ABSTRACT E-BOOK

XXVI

WORLD CONGRESS ON PARKINSON'S DISEASE AND RELATED DISORDERS

A COMPREHENSIVE EDUCATIONAL PROGRAM

PRAGUE /
CZECH REPUBLIC

2022

01 – 04 May

INTERNATIONAL ASSOCIATION PARKINSONISM AND RELATED DISORDERS

www.iaprd-world-congress.com

To quote abstracts, use the following information:
Abstract Title
Abstract Number
Author name
Source: XXVII World Congress on Parkinson's Disease and Related Disorders
Online at www.iaprd-world-congress.com 1 – 4 May 2022

URN: urn:nbn:de:101:1-20220421132421503590 46

Table of Contents

Video Abstracts
Part of the Grand Parade of Movement Disorder

GP 1.01
Brittle dyskinesias after bilateral STN DBS: dissociation of microlesioning effect on tremor versus on dyskinesias

Z. Mari[1], *M. Lee*[1]
[1]Cleveland Clinic, Lou Ruvo Center for Brain Health, Las Vegas, United States

Background: Brittle dyskinesia is a complication described after subthalamic nucleus but (STN) not globus pallidus deep brain stimulation implants in Parkinson's disease (PD) (https://pubmed.ncbi.nlm.nih.gov/24932426/). The benefits of directing stimulation away from potentially dyskinesogenic fibers within target, with the use of segmented contacts, has not been evaluated or reported.
Methods: Case report with video.
Results: We present a case of a 74 years old gentleman with about 8 years history of tremor-predominant PD, who was evaluated by the Cleveland Clinic Patient Management Team and was found to be a good candidate for bilateral STN DBS due to motor complications such as wearing off. He had no history of levodopa induced dyskinesias prior to DBS despite taking relatively large dose of levodopa for poorly levodopa responsive tremor. Immediately post-operatively, with no levodopa or stimulation, he developed severe right leg dyskinesias with complete resolution of his tremor.
Over the ensuing months he continued to struggle with disabling right leg dyskinesias, whereas the dissipation of his microlesioning effect produced recurrence of tremor. Neither dyskinesias nor tremor severity were significantly affected by levodopa status. Dyskinesias were worse with most DBS settings compared to off-stimulation. At the same time DBS remained highly effective in suppressing the tremor. MRI showed accurate tip placement with peri-lead edema and minimal hemorrhage along the left sided implantation track. With the use of directed stimulation it was possible to optimize the balance between stimulation-induced tremor benefits and dyskinesias.
Conclusions: To our knowledge this is the first reported case in which a patient with no history of pre-DBS dyskinesias developed brittle dyskinesias in one limb (right leg) only, with no levodopa or stimulation, simultaneously experiencing recurrence of tremor in both the opposite body side and the other limb of the same body side (right arm). This phenomenon may be due to presumed partial resolution of microlesioning effect (for tremor in 3 limbs), while remaining persistent for dyskinesias in one limb only.

GP 1.02

A late-onset mitochondrial Membrane Protein-Associated Neurodegeneration (MPAN) case with Parkinsonism

T. Saltoğlu[1], *F. Erdoğan Küçükdağli*[1], *Y. Sücüllü Karadağ*[1]
[1]Ankara City Hospital, Neurology, Ankara, Turkey

Background: Neurodegeneration with brain iron accumulation (NBIA) is a group of rare disorders progressing notoriously and characterized by excess iron accumulation located mainly in the basal ganglia and in the substantia nigra. MPAN is thought to be the third most frequent subtype of NBIA after pantothenate kinase- and PLA2G6-associated neurodegeneration (PKAN, PLAN) and caused by mutations in C19orf12 encoding a protein of the mitochondrial membrane.

We present a previously healthy 26-year-old man, the first child of related parents, who had normal developmental milestones and presented with a history of cognitive decline for 3 years. His parents were first cousins in the family history. He developed underperformance in the workplace, urinary incontinence, trembling in his hands, and slowness in movements. He was consulted to our clinic for the slowness of movements, trembling upper limbs, and psychomotor retardation with late-onset.

Methods: On examination, the patient had mental slowness and the mini-mental scale score was 17/30, furthermore, hypophonia and a brisk jaw jerk were detected. There was cogwheel rigidity in upper limbs, bradykinesia, and bilateral resting, postural, and intention tremor more especially in the right hand; the amplitude was small, and frequency exceeded 12 Hz, furthermore spasticity in lower limbs with, exaggerated deep tendon reflexes and bilateral extensor plantar response was included. On T2-weighted MRI of the brain showed symmetrical hypointensity in bilateral globus pallidus with linear streak-like hyperintensity in the medial medullary lamina, between the globus pallidus interna and externa due to iron accumulation.

Results: Genetic tests for PANK2 and PLAG2G6 genes were negative. The test for C19orf12 has proven the patient to be a compound homozygote bearing c.32C>T (p.Thr11Met) that shows mitochondrial membrane protein-associated neurodegeneration.

Conclusions: Consequently, we phenomenologically present a case of late-onset MPAN with parkinsonism that is rare and laboriously diagnosed from one of the NBIA group disorders.

GP 1.04
Belly dancer's dyskinesia: case report

K.I. Carus[1], *E. Kobak Tur*[1], *E. Gozke*[1]
[1]Healt Sciences University, Fatih Sultan Mehmet Training and Research Hospital, Neurology Department, Istanbul, Turkey

Background: Belly Dancer's dyskinesia, also known as diaphragmatic myoclonus, is a rare syndrome involving repetitive, involuntary, and continuous movements of the abdominal wall muscles. This phenomenon is secondary to abnormal excitation of the phrenic nerve via the central nervous system or along the nerve.
Methods: Herein, we present a Belly Dancer's Dyskinesia case in a young female patient with no past pregnancy or surgery history. Her clinical situation is considered secondary to trauma.
Results: A 24 years-old patient with have no past medical, or surgical history presented involuntary and rhythmic body movements for six months. She was in good health until she felt pain in the lumbar region after minor trauma. She had explosive speech and disarticulation, head titubation, tongue tremor, and fast abdominal contraction caused by undulating or circular umbilical movements (Video 1).
The signs were neither distractible nor untrainable to hand tapping and alternating hand movement. Propranolol and Primidone were started separately for this situation. She described mild relief of frequency of the signs but no improvement in the long run. The spinal MRI no specifically reported consequences except a posterior central protrusion indenting to a prominent aspect of the thecal sac and constricting lateral recesses. Thorax CT and ECG were shown no abnormalities. The biochemistry panel and CSF examination were in a normal range. Needle EMG showed spontaneous rhythmic activity in L5 paraspinal muscles and had taken the tremor record for 6-7 Hz. We planned a botulinum toxin injection for the patient.
Conclusions: To our knowledge, it is the first reported abdominal wall dyskinesia case after direct trauma. Even though there are no specific treatments, diagnosis and etiologic examination are essential.

GP 1.05
Speech-induced lower face dystonia – presentation of two cases

J. Kaczyńska[1], *Z. Jamrozik*[1], *P. Janik*[1]
[1]Medical University of Warsaw, Department of Neurology, Warsaw, Poland

Background: Among task-specific dystonias, speech-induced focal dystonias are distinguished. There are few descriptions of speech-induced dystonias involving face, mouth, tongue, mandible, and eyelids in the medical literature.
The presented cases are other examples of this rare and interesting phenomenon.
Methods: We present two patients with speech-induced lower-face dystonia with no history of neuroleptics usage. Both of the patients suffer from speech difficulties caused by mouth and probably tongue dystonia, as speech triggers dystonia symptoms. In both cases, other activities such as eating, drinking, swallowing, and whistling are not disturbed and do not induce dystonia.

Results: The first video shows a 44-year-old patient with disfluent, dystonic speech. In this patient severe lower face dystonia occurs during speaking and disturbs speech. The video also shows that in this case symptoms may be reduced using sensory tric (geste antagoniste): the patient places a pea between his teeth and when speaking holding it, speech improves as symptoms of dystonia become less severe. In this patient symptomatic treatment including botulinum toxin was unsuccessful.
The second video shows a 53-year-old patient, in whom speech-induced dystonia had its onset shortly after dental treatment. The video shows moderate speech disorder due to dystonia of mouth and mild dystonic head tremor. In the further part of the video, effect of levodopa (300mg/day) is visible in the form of symptoms reduction. In the follow-up, she developed slow-progressing asymmetrical parkinsonism with good response to levodopa and her speech difficulties never relapsed.
Conclusions: Both patients presented with task-specific focal dystonia, of unknown cause in the first patient, and in the latter case it was possibly a presenting symptom of parkinsonian syndrome. The response to treatment was different in both cases. Speech-induced focal dystonias are rare, yet interesting phenomenon, and the presented cases complement the knowledge on this topic.

GP 1.06
Combined dystonia syndrome associated with novel PMPCA gene variant

Tiziana De Santis[1], *Antoniangela Cocco*[1], *Stefania Lalli*[1], *Michele Lanotte*[2], *Ilaria Palmieri*[3], *Enza Maria Valente*[3], Alberto Albanese[1]
[1]Department of Neurology, IRCCS Humanitas Research Hospital, Rozzano, Milano, [2]Department of Neuroscience, Psychiatric Institute, University of Turin, Torino, Italy, [3]Department of Molecular Medicine, University of Pavia, Pavia, Italy

Objective: Use of genetic testing has facilitated the finding of new genes associated with inherited combined dystonia syndromes, a clinically and genetically heterogeneous group of rare neurologic disorders characterized by the overlap of dystonia and other movement disorders. Recessive mutations in peptidase mitochondrial processing alpha (PMPCA) gene (9q.34.3) are associated with a wide clinical spectrum, including non-progressive ataxia and encephalopathy combined with hyperkinetic movement disorders. Here we report a combined dystonia/ataxia syndrome associated with two biallelic variants in the PMPCA gene.
Methods: We observed a 29-year-old man, born at term from non-consanguineous parents, who presented with early onset laryngeal dystonia that progressed to generalization. At age 8, he developed spasmodic dysphonia, dysarthria and oromandibular dystonia. Symptoms progressed gradually over the years. At age 15, his parents noticed craniocervical and limb dystonic movements with right predominance. Unsteady gait appeared 10 years later. Psychomotor development and cognition were normal. Brain MRI showed a marked cerebellar atrophy with vermian predominance. DAT imaging showed normal uptake (mildly reduced in the left putamen). The patient did not carry variants in a list of dystonia genes. At age 27, he underwent GPi DBS, but a cerebral abscess complicated this procedure and the leads were removed. After surgery, dystonia and ataxia worsened and the patient progressively became anarthric and wheel-chaired. At age 29, we performed an NGS genetic-testing and skin biopsy.

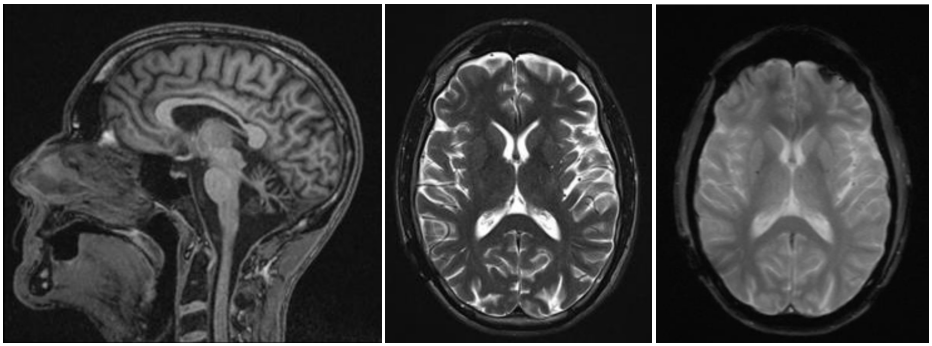


Figure: From left to right - Sagittal FLAIR showing marked vermian and ponto-mesencephalic atrophy, no abnormalities in the basal ganglia observed in axial T2 sequences, no iron deposits in the basal ganglia (axial gradient echo).

Results: Exome sequencing showed two novel compound heterozygous variants in the PMPCA gene (p.Glu207Lys and p.Met251Val).
Conclusion: We report a combined dystonia syndrome associated with compound heterozygous variants in the PMPCA gene. This case highlights the importance of whole exome sequencing in patients with unusual dystonia phenotypes.

GP 1.07
Hemichorea-hemiballismus syndrome with rapidly progressing cognitive decline

J. Kunst[1], V. Vsiansky[1], E. Zatloukalova[1], K. Saxunova[1], M. Balaz[1], I. Rektorova[1], O. Strycek[1]
[1]1st Department of Neurology, St Anne's University Hospital, Faculty of Medicine, Masaryk University, Brno, Czech Republic

Background: We present a case of an 83-year-old female patient who developed right-sided hemichoreatic/hemiballistic involuntary movements over the course of January 2022. This was preceded by a subacute onset of cognitive decline from December 2021. She had a history of arterial hypertension, atrial fibrillation, type II diabetes mellitus and depression.
There was no family history of any movement disorder.
When first examined in the outpatient clinic, a brain CT scan was performed, with no acute pathology described.
The patient declined further examination and oral clonazepam was administered. Before being referred to our outpatient department again, she attempted suicide with acetaminophen overdose, leading to the progression of cognitive decline.

Methods and results: When admitted to our neurology ward in March 2022, the initial neurological examination revealed right-sided hemichoreatic/hemiballistic involuntary movements and cognitive impairment (Mini-Mental state examination 12 points). Laboratory tests showed hyperglycaemia of 19 mmol/l and glycosylated hemoglobin level of 127 mmol/mol. Contrast brain MR scan illustrated changes pathognomonic for the non-ketotic hyperglycaemia in the left striatum.
Moreover, MR revealed multiple bilateral subacute cerebral watershed infarcts. Neurosonologic examination showed non-hemodynamically significant bilateral internal carotid stenosis. Echocardiography demonstrated normal heart function. Glycaemia was lately compensated and tetrabenazine was added to the medication for chorea treatment.
Conclusions: The diagnosis of hemichorea-hemiballismus syndrome associated with nonketotic hyperglycaemia was confirmed on MR scans. Cognitive decline was probably multi-factorial (chronic hyperglycaemic injury, watershed cerebral infarcts). Cerebral infarcts were likely due to acetaminophen overdose and subsequent hypoperfusion of the brain. Compensation of glycaemia and oral tetrabenazine, led to a good improvement in the patient's state.

GP 1.08
Multisystem Erdheim-Chester disease presenting as multiple system atrophy

A.Hassan[1], K.J. Warrington[2], A. Ashrani[3], S. Zanwar[3], K. Kalantari[4], R. Go[3], J. Abeykoon[3], M. Koster[2]
Departments of Neurology[1], Rheumatology[2], Hematology[3], Nephrology[4], Mayo Clinic, Rochester, MN, USA

Background: A 44-year-old male presented to the Ataxia Clinic at Mayo Clinic with a 2-year history of autonomic symptoms (orthostatic dizziness, erectile dysfunction, constipation, voiding difficulty), pancerebellar ataxia, diplopia and sleep-talking. He reported toe discoloration 3 years prior that improved with vasodilators.
Methods: Tests for clinically suspected multiple system atrophy, plus vascular and inflammatory disorders were arranged.
Results: MRI brain showed cerebellar atrophy and atypical patchy FLAIR hyperintensity (brainstem, cerebellar peduncles, mamillary bodies). MRI spine showed extended abnormal T2 cord signal. Autonomic reflex screen was normal and thermoregulatory sweat test showed reduced sweating in the toes. These findings were not consistent with multiple system atrophy.
Additional tests showed raised inflammatory markers (ESR 91, CRP 49) and anemia. CT angiogram showed circumferential thickening of the aorta, peri-renal soft tissue thickening ,and bilateral renal artery stenosis. Bone scintigraphy was consistent with a histiocytic disorder. FDG CT-PET showed extensive uptake in arteries, skeleton and kidneys.
These findings were suggestive of Erdheim-Chester disease. Diagnosis was confirmed by perinephric biopsy for $BRAF^{V600E}$ mutation. Treatment with vemurafenib was initiated with radiographic response.
Conclusions: Erdheim-Chester disease may clinically mimic multiple system atrophy, expanding the phenotype of cerebellar ataxia disorders. Erdheim-Chester disease is a rare multisystem disorder with CNS involvement in 40% of cases. The MRI imaging pattern, CT-PET and bone scintigraphy suggest Erdheim-Chester disease with biopsy-confirmed diagnosis.

Oral Abstracts
Part of the Resident and Trainee presentation session

Part: Parkinson Disease

Imaging and Biomarkers

RT 1.01
Metabolic changes in dementia with Lewy bodies and Parkinson's disease

M. Perovnik[1], *P. Tomše*[2], *J. Jamšek*[2], *M. Trošt*[1]
[1]Unversity Medical Center Ljubljana, Department of Neurology, Ljubljana, Slovenia, [2]Unversity Medical Center Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia

Background: Dementia with Lewy bodies (DLB) is marked by one or more of: parkinsonism, visual hallucinations, fluctuating cognition and REM sleep behaviour disorder with accompanying dementia. Parkinson's disease dementia (PDD) is marked by the appearance of dementia in already established PD. So called "1-year-rule" is commonly used to distinguish between the two.
Methods: We analysed clinical data and FDG PET scans from 21 normal controls (NC), 58 DLB, 20 PD with mild cognitive impairment (PD-MCI) and 22 PDD patients. We compared the groups with two sample t-test of statistical parametric mapping, scaled on pontine metabolism, with age as covariate, $p<0.05$(FWE), cluster size 100 voxels. We calculated the expression of previously derived DLB-related pattern (DLBRP). ANCOVA with post hoc Tukey, age as covariate was used to compare the DLBRP expression.
Results: DLB were older with lower MMSE than NC and PD-MCI ($p<0.01$). DLB had shorter disease duration than PDD ($p<0.01$). DLB showed globally (precuneus, parietal, occipita, inferior temporal lobes) reduced metabolism compared to NC. DLB had reduced metabolism in precuneus, occipital, inferior and middle temporal lobes and cerebellum compared to PD-MCI. DLB had reduced metabolism in putamen, inferior parietal, occipital and bilateral fusiform gyrus ($p<0.001$) and relatively higher metabolism in thalamus compared to PDD. DLBRP expression was higher in DLB vs. NC, DLB vs. PD-MCI ($p<0.001$) and DLB vs. PDD ($p<0.03$).

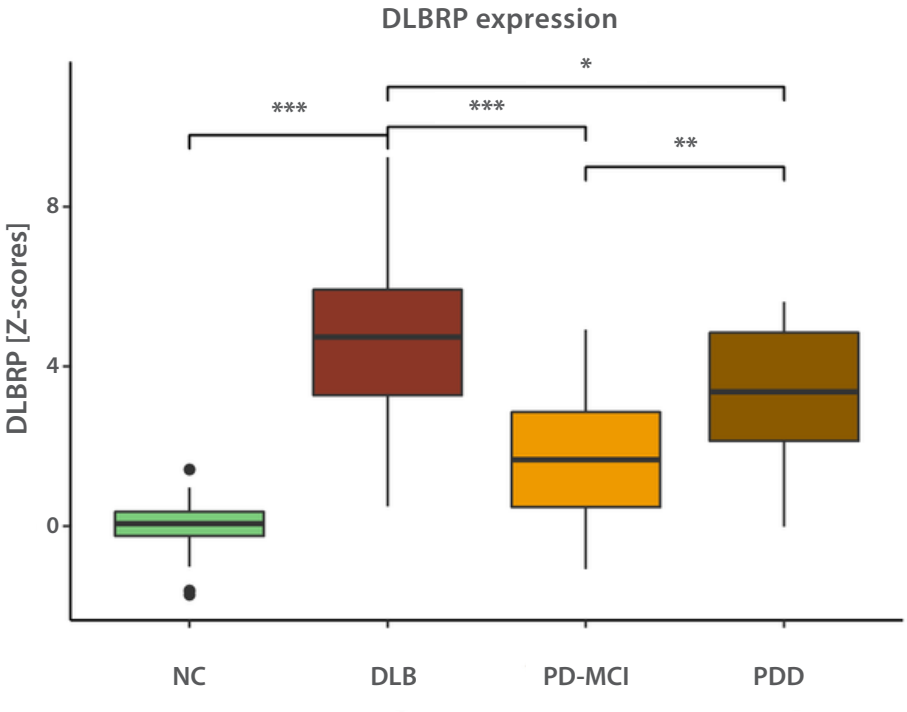


Figure. DLBRP expression

Conclusions: DLB exhibits specific metabolic changes, also in comparison to PD-MCI and PDD. DLBRP is a marker whose expression is higher in DLB than PDD and could be used as a diagnostic biomarker.

Parkinson Disease: Subtypes, natural course

RT 1.02

Correlation of olfactory dysfunction with behavioral symptoms in tremor predominant (TDT) versus akinetic rigid (ART) Parkinson's disease

S. Panambur[1], *S. Paneyala*[1]
[1]JSS Medical College and Hospital, Neurology, Mysore, India

Background: Patients with PD have high prevalence of non motor symptoms like olfactory ,autonomic dysfunctions, sleep disorders and other neuropsychiatric symptoms. Olfactory dysfunction detected in 90% of PD patients and is a potential preclinical marker. Hence, there is a need to identify these symptoms and treat them adequately to optimize the management of patients with PD with an interdisciplinary approach.
Methods: It was a hospital based prospective clinical study over one year including 30 PD patients, sub-classified into ART/TDT. Olfactory function analysed by UPSIT and major behavioral symptoms were assessed using Hamilton's anxiety/Hamilton's depression/Lille apathy rating scale. Psychotic symptoms by the SCOPA- pc scale and impulsive/compulsive behavior by QUIP RS scale.
Results: Analysis of olfactory functions by UPSIT test showed that hyposmia/anosmia was higher in ART (*image 1*).

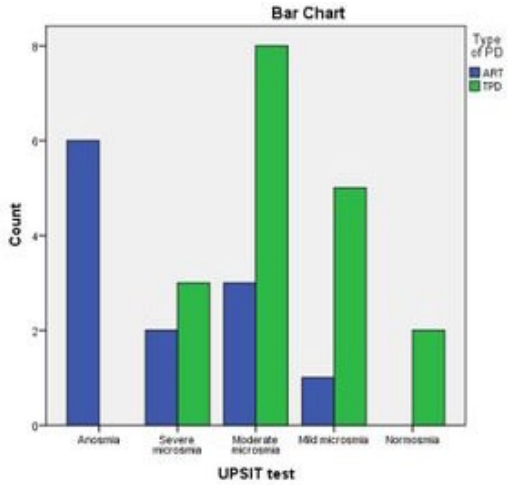


Image 1: UPSIT test in types of PD

Psychotic symptoms analyzed by QUIP RS scale revealed that ART had more severe symptoms with median (IQR) 59(31,87) compared to TDT with median (IQR) 6(2,44) (p value 0.01). SCOPA PC test revealed that ART had more severe symptoms with median (IQR) 10.5(2.5,15.5) compared to TDT with median (IQR) 1(0,2) (p value 0.002). Anxiety analyzed by HAM A test was noted in 12 (100%) ART patients versus 9(50%) TDT patients (p value 0.003).HAM D test and Apathy test were not statistically significant (image 2,3).

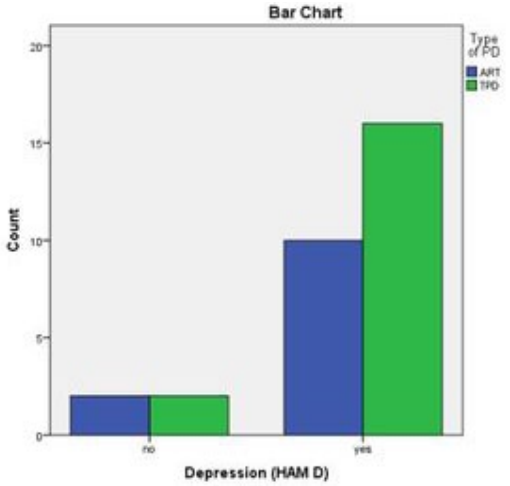


Image 2: HAM D Test in different types of PD

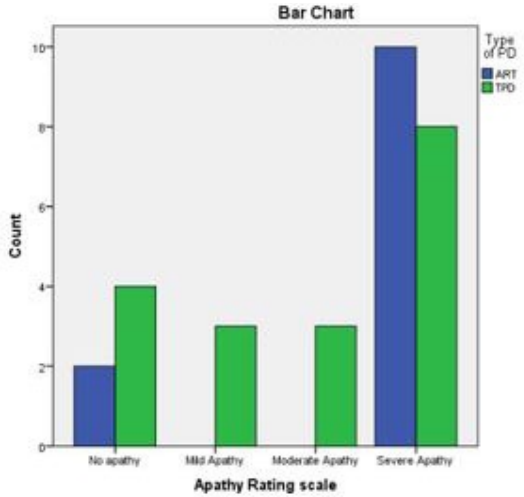


Image 3: Apathy Rating Scale in types of PD

Conclusions: Non motor symptoms have to be given due attention in Parkinson's disease. Anosmia/hyposmia is common in ART subtype. Impulse control disorder/ psychotic symptoms/anxiety are common and statistically significant in ART compared to TPT. The present study didn't reveal statistically significant difference in apathy and depression in subgroups of PD.

Parkinson Disease: Clinical assessment (including devices)

RT 1.03

Comparison of autonomic dysfucntion in patients with Parkinson's disease and progressive supranuclear palsy

J. Malkiewicz[1], *J. Siuda*[1]
[1]Medical University of Silesia, Department of Neurology, School of Medicine, Katowice, Poland

Background: Dysautonomia is common in Parkinson's disease (PD), but also noted by some studies in progressive supranuclear palsy (PSP). The aim of the study was to asses dysautonomia in both diseases.
Methods: 19 PSP and 34 age-matched PD patients were included. Exclusion criteria were heart disease (HD) with NYHA scale result >1, advanced diabetes mellitus (DM), polyneuropathy, renal failure, hepatic cirrhosis, severe respiratory disease, abnormal thyrotropin level, acute infection, electrolyte imbalance. Prevalence of arterial hypertension (AH), HD and DM, cognitive impairment (CI), disease duration and Hoehn-Yahr (HYs) ON and OFF staging were also analyzed. Autonomic dysfunction was evaluated with SCOPA-AUT questionnaire without its sexual domain in 34 PD and 18 PSP patients. Heart rate variability analysis (HRVa) in time (SDNN, RMSSD) and frequency domains (VLF, LF, HF, LF/HF ratio) of 5 minutes ECG was assessed in 30 PD and 12 PSP patients. Orthostatic hypotension (OH) was assessed in 31 PD and 18 PSP patients with 5 minutes tilt-test to 60 degrees angle or active standing test, with cut points 20 and 10 mmHg for systolic and diastolic blood pressure, respectively. U-Mann-Whitney, t-Student, Chi-square and Fisher tests were used in statistical analysis.
Results: PD patients had longer disease's duration PD 10 (7-13) vs 3.5 (2-6), $p<0.001$, lower HYs in ON ($p=0.002$), but not in OFF state. There was not significant difference in number of patients with CI ($p=0.052$), DM and HD, but AH was more common in PD ($p=0.017$). Subjective assessment of autonomic symptoms with SCOPA-AUT questionnaire did not showed significant differences between PD and PSP as well as HRVa. OH was present in 40% of PD patients and any PSP patients ($p=0.007$).
Conclusions: HRVa and SCOPA-AUT questionnaire results are similar in both diseases. Presence of OH usually suggest diagnosis other than PSP.

Parkinson Disease: Therapy (excluding surgical, physical)

RT 1.04

Placebo-controlled study of neurophysiological parameters dynamics in patients with Parkinson's disease stage II after a course of transcranial magnetic stimulation

D. Aravitskaya[1], *A. Demchenko*[1]
[1]Zaporizhzhya State Medical University, Family Medicine, Therapy, Cardiology and Neurology, Zaporizhzhya, Ukraine

Background: Modern principles of Parkinson's disease (PD) treatment include pharmacotherapy and non-drug methods, one of which is transcranial magnetic stimulation (TMS). Today, it's important to study changes in neurophysiological parameters of the CNS in patients with PD for objective assessment of the treatment effectiveness.
Methods: We examined 90 patients (51 women and 39 men) aged 45 to 75 years with PD stage II in Hoehn-Yahr. All patients were randomized into two groups of 45 persons in each for TMS course (10 sessions) in zones of premotor cortex: group 1 patients received a real TMS course, while group 2 patients received placebo-TMS sessions. All patients underwent examination using the SPES SCOPA Motor scale and a neurophysiological study to determine the dynamics of the latent period (LP) of motor evoked potential (MEP) and silence period (SP) before and after TMS treatment.
Results: The mean age, disease duration, and SPES SCOPA Motor Scale score did't differ significantly between patients groups ($p > 0.05$). After TMS-treatment SPES SCOPA Motor score in real TMS-group patients was significantly reduced ($p<0.001$), and no significant changes were found in the placebo-TMS group ($p=0.25$). In real TMS-group after TMS treatment was found significant reduction of MEP latency on the right and left premotor cortex ($p<0.001$ and $p<0.001$, respectively). In the placebo-TMS group wasn't detected significant changes of MEP latency in the right and left premotor cortex ($p=0.06$ and $p=0.08$). It was found significant prolongation of SP latency in both hemispheres ($p>0.001$) after treatment in real TMS patients group. In patients with placebo-TMS after treatment, the SP latency didn't change significantly in both hemispheres ($p=0.36$ and $p=0.30$ respectively).
Conclusions: In patients with PD stage II after real TMS-treatment was detected significantly reducing of SPES SCOPA Motor Scale score, reducing latency of MEP and prolongation of SP latency in both premotor cortex.

Parkinson Disease: Other topics

RT 1.05

Neuroprotective effects of estradiol and progesterone in brain of different age groups of naturally menopausal rats: a therapeutic potential drug for Parkinson's disease

P. Kumar[1], *N. Baquer*[1]
[1]Jawaharlal Nehru University, School of Life Sciences, Delhi, India

Background: Aging of the normal brain is accompanied by changes in its structure, function, and metabolism. Most of these changes increase during menopausal condition in females when the level of 17 β-estradiol (E2) and progesterone (P4) are decreased.
The objective of this study was to determine the effect of E2 and P4 on the activity of acetylcholinesterase (AChE) and monoamine oxidase (MAO), oxidative stress and expression of glucose transporter-1 (GLUT1), tyrosine hydroxylase (p-TH), nerve growth factor (NGF), and testing learning memory, 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. At the end of the treatment period, frontal cortex (FC), striatum (STR), and hippocampus (HP) were isolated for further studies. The learning and memory function were assessed by Morris water maze test.
Results: The results obtained in the present work revealed that normal aging was associated with significant increases in the activity of MAO, lipid peroxidation levels, and a decrease in antioxidant status, GLUT 1, NGF expression, memory functions and AChE activity in rats. There was a significantly increased PPARγ, p-TH expression and alleviated TNF-α, IL-1β in various brain areas compared with the E2, P4 and combined treatment group (E+P). Our data showed that (E+P) group, effectively brought these changes to near normalcy in aging female rats.
Conclusions: Present study elucidates an antioxidant, neuromodulatory and neuroprotective effects of E2, and P4 in aging rats and therapeutic potential for adjunctive therapy along with dopamine replacement in PD.

RT 1.06

Levodopa-induced frequency modulation of cortical EEG activity in the supplementary motor area of dyskinetic Parkinson's disease patients

F. Avantaggiato[1], *A. Canessa*[2,3], *G. Pezzoli*[4], *I.U. Isaias*[1,4]

[1]University Hospital of Würzburg, Department of Neurology, Würzburg, Germany, [2]Fondazione Europea di Ricerca Biomedica (FERB Onlus), Milan, Italy, [3]University of Genoa, Department of Informatics, Bioengineering, Robotics and System Engineering, Genoa, Italy, [4]Parkinson Institute ASST Pini-CTO, Milan, Italy

Background: The clinical phenomenology of Parkinson's disease (PD) has been recently reinterpreted as dysfunctions of task-specific brain circuits, or "circuitopathies", often manifesting as the excessive propagation of cortical-subcortical oscillatory phenomena.

Recently, a dyskinesia-related oscillopathy in the motor network of subjects with PD has been described. Based on previous findings demonstrating altered cortical excitability in the supplementary motor area (SMA) of dyskinetic patients, we hypothesized an involvement of the area in aberrant resonant circuits associated with the development of levodopa-induced dyskinesias (LID) and explored its oscillatory response with TMS/EEG following levodopa intake.

Methods: We enrolled 13 uncomplicated (PD) and 12 dyskinetic parkinsonian patients (PDYSK), evaluated clinically with the MDS-UPDRS and the AIMS scales at baseline and 60 min after a standardized levodopa-challenge. Using an MRI-navigated TMS-EEG system, we stimulated the SMA of their most dopamine-depleted hemisphere identified with SPECT and FP-CIT. We computed the local TMS-induced event-related spectral perturbation (LERSP) at 10 to 2000 ms after stimulus and identified the maximum power frequency on the resulting power spectral modulation profile. We investigated differences due to medication condition and patient group with a repeated measure ANOVA. We used within-subject cluster-based analyses to test for significant LERSP spectral modulations between medication conditions separately for each group.

Results: No difference in age, clinical severity, levodopa equivalent daily dose, and % improvement after levodopa challenge was detected between PD and PDYSK. At baseline, the LERSP was characterized by two frequency peaks, in the low beta and high beta/gamma range, present in both groups.

In uncomplicated PD, no difference was detected in the LERSP and maximum power frequency after levodopa intake, while PDYSK displayed a significant low beta power modulation, coexisting with a shift of the maximum power frequency to lower values.

Conclusions: Our results support a contributory role of the SMA to the "circuitopathy" fostering LID. SMA fundamental frequency shift to the low beta range could represent a marker of transition to a dyskinetic state, possibly due to motor network reorganization in the context of altered synaptic plasticity. This might reflect communication failure along the hyperdirect pathway, potentially amenable to neuromodulatory interventions.

RT 1.07

How choroidal thickness is related with Parkinson's disease? A case control study

A. Fatima[1]
[1]Fatima Jinnah Medical University/Sir Gangaram Hospital, Neurology, Lahore, Pakistan

Background: Parkinson's disease (PD) is a neurodegenerative disorder that leads to the selective loss of dopaminergic neurons substantia nigra pars compacta (SNc).. The clinical manifestations include movement alterations as well as non-motor symptoms, such as dementia, depression, and autonomic dysfunction. MRI assessment feature high iron accumulation. Recently it has been observed that PD affects the retina. Our study aims to find the retinal alterations in PD and their association to clinical and SNc iron-related imaging metrics.
Methods: A case control study was conducted and fifteen patients were included in the study. The patients underwent enhanced depth imaging optical coherence tomography evaluation. Choroidal (vascular) thickness and nerve layers were measured in 4 subregions [superior, inferior, temporal and nasal] and at 3 foveal distances (1, 1.5, and 3mm).
For significantly different metrics, their associations with clinical [levodopa equivalent daily dosage (LEDD), motor and visuospatial function] and SNc susceptibility MRI metrics [R2* and quantitative susceptibility mapping (QSM)] were explored.
Results: Compared to control participants, PD participants had a thicker choroid ($p = 0.005$), but no changes in nerve layers. Higher mean choroidal thickness was associated with lower LEDD ($p < 0.01$) and better visuospatial function ($p < 0.05$). Subregion analyses revealed higher choroidal thickness correlated with lower LEDD and better motor and visuospatial measures. Higher mean choroidal thickness also was associated with lower nigral iron MRI ($p < 0.05$).
Conclusions: The choroid in PD may present increased thickness with better clinical performance and less nigral pathology. compared to healthy individuals; however, more studies and histological analysis are needed to corroborate our findings.

