephone survey system of each of the patients and/or their relatives based on the diagnosis criteria established by the IRSLSSG (International Restless Legs Syndrome Study Group).
**Results:** A total of 1372 patients were found in the database, and a sample of 353 patients was obtained.
The general characteristics of the population are reported in Table 1.
The prevalence of RLS in our patients with PD was 20.4%. No statistical significance was found in the analysis between the Hoehn & Yahr stages of PD and the presence of RLS. In terms of severity, patients most frequently described severe and very severe involvement.
4% of patients presented RLS before the diagnosis of PD.
**Conclusions:** In addition to the results described in the literature, this study provides evidence in a Latin American population of the prevalence of restless legs syndrome in patients diagnosed with Parkinson's disease.

## P_159

## Investigating factors contributing to clinical trial recruitment in Parkinson's disease within the Black community

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**Background:** There is a growing body of literature describing disparities in Parkinson's disease (PD) within the Black population, from PD awareness and diagnosis to management and outcomes. Compounding these disparities is inequitable access to PD trials. Only 1.7% of PD clinical trial enrollees to date have identified as Black or African American. This underrepresentation limits the generalizability and validity of research findings and creates a gap in our understanding of the disease in this population. This study aimed to investigate the facilitators and barriers to PD research engagement within Black people with PD and Black healthy controls.
**Methods:** Thirty participants (15 Black participants with PD and 15 Black healthy controls) completed a survey which included demographics, past research participation, personal/family history of PD, and questions on views toward clinical research. The survey was followed by a semi-structured interview covering (1) perceptions of PD, (2) thoughts and experience with clinical research, and (3) recommendations for engaging the Black community in PD research.
**Results:** Thirteen of the 15 participants with PD and all the healthy controls agreed that they would strongly consider participating in a study if their doctor recommended it, and 11 of 15 participants with PD and 12 of 15 healthy controls were interested in learning about studies they might participate in. Barriers identified included time, transportation, location, lack of awareness of PD and research opportunities, and lack of a trusting relationship with the medical research field. Facilitators to research engagement included transparency and education on PD and research opportunities, culturally congruent research team members, convenience/flexibility, compensation, and academic-community partnerships.
**Conclusions:** There is a significant interest in PD research participation in the Black community. Sustainable, long-term initiatives using community-partnered and -located education, relationship-building, and recruitment are possible solutions to address identified barriers and increase the representation of Black participants in PD clinical trials.

## P_162

## Social and gender inequity on overall survival and access to deep brain stimulation in Parkinson disease patients in Colombia

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**Background:** Lower socioeconomic status (SES) has been linked with higher mortality and lower access to treatments, such as deep-brain stimulation (DBS). These variables can be studied in Colombia with SISPRO, the official healthcare registry, which covers 99% of the population. Access to health-system is granted mainly through two insurance schemes: contributory, for people above certain income thresholds, or subsidized, for low-income population. Subsidized scheme can therefore be a proxy to study low SES. Therefore, our aim is to describe discrepancies on survival and access to DBS in PD in Colombia by gender and affiliation regime.
**Methods:** People over 40 years-old diagnosed with PD registered between January 2017 and December 2021 were characterised according to insurance-scheme. Survival was estimated calculating people on a year-by-year basis. A cessation of consultation for over two years was assumed as death. Procedures categorised as "neurostimulator implantation" or "thalamus or basal ganglia procedures" in patients with PD are described. Costs of DBS were calculated by dividing the total cost by the number of patients with the procedure.
**Results:** Overall survival was 49.7% after 5 years. Women on the contributory-scheme survived 8.9% more than on the subsidized-scheme (48.8% vs 39.9%). Men on the contributory-scheme survived 10.2% more than the subsidized-scheme (52.9% vs 42.7%). A total of 196 DBS were implanted, most of them in Bogotá (54%) and on men (45.4%) and on women (27%) from the contributory-scheme (45.4%), compared to men (15.8%) and women (11.7%) from the subsidized-scheme. Total expenditure on DBS implantation was reported on 23,220 USD.
**Conclusions:** When using insurance schemes as proxies for SES, a lower survival rate is associated with the subsidized-regime for both women and men. Access to DBS implantation is also different when comparing regimes. Further research is necessary in order to broaden information about the impact of SES on treatment and progression of PD.

## P_166

### Relationship between visuo-motor Stroop stepping task reaction time and regional cholinergic denervation in Parkinson disease

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**Background:** Poor response inhibition when stepping increases the risk of falling, which is a major determinant of poorer quality of life in people with Parkinson Disease (PD). Cholinergic denervation in PD may contribute to this increased fall risk through cognitive decline and gait-postural deficits. However, the role of acetylcholine and its interactions with the CNS in gait-postural deficits and response inhibition are not completely understood.
**Methods:** 10 PD patients underwent the Stroop stepping task (SST). The final block is a visuo-motor test involving task switching and inhibition of movements. Average time to successfully respond to incongruent trials in the final block (a measure of response inhibition) was used as the response variable. Subjects underwent brain MRI and FEOBV PET to measure cholinergic system integrity. Pearson's R correlations were computed between regional PET bindings and SST performance to select a set of relevant brain regions. Hierarchical clustering was applied to selected regions to determine which of them most closely associated with the response variable. A simple linear regression model was subsequently fitted to assess the significance of association between regional cholinergic integrity and the response variable.
**Results:** Lower reaction times in the SST were associated with greater average cholinergic integrity in right medial orbitofrontal and bilateral anterior cingulate cortices (r=-0.73 [-1.227, -0.250], P=0.008).
**Conclusions:** Cholinergic integrity in right medial orbitofrontal and anterior cingulum predicts SST response inhibition and may provide a novel fall risk mechanism in PD. These regions play an important role in error processing, executive control, and response inhibition – all of which are involved in the integration of visual, cognitive, and motor processes that subserve gait control. Identifying these cholinergic circuits will aid in the development of targets for pharmacological intervention and neuromodulation approaches to manage gait and balance deficits in PD.

## P_167

### Effect of amyloid on cognitive performance in Parkinson's disease and dementia with Lewy bodies

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**Background:** Concomitant amyloid pathology contributes to the clinical heterogeneity of Lewy body diseases (LBD). In this study, we investigated the pattern and effect of amyloid accumulation on cognitive dysfunction in Parkinson's disease (PD) and dementia with Lewy bodies (DLB).
**Methods:** We retrospectively assessed 205 patients with LBD (91 with DLB and 114 with PD) who underwent $^{18}$F-florbetaben PET and divided into amyloid-positive and amyloid-negative groups depending on global standardized uptake value ratios (SUVRs). We investigated the effect of group on the regional and global SUVRs using general linear models (GLMs) after controlling for age, sex, cognitive status, and the Korean version of mini-mental state examination. Moreover, the effect of amyloid on the cognitive function, depending on the type of LBD, was evaluated using GLMs with interaction analysis.
**Results:** In all evaluated regions including striatum, the DLB group showed a higher SUVR than the PD group. Among amyloid-positive patients, the DLB group had a higher regional SUVR than the PD group in the frontal and parietal cortices. There was a significant interaction effect between amyloid and disease groups in language and memory function. In patients with PD, global amyloid load was negatively associated with language ($\beta$ = -2.03; p = 0.010) and memory functions ($\beta$ = -1.96; p < 0.001). However, amyloid load was not significantly associated with cognitive performance in the DLB group.
**Conclusions:** Although the burden of amyloid was higher in the DLB group, amyloid accumulation was negatively associated with the memory and language function in the PD group only.

## Other Parkinsonian Disorders

### P_169

### Hydrocephalus associated with Chiari-I malformation presenting with Parkinsonism and dystonia

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**Background:** Hydrocephalus is estimated to be present in 7-18% of Chiari type I malformation (CIM), though commonly described in the pediatric population and young adults. Hydrocephalus associated with CIM (HC) typically manifests with gait instability, urinary incontinence, and cognitive dysfunction. Extrapyramidal symptoms (EPS) are less described presentations.
**Methods:** We present a 77-year-old male with HC presenting with EPS.
**Results:** The patient presented with a 5-year history of slowly progressive loss of dexterity, right-hand tremors, shuffling gait, and recurrent falls. His nonmotor profile included cognitive impairment, depression, apathy, urge incontinence, orthostatic hypotension, and hyposmia. His motor exam findings included hypomimia, hypophonia, predominantly right-sided dystonia, rigidity, and bradykinesia. Right leg (RLE) levitation was noted at rest. He had a narrow-based parkinsonian gait with RLE dragging, decreased right arm swing with dystonic posturing, and en-bloc turning with positive retropulsion. No neglect or apraxia appreciated on exam. Levodopa response was not noted.MRI brain revealed hydrocephalus and CIM with 16mm caudal cerebellar ectopia causing cerebrospinal fluid outflow obstruction. Additionally, spinal imaging showed cervical syrinx from C2-3 to T2-3. The DaTscan results were confounded by bupropion use but showed preferential involvement of the right caudate. He was considered a neurosurgical candidate and underwent ventriculoperitoneal shunt with significant motor benefits. His cognition has declined during the 18-month follow-up but maintains improvement in his gait, parkinsonism, and dystonia.
**Conclusions:** To our knowledge, this is the first description of HC presenting in late adulthood with levodopa unresponsive asymmetrical parkinsonism with dystonia. The case details several overlapping features with degenerative parkinsonism, which can lead to delayed diagnosis. Interestingly, the DaTscan showed a preferential caudate involvement which has been reported with hydrocephalus previously. Early recognition with surgical intervention can provide significant symptomatic benefits. Further studies are needed to elucidate the effect of hydrocephalus on the basal ganglia circuitry and overlap with degenerative etiologies.

### P_170

### Comparative analysis of the occurrence of nonmotor disorders in Parkinson's disease and vascular Parkinsonism

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**Background:** In Parkinson's disease (PD) and vascular parkinsonism (VP), non-motor disorders are manifested in different degrees, and their first manifestation can be observed several years before the onset of motor disorders of the disease.
**Methods:** 84 patients with various clinical forms of PK (44 men and 40 women) and 30 patients with vascular parkinsonism (16 men and 14 women) were enrolled for examination. The average age of patients with PK is 56.8±6.5 years, and in vascular parkinsonism it is 67.8±6.9 years. Nonmotor disorders were assessed based on specific neuropsychological tests.
**Results:** Of the 38 patients with PD, olfactory disorders were observed in 84.2% of cases several years ago, while in 15.8% of patients, movement disorders began to be observed. Out of 41 observed sleep disorders, 51.2% of patients had movement disorders before, and 48.8% of patients had them after. 83.7% of patients with depression and anxiety were observed in 43, depression was the first onset, which led to the appearance of tremors and rigidity. 16.3% later developed depression and anxiety. Sensory disorders in the form of pain were observed in 71.7% of 39 patients before movement disorders, while 28.3% of patients began to feel pain later. In the syndrome of VP, almost all symptoms began to be observed after motor disorders.
**Conclusions:** Nonmotor disorders can begin very early in PD, depending on where the degenerative process spreads. A more in-depth analysis of olfactory disorders, sleep disorders, affective disorders, sensory will greatly help in early detection of the disease.

## P_171

### Exposure to Lambda-cyhalothrin induces motor dysfunctions and impairs striatal REDOX homeostasis and β- arrestin-dependent Akt signaling in adult *Wistar* rats

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**Background:** The susceptibility of striatal dopaminergic system to lambda-cyhalothrin (LCT), a new generation type II synthetic pyrethroid pesticide with widespread use for insects and pests mitigation, was previously reported by us. Continuing the leads, the present study has been carried out to understand the involvement of REDOX mechanism and β-arrestin / Akt pathway in an attempt to identify molecular targets involved in LCT induced dopaminergic alterations.
**Methods:** Adult male *Wistar* rats (180±20gm) obtained from CSIR-IITR central animal breeding colony were divided into four treatment groups. Rats in three groups were treated with LCT at any of the doses (0.5 or 1.0 or 3.0 mg/kg body weight, p.o.) for 45 days. The fourth group of rats was given corn oil identically and served as controls. Animals were euthanized 24h after the last dose of LCT, brains were removed and dissected to isolate substantia nigra and corpus striatum and processed for gene expression, immunoexpression, and histological studies using different molecular techniques such as western blotting and RT-PCR respectively.
**Results:** Rats treated with LCT exhibited a significant increase in the mRNA expression and protein levels of Nrf2 and decrease in KEAP-1 and HO-1 in the corpus striatum as compared to controls. Decrease in the levels of dopamine receptor DA-D2 and alterations in the immunoexpression of β-arrestin and Akt was also evident in the corpus striatum of LCT-treated rats. Behavioral studies also evince decreased motor activity and motor co-ordination on exposure to LCT. Further, the histological examination also suggests the detrimental effect of LCT on striatal neurons as evidenced by decrease in % Nissl staining.
**Conclusions:** The results suggest that LCT alters the expression of specific targets involved in the regulation of cellular REDOX homeostasis, DA-D2 receptor signaling and β-arrestin / Akt pathway, which affects the viability of striatal neurons and impairs motor activity in animals.

## P_172

### Failure to predict outcomes of ventriculoperitoneal shunting in normal pressure hydrocephalus patients using multi-variable logistic regression models

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**Background:** There is no uniform decision-making paradigm to determine which patients with idiopathic normal pressure hydrocephalus (iNPH) benefit from ventriculoperitoneal shunt (VPS). We sought to evaluate factors or a combination of factors that influence long-term outcomes in shunted iNPH patients.
**Methods:** Patients with NPH who underwent VPS placement between January 1, 2010 and June 30, 2021 were included in the study. Patient's charts' were retrospectively reviewed to determine gait outcomes closest to 1 year post-VPS and were graded by two individuals using the Clinical Global Impressions Scale - Improvement (CGI-I). A score of ≤2 was considered a meaningful positive outcome. The candidate predictors of outcome analyzed included change in walk time pre- and post-external lumbar drain (ELD) trial, change in step count pre- and post-ELD trial, change in assistive device pre- and post-ELD trial, comorbidity index, iNPH Radscale, presence of dementia, age at time of VPS, degree of white matter disease, and parenchymal volume loss on MRI prior to VPS. A step-down method was used to determine which candidate predictors should be included in multi-variable logistic regression model. Simple logistic regression models were also constructed to assess each candidate predictor individually.
**Results:** Our cohort had a mean age of 75 (SD 6) at time of VPS and 36% were female. 179 patients had CGI-I scores for ambulation and 46% had an average CGI-I score of ≤2. 91 patients had completed data for all of the candidate predictors considered. After using the step-down method to select predictors to include in a logistic regression model, the result was a null model. When evaluating candidate predictors individually, none of the candidate predictors showed evidence of a good fit for predicting CGI-I ambulation scores.
**Conclusions:** In our cohort, none of the candidate predictors of outcome correlated with post-VPS ambulation scores at follow up closest to 12 months.

## P_173

### External lumbar drain trial walk tests as predictors of ambulatory Clinical Global Impression rating after ventriculoperitoneal shunting in NPH

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**Background:** In determining candidacy for ventriculoperitoneal shunt (VPS) implantation for treatment of NPH, external lumbar drain (ELD) trials are routinely performed to assess clinical response to cerebrospinal fluid (CSF) drainage.
Optimal changes to monitor pre- and post-ELD trial are unclear. A common strategy is conducting walk tests before and after ELD. Changes in time and step count are frequently assessed; decreases in these values indicate improvement in ambulation. This study assesses these ELD trial walk test variables, and descriptors derived from walk test observation, as predictors of VPS outcomes.
**Methods:** In a retrospective review of 137 NPH patients, ambulatory outcomes of VPS were graded using the Clinical Global Impression – Improvement (CGI-I) scale at follow-up closest to one-year post-VPS. Time and step changes, along with seven categorical changes in gait (e.g. reduced foot clearance), in a ten-meter walk test after ELD were individually evaluated as predictors of ambulatory CGI-I.
**Results:** The cohort was predominately male (69.3%) with mean age of 75.16 (SD 6.19). After ELD, 80.7% improved on time (mean: 7.31 seconds) and 76.7% improved on step count (mean: 3.58 steps). Approximately 50% significantly improved in ambulation after VPS based on CGI-I. Walk test results were not linearly predictive of post-VPS ambulatory CGI-I. False positive rates (FPRs) were high for time and step changes when considering any improvement to be a positive test (79.7% and 75.4%, respectively); FPRs decreased when raising the positive threshold to 5 seconds/2.5 steps (36.23%/42.03%), 10 seconds/5 steps (20.29%/20.29%), or 15 seconds/7.5 steps (14.49%/10.14%). Increasing thresholds greatly increased false negative rates (FNRs).
**Conclusions:** Results suggest the relationship between ELD walk tests and VPS outcomes is not linear. Increasing positive sco re thresholds substantially reduces FPRs but increases FNRs. ELD walk tests with high thresholds may be useful as a rule in tool for VPS, but negative results should not rule out candidacy.