RT 1.08

Correlation of hypothalamic-pituitary adrenal disorders with cognitive impairment in Parkinsons disease and vascular parkinsonism

D. Akramova[1], *G. Rakhimbaeva*[1], *T. Bobomuratov*[1], *S. Kuranbaeva*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: The clinical features of Parkinson's disease and vascular parkinsonism, cognitive disorders associated with the disease, neuroimaging in Parkinson's disease and vascular parkinsonism, as well as intracranial vascular lesions, elevated serum cortisol levels and serum alpha-fetoprotein alterations are therefore discussed.

Methods: Based on this study, the results of a comprehensive clinical examination of 87 patients were analyzed. Research work was carried out on the basis of the TMA clinic in 2019-2022 years 47 patients with Parkinson's disease (PD) and 40 patients with vascular Parkinsonism (VP). For study hypothalamic-pituitary adrenal disorders we studied the association of cortisol and alpha-fetoprotein (AFP) levels in morning serum. Cognitive status and mental status of patients was assessed by the following tests: Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment-(MoCA test).
Results: The main statistical changes when examining morning serum cortisol in patients were observed in the group of patients with VP, with a mean cortisol value of 264.6 ± 66.4 The correlation with cognitive impairment on the MMSE scale was $r = -0.79$ $p < 0.01$, and the correlation with the MoCA test and cognitive impairment was $r = -0.77$ $p < 0.01$. It was also noted that AFP concentrations in group two patients significantly increased compared to group one patients and practically healthy patients with an increase of 15.3 ± 3.7. and the correlation of cognitive impairment with the MMSE scale was $r = -0.80$ $p < 0.01$, and the correlation of the MoCA test with cognitive impairment was $r = -0.79$ $p < 0.01$. Group 2 patients showed a significant increase in blood sugar levels, $p < 0.01$. On the Beck scale, the presence of severe moderate depression was observed at 72.5% $p < 0.01$. Elevated blood pressure was also dominant in group 2 compared to group 1 and 3 patients. In analysis by neuropsychological scales, it was noted that the overall MMSE scores in the VP patient group were in the range of 2 clearly marked cognitive impairment, while the MoCA test also showed a statistically significant change in clearly marked cognitive impairment. Cognitive impairment was observed in 72.5% of VP patients with $p < 0.01$.
Conclusions: In Parkinson's disease and vascular parkinsonism, there is a significant increase in serum cortisol and alpha-fetoprotein ($p < 0.05$), as well as an increase in the rate of cognitive impairment, that is, the amount of cortisol and the degree of cognitive impairment correlate.

RT 1.09

Sarcopenia in acute ischemic stroke patients and patients with Parkinson's disease

S. Mandjikoska[1], *G. Horvat Pinterić*
[1]University Clinical Center in Maribor, Department of Neurology, Maribor, Slovenia

Background: Sarcopenia is a condition characterized by a progressive generalized loss of skeletal muscle mass and strength. The most common nutritional problem that predisposes an ischemic stroke (IS) is sarcopenia. In patients with Parkinson's disease (PD), sarcopenia may represent the common downstream pathway that, from motor and non-motor symptoms leads to the progressive loss of resilience, frailty, and disability.
Methods: Clinical tests and bioimpedance analyses were used to recognize malnourished patients. We chose the Jansen's formula to calculate the total skeletal muscle mass index (TSMMi) and Cruz-Jentoft's cut-off values to identify sarcopenia.
Results: The nutritional status was performed on 123 patients, of which 72 were with moderate IS (NIHSS 9-15) in acute phase (<7days) and 51 with PD, 47% were women and 53% were men. Their average age was 71.6 years. The average BMI was 27.6 kg/m2 (21.0–35.4) in women and 27.9 kg/m2 (20.8–44.4) in men

with IS, and 24.0 kg/m2 (18.0-34.1 kg/m2) in women and 26.4 kg/m2 (20.2-31.5 kg/m2) in men with PD. Among the 72 participants with IS, the prevalence of sarcopenia was 71.9% in men and 23.7% in women. The prevalence of sarcopenia in patients with PD was 22.6% in men and 15% in women. The average fat percentage in our study in female patients with IS was 41.2%, and half of the females exceeded the upper limit for normal fat (>41%). On the other hand, the average fat percentage value in male patients with IS was 28.0% and only 35.3% of our male patients exceeded the upper limit (>29%). In contrast, the average fat percentage in female patients with PD was 34.1%, and 10% exceeded the upper limit. In male patients with PD the average fat percentage was 21.7%, and only 3.2% exceeded the upper limit for normal fat.

Conclusions: Sarcopenia is a common and unrecognized problem in ischemic stroke patients and patients with Parkinson's disease. Thus, BMI is no longer a sufficient tool for recognizing malnourished patients. Bioimpedance analysis is becoming a golden standard for individual nutritional interventions, which provide a solid basis for an efficient rehabilitation.

Tremors, Myoclonus

RT 1.10
Probabilistic tractography based structural connectivity of the tremor network in tremor dominant Parkinson's disease and essential tremor plus syndrome

S. Prasad[1], *J. Saini*[2], *R.D. Bharath*[2], *P.K. Pal*[3]
[1]National Institute of Mental Health and Neurosciences, Clinical Neurosciences, Neurology, Bangalore, India, [2]National Institute of Mental Health and Neurosciences, Neuroimaging and Interventional Radiology, Bangalore, India, [3]National Institute of Mental Health and Neurosciences, Neurology, Bangalore, India

Background: The basal ganglia-thalamocortical (BGTC) and cerebello-thalamocortical (CTC) networks are implicated in the genesis and propagation of postural and rest tremor, however, the exact contributions across disorders have not been studied. This study evaluated if the role of BGTC and CTC in tremorogenesis differs between tremor dominant Parkinson's disease (TDPD) and essential tremor plus (ETP), and if specific regions differentially contributed to tremor severity.
Methods: Structural connectomes of the BGTC and CTC were generated by probabilistic tractography (n=TDPD:25; ETP:25; HC:22). The Brain Connectivity Toolbox was used for computing standard topological graph measures of segregation, integration and centrality of the structural connectomes. Tremor severity was ascertained using the Fahn-Tolosa-Marin tremor rating scale (FTMRS).
Results: A reduction in participation coefficient (PC) of the right thalamus and precentral gyrus in TDPD was observed compared to HC. No significant differences surviving FDR correction were observed between TDPD and ETP, or ETP and HC. In TDPD, the left side FTMRS score correlated directly with the PC of the right thalamus and caudate. Similarly, right side FTMRS score inversely correlated with PC of the right cerebellar lobule VIII. In ETP, the total FTMRS score directly correlated with the strength of the left SNc. FTMRS part A scores directly correlated with the strength of the left precentral gyrus, supplementary motor area, pallidum, SNc, and eigenvector centrality of the left SNc.
Conclusions: Contrary to expectations the extent of difference between TDPD and ETP was minimal. Results were suggestive of damage to the central pathway common to both the BGTC and CTC in TDPD. Increased participation of the thalamus and caudate, and reduced participation of the cerebellum was found to drive tremor severity in TDPD, whereas a possible role of the SNc and pallidum was observed in ETP.

Part: Other Movement Disorders

Parkinson Disease: Other topics

RT 2.01
Cross-cultural validation of the Cebuano version of a screening questionnaire for Parkinson's disease

D. Dakay[1], *F. Tangcalagan*[1], *E. Villanueva III*[2], *J. Abejero*[3], *G. Saranza*[3]
[1]Chong Hua Hospital Mandaue, Internal Medicine, Mandaue City, Philippines, [2]University of the Philippines, Pathology, Quezon City, Philippines, [3]Chong Hua Hospital, Internal Medicine, Section of Neurology, Cebu City, Philippines

Background:
In the Philippines, actual prevalence of Parkinson's Disease is not yet determined. Although cases can be extrapolated from hospital databases and medical registries, this method may undermine actual case rates. Community cases are missed due to lack of appropriate data collection instruments.
Therefore, a reliable screening tool for Parkinson's disease (PD) that can be used in the hospital and community setting is essential in the timely diagnosis of PD and in epidemiological studies. The most widely used screening questionnaire for PD diagnosis was developed by Tanner et al. Although this questionnaire has been translated to several other languages, translated version must be validated for use in our local setting.
Methods: To achieve a power of 80% with a significance level of 5% in a receiver operating characteristic (ROC) analysis, 75 PD patients and 244 controls were enrolled in the study. The questionnaire consisted of nine individual questions about the motor symptoms of PD. The questionnaire was translated from English to Cebuano by a hired English-Cebuano language specialist.
It was subsequently administered to both PD and controls. Each item was supplied with a "yes", "no" or "don't know" answer. Information on demographics, age of PD onset, Hoehn and Yahr stage and medications were determined.
Results: The overall Cronbach's alpha for internal consistency of the questionnaire was 0.9410. The item on "tremor" had the highest sensitivity (97.26%), while the item on "problems with buttoning" had the highest specificity (100.00%). A cut-off score of >3 obtained the best Youden's index (99.18%) with a sensitivity of 100.00% and a specificity of 99.18%. The questionnaire had an almost perfect predicting ability to diagnose PD based on the computed AUC of 0.9994.
Conclusions: The translated version of the Tanner questionnaire is a validated instrument to identify PD in a literate Cebuano population.

RT 2.02

Patients' with Parkinson disease perceptions of palliative care

A. Kundrick[1], *O. Hogue*[1], *A. Margolius*[1]
[1]Cleveland Clinic Foundation, Neurology, Cleveland, United States

Background: Parkinson disease (PD) affects multiple facets of patients' lives, many of which may not be recognized or addressed by their healthcare team. A growing body of evidence has shown that palliative care improves the quality of life of patients with PD; however, little is currently known about how patients with PD perceive palliative care.
Methods: An 8-question multiple choice survey was created and given to patients diagnosed with probable PD at a movement disorders clinic in a quaternary care center. Patients with less than 2 years of follow up or that had atypical features of PD were excluded from the survey.
Results: There were 106 respondents to the survey. A third of patients reported having never heard of palliative care and an additional 25% had heard of it, but did not know what it was. 88% were reported being familiar with or very knowledgeable about hospice, though 50% of respondents did not know the difference between the hospice and palliative care. 93% had never been offered either service. 37.7% thought their neurologist should discuss advance care planning early in the course of their disease.
Conclusions: In our study, over half of patients with PD were not familiar with palliative care and the majority had never been offered palliative or hospice services even though it could improve their quality of life. Additionally, patients with PD would like to be introduced to advanced care planning by their neurologist early in the course of their disease.

Dystonia

RT 2.03
Isolated lingual dystonia as a presenting symptom of X-linked dystonia parkinsonism

D. Dakay[1], *G. Saranza*[2], *Z. Leonardo*[2], *N. Brüggemann*[3], *A. Westenberger*[3]
[1]Chong Hua Hospital Mandaue, Internal Medicine, Mandaue City, Philippines, [2]Chong Hua Hospital, Internal Medicine, Section of Neurology, Cebu City, Philippines, [3]Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Background: Dystonia is an involuntary, repetitive muscular movements. Oromandibular dystonia, a form of focal dystonia, involves the muscles of the face, jaw and tongue. Isolated lingual dystonia (ILD), a rare subtype of oromandibular dystonia, affects only the tongue. There is paucity of literature regarding causes of ILD. Published case reports of ILD are limited to idiopathic and drug-induced forms. This case report highlights the genetic causation of ILD as confirmed by X-linked dystonia parkinsonism (XDP) haplotype.
Methods: A 43-year-old male complained of involuntary tongue movements aggravated by jaw opening. His concern resulted in speech and swallowing difficulties with consequent weight loss. He was not maintained on any medications. He has no co-morbid illnesses. There were no antecedent events and family history of movement disorders documented. Despite a thorough history, clinical examination and work-up, no cause could be identified. Thus, idiopathic isolated lingual dystonia was initially considered.

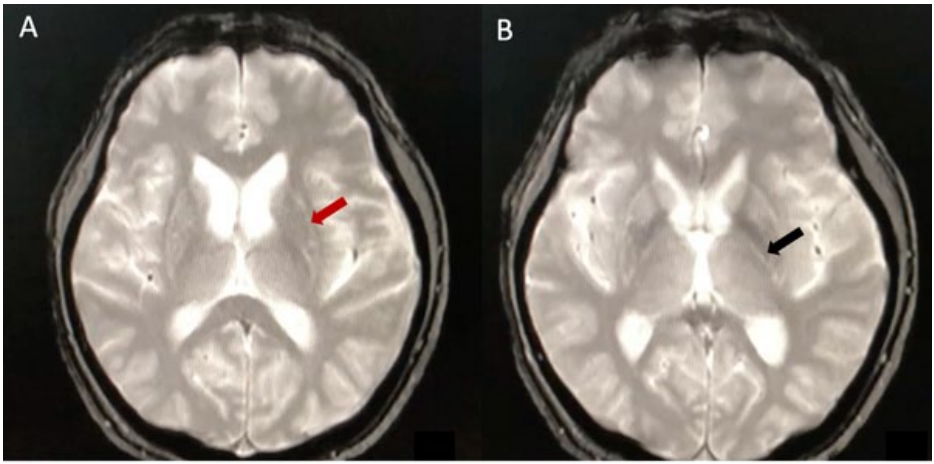


Figure 1. Neuroimaging findings. Cranial MRI (Gradient echo sequence) showed hyperintensities in the putaminal rim (A) and pallidal rim (B).

Results: Routine hematologic, biochemical, and thyroid function studies were all normal. A trial with clonazepam and zolpidem did not afford any symptom improvement. At 2.5 mg of trihexyphenidyl, there was a significant improvement of his lingual dystonia, now speaking more clearly and swallowing without any difficulty. Genetic testing revealed the presence of the XDP haplotype, with 43 CCTTCT repeats in the SVA insertion. On cranial MRI, he had hyperintensities in the bilateral putamen and globus pallidus.
Conclusions: X-linked dystonia parkinsonism (XDP) should be considered in the differential diagnoses of a patient with isolated lingual dystonia (ILD), even in the face of a negative ancestral roots from Panay.

RT 2.04

Structural and functional brain abnormalities in idiopathic cervical dystonia: a multimodal meta-analysis

X. Huang[1], *B. Li*[1], *M. Zhang*[1], *H. Shang*[1], *J. Yang*[1]
[1]West China Hospital of Sichuan University, Department of Neurology, Chengdu, China

Background: Neuroimaging studies have revealed both brain structural and functional abnormalities in patients with Idiopathic cervical dystonia (iCD), but often yield diverse results and no data are available relating these two domains. We aim to find the specific and common neurostructural/functional abnormalities in iCD by conducting separate and multimodal meta-analyses across studies.
Methods: A systematic literature search was conducted to identify relevant publications. Separate meta-analysis for whole-brain voxel-based morphometry (VBM) studies and for functional imaging studies, and then a multimodal meta-analysis across VBM and functional studies in iCD were conducted using anisotropic effect size-based signed differential mapping.
Results: Nine structural studies comprising 152 iCD patients and 188 healthy controls, and thirteen functional imaging studies comprising 194 iCD patients and 206 healthy controls, were included in the meta-analyses. The multimodal analysis showed overlap between anatomic and functional changes, including bilateral supplementary motor areas, bilateral caudate, left putamen and pallidum and bilateral median cingulate/paracingulate gyri. We also found gray matter alterations alone in the bilateral thalamus, bilateral dorsolateral superior frontal gyri, right paracentral lobule, left middle temporal gyrus, right inferior parietal gyrus; and functional abnormalities alone in the bilateral precuneus, right precentral gyrus, right inferior frontal gyrus and superior frontal gyrus, and right cerebellum.
Conclusions: The significant conjoint and dissociated brain structural and functional abnormalities identified in the meta-analyses may help provide new insight into the neuropathology of iCD.

RT 2.05
Botulinum toxin type a for blepharospasm

A. Duarte[1], *H.A. Ghizoni Teive*[1]
[1]Universidade Federal do Paraná, Curitiba, Brazil

Background: Blepharospasm is a type of focal dystonia, characterized by involuntary contraction of eyelids, leading to bilateral eye closure or persistent blinking. Although there is currently no cure, botulinum toxin type A (BTA) has been used as a choice treatment since the eighties. The aim of our study was to quantify the symptoms improvement after BTA application.
Methods: Patients diagnosed with bilateral blepharospasm that apply quarterly botulinum toxin type A at Hospital de Clínicas da Universidade Federal do Paraná, in Brazil, were invited to compose the study sample. Patients that could not understand or sign the consent form were excluded, as well as patients with other associated dystonias (such as oromandibular). Participants were questioned about their symptoms at baseline (3 months after the last application) and two weeks after the application, using the Jankovic Rating Scale (JRS) to quantify the improvement. The responses were noted in an Excel sheet and statistical analysis were performed using the software Jamovi 1.6 (The jamovi project, 2021).
Results: 52 patients were invited to compose the study sample. 9 patients met the exclusion criteria and did not participate in this research. The study had 43 participants, 6 male and 37 female, with a mean age 65,74 (± 10,26). They received a mean of 43,98 (± 9,93) U of botulinum toxin type A (Botox®, by Allergan, diluted in saline solution). The mean score at JRS before the BTA application was 5.12 (± 1.88) and the after was 2.16 (± 1.79), $p < 0.001$. The Shapiro-Wilk test showed that the sample was inside the normality, with a $p = 0.186$ and $W = 0.964$, and the effect size given by the Cohen's d was 4.14.

								95% Confidence Interval				95% Confidence Interval	
			statistic	df	p	Mean difference	SE difference	Lower	Upper		Effect Size	Lower	Upper
A	B	Student's T	27.2	42.0	< .001	41.8	1.54	38.7	44.9	Cohen's d	4.14	3.21	5.07

Table. Paired Samples T-Test

Conclusions: Botulinum toxin type A is effective for the treatment of blepharospasm, capable of acting not only in severity, but also in symptom frequency, and of reducing the JRS score by 57,81%. Further studies are mandatory to determine the influence of other factors in symptom improvement.

Ataxias, hereditary spastic paraparesis

RT 2.06
Patient perspective in hereditary ataxia

S. Gorcenco[1], *C. Karremo*[1], *A. Puschmann*[1]
[1]Lund University, Skane University Hospital, Neurology, Lund, Sweden

Background: Hereditary ataxia is a group of rare disorders. Healthcare providers and public authorities may have limited knowledge about this diagnosis. We asked the patients if they feel well-informed about the diagnosis and whom they usually turn to for support.
Methods: Adult patients with a diagnosis of progressive cerebellar ataxia were identified in the diagnosis register of Scania region or were recruited through a patient organization. All patients were examined clinically. A survey with 32 multiple choice and open-ended questions was distributed through a secure online tool. Written and informed consent was obtained from every participant. Our study is ethically approved.
Results: Participants (N=79) were aged between 22 and 80 years, onset varied from 1 to 73 years. The most common symptom at onset was "impaired balance". The SARA score median was 10 (SD 9,06). Progress was described as slow by 87,3% (N=69). Genetic testing was recalled by 56,9% (N=45) of which 38% (N=30) received a genetic diagnosis. Among patients who had a genetic diagnosis, 76.7% felt "well-informed" (36.7%) or "partly well informed" (40.0%) about their diagnosis. Among patients who did not have a genetic diagnosis, 59.2% felt (fully: 22.4%; partly: 36.7%) well-informed. This difference did not reach statistical significance (Pearson Chi-Square 0,17, Cramer's V 0,2). On the question "what helps you feel better?", "exercise" was the predominant answer 40,5% (N= 32) followed by "social support from close family" and "medication". Patients answered that close family and friends is the first instance they turn to for moral support (N=62).
Conclusions: This patient-perspective study on hereditary ataxia highlights the need to improve the disease-related information that health service providers give to their patients, even when the exact genetic subtype has been established. Physiotherapy and support from close family are important for the wellbeing of patients with hereditary ataxia.

Tremors, Myoclonus

RT 2.07

Non-motor manifestations of myoclonus dystonia on a mixed-ethnicity Filipino female with a novel sgce gene nonsense mutation: a case report

M.A. De Leon[1], *R. Rosales*[1], *C. Klein*[2], *A. Westenberger*[2]
[1]University of Santo Tomas Hospital, Neuroscience and Behavioral Medicine, Metro Manila, Philippines, [2]Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Background: Myoclonus-dystonia is a rare movement disorder with an autosomal dominant inheritance pattern characterized by a combination of myoclonic jerks and dystonia that may have psychiatric manifestations. Our aim is to present neurologic and psychiatric phenotypic characteristics in the first Filipino bi-ethnic myoclonus-dystonia patient and her father.
Methods: We investigated a Filipino myoclonus-dystonia patient with a positive family history. This 21-year-old woman of mixed Filipino-Greek ethnicity presented with involuntary jerking movements of her upper extremities, head, and trunk. Her symptoms affected her activities of daily living which led her to develop moderate depression, mild to moderate anxiety, and mild obsessive-compulsive disorder (OCD). Her 49-year-old Greek father suffered from adolescence-onset myoclonus-dystonia.
Results: Genetic testing revealed a novel epsilon-sarcoglycan (*SGCE*) gene nonsense mutation c.821C>A; p.Ser274* that confirmed our clinical diagnosis.
Conclusions: It is intriguing to consider whether a bi-ethnic origin of our patient would influence the transmission and the expression of the disease. The literature search revealed no genetic or functional study of a myoclonus-dystonia patient with a bi-ethnic origin.
Nevertheless, given that the *SGCE* gene has been found to be maternally imprinted and thus expressed only from the paternal allele in numerous patients worldwide, there is no reason to assume that the Greek or Filipino ethnicity would influence this epigenetic phenomenon.
For co-morbid anxiety, depression, and OCD, this patient was given duloxetine, in addition to clonazepam for the myoclonus and dystonia. She has a 9-month-old half-sister, likewise Filipino-Greek, who is currently asymptomatic. Counseling was provided for the patient and her family as well as close monitoring for symptoms as her younger sister may develop the aforementioned movement disorder in the near future.

Gait Disturbances and Other Movement Disorders

RT 2.08
Idiopathic NPH patients with worse pre-surgical walk test performances demonstrate the greatest improvement in performance post-VPS

A. Kundrick[1], *J. Liao*[1], *P. Salles Gandara*[1], *O. Hogue*[1], *C. Fellows*[2], *T. Charnas*[3], *S. Nagel*[2], *H. Fernandez*[1]
[1]Cleveland Clinic Foundation, Neurology, Cleveland, United States, [2]Cleveland Clinic Foundation, Neurosurgery, Cleveland, United States, [3]Cleveland Clinic Foundation, Cleveland, United States

Background: Currently, there is no uniform decision-making paradigm to determine which patients with idiopathic normal pressure hydrocephalus (iNPH) benefit from ventriculoperitoneal shunt (VPS). To determine surgical candidacy, most institutions perform a standardized walk test before and after an external lumbar drain trial (ELD).
However, many patients have equivocal responses and are still offered shunt surgery because of subjective improvements not captured by the walk test. We sought to determine factors that influence long-term outcomes in shunted iNPH patients.
Methods: Patients who underwent diagnostic ELD trial for suspected iNPH between January 1, 2010 and June 1, 2020, and subsequently underwent VPS placement and post-shunt video-taped walk tests were identified. Each patient's pre-shunt walk test performance was plotted against follow-up performance closest to 12 months and Spearman's correlation analysis was used to determine whether baseline performance was associated with improvement.
Results: Of the 39 patients that had follow-up walk test videos, 72% were male, 38 patients were white and 1 was black, with an average age of 75 years old (SD 5.92). The average time to post-VPS follow up was 7 months (SD 6.6). Twenty-two patients had more than one follow-up walk test.
The median baseline step count was 15 steps (IQR 13.5-19.5) and time to walk was 19 seconds (IQR 15.5-31). At follow-up, median step count improvement was 3 steps (IQR 1.6-6) and median walk time improvement was 5 seconds (IQR 2-11.5). Patients that started with worse baseline walk test performance had greater post-VPS improvement (rho=0.63, $p < .001$).
Thirty-one (79.5%) patients improved more than 10% in step count from baseline, and only 2 worsened.100% of patients improved more than 10% from baseline in walk time.
Conclusions: In this study, patients with worse pre-surgical walk test performances demonstrated the greatest improvement in performance post-VPS.

RT 2.09

Clinical presentation, comorbidities and treatment of GAD antibodies associated Stiff Person Syndrome

G. Lazzeri[1,2], D. Saccomanno[1], F. Arienti[1], E. Monfrini[1,2], I. Trezzi[1,2], S. Corti[1,2], G.P. Comi[1,2], G. Franco[1], A.B. Di Fonzo[1,2]

[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurology Unit, Milan, Italy, [2]Neuroscience Section, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Background: Stiff Person Syndrome (SPS) is a rare autoimmune neurological disorder, characterized by axial and limb muscular stiffness and spasms, due to a loss of physiological GABAergic CNS inhibition. In 60%-80% of patients with classic SPS phenotype antibodies against glutamic acid decarboxylase (GAD) enzyme can be found.

Methods: Patients with a clinical diagnosis of SPS and GAD antibodies, evaluated at Ospedale Maggiore Policlinico, Milan, Italy, between 2013 and 2022, were retrospectively included. The presence of GAD antibodies was screened by quantitative assessment (either Chemiluminescent immunoassay-CLIA or Radioimmunoassay-RIA), and subsequently confirmed by qualitative assessment (indirect immunofluorescence on cerebellum primate and immuno-dot-blot).

Patient	Age	Age at onset	Symptoms at onset	Neurologic examination	Other neurologic manifestations	Comorbidities	Symptomatic treatment	Immunotherapy
#1	75	58	Uncontrolled diabetes	Bilateral UL bradykinesia, lumbar and limb rigidity, exercise induced limbs and lumbar spasms, walks with assistance	- EEG: sporadic bilateral temporal sharp waves - Acute episodes of diffuse spasms with respiratory involvement, tachycardia, tachypnea, sweating, responsive to EV Diazepam	Breast cancer Autoimmune diabetes Anti-TPO+, anti-TG+	Clonazepam Gabapentin	1st line: PEX 2nd line: AZA
#2	33	27	Lumbar pain	Bilateral UL bradykinesia, low back stiffness and spasms, hyperreflexia, right ankle clonus, exaggerated lumbar lordosis, robotic gait	EEG: bilateral fronto-temporal polymorphic sharp theta graphoelements	None	Clonazepam Baclofen	1st line: PEX 2nd line: RTX 3rd line: *thymectomy* (no response)
#3	45	37	Axial and limb rigidity	LL spastic rigidity, brisk DTRs, bilateral patellar and ankle clonus, spastic gait	Ptosis and diplopia (EMG negative for MG, anti-AcHR and anti-Musk negative)	Breast fibrous dysplasia Anti-TPO+, anti-TG+ Anti-PGC+ Vitiligo	Clonazepam Baclofen Gabapentin Botulin toxin	1st line: oral steroid, PEX 2nd line: AZA, MTX 3rd line: RTX 4th line: *thymectomy* (no response)
#4	59	58	Falls	Hypermetric saccades, unsustained bilateral endpoint nystagmus, LL and axial spasms, brisk DTRs	None	Anti-TPO+, anti-TG+	Clonazepam	1st line: IVIg
#5	52	37	Falls	Axial and limbs rigidity, postural instability, reduced arm swing	Ptosis and diplopia (SFEMG compatible with MG, slight positivity of anti-AcHR ab)	Anti-TPO+, anti-TG+	Clonazepam Baclofen Diazepam Pregabalin	1st line: EV steroid, PEX
#6	44	35	Limb rigidity	Sustained bilateral endpoint nystagmus, brisk DTRs, spastic paraparesis	- Episodes of diplopia in the past - Acute painful crisis with spasms, misdiagnosed as acute abdomen or panic attacks, responsive to EV Diazepam	None	Clonazepam Diazepam Baclofen (*intrathecal pump*)	1st line: PEX 2nd line: RTX
#7	52	25	Falls	Axial and LL rigidity	Partial epilepsy, chronic treatment with carbamazepine	Autoimmune diabetes Anti-PGC+ IgA deficiency	Clonazepam Baclofen Diazepam	1st line: oral steroid 2nd line: PEX 3rd line: AZA
#8	49	47	Lumbar pain, falls	Brisk DTRs, right ankle clonus, right limbs spastic rigidity, walks with assistance	EEG: sporadic left temporal sharp waves	ANA+	Clonazepam Baclofen	1st line: IVIg
#9	75	61	LL rigidity	Right LL, axial and abdominal rigidity, painful cramps, walks only with assistance	Axonal polyneuropathy	Autoimmune diabetes Colorectal cancer ANA+ Vitiligo	Clonazepam Diazepam Baclofen Pregabalin Botulin toxin	1st line: EV steroid 2nd line: IVIg

Table 1. Clinical presentation, comorbidities and treatment of 9 anti-GAD SPS patients.

ANA: anti-nuclear antibodies; AZA: azathioprine; DTRs: deep tendon reflexes; IVIg; intravenous immunoglobulins; LL: lower limbs; MTX: methotrexate; PEX: plasma exchange; PGC: parietal gastric cells; RTX: rituximab; TG: thyroglobulin; TPO: thyroperoxidase; UL: upper limbs.

Results: A total of 9 patients were included, all female. The mean age at onset was 40.5 years (25-58). The most common symptoms at onset were unexplained falls and dorso-lumbar pain. Three patients suffered from autoimmune diabetes; positivity to anti-thyreoglobulin, anti-TPO and anti-parietal gastric cells was also detected. One patient had history of partial epilepsy, and other 3 patients had subclinical epileptic activity on EEG. All patients had a good response to symptomatic treatment with clonazepam or baclofen (in 2 cases with intrathecal pump), but were also treated with immunotherapy, with either plasma-exchange or IVIG in inpatient setting, and subsequently with second-line agents (Rituximab, Azatioprine, Methotrexate). Two patients underwent thymectomy, with identification of thymic hyperplasia vera, although with no symptomatic relief.
Conclusions: GAD associated SPS is a protean syndrome, with diverse neurological manifestations combined with autoimmune disorders. A patient-tailored combination of symptomatic drugs and immunotherapies is needed to improve the patients' quality of life.

RT 2.10
Aceruloplasminemia - ultra-rare cause of iron accumulation

A. Antos[1], *T. Litwin*[1], *M. Skowrońska*[1], *A. Przybyłkowski*[2], *H. Zoller*[3], *I. Kurkowska-Jastrzębska*[1], *A. Członkowska*[1]
[1]Institute Psychiatry and Neurology, Warsaw, Poland, 2nd Department of Neurology, Warsaw, Poland, [2]Warsaw Medical University, Department of Gastroenterology and Internal Medicine, Warsaw, Poland, [3]Medizinische Universität Innsbruck, Universitatsklinik fur Innere Medizin I, Gastroenterologie, Innsbruck, Innsbruck, Austria

Background: Aceruloplasminemia is an ultra-rare, adult onset, autosomal recessive disease, one of the neurodegeneration with brain iron accumulation (NBIA). It is caused by mutations in the ceruloplasmin gene (*CP*), encoding ceruloplasmin. Ceruloplasmin is a multicopper oxidase with ferroxidase activity that oxidizes ferrous iron which enables its transfer to transferrin. The rarity of the disease (estimate prevalence about 1:2,000,000 in the Japanese population, no data for other populations) renders early diagnosis challenging.
Methods: Case report
Results: We investigated a 51-year-old male suffering from progressive gait difficulties, blurred speech and cognitive impairment for four years. At the age of 39 years diabetes mellitus was diagnosed and treatment with insulin had been started. Neurological examination showed tremor at rest in upper limbs, postural tremor and ataxia in upper and lower limbs and dysarthria. He had abnormal serum tests of copper and iron metabolism–almost undetectable concentration of serum ceruloplasmin and accordingly decreased concentration of serum copper, but normal urinary copper excretion. Serum iron concentration was normal and serum ferritin was increased, transferrin saturation 24%. Eye exam showed no retinal degeneration and no Kayser-Fleischer rings. Brain MRI showed on T2- and T2*-weighted sequences hypointense signal of caudate, globus pallidus, putamen, thalamus, red nucleus and dentate. In abdomen CT density of the liver was increased, suspected accumulation of iron. Diagnosis of aceruloplasminemia was confirmed by genetic testing, which showed homozygosity for the likely pathogenic sequence variant for gene *CP*(rs746219133), mutation, what confirmed the diagnosis of aceruloplasminemia.

Conclusions: Aceruloplasminemia should be suspected in patients with high ferritin, low to normal transferrin saturation and liver iron overload, diabetes mellitus in young adults, or adult-onset neurological dysfunction with brain MRI changes suggesting iron overload. Typical triad of clinical symptoms of aceruloplasminemia includes neurological disorders, diabetes mellitus and retinal degeneration. Retinal degeneration is more common in patients from Japan than in Europeans.

Poster Abstracts
Part of the Poster Guided Tours (GPT) and Poster Exhibition

Basic Neuroscience (excluding Genetics)

P 001 (GPT)
In silico study of Orexin on subthalamic nucleus neuron electrophysiology towards Parkinson's disease

C. Mahapatra[1], *R. Manchanda*[1]
[1]Indian Institute of Technology Bombay, Bio Sciences & Bio Engineering, Mumbai, India

Background: From the pathophysiological viewpoint, Parkinson's disease (PD) can be recognized as a classic disorder of "brain arrhythmias". The subthalamic nucleus (STN) in the basal ganglia plays the most influential role in basal ganglia motor control including PD. It is well known that both single-spike and burst mode firing patterns of STN control the dopamine-deprived conditions such as PD. Therefore, the modulation of relevant ion channels may be crucial therapeutic consideration for PD. We present an in silico platform to describe how Orexin influences the spike patterns in STN neuron electrophysiology.
Methods: Orexin effects are interpreted by the conductance changes in the inward rectifier ion channels. The inward rectifier ion channels are expressed by the conventional Hodgkin-Huxley formalism
Then the Orexin effects are incorporated into a STN electrophysiological model, where a brief square pulse of varied duration and magnitude is applied as an external stimulus current (Istim) to trigger the action potential (AP).
Results: The electrical activities are initiated in the whole-cell model by injecting Istim of varying magnitude (0.1-0.6nA) and duration (1-5ms). Then, we investigated the modulating effects of inward rectifier currents in two folds. First, we increased the inward rectifier channel maximum conductance by 50% of its control value to get the promising effects in the AP. Then, we varied the Orexin doses to observe its' modulating effects on the electrical properties. Higher Orexin dose reduced the resting membrane potential from –60mV to –65mV by inhibiting the activation of inward rectifier channels.
Conclusions: The opening of the inward rectifier channel always elevates the resting membrane potential. It is documented that the Orexin modulates the firing patterns via both NCX and inward-rectifying channels. As the Orexin depolarizes the STN bursting patterns, the pharmacological targeting of this peptide may shed light on the treatment of PD.