## P_174

### Topography of differential cholinergic vulnerability in Parkinson's disease and atypical Parkinsonisms: a [$^{18}$F]-FEOBV PET study

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**Background:** Cholinergic system changes in Parkinson's disease (PD) have therapeutical implications. Atypical parkinsonism syndromes (APS) have overlapping and APS-specific clinical features with PD that in part may be mediated by disease-specific cholinergic vulnerability. We applied voxel-based principal component analysis (PCA) of [$^{18}$F]-FEOBV vesicular acetylcholine transporter (VAChT) brain PET to investigate the shared and distinct disease-specific vulnerable/resilient cholinergic areas of the brain in PD and different APS subtypes, namely, dementia with Lewy bodies (DLB), multiple system atrophy parkinsonian subtype (MSAp), and progressive supranuclear palsy (PSP).
**Methods:** 9 DLB, 2 MSAp, 45 PD, 8 PSP & 31 normal control (NC) subjects underwent brain VAChT ([$^{18}$F]-FEOBV) PET and MR imaging. We use a scaled subprofile model (SSM) PCA algorithm to generate subprofile model clusters of positively and negatively values based on group discrimination between parkinsonism disorder subtypes (PDS) and NC subjects.
**Results:** Vulnerable cholinergic activity in PSP was mainly in the bilateral insula, bilateral lateral geniculate nuclei (LGN) and left medial geniculate nuclei and right posterior tectum, left caudate, left precentral, right superior temporal, right postcentral, right supramarginal cortices, and thalamus. For MSAp, vulnerable cholinergic activities were present in the bilateral LGN, insula, striatum, middle temporal lobe, supplementary motor area, mid-cingulum, precuneus, paracentral, and thalamus, including right pulvinar. DLB had a vulnerability pattern in the insula, superior temporal (esp. Heschl's) gyrus, calcarine, left caudate, pre-post central cortices, and mid-cingulate. In PD, the vulnerability was mainly in the sup-post temporal, visual and visual association cortices. In all cases, the resilient area was present mainly in the cerebellar and frontal lobes of the brain.
**Conclusions:** Our imaging findings into shared/distinct cholinergic vulnerability regions in different parkinsonism disorders. The current result shows a potential promise in improving the diagnosis of PDS and potential target areas for treatment. A larger study is required to validate and reinforce our findings.

## P_176

### Parkinsonism secondary to mercury poisoning in a Colombian population

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**Background:** Mercury is a heavy metal and its compounds are recognized as potentially hazardous materials. Industrial growth, and especially fluorescent lamps, has increased the exposure and the risk of mercury poisoning. Through environmental studies and case-control studies, demonstrated that mercury is related to the presence of parkinsonism.
**Methods:** Descriptive observational study of patients diagnosed with mercury poisoning and secondary parkinsonism, in a Neurology clinic of the University Hospital between 2015-2020 Sociodemographic, clinical and laboratory, collected in each patient.
**Results:** A total of 10 individuals are reported in whom an intoxication is evidenced by mercury secondary to occupational exposure and that after chelation and management of acute symptoms present parkinsonism. Of the individuals studied, 100% were male and belonged to a company that produces fluorescent lamps; the age range was 38-50 years . In these patients, the range of mercury levels at admission was 93-761 µg / l with controls after chelation in the office neurology lower than 20 µg / l in blood; In addition, intoxication by other heavy metals was ruled out in all patients. 100% of the patients consulted for symptoms due to tremor at rest and bradykinesia, in addition to stiffness, with a positive levodopa test and a score on the MDS-UPDRS-III scale of 5-18.
**Conclusions:** The results of this study suggest that there is a possible association of occupational exposure to mercury (with acute intoxication) and subsequent parkinsonism, however, larger and more methodologically robust studies are required to determine this association. This study is the first in the country to report an empirical association of mercury poisoning and parkinsonism.

## P_180

### Striatal encephalitis: a cause of rapid onset Parkinsonism

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**Background:** Striatal encephalitis is an uncommon cause of secondary parkinsonism. Antibodies most frequently reported with this condition include NMDA receptor, dopamine 2 receptor, LGI1, and anti-recoverin antibodies. We present a patient with basal ganglia lesions on MRI with elevated anti-dopamine 1 and CAM kinase II receptor antibodies.

**Methods:** N/a
**Results:** 72 year-old female with a history of hyperthyroidism and smoking, presented with subacute onset parkinsonism with rapid motor and cognitive decline. Exam showed asymmetric bradykinesia and rigidity with shuffling gait. MRI demonstrated T2/FLAIR and T1 hyperintensities with additional area of enhancement in bilateral caudate and left lentiform nuclei. Workup revealed normal glucose, heavy metals, infection and cancer screen. CSF revealed 3 WBCs, mild protein elevation, elevated IgG index, and absence of oligoclonal bands. Serum and CSF encephalopathy panels were negative except slight elevation in serum GAD antibodies, which decreased on repeat testing. Serum IgG was low. Anti-TPO antibodies were slightly elevated. Cunningham panel demonstrated elevated anti-dopamine 1 antibodies and CAM kinase II antibodies. Brain biopsy demonstrated gliosis and activated microglia. Treatments including levodopa and IVIG led to no objective improvement. Minimal improvement in parkinsonism was noted after IV steroids. Mycophenolate was started outpatient, but patient died 13 months after symptom onset.
**Conclusions:** Our patient had basal ganglia lesions on MRI and activated microglia on brain biopsy to suggest encephalitis as the cause for rapid onset parkinsonism. Commonly reported causes of striatal encephalitis were not found, suggesting possible relation to elevated titers of anti-dopamine 1 and CAM kinase II antibodies. Despite slight elevation in antithyroid peroxidase antibodies, robust improvement was not seen with steroids. While cases of limbic encephalitis have been associated with common variable immunodeficiency, low IgG levels have not been associated with development of striatal encephalitis to our knowledge.

## P_184

### Automatic stridor detection using small training set via patch-wise few-shot learning for diagnosis of multiple system atrophy

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**Background:** Stridor is an uncommon yet distinct non-motor symptom that can aid in the diagnosis and prognostication of multiple system atrophy. Artificial intelligence (AI) may be utilized as a means to develop an automatic stridor detection method. However, the low prevalence of stridor hinders the collection of sufficient data. Therefore, we propose an AI method to detect patients with stridor by combining audio splitting and reintegration with few-shot learning for diagnosis.
**Methods:** We used overnight video-polysomnography data gathered from patients with stridor (19 patients with mul tiple system atrophy) and without stridor (28 patients with parkinsonism and 18 patients with sleep disorders) from October 2013 to May 2022. The audio recordings were pre-processed to extract regions of interest using binary thresholds based on the audio volume. Next, we implemented the patch-wise few-shot learning for sound detection (PFL-SD) AI method to patch-split the processed waveform, train, and arrive at a patient-level diagnosis after merging the original audio waveform with the inferred results (snore vs. stridor). The performance of this design was evaluated in comparison to a conventional method.
**Results:** The proposed method achieved a detection accuracy above 95% using data from only eight patients with stridor for training. Performance improvement of 4 – 13% was achieved compared with a state-of-the-art AI baseline. Moreover, our method determined whether a patient had stridor and performed real-time localization of the corresponding audio patches, thus providing physicians with support for interpreting and efficiently employing the results of this method.
**Conclusions:** This is the first study to propose a method for stridor detection and attempt to validate the few-shot learning method to process medical audio signals. Even with a small training set, a substantial improvement was achieved for stridor detection, confirming the clinical utility of our method compared with similar developments.

## P_185

### Diagnostic utility of movement disorder society criteria for multiple system atrophy

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**Background:** The 2008 criterial for the diagnosis of multiple system atrophy (MSA) has been widely used for more than 10 years, but the sensitivity is low, particularly for patients in early stage. Recently, a new MSA diagnostic criteria was developed. The aim of the study was to assess and compare the diagnostic utility of the new Movement Disorders Society (MDS) MSA criteria with the 2008 MSA criteria.

**Methods:** This study included patients diagnosed with MSA between January 2016 and October 2021. All patients underwent regular face-to-face or telephonic follow-ups every year until October 2022. A total of 587 patients (309 males and 278 females) were retrospectively reviewed to compare the diagnostic accuracy of the MDS MSA criteria to that of the 2008 MSA criteria (defined by the proportion of patients categorized as established or probable MSA).
**Results:** The sensitivity of MDS MSA criteria (93.2%, 95% CI = 90.5-95.2%) was significantly higher than that of 2008 MSA criteria (83.5%, 95% CI = 79.8-86.6%) (*P*<.001). Additionally, the sensitivity of MDS MSA criteria was maintained robust across different subgroups, defined by diagnostic subtype, disease duration, and symptom of onset. Importantly, the specificities were not significantly different between MDS MSA criteria and 2008 MSA criteria (*P*>.05).
**Conclusions:** The present study demonstrated that the MDS MSA criteria exhibited good diagnostic utility for MSA. The new MDS MSA criteria should be considered as a standard for the diagnosis of MSA in clinical practice and future therapeutic trials.

### P_186

### Idiopathic normal pressure hydrocephalus features on MRI in patients with pathologically confirmed progressive supranuclear palsy

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**Background:** Idiopathic normal pressure hydrocephalus (iNPH) is characterized by a clinical triad of gait disturbance, cognitive impairment, and urinary incontinence. In addition to the triad, ventriculomegaly on neuroimaging is a core feature of iNPH. The presence of high Evans index (EI) and disproportionately enlarged subarachnoid-space hydrocephalus (DESH) are widely used as imaging biomarkers for iNPH. Recently, several studies have reported that iNPH could mimic other neurodegenerative disorders, especially progressive supranuclear palsy (PSP), although most of these reports were based on clinical diagnoses. To date, clinical and neuroimaging findings of iNPH in autopsy-confirmed PSP patients have not been systematically investigated.
**Methods:** We retrospectively reviewed medical records of 113 patients with autopsy-confirmed PSP in the Mayo Clinic brain bank. iNPH-like clinical and neuroimaging findings, including high EI and DESH, were assessed. Finally, we performed logistic regression analyses to investigate the relationships between the clinical triad of iNPH with high EI or triad with DESH.
**Results:** Of 113 patients, gait disturbance, cognitive impairment, urinary incontinence and the iNPH triad were present in 98 (87%), 74 (66%), 48 (42%), and 33 (29%), respectively. The most common clinical diagnosis was PSP (66; 58%), followed by corticobasal degeneration (7; 6%) and primary progressive apraxia of speech (5; 4%). Thirty-five patients (31%) were diagnosed with other neurological disorders; none was diagnosed with iNPH. The mean EI was 0.28 ± 0.04. Thirty-six patients (32%) had EI of ≥0.30. Five patients (4%) had DESH. In a logistic regression analysis, there were no significant differences between the presence of the clinical iNPH triad and high EI or DESH (high EI p = 0.64; DESH p = 0.50).
**Conclusions:** A subset of PSP patients has the clinical triad of iNPH; therefore, it is challenging to differentiate iNPH from PSP. Additionally, EI may not be specific in the context of PSP.

## Dystonia

### P_188

### Initial experience in Bolivia with HU-014 (a non-FDA-approved botulinum toxin A) for movement disorders

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**Background:** In Bolivia, a lower middle-income country, access to botulinum toxin is limited. Most neurologists in this country need to familiarize themselves with its application. Besides, availability, cost, and lack of insurance coverage impede its use for common indications (i.e., a hemifacial spasm or focal dystonia).
Recently, HU-014 (Hutox), a non-FDA- approved botulinum toxin type A manufactured in Korea, became available in Bolivia as a cheaper alternative to incobotulinumtoxin-A. HU-014 has demonstrated effectiveness in post-stroke upper limb spasticity in an open-label study and noninferiority in treating glabellar lines compared to onabotulinumtoxin-A in a 1:1 dose ratio RCT. However, evidence of its use in movement disorders still needs to

be provided.
We aim to inform our initial experience treating movement disorders with HU-14 toxin.
**Methods:** Two patients with a hemifacial spasm (a 62-years-old woman and a 53-years-old man) and a 61-years-old woman with a blepharospasm were injected with 35 IU, 25 IU and 42 IU of HU-014 toxin, respectively. Their outcome was assessed three months later using a Blepharospasm Disability Index, Jankovic Rating Scale, or The Hemifacial Spasm Grading Scale.
**Results:** All the subjects improved their functionality scores and reported significant benefits three months after a single HU-014 injection.
**Conclusions:** The availability of new and accessible therapeutic alternatives is crucial to improve the quality of life of Bolivian patients with movement disorders. To our knowledge, this is the first report on the use of HU-014 for hemifacial spasm and blepharospasm. Clinical trials are pending to establish its effectiveness in movement disorders. Still, based on our nascent experience, this is a reasonable and cost-effective intervention for Bolivian patients. Neurologists' training and public policy changes are also necessary to take better care of our patients in Bolivia.

## P_189

## Hemidystonia-hemiatrophy syndrome: first case report in Bolivia

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**Background:** Hemi-dystonia (HD) hemi-atrophy (HA) is a rare syndrome characterized by dystonia involving one hemibody plus ipsilateral body atrophy, often preceded by a cerebral injury.
**Methods:** Case report.
**Results:** A thirty-two-year-old woman with unremarkable perinatal history began with motor difficulties on her left arm at age 5. Two years later, she developed a tiptoe dystonic posture on her left foot when walking, followed by permanent flexion of her left hip and knee. Involuntary twisting movements on her left arm progressively increased in severity until adolescence, plateauing afterward. She denied previous head trauma and any history of CNS infection, stroke, seizures, or cognitive or psychiatric disturbance. Her family history was unremarkable. On examination at 30, she had thoracolumbar scoliosis, left HD-HA, with shortening of her left leg and severe hip and knee flexion.
Her brain CT was unremarkable; a brain MRI showed a subtle right lateral ventricle enlargement, possibly due to a right cerebral hemiatrophy. Her electroencephalogram revealed right temporoparietal slowing but no seizures. An EMG and NCS show no neuropathy.
Multiple drug trials (i.e., levodopa, benzodiazepines, anticholinergics, and baclofen) for symptomatic relief have been ineffective. Botulinum toxin injections provided transient and partial relief, requiring muscle-tendon lengthening surgery at 25. To date, the patient has not been able to access a neurosurgical treatment (i.e., DBS) that, according to a limited number of reports, has shown promising results in secondary hemi-dystonia
**Conclusions:** To know the phenomenology is essential to recognize this rare disorder with limited reports in the literature. The need for genetic studies is a limitation of our report. To our knowledge, this is the first case of a patient with HD-HA syndrome reported in Bolivia.

## P_190

## A novel THAP1 variant presenting with early onset generalized dystonia

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**Background:** *DYT6 or DYT-THAP1* is a genetic dystonia caused by pathogenic mutations in the THAP1 gene. It predominantly presents with early-onset segmental or generalized dystonia with preferential craniocervical and upper limb involvement.
**Methods:** We report a novel mutation in the THAP1 gene presenting with childhood-onset generalized dystonia in a family.
**Results:** A 37-year-old female (proband) presented with dystonia starting at 12 years, initially developed right-sided neck tilting, progressing to left-side predominant abnormal posturing of the arm and leg within a few years. With time she developed truncal posturing with worsening speech and swallowing functions. All her symptoms developed during her teenage years with slow progression since then. Pertinent exam findings included a high arched palate, mild dysarthria, facial and oromandibular dystonia, right laterocollis with left torticollis, and mild left more than right-hand dystonia with minimal leg involvement. Mild truncal leaning to the right was noted. Her Burke-Fahn-Marsden Dystonia Rating scale was 44.

Her parents and siblings are asymptomatic. Her 15-year-old daughter is symptomatic with the onset of dystonia at seven years, starting with cervical involvement. She has a similar phenotype.
GeneDx dystonia panel reported a heterozygous THAP1 mutation, c.61T>G for the proband classified as a variant of unknown significance. The daughter also carries the same variant.
**Conclusions:** The c.61T>G mutation changes the amino acid at position 21 from serine to alanine in exon one. This variant is not observed frequently in large population cohorts. Other variants at nucleotide positions 61 and 62, changing serine to threonine, cysteine, and phenylalanine, have been associated with dystonia. To our knowledge, this is the first description of this variant in a family with early-onset generalized dystonia with craniocervical predominance. Interestingly, the daughter was symptomatic earlier than the proband. Further studies are needed to elucidate the clinical heterogeneity in DYT-THAP1.

## P_191

### *CACNA1A* variant can be associated with generalized dystonia

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**Background:** Mutations in the *CACNA1A* gene have been correlated with episodic ataxia type 2, spinocerebellar ataxia type 6, and familial hemiplegic migraine type 1. Dystonia is not enlisted among the typical clinical manifestations of *CACNA1A* mutations.
We report the case of patient with a novel missense mutation of the *CACNA1A* gene presenting headache, head and arm tremor, slowly progressive dystonia associated with episodic painful focal dystonic attacks, and unexplained falls.
**Methods:** A 57-year-old woman was referred because of neck dystonia associated with head and arms tremor since the age of 15 years. At the age of 47, in 2012, she presented an increase in tremor amplitude led to suspect an essential tremor. In 2019 she showed mild dysarthria, right torticollis with dystonic head tremor and both arms, adiadochokinesia without limb ataxia, gait with dystonic head posture, and no cerebellar features. Moreover, she reported paroxysmal dystonia attacks (3-4 per week) of the left paravertebral muscles and lower extremity with intense pain occurring without apparent provoking factors.
**Results:** The BFMDRS score was 14, and she tried therapy with levodopa/benserazide up to 300 mg/die with no improvement.
Dystonia genetic panel showed a heterozygous mutation in the *CACNA1A* gene (NM_023035.2:c.1630C>T p.(Arg544Trp). In 2020 due to worsening dystonia (BFMDRS score 29,5), she underwent evaluation for GPi-DBS surgery. However, brain MRI showed cortical atrophy, and she was exclude d
**Conclusions:** *CACNA1A* mutations are associated with a broad spectrum of neurological manifestations, with a frequent overlap of headache and neurological signs related to the involvement of the cerebellum. Few dystonic symptoms have been reported so far; however, the link between dystonia and *CACNA1A* mutations is increasingly evident, although the prevalence, incidence, and pathogenesis still need to be elucidated.

## P_192

### Distal lower extremity task specific dystonia symptoms in runners

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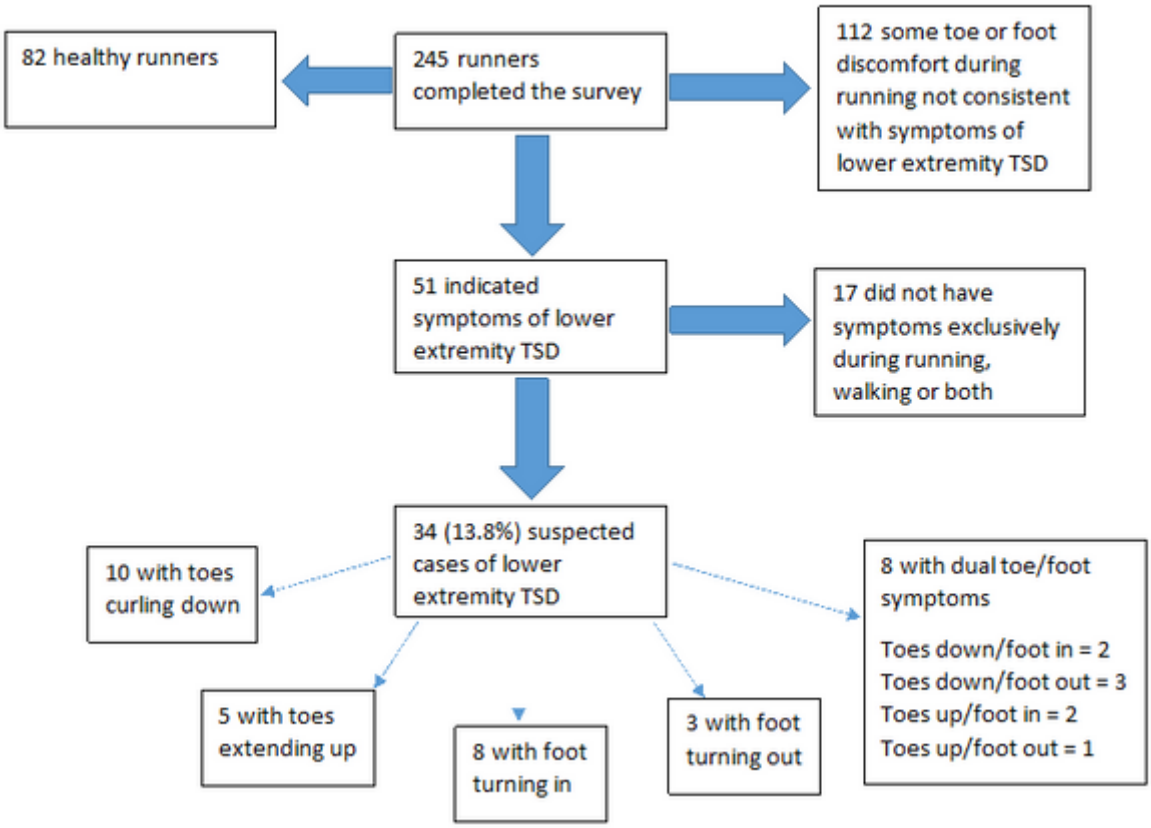
**Background:** Task specific dystonia (TSD) occurs only when performing a specific action and it has been well described in the upper extremities and mouth but there is less literature for the lower extremities. Its etiology is thought to be multifactorial with genetic and environmental risk factors.
**Methods:** We included people older than 19 that ran at least once a week over the last year and collected the data via an online survey. We assessed the presence of foot and toe symptoms suggestive of TSD (foot turning, toes curling, toes extending or some combination) and when they occurred, running experience, weight training, cross training, shoe brand, special equipment, past injuries, position of foot strike, medications, personal medical history and family neurological history. We analyzed the difference in this data between those with symptoms suggestive of TSD and the healthy runners

**Results:**

Figure 1. Flow of participants




116 participants were included in the final analysis. The prevalence of concerning symptoms for TSD in runners was higher than it has been reported in the literature., tThere was a statistically significant higher number of women in the affected group and that mid strike was the most common position of foot in the healthy group
**Conclusions:** In our population, suspected TSD runners were more likely to be female and have rear or forefoot strike.

## P_193

### Temporomandibular dystonia as a cause of temporomandibular joint degeneration: case report

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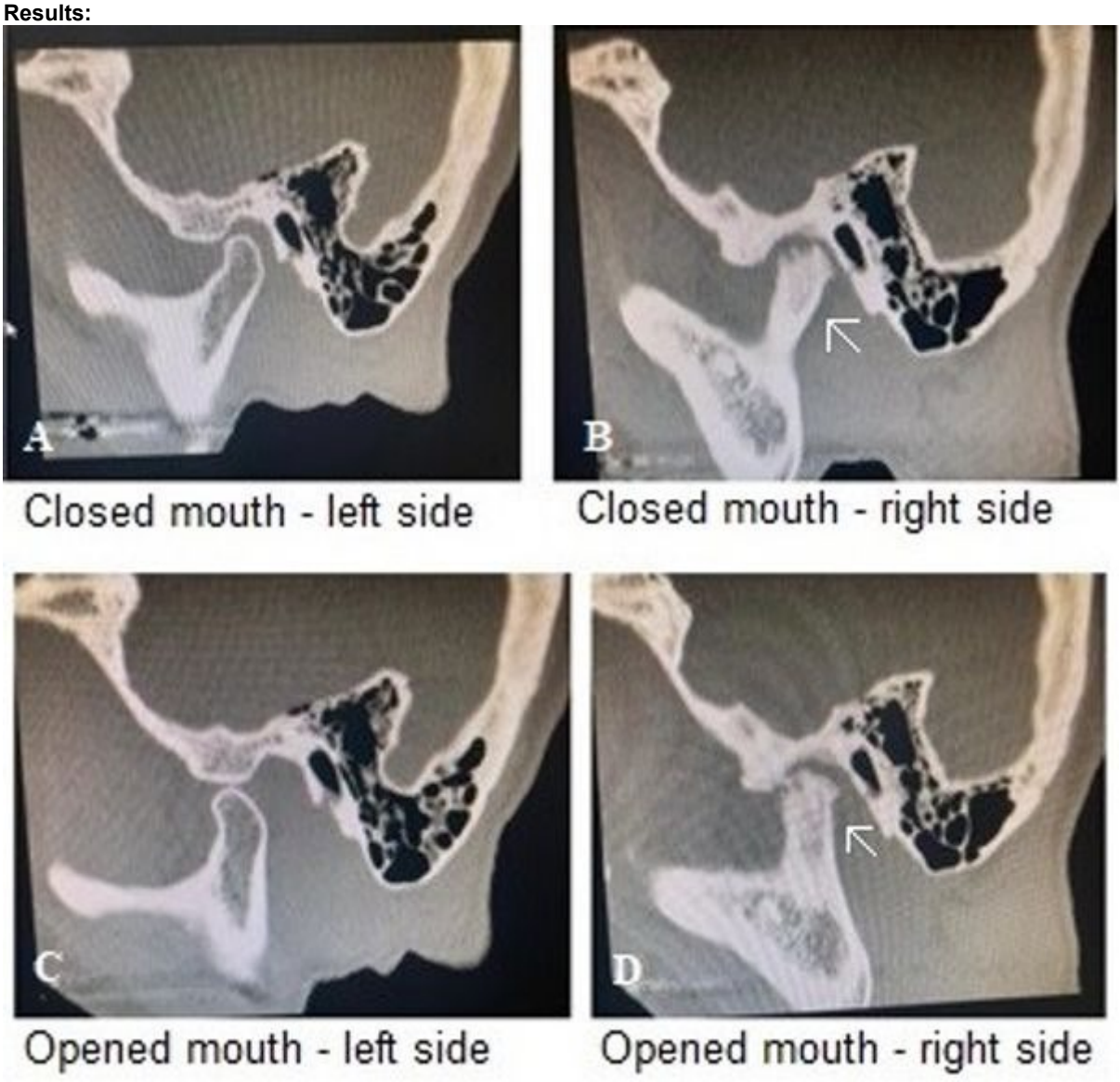
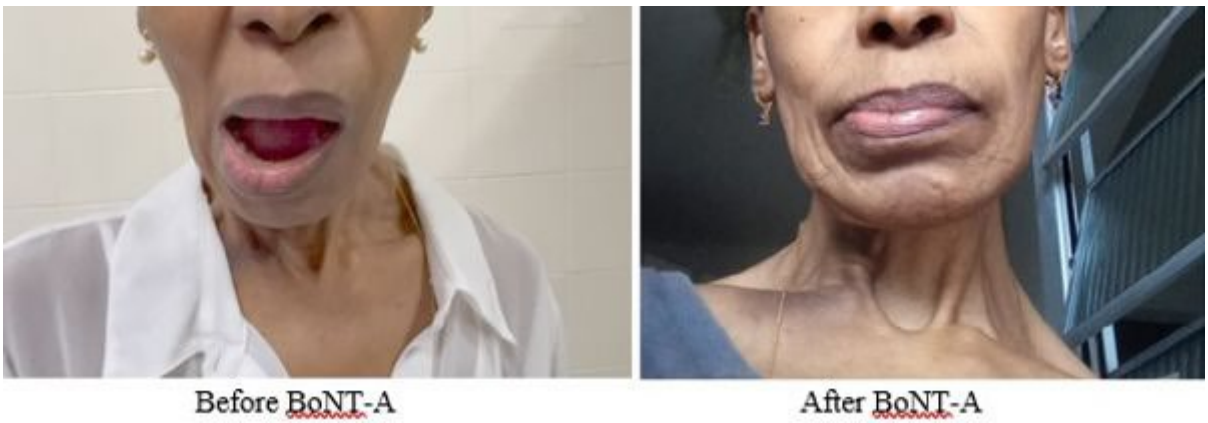
**Background:** Temporomandibular disorders (TMD) can have multiple etiologies, including oromandibular dystonia (OMD). However, in a few cases, the OMD can evolve from cervical dystonia (CD), and it can lead to serious bone degeneration.
**Methods:** The purpose of this case report of a 64-year-old woman presenting to the Outpatient Neurology Clinic of the Federal University of Bahia, is to illustrate the development of OMD with temporomandibular joint (TMJ) dysfunction, after 10 years of CD. Clinical examination showed bone degeneration of the mandibular ramus and right TMJ click.

**Results:**




Computerized tomography of TMJ. B) Indicate sclerosis and degeneration of right condyles and mandibular ramus. D) Show the lack of condyle translation during opened mouth. B and D shows degeneration and narrowing of the right mandibular fossa. A and C shows normal TMJ.




Patient with a history of CD presenting with OMD, and TMJ dysfunction treated with botulinum neurotoxin type A (BoNT-A) injections in the right lateral pterygoid muscles.
After the BoNT-A injections, the patient had improved in swallowing, and in pain.

**Conclusions:** This case highlights the importance of close follow-up of CD patients, to identify new dystonic muscles. In our patient, lateral pterygoid muscle involvement was followed by several comorbidities, such as dysphagia, and jawbone abnormalities.

## P_195

### Oculogyric crisis as a result of dopamine blocking agent withdrawal

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**Background:** Oculogyric crisis (OGC) is a form of dystonia in extraocular muscles which is described as conjugate eye deviation mostly in an upward direction. These dystonic movements can last seconds to hours long. Oculogyria is first reported as a finding associated with post-encephalitic parkinsonism, and later was found to be mostly seen as an extrapyramidal side effect of dopamine blocking agents. While OGC is mostly reported as an acute life-threatening dystonia secondary to high dose D2 blocking agents, tardive forms of OGC is also described with chronic exposures. Here we report a patient who developed OCG after discontinuation of risperidone.
**Methods:** Case report of a 61 year-old left-handed female with past medical history of epilepsy, schizophrenia, drug-induced lupus, gastroparesis (on J-tube) who was evaluated due to abnormal eye movements.
**Results:** These movements had started around 2 months prior to the visit date and after patient had received her J-tube. By the time of evaluation, movements were dystonic upward gaze deviation that lasted less than one second and were happening multiple times in a minute. Her sister initially noted these movements while patient was unaware of them. Patient has been residing in a nursing facility and upon further questioning it was noted that her risperidone, which she was taking for over 20 years, was not given since her J-tube was placed. Patient was followed up in one month with some reduction in movement frequency.
**Conclusions:** OGC is a rare form of dystonia that has been mainly reported acutely after dopamine blocking agent exposure or as a tardive form of dystonia with chronic exposures. Treatment is discontinuation of the dopamine blocking agent or starting an anti-cholinergic medicine. Our patient started to develop oculogyria upon abandoning her long-standing neuroleptic medicine. Therefore, any modification of dopamine blocking medicines should be done cautiously to avoid this serious side effect.

## P_196

### Benefit of multiple incobotulinumtoxinA injections for pain reduction in adults with cervical dystonia: an analysis of pooled data

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**Background:** The long-term effects of repeated incobotulinumtoxinA (incoBoNT-A) injections on cervical dystonia (CD)-related pain were assessed in a pooled analysis of studies in adults with CD.
**Methods:** Pooled data from four phase 3 and 4 studies in adults with CD-related pain at baseline (N=678) were analysed over five incoBoNT-A injection cycles. Pain was assessed at each injection visit (IV) and control visit (CV) 4 weeks post-injection using the TWSTRS-pain severity subscale or a pain VAS. Both pain scales were analysed using a score range 0–10 and pain was categorised as mild (>0–<3.5), moderate (3.5–<6.5) or severe (6.5–10). Response was defined as ≥30% or ≥50% reduction in baseline pain score, reflecting at least moderate or substantial clinically important improvements, respectively. Complete pain relief (pain score=0) was evaluated at each IV and CV. Pain scores in the subgroup of patients not taking concomitant pain medication (N=379) were also examined.
**Results:** Baseline pain was moderate or severe for 64% of patients. Pain reduction was observed over multiple treatment cycles; response rates and % with complete pain relief tended to increase over the 5 injection cycles (Table). A cumulative effect was demonstrated in the proportion of patients whose pain had not returned to baseline levels by the next IV. Pain responses were generally slightly higher in the subgroup not taking

concomitant pain medication (Table).

| | Patients (%) with pain response at Control Visit (CV) 4 weeks after incoBoNT-A injection | | | | |
|---|---|---|---|---|---|
| | CV1 | CV2 | CV3 | CV4 | CV5 |
| **All patients** | N=669 | N=263 | N=235 | N=215 | N=179 |
| ≥30% pain reduction from baseline | 48.1% | 49.8% | 54.0% | 57.2% | 53.1% |
| ≥50% pain reduction from baseline | 34.4% | 34.2% | 40.4% | 39.1% | 40.2% |
| Complete pain relief | 10.3% | 11.8% | 13.2% | 12.6% | 16.8% |
| **No pain medication** | N=379 | N=116 | N=107 | N=101 | N=86 |
| ≥30% pain reduction from baseline | 54.4% | 49.1% | 57.9% | 57.4% | 55.8% |
| ≥50% pain reduction from baseline | 41.4% | 32.8% | 46.7% | 37.6% | 45.4% |
| Complete pain relief | 13.2% | 14.7% | 16.8% | 14.9% | 22.1% |

*Table. Pain severity results at each control visit for all patients with a pain assessment at that visit and in the subgroup not taking concomitant pain medication*

**Conclusions:** Patients with CD-related pain experienced clinically important and sustained reductions in pain during repeated incoBoNT-A injections with or without concomitant pain medication, confirming the benefits of long-term incoBoNT-A treatment.