P 002
Orthostatic hypotension: a mini-review

A. Ovchynnykova[1], *Y. Trufanov*[1], *N. Svyrydova*[1]
[1]Shupyk National Healthcare University of Ukraine, Neurology, Kyiv, Ukraine

Background: Last data claimed that nearly 25% of neurology patients had age-related orthostatic hypotension (OH) [1].
Residents of nursing homes and patients with persisting autonomic dysfunction are at the highest risk of having OH and its dramatic effects as trauma or even sudden death [2].
Methods: PubMed and Google Scholar resources were used to write the review.
Results: OH is influenced by physiological reflex disruption [1, 3].
Changing position from supine to standing leads to collection of 500-700 ml of vein blood under the heart [1, 4].
It requires a boost in sympathetic effect on vessels and heart to enhance venous return. Therefore, OH is lowering of blood pressure at least 20 and/or 10 mmHg according to systolic and diastolic BP at the third minute of standing. If a heart rate increases by less than 15 beats, it implies neurogenic OH [4].
Symptoms depend on hypoperfused tissue or organ and are divide into cerebral (dizziness, blurred vision, cognitive slowing, syncope), muscular (low backache, coat-hanger ache) and non-specific features (general weakness, fatigue) [3].
Severities of symptoms distinguished by four functional classes of OH [2]. Diagnosis is usually clear after taking patient history and a bedside orthostatic test, but some cases require ambulatory blood pressure monitoring, tilt-table test, plasma noradrenaline level and depend on the cause. EMG, QSART, autoimmune antibodies, chest CT, serum and urine electrophoresis, fat-pad biopsy and genetic testing can be utilised [4].
Posture test should not be routine [1].
Management includes pharmacology and non-pharmacology interventions. First strategy leads to lifestyle changes, and second one is taking medicine such as fludrocortisone, midodrine, droxidopa, atomoxetine, pyridostigmine [1, 2, 4].
Conclusions: OH is wide-spread problem with various probable causes [4] and symptoms need to be further investigated to understand the impact of hypoperfusion on target organs and look for the most effective treatment strategies.

Imaging and Biomarkers

P 006 (GPT)

Preclinical diagnosis of Parkinson's disease: upgraded and new approaches

M. Ugrumov[1]
[1]Institute of Developmental Biology, Russian Academy of Sciences, Laboratory of Neural and Neuroendocrine Regulations, Moscow, Russian Federation

Background: Among the priorities in neurology is the development of preclinical diagnosis of Parkinson's disease (PD), mainly by searching biomarkers in body fluids of patients at the clinical stage. The drawback of this approach is that biomarkers found in patients at the clinical stage should a priori differ from biomarkers at the preclinical stage.
The objectives of this study were:
i. to select among biomarkers found in blood and tears of PD patients, biomarkers that are characteristic of an animal model of PD at the preclinical (presymptomatic) stage;
ii. to develop a provocative test for detection of latent failure of the nigrostriatal system in presymptomatic animals.
Methods: HPLC, ELISA, Western blot, real time PCR were used to assess changes in blood and tears in untreated PD patients at the early clinical stage and in presymptomatic MPTP-treated mice. Moreover, we used α-methyl-p-tyrosine, a reversible inhibitor of dopamine synthesis, to decrease the striatal dopamine level in presymptomatic mice to a threshold level of 30% that should provoke short-term motor disorders.
Results: According to our data, only 17-25% of biomarkers (monoamines, protein neurotoxins, miRNAs, sphingolipids, etc.) found in the blood and tears of PD patients are also characteristic of presymptomatic MPTP-treated mice. We believe that only these biomarkers can be used for PD preclinical diagnosis. Moreover, we developed a provocative test to detect dopaminergic failure in presymptomatic mice with 55% loss of dopamine in the striatum. Indeed, an inhibitor of dopamine synthesis in a preselected dose caused a reversible 30% decrease in striatal dopamine and motor disorders in presymptomatic MPTP-treated mice, but not in the control.
Conclusions: We have upgraded the methodology for the development of preclinical PD diagnosis by comparing biomarkers found in patients and in presymptomatic MPTP-animals, and for the first time developed a provocative test for preclinical PD diagnosis.

P 007 (GPT)

Head-to-head comparison of [^{18}F]-FDOPA PET and [^{123}I]-FP-CIT SPECT for assessing nigrostriatal degeneration in patients with a clinically uncertain parkinsonian syndrome

E. Wallert[1], E. Letort[2], F. van der Zant[3], A. Winogrodzka[4], H. Berendse[5], M. Beudel[6], R. de Bie[6], J. Booij[1], P. Raijmakers[7], E. van de Giessen[8]

[1]Amsterdam UMC, Location AMC, Department of Radiology & Nuclear Medicine, Amsterdam, Netherlands, [2]Northwest Clinics, Location Alkmaar / Spaarne Gasthuis, Location Haarlem, Department of Radiology and Nuclear Medicine, Haarlem, Netherlands, [3]Northwest Clinics, Location Alkmaar, Department of Radiology and Nuclear Medicine, Alkmaar, Netherlands, [4]Northwest Clinics, Location Alkmaar, Department of Neurology, Alkmaar, Netherlands, [5]Amsterdam UMC, Location VUmc, Department of Neurology, Amsterdam, Netherlands, [6]Amsterdam UMC, Location AMC, Department of Neurology, Amsterdam, Netherlands, [7]Amsterdam UMC, Location VUmc, Department of Radiology & Nuclear Medicine, Amsterdam, Netherlands, [8]Amsterdam UMC, Location AMC and VUmc, Department of Radiology & Nuclear Medicine, Amsterdam, Netherlands

Background: Two commonly used imaging techniques to aid in the diagnosis of neurodegenerative parkinsonian syndromes are single-photon emission computed tomography with [^{123}I]-FP-CIT (DAT-SPECT) and positron emission tomography with [^{18}F]-FDOPA (FDOPA-PET). We provide a unique series of parkinsonian patients who received both FDOPA-PET and DAT-SPECT in routine clinical practice and assess potential differences between these techniques.

Methods: We identified 10 patients who visited a neurologist at a movement disorder clinic with clinically uncertain parkinsonian syndrome (CUPS) and received an FDOPA-PET scan. In the patients presented, the diagnosis remained uncertain after the FDOPA-PET scan. Therefore, an additional DAT-SPECT was performed.

Results: There was discrepancy in the results of the FDOPA-PET and DAT-SPECT scans in 7 patients, including 6 patients who were reportedly normal on FDOPA-PET but abnormal on DAT-SPECT (Table 1).

	Age	Disease duration in years	Result FDOPA-PET Report	Result DAT-SPECT Report	Months between scans	Final diagnosis
Patient 1	68	0.75	normal uptake	severely reduced uptake	2	Possible MSA-P
Patient 2	51	3	Slightly reduced uptake	severely reduced uptake	3	PD
Patient 3	66	1	normal uptake	reduced uptake	<1	PD
Patient 4	65	0.75	normal uptake	normal uptake	7	Inconclusive
Patient 5	60	8	normal uptake	reduced uptake	11	Probable MSA-P
Patient 6	70	3	normal uptake	severely reduced uptake	7	PD
Patient 7	77	3.5	normal uptake	reduced uptake	6	PD
Patient 8	69	0.7	normal uptake	normal uptake	3	Inconclusive (passed away)
Patient 9	76	1	asymmetric slightly reduced uptake	reduced uptake	9	PD
Patient 10	67	2	normal uptake	Reduced uptake	15	PD

Table 1. Case overview with clinical and imaging information.

Conclusions: In patients with CUPS, DAT-SPECT may show a more pronounced reduction in striatal uptake than FDOPA-PET. This is in line with limited available data and may indicate compensatory downregulation of the dopamine transporter and/or upregulation of DOPA decarboxylase activity in early disease stages.

P 008
White matter connectivity networks predict early dementia conversion in Parkinson's disease

S.J. Chung[1,2], Y. Kim[3], J.H. Jung[4], H.S. Lee[5], B.S. Ye[2], Y.H. Sohn[2], Y. Jeong[6], P.H. Lee[2]
[1]Yongin Severance Hospital, Department of Neurology, Yongin-si, Korea, Republic of, [2]Yonsei University College of Medicine, Department of Neurology, Seoul, Korea, Republic of, [3]Korea Advanced Institute of Science and Technology, Program of Brain and Cognitive Engineering, Daejeon, Korea, Republic of, [4]Inje University Busan Paik Hospital, Department of Neurology, Busn, Korea, Republic of, [5]Yonsei University College of Medicine, Biostatistics Collaboration Unit, Seoul, Korea, Republic of, [6]Korea Advanced Institute of Science and Technology, Department of Bio and Brain Engineering, Daejeon, Korea, Republic of

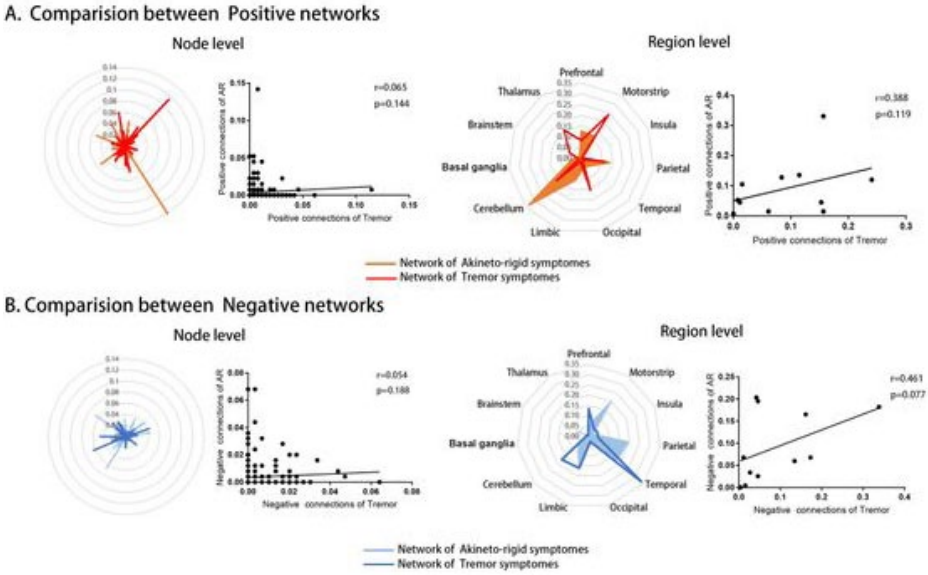
Background: Several clinical and neuroimaging biomarkers have been proposed to identify individuals at high risk for dementia conversion in Parkinson's disease (PD). This study aimed to explore whether white matter (WM) connectivity disruption can predict the dementia conversion in patients with newly diagnosed PD with mild cognitive impairment (PD-MCI).
Methods: Neuroimaging analyses of WM structural connectivity were performed in 75 patients with drug-naïve PD-MCI who underwent serial cognitive assessments during the follow-up period (>5 years). The patients were classified into either the PD with dementia (PDD) high-risk group (PDD-H, n = 38) or low-risk group (PDD-L, n = 37), depending on whether they converted to dementia within 5 years of PD diagnosis. We conducted degree-based statistics (DBS) analyses based on a graph-theoretical concept to identify the subnetworks whose WM connectivity was disrupted in the PDD-H group compared with the PDD-L group. We also performed partial correlation analyses to investigate whether the network connectivity strength was correlated with either the cognitive composite scores or the estimated risk score for PDD conversion within 5 years.
Results: The PDD-H group showed poorer cognitive performance on frontal/executive, visual memory/visuospatial, and attention/working memory/language function than the PDD-L group at baseline assessment, even though there was no difference in parkinsonian motor deficits severity, disease duration, and years of education. The PDD-H group exhibited more severely disrupted WM connectivity in both frontal and posterior cortical regions with eight hub nodes in the DBS analysis. The strength of structural connectivity within the identified subnetworks was correlated with the composite scores of the frontal/executive function domain and the risk score of PDD conversion within 5 years.
Conclusions: The present study demonstrated that disrupted WM connectivity in frontal and posterior cortical regions, which was correlated with frontal/executive dysfunction, could be used as a marker for early dementia conversion in patients with PD-MCI.

P 009 (GPT)

Distinct whole-brain functional connectomics of parkinsonian akinetic-rigid and tremor : a preliminary study in drug-naïve Parkinson's disease

H. Wu[1], *M. Zhang*[1]
[1]The Second Affiliated Hospital, Zhejiang University School of Medicine, Radiology, Hangzhou, China

Background: Parkinson's disease (PD) is characterized by two paradoxically related symptoms: akinetic-rigid (AR) and tremor. Identifying and comparing functional connectomics specific to them can improve understanding of their genesis and provide evidence of their distinct neural basis.
Methods: Rs-fMRI data of 78 drug-naive patients were analyzed using connectome-based predictive modeling (CPM) to identify the association between symptoms and whole-brain connections. Based on the relationship between connection strength and symptom severity, all connections were divided into positive and negative networks and then summarized at the node and region levels.
Correlation analysis was used to compare the node- and region-level contributions between networks and overlap connections were detected. Post-medication data of 30 patients were used to determine whether the identified symptom-connectome correlation remained after medication.



Figures. Comparison of nodes/regions contributions between Akinetic-rigid (AR)- and tremor- positive (A) and negative (B) networks. Each dot presented the contribution of each node or region to the predictive network.

Results: CPM identified AR-related (r=0.28, p=0.018) and tremor-related connectomics (r=0.32, p=0.025). No significant correlation was detected between AR-positive and tremor-positive networks or between AR-negative and tremor-negative networks at either node or region level, and only four overlapped connections were observed between two connectomics, indicating that their connection patterns were pretty different. In the post-medication validation, AR-related connectome remained significant prediction (r=0.605, p<0.001), while tremor-related connectome did not (r=0.017, p=0.366).
Conclusions: The whole-brain functional connectomics specific to AR and tremor were identified within drug-naïve PD patients. Their distinct connection pattern may provided novel evidence for the different underlying neural bases between PD motor symptoms.

P 010
Prediction of Parkinson's disease with dual-phase [18F] FP-CIT PET image through deep learning algorithm

S.-M. Cheon[1], *Y.J. Jeong*[2], *D.-Y. Kang*[2]
[1]Dong-A University College of Medicine, Neurology, Busan, Korea, Republic of, [2]Dong-A University College of Medicine, Nuclear Medicine, Busan, Korea, Republic of

Background: Parkinson's disease (PD) is known to be difficult to make an accurate diagnosis in the early stage of the disease. The purpose of this study is to differentiate PD from other degenerative parkinsonism with dual-phase [18F] FP-CIT image through deep learning (DL) algorithms.
Methods: The study retrospectively analyzed [18F] FP-CIT image of 231 patients and 139 control. Clinical diagnosis of patients were PD (115), DLB (14), PSP (34), MSA-C (44) and MSA-P (24). Dual-phase [18F] FP-CIT image was analyzed through three models of DL, long short-term memory (LSTM) model, neural network (NN) model, and combined model (LSTM+NN).
Results: Accuracy of LSTM model was 80.1%, 62.1% with NN model, and 90.1% with combined model. Overall, the accuracy of the early-phase FP-CIT PET image was 80.0%, 62.0% with delayed-phase FP-CIT PET image, and 91.0% with the dual-phase FP-CIT PET image.
Conclusions: The results of this study suggest that combined model using dual-phase FP-CIT could provide more accurate PD prediction than other DL models using delayed-phase FP-CIT image alone.

P 011
Association between plasma cytokines and motor, non-motor symptoms in Parkinson's disease

K. Abdurakhmonova[1], *G. Rakhimbaeva*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: Inflammatory response in Parkinson's disease(PD) is still to be understood. The majority of PD patients experience motor and non-motor symptoms(NMS)during this disease. Purpose of this study is to determine correlation between plasma cytokines and motor and NMS in PD patients.
Methods: 48 PD patients with NMS were enrolled in this study. Unified Parkinson's Disease Rating Scale (UPDRS) and the modified Hoehn & Yahr (H&Y) scale were used to score disease progression and stage, respectively. Montreal Cognitive Assessment (MoCA) was used to assess cognitive impairment (CI). Anxiety and dementia were assessed by using the Hospital Anxiety and Depression Scale (HADS). Cytokine levels such as IL-6 and IL-17 were measured in all patients.
Results: IL-6 correlated with H&Y and UPDRS score positively in PD patients ($p < 0.05$, $r = 0.29$ and 0.36 respectively. IL-17A was correlated with the HADS scale ($p < 0.05$, $r = 0.39$) and negatively correlated with MoCA score ($p < 0.05$, $r = 0.38$). According to the gender specific correlations, in male patients, IL-6 levels positively correlated with H&Y and UPDRSIII ($p < 0.05$, $r = 0.4$ and 0.44 respectively), but negatively correlated with MoCA score ($p < 0.05$, rho = –0.39). In female patients IL-17A levels positively correlated with H&Y as well as with HADS ($p < 0.05$, $r = 0.49$ and 0.76 respectively.
Conclusions: In conclusion, we can say that, that the pro-inflammatory cytokine IL-6 positively correlates with motor scores while IL-17A correlates with NMS, specifically mood and cognition scores. Moreover, it may be important to investigate sex specific alterations in peripheral cytokines in PD patients.

P 012 (GPT)
Understanding correlation between diffusion MRI-derived white-matter organization and clinical measures in Parkinson's disease patients with freezing of gait

V. Mishra[1], *K. Sreenivasan*[1], *J. Longhurst*[2], *A. Ritter*[1], *Z. Mari*[1]
[1]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States, [2]Saint Louis University, St Louis, United States

Background: The pathophysiology of freezing of gait (FoG) in Parkinson's disease (PD) is incompletely understood. We hypothesized that a differential correlation between the white matter (WM) organizational change as measured using diffusion MRI (dMRI) and the clinical measures will exist between PD-FoG+ and PD-FoG- patients.
Methods: Thirty-eight PD patients were recruited at our center. Each participant underwent a comprehensive clinical examination including Unified Parkinson's Disease Rating Scale score, disease duration, FoG questionnaire, and Levodopa Equivalent Dose in a clinically defined OFF state. PD patients were

classified as FoG+ based on observation of FoG during physical therapy evaluation by a trained physical therapist (JL) and were verified by the neurologists (AR and ZM) via a video review. 17 PD-FoG+ and 21 PD-FoG- patients were identified in our cohort. We collected high spatial (1.5mm^3) and high angular (71 unique directions) resolution dMRI each at three shells (b=500s/mm^2, b=1000s/mm^2, and b=2500s/mm^2) using HCP sequence on a 3T Siemens Skyra. Both conventional single tensor diffusion tensor (DTI) metrics and advanced dMRI metrics such as free-water (FW)-corrected DTI metrics, diffusion kurtosis (DKI) measures, and neurite orientation dispersion and density (NODDI) measures, were estimated in each voxel. Correlation between the clinical measures and various dMRI-derived voxelwise measures at the center of the WM tracts was conducted using non-parametric statistics and significance was established at family-wise error correction of $p_{corr}<0.05$.

Results: Regardless of the fitting technique utilized, left lateralization was observed when the correlation between clinical variables and dMRI-derived measures was found to be significantly different.

Conclusions: Analysis of our dataset confirms our hypothesis of a differential correlation between PD-FoG status and clinical variables with remarkable left lateralization of axonal damage in PD-FoG+ patients. Furthermore, irrespective of the FoG status, our data suggest widespread Wallerian degeneration in PD patients across corpus-callosum.

P 013
Understanding correlation between diffusion MRI-derived white-matter organization and neuropsychological measures in Parkinson's disease patients with freezing of gait

V. Mishra[1], *K. Sreenivasan*[1], *J. Longhurst*[2], *J. Caldwell*[1], *A. Ritter*[1], *Z. Mari*[1]
[1]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States, [2]Saint Louis University, St Louis, United States

Background: The pathophysiology of freezing of gait (FoG) in Parkinson's disease (PD) is incompletely understood. We hypothesized that a differential correlation between the white matter (WM) organizational change as measured using diffusion MRI (dMRI) and the neuropsychological measures will exist between PD-FoG+ and PD-FoG- patients.

Methods: Thirty-eight PD patients and 17 healthy controls (HC) were recruited at our center. Each participant underwent a comprehensive neuropsychological examination evaluating various domains in a clinically defined OFF state for all PD patients. PD patients were classified as FoG+ based on observation of FoG during physical therapy evaluation by a trained physical therapist (JL) and were verified by the neurologists (AR and ZM) via a video review. 17 PD-FoG+ and 21 PD-FoG- patients were identified in our cohort. We collected high spatial (1.5mm^3) and high angular (71 unique directions) resolution dMRI each at three shells (b=500s/mm^2, b=1000s/mm^2, and b=2500s/mm^2) using HCP sequence on a 3T Siemens Skyra. Both conventional single tensor diffusion tensor (DTI) metrics and advanced dMRI metrics such as free-water (FW)-corrected DTI metrics, diffusion kurtosis (DKI) measures, and neurite orientation dispersion and density (NODDI) measures, were estimated in each voxel.

Correlation between the neuropsychological measures and various dMRI-derived voxelwise measures at the center of the WM tracts was conducted using non-parametric statistics and significance was established at familywise error correction of $p_{corr}<0.05$.

Results: Only DKI and NODDI measures showed a significant correlation between dMRI-derived measures and neuropsychological scores evaluating verbal learning and visuospatial memory.

Conclusions: Analysis of our dataset confirms our hypothesis of a differential correlation between PD-FoG status and neuropsychological variables, although the findings were subtle. Analysis with a larger sample size is warranted to confirm the findings.

P 014 (GPT)
Effects of levodopa on functional connectivity in Parkinson's disease patients with Mild Cognitive Impairment

K. Sreenivasan[1], *X. Zhuang*[1], *A. Ritter*[1], *J. Caldwell*[1], *D. Cordes*[1], *Z. Mari*[1], *V. Mishra*[1]
[1]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States

Background: Several studies have identified altered functional connectivity involving several cortical-subcortical regions in Parkinson's disease patients with mild cognitive impairment (PD-MCI)[1,2]. However, the effects of levodopa which is the most used medication for PD[3] on functional connectivity is still unclear. We aim to investigate the effect of levodopa on functional connectivity in PD-MCI and PD without MCI (PD-NC).

Methods: Preliminary analyses were performed using 23 PD-MCI and 15 PD-NC patients from the Center for Neurodegeneration and Translational Neuroscience. All participants underwent resting-state functional magnetic resonance imaging using a 3T scanner during the levodopa OFF and ON states. After standard pre-processing connectivity matrices were obtained for each subject. Nonparametric statistical tests[4] were used to identify the differences between the groups (PD-MCI vs PD-NC (OFF and ON states); PD-NC and PD-MCI (OFF vs ON)).

Results: (a) OFF versus ON: The PD-MCI group showed significantly higher connectivity involving mainly the frontal regions in the OFF state. The PD-NC group also showed significantly higher connectivity in the OFF state but mainly involved the occipital regions.

(b) OFF state: Compared to PD-NC, the PD-MCI showed greater strength in 3 connections involving temporal regions and reduced strength in 3 connections involving mainly frontal and parietal regions.

(c) ON: The majority of the connections mainly involving frontal and temporal regions showed increased connectivity in PD-MCI when compared to the PD-NC group. The functional connectivity between the different cortical regions was reduced in both PD-MCI and PD-NC with levodopa, but to a greater degree in the PD-NC.

Conclusions: We observed hyperconnectivity in the OFF state in both PD groups and this was mitigated by levodopa therapy. However, the levodopa therapy had more effect in PD-NC compared to the PD-MCI. Therefore, our findings suggest that levodopa affects functional connectivity to a lesser extent in the PD-MCI group.

P 015
Tissue biomarker for the detection of dementia with Levi bodies

D. Azizova[1]
[1]Tashkent Medical Academy, Medical Biochemestry, Tashkent, Uzbekistan

Background: Scientists from the Banner Sun Health research institute (Sun City, Arizona, USA) studied 228 histological preparations obtained by postmortem examination, including samples with diseases of Levi bodies: 46 with Parkinson's disease, 28 with dementia with Levi bodies, 9 with concomitant disease of Levi bodies, 33 with Alzheimer's disease with Levi bodies and two with progressive supranuclear palsy with Levi bodies.
The drugs of the control group, defined as people without synucleopathy associated with Levy's disease of the body affecting the central nervous system, included 79 samples from healthy elderly people, 15 from people with Alzheimer's disease, 12 from people with progressive supranuclear palsy, 2 from individuals with corticobasal degeneration and 2 from individuals with multiple systemic atrophy.
Methods: Tissue sections of the submandibular gland of exposed people were stained with an immunohistochemical method to detect serine phosphorylated α-synuclein 129.
Results: Researchers found a submandibular alpha-synuclein pathology in 42/47 (89%) of exposed patients with Parkinson's disease and in 20/28 (71%) opened patients with dementia with Levy bodies, but not one of 110 representatives of the control group.
The authors concluded that the findings could help with further clinical studies of a diagnostic biopsy of the submandibular gland in vivo to detect Parkinson's disease and dementia with Levi bodies.
Accurate diagnosis using a peripheral biopsy will help select patients for clinical trials and can be used to check other biomarkers.
Conclusions: Low diagnostic accuracy made it difficult to conduct effective clinical trials involving living people in the search for new drugs. With better diagnostic accuracy, clinical trials would have a higher chance of success and could be completed faster and have lower cost. In the next step, biopsy of the submandibular gland will be necessary for living people with dementia with Levi bodies to confirm the autopsy results.

P 016 (GPT)
Gray matter abnormalities in myotonic dystrophy type 1: a voxel-wise meta-analysis

Q. Jiang[1], *J. Lin*[1], *C. Li*[1], *Y. Hou*[1], *H. Shang*[1]
[1]West China Hospital, Sichuan University, Neurology, Chengdu, China

Background: A growing number of voxel-based morphometry (VBM) studies have demonstrated widespread gray matter (GM) abnormalities in myotonic dystrophy type 1 (DM1), but the findings are heterogeneous. This study integrated previous VBM studies to identify consistent GM changes in the brains of patients with DM1.

Methods: Systematic retrieval was conducted in Web of Science, Pubmed, and Emabase databases to identify VBM studies that met the inclusion requirements. Data was extracted. The Seed-based d Mapping with Permutation of Subject Images (SDM-PSI) software was used for meta-analysis of voxel aspects.
Results: A total of 8 VBM studies were included, including 176 patients with DM1 and 198 healthy controls (HCs). GM volume in patients with DM1 was extensively reduced compared with HCs, including bilateral rolandic operculum, bilateral posterior central gyrus, bilateral precentral gyrus, right insula, right heschl gyrus, right superior temporal gyrus, bilateral supplementary motor area, bilateral middle cingulate gyrus/paracingulate gyrus, left paracentral lobule, and bilateral caudate nucleus. Meta-regression analysis found that regional GM abnormalities were associated with disease duration and ROCF-recall scores.
Conclusions: DM1 is not only a disease of muscle injury, but also a multi-system disease involving brain motor and neuropsychiatric regions, providing a basis for the pathophysiological mechanism of DM1.

P 017
Alterations in the HSP70 system in PBMC accompanying Parkinson's disease

J. Vavilova[1], *A. Boyko*[1], *E. Kovalenko*[1], *A. Sapozhnikov*[1]
[1]Shemyakin Ovchinnikov Institute Of Bioorganic Chemistry, Moscow, Russian Federation

Background: PD is attributed to selective loss of dopaminergic neurons as a result of α-synuclein accumulation, which leads to the disruption in the substantia nigra pars compact. It is known that α-synuclein aggregates accumulate in the neurons due to disruption of cellular proteostasis in PD. In considered proteostasis system include heat shock proteins of the 70 kDa family (HSP70).
We focused on studying this system in peripheral blood mononuclear cells (PBMC) in PD.
Methods: 26 patients with Parkinson's disease (PD) and 36 age-matched healthy donors (HD) were recruited for the study. Intracellular levels of HSP70 were determined in intact PBMC (HSP70basal) and exposed to heat shock (water bath at 43°C for 10 min) (HSP70heat) by indirect immunofluorescent staining followed by flow cytometry analysis using BRM-22 antibody recognizing a conservative epitope for constitutive Hsc70 and inducible Hsp70. Then, we analyzed the basal transcriptional activity of *HSPA1A* and *HSPA6* encoding stress-inducible proteins Hsp70 and Hsp70B', respectively by real-time PCR.
Results: There were no significant differences in the HSP70basal and HSP70heat levels between PD and HDs. Correlation analyses were revealed the increase in HSP70basal level in PBMC was parallel to the increase in HSP70heat level in both PD and HDs. Thus, it can be concluded the disruption of the release of HSP70 from complexes with proteins by short-term heat shock does has not been detected in PBMC in PD. A significant increase of the basal transcriptional activity *HSPA6* gene in PBMC in PD vs HDs was demonstrated. Interestingly, there was a strong correlation between the basal transcriptional activity of *HSPA1A* and *HSPA6* genes in PBMCs of both PD and HDs. Thus, we observe a simultaneous and possibly dependent increase in the main stress-induced genes as *HSPA1A* as *HSPA6* in PBMC in PD.
Conclusions: These findings could be used as a diagnostic marker for PD.

P 018

Cholinergic brain network deficits associated with vestibular sensory conflict deficits in Parkinson's disease: correlation with postural and gait deficits

N. Bohnen[1], *P. Kanel*[1], *P. Scott*[1], *R. Koeppe*[1], *M. van Emde Boas*[1], *R. Albin*[1], *K. Kerber*[1], *M. Muller*[1]
[1]University of Michigan, Neurology & Radiology, Ann Arbor, United States

Background: To examine regional cerebral vesicular acetylcholine transporter (VAChT) ligand [F] fluoroethoxybenzovesamicol ([F]-FEOBV) PET binding in Parkinson's disease (PD) patients with and without vestibular sensory conflict deficit (VSCD). To examine associations between VSCD associated cholinergic brain deficits and postural instability and gait difficulties (PIGD).
Methods: PD persons (n=92; M70/F22; mean age 67.6 7.4 years) completed clinical assessments for imbalance, falls, freezing of gait (FoG), modified Romberg sensory conflict test and underwent VAChT PET. Volumes-ofinterest (VOI)-based analyses included detailed thalamic and cerebellar parcellations. VSC-Dassociated VAChT deficit VOI selection used stepwise logistic regression analysis. Vesicular monoamine transporter type 2 (VMAT2) [C] dihydrotetrabenazine (DTBZ) PET imaging was available in 54 patients. Analyses of covariance were performed to compare VSCD-associated cholinergic deficits between patients with and without PIGD motor features while accounting for confounders.
Results: PET sampling passed acceptance criteria in 73 patients. This data-driven analysis identified cholinergic deficits in five brain VOIs associating with the presence of VSCD: Medial geniculate nucleus (MGN) ($P<0.0001$), parahippocampal gyrus ($P=0.0043$), inferior nucleus of the pulvinar ($P=0.047$), fusiform gyrus ($P=0.035$) and the amygdala ($P=0.019$).
Composite VSCD-associated [F] FEOBV binding deficits in these 5 regions was significantly lower in patients with imbalance (-8.3%, $F=6.5$, $P=0.015$; total model: $F=5.1$, $P=0.0008$), falls (-6.9%, $F=4.9$, $P=0.03$; total model $F=4.7$, $P=0.0015$), and FoG (-14.2%, $F=9.0$, $P=0.0043$; total model $F=5.8$, $P=0.0003$), independent of age, duration of disease, gender and nigrostriatal dopaminergic losses. Post-hoc analysis using MGN VAChT binding as the single cholinergic VOI demonstrated similar significant associations with imbalance, falls and FoG.
Conclusions: Vestibular sensory conflict deficit-associated cholinergic network changes localize to distinct structures involved in multi-sensory, in particular vestibular, and multimodal cognitive and motor integration brain regions. Relative clinical effects of VSCD cholinergic network deficits were largest for FoG followed by postural imbalance and falls. The cholinergic medial geniculate body was the most significant predictor region.

P 019

The feasibility of using loss of "swallow tail sign" on 3T – susceptibility weighted MRI in diagnosis of Parkinson's disease

U.N.L. Ha[1], *T.V. Nguyen*[1], *K.N.C. Vo*[1], *T.T.H. Dang*[1], *T.N. Tran*[1]

[1]University Medical Center, University of Medicine and Pharmacy Ho Chi Minh City, Ho Chi Minh, Vietnam

Background: Parkinson's disease (PD) is the second most common neurological disorder and the most prominent movement disorders. However, it is sometimes challenging to distinguish between PD and other conditions, especially in the beginning stage of the disease. Loss of "swallow tail sign" (STS) which is the healthy appearance of nigrosome-1 on iron-sensitive magnetic resonance imaging (MRI) has been recognized at a helpful marker in the diagnosis of PD

Methods: This is a prospective cross sectional study. We recruited two groups of patients with and without PD. Those without PD who came to the hospital because of other conditions were examined by a neurologist specializing in movement disorders to make sure that they did not have Parkinsonism.

Both groups of participants underwent a routine high resolution 3T – susceptibility weighted (SWI) MRI. Two trained neuroradiologist blind- rated and independently classified the MRI images into PD and non-PD based on the presence or absence of swallow-tail sign then reached a consensus on final results. The reliability of using high resolution 3T – SWI MRI as a diagnostic tool of PD was determined by the absolute inter-rater agreement (Cohen's kappa coefficient).

The validity was assessed by the sensitivity and specificity of the MRI results in comparison with clinical diagnostic as the gold standard.

Results: 52 PD and 35 non-PD subjects have joined our study. The mean ages of two groups of participants were 51.63 for PD and 49.43 for non-PD. The reliability of the nigrosome-1 detection using 3T – SWI MRI was at a substantial level with kappa value = 0.739. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy resulted 94.34%, 91.67%, 94.55%, 91.89% and 94.38% respectively.

Conclusions: Assessing the substantia nigra on high resolution 3T – SWI MRI for the typical "swallow – tail" appearance is a promising neuroimaging marker for the diagnosis of PD

P 020

Features of MRI signs in patients with Parkinson's disease

A. Ismatov[1], *D. Tolibov*[1], *G. Rakhimbaeva*[1]
[1]Tashkent Medical Academy, Neurology, Tashkent, Uzbekistan

Background: Parkinson's disease (PD) involves widespread damage to various areas of the cerebral cortex. We aimed to establish using MRI the presence of differences in the thickness of the cortical layer in patients with early and advanced stages of PD.
Methods: We examined 22 patients with PD, with stages 2 (group 1) and 3 (group 2) according to the Hoehn-Yar functional scale, of which 12 patients had an akinetic-rigid form of the disease (54,5%), the rest patients had a mixed form of PD (45.5%). The examination protocol consisted of a clinical assessment of the condition of patients with the determination of the stage of the disease, as well as an MRI study on a magnetic resonance tomography.
Results: Complications of the course of the disease in the 2nd stage of PD were represented by moderate cognitive deficit, increased daytime sleepiness, and depressive disorders. In the 3rd stage of the disease, cognitive impairments ranged from moderate to dementia, there was also a significant increase in the severity of daytime sleepiness and night sleep disturbances, and deepening of depression. In patients with PD, we found significant differences in the thickness of the cortex in both the left and right hemispheres of the brain. One of the most interesting results obtained is degeneration in the visual cortex. Pathology of the posterior dorsal cingulate gyrus (group 1-2.758; group 2-2.624; p= 0.017) affects the performance of operations with episodic memory and the ability to understand and realize the opinions of other people. There is a decrease in the thickness of the cortical layer (group 1-2.21; group 2-2.11; p= 0.044), which negatively affects cognitive and mental disorders that develop in patients with PD. Changes in the fusiform gyrus (Group 1-1.83; Group 2-1.75; p=0.042) has a negative impact primarily on the state of cognitive functions of patients and is one of the mechanisms for the development of hallucinations. Despite the fact that there were no significant differences in the thickness of the cortex among the structures of the parietal lobe, graphic post-processing visualizes very bright differences between patients with the 2nd and 3rd stages of the disease.
Conclusions: The data obtained make it possible to establish a connection between non-motor manifestations of PD and degeneration of certain cortical areas of the brain. In this regard, it is necessary to further develop and improve high-tech methods that will contribute to clarifying the issues of pathogenesis and predicting the course of PD.

P 021

Correlation specificity of neuroimaging changes with clinic syndromes in Parkinson's disease, vascular parkinsonism and chronic cerebral ischemia

S.-J. Khamdamov[1], *D. Akramova*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: Although the problem of Parkinson's disease has attracted the attention of researchers for many years, thousands of innovations about the clinic, treatment methods, and principles of differential approach have been discovered, today the pathogenesis of disease development, differential diagnosis and treatment of complications, and disease prevention are still lame not only from a scientific, but also from a practical point of view.

Methods: Based on this study, the results of a comprehensive clinical examination of 117 patients were analyzed. Research work was carried out on the basis of the Tashkent medical academy clinic in 2019-2022. To assess the characteristics of vascular disorders in Parkinson's disease 47 patients with Parkinson's disease, 40 patients with vascular Parkinsonism and the third group of 30 patients with chronic cerebral ischemia.

Results: The factors for Parkinson's disease and vascular Parkinsonism, the onset of the disease, the clinical course, and the degree of autonomic, psycho-emotional and cognitive impairment all differ dramatically from each other. The main factor for VP development was hypertonia 86.5% ($p<0.05$), CCI 72.5% ($p< 0.05$), diabetes mellitus 40% ($p<0.05$), strokes 55.5% ($p<0.05$) and their combination, factors were seen in 82.3% of cases ($p<0.05$); On neuroimaging examination, moderate periventricular edema was recorded in 49.7 ± 2.4% ($p<0.05$) in PD, 62.4 ± 2.3% in VP ($p<0.05$), and 55.7 ± 3 .4% ($p<0.05$) with CCI.

Also, subcortical leukoaraiosis separately and with small leukoaraiosis with multihyperintensity in different localizations in T2 mode in 51.4% ($p<0.05$) in PD, 74.8% ($p<0.01$) in VP, 49.3% of CCI. Ischemic changes in the subcortical nuclei were observed in 49.2% ($p<0.05$) in the first group, 76.2% ($p<0.01$) in the second group and 38.9% in the third group.

The results of MRI analysis showed a correlation between the correlation between periventricular edema and growth and posture disorder r =-0.31, correlation between impaired coordination r = 0.71, memory impairment r = 0.31 and association with emotional labilit r -0.31. The process of long-term cerebral vascular disorders in vascular parkinsonism changes the morphological structure of the brain tissue. In particular, vascular changes are clinically significant in terms of their effect on the pathophysiological form of vascular parkinsonism, the appearance of neuroimaging and the clinical form of the disease.

Conclusions: These correlations were based on the origin of memory impairment and emotional instability due to the association of the limbic region of the brain, in particular the Cingularis gyrus, with an increase in the ventricular system of the brain.

P 022

The distinctive functional connectivity of the cholinergic nucleus basalis of Meynert in Parkinson's disease across different cognitive status

M. Nazmuddin[1,2], *T. van Laar*[2], *P. Zeidman*[3]

[1]Dr. Soetomo Teaching Hospital, Faculty of Medicine Airlangga University, Neurology, Surabaya, Indonesia, [2]University Medical Centre Groningen, University of Groningen, Neurology, Groningen, Netherlands, [3]Wellcome Centre for Human Neuroimaging, London, United Kingdom

Background: Current longitudinal structural MRI and cross-sectional cholinergic-based PET studies on early-stage PD subjects revealed that the degeneration of the cortically-projecting cholinergic nucleus, the nucleus basalis of Meynert (NBM), is a crucial contributing factor to cognitive sequelae in Parkinson's disease (PD).

In this study, we aimed to investigate the difference in the NBM functional connectivity between cognitively-normal PD (CN-PD) and cognitively-impaired (CI-PD).

Methods: We analyzed the resting-state functional MRI (rs-fMRI) data of healthy control (HC) and PD subjects obtained from the Parkinson's Progression Markers Initiative (PPMI) database. PD subjects were dichotomized into CN-PD and CI-PD based on their cognitive status at the time of image acquisition. Seed-based analysis with the NBM as the region-of-interest was conducted.

Results: Twenty HC, 63 CN-PD, and 18 CI-PD with at least one rs-fMRI data and complete cognitive status data were included in the study. We are currently working on the seed-based analyses of the rs-fMRI data to find any distinctive pattern between CN-PD and CI-PD relative to HC.

Conclusions: We hypothesize that the NBM functional connectivity pattern to several cortical areas will be different between CN-PD and CI-PD.

This study will provide further evidence on the significant role of the NBM pathology in PD from the functional imaging perspective in addition to the results of previous structural imaging studies.

Neurosurgery (including Deep Brain Stimulation)

P 024 (GPT)

Reprogramming frequency in clinical practice: 6-months post-implantation of DBS for Parkinson's disease subjects in ADROIT

S. Groppa[1], A. Schnitzler[2], Y. Bezchlibnyk[3], J. Pilitsis[4], C. Giordana[5], L. Verhagen[6], M. Frassica[7], B. Cheeran[8], S.-Y. Chen[9]

[1]Johannes Gutenberg Universität Mainz, Mainz, Germany, [2]Medizinische Einrichtungen der Universität Düsseldorf, Düsseldorf, Germany, [3]University of South Florida, Neurology, Tampa, United States, [4]Albany Medical Center, Albany, United States, [5]CHU Hopital Pasteur, Nice, France, [6]Rush University Medical Center, Chicago, United States, [7]Abbott, Plano, United States, [8]Abbott, Austin, United States, [9]Hualien Tzu Chi Hospital, Hualien, Taiwan, Province of China

Background: After initial programming of a newly implanted DBS system, patients typically require additional titration visits to approach the optimal settings for treating their Parkinson's disease symptoms. Depending upon a host of factors, the true frequency of those visits can vary considerably, which may impact when this optimal outcome is reached for the patient. The frequency at which these visits occur in current clinical practice is of interest to further patient care.

Methods: ADROIT is a large, international, prospective, multicenter, post-market, observational study at up to 50 centers worldwide that collects long-term safety and effectiveness data on Abbott DBS systems in the real-world setting. Programming frequency within the first 6-months of DBS will be visualized by geography and demographics for Parkinson's disease subjects in ADROIT.

Results: As of December 2021, 184 Parkinson's Disease subjects in ADROIT enrolled for newly implanted DBS systems and completed baseline assessments. Of those subjects, 79 at 21 sites (11 U.S., 8 Europe, 2 Asia-Pacific) have received new DBS Systems with leads in the subthalamic nucleus (STN) or globus pallidus internus (GPi) and completed 6-month visits. The STN was the chosen target for 71 subjects, and the GPi for 8 subjects. Initial analysis of reprogrammings after initial programming out to the 6-month visit show Asia-Pacific sites have 3.9 ± 2.1 (N=12) visits, European sites 3.3 ± 3.3 visits (N=39) and U.S. sites 2.8 ± 2.0 visits (N=28).

Conclusions: DBS technology is advancing beyond hardware improvements toward enhancing patient access and convenience. Programming frequency and its impact upon patient outcomes is of interest to the community, and clinical evidence from real-world cases can help inform the improvement of patient care. This interim report of the ADROIT study will investigate the variability in programming visits in the first 6 months of newly implanted and programmed DBS.

P 025
Deep brain stimulation of posterior subthalamic area for Holmes Tremor

H. Kamo[1], G. Oyama[1,2], M. Ito[3], H. Iwamuro[4,2], A. Umemura[4,2], N. Hattori[1,2]
[1]Juntendo University School of Medicine, Neurology, Tokyo, Japan, [2]Juntendo University Graduate School of Medicine, Research and Therapeutics for Movement Disorders Juntendo University Graduate School of Medicine, Tokyo, Japan, [3]Juntendo University School of Medicine, Psychiatry, Tokyo, Japan, [4]Juntendo University School of Medicine, Neurosurgery, Tokyo, Japan

Background: Holmes tremor (HT) is a refractory tremor related to abnormality of the cortico-basal ganglia loop and cerebellothalamic tract. Various drug treatments have been tried, but there is no established treatment method. In medically refractory cases, Thalamic deep brain stimulation (DBS) has been historically performed. Recently, the posterior subthalmic area (PSA) has been also applied for HT. We present two cases of PSA-DBS for HT.
Methods: We conducted a retrospective chart review of two patients with HT and underwent PSA-DBS. The patients who were diagnosed as HT subsequent to brain hemorrhage were performed DBS in PSA because of refractory to medical therapy.
Results: The Fahn-Tolosa-Marin Tremor Rating Scale immediately improved 1 month after the operation without obvious complications in both patients (64.3% and 21.9% respectively).
Conclusions: Good improvement in HT was obtained with PSA-DBS in our patients. It has not been concluded where the most appropriate target for improving HT symptoms is, including thalamus and PSA. Long-term observation and accumulation of the cases as well as randomized studies are needed.

P 026 (GPT)
Identification of suboptimal response to STN-DBS in Parkinson's disease

I. Rektor[1], M. Bočková[2], E. Výtvarová[3], M. Lamoš[4], P. Klimeš[5], P. Jurák[5], S. Goldemundová[2], M. Baláž[6]
[1]Masaryk University, CEITEC and Movements Disorders Centre, Hosp. St. Anne, Brno, Czech Republic, [2]Masaryk University, CEITEC and 1st Dept. of Neurology, St. Anne Hosp., Brno, Czech Republic, [3]Masaryk University, Faculty of Informatics, Brno, Czech Republic, [4]Masaryk University, CEITEC, Brno, Czech Republic, [5]Czech Academy of Sciences, Institute of Scientific Instruments, Brno, Czech Republic, [6]Masaryk University, CEITEC and Movements Disordesr Centre, Hosp. St. Anne, Brno, Czech Republic

Background: Although deep brain stimulation of the subthalamic nucleus (STN-DBS) in Parkinson's disease (PD) is generally a successful therapy, insufficient clinical effect can complicate the treatment in some patients. The degree of response to STN-DBS is individual and hardly predictable.
Methods: We studied clinical parameters and cortical oscillations related to STN-DBS to identify patients with suboptimal responses. High-density EEG was recorded during a visual oddball three-stimuli paradigm in DBS "off" and "on" conditions in 32 PD patients with STN-DBS. Pre-processed data were reconstructed into the source space, the time–frequency and network analysis based on graph theory were evaluated. Data were correlated to the behavioral and motor parameters.

Results: We identified a subgroup of six patients with longer reaction times (RT) during the DBS "on" state than in the DBS "off" state after target stimuli. These subjects had lower UPDRS score improvement after DBS and worse performance in memory tests compared to the other subjects (n=26). The alpha and beta power decrease (event-related desynchronizations, ERD) was reduced in the DBS "on" condition in these patients. In the majority of patients (n = 26), STN-DBS did not lead to changes in global network organization in large-scale brain networks.
In the suboptimal responders, global connectivity in the 1–8 Hz frequency range and regional node strength in frontal areas were detected. The important role of the supplementary motor area for the optimal DBS response was demonstrated by the increased node strength and eigenvector centrality in good responders. This response was missing in the suboptimal responders.
Conclusions: A subgroup of PD patients with a suboptimal response to STN-DBS was identified. Evaluation of RT could serve as a biomarker for responsiveness to STN-DBS. Cortical topologic architecture is modified by the response to STN-DBS leading to a dysfunction of the large-scale networks in suboptimal responders.

P 027
Necessity and feasibility of remote tele-programming of deep brain stimulation systems in Parkinson's disease

C. Esper[1], A. Merola[2], L. Himes[3], N. Patel[4], Y. Bezchlibnyk[5], D. Falconer[6], D. Weiss[7], C. Luca[8], B. Cheeran[3], Z. Mari[9]
[1]Emory University School of Medicine, Department of Neurology, Atlanta, United States, [2]The Ohio State University Wexner Medical Center, Department of Neurology, Columbus, United States, [3]Abbott Neuromodulation, Austin, United States, [4]Rush University Medical Center, Department of Neurological Sciences, Chicago, United States, [5]University of South Florida Morsani School of Medicine, Department of Neurosurgery and Brain Repair, Tampa, United States, [6]Inova Parkinson's and Movement Disorders Center, Alexandria, United States, [7]Centre for Neurology, Department for Neurodegenerative Disease, and Hertie Institute for Clinical Brain Research, Tübingen, Germany, [8]University of Miami Miller School of Medicine, Miami, United States, [9]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States

Background: Deep brain stimulation (DBS) outcomes for patients with Parkinson's disease (PD) depend on stimulation parameters optimized over multiple programming sessions, requiring frequent travel to a DBS center, which presents challenges for those with limited access. Management of DBS through telemedicine in the USA and Europe was limited until recent FDA approval of a remote tele-programming solution where clinicians can provide synchronous audio-visual telemedicine and remotely program DBS systems. The Parkinson's Foundation hosted a collaborative survey with Abbott Labs to (1) assess the availability and accessibility to DBS specialists and (2) assess the usability of the telehealth interface [NeuroSphere™ Virtual Clinic] for synchronous tele-programming of DBS.
Methods: Two validated survey instruments were used to assess telemedicine need and usability of the telehealth interface for DBS programming among PD patients: The Effective Accessibility and Accommodation survey (EAA) and the Telehealth Usability Questionnaire (TUQ).

Results: Results from the EAA (n=47) revealed that over a third of patients reported not being able to easily get to a clinic for various reasons such as distance to a clinic. Over a quarter reported it would be difficult to contact their clinic for advice. Disease duration was associated with difficulty accessing care ($r = .30$, $p = 0.04$).
Results from the TUQ (n=41) revealed overall satisfaction with the Virtual Clinic DBS remote programming telehealth interface and care provided. Most respondents reported that remote tele-programming visits are similar in quality to in-person visits.
Conclusions: This study provides support for the use of telehealth and tele-programming for DBS management in PD. DBS is an underutilized procedure, despite its proven efficacy, and disparities in access to care are significant. The ability to use remote technologies may increase access to DBS and mitigate the disparities that currently prevent access to care.

P 028
Hemorrhagic risk in patients who undergo deep brain stimulation on chronic antiplatelet or anticoagulation therapy

L. Jackson[1], *K. Lee*[1], *K. Miller*[1], *B. Klassen*[1], *A. Hassan*[1]
[1]Mayo Clinic, Rochester, United States

Background: Deep brain stimulation (DBS) is the main surgical treatment for medically refractory movement disorders. Many patients are older with medical comorbidities necessitating antiplatelet or anticoagulation use. There is limited data on intracranial bleeding or thromboembolic complications surrounding use of chronic antiplatelet or anticoagulation treatment for patients who undergo DBS surgery.
Methods: All patients who underwent DBS at Mayo Clinic, Rochester between July 2020 and May 2021 were retrospectively reviewed. Baseline demographic and clinical data was extracted, and hemorrhage and thromboembolic complications were assessed post-operatively.
Results: Ninety-three patients (mean 64.1 years old, ± 11.8, 60% male) underwent DBS during the study period, (54 essential tremor, 33 Parkinson disease, 4 dystonia, 1 multiple sclerosis-related tremor, 1 Tourette's syndrome). Thirty (32%) were prescribed chronic antiplatelet medication and 8 (9%) were on anticoagulation.
There were no hemorrhage complications, and one thromboembolic complication in the 63 patients not taking antiplatelet/anticoagulation therapy. Antiplatelet medication was held preoperatively for a mean 10.7 days (± 3.8) , and anticoagulation was held for a mean of 7.8 days (±2.8).
Intracranial hemorrhage occurred in 3/30 (10%) of antiplatelet-treated patients, and in 3/8 (43%) of anticoagulation-treated patients after a mean 31 and 7 days post-operatively.
Thromboembolic complications occurred in 3/38(8%); 2 anticoagulation-treated, and 1 antiplatelet-treated, after a mean of 9 and 16 days. Age was not associated with hemorrhage or thrombosis (p=0.2393, p=0.3820).
Hemorrhage was less likely with longer duration holding antiplatelet or anticoagulation preoperatively (p=0.048), but it was not associated with time held postoperatively (p=0.2563). Thromboembolic risk was not associated with length of time held before or after surgery (p=0.4332, p=0.3482).

Conclusions: DBS-associated hemorrhage and thromboembolic complication are higher in patients taking anticoagulant versus antiplatelet therapy. Longer time holding these medications preoperatively, but not postoperatively, is associated with lower hemorrhage occurrence. These findings can help guide risk management of intracranial vascular complications.

P 029 (GPT)
Eleven-year outcomes from the deep brain stimulation in early-stage Parkinson's disease pilot clinical trial

M. Hacker[1], J. Meystedt[1], M. Turchan[1], K. Harper[1], B. Eoff[1], K. Cannard[2], R. Fan[1], F. Ye[1], T. Davis[1], P. Konrad[3], D. Charles[1]

[1]Vanderbilt University Medical Center, Nashville, United States, [2]Walter Reed National Military Medical Center, Bethesda, United States, [3]West Virginia University School of Medicine, Morgantown, United States

Background: The deep brain stimulation (DBS) in early-stage Parkinson's disease (PD) pilot trial randomized 30 patients (Hoehn & Yahr II off; medication duration 0.5-4 years; without dyskinesia/motor fluctuations) to optimal drug therapy (early ODT) or bilateral subthalamic nucleus (STN) DBS plus ODT (early DBS+ODT; NCT00282152; IDEG050016; VanderbiltIRB#040797). This study reports 11-year outcomes of patients who completed the early DBS trial.

Methods: Attempts were made to contact all 29 subjects who completed the two-year trial to participate in an 11-year follow-up study (VanderbiltIRB#180766). Mixed-effects models compared overall trend in outcomes for randomization groups (fixed effects: assigned treatment, year, their interaction; random effect: subject) to account for repeated measures.

Results: Twelve subjects participated in this 11-year follow-up study (n=8 early ODT, n=4 early DBS+ODT). Eighteen subjects did not participate: withdrew after baseline (n=1 early ODT), lost to follow-up (n=2 early DBS+ODT), declined (n=1 early DBS+ODT), severe disability (n=1 early ODT, n=1 early DBS+ODT), deceased (n=5 early ODT, n=7 early DBS+ODT). Participating subjects were 70.0±4.8 years old with a PD medication duration of 13.7±1.7 years (early DBS duration 11.5±1.3 years, n=4). Three early ODT subjects received STN-DBS as standard care (DBS duration 6.5±2.0 years, n=3).

Early ODT subjects had worse motor complications (UPDRS-IV) than early DBS+ODT subjects over the 11-year follow-up period (between-group difference=3.5 points; $P_{interaction}$=0.033). Early DBS+ODT was well-tolerated after 11 years and showed comparable outcomes to ODT subjects for UPDRS-III, PDQ-39, and LEDD.

Conclusions: In this limited cohort available for follow-up 11 years after randomization in the DBS in early-stage PD pilot trial, early DBS+ODT subjects had fewer motor complications than early ODT subjects. These results should be interpreted with caution, because only 40% of pilot trial subjects participated in this 11-year follow-up study. The FDA has approved a randomized, double-blind pivotal clinical trial evaluating DBS in early-stage PD (IDEG050016).

P 030 (GPT)

Improving the accuracy of DBS and other stereotactic neurosurgeries using a 3D-printed skull for preoperative target practice

H. Singh[1], *N. Sawal*[2], *S. Arjun*[3], *M. Matta*[3]
[1]Government Medical College and Hospital, Intern, Chandigarh, India, [2]Fortis Mohali, Neurology, Mohali, India, [3]Government Medical College and Hospital, Chandigarh, India

Background: Stereotactic Neurosurgery is the technique of accurately reaching a target inside the brain using an external frame of reference. A number of potential sources of error have been identified in frame-based stereotactic neurosurgery; distortion of the frame over time, a difference in the torque used for screw fixation, or simply an inexperienced surgeon. In our centre, we wanted to perform a GPi-DBS using a stereotactic frame that we were previously unfamiliar with.
Therefore, we decided to 3D-print the patient's skull, which enclosed within it, GPi targets for pre-operative target practice.
Methods: CT images were used to make a 3D model of the patient's skull using [Fig. 1]. FGATIR-MRI sequence was used to visualise the GPi. The Bregma was used as a reference point for calculating the coordinates in the MRI images. Using the bregma as a reference, these coordinates were used to create two 5mm targets representing the GPi in the 3D-model of the CT [Fig. 1].

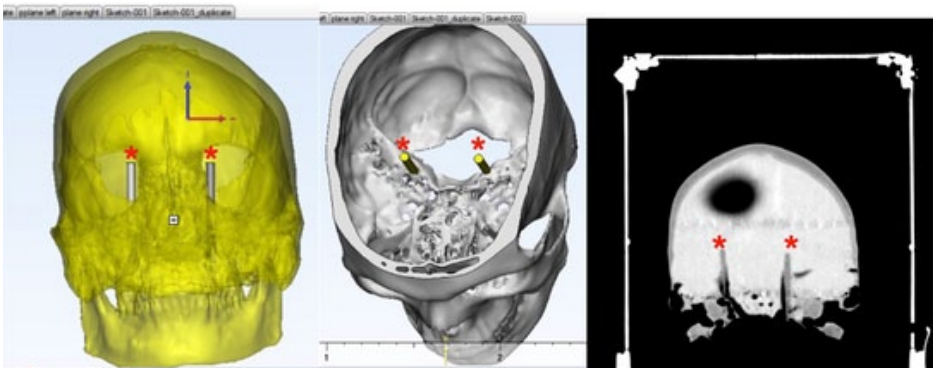


Figure 1. A 3D model of the patient's skull with GPi targets (shown as red asterisks)

Results: The frame was fixed to the skull, GPi-targets enclosed within the skull were visualised in the pre-operative CT. An RF-electrode was inserted at the intended target and visualised in a postoperative CT [Fig. 2]. The trajectory was 3.035mm too-medial and 0.486mm too-anterior from the intended target. Fixation screws were adjusted and the accuracy in the subsequent attempt was <0.5mm.

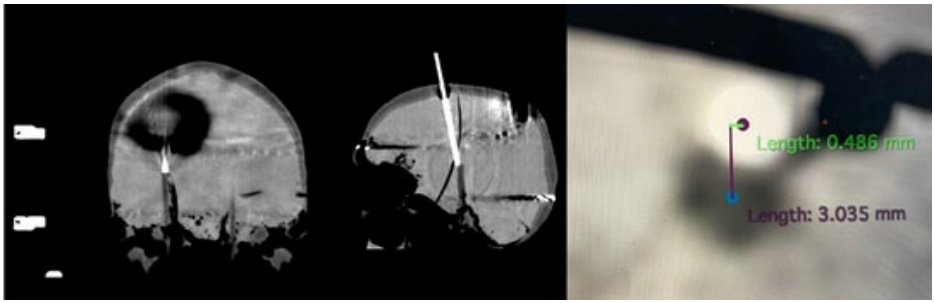


Figure 2. Post-op CT of the 3D-printed skull to assess the accuracy of the procedure.

Conclusions: A 3D-printed skull with surgical targets could help train young functional neurosurgeons. This approach shall also allow neurosurgeons to rapidly transition between the various manufacturers of stereotactic frames, micro-drives and planning stations.

P 031 (GPT)
Clinical milestones demonstrate compression of morbidity in patients with Parkinson's disease treated by deep brain stimulation of the subthalamic nucleus

N. Schnalke[1], A. Konitsioti[1], M. Kurz[1], W. Polanski[2,2], P. Themann[3], M. Wolz[4], S. Sobottka[2], H. Reichmann[1], B. Falkenburger[1], L. Klingelhoefer[1]

[1]Universitätsklinikum Dresden an der Technischen Universität Dresden, Department of Neurology, Dresden, Germany, [2]Universitätsklinikum Dresden an der Technischen Universität Dresden, Department of Neurosurgery, Dresden, Germany, [3]Rehabilitationszentrum Niederschoena, Hetzdorf, Germany, [4]Klinikum Meißen, Department of Neurology, Meißen, Germany

Background: Deep Brain Stimulation of the subthalamic nucleus (STN-DBS) is an effective treatment for motor symptoms of Parkinson's Disease (PD). The occurrence of hallucinations, dementia, nursing home placement and falls in PD patients with best medical therapy (BMT) were suggested as clinical milestones initiating the final disease stage by Kempster et al. In this study, we investigated the long-term progression of motor and non-motor symptoms and health-related quality of life (HrQoL) in patients with STN-DBS. In order to determine the functional relevance of the clinical milestones in PD patients with STN-DBS, we measured their occurrence in a well described cohort of PD patients with STN-DBS.
Methods: The occurrence of milestones was determined for 162 consecutive patients who underwent STN-DBS at our center. A subgroup of 115 patients was enrolled in a more detailed prospective analysis of PD symptoms.
Results: After STN-DBS, levodopa equivalent daily dose was reduced, motor function and HRQoL improved, non-motor symptoms and cognition remained stable. These effects are in line with previous studies in PD patients with STN-DBS. In our cohort, milestones occurred on average 13 years after diagnosis of

PD, which is later than reported for patients with BMT. Measures of motor function, cognition and HrQoL significantly worsened one year after occurrence of any milestone, confirming that milestones are functionally relevant. Mean survival in our cohort was 5 years after the occurrence of any milestone, thus similar as without STN-DBS.

Conclusions: The occurrence of clinical milestones in the course of PD is functionally relevant and marks the transition to the final stage of the disease. Disability-free life expectancy is longer in patients with STN-DBS than in PD patients with BMT. However, STN-DBS does not prolong survival after the occurrence of the first milestone. Thus, in patients with STN-DBS morbidity is compressed into the final stage of the disease.

P 032
Possible impact of subthalamic deep brain stimulation on glycemic variability and lipid profile in patients with Parkinson's disease

J. Samborska-Ćwik[1], *S. Szlufik*[1], *A. Marszalek*[2], *D. Koziorowski*[1]

[1]Medical University of Warsaw, Department of Neurology, Warsaw, Poland, [2]Medical University of Warsaw, Students' Scientific Association of the Department of Neurology, Warsaw, Poland

Background: Being valuable alternative for pharmacotherapy in advanced Parkinson's disease (PD), subthalamic nucleus deep brain stimulation (STN-DBS) is suspected to affect negatively cardiometabolic profile of patients (including body mass, lipid profile). In our study we investigated whether it may have similar effect on glucose metabolism.

Methods: Two groups of patients with PD were included: 20 treated pharmacologically (PHT group) and 20 newly qualified for STN-DBS (DBS group) - with the first assessment prior to the surgery. BMI, plasma concentrations of the total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides (TG), and glucose level during three-point oral glucose tolerance test were measured thrice (median intervals between visits 12 and 14 months respectively).

Results: A significant difference between two groups was noted according to changes in BMI (-0,56 kg/m^2 in the PHT and +1 kg/m^2 in the DBS, p=0,01), serum concentration of TG (-6,1 mg/dl in PHT vs +39 mg/dl in DBS, p<0,01) and HDL-C (-1,3 mg/dl PHT and -8,4 mg/dl in DBS, p=0,01) in the course of the study. Level of TG was significantly higher in DBS group during last visit (142,8 vs 95,6 mg/dl, p=0,04).

Conversely, mean glucose level after oral glucose administration was lower in DBS than in PHT group (147,4 vs 120,2 mg/dl, p=0,03 after 1 hour and 109,9 vs 82,3 mg/dl, p<0,01 after 2 hours) during second visit. Also inter-visit changes in fasting glucose levels (8,4 mg/dl in PHT and -5,8 mg/dl in DBS, p=0,02) differed over study duration.

Conclusions: Our observations are in the agreement with other reports indicating less favourable changes in BMI and some lipid fractions during course of the disease in patients treated surgically. Interestingly, reverse trend was observed for glucose metabolism parameters suggesting that other mechanisms than simple body mass changes are involved in early biochemical changes after STN-DBS in PD patients.

P 033 (GPT)

Compared effects of magnetic-resonance guided ultrasound (MRgFUS) and deep brain stimulation (DBS) in a 58 year old Parkinson's disease patient

E. Papić[1], V. Komen[2], G. Rožmarić[3], V. Vuletić[1]

[1]Faculty of Medicine, University of Rijeka, Department of Neurology, Rijeka, Croatia, [2]Clinical Hospital Center Rijeka, Clinic of Neurology, Rijeka, Croatia, [3]Faculty of Medicine, University of Rijeka, Rijeka, Croatia

Background: Magnetic resonance guided ultrasound (MRgFUS) is a non-invasive technique recently established as a potential alternative to the already well known deep brain stimulation (DBS) in movement disorders such as essential tremor and Parkinson's disease (PD).

To the best of our knowledge, there are no reported cases of DBS following unsuccessful MRgFUS. As these methods overlap in treatment targets, we present the case of a patient with Parkinson's disease who was treated with both of them.

Methods: MRgFUS has been used experimentally for the treatment of Parkinson's disease since the beginning of the last decade, with some studies showing promising, even if short-term effects. It's a noninvasive method, using thermoablation to create intracranial lesions. On the other hand, DBS has become a mainstay in the treatment of PD, with studies reporting long-term efficacy for more than ten years. However, as an invasive method, it has multiple side-effects.

Results: A 58-year-old patient, a dentist by profession, developed his first symptoms in 2003, presenting with right-sided tremor which slowly progressed over time, affecting his ability to work and his quality of life. He was treated with various medications to slight effect and was eventually treated with MRgFUS with the lesion formed in the pallidothalamic tract.

However, his symptoms showed little improvement, and his tremor returned after a couple of weeks. In 2016 he was implanted with bilateral STN DBS and showed dramatic improvement. In follow-up examinations in 2021 he showed sustained improvement with DBS, with gradual changes to stimulation parameters.

Conclusions: Bilateral STN DBS greatly improved our patient's quality of life and enabled him to continue his work as a dentist. Even though focused ultrasound didn't prove beneficial in his case, it is still early to assess this method's true potential in PD. More research is required in this field.

P 034

Marked worsening of hypophonia, dysphagia and sialorrhea S/P bilateral STN DBS: a case report.

K. Papesh[1], J. Nguyen[2], Z. Mari[3]

[1]Advanced Neurology of Colorado, Movement Disorders, Fort Collins, United States, [2]Cleveland Clinic Lou Ruvo Center for Brain Health, Movement Disorders, Las Vegas, United States, [3]Lou Ruvo Center for Brain Health, Movement Disorders, Las Vegas, United States

Background: Dysphagia is a common and dangerous symptom affecting people living with Parkinson's disease (PD). It increases the risk four-fold for aspiration pneumonia, greater disease burden, and significantly higher mortality. Speech disorders, such as hypophonia can affect up to 90% of those living with PD (Dashtipour et al, 2018). Deep brain stimulation (DBS) as an advanced therapy to treat motor symptoms of PD may have a negative impact on speech, swallowing and sialorrhea. STN DBS may impair the jaw opening and closing velocity leading to difficulty with managing oral secretions, and dysphagia.

In a previous longitudinal study, newly reported and worsening of dysphagia was reported in 10% of patients at a 30-month post DBS follow up. Here we present a case report of a patient with treated with bilateral STN DBS with immediate life-altering dysphagia and marked worsening sialorrhea and speech disturbance following DBS implant.

Methods: For this case report, retrospective chart review and subjective history from patient and caregiver was collected. The chart review and patient log trending symptomatic management were assessed for extent of impairment, disability in swallowing and speech function.

Results: A 70-year old male with 15 year history of tremor-predominant Parkinson's disease who had history of mild sialorrhea and hypophonia received deep brain stimulation implants bilaterally in STN. Post-implant of DBS, this patient developed life-altering changes and progression in sialorrhea and hypophonia, as well as a newly developed dysphagia to the extent of requiring feeding tube placement.

Conclusions: Bilateral STN DBS may contribute to a negative impact with bulbar side effects such as dysphagia, hypophonia and sialorrhea. While similar findings have been reported both retrospectively/anecdotally and in prospective studies, awareness of the severity and impact of these complications remains low.

P 035

Feasibility of large-scale systematic data collection in a quality improvement registry of deep brain stimulation in Parkinson's disease

J. Jimenez-Shahed[1], *M. York*[2], *J. Kirk*[3], *A. Berg*[4], *J. Schwalb*[5], *M. Siddiqui*[6], *J. McInerney*[4]
[1]Icahn School of Medicine at Mount Sinai, New York, United States, [2]Baylor College of Medicine, Houston, United States, [3]n/a, Boston, United States, [4]Penn State University, Hershey, United States, [5]Henry Ford Health System, Detroit, United States, [6]Wake Forest School of Medicine, Winston-Salem, United States

Background: RAD-PD is a multicenter quality improvement patient registry for patients with Parkinson's disease (PD) who are candidates for deep brain stimulation (DBS) surgery. The project goals are to describe best practices, adverse effects and their determinants, health economics, and disparities in outcome related to DBS treatment.
Methods: In this pilot period, 20 sites were selected and activated. A data repository was built in the Research Electronic Data Capture portal, a secure web application for building and managing online surveys and databases. Patients are recruited from sites' individual practices when they are considered eligible for consideration of DBS. Sites collect clinically measured scales, disease related information, and demographics into the portal and deploy surveys to patients that include a variety of patient reported outcomes.
Data is reviewed for completeness in order to be retained in the registry. Participant information is benchmarked for sites in a study dashboard. Quarterly site calls are conducted to review best practices and data trends. Patient report cards will be distributed at follow-up timepoints.
Results: Since project launch, informed consent has been obtained for >250 individuals with PD. The COVID-19 pandemic has affected site onboarding, subject enrollment and surgical data collection. There are 113 complete baseline datasets, 67 complete surgery datasets, and 18 complete 6-month follow-up datasets. Baseline clinical characteristics of enrolled subjects are heterogeneous. Surgical techniques vary amongst sites. Barriers to data collection are assessed and mitigated in order to streamline workflows and data management efforts.
Conclusions: Longitudinal, standardized multicenter data collection related to DBS treatment in patients with PD is feasible. Data from RAD-PD will generate real world evidence that will improve understanding of factors related to outcomes disparities after DBS.