**P_197**

### Pain reduction in adults with cervical dystonia following a single injection of incobotulinumtoxinA: a pooled analysis

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**Background:** Pain is a common and disabling symptom of cervical dystonia (CD). This pooled analysis evaluated the effects of a single injection of incobotulinumtoxinA (incoBoNT-A) on pain in adults with CD-related pain.
**Methods:** Pain severity data were pooled from four phase 3 and 4 studies of incoBoNT-A for the treatment of CD in adults. CD-related pain was assessed at baseline and 4 weeks after a single injection of incoBoNT-A using the TWSTRS-pain severity subscale or a pain VAS. Both were analysed using a score range 0–10 and pain was categorised as mild (>0–<3.5), moderate (3.5–<6.5) or severe (6.5–10). Response was defined as ≥30% or ≥50% reduction from baseline pain severity score. Percentage of patients with complete pain relief (pain score=0) at 4 weeks after incoBoNT-A injection was determined. Sensitivity analyses evaluated pain responses in the subgroup of patients not taking concomitant pain medication. Change in pain severity from baseline to Week 4 was assessed using a one-sample t-test.
**Results:** Of the 678 patients with pain at baseline, 36.4% had mild pain, 42.9% moderate pain and 20.7% severe pain; mean pain severity score was 4.26 (SD 2.32). At Week 4 after incoBoNT-A injection, there was a significant reduction from baseline in mean pain severity score (−1.25 (SD 2.04; p<0.0001), a shift to a lower level of pain severity, response rates reflected clinically important improvements (48.1% had ≥30% pain reduction and 34.4% had ≥50% pain reduction), and 10.3% were pain free. Of the 678 patients, 64.2% were not taking concomitant pain medication and had a baseline mean pain severity score of 3.83(SD 2.41). Pain improvements in this subgroup were consistent with those in the total population.
**Conclusions:** These results show significant pain reduction in patients with and without concomitant pain medication following a single injection of incoBoNT-A in patients with CD.

## Chorea, Athetosis, Ballism, Tics

## P_198

### Extrapyramidal and movement disorder, unspecified

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**Background:** Different clinical manifestations of extrapyramidal disorders and its peculiarity makes the disease both easy and difficult to diagnose.
We present the case of a 23-year-old girl, the first child from unrelated parents, has two sisters (healthy). From the anamnesis, heredity is not burdened. The disease began at the age of five after febrile convulsions, the onset of the disease with a tremor of the limb and the transition to the trunk, with slow progression. In the last three months, there have been unprovoked convulsive seizures and a slow decline in intelligence. During 10 days of inpatient treatment, three generalized tonic-clinic epileptic seizures were observed.
**Methods:** When trying to move, the patient showed non-voluntary movements of the upper and lower extremities and mimic muscles, more like a tremor of the arms and torso. Speech impairment was assessed as dysarthria. Deep reflexes are evoked, there are no pathological pyramidal symptoms. Intention tremor and cognitive decline were identified, the score on the mini-mental scale was 18/30. An MRI study showed an expansion of the lateral ventricles up to 21 mm and a descent of the cerebellar tonsils into the foramen magnum by 2–3 mm. No epileptiform waves were observed on a 30-minute EEG routine.
**Results:** The absence of significant pathology in laboratory studies, inability to conduct genetic tests and the atypical disease`s course, made it difficult to make a diagnosis. The treatment was symptomatic, tiapride hydrochloride at a daily dose of 100 mg did not significantly reduce involuntary movement, against the background of carbamezepine at a daily dose of 400 mg epileptic seizures were not stopped.
**Conclusions:** The presence of hyperkinesis, intention tremor, convulsive syndrome and a rather slow disease`s course, absence of a genetic background, significant deviations in laboratory and instrumental studies, increase the significance of genetic tests.

## P_200

### Post-pump hemichorea in an adult: a case report

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**Background:** Post-pump chorea is the development of chorea after surgery utilizing cardiopulmonary bypass. While usually bilateral, there are cases of post-pump hemichorea reported in children. Here we present a case of post-pump hemichorea in an adult patient.
**Methods:** Case report.
**Results:** A 65-year-old woman with a known history of a thoracic aortic aneurysm presented to the emergency department after being found down. CT angiography of head and neck showed an aortic dissection extending into the innominate and left extracranial carotid arteries, sparing the intracranial circulation. Initial CT head without contrast was normal, but CT perfusion showed reduced cerebral perfusion bilaterally. She underwent emergent aortic dissection repair utilizing cardiopulmonary bypass and hypothermia. After the surgery, she developed involuntary right lower extremity movements. Subsequent CT head and CT perfusion 2 days after the procedure showed no definite abnormalities. After discharge, the movements progressed to involve her right arm. MRI brain 6 weeks after the procedure showed small areas of resolving ischemia involving a cortical ribbon of the right parietal lobe and a punctate focus in the left centrum semiovale, without basal ganglia involvement. She was evaluated in the Movement Disorders clinic 3 months after the acute presentation. Exam at that time identified right hemichorea with a component of dystonia in the distal right lower limb. She preferred to avoid dopamine receptor blocking medications; therefore, she was started on amantadine for chorea and botulinum toxin injections for right leg dystonia, with improvement of symptoms.
**Conclusions:** To our knowledge, this is the first case report of post-pump hemichorea in an adult, a potential complication from surgery involving cardiopulmonary bypass. Notably, we cannot exclude a small, MRI-negative ischemic stroke involving the left basal ganglia. In our opinion, the punctate infarct in the left centrum semiovale is unlikely to be causative.

## P_202

### Late-onset chorea-dystonia related to a novel ADCY5 variant

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**Background:** Adenylyl cyclase 5 (ADCY5) gene mutations cause “hyperkinetic" phenotypes. Most affected individuals have an onset before the age of 5. However, early-adulthood onset has been rarely described. Typical features include perioral-periorbital myokymia and paroxysmal dystonia/chorea affecting the upper body, evolving from bouts to permanent hyperkinetic movements. Other clinical features comprise ataxic gait, delayed psychomotor development, or pyramidal signs.
**Methods:** We aim to present an illustrative case of late-onset chorea-dystonia related to the ADCY5 gene; we also review the literature on late-onset ADCY5 cases.
**Results:** A 63-year-old woman had a history of psychomotor developmental delay and obstructive pulmonary disease since birth. Her family history was remarkable for facial myokymia affecting three consecutive generations. At 54, fluctuating dystonia of her right upper limb spread to her neck, face, and trunk, adding paroxysms of choreoathetosis, which become permanent with diurnal fluctuation (worse in the afternoon). Laboratory tests and brain and cervical spine MRI were unremarkable; Huntington's genetic test was negative. Subsequently, a dystonia genetic panel revealed a novel heterozygous ADCY5 c.3163C>T (p.Arg1055Cys) variant of uncertain significance. Other relatives were studied for this variant.
We reviewed 126 cases described in the literature, of which eight had an onset of chorea/dystonia after age 10. The older age at onset previously reported was 30. A more detailed description of kindred and review will be available on the poster.
**Conclusions:** This report expands age at onset limits of *ADYC5*-related chorea-dystonia. Regardless of age, family history, diurnal fluctuation, and facial myokymia are clues for suspecting *ADYC5*-related disorders.

## P_203

## A paradoxical phenomenon: hemichorea-hemiballismus resolution after stroke in moyamoya disease

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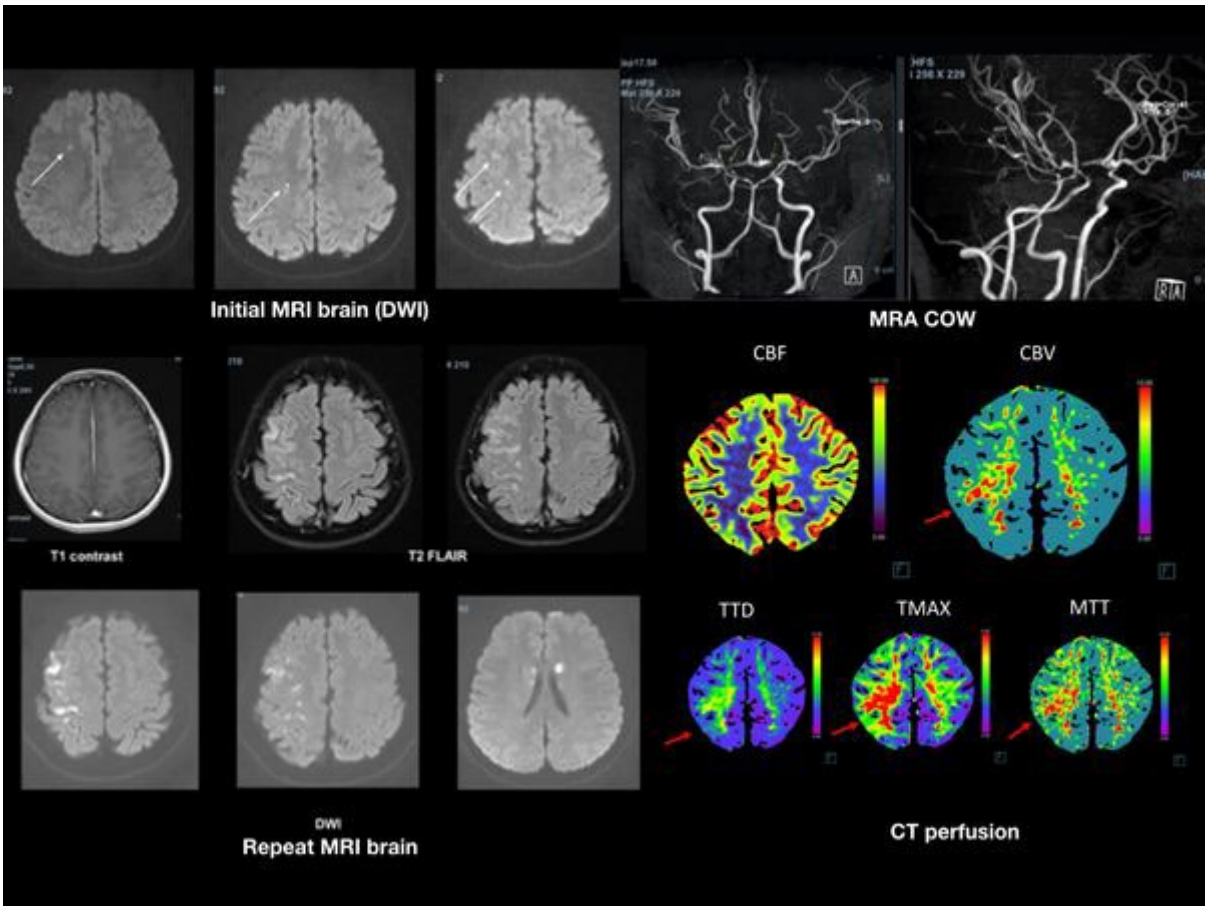
**Background:** Moya-moya disease is characterised by occlusion of the supraclinoid ICA resulting in formation of "moya-moya vessels" at the base of the brain which mimics a puff of smoke on angiogram. The clinical presentation of moya-moya disease includes TIA, stroke, seizures, headache and cognitive impairment. Hemichorea is an uncommon presentation of moya-moya disease found in 6% of patients.
**Methods:** We present a 26-year-old woman with left hemichorea-hemiballismus which resolved after an ischemic stroke.
**Results:** A 26-year-old woman with migraine-like headaches for 2 years presented with sudden onset of left sided involuntary movements while crying after arguing with her mother. She had no exposure to neuroleptics or antiemetics, prior upper respiratory tract infection or fever. There was no significant family history. Examination shows left hemichorea-hemiballismus without facial dyskinesia. Otherwise, her eye movements and saccades were normal with no cerebellar signs or long tract signs.
MRI FLAIR showed “Ivy” sign, MRI T1 showed leptomeningeal enhancement while MRI DWI showed internal watershed infarction. MRA COW showed distal right ICA, bilateral proximal A1 and M1 stenosis with prominent bilateral curvilinear lenticulostriate vessels. Genetic testing of RNF213 and GUCY1A1 were negative. CT perfusion parameters corresponded to a substantial area of penumbra over the right MCA territory without an established infarct core.
Eight days later, she presented with sudden left hemiplegia and subsequent five days improvement of muscle power with complete resolution of the left hemichorea. Three months later, she showed full muscle power with no re-emergence of hemichorea-hemiballismus.




**Conclusions:** This interesting 'stroke of luck' case depicts resolution of hemichorea-hemiballismus post stroke in a patient with moya-moya disease.

## P_206

## Crushing valbenazine capsule contents for potential addition to soft foods or administration via G-tube

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**Background:** Once-daily valbenazine is FDA-approved for tardive dyskinesia and has shown efficacy for chorea associated with Huntington disease. Dysphagia can occur with both of these movement disorders. Therefore, three studies were conducted to assess the suitability of crushing the contents of valbenazine capsules (40 mg, 80 mg) and mixing them with soft foods/liquids or administering dissolved contents through a gastrostomy tube (G-tube).
**Methods:** In Study 1, whole valbenazine capsules and crushed capsule contents were dissolved in a warm solution. Samples were collected serially over 1 hour (from 10 to 60 min) for analysis. In Study 2, crushed valbenazine capsule contents (both doses) were mixed into applesauce, yogurt, and pudding; crushed contents (40 mg) were also added to buffer solutions (pH 1.2, 4.5, 6.8) and fed-state simulated gastric fluid (FeSSGF). In Study 3, crushed valbenazine capsule contents (both doses) were dissolved in various temperatures of tap water and added to a G-tube, with and without a cup rinse. In Studies 2 and 3, conditions that yielded 90-110% valbenazine recovery were considered acceptable for administration.
**Results:** In Study 1, rapid and complete drug release (>98% in 15 min) was observed, independent of preparation (whole capsules, crushed contents) or dose (40 mg, 80 mg). In Study 2, recovery of crushed capsule contents was acceptable within 2 hours of addition to tested foods, buffers, or FeSSGF (recovery rang e: 92-102%), with minimal degradants detected. In Study 3, acceptable recovery was found when crushed capsule contents were dissolved in hot or cold water and added to a G-tube with a cup rinse (recovery range: 91-97%).
**Conclusions:** Crushing valbenazine capsule contents did not impact in vitro dissolution performance. Mixing the contents with soft foods or liquids across a broad pH range or delivering them dissolved in tap water via G-tube may be acceptable methods for administering valbenazine.

## P_207

### A paradoxical phenomenon: hemichorea-hemiballismus resolution after stroke in moyamoya disease

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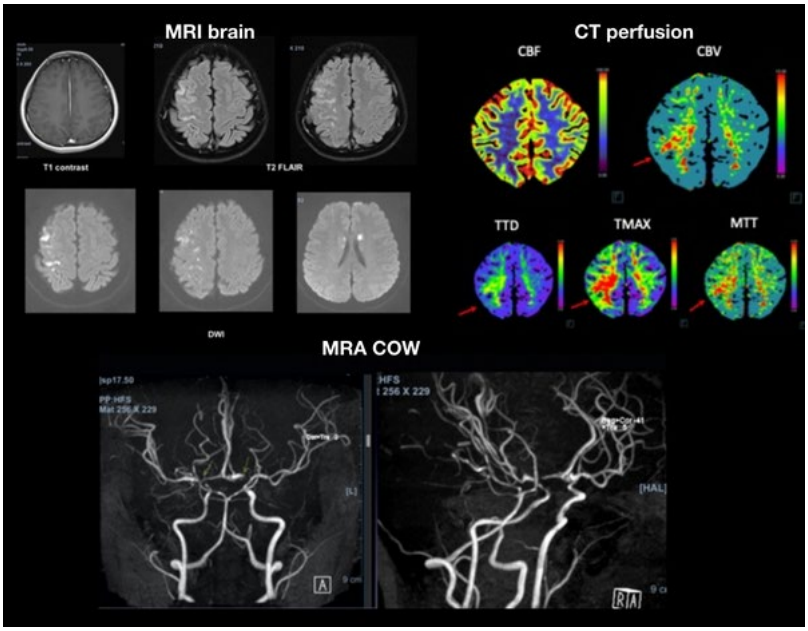
**Background:** Moya-moya disease is characterised by occlusion of the supraclinoid ICA resulting in formation of a fine vascular network at the base of the brain mimicking a puff of smoke (maya-moya) on angiogram. The common clinical presentation of moya-moya disease includes TIA, stroke, seizures, headache and cognitive impairment.
**Methods:** We present a 26-year-old woman with left hemichorea-hemiballismus which resolved after an ischemic stroke.
**Results:** A 26-year-old woman with migraine-like headaches for 2 years presented with sudden left sided involuntary movements while crying after arguing with her mother. She had no exposure to neuroleptics or antiemetics, prior upper respiratory tract infection or fever. No significant family history noted. Examination showed left hemichorea-hemiballismus without facial dyskinesia. Otherwise, her eye movements and saccades were normal without cerebellar or long tract signs.
MRI FLAIR showed “Ivy” sign, leptomeningeal enhancement on T1-weighted images and internal watershed infarction on MRI DWI. MRA COW showed distal right ICA, bilateral proximal A1 and M1 stenosis with prominent bilateral curvilinear lenticulostriate vessels. Genetic testing of RNF213 and GUCY1A1 were negative. CT perfusion parameters corresponded to a substantial area of penumbra over the right MCA territory without an established infarct core.
Eight days later, she presented with sudden left hemiplegia and subsequent 5 days partial improvement of muscle power with complete resolution of the left hemichorea. Three months later, she showed full muscle power without re-emergence of hemichorea.




**Conclusions:** Hemichorea is an uncommon presentation of moya-moya disease. This interesting 'stroke of luck' case depicts resolution of hemichorea post stroke in a patient with moya-moya disease.

## P_209

### Indirect treatment comparison of valbenazine with deutetrabenazine for improvement in total maximal chorea core in Huntington disease

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**Background:** Chorea is a hallmark motor symptom of Huntington Disease (HD). Tetrabenazine and deutetrabenazine are currently approved by the FDA for the treatment of chorea associated with HD. Valbenazine is currently under FDA review for that indication. There is no available comparison between the efficacy of deutetrabenazine and valbenazine in the treatment of chorea associated with HD. We conducted an Indirect Treatment Comparison (ITC) between these 2 drugs.
**Methods:** The outcome of interest of this indirect comparison based on clinical trial data was the mean change in total maximal chorea (TMC) score. For deutetrabenazine and placebo, the mean change and 95% confidence interval values were digitally extracted from the chart in the pivotal trial publication (First-HD). For valbenazine and placebo, the values were obtained from the clinical study report (KINECT$^{TM}$-HD). The mean change for drug versus placebo was estimated using the inverse variance method. An ITC of valbenazine versus deutetrabenazine was conducted using the Bucher method at 2,4,6 weeks and at maintenance (average of weeks 9 and 12 for deutetrabenazine, and of weeks 10 and 12 for valbenazine).
**Results:** The ITC of the TMC score improvement significantly favored valbenazine over deutetrabenazine at 2 and 4 weeks. The relative treatment effect for valbenazine versus deutetrabenazine was -1.87 (95%CI: -3.23,-0.52, $p<0.05$) at 2 weeks, and -1.84 (95%CI: -3.43,-0.25, $p<0.05$) at 4 weeks. At 6 weeks and at maintenance, the difference of valbenazine versus deutetrabenazine demonstrated a relative treatment effect of -0.84 (95%CI: -2.45,0.78, p=NS) and -0.77 (95%CI: -2.42,0.87, p=NS), respectively.
**Conclusions:** In this indirect comparison of valbenazine and deutetrabenazine, valbenazine seems to improve chorea earlier, which is compatible with its shorter titration schedule, and to have a similar therapeutic effect compared to deutetrabenazine during the maintenance phase. Subsequent analyses will include indirect comparisons of treatment effects on other endpoints, including safety outcomes.

## P_210

## Once-weekly robotic-assisted gait training preserves walking function in Hereditary Spastic Paraplegia: a case report

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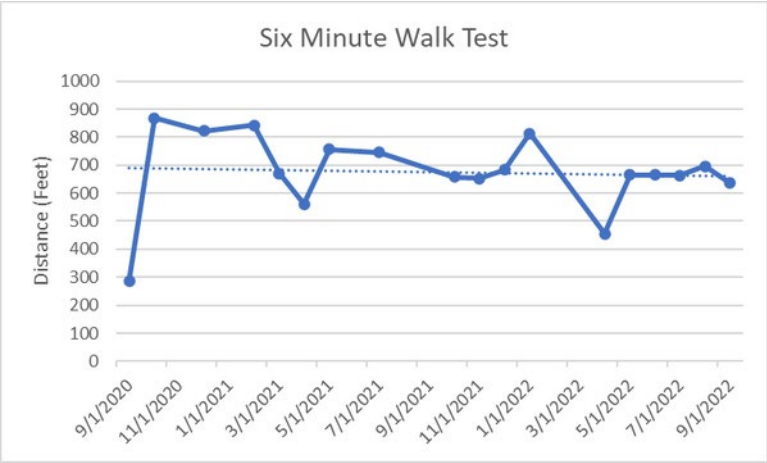
**Background:** Hereditary spastic paraplegia (HSP) describes various genetic disorders presenting with lower extremity spasticity, progressive weakness, and general disability. Many patients with HSP participate in physical therapy (PT). PT interventions address functional impairments but limited efficacy trials are available to define treatment recommendations. Robotic-assisted gait training (RAGT) has emerged as a means of improving mobility in neurologic disorders. Various exoskeletons, ranging from treadmill-based to overground, achieve walking even in the presence of total paralysis. Treadmill-based RAGT has been examined in HSP and achieved meaningful improvements in measures of balance and mobility. The treadmill-based system may be inferior to overground walking exoskeletons as the restrictions in direction and excessive force guidance may limit responsiveness to therapy.
**Methods:** A 70-year-old male patient with HSP was referred to outpatient PT for spastic gait. He briefly completed a twice-weekly PT plan of care, but he commutes approximately 90 miles and could only realistically participate in once-weekly PT. The original twice-weekly plan lasted for approximately three months, during which time he was prescribed bilateral carbon fiber ankle foot orthoses (AFO) in addition to PT interventions. He has since completed over 70 visits once weekly, aside from interruptions due to ITB surgery (3/2021), exercise-contraindicated hypertension requiring medical management (7/2021), and primary PT out on short-term disability (2/2022). All PT sessions lasted one hour. Sessions exclusively used RAGT for walking, stair negotiation, and novel strength training.
**Results:**




BTemia Keeogo Dermoskeleton

**Conclusions:** Maintenance PT using RAGT may provide sufficient training effect and carryover to benefit persons with HSP and spastic gait disorder.

## Ataxias, Hereditary spastic paraparesis

### P_211

### Short-term efficacy of repetitive transcranial magnetic stimulation in SCA3: a prospective, randomized, double-blind, sham-controlled study

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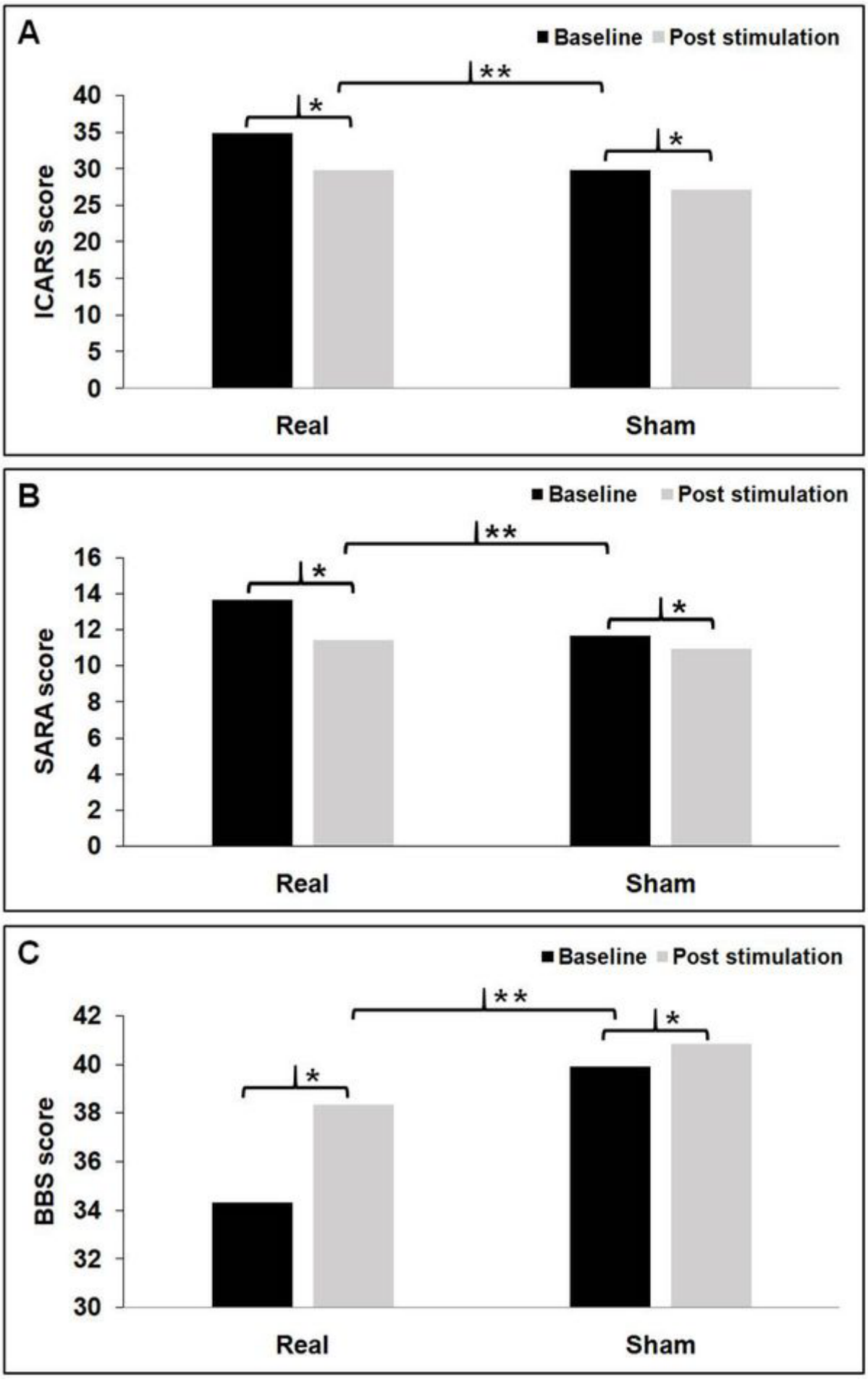
**Background:** Spinocerebellar ataxia type 3 (SCA3) is the most common autosomal dominant ataxia globally. No effective treatment is currently available for SCA3. Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive form of brain stimulation, demonstrated to improve symptoms in patients with neurodegenerative cerebellar ataxias. The present study investigated whether treatment with rTMS over the cerebellum for 15 consecutive days improved measures of ataxia in SCA3 patients.
**Methods:** A double-blind, prospective, randomized, sham-controlled trial was carried out on 44 SCA3 patients. Participants were randomly assigned to two groups: real or sham stimulation. Each participant underwent 30 minutes of 1Hz rTMS stimulation (a total of 900 pulses) for 15 consecutive days. The primary outcome measure was the score on the International Cooperative Ataxia Rating Scale (ICARS), and secondary outcomes were from the Scale for the Assessment and Rating of Ataxia (SARA) and the Berg Balance Scale (BBS).
**Results:**


A
Baseline
Post stimulation
**
*
*
ICARS score
40
35
30
25
20
15
10
5
0
Real
Sham
B
Baseline
Post stimulation
**
*
*
SARA score
16
14
12
10
8
6
4
2
0
Real
Sham
C
Baseline
Post stimulation
**
*
*
BBS score
42
40
38
36
34
32
30
Real
Sham

Nausea was the only adverse effect reported by 2 participants from the sham and real group. After 15 days of treatment, there was a significant improvement in all performance scores in both real and sham stimulation groups. However, compared to the sham group, the improvements were significantly larger in the real group for the ICARS (P = 0.002), SARA (P = 0.001), and BBS (P = 0.001).
**Conclusions:** A 15 days treatment with rTMS over the cerebellum improves the symptoms of ataxia in SCA3 patients. Our results suggest that rTMS is a promising tool for future rehabilitative approaches in SCA3.

## P_213

### A long-term effect of miglustat on Niemann-Pick type C: an 8-years follow-up of dystonia and ataxia

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**Background:** Niemann-Pick type C (NPC) is a rare, autosomal recessive disease with visceral, psychiatric and neurological symptoms. Miglustat is the only disease-modifying therapy for NPC. However, the long-term effects of Miglustat are lacking. WE report an 8-years effect of Miglustat on cognition & neurological symptoms (dystonia and ataxia) in a NPC patient.
**Methods:** A 31-year-old female patient visited our clinic in 2014. Her symptoms began with clumsiness in the right hand at the age of 19. Initial symptoms were followed by psychosis, cognitive impairment, and gait disturbance, which gradually worsened over the next several years. On examination, she had vertical supranuclear gaze palsy. She independently performed daily living activities. Her Mini-mental status examination (MMSE) score was 23/30. An abdominal CT scan revealed hepatosplenomegaly. A dopamine transporter image revealed mildly decreased uptake in the striatum. NPC gene sequencing showed a compound heterozygous mutation, with aberrations in exon 9 (c.1552C>T) and exon 18 (c.2780C>T). A filipin staining test was also positive.
The patient was evaluated for dystonia and ataxia using the Dystonia Movement Scale (DMS, maximum score 120) and Scale for the assessment and rating of ataxia (SARA, maximum score 40) before and 8 years after the administration of miglustat. Cognition was evaluated using MMSE. 600mg of miglustat a day was given to the patient.
**Results:** The baseline scores of DMS & SARA were 29 & 13. They changed to 42 & 22 after the administration of miglustat for 8 years. MMSE score declined from 24 to 19. No serious adverse effect except intermittent loose stool leading to slight weight loss was found.
**Conclusions:** In spite of continuous administration of miglustat, her condition gradually progressed. Considering the average survival of NPC, however, it was suggested that miglustat have a disease modifying effect in long-term period and contribute to improved survival.

## P_215

### Correlation of age onset and Mitochondrial DNA haplogroup in Indian Spinocerebellar ataxia type 2 (SCA2) patients

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[1]All India Institute pf Medical Sciences, Neurology, New Delhi, India, [2]CSIR-Institute of Genomics and Integrative Biology, Genomics, Delhi, India

**Background:** Spinocerebellar Ataxia type 2(SCA2) is an autosomal dominant polyglutamine ataxia caused by an unstable expansion of a CAG tract in the ATXN2 gene. Mitochondrial dysfunction has been linked to the age at onset (AO) modifiers of several neurodegenerative disorders, including SCA2. Expanded CAG repeats not entirely explains AO in SCA2 patients and show up the existence of disease modifiers of AO. mtDNA haplogroups linked to clinical manifestations in several polyglutamine disorders which are suggesting that they may act as disease modifiers in SCA2.
**Methods:** To investigate if mtDNA haplogroups contribution to AO of SCA2, we performed sanger sequencing of D-LOOP and hypervariable regions of Mitochondrial genome of 122 patients from mixed Indian population. mtDNA haplogroups were obtained after sequencing the mtDNA D-loop and hypervariable regions.
**Results:** The major haplogroups found were H,L,U,W,M,G,A,N,J,I,T, R and D,whereases the frequency of haplogroup in SCA2 patients, were H(32.79%),L(4.10%),U(11.48%),W (0.82%),M(36.07%),G(0.82%),A(1.64%),N(4.92%),J(1.64%),I(1.64%),T(2.46%),R(0.82%), D(0.82%)respectively.AO was significantly different at the same expanded CAG repeats in SCA2 patients, which are showing the existence of other non-CAG factors role in the age onset modifiers. We observed the most frequent mtDNA haplogroups H,L,U,M and N whereases A,J,G,I,T,R,W and D haplogroups clusters were observed less in Indian SCA2 patient's groups. The frequency of H,L,U,M and N mtDNA haplogroups were

32.79%,4.10%,11.48%,36.07% and 4.92% respectively. Further, we considered these mtDNA haplogroups H,L,U, M and N to rule out as AO modifier factor in SCA2. For this, we performed an ANCOVA test between haplogroups and AO of SCA2 patients. However, our analysis there was no significant association found between mtDNA haplogroup clusters and AO of SCA2 patients' groups with a p-value of 0.453.
**Conclusions:** These findings suggest that age onset modifiers of SCA2 AO patients, mtDNA haplogroups analysis should perform in worldwide SCA2 patient's samples to exploration of mtDNA haplogroup role in disease age modifiers variability.