P 036 (GPT)

Subthalamic recordings in chronically implanted parkinsonian patients

C. Palmisano[1], I. Hanafi[1,2], J. Del Vecchio Del Vecchio[1,2], N. Pozzi[1], M. Reich[1], P. Capetian[1], C. Matthies[3], J. Volkmann[1], I.U. Isaias[1,2]

[1]University Hospital of Würzburg, Neurology, Würzburg, Germany, [2]Julius Maximilian University, Würzburg, Germany, [3]University Hospital of Würzburg, Neurosurgery, Würzburg, Germany

Background: Adaptive deep brain stimulation (aDBS) in Parkinson's disease (PD) aims to improve the efficacy of DBS and reduce battery consumption. Postoperative recordings with externalized leads indicated subthalamic beta activity (STN-LFP, 13-30 Hz) as a possible biomarker for aDBS in PD patients.

However, recent studies in chronically implanted PD patients have been controversial in identifying exaggerated STN-LFP beta activity.

The recent market release of a new device for DBS (Percept PC, Medtronic) allows for monitoring beta activity in large cohorts of chronically implanted patients at multiple follow-ups. Assessing the quality of recordings performed with this device is the first step toward developing aDBS protocols.

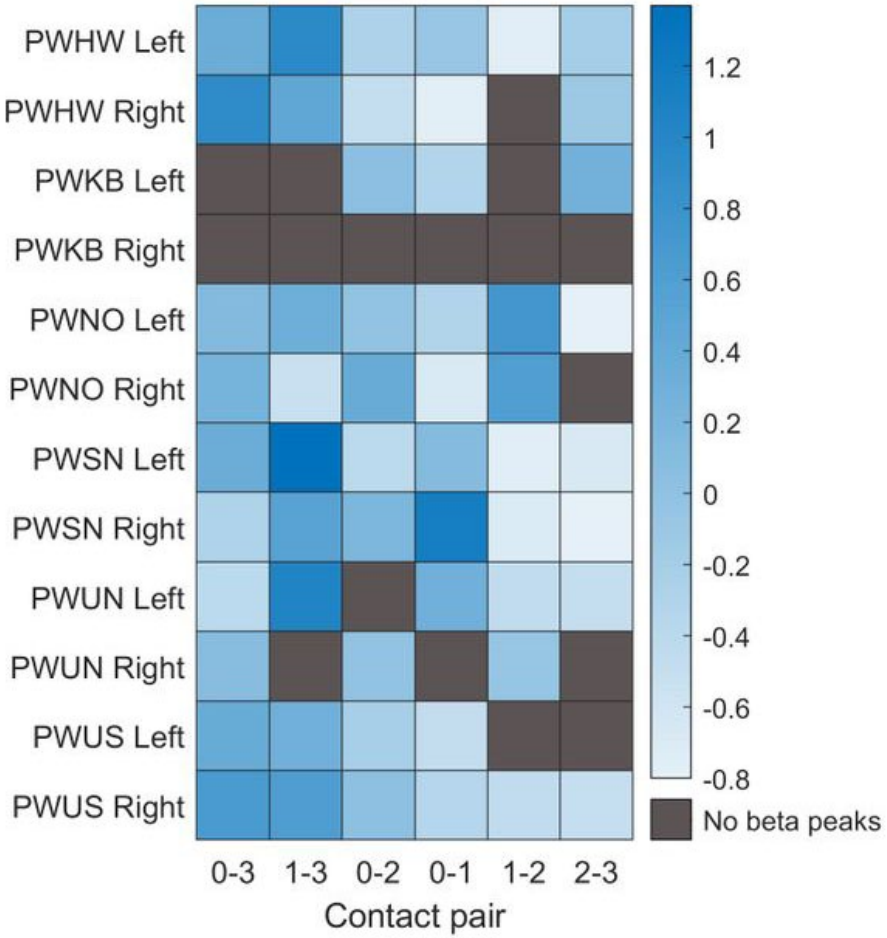
Methods: STN-LFP were recorded with chronically implanted leads (B33005/B33015, Medtronic PLC) and the Percept PC device in PD patients at one week [1w] (4/6 patients), six weeks [6w] (6/6 patients) and three months [3m] (5/6 patients) of follow-up.

At each follow-up, we performed BrainSense *Survey* recordings (i.e., stimulation-off 22s bilateral recordings from all contact combinations) and BrainSense *Setup* recordings (i.e., stimulation-off and -on 22s bilateral recordings from non-adjacent contact pairs). We computed the average percentage of contact pairs labelled as artefactual in both modalities.

We identified cardiac-related artefacts by visual inspections of the signals. We computed the power spectral density of the BrainSense *Survey* recordings performed at 6w follow-up and identified the beta peaks.

Results: At the three follow-ups, the mean percentage of contacts labelled as artefactual by the device was 30.2±28.7%, 11.7±10.8%, 6.9±17.0% in stimulation-off and 25±50%, 36.7±29.8%, 23.0±22.9±% in stimulation-on condition.

The cardiac artefact was present at all follow-ups and in both stimulation conditions in all patients except for one. Beta peaks were detected in 74.6% of non-artefactual contact pairs, in all but one STN. The highest beta peaks were located at an average frequency of 19.8±4.6 Hz (Fig. 1).



Conclusions: Artefacts in stimulation-off significantly decreased at the 6w and 3m follow-up, while artefacts in stimulation-on and cardiac-related artefacts still contaminated the signals.
Despite this, our results confirm the presence of beta peaks in STN-LFP of PD patients and support its study as a possible biomarker for aDBS.

P 037

Rare neurological indications for Deep Brain Stimulation treatment: experience at the University Medical Center Ljubljana

S. Ibrulj[1], *M. Trošt*[1], *D. Flisar*[1], *M. Benedičič*[2], *D. Georgiev*[1]

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

Background: Deep brain stimulation is (DBS) is the operative method of microelectrode placement and stimulation of basal ganglia for the symptomatic treatment of movement disorders. The currently established indications for DBS treatment are advanced Parkinson's disease (PD), idiopathic dystonia (D) and essential tremor (ET).

Recent clinical studies have shown successful results in implementing DBS for treatment of other, rare neurological and psychiatric syndromes i.e. Tourette's syndrome, Huntington's chorea, tardive dystonia and epilepsy, which have not yet been established as indications for DBS. Routine clinical application in these is limited due to the ambiguity of appropriate anatomical target choice, poor understanding of disease patophysiology and DBS' effect on them. The disease spectrum for DBS treatment is expanding thanks to the empirical results of existing clinical studies. Our aim is to present 13 cases of rare neurological syndromes which were treated with DBS in our center.

Methods: We analyzed all patient records for those treated with DBS at the Department of Neurology of the University Medical Center in Ljubljana between January 2008 and November 2021. 131 patients were treated with DBS, of those 118 were treated for PD, dystonia or ET. 13 patients had DBS implemented for symptomatic treatment of other types of movement disorders.

Results: Between January 2008 and November 2021 DBS was implemented to 6 patients (4 F) with Huntington's chorea, 4 patients (2 F) with the dyskinetic type of cerebral palsy, 1 patient with PKAN generalized dystonia, 1 patient with dystonia-deafness syndrome and 1 patient with Gilles de la Tourette syndrome. The target in all patients was the globus pallidus internus (GPi), bilaterally.

Conclusions: The spectrum of neurological and psychiatric disorders that can be successfully symptomatically treated with DBS is expanding. Our experience shows success in treating some rare neurological diseases presenting with movement disorders, which are currently not routinely treated with DBS.

P 038

An experimental paradigm for testing effect of alternating-frequency deep brain stimulation on gait, in Parkinson disease

J. Liao[1], R. Kaya[1], J. Yu[1], M. Koop[2], A. Rosenfeldt[2], J. Alberts[2], K. Baker[3], H. Fernandez[1]

[1]Cleveland Clinic Neurological Institute, Cleveland, United States, [2]Cleveland Clinic Lerner Research Institute, Biomedical Engineering, Cleveland, United States, [3]Cleveland Clinic Lerner Research Institute, Neurosciences, Cleveland, United States

Background: Gait impairment remains a crucial unmet need in Parkinson Disease (PD). High frequency (HF) ~130Hz deep brain stimulation (DBS) of the subthalamic nucleus (STN) 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 including gait; however, key questions remain.

We developed a paradigm to evaluate, using quantitative kinematic and neural measures, the effect of alternating-frequency (AF) interval on motor function, to identify intervals that maximize motor benefits, as well as to gain insight into the mechanism of AF DBS.

Methods: We used literature and incremental feasibility tests to develop a paradigm that enables open environment ambulation using a wireless headset to display an augmented-reality obstacle course. An ambulatory EEG system was used to record EEG signals, with STN local field potentials recorded via Medtronic Percept. Stride time coefficient of variation and per-step task performance were captured using body-worn kinematic sensors. AF stimulation intervals were selected based upon Jia 2018 (PMID 30637270), who observed that 10-30s intervals improved gait and UPDRS. Six DBS conditions were selected, including constant HF, constant LF, 10s-HF/10s-LF, 50s-HF/50s-LF, 10s-HF/50s-LF, and 50s-HF/10s-LF. Tasks are repeated OFF and ON meds.

Results: All participants to date (n = 4) tolerated the augmented-reality obstacle course, supporting the overall feasibility and safety of the approach. Gait-related electrophysiology and kinematics can be simultaneously captured, with motion- and stimulation-related artifact mitigated offline.

Conclusions: The experimental paradigm of a recruiting clinical trial is presented, comparing various alternating-frequency DBS conditions on gait. Additional data continue to be gathered to fully understand the usability of the system and its capability to reliably elicit and quantify freezing of gait and other gait-related dysfunction.

P 039 (GPT)

STN DBS improves balance disorders in Parkinson's disease patients and impacts the disease progression

S. Szlufik[1], M. Kloda[1], I. Potrzebowska[1], K. Jaros[2], A. Gędek[2], A. Przybyszewski[3], T. Mandat[4], D. Koziorowski[1]
[1]Medical University of Warsaw, Department of Neurology, Faculty of Health Sciences, Warszawa, Poland, [2]Medical University of Warsaw, Department of Neurology, Students' Scientific Group, Faculty of Health Science, Warszawa, Poland, [3]Polish Japanese Academy of Information Technology, Department of Informatics, Warsaw, Poland, [4]Maria Sklodowska Curie Memorial Oncology Center, Department of Neurosurgery, Warsaw, Poland

Background: Subthalamic nucleus deep brain stimulation (STN DBS) can influence on balance and gait disorders, but there are still some conflicting information. Therefore the aim of this study was to evaluate the impact of STN DBS on balance disorders in PD patients.
Methods: DBS-group consisted of 28 PD patients who underwent bilateral STN DBS. Control group (BMT-group) consisted of 24 patients who did not undergo surgical intervention and were treated only with pharmacotherapy.
UPDRS III scale and balance tests (UpAndGo Test, Tandem Walk Test) were measured during 3 visits: V1 (which was preop visit for DBS group), V2 and V3 in all DBS/pharmacotherapy phases. The mean periods between visits were 9±3months.
Results: There are statistically significant differences in all balance tests on each visit between Total-On and Total-off in both study groups ($p<0,05$). There are statistically significant differences in all balance tests in V2 and V3 visits between DBS-on/BMT-off and Total-off as well as BMT-on/DBS-off and Total-off, but values of the balance tests achieved in the DBS-on/BMT-off phase are significantly lower and tend to increase slower than those achieved in DBS-off/BMT-on.
Conclusions: STN DBS can improve balance disorders in PD patients more than pharmacological treatment. STN DBS may have an impact on PD progression.

P 040

Is there any difference between directional vs omnidirectional lead for treatment in Parkinson's disease?

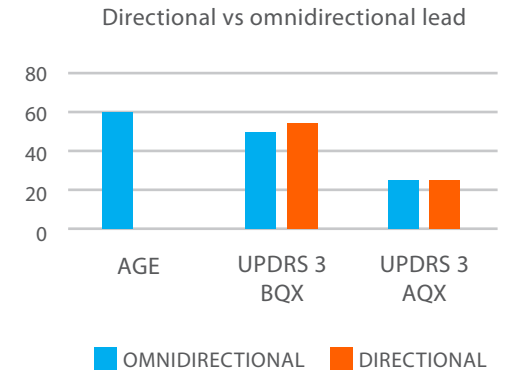
O. Bernal-Pacheco[1,2], M. Fonseca Ramos[3]
[1]Universidad Militar Nueva Granada, Neurology, Bogotá, Colombia, [2]Instituto Ortopedico Roosevelt, Neurology, Bogota, Colombia, [3]Instituto Ortopedico Roosevelt, Neurology, Bogotá, Colombia

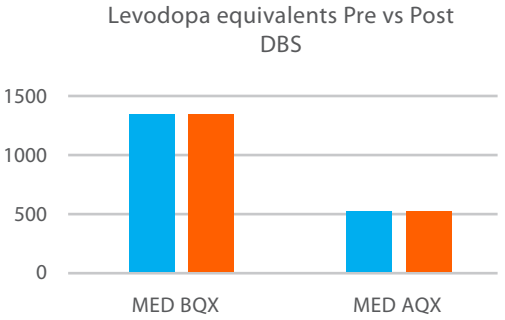
Background: Deep Brain Stimulation (DBS) is one of the most important tools for the treatment of patients with advanced Parkinson Disease. New devices such as leads with directional stimulation have been developed trying to get even more control of symptoms without induce bothersome and non-tolerable side effects, and looking for a better outcome in movements disorders, quality of life and activities of daily living.

Methods: This is a descriptive study of patients with Parkinson Disease who underwent a DBS surgical treatment in the Roosevelt Institute, between June 2019 and August 2021 and followed for at least six months after implantation. 28 patients (56 leads) were implanted with directional lead and 56 patients (112 leads) were implanted with omnidirectional lead. All patients were random assigned to one or the other arm.

Results: There were non demographical diferences, with 23 female (41%) and 33 male in the omnidirectional lead group with a median age of 62 years (46-74) and 10 female (45%), 18 male (38-75) with a median age of 61 years in the lead directional group. The UPDRS 3 in the group omnidirectional lead was 52 pts (42-76) vs 51 pts in the directional group (30-76). The UPDRS 3 post DBS were similar after the treatment with a median of 25 pts in both groups. We diminish 61% of medications according to levodopa equivalents in both groups.

Conclusions: In our population, we didn´t find any clinical or pharmacological difference in the follow up after six months of patients with PD that underwent to DBS with directional or omnidirectional lead.





Keywords: Deep Brain Stimulation; Parkinson Disease; Directional Lead

Behavior, Cognition, Psychiatry

P 041 (GPT)

Clinical evaluation of neuropsychiatric symptoms in patients with Parkinson's disease during COVID-19 pandemic: risk factors

M. Salokhiddinov[1], *R. Nuriddinov*[1]
[1]Zangiota №2 Republic COVID Specialised Center, Zangiota, Uzbekistan

Background: The coronavirus disease pandemic of 2019 (COVID-19) and the consequent state of emergency drove people to focus on the infection and put chronic disease treatment on the back burner. Because they were believed to be at a higher risk for a serious sickness, older persons, who frequently have underlying medical disorders, have an elevated mental burden.
Methods: From April 22, 2020, to May 15, 2020, a cross-sectional hospital-based survey was undertaken. Patients with Parkinson's disease and their family members were mailed questionnaires about neuropsychiatric symptoms. Motor symptoms in PD patients were assessed via telephone interview using the MDS-UPDRS part 2. The study enrolled a total of 71 responders (39 PD patients and 32 controls).
Results: Patients with Parkinson's disease (PD) had a lower percentage of females (25 percent) than healthy controls (74 percent). Patients with Parkinson's disease (45%) had more participants with clinical depression (PHQ-9 score 10) than controls (9%; p = 0.002).
Clinical depression (PHQ-9 score 10) and anxiety (GAD-7 score 7) were found to be associated with a low MDS-UPDRS part 2 score (odds ratio, 1.32; 96% confidence interval, 1.05–1.78; P = 0.020; odds ratio, 1.14; 95% confidence interval, 1.12–1.65; P = 0.011).
Our study showed that clinical depression and anxiety are more common among people who scored highly on the MDS-UPDRS part 2. Reducing exercise time during the COVID-19 pandemic has been linked to an increase in both motor and non-motor symptoms.
Conclusions: Since high MDS-UPDRS part 2 scores in Parkinson's disease patients are strongly linked to the development of severe depression and anxiety as well as other neuropsychiatric symptoms, these individuals may require special treatment in the event of another great disaster.

P 042
Homologs and order of duplication of insulin-like growth factor in humans

A. Venger[1], *O. Venger*[2]
[1]Odessa National Medical University, Department of Microbiology, Virology and Immunology, Odesa, Ukraine, [2]State institution 'South Ukrainian National Pedagogical University named after K. D. Ushynsky', Department of General Disciplines and Clinical Medicine, Odesa, Ukraine

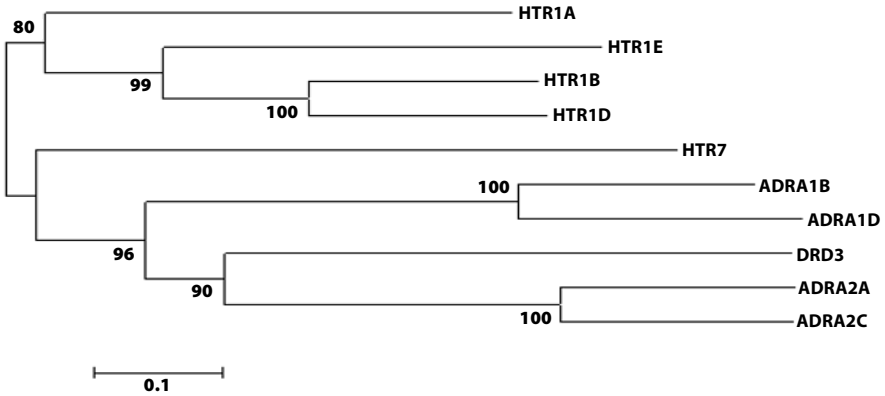
Background: As claimed by a hypothesis about schizophrenia widely indicated by studies in areas of epidemiology, genetics and neuroimaging, if an adult suffers from severe mental illness, the central nervous system must have developed in a disruptive manner [1].
Being a type of insulin-like protein, insulin-like growth factor (IGF) is an integral component of the cell system in human bodies that serves as a communication channel regarding the physiological circumstances [2].
Previously there was convincingly demonstrated that IGF has an indispensable and crucial role to play in nerve growth. The interesting fact is that individuals suffering from IGF gene mutations are vulnerable to physically disabled growth, nanocephaly or intellectual disability.
The aim of this work was to detect homologs and order of duplication of IGF in humans.
Methods: The order of duplication was inferred using the Neighbor-Joining method. The optimal tree with the sum of branch length = 8.28086334 is shown. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (500 replicates) is shown next to the branches.
Results: The dendrogram was successfully built and consisted of two clusters.
In the first cluster IGF-1 and IGF-2 are situated.
The second cluster contains FREM3 (FRAS1 related extracellular matrix 3), NIBAN1 (niban apoptosis regulator 1), KIF3B (kinesin family member 3B), SSASKS (solute carrier family 10 member 7), TSPAN5 (tetraspanin 5) and INSIGF (a protein coding gene) amino acid sequences.
Conclusions: Most of these members are cell-surface proteins that are characterized by the presence of four hydrophobic domains. The proteins mediate signal transduction events that play a role in the regulation of cell development, activation, growth and motility. The fulfilled research gives possibility to anticipate the properties of the studied genes as they are very familiar according to amino acid sequences of their products.

P 043

Paralogs and order of duplication of serotonin 1A receptor in humans

O. Venger[1], *A. Venger*[2]
[1]State Institution 'South Ukrainian National Pedagogical University named after K. D. Ushynsky', Department of General Disciplines and Clinical Medicine, Odesa, Ukraine, [2]Odessa National Medical University, Department of Microbiology, Virology and Immunology, Odesa, Ukraine

Background: The serotonin neurotransmitter system generally, and serotonin 1A receptor (HTR1A) particularly, have been wildly involved in the pathophysiology of mood and anxiety disorders. Thus, the serotonergic system and HTR1A are shown to be involved in major depressive disorder (MDD).
Attentiveness to depression is caused by high prevalence and increasing frequency of this disease in the world and its negative influence on the ability to work and social activity of a human. Both the study of polymorphisms of gene-candidates and consequences of their effects can help to define degree of disposition to depressive disorders.
The aim of this work was to detect paralogs and order of duplication of HT1AR in humans.
Methods: The order of duplication was inferred using the Neighbor-Joining method. Optimal tree with sum of branch length = 3.74122546 is shown. Percentage of replicate trees in which associated taxa clustered together in the bootstrap test (500 replicates) is shown next to the branches.



Results: The dendrogram with products of HTR7, HTR1A, HTR1B, HTR1E, HTR1D, ADRA1B, ADRA1D, ADRA2A, ADRA2C and DRD3 amino acid sequences was successfully built and consisted of two clusters. In the first cluster HTR1A, HTR1B, HTR1E, HTR1D are situated. The second cluster contains HTR7, ADRA1B, ADRA1D, ADRA2A, ADRA2C and DRD3 amino acid sequences.
Conclusions: Thus, downregulation of HTR1A palmitoylation is mechanism involved in depression, making restoration of HTR1A palmitoylation a promising clinical strategy for treatment of MDD. Current work gives opportunity to predict properties of studied genes as they are very close according to amino acid sequences of their products.

P 044
Evaluation of the adaptive capacity of patients with Parkinson's disease

S. Djalilova[1]
[1]Tashkent Medical Academy, Neurology and Medical Psychology, Tashkent, Uzbekistan

Background: Adaptive behavior of patients with PD gives the patient the opportunity to effectively recover from the rehabilitation regime.
Methods: The study included patients with Parkinson's disease on stage 0–2, with progredient transition, tremor, tremor-regid type (Hoehn, Yahr, 1967). The mean age of the patients was 52.8 ± 3.2. The duration of the disease was 3.8 ± 0.2 years.
Patients were studied in two groups.
Main group: 24 patients, consisting of patients with PD tremor type.
Comparison group: 24 patients were patients belonging to the vibration-regid type of PD.
The nonadaptative behavior and the mental response to the disease were studied using the Tipe of Attitude Towards the Disease (TATD) questionnaire. (L.I. Vasserman 2005).
Results: According to the TATD, patients of main group belong to the second block of maladaptive typologies because of the high level of anxiety about their disease (17%) compared to the tremor-type, tremor-bradykinetic type (13%). Including in this category of patients does not leave a feeling of high anxiety about their disease ($\rho \geq 0,05$).
However, patients in both groups reported an ergopathic response to the disease equally (5%:3%), but less frequently observed than in other typologies ($\rho \geq 0,03$). It was also established that in both groups of patients the response to the disease was melancholic, but in the tremor-bradykinetic type this typology was observed 3 times more common (1: 3.02).
Conclusions: It should be noted that the ergopathic type of all of the typologies whose patient adaptation features are highly described, appeared in a lower percentage, equally in both groups (1: 1.02). However, among the typologies with a high degree of maladaptation - the anxiety type Parkinson's disease was found to be more common in the form of tremors (85%) and the melancholic type was predominant in the form of tremors - bradykinetics (45%).

P 045
Non-permitted food colorants induced cognitive impairment and neurotoxicity in hippocampus of rats

P. Biswas[1], *D. Bose*[1], *R.S. Yadav*[1]
[1]Dr. Harisingh Gour Vishwavidyalaya (A Central University), Sagar – 470003 (MP), India, Department of Criminology & Forensic Science, School of Applied Sciences,, Sagar, India

Background: Food products are artificially coloured to make attractive mixtures to lure consumers because they not only attract but enhance appetite. Non-permitted food colourants (NPFCs) (prohibited one) injudiciary still reported but their neurobehavioral and neurotoxicity consequences are not well re-

ported. The present study was focused to investigate the effects of NPFCs (metanil yellow-MY, malachite green-MG and sudan III-SIII) on learning and memory of rats, oxidative stress, mitochondrial complex activity, neuroenzyme activity, neurotransmitters and histopathology in the hippocampus of rats.
Methods: Rats were divided into 5 groups and treated with MY (430 mg/kg), MG (13.75 mg/kg), SIII (250 mg/kg), mixture (YGR) (MY 143.33 + MG 4.52 + SIII 83.33 mg/kg) and 1 % gum acacia serve as control p.o. for 60 days. Learning and memory were assessed through Y maze and Morris water maze then one rat from each group was transcardially perfused for histopathology and the remaining were decapitated for hippocampus isolation and processed for biochemical, neurochemicals, neurotransmitters analysis through valid standard protocols.
Results: The treatment groups showed impairment in learning and memory and a significantly enhanced oxidative stress (higher lipid peroxidation, decreased level of reduced glutathione, superoxide dismutase and catalase activity), reduced mitochondrial complex enzyme activity (I and II), higher acetylcholinesterase activity, lower monoamine Oxidase –B activity in the hippocampus of rats. Levels of serotonin, dopamine and nor-adrenaline were higher in treatment groups compared to the control. Finally, significant damage in the architectures of neurons of hippocampus was observed in the treatment groups.
Conclusions: The results of the present study demonstrated that chronic exposure of NPFCs impaired learning and memory due to cholinergic and dopaminergic dysfunctions and an increase in the level of serotonin, dopamine and nor-adrenaline and neuronal damages due to enhanced oxidative stress and mitochondrial dysfunction which could be further associated with impaired motor dysfunction and pathological alterations like neurodegenerative diseases.

P 046
Correlation between NREM Sleep EEG characteristics and Mild Cognitive Impairment in patients with Parkinson's disease

K. Abdurakhmonova[1], *G. Rakhimbaeva*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: Purpose of the study was to assess the relevance between NREM Sleep EEG characteristics and Mild Cognitive Impairment (MCI) in patients with Parkinson's disease (PD)
Methods: 34 patients were enrolled in this study and were divided into two groups according to the cognitive status. First group consists of 18 patients with PD-MCI while second group includes 16 patients with PD and normal cognitive function(PD-NCF). All patients underwent an overnight polysomnography study (PSG). Sleep EEG signals were removed and clarified from the PSG and subjected to a conventional power spectral analysis and detrended fluctuation analysis (DFA) during wakefulness, nonrapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep.
Results: The alpha activity and fast ratio (alpha + beta/delta + theta) were lower during wakefulness and NREM sleep in patients with PD-MCI than in those with PD-NCF ($p < 0,05$). DFA increased in patients with PD-MCI during wakefulness and NREM sleep compared to those with PD-NCF ($p < 0,05$).
The results showed that PD-MCI patients had a decreased EEG fast ratio ($0,63 \pm 0,22$ vs $1,23 \pm 0,59$, $p = 0,001$) and increased DFA ($0.87 \pm 0,12$ vs $0,78 \pm 0,12$, $p = 0,005$) during NREM compared to PD-NCF patients

($p < 0{,}005$). Mild cognitive dysfunction was positively correlated with DFA in NREM ($r = 0{,}432$, $p = 0{,}005$) and negatively correlated with the fast ratio in NREM ($r = -0{,}524$, $p = 0{,}001$) in channel O1 during NREM sleep.

Conclusions: In conclusion, this study showed that the power spectral analysis and DFA characteristics of NREM sleep EEG were related to MCI in patients with PD. DFA can provide an estimation for cognitive function. Slowing of EEG activity during NREM sleep may reflect the decline in NREM physiological function and is therefore a marker in patients with PD-MCI.

P 047 (GPT)
The role of dopaminergic therapy on cognition in Parkinson's disease

L. Montaser Kouhsari[1], *A. Bakkour*[2], *D. Shohamy*[3,4]

[1]Stanford University, Neurology, Palo Alto, United States, [2]University of Chicago, Psychology, Chicago, United States, [3]Columbia University/ The Mortimer Zuckerman Mind Brain Behavior Institute, Psychology, New York, United States, [4]Columbia University | Zuckerman Institute, Psychology, New York, United States

Background: Parkinson's Disease (PD) is a neurodegenerative disease that causes debilitating cognitive deficiencies in addition to motor impairments. Although dopaminergic medications are designed to improve motor symptoms, their effect on cognition is complex and varies based on individual differences. Recent studies have used verbal Digit Span as a tool to study working memory in PD patients and have shown that Digit Span Backward can be used as a screening tool for mild cognitive impairment (MCI) in PD.

Our previous work demonstrated that Digit Span performance could discriminate patients whose working memory benefits from dopaminergic therapy.

Our goal was to assess whether Digit Span performance reveals the dopamine effect on decision-making impacted by memories.

Methods: Participants (25 PD patients without MCI) performed a Digit Span task ON and OFF dopaminergic medication. While OFF medication using a median split, they were divided into low and high working memory capacity groups (LM and HM). Consequently, they performed a decision task and made choices between pairs of familiar food items. The reaction time (RT) and choice performance were measured.

Results: Working memory performance varied across participants. We found the performance improvement due to dopaminergic therapy in the Verbal Digit Task was restricted to LM group; the HM group was not affected. The decision-making task revealed that dopamine increased RT in the HM group more than in the LM group. This increase in RT only was beneficial for the LM group resulting in improved performance.

Conclusions: This study offers evidence that working memory measured with the Verbal Digit Span test can be used as a screening tool for the effect of dopamine on other cognitive tasks. Moreover, the dopaminergic medication affects decision-making performance in PD patients, but this effect depends on the underlying baseline of the PD patients.

P 049

Early onset dementia with parkinsonism in a patient with pathogenic mutations in CSF1R and ABCD1 gene

G. Novotni[1], N. Tanovska[2], I. Barbov[3], F. Stojkovska[3], V. Aleksovski[3], K. Karanfilovik[3], M. Pendaroska[3], D. Stoilkovski[3], A. Jovkovska Gerasovska[3], A. Angelova[3], K. Aleksovska[3], S. Hasani[3], D. Plasheska Karanfilska[4], A. Novotni[5]

[1]University Ss Cyril and Methodius, Medical Faculty, University Clinic of Neurology, Neuroimmunology, Dementia Outpatient Clinic, Skopje, The Republic of North Macedonia, [2]University Ss Cyril and Methodius, Medical Faculty, University Clinic of Neurology, Neuroimmunology, Skopje, The Republic of North Macedonia, [3]University Ss Cyril and Methodius, Medical Faculty, University Clinic of Neurology, Skopje, The Republic of North Macedonia, [4]Macedonian Academy of Sciences and Arts, Genetic Laboratory 'Prof. Georgi Efremov', Skopje, The Republic of North Macedonia, [5]University Ss Cyril and Methodius, Medical Faculty, University Clinic of Psychiatry, Skopje, The Republic of North Macedonia

Background: Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) is a rare autosomal dominant genetic disease due to mutations in CSF1R gene, with complex underlying mechanisms that lead to white matter damage.

On the other hand, ABCD1 gene mutations have been found to cause another rare genetic disease, X-linked adrenoleukodystrophy.

Both these conditions are characterized by progressive development of white matter changes and consequent varying degrees of cognitive and movement problems.

Methods: A case study, discussing the coexistence of two pathogenic mutations in CSF1R and ABCD1 gene respectively, in a 46-year-old male with early onset and rapid progressive cognitive decline resembling frontotemporal dementia and parkinsonism is presented.

Results: The disease history is presented followed by the diagnostic work-up.

A 46 yo male, developed a severe dementia within less than a year, initially presented with inappropriate behavior, followed by apathy, poor planing and judgment, perseverations, verbal fluency difficulties with agrammatism, soon leading to aphasia. Ten months after the initial cognitive symptoms, movement problems occurred, presented with L-dopa non-responsive parkinsonism (bradykinesia, hypomimia, tremor and rigidity) later associated with presence of pathological reflexes and apraxia. Three years after the initial symptoms onset, the patient is bedridden with severe swallowing difficulties and emotional incontinence.

After completing a thorough diagnostic work-up to exclude reversible causes for dementia, infectious, vascular, autoimmune, and paraneoplastic conditions, the neurodegenerative spectrum of disorders was implied as an underlying cause for the clinical syndrome presented. The white matter changes on the repeated brain MRI scans suggested a leukodystrophy pattern which led to the genetic testing.

Using NGS (Next Generation Sequencing) and analyzing 4800 clinically relevant genes we concluded that both of the pathogenic mutations found in each of the genes CSF1R (c.2381T>C(p.Ile794Thr) and ABCD1, could possibly explain the clinical syndrome presented, but having plasma levels of very long-chain fatty acids (VLCFA) within referent range, puts weight on the ALSP diagnosis.

The follow up of our patient is of immense importance as having these rare genetic conditions coexisting in a same patient is a rarity of its own that rises diagnostic, therapeutic, and academic dilemmas.

Conclusions: Genetic testing should be included in the diagnostic work-up when evaluating an early onset, rapid progressive dementia associated with atypical parkinsonism, as rare diseases are misdiagnosed, often labeled with more common diagnosis. Even though there might not be a cure for most of them, disclosing the correct diagnose and offering genetic counseling is of no less importance.

P 050
Brain atrophy correlates with neuropsychological examination in Parkinson's disease patients

S. Szlufik[1], K. Duszynska-Was[1], K. Szalata[2], P. Romaniuk[2], M. Karolak[2], A. Drzewinska[1], D. Koziorowski[1]
[1]Medical University of Warsaw, Department of Neurology, Faculty of Health Sciences, Warszawa, Poland, [2]Medical University of Warsaw, Department of Neurology, Students' Scientific Group, Faculty of Health Science, Warszawa, Poland

Background: The neuropsychological examination and MRI are very important parts of PD patients' assessment before DBS procedure. So far, it is not clear if the brain atrophy in PD patients correlates with the neuropsychological deficits what would be a crucial predictive factor of post-DBS neuropsychological deterioration.
The aim of this study was to evaluate the estimate the possible correlations between brain atrophy in Parkinson's disease patients with the neuropsychological examination.
Methods: The study group consists of 62 PD patients who were the candidates to DBS STN procedure, from which 53 patients performed all neuropsychological tests and preoperative MRI. The brain atrophy parameters were measured by two independent evaluators.
Results: The brain cortical and subcortical atrophy parameters correlate with the neuropsychological evaluations, mainly in executive functions, language functions as well as concentration of attention and working memory ($p<0,05$).
Conclusions: Brain atrophy may be a neuroimaging biomarker of the level of cognitive decline in PD patients.