## Tremors, Myoclonus

### P_216

### A genetic pearl for counseling patients with SGCE positive myoclonus-dystonia

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**Background:** Myoclonus-dystonia syndrome is most commonly caused by an autosomal dominant (AD) mutation in the epsilon sarcoglycan gene (SGCE). However, there may be reduced penetrance within a family due to maternal imprinting 95% of the time. This is important to consider as 1) patients may not have a clear family history leading to diagnostic confusion, and 2) the risk of having a clinically affected child differs for females versus males.
**Methods:** A case demonstrating the genetics of SGCE-positive myoclonus-dystonia.
**Results:** The patient is a 34-year-old woman from Puerto Rico who developed jerky arm movements at age 3 which progressed over time, worsened with action, and improved with alcohol. Additionally, she developed a jerky tremor of the neck and difficulty writing. At age 8 she suffered from generalized tonic-clonic seizures that resolved with levetiracetam. Subsequent MRI and EEGs were unremarkable. Her brother and two female cousins have similar movements, but no one in prior or successive generations is affected. Her exam is remarkable for left laterocollis, left torticollis, right dystonic finger flexion, and axial and upper extremity myoclonus that worsens with action.
Despite lack of AD inheritance pattern in her family, clinical suspicion for myoclonus dystonia was high so she underwent single gene testing for SGCE which resulted positive. She likely inherited the mutation from her clinically unaffected father who inherited a maternally imprinted mutation from his mother. The patient was counseled that provided her daughters inherited the mutation, due to maternal imprinting there is only a 5% risk they will be clinically affected. Likewise, there is a 5% risk each of her grandchildren will be clinically affected. Great-grandchildren of any male mutation carriers; however, will have a 50% chance of expressing the phenotype.
**Conclusions:** A female patient with the SGCE mutation has a 50% chance of passing on the mutation with only 5% penetrance.

### P_217

### The cameraperson sign in the diagnosis of functional tremor

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**Background:** Functional tremor (FT) is one of the most common forms of functional movement disorder (FMD). Its diagnosis can often be challenging. A growing literature highlights the role of telemedicine in the care of patients with hyperkinetic disorders. Identifying positive signs like tremor variability, distractibility, and entrainment supports a diagnosis of FT. In this case series, we identify another examination technique which could be of value when assessing FT.
**Methods:** In our Movement Disorders clinic, charts were retrospectively reviewed for relevant clinical information. Video examinations were conducted. Obtained videos were either synchronous, via the use of screen recording software during telehealth visits or asynchronous, from self-recorded home videos. In both cases, patients were instructed to self-record their tremor using their phone cameras.
**Results:** Three patients with FT or comorbid FT were identified as demonstrating a unique examination sign. Videos showed an improvement or suppression of the tremor when the affected hand held the phone. When compared to a fourth patient with tremor-dominant Parkinson's disease serving as a control, this sign was not observed.

**Conclusions:** We propose that the cameraperson sign may be of value in diagnosing FT. Patient-recorded videos of their tremor can be a convenient and practical way of evaluating suspected FT, especially when paroxysmal or variable symptoms limit the usefulness of classic signs often assessed in the clinic.

## P_219

### Essential1: results from a phase 2 trial evaluating the tolerability, safety and efficacy of ulixacaltamide in adults with essential tremor

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**Background:** Essential tremor (ET) is the most common movement disorder with clear need for novel therapies. Approximately 50% of patients seeking pharmacological therapy discontinue medications due to limited efficacy and poor tolerability. Ulixacaltamide (PRAX-944) is a selective small molecule T-type calcium channel blocker in development for treatment of ET and other movement disorders.
We previously demonstrated tolerability of pharmacodynamically-active doses of ulixacaltamide (up to 120mg) in healthy participants (ACTRN12620000675921), and preliminary evidence of tremor reduction in adults with ET (NCT05021978). The PRAX-944-222 (Essential1) trial (NCT05021991) further explores the efficacy and safety of 60 and 100mg once-daily (QAM) ulixacaltamide in adults with ET.
**Methods:** This 8-week double-blind, placebo-controlled, randomized study with optional 19-week Extension, enrolled 133 adults with moderate-to-severe ET defined by TETRAS–ADL subscale ≥20, sum of items 6 and 7 (handwriting and spiral drawings) on TETRAS–PS >4 (item 6, >0), and CGI–S score ≥ “moderate”. Eligible participants had to discontinue primidone prior to baseline; or be stable on their permitted medications for 1 month prior to screening. Participants were randomized to titrated doses of 60, or 100mg ulixacaltamide QAM or placebo. Safety and efficacy assessments were captured across 3 study periods: Screening/Baseline (up to 28 days); Intervention (56 days); Safety Follow-Up (14 days).
**Results:** The primary efficacy endpoint is change from baseline to Day 56 on the modified ADL, a composite scale calculated from items 1–11 of the TETRAS-ADL, and 6 and 7 of the TETRAS-PS. Mixed model repeated measures will be applied to assess the difference between pooled ulixacaltamide and placebo. Enrolment began in October 2021, with results expected late Q1 2023.
**Conclusions:** Expanding on preliminary findings, the Essential1 trial further examines the efficacy, safety and tolerability of ulixacaltamide in adults with ET, and will determine optimal doses and endpoints for evaluation in registrational studies.

## P_220

### Atypical midbrain head tremor presenting as like Bobble-head doll syndrome after successful brain surgery of hemorrhagic cavernous hemangioma

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**Background:** Bubble-head doll syndrome (BHDS) is a rare and unique movement disorder most commonly affecting children younger than 5 years of age. It is characterized by continuous or episodic involuntary forward and backward and side to side movement of the head at the frequency of 2-3 Hz. The phenomenology of BHDS is related to cystic lesions and swelling of the third ventricle in the brain. But, Bobble-head doll syndrome after successful surgery of hemorrhagic cavernous hemangioma is not reported in the literature. Our aim is to report unusual case of woman who developed atypical midbrain head tremor presenting as like Bobble-head doll syndrome after successful surgery of hemorrhagic cavernous hemangioma.
**Methods:** Single case report and description of clinical characteristics.
**Results:** A 49-year-old Korean woman was referred to our neurologic department due to involuntary movements of head presenting as Bubble-head doll syndrome. She presented relatively subacute-onset head tremor after successful surgery of hemorrhagic cavernous hemangioma. Her tremorous symptoms of head had more aggravated in a sitting position and neurologic examination revealed myorrhythmic, right hand tremor during action. After the introduction of levodopa medication, her atypical tremorous symptoms of head and right hand gradually improved.
**Conclusions:** To our knowledge, this is the first case report of prominent atypical midbrain head tremor presenting as like Bobble-head doll syndrome after successful brain surgery of hemorrhagic cavernous hemangioma. As like this case, if there is acute or subacute-onset, not-fixed, continual head tremor as Bubble-head doll syndrome after brain surgery, it should be considered diagnosis of midbrain head tremor.

## P_221

### Accelerometric quantification of FTM tremor measurements in ET patients: a pilot study

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**Background:** Disease status, progression and treatment effect of Essential Tremor (ET) patients are currently assessed using subjective visually-scored scales, like the Fahn-Tolosa-Marin Clinical Rating Scale for Tremor (FTM). Precise and rater-independent monitoring of tremor is essential in improving the clinical care for ET patients. Therefore, the focus of this study is translating FTM tremor tests to an objective accelerometry-based method for rating tremor severity according to FTM-criteria.
**Methods:** Thirteen ET patients and 13 age- and sex-matched healthy participants underwent FTM-tests to rate tremor severity, while tri-axial accelerometric measurements were performed at the index fingers. Tremor severity according to FTM-criteria was assessed by four independent raters via video recordings. Quantitative measures were calculated from the accelerometric data, such as area-under-the-curve of power in the 4–8Hz range and maximal tremor amplitude. Thresholds for the scoring algorithm were calculated based on acceleration data of the healthy group. Agreement between accelerometric tremor scores and clinically rated FTM-scores were examined. The inter-rater variability of the clinical FTM assessment and the test-retest reliability of our accelerometric approach were investigated.
**Results:** The acceleration data were in line with a logarithmic relationship between FTM-ratings and tremor amplitude shown in previous research. The agreement between accelerometric scores and FTM-ratings was strong for rest and kinetic tremor tests (>72.7%). However, a poor agreement between accelerometric postural tremor data and clinical FTM-ratings (κ=0.459) was found, although their logarithmic relationship was substantial ($R^2$>0.653). These discrepancies could be explained by objective measurements outperforming clinical scales at the level of the individual patient.
**Conclusions:** This pilot study showed that FTM tremor assessments can be quantified using tri-axial accelerometry-based measurements. The found test-retest reliability of the accelerometric tremor scoring algorithm indicates that our accelerometry-based approach is a promising one. The proposed technology could diminish rater-dependency of FTM tremor measurements and enable physicians to monitor ET patients more objectively.

## P_222

### Burden of essential tremor: associated morbidities, healthcare resource utilization and costs in commercially insured patients on drug therapy

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**Background:** Patients with ET have been shown to have a higher number of comorbidities than non-ET patients, and this could lead to greater medication use. Previous research has demonstrated a high frequency of side effects due to pharmacotherapy in ET, yet data on the economic consequences are limited. Understanding the relationship between the medical complexity of ET patients, concurrent medication use and downstream economic consequences is crucial. This analysis aimed to compare economic consequences, including healthcare resource utilization (HCRU) and costs, of associated morbidities (AMs) among commercially insured adult essential tremor (ET) pa tients taking multiple medications.
**Methods:** Using the MarketScan database (1/1/2017- 6/30/2020), ET patients aged 22-64 (n=22,641) were stratified into subgroups taking 0, 1, and 2 of commonly prescribed ET drugs (propranolol, primidone, topiramate, gabapentin, and atenolol).
**Results:** In the two years following index date, AMs increased with additional ET drugs: anxiety 31.9% vs. 40.6% vs. 44.0% (0, 1, 2 medications, respectively); depression 22.7% vs. 33.3% vs. 42.5% (0, 1, 2 medications, respectively); falls 3.4% vs. 5.0% vs. 8.6% (0, 1, 2 medications, respectively); substance abuse 5.4% vs. 8.6% vs. 12.1% (0, 1, 2 medications, respectively). Additionally, over the two-year period, HCRU and costs increased as patients took additional ET medications. Rates of all cause inpatient admissions and emergency room visits (costs) were 12.6% and 30.2% ($29,670) vs. 16.7% and 35.8% ($39,603) vs. 26.8% and 45.1% ($63,765) (0, 1, 2 ET medications, respectively).

**Conclusions:** AMs, HCRU and costs escalate with each additional ET medication. Effective ET treatments, both pharmacologic and non-pharmacologic, with fewer AMs may mitigate downstream HCRU and costs.

## P_223

### A phase 2b, randomized, dose-response study of SAGE-324/BIIB124 for the treatment of essential tremor: KINETIC 2 trial in progress

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**Background:** Essential tremor (ET) is a common movement disorder and gamma-aminobutyric acid (GABA) dysregulation has been implicated in its pathophysiology. SAGE-324/BIIB124 (SAGE-324) is an investigational GABAA receptor–positive allosteric modulator. In a prior phase 2 trial, patients with ET receiving 60 mg of SAGE-324 once daily experienced a statistically significant reduction in upper limb tremor as assessed by change from baseline (CFB) in The Essential Tremor Rating Assessment Scale-Performance Subscale [TETRAS-PS] Item 4 at Day 29 (primary endpoint) compared with those receiving placebo; 33/34 (97.1%) patients in the SAGE-324 group had ≥1 treatment-emergent adverse event. KINETIC 2 (NCT05173012) is a phase 2b, double-blind, randomized, placebo-controlled, dose-response study designed to evaluate SAGE-324 for the treatment of ET.
**Methods:** The ongoing KINETIC 2 trial is planned to enroll approximately 160 patients. Key eligibility criteria include: age 18-80 years; ET diagnosis (isolated tremor syndrome consisting of bilateral upper limb action tremor for ≥3 years with or without tremor in other locations); no other relevant neurological signs; a TETRAS-PS Item 4 score of ≥12 at screening and at baseline with a total score of ≥6 for the dominant upper limb; a TETRAS-Activities of Daily Living (ADL) score of ≥20 at screening.
Patients are randomized 1:1:1:1 (placebo or SAGE-324: 15 mg, 30 mg, or 60 mg [uptitrated from 15 mg]; oral, daily at night).
The primary endpoint is CFB in TETRAS-PS Item 4 score on Day 91; the secondary endpoint is CFB in TETRAS-ADL composite score. Safety and tolerability of SAGE-324 will be assessed.
**Results:** KINETIC 2 is estimated to complete in 2024.
**Conclusions:** The phase 2b KINETIC 2 trial was designed to evaluate SAGE-324 dose-response on clinically relevant endpoints and safety. Enrollment is ongoing, and the results will inform future SAGE-324 clinical development.
This study is sponsored by Sage Therapeutics Inc. and Biogen Inc.

## P_225

### Clinical effectiveness of transcutaneous afferent patterned stimulation therapy for essential tremor in a real-world setting: a randomized pragmatic trial

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**Background:** Transcutaneous afferent patterned stimulation (TAPS) is a non-invasive therapy delivering calibrated stimulation to the median and radial nerves of the wrist. This study evaluated the clinical benefit of adding TAPS to essential tremor patient's care plan.
**Methods:** This randomized pragmatic trial recruited 300 essential tremor patients from AETNA's Commercially Insured and Medicare Advantage Plans. Patients were randomized 1:1 to 1-month of standard of care (SOC) or treatment (TX; use of TAPS as-needed). Patients reported Bain & Findley Activities of Daily Living (BF-ADL) dominant hand scores and measured tremor power using an on-device accelerometer (after TAPS in the TX arm; daily in the SOC arm). The pre-specified endpoints were tremor power (primary) and improvement in BF-ADL (secondary) between TX and SOC (ClinicalTrials.gov NCT05540626).
**Results:** 261 patients had completed the 1-month trial as of 1/24/23 (131 in SOC, 130 in TX). Patients in TX used therapy and measured tremor 5.33 (0.52) (mean (SD)) times per week, and patients in SOC measured tremor 5.95 (0.81) times per week. TAPS significantly improved (i.e. lowered) tremor power, from 0.017 (0.003) $(m/s^2)^2$ in TX versus 0.079 (0.038) in SOC $(m/s^2)^2$ (geometric mean (SE); $p<0.0001$; primary endpoint). 84% of patients experienced tremor reduction, and 43% of patients experienced at least 50% improvement. TAPS also increased BF-ADL improvement, from 0.223 (0.049) in TX versus 0.073 (0.039) in SOC (mean (SE) improvement per task;

*p*=0.0047). Six patient reported complaints were determined to be adverse events, and included temporary wrist skin irritation, sores, discomfort, or dizziness.
**Conclusions:** Interim results demonstrate that TAPS significantly improved tremor power and BF-ADLs in patients with essential tremor compared to SOC.

### P_226

### Reduced cerebellar volume and preserved white-matter integrity in Essential Tremor: a UK Biobank nested case-control study

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**Background:** Essential Tremor (ET) is a common tremor disorder in adults with uncertain pathophysiology, possibly involving cerebellar degeneration and dysfunction of the cerebello-thalamo-cortical circuit. Previous MR-based imaging studies have demonstrated cerebellar grey matter volume loss, and changes in white-matter microstructure. We aimed to determine if these findings could be seen in an unstudied population. We hypothesized that subjects with ET would have smaller motor-cerebellar lobules (reduced volume) compared to controls. We also predicted that the white-matter microstructure of the cerebellar peduncles and thalamocortical-projections would be disrupted in these subjects.
**Methods:** We conducted a retrospective nested case-control study using data from the UK Biobank, a prospective cohort of >500,000 individuals, aged 40-69, enrolled between 2006 and 2010. Participants with diffusion-weighted brain MRI scans were included. ET cases (n = 31) were ascertained using ICD10 codes (G25) and matched (3:1) by age, sex, imaging site, and medical comorbidities, to controls without a neurologic diagnosis (ICD10 G-coded). Diffusion metrics were extracted from relevant tracts, along with grey matter volumes of the cerebellum, thalamus, and basal ganglia. T-tests (Benjamini-Hochberg FDR = 0.05) were used to compare means. Serial multivariable linear regressions were performed to control for age, sex, and whole-brain volume.
**Results:** In subjects with ET, volumes of the globus pallidus and cerebellar lobules VII and VIII were significantly reduced. Lower volumes of lobules I, II, V, VI, and IX were also observed after controlling for covariates. White-matter tracts showed no significant differences, except for lower orientation dispersion of the superior-thalamic-radiations in subjects with ET.
**Conclusions:** These results confirm and extend previous findings of reduced cerebellar volumes in subjects with ET. However, we did not observe disrupted white matter network microstructure in this population. Our findings are consistent with the hypothesis that the basal ganglia and cerebellum are both involved in the generation of ET.