Parkinson Disease: Genetics

P 051 (GPT)
Polygenic resilience inheritance modulates the penetrance of Parkinson's disease genetic risk factors

H. LIU[1], M. Dehestani[1], C. Blauwendraat[2], M.B. Makarious[2], H. Leonard[2], J.J Kim[2], C. Schulte[1], A. Noyce[3], B.M Jacobs[3], I. Foote[3], M. Sharma[4], M. Nalls[2], A. Singleton[2], T. Gasser[1], S. Bandres-Ciga[2]
[1]Hertie Institute, Neurodegeneration Department, Tuebingen, Germany, [2]National Institutes of Health, Laboratory of Neurogenetics, Molecular Genetics Section, National Institute on Aging, Bethesda, United States, [3]Queen Mary University of London, London, London, United Kingdom, [4]Institute for Clinical Epidemiology and Functional Biometry, University of Tuebingen, Tuebingen, Germany

Background: There is very little known about the genetic architecture of resilience in Parkinson's disease (PD). The aim of the current study is to understand why some individuals avoid developing PD in spite of being at high genetic risk, using the largest datasets of individual-level genetic data available to date.
Methods: Polygenic risk score was calculated to identify controls and matched PD cases with the highest burden of genetic risk for PD in the discovery cohort (IPDGC, 7,204 PD cases and 9,412 controls) and validation cohorts (COURAGE-PD, 8,968 cases and 7,598 controls; UKBB, 2,639 PD cases and 14,301 controls; AMP-PD, 2,248 cases and 2,817 controls).
A genome-wide association study meta-analysis was performed on these individuals to understand genetic variation associated with resistance to disease. Based on these estimates, we further constructed a polygenic resilience score, performed MAGMA gene-based analyses and explored the functional enrichment of resilience variants in molecular processes, cell types, and tissues.
Results: A higher polygenic resilience score was associated with a lower risk for PD (Beta= -0.130, SE = 0.022; P = 2.34e-09). Although no single locus reached genome-wide significance, MAGMA gene-based analyses nominated TBCA as a putative gene that merits further study. Subsequent functional enrichment analysis highlighted specific biological sub-processes underlying histone methylation, synaptic transmission, and molecule binding as potential pathways harboring resilience alleles that could mitigate the effects of PD risk loci.
Conclusions: The present study represents a comprehensive assessment of heritable genetic variation contributing to PD resistance. We perform the first GWAS of PD resilience to polygenic PD risk and conduct comprehensive follow-up analyses highlighting novel pathways potentially contributing to PD resilience. We show that a genetic resilience score can modify the penetrance of known and unknown PD genetic risk factors and therefore protect individuals carrying a high-risk genetic burden from developing PD.

P 052

Autophagy-lysosomal and mitochondrial polygenic risk scores in Parkinson's disease

M. Dehestani[1], *H. Liu*[1], *C. Schulte*[1], *V. Bansal*[2], *T. Gasser*[1]

[1]Hertie Institute for Clinical Brain Research, University of Tuebingen, Department of Neurodegenerative Disease, Tuebingen, Germany, [2]German Center for Neurodegenerative Disease DZNE, Tuebingen, Germany

Background: Polygenic Risk Scores (PRS) are calculated as the weighted number of genetic risk alleles in an individual's genome, with the risk alleles and their weights typically derived from the results of genome-wide association studies (GWAS). Pathway-specific PRS are genetic scores based on SNPs corresponding to genes involved in major disease pathways and can be used for stratification of patient cohorts for treatment trials targeting specific disease mechanisms.

The aim of this study is to assess and compare the predictive value of pathway PRS , including mitochondrial (Mito) and autophagy-lysosomal pathways (ALP), to PRS generated from all GWAS hit SNPs (Hit model) in predicting Parkinson's disease (PD) status as well as relevant clinical outcomes.

Methods: PRS models were constructed using the clumping-and-thresholding approach in a German population comprising 686 cases and 544 controls using data from the largest and most recent PD GWAS. Their predictive power and predictive accuracy were measured precisely in a training population and subsequently were tested in an independent population.

Results: We show that the pathway PRS can predict PD status and certain clinical outcomes including age of onset and cognitive score. We also demonstrated that both Mito and ALP PRS is significantly associated with later age of onset. Also, significant negative correlation was observed between Mito PRS and cognitive scores.

Conclusions: Our results add to accumulating evidence supporting the involvement of mitochondrial and autophagy-lysosomal pathways in PD. They may help to identify patients with the highest genetic risk attributable to these pathways.

P 053 (GPT)

Diagnostic utility of whole-exome sequencing in early onset and familial Parkinson's disease: Preliminary findings in a regional centre study

V. Rački[1,2], M. Hero[1,2], G. Rožmarić[3], V. Vuletić[1,2]

[1]Faculty of Medicine, University of Rijeka, Department of Neurology, Rijeka, Croatia, [2]Clinical Hospital Center Rijeka, Clinic of Neurology, Rijeka, Croatia, [3]Faculty of Medicine, University of Rijeka, Rijeka, Croatia

Background: Parkinson's disease guidelines lack clear criteria for genetic evaluation and testing. Parkinson's disease is a multifactorial disease, and an estimated 5-10% can be contributed to monogenic causes. Identifying those patients remains a diagnostic challenge. The latest recommendations by EFNS/MDS-ES regarding Parkinson's disease genetic testing suggest that its' rationale should be assessed individually and performed only for a few select genes. Exome sequencing enables us to simultaneously analyse a large number of genes. We aimed to assess the clinical application of genetic testing for early onset and familial Parkinson's disease, by using exome-sequencing of evidence-based Parkinson's disease-associated gene panel.

Methods: Our study cohort includes patients from the Clinic of Neurology at the Clinical Hospital Centre Rijeka, referred to genetic testing during 2021. The inclusion criteria were confirmed clinical Parkinson's disease diagnosis based on United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria, and either sporadic early onset Parkinson's disease (<50 years) or familial Parkinson's disease with at least one affected 1st-degree relative. 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.

Results: We have performed exome sequencing in 25 Parkinson's disease patients, of which 14 were early onset and 11 were familial patients. Causative pathogenic mutations have been confirmed in 3 patients (12%, GBA n=2, LRRK2 n=1), while variants of uncertain significance were found in 9 patients (36%, ATP13A2 n=2, LRRK2, SNCA, PSEN1, GCDH, HEXA, SORL1, THAP1 n=1 for each).

Conclusions: 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 054
Biomarkers of Parkinson's disease

A. Kondybayeva[1], A. Aralbayeva[2], S. Kamenova[1], A. Akimniyazova[1], A. Pyrkova[3], A. Ivashchenko[3], K. Kuzhybayeva[1]

[1]Al-Farabi Kazakh National University, Faculty of Medicine and Health Care, Almaty, Kazakhstan, [2]Asfendiyarov Kazakh National Medical University, Neurology, Almaty, Kazakhstan, [3]Al-Farabi Kazakh National University, Faculty of Biology and Biotechnology, Almaty, Kazakhstan

Background: Parkinson's disease (PD) exhibits the second-highest rate of mortality among neurodegenerative diseases. PD is difficult to diagnose and treat due to its polygenic nature.

Methods: In recent years, numerous studies have established a correlation between this disease and miRNA expression; however, it remains necessary to determine the quantitative characteristics of the interactions between miRNAs and their target genes.

Results: In this study, using novel bioinformatics approaches, the quantitative characteristics of the interactions between miRNAs and the mRNAs of candidate PD genes were established. Of the 6,756 miRNAs studied, more than one hundred efficiently bound to mRNA of 61 candidate PD genes. The miRNA binding sites (BS) were located in the 5'-untranslated region (5'UTR), coding sequence (CDS) and 3'-untranslated region (3'UTR) of the mRNAs.

In the mRNAs of many genes, the locations of miRNA BS with overlapping nucleotide sequences (clusters) were identified. Such clusters substantially reduced the proportion of nucleotide sequences of miRNA BS in the 5'UTRs, CDSs, and 3'UTRs. The organization of miRNA BS into clusters leads to competition among miRNAs to bind mRNAs.

Differences in the binding characteristics of miRNAs to the mRNAs of genes expressed at different rates were identified. Single miRNA BS, polysites for the binding for one miRNA, and multiple BS for two or more miRNAs in one mRNA were identified. Evolutionary changes in the BS of miRNAs and their clusters in 5'UTRs, CDSs and 3'UTRs of mRNA of orthologous candidate PD genes were established.

All tables can be found here.

Conclusions: Based on the quantitative characteristics of the interactions between miRNAs and mRNAs candidate PD genes, several associations recommended as markers for the diagnosis of PD.

P 055 (GPT)

PLA2G6-associated neurodegeneration in three different populations-case series

L. Milanowski[1,2], R. Hanna AL-Shaikh[2], V. Holla[3], K. Kurihara[4], R. Yadav[3], N. Kamble[3], B. Muthusamy[5], D. Koziorowski[1], S. Szlufik[1], D. Hoffman-Zacharska[6], S. Fujioka[4], O.A. Ross[7], K. Wierenga[8], Z.K. Wszolek[2], P.K. Pal[3]

[1]Medical University of Warsaw, Faculty of Health Science, Department of Neurology, Warsaw, Poland, [2]Mayo Clinic, Department of Neurology, Jacksonville, United States, [3]National Institute of Mental Health & Neurosciences, Department of Neurology, Bengaluru, India, [4]Fukuoka University, Department of Neurology, Fukuoka, Japan, [5]Bengaluru, India and Manipal Academy of Higher Education, Institute of Bioinformatics, Manipal, India, [6]Institute of Mother and Child, Department of Medical Genetics, Warsaw, Poland, [7]Mayo Clinic, Department of Neuroscience, Jacksonville, United States, [8]Mayo Clinic, Department of Clinical Genomics, Jacksonville, United States

Background: The PLA2G6-associated neurodegeneration (PLAN) is extremely rare autosomal recessive genetic disease caused by variants in the PLA2G6 gene. PLAN disorders are classified as infantile neuroaxonal dystrophy (INAD), a juvenile onset form called atypical neuroaxonal dystrophy (NAD) or an adult-onset type called PLA2G6-related dystonia-parkinsonism.

However, there are patients placed between these categories showing that there is much more complicated phenotypic picture of those disorders. The aim of this study was clinical and molecular characterization of newly diagnosed patients from three different populations.

Methods: Eleven patients (1 from Poland, 1 from Japan, and 9 from India) were presented to four different institutions in four different countries. All patients underwent a comprehensive chart review to document their clinical visits and track their disease course, family history, symptoms of onset, disease progression, findings on neurological and neuropsychological evaluation, neurophysiologic studies, radiologic studies, and ophthalmologic exam findings.

Results: We reviewed clinical data for all 11 patients (3 with adult dystonia-parkinsonism and 8 with atypical neuroaxonal dystrophy). Ages at onset ranged from 1 to 36 years, with a median of 15 and a mean of 14.5 years. Electroencephalography was abnormal in two patients. Nerve conduction studies demonstrated sensory motor axonal neuropathy in one patient. Visual evoked potentials were conducted in two patients and were normal. Brain MRI scans were performed for all 11 patients. Magnetic resonance angiography was performed for one patient and SPECT was conducted for 3 patients.

Conclusions: The PLAN is very heterogenous condition. The PLA2G6 gene analysis should be always considered in patients with early onset parkinsonism, especially with early neuropsychiatric manifestations or in newborns with psychomotor regression and slower development with concomitant movement disorders.

P 056 (GPT)
Plasma miR-153 and miR-223 levels as potential biomarkers in Parkinson's disease

W. Chen[1]
[1]Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Department of Neurology, Shanghai, China

Background: Small molecule RNAs (miRNAs)could induce down-regulation of α-synuclein (SNCA)expression by binding the 3′ untranslated region of SNCA, thus playing an important role in the pathogenesis of Parkinson's Disease (PD).Recent studies suggest that SNCA related miRNAs in cerebrospinal fluid and saliva are promising PD biomarkers. Research on those miRNAs in plasma is rare in PD patients.
Methods: MiR-7, miR-153 and miR-223 levels were detected in plasma of 75 PD patients and 73 normal controls (NCs) via real-time quantitative polymerase chain reaction. The receiver operating characteristic (ROC) curves were delineated to evaluate their diagnostic value in PD. In addition, their associations with demographic, key motor and non-motor symptoms were explored by serial scales.
Results: The expression levels of plasma miR-153 and miR-223 were significantly decreased in PD patients relative to NCs. The area under the ROC curve separating PD from NCs was 63.1% for miR-153 and 86.2% for miR-223. Plasma miR-153 level in de novoPD was lower than that in treated patients (p=0.006), its level increased gradually with disease duration (r=0.358, p=0.002) and Unified Parkinson's Disease Rating Scale part III score (r=0.264, p=0.022). Plasma miR-223 level was decreased in patients with clinical probable rapid eye movement sleep behavior disorder (cpRBD) compared with those without cpRBD (p<0.001), and its level was negatively associated with RBD screen questionnaire score (r=-0.334, p=0.003). Multiple linear regression analysis revealed that disease duration(p=0.049) was the independent associated factor of miR-153 level; whereas, RBDSQ(p=0.009) was related to miR-223 level in PD.
Conclusions: Plasma miR-153 and miR-223 level could be potential biomarkers of PD.

P 057
Genetic heterogeneity on sleep disorders in Parkinson's disease: a systematic review and meta-analysis

J. Huang[1], *Y. Cheng*[1], *C. Li*[1], *H. Shang*[1]
[1]West China Hospital, Sichuan University, Department of Neurology, Laboratory of Neurodegenerative Disorders, Rare Diseases Center, National Clinical Research Center for Geriatrics, Chengdu, China

Background: The conclusion of the association between causative genes of Parkinson's disease (PD) and sleep disorders in PD have not been consistent.
Methods: We performed a systematic review and meta-analysis to investigate the role of genetics on sleep disorders in patients with PD and asymptomatic genetic carriers of PD. We calculated the odds ratios (ORs) for binary variables and standard mean difference (SMD) for continuous variables with 95% confidence intervals (CIs) using the Mantel-Haenszel statistical method.

Results: Seventeen studies on glucocerebrosidase (*GBA*), 25 studies on Leucine-rich repeat kinase 2 (*LRRK2*) and 7 on parkin (*PRKN*) genes were selected for quantitative analysis, and 3 studies on alpha-synuclein gene (*SNCA*) for qualitative analysis. PD patients carrying *GBA* variants had a significantly higher risk and severity for rapid-eye-movement behavior disorders (RBD) (OR, 1.82; 95% CI, 1.21-2.74; SMD, 0.33; 95% CI, 0.21-0.45). Asymptomatic carriers with *GBA* variants had higher severity of RBD during follow-up. PD patients with *LRRK2* G2019S variants had lower risk and severity for RBD compared with those without *LRRK2* G2019S. Variants of *GBA*, *LRRK2* and *PRKN* did not affect the risk and severity of excessive daytime sleepiness (EDS) and restless legs syndrome (RLS) in PD.
Conclusions: We found several PD causative genes associated with sleep disorders in PD patients at clinical stages, as well as asymptomatic stages. *GBA* variants increase the risk and severity of RBD in the clinical stages of PD and severe the symptom of RBD in the prodromal stages of PD. *LRRK2* G2019S was negatively associated with RBD in patient with PD. These findings provide evidence that genetic heterogeneities play a role in the development of sleep disturbance, especially RBD, in PD and in the prodromal stage of PD.

P 058
On the question of genetic predisposition to Parkinson's disease

K. Daminova[1], *D. Akramova*[1,1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: The initial purpose of the work is to study the clinical and geneological features of Parkinson's disease.
Methods: The study included 213 patients with PD, 90 (42.25%) women, 123 (57.75%) men, whose average age was 46.17 ± 0.63 years, mainly of Uzbek nationality. A control group of 20 healthy people of Uzbek nationality of the same age without signs of PD.To exclude other causes of Parkinson's syndrome, patients underwent CT or MRI of the brain.
Results: Due to the supposed differences in the pathogenesis of early and late forms of PDThe subgroup of early parkinsonism consisted of 79 (37.09%) patients in whom the symptoms of the disease manifested before the age of 45, and 76 (35.68%) patients with a burdened family history, the subgroup of late parkinsonism accounted for 58 (27.23%) patients with an age of onset of primary parkinsonism> 45 years. A detailed pedigree was compiled, which included information about diseases in 2-3 generations of the family. Genetic material was collected from both parental lines by cross-examining both parents, sometimes grandparents. A total of 1741 people were analyzed in the model population.
The data obtained were compared with the generalized family response of 20 practically healthy people, in the model population of which 168 people were analyzed, of which the occurrence of PD was not noted. A burdened family history of PD was observed in 76 (35.68%) cases, 44 men (57.89%), 32 women (42.11%). In families of probands, PD in generations in relation to the total number of patients with each concentration is III - 16 (21.05%); II- 23 (30.26%); I- 37 (48.68%).
Conclusions: It turned out that PD is more often affected by relatives of the I degree of kinship 37(48.68%), which in relation to the total number of patients with this concentration is 35.68%, and men accounted for 44(20.66 ± 2.08%) cases.

P 059

Parkin gene may rescue mitochondrial dysfunction induced by FUS expression in Drosophila

E.J. Choi[1], *S.J. Cha*[2], *D.G. Lee*[3], *K. Kim*[4]

[1]Soonchunhyang University, Gumi Hospital, Neurology, Gumi, Korea, Republic of, [2]Soonchunhyang University, Department of Medical Biotechnology, Asan, Korea, Republic of, [3]UBC Faculty of Medicine, Vancouver, Canada, [4]Soonchunhyang University, Medical Biotechnology, Asan, Korea, Republic of

Background: Parkin gene encodes an ubiquitin ligase (E3), as we know, induces mitophagy to control mitochondria quality. And loss of Parkin gene results in degradation of mitochondria. Parkin, PINK1 and DJ-1 are associated with mitophagy and mitochondria homeostasis. FUS is a DNA/RNA-binding protein for RNA processing, splicing, transport, and translation, by regulating cellular localization and degradation. We would do this study to understand the characteristics or the interaction between Parkin gene and FUS expression in mitochondria of Drosophila, fruit flies.

Methods:

A. Drosophila stocks. All Drosophila stocks were kept under standard food conditions, normal temperature conditions (25°C), and normal humidity conditions (60%). Those flies were obtained from the Bloomington Drosophila Stock Center, Baylor College of Medicine and University of Pennsylvania.

B. Western blot analysis.

C. Locomotive activity assay.

D. Immunohistochemistry.

E. Blue native polyacrylamide gel electrophoresis (BN-PAGE).

F. ATP assay. A 27-day-old fly thorax was homogenized in 100 µL of extraction buffer (6 M Guanidine-HCl, 100 mM Tris, 4 mM EDTA, pH 7.8) to inhibit ATPase.

Results:

1. Parkin rescues the locomotive defect in FUS-expressing flies.
2. Total FUS expression is unaffected by Parkin in heads extracts.
3. FUS-induced mitochondrial dynamic imbalance is not related to rescue effects for Parkin.
4. Down-regulation of complex I and III subunits is compensated by Parkin over-expression.

Conclusions: From this study, we could suggest the first, Parkin was able to rescue the healthy phenotype from the FUS-induced defective phenotype, including impaired locomotive ability and mitochondrial dysfunction. The second, locomotive disability of FUS-overexpressing flies was alleviated by Parkin and the Parkin is we screened as a novel genetic modifier.

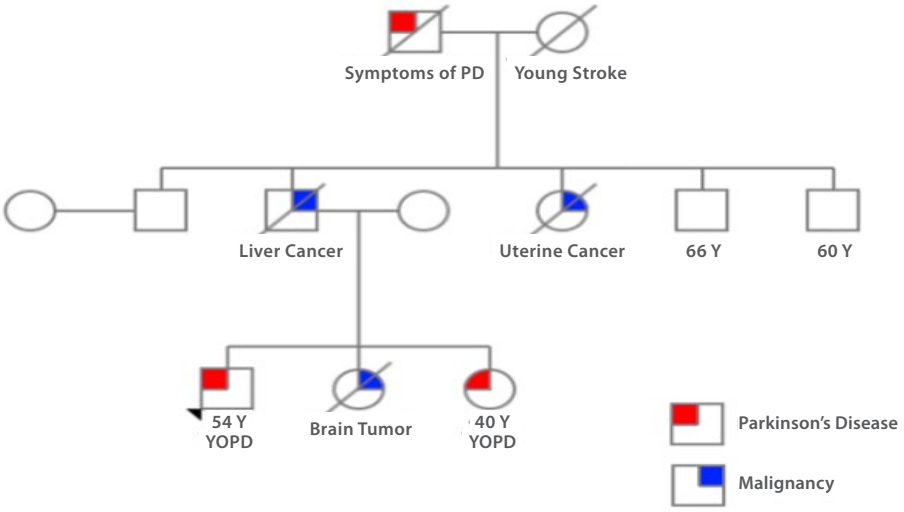
Finally, Parkin is the neuroprotective regulator for FUS-induced proteinopathy and it recovered the protein levels of mitochondrial complexes I and III by Parkin overexpression and FUS flies.

P 060 (GPT)

Heads - It's Parkinson's; tails - it's cancer, a kindred of Parkinsonism and Malignancies

M. Matta[1], *H. Singh*[1], *N. Sawal*[2], *S. Arjun*[1]
[1]Government Medical College and Hospital, Chandigarh, India, [2]Fortis Mohali, Neurology, Mohali, India

Background: Patients with Parkinson's Disease (PD) have increased risk of Melanoma and Prostate Cancer. PARK2, DJ-1 and LRRK2 are genes implicated in both Familial PD and cancer. A 54-year-old male presented to us with generalised stiffness of body for 15 years, starting first from the right lower-limb. His sister also presented with stiffness in her left lower limb for two years, involving right-limb for last 6 months, starting distally and gradually involving whole of limb.
We had examined 11 members of a three-generation family, where three individuals had features suggestive of Parkinson's disease and three subjects had a history of cancers. His father had Liver cancer, paternal-aunt had Stomach malignancy and younger sister had a Brain Tumour. The individuals who had a malignancy were spared from PD.



Methods: Only two subjects of the eleven examined were wiling for a Genetic analysis, which was done using Whole-Exome-Sequencing (WES).
Results: In our kindred there is family history of Parkinsonism, there is family history of cancers. Interestingly family members having Parkinsonism are not having malignancies and members having malignancy are not having Parkinsonism. Analysis of WES data allowed us to identify a novel homozygous deleterious non-synonymous variation (D479H) in ZNF837 (Zinc Finger Protein 837) in the index case and his sister.
Conclusions: This study is first to report any disease association of ZNF837 gene, that too with a neurodegenerative phenotype.

P 061 (GPT)
Green tea intake and Parkinson's disease progression: a Mendelian randomization study

C. Li[1], J. Lin[1], T. Yang[1], H. Shang[1]
[1]West China Hospital Sichuan University, Neurology, Chengdu, China

Background: Epidemiological studies have suggested green tea intake was associated with risk of Parkinson's disease (PD). However, whether green tea has an effect on PD progression is unknown.
Methods: To evaluate the role of green tea intake in PD progression, we conducted a two-sample Mendelian randomization analysis using summary statistics from genome-wide association study of green tea intake (N=64,949), age at onset (N=28,568) and progression (N=4,093) of PD.
Results: One standard deviation increase in genetically determined green tea intake was significantly associated with slower progression to dementia (OR:0.87, 95% CI:0.81~0.94, P: 3.48E-04) after Bonferroni correction. Meanwhile, higher green tea intake was nominally associated with slower progression to depression, and lower risk of dementia, depression, hyposmia and insomnia at baseline. The results were robust under all sensitivity analyses.
Conclusions: These results facilitate novel therapeutic targets to slow down the progression of PD in clinical trials.

P 062 (GPT)
Genomic analyses of a large Swedish multi-incident kindred with autosomal dominant Parkinson's disease with dementia

E. Ygland Rödström[1], A. Soto-Beasley[2], E. Englund[3], E. Kafantari[1], D.W. Dickson[2], Z.K. Wszolek[4], A. Puschmann[5], O.A. Ross[6]
[1]Lund University, Skåne University Hospital, Department of Clinical Sciences Lund, Neurology, Lund, Sweden, [2]Mayo Clinic, Department of Neuroscience, Jacksonville, United States, [3]Lund University, Skåne University Hospital, Department of Clinical Sciences Lund, Oncology and Pathology, Lund, Sweden, [4]Mayo Clinic, Department of Neurology, Jacksonville, United States, [5]Lund University, Skåne University Hospital, Department of Clinical Sciences Lund, Neurology, Lund, Lund, Sweden, [6]Mayo Clinic, Department of Neuroscience, Department of Clinical Genomics & Mayo Graduate School Neuroscience Track, Jacksonville, United States

Background: The known genetic causes for Parkinson's disease (PD) only explain a small proportion of the familial aggregation of PD. Despite intensive efforts by researchers internationally, identifying and confirming additional monogenic causes for PD has been difficult.
Methods: We examined 16 members of a large family with multi-incident PD and dementia. Eight members were examined by whole exome (WES) or whole genome sequencing. Rare variants co-segregating with the disease were evaluated based on their distribution in additional family members and known gene functions. WES data from 843 PD cases and 885 controls were screened for the two most highly ranked candidate variants and used for gene burden analysis.

Results: Clinically, all affected family members had typical PD with cognitive decline. Two affected individuals showed typical PD neuropathology. Out of nine genetic variants identified, we highlighted two as good candidates for causing this family's PD.
However, co-segregation with PD was imperfect and this study was complicated by the fact that some genotyped family members showed mild motor symptoms of uncertain cause, or cognitive decline without apparent motor dysfunction. Gene burden analysis showed no difference between cases and controls in the frequency of potentially deleterious variants in the top-candidate genes.
Nonetheless, factors that could indicate an impact of either of the two top-candidate genetic variants were found as one of the variants was identified in one additional familial PD proband from the case series and genetic variants in the other top-candidate gene had previously been associated with an increased risk for PD in humans.
Conclusions: Our study was not able to determine a single high-impact variant as the cause of PD with cognitive decline in the family despite detailed clinical and genetic assessments, but we nominate two potential candidate variants. Reduced penetrance and phenocopies may complicate genomic studies of families with PD.

P 063

Leucine-rich repeat kinase2 (LRRK2) associated Parkinson's disease: less vulnerable during Covid-19 pandemic?

A. Gharbi[1], *I. Kacem*[1,2], *I. Sghaier*[1], *S. Mrabet*[1,2], *A. Souissi*[1], *A. Gargouri*[1,2], *A. Nasri*[1,2], *R. Gouider*[1,2]
[1]Razi University Hospital, Department of Neurology, LR18SP03, Manouba, Tunisia, [2]Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

Background: COVID-19 pandemic constitutes a major global stressful event of exceptional international scope. To our knowledge, there were no previous studies exploring the impact of such an event on genetic groups of Parkinson's disease (PD).
Our aim was to determine short and long-term impact of COVID-19 on motor(MS) and non-motor(NMS) symptoms among Tunisian PD patients according to LRRK2-carrying status.
Methods: In a longitudinal retrospective study, a survey assessing changes of MS and NMS in PD patients was conducted in two steps: T1 (short-term) in May-June2020 and T2 (long-term) in May-June2021. Resilience was evaluated with the Brief Resilience Scale (BRS). Participants were screened for G2019S-*LRRK2* mutation.
Results: We included 110 patients (37% *LRRK2*-PD) for T1-survey and 52 among them (40% *LRRK2*-PD) in T2. *LRRK2*-PD had less perceived aggravation. Significant differences emerged mainly on long-term for NMS concerning dysautonomic symptoms, RBD (p=0.0078), memory disorders (p=0.0137), decreased appetite (p=0.024), apathy (p=0.035), anxiety (p=0.0114) and depression (p=0.045), all more affected in non-*LRRK2*-PD.
In this group, anxiety and depression were associated to aggravation of all MS and several NMS. *LRRK2*-PD patients tended to be more resilient (80% vs 68%). Yet, resilience was associated with absence of aggravation of MS and NMS only in non-*LRRK2*-PD.

Conclusions: This is the first study to explore the potential short and long-term effects of COVID-19 pandemic on subjective perceived changes of MS and NMS in particular genotypic PD subgroups. *LRRK2*-PD patients had less perceived aggravation and were more resilient; while non-*LRRK2*-PD had more long-term-impaired NMS linked to anxiety, depression and limited resilience.

P 065
Exploration of the Immune-related genes Signatures and potential Molecular Mechanisms shared between AD and PD

K. Zhou[1], *Y. Song*[2], *L. Jin*[3]
[1]Tongji University, Department of Neurology, Tongji Hospital, School of Medicine, shanghai, China, [2]Tongji University, Fundamental Research Center, Department of Neurology and Neurological Rehabilitation, Shanghai Yangzhi Rehabilitation Hospital, School of Medicine, shanghai, China, [3]Tongji University, Fundamental Research Center, Department of Neurology and Neurological Rehabilitation, Shanghai Yangzhi Rehabilitation Hospital, School of Medicine;, shanghai, China

Background: Alzheimer's disease (AD) and Parkinson's disease (PD) are the two most common chronic neurodegenerative disorders. Neuroinflammatory is involved in the pathogenesis of both AD and PD, but the specific mechanisms shared remain limited. This study aims to screen the potential immune-related genes (IRGs) and assess their value on the prognosis and progression of the two disorders.
Methods: Differentially expressed genes (DEGs) in two diseases were explored based on the GEO datasets. The shared IRGs were identified by taking the intersection among the IRGs downloaded from the ImmPort database and DEGs in AD and PD. We identified the hub IRGs with protein-protein interaction (PPI) networks based on six different algorithms. To explore the multiple biological functions of these shared IRGs, we performed a series of function and pathway enrichment analyses. Finally, the expression levels of these shared IRGs were validated based on a PD dementia (PDD) dataset and evaluated the diagnostic performance by ROC curves.
Results: A total of 375 potential IRGs in AD and 97 in PD were detected, respectively. And 36 overlapped shared IRGs by the two disorders were detected. 11 hub IRGs (SLIT2, SLIT1, SEMA6D, SEMA3G, FLT1, CXCR4, PPARG, SOCS3, FGF13, AGRP, FGF11) were identified among the 36 shared IRGs by a PPI network through 6 different algorithms. The enrichment analysis mainly focused on regulating cytokine-mediated signaling pathways. Finally, combining the ROC analysis and verification analysis showed, these shared hubs IRGs (CXCR4 and FLT1) have brilliant prognostic values (AUC>0.7) and whose expression level was statistically significantly elevated ($p<0.05$) in the PDD brain samples compared with the age-matched controls.
Conclusions: This work highlighted the existence of shared immune-related mechanisms between AD and PD and described the CXCR4 and FLT1 as candidate biomarkers for developing novel strategies for prognostic evaluation, and therapeutic decision making for AD and PD patients.

P 066 (GPT)

Charcot-Marie-Tooth Disease associated with Parkinson Disease, about a case

H. Pacheco Mendoza[1], *V. Alvarez Rivera*[1]
[1]Universidad Nacional Autonoma de Mexico, Mexico City, Mexico

Background: Charcot-Marie-Tooth disease (CMT) is a peripheral neuropathy accompanied by weakness, atrophy, pes cavus, tremor, hearing loss and changes in sensitivity. In Parkinson Disease (PD), patients course with bradykinesia, rigidity, tremor, and postural instability. The presentation of both pathologies in a same individual is rare and cases are related to mutations of the *LRSAM1* gene.
Methods: An 81-year-old woman with a history of 2 grandchildren with MTC. Onset at age 17 with deformity in both feet and high plantar arch. He presented generalized weakness and changes in sensitivity, progressed slowly over time with difficulty walking and falls. At 75 years, she presented bradykinesia, generalized and tremor in upper limbs, in addition to cognitive impairment. This a novel case of a Mexican patient who came to Internal Medicine hospitalization, due to liver failure. After it's first evaluation, we found out that patient course with both CMT and PD.
We recorded (previously patient consent sign) and performed several scales in her evaluation, such as UPDRS, MDS-UPDRS, NMSS, PDQ-39, MMSE and MoCA test, also a Levodopa test to evaluate PD, SARA and ICARS and clinical examination to evaluate CMT. We also performed neuroimage studies to a better characterization of both entities.
Results: A levodopa test was performed, with improvement in motor symptoms, cognitive tests with severe cognitive impairment, clinimetric scales for moderate ataxia. Simple tomography of the skull with cortico-subcortical atrophy and Magnetic resonance imaging (T1, T2, Flair, Swan).
Conclusions: Few cases of CMT and PD have been reported in the literature, finding 2 altered genes that could be the link between both entities. In addition, there is another important factor, limb ataxia, which has also been found to be related to PD and CMT. There is the possibility of a relationship between both diseases, however, it would be necessary to carry out genetic studies to be able to identify them due to the great heterogenicity of both neurological diseases.

Parkinson Disease: Subtypes, natural course

P 067
Relationship between risk and protective factors and clinical features of Parkinson's disease

M. Costanzo[1], D. Belvisi[2], R. Pellicciari[3], A. Fabbrini[2], G. Ressa[4], S. Pietracupa[1], M. De Lucia[1], N. Modugno[1], F. Magrinelli[5], C. Dallocchio[6], T. Ercoli[7], A. Nicoletti[8], M. Zappia[8], P. Solla[7], M. Bologna[2], G. Fabbrini[2], M. Tinazzi[5], A. Conte[2], A. Berardelli[2], G. Defazio[7]

[1]IRCCS Neuromed, Pozzilli, Italy, [2]Sapienza, University of Rome, Department of Human Neurosciences, Rome, Italy, [3]"Aldo Moro" University of Bari, Department of Basic Medical Sciences, Bari, Italy, [4]Albert Einstein College of Medicine, Department of Developmental and Molecular Biology, New York, United States, [5]University of Verona, Department of Neurosciences, Verona, Italy, [6]ASST Pavia-Ospedale Civile di Voghera, Voghera, Italy, [7]University of Cagliari, Department of Medical Sciences and Public Health, Cagliari, Italy, [8]University of Catania, Department G.F. Ingrassia, Catania, Italy

Background: Non-genetic risk and protective factors play a relevant role in PD development but the relationship between these factors and PD clinical features is unknown. The aim of the present multicenter study was to investigate possible associations between risk/protective factors and clinical manifestations in a large sample of PD patients.

Methods: Six hundred ninety-four patients with PD participated in the study. Patients underwent a clinical evaluation assessing motor and non-motor symptom severity. Motor symptoms were evaluated by the International Parkinson and Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale part III. Non-motor symptoms were evaluated by the Non-Motor Symptoms Scale. Risk and protective factors were previously identified in the present population and included coffee consumption, cigarette smoking, and physical activity as protective factors and a family history of PD, dyspepsia, and exposure to toxic agents and general anesthesia as risk factors. Linear regression models were used to identify possible associations between risk/protective factor profile and clinical variables.

Results: Coffee consumption was associated with an older age at onset and milder motor symptom severity. Non-motor symptom severity was found to be positively associated with dyspepsia and inversely associated with physical activity. We did not find any association between risk/protective factor profile and motor subtype of patients.

Conclusions: Risk and protective factors of PD development are associated with PD clinical features. This finding may represent the first step in the development of new preventive approaches able to slow disease onset and mitigate the extent of clinical manifestations.

P 068 (GPT)

Amantadine treatment in Parkinson's disease patients as a modulatory factor of SARS-Cov-2 infection

S. Szlufik[1], *A. Chudzik*[2], *A. Przybyszewski*[2], *D. Koziorowski*[1]

[1]Medical University of Warsaw, Department of Neurology, Faculty of Health Sciences, Warszawa, Poland, [2]Polish Japanese Academy of Information Technology, Department of Informatics, Warsaw, Poland

Background: Amantadine has been used for the prevention and treatment of viral influenza A, but more recently it is used mainly in PD patients. Previous studies showed a possible impact of amantadine on COVID-19 severity in patients using this drug due to other (neurological diseases, mainly PD). Therefore the aim of this study was to evaluate the possible impact of amantadine on the SARS-Cov-2 infection in Parkinson's disease (PD) patients.

Methods: It was a nation-wide survey performed in Polish PD population from 01.2021 till 01.2022. All members of Polish PD foundations have been asked to answer a survey – 140 PD patients filled the questionnaire consisting of 35 questions concerning the amantadine treatment, Parkinson's disease and SARS-Cov-2 infection history. The patients were divided into 2 groups: group A+ which was treated with amantadine (57 cases) and group A- (83 non-amantadine takers).

Results: We have observed more slight symptoms and progression of SARS-Cov-2 infection in PD patients taking amantadine (8 patients COVID-19+) than in PD patients not taking amantadine (12 patients COVID-19+). The symptoms of COVID-19 in A+ group were slight weakness, sweating or none of symptoms whereas group A- mainly demonstrated cough, smell loss, high temperature – one of group A- patients was hospitalized.

Conclusions: Amantadine treatment in PD patients can reduce the severity of SARS-Cov-2 infection in PD patients.

Parkinson Disease: Clinical assessment (including devices)

P 069
Effect of ventricular metrics on the treatment response in Parkinson's disease

J.-J. Lee[1], *J.S. Baik*[2]
[1]Ilsan Paik Hospital, Inje University College of Medicine, Department of Neurology, Goyang, Korea, Republic of, [2]Sanggye Paik Hospital, Inje University College of Medicine, Department of Neurology, Seoul, Korea, Republic of

Background: A myriad of factors affects the mechanism of actions on balance and gait in Parkinson's disease (PD). We sought to explore the impact of cerebral ventricular metrics on treating patients with PD.
Methods: The current registry-based retrospective cohort study enrolled 101 drug naïve and de novo patients with PD, whom were stratified by the level of Unified Parkinson's Disease Rating Scale (UPDRS) improvement in 1 year, following as a group of the Best (n = 31; UPDRS III, >10), the Moderate (n = 43; UPDRS III, 5-10), and the Modest (n = 27; UPDRS III, <5). The parameters of ventricular metrics include Evan's index (EI), frontal-occipital horn ratio (FOHR), callosal angle (CA), callosal height (CH), and temporal horn width (THW).
Results: The Best group demonstrated significantly the least metrics in ventricular dimension including EI (vs the Moderate vs the Modest; 0.23 ± 0.02 vs 0.24 ± 0.02 vs 0.26 ± 0.03; *p*, <0.001), FOHR (0.64 ± 0.05 vs 0.65 ± 0.05 vs 0.68 ± 0.05; *p*, 0.025), CA (111.12 ± 9.99 vs 112.43 ± 9.73 vs 98.14 ± 11.27; *p*, <0.001), and CH (22.02 ± 5.94 vs 22.05 ± 5.48 vs 25.89 ± 9.32; *p*, 0.048). Better improvement of the UPDRS III score were observed in patients with smaller ventricular metrics apiece (EI, correlation coefficient (*r*), 0.637; FOHR, *r,* 0.405; CA, *r*, -0.437; CH, *r,* 0.366).
Furthermore, every ventricular parameters were found to predict effectively the treatment response in patients with PD (regression coefficient, *ß* (SE); EI, 4.276 (0.921), *p* <0.001; FOHR, 4.199 (0.844), *p* <0.001; CA, 4.754 (1.458), *p* = 0.002; CH, 3.864 (0.874), *p* <0.001; THW, 2.500 (1.132), *p* = 0.030).
Conclusions: Our data demonstrated a negative effect of enlarged ventricle on treating PD patients who were void of evident ventriculomegaly. Larger dimension of ventricle might predict poor treatment response and prognosis in PD.

P 070

Continuous wavelet transforms to improve the accuracy of motor assessments of Parkinson's disease

T. Kosuri[1]
[1]Johns Hopkins University, Baltimore, United States

Background: Routine clinical and research assessments of persons with potential Parkinson's Disease (PD) involve the use of visual observation for structured review. Visual observation of structured examinations introduces inaccuracies, motivating the need to obtain precise measurements with instrumentation. We sought to develop a protocol to utilize continuous wavelet transforms (CWTs) to rate the severity of movements to obtain optimal classifications of PD.
Methods: We expressed CWTs of repetitive movements (finger tapping, hand motion, leg agility, pronation/supination, toe-tapping) for participants with PD as panels (Figure) for rating by visual inspection. Trained raters were instructed to check a box for an overall rating of:

0 normal
1 minimal
2 mild
3 moderate
4 worse

For individual abnormalities:

a interruptions
b slowing
c decreased amplitudes

The representations of the CWTs of a single extremity without identification of laterality were presented as panels to be scored by raters. Each panel contained six images corresponding to the axes of the positions of the accelerometers on the finger and wrist for the upper extremity or the toe and ankle for the lower extremity.
Results: Raters classified transforms by scoring particular abnormalities in the CWTs. Interruptions were identified on the CWTs as breaks in continuous horizontal segments of line; slowing was demonstrated by a negative sloping line; amplitude decrements were evident while examining the warmth of color. Therefore, lines of diminishing warmth from left to right were deemed to show decreasing amplitude.

i. 0 (no amplitude decrements, slowing, or interruptions seen)
ii. 1 (amplitude decrement seen by decrease in warmth of color)
iii. 2 (3-5 interruptions seen by halts in CWT)
iv. 3 (moderate slowing seen by negative sloping line)

Conclusions: A methodology for scoring CWTs of accelerometers on the extremities by a team of trained raters has generated a valuable dataset (Zieglelman, et al., 2020) for analysis and interpretation.

P 071 (GPT)
Prevalence and associated factors of malnutrition in patients with Parkinson's disease using CONUT and GNRI

Z. Jiang[1], R. Ou[1], Y. Chen[1], L. Zhang[1], Q. Wei[1], Y. Hou[1], X. Gu[1], B. Cao[1], K. Liu[1], H. Shang[1], W. Song[1]
[1]Sichuan University, Department of Neurology, West China Hospital, Chengdu, China

Background: Parkinson's disease (PD) is a common neurodegenerative disease, but its nutritional problems have not received enough attention. This study aims to identify the prevalence and associated factors of malnutrition in PD patients using two simple nutritional tools.
Methods: We conducted a large-scale cross-sectional study with 1478 PD patients and equal healthy controls (HC). The controlling nutritional status score (CONUT) and geriatric nutritional risk index (GNRI) were used for malnutrition stratification.
Results: By CONUT or GNRI, the prevalence of malnutrition in PD patients was higher than that in HC (40.7% vs. 25.3% and 11.1% vs. 2.1%, respectively). Subgroup analyses by gender or body mass index could not change the result.
The binary logistic regression model showed that malnutrition in PD was associated with male sex (OR=0.600, *P* <0.001), older age (OR=1.015, *P*=0.003), lower body mass index (BMI) (OR=0.942, *P* <0.001), higher levodopa equivalent daily doses (LEDD) (OR=1.001, *P* <0.001), worse motor symptoms (OR=1.012, *P*=0.004), more serious perceptual problems/hallucinations (OR=1.067, *P*=0.019) by CONUT.
In comparison, older age (OR=1.045, *P* <0.001), lower blood lymphocyte count (OR=0.607, *P*=0.006), lower serum total cholesterol levels (OR=0.991, *P* <0.001), dyskinesia (OR=2.231, *P*=0.002), worse motor symptoms (OR=1.016, *P*=0.015), more severe depression (OR=1.028, *P*=0.008) and perceptual problems/hallucinations (OR=1.061, *P*=0.033) were associated with malnutrition in PD by GNRI.
Conclusions: Our study indicated that malnutrition is more prevalent in PD patients than HC. Multidimensional risk factors for malnutrition in PD should be taken seriously.

P 072
Characteristic of impulse control disorders in Polish patients with Parkinson's disease

M. Toś[1], J. Siuda[1], A. Grażyńska[2]
[1]Medical University of Silesia, Department of Neurology, Katowice, Poland, [2]Medical University of Silesia, Department of Radiology and Nuclear Medicine, Katowice, Poland

Background: Parkinson's disease (PD) is characterized by typical motor symptoms and numerous non-motor symptoms (NMS). Impulse Control Disorders (ICDs) are the group of NMS with growing research interest.
The most frequently undertaken compulsive activities in PD include: pathological gambling, compulsive sexual behavior, compulsive buying, and binge-eating. The incidence of ICDs varies greatly depending on a country where the study was conducted.

In the European population, the prevalence of ICD ranges from 23.48% in the Spanish population to as much as 34.8% in the Finnish population. Our study aims to determine the incidence and risk factors of ICDs in the Polish population of patients with PD, since there were no such studies so far.

Methods: The study included 135 patients with idiopathic PD hospitalized between 2020 and 2021 in the Department of Neurology of the Medical University of Silesia. The occurrence of impulse control disorders was evaluated by the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP). The disease severity was assessed with the MDS-UPDRS and modified Hoehn-Yahr staging. Data about gender, age, PD duration, age at onset, and pharmacotherapy were also collected.

Results: ICDs were identified in 27.41% of PD patients in our group (pathological gambling in 5.19%, compulsive sexual behavior in 11.11%, compulsive buying in 10.37%, and binge-eating in 12.59%). 8.89% had 2 or more ICDs. Impulse control disorders were more common in PD patients treated with a dopamine agonist than those only on levodopa monotherapy (36.90% vs 11.76%; P=0.0015). Additional variables associated with ICDs were: longer disease duration, using higher doses of L-dopa, presence of motor complications, and sleep disorders.

Conclusions: The prevalence of ICDs is high in the Polish PD patients population. As expected, treatment with dopamine agonists was the major factor associated with the development of ICDs. Further studies are needed to better characterize ICDs in Polish PD patients.

P 074 (GPT)

Comparison of voice parameters, self-assessment of speech and sialorrhea levels in Parkinson's disease patients with and without swallowing problems

M. Sapmaz Atalar[1,2], *Ş.N. Oğur*[2], *G. Genç*[3]

[1]Bahçeşehir University, Neuroscience, İstanbul, Turkey, [2]University of Health Sciences, Speech and Language Therapy, İstanbul, Turkey, [3]University of Health Sciences, Şişli Etfal Training and Research Hospital, Neurology, Istanbul, Turkey

Background: Parkinson's disease (PD) is associated with a number of disorders that negatively affect the quality of life of patients including swallowing problems (SP), voice impairment, speech disorders and sialorrhea in addition to the cardinal motor findings of the disease.

We aimed to compare the voice parameters, self-assessment of speech and sialorrhea levels of PD patients with swallowing problems (PD-SP), and without SP (PD-nSP) to investigate the ability of these features in distinguishing PD-SP from PD-nSP.

Methods: 44 PD patients (20 PD-SP and 24 PD-nSP) were included. PD-SP were defined as the patients having Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part II-item 3 score ≥ 1.

Acoustic voice analysis including shimmer, jitter, harmonic to noise ratio, fundamental frequency (F0), standard deviation of F0, minimum F0 and maximum F0 was done using the Praat software via /a/ prolongation. The maximum phonation time (MPT), the longest periods of sustained pronunciation of /a/, was evaluated.

Voice Handicap Index (VHI), self assessment of speech on visual analog scale (VAS), Sialorrhea Clinical Scale for PD-Turkish (SCS-TR) and 10-item Eating Assessment Tool (EAT-10) were also performed.
All tasks were done during the "ON state" of all patients.
Results: There were 30 men and 14 women in our cohort. Mean age was 64,4 ± 9,8 years. Compared with PD-nSP, F0, maximum F0 values were increased, and the maximum phonation time (MPT) was decreased in PD-SP ($p<0,05$). VHI, VAS-Speech, SCS-TR and EAT-10 scores were higher in PD-SP ($p<0,05$).
Conclusions: This study reveals that PD-SP experienced more severe voice impairment, speech problems, and sialorrhea than PD-nSP. Developing diagnostic clinical evaluation tools to better understand the natural history and underlying pathophysiology of PD-SP and conducting studies on different treatment approaches will not be only promising for PD patients but also a guide for health professionals in the future.

P 075
Reliability and validity study of a Turkish version of the Sialorrhea Clinical Scale for Parkinson's disease (SCS-TR)

M. Sapmaz Atalar[1,2], G. Genç[3]
[1]Bahçeşehir Universty, Neuroscience, İstanbul, Turkey, [2]University of Health Sciences, Speech and Language Therapy, İstanbul, Turkey, [3]University of Health Sciences, Şişli Etfal Training and Research Hospital, Neurology, Istanbul, Turkey

Background: To evaluate the validity and reliability of the Turkish version of the Sialorrhea Clinical Scale for Parkinson's disease (SCS-PD) for use in clinical settings.
Methods: The original English version of SCS-PD has been adapted to Turkish (SCS-TR) in accordance with international guidelines. 41 patients with Parkinson's Disease (PD) and 31 healthy people were included in our study. SCS-TR, Movement Disorders Society United Parkinson's Disease Rating Scale (MDS-UPDRS) Part II (functional subscale 2.2 Saliva and drooling), Drooling Frequency and Severity Scale (DFSS) and The Non-Motor Symptoms Questionnaire (NMSQ) (1st question evaluating saliva) were administered to both groups. The adapted scale was re-tested in PD patients 2 weeks later.
Results: A statistically significant relationship was determined between the SCS-TR scale score and all similar scale scores (NMSQ, MDS-UPDRS, DFSS) ($p<0.001$). The correlation between SCS-TR and similar scales scores was high, linear and positive (84.8% for MDS-UPDRS, 72.3% for DFSS and 70.1% for NMSQ). The Cronbach's alpha coefficient for the evaluation of the reliability of the sialorrhea clinical scale questionnaire was found to be 0.881 which indicates a very good internal consistency. Spearman's correlation test evaluating the relationship between the scores of the preliminary test and re-test of SCS-TR showed a high level, linear and positive relationship.
Conclusions: SCS-TR is consistent with the original version of SCS-PD. As its validity and reliability in Turkey have been shown by our study, it can be used for the evaluation of sialorrhea in Turkish PD patients.

P 076

Utilizing technology-based outcome measures in the natural setting to answer intriguing clinical questions in Parkinson disease

O. Phillips[1], *P. Salles*[2], *J. Liao*[1], *J. Yu*[1], *H. Fernandez*[1]

[1]Cleveland Clinic, Center for Neurological Restoration, Cleveland, United States, [2]Centro de Trastornos del Movimiento, Santiago, Chile

Background: The gold standard in the assessment of Parkinson disease (PD) motor symptoms is through evaluation of the quality and severity of movements during office visits. However, this provides only a snapshot with limited assessment in the natural setting of motor fluctuations such as end-of-dose wearing off, the most common indication of several often cost-prohibitive medications with modest efficacy. Furthermore, discrepancies exist between PD patients' motor function in clinic compared to in their natural setting, analogous to the "white coat phenomenon" observed with blood pressure measurements. However, measuring this discrepancy is challenging using current methods. Wearable kinetic devices can inexpensively, noninvasively, and nearly continuously measure PD symptom severity inside and outside the office setting to explore these phenomena.

Methods: We designed two pilot clinical trials, both utilizing wearable kinetic devices, to answer two related questions:

1. Quantify motor performance discrepancies at home versus in clinic and
2. Compare efficacy of cost-effective behavioral interventions versus pharmacological management of motor fluctuations.

Results: First, wearable kinematic devices will quantify discrepancies in motor measures inside vs outside the clinical environment, correlated with participants' clinical scores of anxiety, depression, fear of negative evaluation, and apathy. Second, wearable kinematic devices will analyze movements to determine change in wearing off with behavioral versus pharmacologic interventions.

Expected outcomes are that behavioral compliance-based treatment is noninferior to conventional pharmacologic treatment in the quantity of off time, and that patients with higher ratings of anxiety, depression, and fear of negative evaluation have greater variance in PD motor measures in and out of the clinical setting, whereas participants with higher ratings of apathy have less variability.

Conclusions: Creative new methods utilizing wearable kinematic devices may now allow us to answer relevant under-explored questions in PD.

P 077

Application of the Chinese version of the Montreal cognitive assessment-basic for assessing Mild Cognitive Impairment in Parkinson's disease

W. Chen[1]

[1]Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Department of Neurology, Shanghai, China

Background: Mild cognitive impairment (MCI) is a common and pivotal non-motor symptom in Parkinson's disease (PD). It is necessary to use the appropriate tools to characterize the cognitive profiles and identify the subjects at risk of MCI in clinical practice.

Methods: A cohort of 207 non-demented patients with PD and 52 age- and gender-matched cognitively normal controls (NCs) underwent the Chinese Version of Montreal Cognitive Assessment-Basic (MoCA-BC) evaluation. Patients with PD also received detailed motor and non-motor evaluation by serial scales. Cognitive profiles were investigated in patients with PD-MCI, relative to patients with normal cognition (PD-NC) and cognitively NCs. In addition, differences in demography, major motor and non-motor symptoms were compared between patients with PD-MCI and PD-NC.

Results: There were 70 patients with PD-MCI, occupying 33.8% of the total patients. Patients with PD-MCI had impairment in multiple cognitive domains, especially in executive function, memory and visuospatial function on MoCA-BC, relative to cognitively NCs or PD-NC. Compared with PD-NC patients, PD-MCI patients were older ($p = 0.002$) and had a later onset age ($p = 0.007$) and higher score of the Unified Parkinson's Disease Rating Scale (UPDRS) part III ($p = 0.001$). The positive rate of clinical possible rapid eye movement sleep behavior disorder (cpRBD) in the PD-MCI group was significantly increased relative to the PD-NC group ($p = 0.003$). Multivariate logistic analysis showed that older age (OR = 1.06; $p = 0.012$), higher score of UPDRS-III (OR = 1.03; $p = 0.018$) and the presence of cpRBD (OR = 2.10; $p = 0.037$) were independently associated factors of MCI in patients with PD.

Conclusions: Executive function, memory and visuospatial function are the main impaired cognitive profiles in PD-MCI via MoCA-BC. Aging, motor severity and RBD may be independently related factors of MCI in PD.

P 078

REM sleep behavior disorder correlates with constipation in *de novo* Chinese Parkinson's disease patients

Y. Chen[1], *Q. Xu*[1], *L. Wu*[1], *M. Zhou*[1], *Y. Lin*[1], *Y. Jiang*[1], *Q. He*[1], *L. Zhao*[1], *Y. Dong*[1], *J. Liu*[1], *W. Chen*[1]
[1]Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Department of Neurology, Shanghai, China

Background: Constipation, rapid eye movement sleep behavior disorder (RBD) and hyposmia are common prodromal symptoms of Parkinson's disease (PD), and they may represent two distinct types of disease origin, from the body or the brain.
Our study aimed to compare the clinical characteristics of *de novo* PD patients with and without constipation, and identify which prodromal symptoms were associated with constipation.
Methods: A total of 111 *de novo*, drug naïve Chinese PD patients were consecutively enrolled from Jan 2017 to Sept 2021. Patients were classified into PD with and without constipation based on item 5 of the Scales for Outcomes in Parkinson's disease- Autonomic Dysfunction (SCOPA-AUT).
The demographic data, motor and nonmotor symptoms were compared between the two groups. The associated factors of constipation were analyzed by the multivariate logistic regression analysis.
Results: In total, 44.1% (n=49) of *de novo* PD patients had constipation. PD patients with constipation were older (p=0.028), had higher proportions of Hoehn and Yahr (H-Y) stage 2 (p=0.002), clinical possible RBD (cpRBD) (p=0.002) and depression (p=0.023), as well as marginal increase of hyposmia (p=0.058) and freezing of gait (p=0.069).
After adjusting for H-Y stage and other confounding factors, cpRBD (OR=3.508, p=0.009), rather than hyposmia or depression, was closely related to constipation in *de novo* Chinese PD patients.
Conclusions: RBD is closely associated with constipation in *de novo* Chinese PD patients. Our results support the theory that prodromal symptoms that represent the same pathological origin are closely related to each other.

P 079 (GPT)

Comparison of autonomic dysfunction in essential tremor and Parkinson's disease: a pilot study

J. Malkiewicz[1], *J. Siuda*[1]

[1]Medical University of Silesia, Department of Neurology, School of Medicine, Katowice, Poland

Background: Differential diagnosis of essential tremor (ET) and Parkinson's disease (PD) might be difficult especially in early stage of the diseases. The aim of the study was preliminary assessment of potential parameters of dysautonomia, which might be useful in differential diagnosis of PD vs ET.

Methods: 11 ET and 40 age-matched PD patients were included. Exclusion criteria were heart disease with NYHA scale result >1, advanced diabetes mellitus, polyneuropathy, renal failure, hepatic cirrhosis, severe respiratory disease, abnormal thyrotropin level, acute infection, electrolyte imbalance and non-sinus heart rhythm.

Autonomic dysfunction was evaluated with SCOPA-AUT questionnaire without its sexual domain. Heart rate variability analysis (HRVa) in time (SDNN, RMSSD) and frequency domains (VLF, LF, HF, LF/HF ratio) of 5 minutes ECG was also used. Orthostatic hypotension (OH) was assessed with 5 minutes tilt-test to 60 degrees angle, with cut points 20 and 10 mmHg for systolic and diastolic blood pressure, respectively. U-Mann-Whitney test and Fisher's exact test were used in statistical analysis, continuous data are presented as median (lower quartile-upper quartile), nominal as percentages.

Results: Subjective assessment of autonomic symptoms with SCOPA-AUT questionnaire showed significant differences between PD and ET (PD 14 (10-21) pts vs ET 8 (3-12) pts, p=0.024). In SCOPA-AUT domains analysis PD patients had higher scores in all domains, but only results for gastrointestinal domain reached significance (PD 4.5 (2-7) pts vs ET 1 (1-2) pts, p=0.003). HRVa revealed higher values of all analyzed parameters with exception of LF/HF ratio in ET, significant differences ($p<0.05$) were found in RMSSD 21.9 (20.2-23.5) vs 13.6 (8.5-21.2) ms, VLF 528.4 (223.1-740.3) vs 157.8 (99.3-327.2) ms2, LF 228.8 (155.1-282.2) vs 77.9 (35.9-189.9) ms2. OH was present in 43% of PD patients and none of ET patients (p=0.019).

Conclusions: Gastrointestinal symptoms, orthostatic hypotension and short-term HRVa might be potentially useful parameters in differentiation of ET and PD, however larger study are needed.

P 080

Preliminary verification of a Kinect-based system for evaluating postural abnormalities in patients with Parkinson's disease

R. Hong[1], Z. Wu[1], T. Zhang[1], Z. Zhang[1], A. Lin[1], X. Su[2], Y. Jin[2], Y. Gao[2], K. Peng[1], L. Li[1], L. Pan[1], H. Zhi[2], Q. Guan[1], L. Jin[3,1,4]

[1]Tongji University, Neurological Department, Tongji Hospital, Shanghai, China, [2]IFLYTEK Suzhou Research Institute, Suzhou, China, [3]Tongji University, Department of Neurology and Neurological Rehabilitation, Shanghai, China, [4]Shanghai Clinical Research Center for Aging and Medicine, Shanghai, China

Background: Postural abnormalities are common disabling complications in patients with Parkinson's Disease (PD) leading to pain, balance dysfunction and walking difficulties. At present, there is no recognized objective and quantitative evaluation method for postural abnormalities in PD.
In this study, we initially tested the reliability and validity of a Kinect-based system developed by our team with a cohort of small sample size.
Methods: Fifteen individuals with PD were enrolled. An Azure Kinect depth camera based system was used to collect the postural images of PD patients during bipedal quiet standing, after which eight quantified coronal and sagittal features (F1-F8) reflecting the severity of postural abnormalities were automatically obtained by algorithms. Two professionally trained doctors (namely doctor1 and doctor2) individually measured F1 to F8 as previously defined with the free NeuroPostureApp© (http://www. neuroimaging. uni-kiel.de/NeuroPostureApp). The intraclass correlation coefficient (ICC) was used to evaluate the consistency among the three sets of testing results.
Results: There was moderate to high consistency between the results of doctor1 and doctor2 in F1, F3, F4, F5 and F6. Moreover, there was moderate to high consistency between the results of the system and doctor1 in F1, F2, F4, F5 and F7 and there was moderate to high consistency between the results of the system and doctor2 in F1, F4, and F5. However, the consistency between the results of the system and two doctors in F3 and F8 was very low.
Conclusions: The Kinect-based system for evaluating postural abnormalities in PD was generally reliable and valid and a study with a much larger sample size is needed to further verify this.

P 081

A novel summary index derived from Kinect to evaluate the severity of postural abnormalities in patients with Parkinson's Disease

R. Hong[1], T. Zhang[1], Z. Zhang[1], Z. Wu[1], A. Lin[1], X. Su[2], Y. Jin[2], Y. Gao[2], K. Peng[1], L. Li[1], L. Pan[1], H. Zhi[2], Q. Guan[1], L. Jin[3,1,4]

[1]Tongji University, Neurological Department, Tongji Hospital, Shanghai, China, [2]IFLYTEK Suzhou Research Institute, Suzhou, China, [3]Tongji University, Department of Neurology and Neurological Rehabilitation, Shanghai, China, [4]Shanghai Clinical Research Center for Aging and Medicine, Shanghai, China

Background: The quantitative and overall assessment of posture is important to monitor the progress of Parkinson's Disease (PD) and measure treatment effect. We aimed to propose a new summary index, the Index for Postural Abnormalities (IPA) based on Kinect and explore its clinical value.

Methods: Seventy individuals with PD and thirty age-matched healthy controls (HCs) were enrolled. All participants were tested using a Kinect-based system during bipedal quiet standing with IPA automatically obtained by algorithms. Spearman correlation analysis was adopted to explore the correlations between IPA and various clinical data. The cut-off values of IPA were identified using receiver operating characteristic (ROC) curves.

Results: Significant correlations were detected between IPA and the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score (r_s=0.369, p=0.002), MDS-UPDRS-III total score (r_s=0.431, p<0.001), MDS-UPDRS-III 3.13 score (r_s=0.573, p<0.001), MDS-UPDRS-III-bradykinesia score (r_s=0.311, p=0.010), the 39-item Parkinson's Disease Questionnaire (PDQ-39) (r_s=0.272, p=0.0027) and the Berg Balance Scale (BBS) score (r_s=-0.350, p=0.006).

The ROC curves showed that the cut-off value of IPA for distinguishing PD from HCs was 12.96 with 97.14% of sensitivity, 100.00% of specificity and the area under the curve (AUC) was 0.999 (0.997-1.002, p <0.001). The cut-off value of IPA for distinguishing PD with and without postural abnormalities was 20.14 with sensitivity, specificity and AUC of 77.78%, 73.53% and 0.817 (0.720–0.914, p <0.001) severally.

Conclusions: IPA was significantly correlated to the clinical manifestations of PD patients, and could be used to reflect the global severity of postural abnormalities in PD with important value for differential diagnosis.

P 082
Assessment of pain syndrome in Parkinson's disease in Uzbekistan

G. Goyibova[1], *G. Rakhimbaeva*[2], *K. Sobitjon*[2]
[1]Tashkent Pediatric Medical Institute, Department of Neurology, Tashkent, Uzbekistan, [2]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan

Background: Pain syndrome, one of the leading non-motor manifestations of PD, may be associated with Parkinson's disease itself, or be the result of anti-Parkinsonian therapy.
Methods: 35 patients with Parkinson's disease were examined. The main group included 25 patients with PD with pain, the comparison group consisted of 10 patients with PD without pain. Pain syndrome was assessed on the basis of modern classification of pain syndrome.
Results: The results of the study showed the dependence of the severity of pain syndrome, depression, the degree of movement disorders, and daily activity on the nature of the pain syndrome in myofascial and central algia. Direct dependence of the nature of the pain syndrome on the duration of PD was revealed.
At the stage of confirming the diagnosis of PD and in the first 3 years of the disease, humeroscapular periarthropathies and spondyloarthrosis predominated in patients with algia in the humeroscapular region and lower back.
The longer patients suffered from Parkinson's disease, the more likely they were to have central algia. The pain syndrome in PD at any of its stages was affected by therapy with antiparkinsonian drugs. Antiparkinsonian drugs not only improved the motor activity of patients but also reduced the severity of pain.
After the start or correction of antiparkinsonian therapy in the group of PD patients with pain syndrome, both the general symptoms of the disease and the pain syndrome decreased. Pain syndrome according to VAS decreased by 3 points.
Conclusions: The nature of the pain syndrome depends on the rate of progression, the severity of the disease, and the duration of the disease: in the initial stages of PD, myofascial pains are more common, as the disease progresses, they give way to central algias, mainly on the side of greater motor deficit. Adequate antiparkinsonian therapy reduces the severity of pain.

P 083
Real-world, digital sleep biomarkers capture of Parkinson's disease impact

J.H. Chang[1], *D. Bhatti*[1], *T. Mieth*[1], *A. Tartaglia*[1], *M. Rizzo*[1], *J. Bertoni*[1], *J. Merickel*[1]
[1]University of Nebraska Medical Center, Neurological Sciences, Omaha, United States

Background: Parkinson's disease (PD) is commonly associated with sleep dysfunction that links to clinically validated disease severity. Advents in real-world sleep monitoring with wrist-worn actigraphy show promise for developing remote, digital health biomarkers of PD patient sleep dysfunction. Relationship between sleep dysfunction measured by actigraphy and disease severity has not been fully explored.

The goal of this study was to determine metrics of real-world sleep that index PD disease severity to advance future research aimed at developing digital health biomarkers, tracking PD disease impact from a patient's daily behavior.

Methods: Twenty-nine, idiopathic and not-demented PD patients (age = 67.44 ± 5.79, 20 males, median Hoehn & Yahr stage = 2) were monitored for 4 weeks using a wrist-worn ActiGraph to quantify nightly total sleep time (TST), wake after sleep onset (WASO), and sleep fragmentation index (SFI). A neurologist assessed each patient's PD using the MDS-UPDRS, measuring symptoms severity in non-motor and motor experiences of daily living and motor complications. Average sleep (TST, WASO, and SFI) across 4 weeks was compared to MDS-UPDRS subscale scores using Pearson correlations.

Results: Worse sleep fragmentation, indexed by more frequent awakenings/movement during sleep, significantly associated with worse non-motor experiences of daily living ($r = 0.48$, $p < .01$). Associations with TST and WASO were not detected. None of the associations between sleep and other UPDRS subscale scores were found.

Conclusions: These pilot results indicate that sleep fragmentation may serve as a remote, digital health biomarker to quantify a PD patient's daily activities decline from non-motor symptoms, in line with our previous research showing preliminary predictive utility for capturing PD cognitive decline from sleep fragmentation. Improving real-world monitoring of PD disease impact from clinically validated, digital health biomarkers is critical for advancing early intervention and treatment approaches to mitigating quality of life decline in PD patients.

P 084
Olfactory dysfunction and severity of tremor - is there a connection?

D.D. Pokhabov[1,2], *V. Abramov*[2], *M. Sadovsky*[1], *D.V. Pokhabov*[1,2]
[1]Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation, [2]Federal Siberian Research Clinical Center, Department of Neurological Diseases, Krasnoyarsk, Russian Federation

Background: Parkinson's disease (PD) and essential tremor (ET) are among the leading neurological diseases worldwide. Varying in manifestation, it exhibits some differences: rest tremor for PD and postural-kinetic for ET. Olfactory dysfunction is the first manifest of PD often preceding the movement disorders. Our aim was to obtain tremor data of PD and ET patients and the results of their olfactory function, which can help verify our scientific hypothesis on the inverse relation between tremor manifestation and olfactory dysfunction: lower tremor is accompanied with worse smell perception, and vice versa.

Methods: We had three groups of patients: suffering from PD, ET and healthy people. An examination procedure of olfactory function was based on extended olfactory Sniffin' sticks test with three parameters: threshold, identification and discrimination. For tremor testing we used wireless device to monitor electrophysiological signals with three main characteristics: skin electromyogram (SEMG), gyroscope and accelerations. We used an elastic map technique to cluster and analyze all data.

Results: Proven inverse relation between tremor level and olfactory dysfunction is the core result of our work. Indeed, ET patients showed better olfactory function results accompanied by stronger tremor, as compared to PD patients: lower tremor with worse smell perception.

	Threshold	Discrimination	Identification		Total amount
	Average result	Average result	Average result	Odor knowledge	
Healthy people	5,11 ± 2,32	11,53 ± 2,28	11,28 ± 2,18	Best: garlic Worse: lemon and liquorice	Anosmia-3 Hyposmia-32 Norm-29
PD patients	2,44 ± 1,91	8,76 ± 2,47	6,87 ± 2,69	Best: fish Worse: lemon and apple	Anosmia-14 Hyposmia-30 Norm-1
ET patients	3,85 ± 2,34	10 ± 2,65	10,08 ± 2,47	Best: garlic Worse: lemon	Anosmia-2 Hyposmia-31 Norm-7

Conclusions: Combination of olfactory testing and tremor records improves significantly the discrimination of PD patients from those with ET, as well from healthy people. The presented results could be implemented for early differential diagnostics of PD vs. ET, as well as for the improvement of individual therapy course for such patients.

P 086
The impact of non motor symptoms on quality of life in patients with young onset Parkinson's disease

K. Abdurakhmonova[1], *G. Rakhimbaeva*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: Purpose of the study was to determine the association between non-motor symptoms (NMS) and health-related quality of life (HRQoL) in patients with young onset Parkinson's disease (YOPD).
Methods: 64 patients with an age ranged from 25 to 40 were enrolled in this study. 39-item Parkinson's Disease Questionnaire (PDQ-39), MDS Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Non-Motor Symptoms Scale (NMSS) were used to assess patients.
Results: Pearson correlation coefficients demonstrated statistically significant positive correlations between PDQ-39SI scores and disease duration $r = 0.221$, $p < 0.05$; UPDRS score part I $r = 0.524$, $p < 0.001$; part II, $r = 0.521$, $p < 0.001$; part III $r = 0.379$, $p < 0.001$; part IV $r = 0.248$, $p = 0.01$, while the Spearman rank correlation coefficients showed positive correlations of PDQ-39SI and scores of each NMSS domain including cardiovascular $r= 0.328$, $p = 0.002$, sleep/fatigue $r = 0.481$, $p < 0.001$, mood/ cognition $r = 0.478$, $p < 0.001$, perceptual problems/hallucinations $r = 0.182$, $p <0.05$, attention/memory $r = 0.326$, $p = 0.002$, urinary $r = 0.258$, $p = 0.01$ and miscellaneous $r = 0.298$, $p = 0.004$.
Independent predictors of worsening HRQoL as measured by PDQ-39SI score were NMSS domain 2 - sleep/fatigue $F(4,84) = 2.116$, $p = 0.04$; NMSS domain 3 - mood/cognition $F(4,84) = 2.798$, $p = 0.005$, NMSS domain 5 - attention/memory $F(4,84) = 2.448$, $p = 0.01$ and MDS-UPDRS part III (motor symptoms) $F(4,84) = 3.254$, $p = 0.002$.
Conclusions: The study showed that non-motor symptoms such as to sleep/fatigue, mood/cognition and attention/memory domain are as independent predictors of HRQoL in individuals with YOPD.