## Gait Disturbances and Other Movement Disorders Parkinsonian Disorders

### P_227

### Trazodone-associated Parkinsonism with tremor: a case series and literature review

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**Aim:** To describe a case series of trazodone-associated parkinsonism with tremor, including three cases with hand tremor and one patient who had both hand tremor and head tremor.
**Background:** Trazodone is a commonly prescribed atypical antidepressant that has been associated with movement disorders. Inhibition of dopaminergic neurotransmission by trazodone can lead to extrapyramidal features, including parkinsonism with tremor.
**Methods:** We report on four patients who developed parkinsonism with tremor after starting trazodone. Three patients presented with hand tremor, while the fourth had both hand tremor and chin tremor. We reviewed the literature for previously reported cases of trazodone-associated movement disorders.
**Results:** In all four cases, a probable association between trazodone use and the development of parkinsonism with tremor was established based on Naranjo criteria scores. The patients had complete resolution of symptoms after discontinuing trazodone. Literature review revealed eight cases of trazodone-associated movement disorders, including parkinsonism, dystonia, and akathisia.
**Conclusions:** Trazodone use can cause parkinsonism with tremor, and physicians should be aware of this rare adverse effect, especially when prescribing the drug to the elderly. In elderly patients with movement disorders,

trazodone use should be evaluated as a potential cause to avoid misdiagnosis of degenerative disorders. Timely recognition and cessation of trazodone can improve patient quality of life. Further research is needed to understand the mechanism of trazodone-induced parkinsonism and to identify potential risk factors.

## P_228

### The spectrum of phenomenology in painful leg and moving toes syndrome (PLMT): a way towards creating diagnostic criteria

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**Background:** Painful legs moving toes syndrome (PLMT) is a rare movement disorder involving abnormal movements in the lower extremity, typically following damage to soft tissue or peripheral nerves. Debilitating pain is a common feature that often doesn't respond to even invasive treatment. There is no uniform description of the phenomenology and thus PLMT may be underrecognized and underreported. The exact generator of these movements is uncertain but there is evidence to suggest it's mediated by the peripheral nervous system. As the description of PLMT is broad, we describe five newly diagnosed cases to help better refine the diagnosis and improve its recognition in hopes of establishing future diagnostic criteria.
**Methods:** Five patients were newly diagnosed PLMT from July 2022-January 2023 at Loma Linda University outpatient neurology clinic. Comprehensive histories, neurologic examinations were performed. EMGs and MRIs were obtained when available. Patients signed consent forms for videotaping. A literature review was performed.
**Results:** Each patient had a history of preceding nerve or structural injury involving the affected extremity, which correspond to EMG and MRI lumbar spine findings. Toe movements were common to all cases but others had bilateral and proximal leg movements. Choreiform and myoclonic movements were identified. Pain was present and was the most bothersome symptom in four patients. An average of 4.6 medications were taken without symptom relief. Chemodenervation only helped toe movements in one case but did not relieve the pain.
**Conclusions:** Our case series had variable phenomenology, including myoclonic and choreoathetosis. Each patient suffered a preceding structural and/or neurologic injury, suggesting the movements may be mediated by peripheral nerves.The prevalence of these injuries in our population would suggest that this is a more common disorder. We hope to refine the diagnosis of PLMT and establish diagnostic criteria, thereby increasing its recognition.

## P_230

### Restless limb syndrome and insomnia: co-morbidities in rural Indian migraine patients

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**Background:** Restless limb syndrome (RLS) and insomnia are common yet under-recognised comorbidities in patients with migraine. This study aimed to assess the prevalence of RLS in patients with migraine in rural India, its impact on quality of life and sleep, and the relationship between RLS severity, migraine severity, and patient demographics.
**Methods:** Consecutive consenting adults with migraine attending the neurology clinic of a rural charitable medical teaching university hospital in Western India between January 2021 to August 2022 were assessed using a structured proforma. RLS was diagnosed using IRLSSG criteria and assessed by IRLS instrument. Migraine severity was assessed by HIT-6 scale and MIDAS. Sleep was assessed by Insomnia severity index. Prevalence of RLS and insomnia and its relationship with co-morbidities and pharmacological treatment were assessed.
**Results:** Of the 109 participants with migraine, 22 had RLS and 54 had insomnia; all patients with RLS had insomnia. Presence of RLS and migraine correlated with presence of anaemia but not with other medical comorbidities or particular drug therapy. The participants had moderate to severe migraine. Mean IRLS score was 16.4, and mean insomnia index score was 5.2. 14 patients with RLS required dopamine agonist therapy.
**Conclusions:** RLS and insomnia are important co-morbidities in patients with migraine. Female gender and anaemia increase the odds of having RLS. Assessment and treatment for co-morbid RLS is important in patients with migraine to improve their quality of life and sleep.

## P_231

### Anticholinergics should not be used to treat tardive dyskinesia: insights from an expert panel

## of psychiatry and neurology healthcare professionals

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**Background:** Tardive dyskinesia (TD) is a persistent and often disabling hyperkinetic movement disorder associated with prolonged exposure to dopamine receptor blocking agents. Treating TD with anticholinergics is still common, despite a lack of supportive evidence and the potential to exacerbate TD.
**Methods:** In November 2020, 8 movement disorder experts from neurology and psychiatry convened to gather insights on the challenges of differentiating TD from other drug-induced movement disorders (DIMDs) and to discuss appropriate treatments for TD and other DIMDs. A follow-up meeting was held in June 2021 to consolidate these insights. Key recommendations based on these panel discussions are presented.
**Results:** The panel emphasized that while anticholinergics can help with managing some DIMDs, current evidence indicates that they are ineffective against—and may even worsen—TD symptoms. Therefore, in accordance with APA guidelines, the use of FDA-approved vesicular monoamine transporter 2 (VMAT2) inhibitors indicated for TD should be considered as first-line treatment for TD. The panel noted that TD is often described as an “extrapyramidal symptom,” leading to difficulty differentiating TD from other DIMDs and inappropriate treatment of TD with anticholinergics. The panel agreed that prophylactic anticholinergic use is generally not recommended and should only be considered in patients at high risk of acute dystonia. They cautioned against chronic anticholinergic use, especially in elderly patients and those with cognitive disorders or substance abuse problems. Abrupt anticholinergic discontinuation can result in cholinergic rebound; thus, when used appropriately, anticholinergics should be prescribed at minimally effective doses and slowly tapered for successful discontinuation.
**Conclusions:** These findings align with current treatment guidelines for TD, including the lack of evidence for anticholinergic use and recommended first-line treatment with approved VMAT2 inhibitors. Conclusions from this panel highlight the need for continued education on DIMD differentiation, inappropriate and appropriate use of anticholinergics, and safe anticholinergic dosing until discontinuation is possible.

## P_232

## Relationship between frontal lobe dysfunction and fear of falling in people with Parkinson's disease

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**Background:** To evaluate relationship between frontal lobe dysfunction and fear falling during the daily activities in people with Parkinson's disease (PwPD).
**Methods:** Twenty-four PwPD diagnosed by a certified neurologist (mean HY 2.7 stage, mean age 76.9±6.9, female 62%) were included. Fall anxiety and frontal lobe function were assessed using the Modified Fall Efficacy Scale-Japanese Version (MFES-J) and Frontal Assessment Battery (FAB), respectively. The study participants were divided into the two subgroups based on FAB total score: PwPD with a score of 12 or more were classified as the normal group, and those with a score of 11 or less were classified as the frontal lobe dysfunction group. The Mann-Whitney U test was used to compare the MFES-J subitems and total scores between the two groups. The FAB results and the MFES-J total scores and subitems were analyzed by Spearman's rank correlation coefficient.
**Results:** Compared to the normal group, subscores of the following MFES-J subitems "preparing meals," "using buses and trains," and "gardening and hanging the laundry" were significantly higher in the frontal lobe dysfunction group ($p < 0.05$). FAB total score was significantly associated with the MFES-J total score as well as the each following MFES-J subscore ‘dressing’, ’preparing meals’, ‘doing housework’, ‘using buses and trains’, and ‘gardening and washing clothes’ ($r > 0.50$, $p < 0.05$).
**Conclusions:** As a result, frontal lobe dysfunction in PwPD was supposed to be associated with fear of falling.

## P_233

## A follow-up study of diffusion tensor imaging after ventricular shunt in a patient with idiopathic normal pressure hydrocephalus

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**Background:** Idiopathic normal pressure hydrocephalus (iNPH) is a potentially reversible neurological disease, that causes gait disorders, cognitive impairment, and urinary incontinence. The symptoms and neuroimaging findings of iNPH are similar to other neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD). All of these clinical entities mainly occur in elderly patients and so iNPH is often misdiagnosed as other neurodegenerative diseases. VVentriculoperitoneal shunting (VPS) is an effective treatment for iNPH patients that can significantly improve neurological function, while, most persons suffering from iNPH do not receive treatment. Diffusion tensor imaging (DTI) is a powerful magnetic resonance (MR) technique for investigating cerebral microstructure. Diffusion characteristics change rapidly after injury and quantitative measurements are altered in tissue damage.
**Methods:** We report on a 67-year-old male patient with iNPH who was evaluated by diffusion tensor imaging (DTI) follow-up study before and after a ventricular shunt operation. Before the ventriculoperitoneal shunt and at 6, and 18 months after the drainage, gait disturbance, mini-mental state examination (MMSE) score, and the idiopathic normal pressure hydrocephalus grading scoring scale (iNPHGS) were assessed. Three longitudinal DTIs analyzed by tract-based spatial statistics (TBSS) were acquired from the patient (pre-shunt, post-shunt 6 months, and post-shunt 18 months).
**Results:** Significant improvements were noticed in walking difficulties and cognitive decline. The white matter skeletons in the corpus callosum decreased before the shunt operation compared with age-matched healthy controls and increased at 18 months after the shunt operation. (There were three pre-operative and post-operative DTI images of this patient, but they cannot be uploaded successfully for some reason.)
**Conclusions:** Our report suggested that shunt surgery is effective in iNPH patients and DTI analyzed by TBSS is a quantifiable, qualified biomarker for the evaluation of neurologic injury and treatment effect.

## P_234

### Prevalence and impact of restless legs syndrome in patients with stroke in a rural medical teaching hospital in India

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**Background:** Restless Legs Syndrome (RLS) is a nervous system disorder that causes an overpowering urge to move your legs. RLS symptoms are found in 5 to 15% of the general population. Although the majority of primary RLS patients appear to be idiopathic in nature, various underlying medical problems can cause secondary RLS.
**Methods:** This cross-sectional observational study done in a rural tertiary care medical teaching hospital, in between January 2021 to August 2022, aimed to study the prevalence and clinical features of RLS in stroke and to assess the quality of life and sleepiness in stroke patients with/without RLS using the PHQ-9 [Patient Health Questionnaire-9] and ESS [Epworth sleepiness scale], respectively. A total of 106 patients with stroke were included, and their demographic profile and stroke-related details were recorded. RLS was diagnosed using the IRLSSG diagnostic criteria, and severity was assessed using the IRLS [International RLS] rating scale. Quality of life and sleepiness were assessed using the PHQ-9 and ESS scales, respectively.
**Results:** The prevalence of RLS was 15.1% in stroke patients, with a higher prevalence among older, female, unilateral, and hemorrhagic stroke patients. Patients with RLS had significantly higher PHQ-9 and ESS scores, and these scores increased with the severity of RLS. The correlation between the severity of RLS and quality of life and sleepiness was statistically significant.
**Conclusions:** Around 15% of stroke patients have symptoms of RLS, which can lead to poor quality of life and increased daytime sleepiness. Screening all stroke patients for RLS may have a significant impact on public health. Healthcare workers should be trained to diagnose and manage RLS in individuals with stroke to prevent the associated distresses.

## P_235

### Does the preoperative iNPH radscale predict clinical outcomes post-ventriculoperitoneal shunt placement (VPS) in patients with normal pressure hydrocephalus (NPH)?

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**Background:** NPH is treated by placement of a VPS; however, there is no standardized approach to determining surgical candidacy. The iNPH Radscale is an established scoring system for CT/MRI scans that evaluates seven radiographic features characteristic of iNPH. A Radscale score of ≥8 suggests a high probability of an iNPH

diagnosis. This study aimed to assess whether the pre-surgical iNPH Radscale could be used to help determine surgical candidacy.
**Methods:** Patients with a clinical diagnosis of NPH who underwent VPS placement between 1/1/10 and 6/30/21 were included in the study. The seven Radscale parameters were measured on patients' pre-surgical MRIs. Patient charts were reviewed to determine clinical ambulation, cognition, and urination outcomes closest to one year post-VPS and were graded using the Clinical Global Impression Scale-Improvement (CGI-I). Chi-square and ANOVA were used to determine the relationship between total Radscale scores and CGI-I scores. The Fisher's Exact Test was used to determine the association between each Radscale parameter and CGI-I scores.
**Results:** Out of 180 patients, 134 had complete Radscale scores and were included in this analysis. Fifty-nine percent had scores of ≥8, and 41% had scores <8. Forty-seven percent had CGI-I ambulation scores that reflected "much" or "very much" improvement, and 45% demonstrated minimal to no improvement or worse outcomes. There was no evidence of a significant association between the total Radscale score and CGI-I ambulation, cognition, and urination scores after VPS; nor was there evidence of a significant association between the individual Radscale parameters and CGI-I outcomes.
**Conclusions:** This study suggests both total and sub-scores of the iNPH Radscale ratings based on pre-VPS placement imaging have no clear association with clinical improvement in NPH patients after VPS placement. Further research is needed to identify preoperative parameters that are predictive of positive shunt response.

## P_236

## Expanding the phenotypic spectrum of CSF1R variant carriers

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**Background:** Most CSF1R variants are detected in the monoallelic or bi-allelic state. However, little is known about the carriers of two different (compound heterozygous) CSF1R variant carriers.
**Methods:** We analyzed history, clinical, neuroimaging and genetic data of our patient with compound heterozygous CSF1R variants.
**Results:** A 30-year-old Caucasian male with a positive maternal family history of early-onset (6th decade of life) dementia, developed neuropsychiatric symptoms, cognitive decline, decreased control over right limbs, and urine and stool incontinence. On neurological evaluation at 31 years, he scored 15 points on MoCA and presented with right-sided alien limb syndrome, bilateral pyramidal signs, action and resting hand tremor, and abnormal graphesthesia. In the next 12 months, his symptoms rapidly progressed. Repeated brain MRI evidenced progressive white matter changes, and generalized atrophy most prominent in the corpus callosum. Additionally, CT revealed stepping-stone calcifications in the pericallosal area. Genetic testing revealed compound heterozygous CSF1R variants, a pathogenic one (Ile794Thr), and in the other allele one of uncertain significance (Glu916Lys). In-silico prediction models indicated low pathogenic likelihood of the Glu916Lys variant (CADD: 9.77, SIFT: 0.76, PolyPhen: 0.014); however, it was very rare in the general population (0.02% in gnomAD). The analysis of 12 CSF1R–related leukoencephalopathy cases due to the Ile794Thr variant showed a mean age of onset of 42 years (range 28-60).
**Conclusions:** Compound heterozygous CSF1R variants may present with earlier age of onset and more rapid disease progression than monoallelic CSF1R variant carriers. This mechanism may explain the clinical variability of CSF1R-leukoencephalopathy observed in some families.

## P_240

## Subcortical, limbic and neocortical dopaminergic innervation determines response to levodopa in older adults with slow walking and minimal Parkinsonian signs

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**Background:** Mild Parkinsonian signs (MPS), characterized by gait and balance abnormalities, rigidity, and tremor are common among older adults. While not as severe as Parkinson's disease (PD), MPS is correlated with an increased risk of disability and mortality. As PD is characterized by the loss of dopaminergic neurons in the substantia nigra, it has been hypothesized that these PD-like symptoms may be associated with age-related dopaminergic cell loss. In this feasibility study, we explore the relationship between baseline dopaminergic innervation and the effects of carbidopa-levodopa on gait related symptoms in older adults with MPS.

**Methods:** We examined 11 individuals with MPS (F=5/M=6) who completed an extensive gait and balance protocol with APDM sensors, 6 of whom (F=2/M=4) completed dopaminergic PE2i PET imaging. Varimax rotated PCA was applied to gait variables to yield gait feature categories. A Voxel-wise mixed linear model was performed to assess the significance of treatment by PE2i binding with coefficient p-values corrected for false discovery rate.
**Results:** PCA yielded four distinct categories of gait features: festination of gait, cadence, speed, and turn-related gait features. Festination of gait ($\beta$=-0.26, p=0.050), cadence ($\beta$=0.69, p=0.001), and speed ($\beta$=0.66, p=0.020) improved with carbidopa-levodopa therapy. The positive effect of carbidopa-levodopa on gait among older adults with MPS depended on lower dopaminergic terminal integrity in the basal ganglia, centro-cingulate cortex, right parietal operculum, right parieto-insular vestibular cortex, right amygdala, and right hippocampus.
**Conclusions:** Carbidopa-levodopa therapy was effective at improving gait in older non-PD adults with slow walking and MPS. The effectiveness of treatment was dependent on dopaminergic losses in neocortical, limbic, and striatal regions which are important in movement, sensory integration, and emotional and spatial processing.

## P_241

### The Clinician's Tardive Inventory (CTI): an integrated phenomenological and functional measure of Tardive Dyskinesia

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**Background:** Currently, clinician-rated Tardive Dyskinesia (TD) symptom scales have not kept up with expanding spectrum of phenomenology. The objective was to develop/test the reliability of a new instrument.
**Methods:** A movement disorder neurologist devised the scale outline. A steering committee (4 neurologists and 2 psychiatrists) provided revisions to reach consusus The CTI assesses abnormal movement frequency of the eye/eyelid/face, tongue/mouth, jaw, limb/trunk, complex movements (e.g., handwringing, self-caressing) and vocalizations. It rates symptoms from 0-3 (0 = absent, 1 = infrequent/intermittent or only present with activating maneuvers, 2 = frequent intermittent, brief periods without movements, 3 = constant/nearly constant). Functional impairments including activities of daily living (ADL), social impairment, symptom bother, and harm are rated 0-3 with 0 = patient is unaware/ unaffected, symptoms
1 = mildly,
2 = moderately,
3 = severely impact patient.
Following institutional review board approval, the CTI underwent inter-rater and test-retest reliability testing. TD examination videos were obtained and reviewed by 2 movement disorder specialists to determine adequacy. Vignettes were created including symptom descriptions, functional, social, or occupational impairments. Four clinicians rated each video/vignette. Selected videos/vignettes underwent intra-rater retest. Interrater agreement was analyzed via 2-way random-effects interclass correlation (ICC) and test-retest agreement assessment utilizing Kendall's tau-b.
**Results:** 45 video/vignettes were assessed for interrater reliability, and 16 for test-retest reliability. ICCs for movement frequency were: anatomic symptom summary score .92; abnormal eye movement .89; abnormal tongue/mouth movement .91; abnormal jaw movement .89; abnormal limb movement .76; complex movement .87; abnormal vocalization .77; and functional impairments including total impairment score .92; harm .82; social embarrassment .88; ADLs .83; and symptom bother .92; Retests were conducted on mean (SD) 15 (3) days later with scores ranging from .66-.87.
**Conclusions:** The CTI is a new instrument with good reliability in assessing TD symptoms and functional impacts. Future validation study is warranted.

## P_243

### Sustained treatment response with long-term valbenazine in patients with tardive dyskinesia

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**Background:** Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotics and other dopamine receptor blocking agents. Valbenazine is a highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor approved for the treatment of TD. Data from a 48-week, open-label study of once-daily valbenazine (KINECT 4 [NCT02405091]) were analyzed post hoc to assess treatment response patterns.
**Methods:** Data from KINECT 4 treatment completers (participants who reached the Week 48 visit) were analyzed post hoc. Analyses were conducted at Week 8 (first study visit after dose-optimization period) and Week 48 (end of treatment) using the following thresholds: ≥50% and ≥70% improvement from baseline in Abnormal Involuntary Movement Scale (AIMS) total score; rating of “much improved” or “very much improved” (score ≤2) on Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD) and Patient Global Impression of Change (PGIC).
**Results:** Of 167 participants, 103 (62%) were treatment completers and included for analysis. The proportion of completers who met AIMS response thresholds at Weeks 8 and 48, respectively, were as follows: ≥50% improvement (39% and 86%); ≥70% improvement (17% and 52%). Of 40 participants with AIMS ≥50% improvement at Week 8, 95% also met this threshold at Week 48 (“sustained response”). Of 63 participants with <50% AIMS improvement at Week 8, 81% achieved the ≥50% response threshold at Week 48. The proportion of participants meeting thresholds for global response increased from Week 8 to Week 48 for CGI-TD (from 50% to 92%) and PGIC (from 53% to 88%).
**Conclusions:** Post hoc analyses of KINECT 4 data showed that the proportion of participants meeting rigorous response thresholds increased over time. After 48 weeks of treatment with once-daily valbenazine, >80% of participants demonstrated robust improvements in TD, as assessed using the AIMS (≥50% improvement), CGI-TD (score ≤2), and PGIC (score ≤2).

### P_244

### Gait during turning associates with imbalance and falls in PD: 3D video based analysis from a single camera

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**Background:** This study aimed to investigate the relationship between gait parameters during turning and postural imbalance and falls in Parkinson's disease (PD).
It is widely recognized that impaired gait during turning is associated with falls in PD patients. However, conventional gait analytic tools including pressure mat systems cannot provide comprehensive gait analysis during turning.
**Methods:** We prospectively enrolled early or de novo PD patients at the Seoul National University Hospital outpatient clinic from March 2022 to February 2023. We collected clinical variables including age, sex, and disease duration and evaluated them using the MDS-UPDRS scale. All participants underwent previously established 3D video-based gait analysis using a single RGB camera (*Gaitome*) and balance analysis (Pedoscan system). Participants were instructed to walk (forward, turn 180 degrees, and walk back) in a 7-meter walkway five times. Gait phases were segmented into straight walking and turning phases, and turning time and number of steps were automatically calculated. We analyzed the correlation of turning-related gait parameters with center of pressure (COP) deviation measured from the Pedoscan system.
**Results:** We enrolled 26 PD participants in the study. The mean age was 72.35 ± 13.04, with a disease duration of 2.31 ± 1.49. Mean turning time correlated with static and total COP movement ($R = 0.55$, $p = 0.010$), and mean step length during turning correlated with total COP movement ($R = -0.77$, $p = 0.039$) on Pedoscan analysis.
**Conclusions:** Our study showed that turning-related gait variables estimated by video-based gait analysis were significantly correlated with postural instability. Future studies should investigate different clinical syndromes with postural instability and differentiate subtypes of parkinsonian syndrome.

## Rehabilitation, Nursing/Physiotherapy, Other Allied Health; Patient Participation

### P_245

### Outcome measurement and goal-setting recommendations in the multipattern treatment of shoulder spasticity with Botulinum Neurotoxin

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**Background:** Botulinum neurotoxin (BoNT) is a first-line treatment for post-stroke spasticity, helping reduce pain and involuntary movements and restore function. Clinical trials have reported improvements in pain and function after shoulder-muscle BoNT injections. The aim was to present expert consensus on choice of outcome measurement scales and goal-setting recommendations for BoNT in the treatment of shoulder spasticity.
**Methods:** Following a pre-meeting survey, a two-part meeting was held online in late 2021. Five European experts with ~100 years' cumulative experience in post-stroke spasticity gave presentations on shoulder spasticity and treatment with BoNT injections, followed by discussion.
**Results:** Although velocity-dependent increase in muscle tone is often a focus of patient assessment, it is only one component of spasticity and a wider range of measurements is required. For outcome measurement following BoNT shoulder muscle injection, shoulder-specific scales are recommended: AS-SSS, SAAPS and shoulder-relevant items of the ArmA measure, plus standard measurements.
Goal-setting is an essential part of the multiprofessional management of spasticity; goals should be patient-centric, realistic and achievable; functional-focused goal statements and a mix of short (3–6 month) and long-term (9–18 month) goals are recommended. Goals can be grouped into symptomatic, passive function, active function, personal factors and global mobility, measured with the Goal Attainment Scale.
**Conclusions:** Clinical evaluation tools, goal-setting and outcome expectations for multi-pattern BoNT shoulder-spasticity treatment should be defined by the entire team, ensuring patient and caregiver involvement. These recommendations will benefit clinicians who may not be familiar with injecting shoulder muscles and assessing treatment outcomes.

## P_246

## Feasibility of Parkinson's disease treatment utilizing therapy dog with American Kennel Club Canine Certified Therapy Dog

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**Background:** Although animal-assisted therapy generates benefits for individuals with neurological disorders (Rodríguez-Martínez, et al., 2021), the use of animals to benefit people with Parkinson's Disease (PD) needs evaluation. We seek to determine if an American Kennel Club Certified Therapy Dog (AKCCTD) (American Kennel Club, 2022) can be incorporated in the evaluation and treatment of PD in a rehabilitation hospital.
**Methods:** Participants will be patients with PD who will undergo routine evaluation and treatment with physical therapy (PT), occupational therapy (OT), speech and language pathology (SLP), psychology, and physiatry. Mini-Mental State Examination (Folstein, et al., 1975) is administered on admission. Inpatient Rehabilitation Facility Resident Assessment Instrument (IRF–PAI), Self-Care (Activities of Daily Living) and Mobility Items (American Occupational Therapy Association, 2022) and Patient Health Questionnaire-9 (PHQ-9), (Kroenke and Spitzer, 2002) will be administered on admission and weekly to identify the progress of the patient. Treatment sessions and evaluations will utilize an AKCCTD to provide comfort and encouragement.
**Results:** Figures show AKCCTD and owner. Table 1. Rehabilitation hospital patient characteristics.

| Period | 2022 | 1 January to 16 February 2023 |
|---|---|---|
| Number (N) | 41 | 5 |
| Mean length of stay in days | 13.8 | 12.2 |
| Mean age in years | 5.7 | 74.2 |
| Community placement | 82.9% | 100% |
| Mobility improvement | 30.6 | 35.6 |

*A higher Mobility improvement score indicates improved mobility.


**Conclusions:** Treatment of patients with PD utilizing AKCCTD in a rehabilitation hospital is feasible.

**P_247**

**Maintaining and improving individual gains made in physical therapy (PT) by using a dynamic standing protocol post-physical therapy sessions**

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**Background:** A gap in current clinical practice is that post-PT gains are quickly lost in persons with Parkinson's disease (PD). We conducted a single-blinded randomized controlled trial to investigate the effects of a Dynamic Standing Desk (DSK) in the home environment. This desk facilitates a decrease in sedentary behavior as well as weight-shifting and stepping. The Hypothesis was that using this desk would help maintain the gains after the individual PT sessions.
**Methods:** Twenty-four persons with PD were recruited. A total of 14 participants were fully completed the study. All participants received 12 45-minute PT sessions (standard of care). After completion of PT, they all participated in a weekly exercise group of their choice (standard of care). 6 participants were randomized to the DSK group and 8 to the control group. A paired t-test was used to compare 2 visits ($p<0.2$).
**Results:** Results showed that, the post-PT extension of in-home desk group had an improvement of 36.11% of hip abductor strength (p=0.085), 45.71% improvement of MDS-UPDRS II (p=0.119), 65.06% of PDQ-39 (p p=0.127), 19.35% of the short Fall efficacy scale (sFES) (p=0.189), 22.22% of the short Activities-specific Balance Confidence scale (sABC) (p=0.156), and 44.83% decrease of sitting hours per week (p =0.078), 0.17% of Appendicular lean muscle index (ALMI)(kg/m2) (p =0.169), 0.08% of left leg lean muscle mass (p =0.078) ,0.17% of right leg lean muscle mass (p =0.166), 0.1% of trunk fat mass (p=0.099), 0.11% of lumbar bone mineral density (BMD) (p=0.107) compared to immediately after the PT sessions.
**Conclusions:** The Post Physical Therapy intervention in the home environment was feasible, save and well received. Results showed that the decrease in sedentarism combined with weight shifting and stepping resulted in better retention of the individual gains and further improvement in some important outcome measures.

## P_250

### Functional outcomes of an intensive multimodal rehabilitation intervention for moderately advanced Parkinson's disease

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**Background:** Dedicated neurorehabilitation is an essential part of the comprehensive care regimen for PD patients. Intensive multimodal therapy may be especially efficacious for motor and non-motor symptoms in moderately advanced patients, who are at higher risk of falling and losing independent function. Few studies have been conducted in inpatient setting, where pharmacological intervention and therapies can be personalized. Here we present initial functional and quality of life outcomes for patients who participated in our rehabilitation program.
**Methods:** 152 patients with PD (H&Y Stage 3-4) were admitted to the Parkinson's neurorehabilitation unit. Admission criteria included loss of independence in key life function and falls within the past year. Patients participated in a structured multidisciplinary inpatient program with an emphasis on physical, occupational, and speech therapies, and tailored pharmacotherapy. The average length of stay was 14.8 days. A variety of clinical and self-reported scales were completed at admission and discharge: Beck's Depression Inventory (BDI), Sleep Scale (PDSS), Timed Up and Go (TUG), Vocal Volume, Parkinson's Disease Questionnaire (PDQ-39), and the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Statistical methods utilized were two-sample paired t-tests and correlation analyses.
**Results:** The following results were statistically significant ($p \leq 0.05$)–BDI scores decreased: M=16.58 (SD±10.33) to M=12.19 (SD±8.11); PDSS scores increased: M=89.14 (SD±26.04) to M=106.19 (SD±23.98); TUG scores decreased: M=55.73 (SD±43.71) to M=39.33 (SD±31.14); Vocal Volume scores increased: M=54.80 (SD±4.94) to M=60.18 (SD±5.47); PDQ-39 scores decreased: M=43.41 (SD±17.76) to M=37.28 (SD±18.51); MDS-UPDRS scores decreased: M=108.14 (SD±27.89) to M=70.24 (SD±27.61).
**Conclusions:** Neurorehabilitation is integral in the holistic treatment of PD as medications have limited efficacy in advanced stages of this progressive disease. This study indicates that individualized, multimodal rehabilitation intervention in moderately advanced PD has a global impact on functional status.

## P_251

### Virtual reality table tennis in people with Parkinson disease

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**Background:** Rehabilitation is recommended for people with Parkinson disease (PwPD), and various rehabilitation methods have been introduced. Table tennis is one of the rehabilitations which was reported to be effective for motor symptoms of PwPD. A growing body of evidence is accumulating to demonstrate that rehabilitation utilizing virtual reality (VR) is also effective for PwPD. We investigated the effectiveness of VR table tennis for PwPD.
**Methods:** This 2-month prospective study investigated if VR table tennis exercise program could improve symptoms related to Parkinson disease. Four PwPD patients with Hoehn & Yahr stage ≤4 were recruited. Patients participated in a 40-minute VR exercise session in addition to conventional occupational and speech therapies twice weekly. All patients were assessed with the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) before and after the study. The VR model used for the study is the Oculus Quest 2 provided by the Meta Platforms, and we also used a software called 'Eleven Table Tennis'. This study was approved by the Medical Research Ethics Review Committee of Murakami Karindoh Hospital and informed consent was obtained from each participant at enrollment (No: 2022-4).
**Results:** The mean age of disease onset is approximately 74 years, and the mean disease duration is 7.5 years. Among the four participants, number of people who showed improvement more than minimal clinically important difference (MCID) for MDS-UPDRS part I, II, III, and IV were 2, 1, 2, 1, respectively. In addition, two patients showed improvement (-3 points) nearly closed to MCID for MDS-UPDRS part II. No one showed significant improvement on MDS-UPDRS parts I and IV. No one had adverse events such as falls or pain during the study periods.
**Conclusions:** A VR table tennis exercise program may be safe and improve activities of daily living and motor symptoms in PwPD.

## P_168

## Real world outcomes of patients managed with oral medication vs. device-aided therapies: results from the University of Florida INFORM Database

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**Background:** Management of patients with advanced Parkinson's disease (aPD) varies as only a small subset receive device-aided therapies such as, carbidopa-levodopa enteral suspension (CLES) or deep brain stimulation (DBS), while many remain on complex multi-drug oral regimens. Limited data are available on long-term clinical outcomes in patients with advancing disease who remain on oral treatment compared to those who switch to device-aided therapies.
**Methods:** Patient records from the University of Florida Norman Fixel Institute for Neurological Disease INFORM database were retrospectively analyzed. Key inclusion criteria were PD diagnosis > 5 years, moderate motor fluctuations and/or dyskinesia at least 25% of the day, and treatment with levodopa ≥ 4 times/day or a levodopa equivalent dose > 400 mg/day. Eligible patients were divided into two cohorts: "Continued" oral dopaminergic therapy vs "Transitioned" to device-aided therapy (DBS or CLES). Quality of life (QoL) assessed by the Parkinson's Disease Questionnaire (PDQ-39) from baseline to month (M) 12 is the primary endpoint.
**Results:** A total of 614 patient records were evaluated with 295 included in the "Continued" oral dopaminergic therapy cohort and 319 in the "Transitioned" to device aided therapy cohort. Baseline demographics and clinical characteristics were similar between cohorts. There was a clinically meaningful improvement in PDQ-39 summary index with the mean (SD) change from baseline to M12 of -5.0 (7.70) for the "Transitioned" to device aided therapy cohort compared to 0.9 (5.21) for the "Continued" cohort (group difference of 5.89 [95% CI: 4.85-6.94; *P* <.0001]). Improvement in QoL may have been driven by improvements in motor symptoms. Additional outcomes to be included in the presentation.
**Conclusions:** Eligible patients that transitioned to device-aided therapies had clinically meaningful improvements in the patient reported QoL measure (PDQ-39) compared to matched patients remaining on oral therapy.