P 087
Evaluation of extrapyramidal diseases with Parkinson's disease in patients suffering from stroke in Tashkent region, Uzbekistan

J. Sabirov[1], *U. Azamat*[1], *R. Yuldashev*[1]
[1]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan

Background: Much attention has appealed to the frequency of stroke and neurodegenerative diseases correlated with the age of the patient. To determine the incidence and clinical characteristics of PD in patients with stroke.
Methods: An analysis was made of patients with PD and acute cerebrovascular accidents in the acute stage. The main age of patients with stroke in combination with PD was 68.4 years (from 64 to 85 years). In the Primary Vascular Department for patients with stroke in 2020. 843 patients were treated: with cerebral infarction (CI) - 638, with hemorrhagic stroke - 83, and 122 patients with a transient ischemic attack (TIA).

Results: Among all patients, extrapyramidal symptoms were described by doctors in 187 patients. At the same time, PD was found in 15 patients: 11 in patients with CI, 2 in patients with intracerebral hemorrhage, 1 in a patient with TIA.
Damage to the middle cerebral artery was detected in 7 patients with MI (5 on the left, 2 on the right) and 1 patient with TIA (on the left); anterior cerebral artery - in 3; posterior cerebral artery - in 1 patient with infarction of the left cerebellar hemisphere. PD was diagnosed for the first time in 3 patients who were treated for cerebral infarction.
The trembling form of PD was detected in 2 patients out of 15, the hypokinetic-rigid form was found in 5 patients, and the mixed form was found in 8 patients with an established diagnosis of PD. Non-motor symptoms of PD proceeded in the form of constipation, cognitive impairments and emotional-volitional disorders of varying severity (100%), psychotic disorders (4 - 26.6%) mainly in the form of illusions and hallucinations, insomnia (8 - 53.3%), orthostatic hypotension (2-13.3%).
Conclusions: In the acute stage of stroke, extrapyramidal disorders are detected in every fifth patient, while PD occurs in 2.35%.

P 088
Clinical correlations of Parkinson's disease and vascular parkinsonism: a retrospective review from Uzbekistan

A. Umarov[1], *S. Kuranbaeva*[1], *G. Goyibova*[2]
[1]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan, [2]Tashkent Pediatric Medical Institute, Department of Neurology, Tashkent, Uzbekistan

Background: We aimed to study evidence for or against the role of narrowing lesions of the main brain arteries in progressing of parkinsonism, and to identify clinical signs that suggest a vascular origin.
Methods: We provide a Retrospective review in history materials of 231 patients with Parkinson's disease (PD) and Vascular Parkinsonism (VP), 46 and 185 respectively; for the period from 2010 to 2016y. We divided the patients into 2 groups (VP and PD) and compared the clinical features.
Results: Both groups were differentiated in terms of evidence of cerebrovascular disease ($P<.001$ to $P<.00001$). Patients with VP were older, more likely to present with gait difficulty rather than tremor, and less likely to respond to the use of levodopa compared with patients with PD ($P<.00001$). Patients with VP were also significantly more likely to have predominant lower-body involvement, postural instability, a history of falling, dementia, corticospinal findings, incontinence ($P<.00001$), and pseudobulbar affect ($P<.05$).
Conclusions: These differences in clinical features suggest different pathogenesis of parkinsonism in these 2 patient groups. The strong evidence of cerebrovascular disease in the VP group and the differences in clinical features support the concept of VP as a distinct clinical entity.
We conclude that compared with PD, patients with parkinsonism associated with vascular disease are more likely to present with gait difficulty and postural instability rather than tremor, have a history of stroke and risk factors for stroke, and fail to respond to levodopa therapy.

P 089 (GPT)
Correlation between age and positive and negative affect in Parkinson's disease

A. Almaraz-Espinoza[1], A. Banegas-Lagosa[1], E. Robles[1], P. Bazan-Rodriguez[2], E.S. Velazquez-Ávila[1], A. González-Cantú[3], A. Cervantes-Arriaga[2], M. Rodriguez-Violante[2], D. Martinez-Ramirez[1]
[1]Tecnológico de Monterrey, Monterrey, Mexico, [2]Laboratorio Clinico de Enfermedades Degenerativas, Instituto Nacional de Neurologia y Neurocirugia, Ciudad de Mexico, Mexico, [3]Christus Muguerza Alta Especialidad, Monterrey, Mexico

Background: Assess the age of diagnosis with the positive and negative effects in a cohort with PD in Mexico. Develop a model that can be used to predict the PANAS scores.
Methods: An observational, cross-sectional study was performed to identify factors associated with the positive and negative affect in a cohort with PD (n = 77) in Mexico. The Positive and Negative Affect Schedule (PANAS) were utilized to evaluate well-being. A univariate analysis was performed to identify any significant correlations between the variables. A multiple linear regression analysis was conducted to identify the predictors of the outcome scales.
Results: The negative affect scores were significantly correlated to age of diagnosis, disease duration, and residency. The univariate analysis showed that the Positive Affect Schedule (PAS) score was not significantly associated with the age at diagnosis.
In contrast, the analysis revealed a strong correlation between the age at diagnosis and Negative Affect Schedule (NAS) score.
Conclusions: We need to better understand the state of positive and negative emotions in young patients with PD so we can offer a more complete approach in their management.

P 091
Validation of patient administered psychosis questionnaire for screening Parkinson's disease patients for psychosis.

V. Koneru[1], A. Cole[2], K. Crist[3], A. Espay[4], D. Weintraub[5], W. Ondo[1]
[1]Houston Methodist Neurological Institute, Neurology, Movement Disorders, Houston, United States, [2]University of Texas at Austin, Steve Hicks School of Social Work, Austin, Texas, United States, [3]Houston Area Parkinson Society, Executive Directo, Houston, Texas, United States, [4]University of Cincinnati Gardner Neuroscience Institute, Neurology, Movement Disorders, Cincinnati, Ohio, United States, [5]University of Pennsylvania, Psychiatry, Philadelphia, PA, United States

Background: Psychosis is a common feature in Parkinson's disease (PD) and is a major cause of caregiver burden, nursing home placement, and mortality. Psychosis symptoms are often not volunteered during the clinic visit due to embarrassment or lack of insight. There is no widely accepted screening scale. We conducted a study to compare a self-administered psychosis screening questionnaire with the "gold standard" PD psychosis scale.

Methods: A self-administered screening questionnaire was developed through a modified Delphi method by a committee formed by neurologists, a psychiatrist, and patient advocates. After several rounds of revisions including after test subject input, a finalized self-administered screening questionnaire was provided to consecutive PD patients in clinic, and separately to their caregivers when available. Later, the PD psychosis scale (structured interview) was administered by movement disorders specialist physicians without knowledge of the self-administered screening questionnaire responses.
Results: A total of 250 consecutive patients with PD, mean age of 62.7± 10.5 years, mean duration 8.0± 6.1 years, 64.8% (162/250) male, were included in the study. The screening questionnaire showed any psychosis (any of the 4 questions positive) in 34% (84/250) patients. Compared to the gold standard PD psychosis scale, sensitivity was 88.9% and specificity was 92.4%, with a positive predictive value of 95.2%.
Conclusions: This self-administered screening questionnaire showed good sensitivity and specificity compared to a gold-standard administered scale. Since the questionnaire is not limited to patients and can be administered by caregiver, it is utilizable in patients with dementia as well.

Parkinson Disease: Therapy (excluding surgical, physical)

P 092

Long-term motor and non-motor symptom benefits in patients with advanced Parkinson's disease treated with Levodopa-Carbidopa Intestinal Gel: DUOGLOBE final analysis

K.R. Chaudhuri[1], N. Kovács[2], F.E Pontieri[3], J. Aldred[4], P. Bourgeois[5], T.L Davis[6], E. Cubo[7], M. Anca-Herschkovitsch[8], R. Iansek[9], M.S Siddiqui[10], M. Simu[11], L. Bergmann[12], P. Kukreja[12], O. Ladhani[12], J. Jia[12], D.G Standaert[13]

[1]Parkinson's Foundation International Centre of Excellence, King's College Hospital, and King's College Institute of Psychiatry, Biomedical Research Centre, Psychology & Neuroscience, London, United Kingdom, [2]University of Pécs, Department of Neurology, Pécs, Hungary, [3]Sapienza University of Rome, Department of Neurological Sciences, Mental Health & Sensory Organs, Rome, Italy, [4]Selkirk Neurology, Spokane, United States, [5]AZ Groeninge, Department of Neurology, Kortrijk, Belgium, [6]Vanderbilt University Medical Center, Department of Neurology, Nashville, United States, [7]Hospital Universitario Burgos, Neurology Department, Burgos, Spain, [8]Edith Wolfson Medical Center, Department of Neurology, Holon, Israel, [9]Kingston Centre, Monash Health, Melbourne, Australia, [10]Wake Forest School of Medicine, Department of Neurology, Winston Salem, United States, [11]Victor Babes University of Medicine and Pharmacy, Department of Neurology, Timisoara, Romania, [12]AbbVie Inc., North Chicago, United States, [13]University of Alabama at Birmingham, Department of Neurology, Birmingham, United States

Background: In clinical trials, levodopa-carbidopa intestinal gel (LCIG) reduced motor and non-motor symptoms in patients with advanced Parkinson's disease (PD). Prospective, long-term data on LCIG use in a real-world setting are limited. This analysis evaluates the long-term effectiveness and safety of LCIG during routine clinical practice in patients with advanced PD.

Methods: DUOGLOBE (NCT02611713) was an observational, multinational (including US-sites), prospective study enrolling LCIG-naïve patients treated in routine clinical practice with a 3-year follow-up. The change in patient-reported "Off" time was the primary outcome. Additional assessments included Unified Dyskinesia Rating Scale (UDysRS), Non-Motor Symptom Scale (NMSS), Parkinson's Disease Sleep Scale (PDSS-2), health-related quality of life (HR-QoL; Parkinson's disease Questionnaire 8 [PDQ-8]), Modified Caregiver Strain Index (MCSI), and serious adverse events (SAEs). Final outcomes at month (M) 36 are presented.

Results: Among 195 patients, baseline "Off" time, UDysRS, and NMSS total scores showed substantial disease burden. Overall, 89 patients completed the 3-year follow-up. About one-third of patients were treated with LCIG monotherapy or LCIG with only supplemental oral levodopa. The mean total LCIG dose was stable across all time points. Significant improvements were sustained through M36 in patient-reported "Off" time ($P<.001$), UDysRS ($P<.05$), PDSS-2 ($P<.001$), and NMSS total scores ($P<.01$). Patient-reported HR-QoL and MCSI scores were significantly improved through M24 ($P<.01$) and M30 ($P<.05$), respectively.

About half of discontinuations were primarily due to non-safety reasons; 31% of patients who discontinued the study did continue LCIG. The most common SAEs were falls and (worsening of) PD (4.1% [n=8]). Device-related issues were reported by 11.8% of patients (n=23).
Conclusions: In this final analysis from the first fully prospective, 3-year, real-world study of LCIG, patients with advanced PD treated with LCIG exhibited significant and sustained improvements in motor and non-motor symptoms that were maintained for 3 years. Safety was consistent with the established LCIG safety profile.

P 093

Design of the Remote Optimization Adjustment and Measurement for Deep Brain Stimulation (ROAM-DBS) randomized prospective outcomes study of remote programming

T. Tomlinson[1], M. Feldman[2], A. Gharabaghi[3], S. Groppa[4], L. Luo[5], H. Lu[6], C. Luca[7], V. Marshall[8], A. Merola[9], A. Schnitzler[10], L. Verhagen[11], B. Walter[12], C. Wu[13], S.E. Zauber[14], B. Cheeran[1]
[1]Abbott Laboratories, Neuromodulation, Plano, United States, [2]Dartmouth-Hitchcock Medical Center, Neurology, Lebanon, United States, [3]Institute for Neuromodulation and Neurotechnology, Eberhard Karls University of Tuebingen, Neurosurgery and Neurotechnology, Tuebingen, Germany, [4]University Medical Center of the Johannes Gutenberg-University Mainz, Section of Movement Disorders and Neurostimulation, Biomedical Statistics and Multimodal Signal Processing Unit, Department of Neurology, Focus Program Translational Neuroscience, Mainz, Germany, [5]Beth Israel Deaconess Medical Center, Neurology, Boston, United States, [6]Swedish Health System, Seattle, United States, [7], University of Miami Miller School of Medicine, Neurology, Maimi, United States, [8]Queen Elizabeth University, Neurology, Glasgow, United Kingdom, [9]The Ohio State University Wexner Medical Center, Madden Center for Parkinson Disease and Other Movement Disorders, Department of Neurology, Colombus, United States, [10]Heinrich-Heine-Universität Düsseldorf, Institute of Clinical Neuroscience and Medical Psychology, Düsseldorf, Germany, [11]Rush University, Neurological Sciences, Chicago, United States, [12]University Hospitals Cleveland Medical Center, Parkinson's & Movement Disorders Center, Cleveland, United States, [13]Thomas Jefferson University, Neurosurgery, Philadelphia, United States, [14]Indiana University School of Medicine, Neurology, Indianapolis, United States

Background: The recent introduction of DBS Remote Programming (RP) platforms alleviates some of the burden of DBS programming, allowing stimulation changes without requiring that patients travel to the clinic. As many as a third of DBS patients cannot easily travel to a clinic, and a quarter report difficulty contacting the clinic for advice. The ROAM-DBS randomized controlled study will determine if outcomes with RP are comparable to in-clinic programming.
Methods: Patients receiving new Abbott DBS implants for Parkinson's Disease will be offered to participate in the ROAM-DBS study. After initial programming, subjects will be randomized to receive additional programming in-clinic only or with RP. The latter group may receive in-clinic visits as necessary. After each programming session subjects will report changes in symptomology relative to initial programming using the Patient's Global Impression of Change (PGI-C) scale. Additionally, subjects will wear a smartwatch for

continuous measurement of tremor and dyskinesia and will provide monthly PDQ-39 evaluations for the first 3 months after initial programming. Finally, all subjects will have MDS-UPDRS evaluations at 6 months and 1 year after initial programming.

Results: The primary endpoint of ROAM-DBS is the time taken for subjects to report a 1-point improvement in the PGI-C score after initial programming. The hypothesis of ROAM-DBS is that RP results in more rapid improvement in symptoms by enabling more frequent programming sessions. Secondary analyses will describe the change in tremor and dyskinesia, PGI, and PDQ-39 in the first 3 months after initial programming. Improvement in MDS-UPDRS scores after 1 year will be compared in those receiving RP vs. in-person programming to determine if similar outcomes are achieved.

Conclusions: The ROAM-DBS study will analyze the outcomes of DBS RP and clarify whether scheduling flexibility and reduced burden associated with RP may result in more rapid improvement compared to in-clinic only follow-up.

P 094 (GPT)

Vodobatinib, a potent, orally bioavailable brain-penetrating inhibitor of c-Abl as a potential neuroprotective agent for treatment of Parkinson disease

R.R. Walsh[1], *S.P. Piccoli*[1], *R.S. Talluri*[1], *S. Mandhane*[1], *D. Love*[1], *O. Hurko*[1], *S.-L. Yao*[1], *V. Ramanathan*[1], *N. Damle*[1]
[1]Sun Pharma Advanced Research Company (SPARC), Neurology, Princeton, United States

Background: Preclinical evidence suggests that c-Abl is critical for pathogenesis of Parkinson Disease (PD). Vodobatinib is a potent, orally bioavailable inhibitor of c-Abl currently being evaluated in patients with PD in the PROSEEK clinical trial. Nilotinib, a multikinase inhibitor of c-Abl, was recently shown to be unsuccessful in slowing PD progression (Simuni et al. 2021). This failure of nilotinib at its maximally permissible dose of 300mg was attributed to insufficient brain penetration because the concentration of nilotinib in the CSF was found to be 7-fold lower than its IC50 for c-Abl. Here we demonstrate that vodobatinib can adequately penetrate the blood brain barrier to provide potential beneficial effects in PD.

Methods: Vodobatinib and nilotinib were evaluated for inhibition of c-Abl enzymatic activity. Human healthy volunteers were dosed orally at 3 dose-levels of vodobatinib 7 days prior to intrathecal sampling of CSF over 24 hours for drug level measurement.

Results: Vodobatinib (IC50 0.9nM) is a more potent c-Abl inhibitor than nilotinib (IC50 20nM). Oral dosing of vodobatinib for 7 days in three cohorts of healthy adult volunteers (six per cohort) demonstrated that observed steady state levels of 2.9-12nM of vodobatinib in CSF over a 24 hour period exceeded IC50 of c-Abl inhibition. Cmax : IC50 ratio of vodobatinib dosed daily at 384mg was 13, which greatly exceeded the published ratio of 0.24 for nilotinib dosed at 300mg. These results suggest that vodobatinib levels in the brain can be maintained over the treatment period to ensure optimal inhibition of c-Abl.

Conclusions: Higher potency and efficient brain penetration of vodobatinib suggest that vodobatinib offers a better opportunity than nilotinib to test whether c-Abl inhibition ameliorates disease progression in PD.

P 095

Local field potential and clinical symptoms of Parkinson's disease patients implanted with adaptive deep brain stimulation

G. Oyama[1], *H. Kamo*[1], *M. Ito*[2], *H. Iwamuro*[3], *A. Umemura*[3], *N. Hattori*[1]
[1]Juntendo University, Neurology, Tokyo, Japan, [2]Juntendo University, Psychiatry, Tokyo, Japan, [3]Juntendo University, Neurosurgery, Tokyo, Japan

Background: Deep brain stimulation (DBS) is a well-established treatment in advanced Parkinson's disease (PD). However, motor fluctuation re-emerges after DBS implantation because the therapeutic window progressively becomes narrower. Adaptive DBS (aDBS), which can automatically adjust real-time stimulation amplitude based on continuous feedback from local field potentials (LFP) that represents the patient's clinical state has been available in clincal use in Japan. The objective of this study is to describe the association between LFP and clinical symptoms in the real-world data of patients with PD who were implanted with aDBS.
Methods: We retrospectively reviewed 17 patients applied with aDBS in our institution (2020-2021). LFP, Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDSUPDRS) part1-4, Mini-Mental State Examination (MMSE), Levodopa Equivalent Daily Dose (LEDD) were monitored at the pre-operative, 1-month, and 3 -month post-operative period.
Results: There were 12 cases of new implantation and 5 cases of implantable pulse generator exchange. aDBS could be set on both sides in 5 patients and on one side in 4 patients at the time of 3 months after surgery. MDS-UPDRS part 4 score at 1-month postoperative state and LEDD at 3-month postoperative state were lower than the baseline. There is a correlation between LFP peak power and MDS-UPDRS part III score at 3-month after surgery ($p < 0.01$, regression analysis using least squares method).
Conclusions: We presented a correlation between LFP and motor symptoms at 3-month after surgery. Since this study is conducted in the early postoperative period, the micro-lesioning effect and insufficient stimulation amplitude could influence the outcome. We need to collect more data to assess the benefit of aDBS.

P 096

Efficacy of incobotulinumtoxinA in subjects with sialorrhea, assessed using the modified Radboud Oral Motor inventory for Parkinson's disease (mROMP)

W. Jost[1], O. Michel[2], C. Oehlwein[3], J. Slawek[4], A. Bogucki[5], S. Ochudlo[6], M. Banach[7], F. Pagan[8], B. Flatau-Baqué[9], J. Csikós[9], A. Blitzer[10]

[1]Parkinson-Klinik, Ortenau, Baden-Württemberg, Germany, [2]University Hospital Brussels, Brussels, Belgium, [3]Neurological Outpatient Clinic for Parkinson Disease and Deep Brain Stimulation, Gera, Germany, [4]Medical University of Gdansk, Gdansk, Poland, [5]Medical University of Łódź, Łódź, Poland, [6]Medical University of Silesia, Katowice, Poland, [7]Collegium Medicum, Jagiellonian University, Krakow, Poland, [8]Georgetown University, Washington D.C., United States, [9]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [10]Icahn School of Medicine at Mt. Sinai, New York, United States

Background: SIAXI (NCT02091739), a double-blind, randomized, Phase III study, assessed the efficacy and safety of incobotulinumtoxinA in subjects with sialorrhea. Here we report outcomes on modified Radboud Oral Motor Inventory for Parkinson's disease (mROMP) subscales.

Methods: Subjects with sialorrhea due to Parkinson's disease, atypical Parkinsonism, stroke, or traumatic brain injury were randomized (2:2:1) to incobotulinumtoxinA 75 or 100 U, or placebo distributed in bilateral parotid and submandibular glands in a single injection cycle (16±2 week duration). The change from baseline in drooling, speech, and swallowing symptoms was assessed using mROMP. At screening, baseline, 4, 8, 12, and 16 weeks post-treatment, subjects rated 24 items on a 5-point Likert scale from 1 (normal) to 5 (worst score) based on their recollection of the last 7 days (Kalf JG et al. *Arch Phys Med Rehabil* 2011; 92: 1152–1158).

Results: 184 subjects were randomized to incobotulinumtoxinA 75 U (n=74), 100 U (n=74), or placebo (n=36); 173 subjects completed the main period. mROMP drooling scores improved from baseline to all post-treatment visits in both active treatment groups vs placebo. In the incobotulinumtoxinA 75 U, 100 U, and placebo groups, respectively, the greatest mean (standard deviation) improvements were at Weeks 8 (–6.29 [6.52], –6.58 [5.90], and –1.26 [4.91]) and 12 (–6.77 [6.05], –6.40 [5.20], and –1.77 [4.54]) post-treatment. Mean mROMP speech symptom scores improved at all post-treatment visits with no obvious differences between groups. There was no worsening in mean mROMP swallowing symptoms.

Conclusions: IncobotulinumtoxinA resulted in clinically relevant improvement in subjects with sialorrhea.

P 097 (GPT)

Real-world effect of age on long-term effectiveness and safety of levodopa-carbidopa intestinal gel: post hoc analysis from the DUOGLOBE study

M. Simu[1], K.R. Chaudhuri[2], N. Kovács[3], F.E Pontieri[4], J. Aldred[5], P. Bourgeois[6], T.L Davis[7], M. Anca-Herschkovitsch[8], R. Iansek[9], M.S Siddiqui[10], L. Bergmann[11], O. Ladhani[11], T. Gao[11], D.G Standaert[12], E. Cubo[13]

[1]Victor Babes University of Medicine and Pharmacy, Department of Neurology, Timisoara, Romania, [2]Parkinson's Foundation International Centre of Excellence, King's College Hospital, and King's College Institute of Psychiatry, Biomedical Research Centre, Psychology & Neuroscience, London, United Kingdom, [3]University of Pécs, Department of Neurology, Pécs, Hungary, [4]Sapienza University of Rome, Department of Neurological Sciences, Mental Health & Sensory Organs, Rome, Italy, [5]Selkirk Neurology, Spokane, United States, [6]AZ Groeninge, Department of Neurology, Kortrijk, Belgium, [7]Vanderbilt University Medical Center, Department of Neurology, Nashville, United States, [8]Edith Wolfson Medical Center, Department of Neurology, Holon, Israel, [9]Kingston Centre, Monash Health, Melbourne, Australia, [10]Wake Forest School of Medicine, Department of Neurology, Winston Salem, United States, [11]AbbVie Inc., North Chicago, United States, [12]University of Alabama at Birmingham, Department of Neurology, Birmingham, United States, [13]Hospital Universitario Burgos, Neurology Department, Burgos, Spain

Background: Limited data on how age may impact levodopa-carbidopa intestinal gel (LCIG) effectiveness and safety exist. This analysis assess the real-world effect of age on the long-term effectiveness and safety of LCIG treatment in patients with advanced Parkinson's disease (PD).

Methods: DUOGLOBE (NCT02611713) was a prospective, multinational, 3-year, observational study of LCIG-naïve patients treated in routine clinical practice. This post hoc analysis assessed change from baseline in "Off" time, Unified Dyskinesia Rating Scale (UDysRS), Non-Motor Symptom Scale (NMSS), Parkinson's Disease Sleep Scale (PDSS-2), Unified Parkinson's Disease Rating Scale (UPDRS) II and III, Parkinson's disease Questionnaire 8 (PDQ-8), and serious adverse events (SAEs) by age (<65, 65-75, >75 years of age). Measurements up to month (M) 36 were analyzed.

Results: Among 195 patients, 44/95/56 patients were aged <65/65–75/>75 years (range: 43–90 years), with a PD duration of 9.4/11.4/12.6 years, respectively. All groups showed highly significant improvements in "Off" time through M36 ($P<.001$). UDysRS significantly improved at M12 for <65 and through M24 in 65–75 (both $P<.01$). Patients <65 showed the greatest significant and sustained improvements through M36 in NMSS ($P<.001$), and PDSS-2 ($P<.01$) total scores. UPDRS II scores worsened the least in <65 over time. Patients <65 showed numerical improvements in UPDRS III scores through M36; scores significantly worsened in other groups ($P<.05$). PDQ-8 scores showed the greatest significant improvement in <65 through M24 ($P<.01$), and significant improvements at M12 in 65–75 ($P<.01$). SAEs and discontinuation rates were lower in patients <65 and were similar in 65–75 and >75 groups.

Conclusions: This post hoc analysis of a large observational study suggests that patients of various ages may benefit from LCIG treatment, with patients >75 having a comparable safety profile with 65–75, and improvements in patients <65 appeared more pronounced for some outcomes; further research is needed.

P 098

Long-term incobotulinumtoxinA treatment for chronic sialorrhea: efficacy and safety over 64 weeks

W. Jost[1], A. Friedman[2], O. Michel[3], C. Oehlwein[4], J. Slawek[5], A. Bogucki[6], S. Ochudlo[7], M. Banach[8], F. Pagan[9], B. Flatau-Baque[10], U. Dorsch[10], J. Csikos[10], A. Blitzer[11]

[1]Parkinson-Klinik, Ortenau, Wolfach, Germany, [2]Medical University of Warsaw, Warsaw, Poland, [3]University Hospital Brussels, Brussels, Belgium, [4]Neurological Outpatient Clinic for Parkinson Disease and Deep Brain Stimulation, Gera, Germany, [5]Medical University of Gdansk, Gdansk, Poland, [6]Medical University of Łódź, Łódź, Poland, [7]Medical University of Silesia, Katowice, Poland, [8]Jagiellonian University Medical College, Krakow, Poland, [9]Georgetown University, Washington D.C., United States, [10]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [11]Icahn School of Medicine at Mt. Sinai, New York, United States

Background: Botulinum neurotoxin (BoNT) is an effective treatment for chronic sialorrhea; however, reliable and robust evidence supporting long-term efficacy and safety is lacking. This study investigated the efficacy and safety of repeated incobotulinumtoxinA injections for chronic sialorrhea over 64 weeks.
Methods: Adults with sialorrhea were randomized (2:2:1) to incobotulinumtoxinA 75 U, incobotulinumtoxinA 100 U (n = 74 each), or placebo (n = 36) in the double-blind, placebo-controlled main period (NCT02091739). Eligible subjects entered the extension period and received dose-blinded incobotulinumtoxinA 75 or 100 U in three further 16 ±2-week injection cycles. Efficacy and safety assessments in subjects who received incobotulinumtoxinA throughout the study included unstimulated salivary flow rate (uSFR), subjects' Global Impression of Change Scale (GICS), Drooling Severity and Frequency Scale (DSFS), modified Radboud Oral Motor Inventory for Parkinson's Disease (mROMP) drooling, speech, and swallowing symptom scores, and incidence of adverse events (AEs).
Results: In total, 173/184 subjects (94%) completed the main period and entered the extension period; 141 subjects received incobotulinumtoxinA 75 U (n = 69) or 100 U (n = 72) in both periods. Mean uSFR decreased consistently with repeated incobotulinumtoxinA 75 and 100 U treatment and by −0.16 and −0.17, respectively, at the end-of-study visit. Subjects' GICS, DSFS, and mROMP drooling scores also improved at all assessments. mROMP speech and swallowing scores remained stable. The most common treatment-related AEs during the extension period were dry mouth (4.4% and 11.1%) and dysphagia (1.5% and 4.2%).
Conclusions: Data support long-term efficacy and safety of repeated incobotulinumtoxinA treatment for sialorrhea, with no additional safety concerns reported over 64 weeks.

P 099

Attainment of physiologic salivary flow rate with long-term incobotulinumtoxinA treatment for sialorrhea in Parkinson's disease and other neurologic conditions

W. Jost[1], F. Pagan[2], A. Friedman[3], O. Michel[4], C. Oehlwein[5], J. Slawek[6], A. Bogucki[7], S. Ochudlo[8], M. Banach[9], B. Flatau-Baqué[10], J. Csikos[10], A. Blitzer[11]

[1]Parkinson-Klinik, Ortenau, Wolfach, Germany, [2]Georgetown University, Washington D.C., United States, [3]Medical University of Warsaw, Warsaw, Poland, [4]University Hospital Brussels, Brussels, Belgium, [5]Neurological Outpatient Clinic for Parkinson Disease and Deep Brain Stimulation, Gera, Germany, [6]Medical University of Gdansk, Gdansk, Poland, [7]Medical University of Łódź, Łódź, Poland, [8]Medical University of Silesia, Katowice, Poland, [9]Collegium Medicum, Jagiellonian University, Krakow, Poland, [10]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [11]Icahn School of Medicine at Mt. Sinai, New York, United States

Background: We investigated the effect of repeated incobotulinumtoxinA injections on salivary flow rate in adults with chronic sialorrhea due to Parkinson's disease (PD), atypical parkinsonism, stroke or traumatic brain injury in the 64-week SIAXI study.

Methods: SIAXI (NCT02091739) was a pivotal double-blind, randomised, placebo-controlled phase 3 study with a 48-week extension period (EP). In the main phase (MP) subjects were randomised (2:2:1) to incobotulinumtoxinA 75 or 100 U (n=74 each), or placebo (n=36) in a single injection cycle (IC). At completion, eligible patients entered the EP and received three further incobotulinumtoxinA ICs (each 16±2 weeks) of 75 U or 100 U. Outcomes assessed in subjects who received incobotulinumtoxinA in all four ICs included: unstimulated salivary flow rate (uSFR), modified Radboud Oral Motor Inventory for Parkinson's Disease (mROMP) speech symptom scores and dental adverse events (AEs).

Results: In total, 140/148 subjects, who received incobotulinumtoxinA 75 U (n=68) or 100 U (n=72) in all ICs, completed the MP and entered the EP. With incobotulinumtoxinA 75 U and 100 U, respectively, mean (SD) uSFR decreased in all ICs from MP baseline at all visits (0.42 [0.28] and 0.40 [0.27] g/min; including subjects who did not continue to EP) and at the end-of-study visit (0.26 [0.24] and 0.22 [0.18] g/min). Maximal reductions were observed at 4 weeks and sustained at 16 weeks post-injection in all ICs. The most common dental AE was tooth extraction (4.4% and 5.6%) unrelated to treatment. Treatment-related gingivitis was reported in one 100 U recipient.

Conclusions: Data demonstrate a consistent reduction in salivary flow rate at each IC, within normal physiological levels. Subjects did not reach a level of hyposalivation. Stable mROMP speech symptom scores suggest that sufficient saliva remained in the oral cavity to prevent speech impairment. Assessment of dental health showed no safety issues due to hyposalivation.

P 100
Placebo-controlled, randomized, double-blind study of incobotulinumtoxinA for sialorrhea

W. Jost[1], A. Friedman[2], O. Michel[3], C. Oehlwein[4], J. Slawek[5], A. Bogucki[6], S. Ochudlo[7], M. Banach[8], F. Pagan[9], B. Flatau-Baqué[10], J. Csikos[10], C.J. Cairney[11], A. Blitzer[12]

[1]Parkinson-Klinik, Ortenau, Wolfach, Germany, [2]Medical University of Warsaw, Warsaw, Poland, [3]University Hospital Brussels, Brussels, Belgium, [4]Neurological Outpatient Clinic for Parkinson Disease and Deep Brain Stimulation, Gera, Germany, [5]Medical University of Gdansk, Gdansk, Poland, [6]Medical University of Łódź, Łódź, Poland, [7]Medical University of Silesia, Katowice, Poland, [8]Collegium Medicum, Jagiellonian University, Krakow, Poland, [9]Georgetown University, Washington D.C., United States, [10]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [11]CMC - McCann, Glasgow, United Kingdom, [12]Icahn School of Medicine at Mount Sinai, New York, United States

Background: This pivotal phase III study, SIAXI, investigated the efficacy and safety of incobotulinumtoxinA for the treatment of chronic sialorrhea due to Parkinson disease (PD), atypical parkinsonism, stroke, or traumatic brain injury (TBI).

Methods: Adult patients with PD (70.7%), atypical parkinsonism (8.7%), stroke (19.0%), or TBI (2.7%) were randomized (2:2:1) to double-blind treatment with placebo (n = 36), or total doses of incobotulinumtoxinA 75U (n = 74) or 100U (n = 74), in a single treatment cycle. The coprimary endpoints were change in unstimulated salivary flow rate from baseline to week 4, and patients' Global Impression of Change Scale score at week 4. Adverse events were recorded throughout.

Results: A total of 184 patients were randomized. Both incobotulinumtoxinA dose groups showed reductions in mean unstimulated salivary flow rate at week 4, with a significant difference vs placebo in the incobotulinumtoxinA 100 U group (p = 0.004). Patients' Global Impression of Change Scale scores also improved at week 4, with a significant difference vs placebo in the incobotulinumtoxinA 100 U group (p = 0.002). A lasting effect was observed at week 16 post injection. The most frequent treatment-related adverse events in the incobotulinumtoxinA 75 U and 100 U groups were dry mouth (5.4% and 2.7% of patients) and dysphagia (2.7% and 0.0% of patients).

Conclusions: IncobotulinumtoxinA 100 U is an effective and well-tolerated treatment of chronic sialorrhea in adults.

P 101

Long-term motor and non-motor symptom benefits of levodopa-carbidopa intestinal gel by baseline Hoehn & Yahr stage: DUOGLOBE post hoc analysis

F.E Pontieri[1], K.R. Chaudhuri[2], J. Aldred[3], P. Bourgeois[4], T.L Davis[5], E. Cubo[6], M. Anca-Herschkovitsch[7], R. Iansek[8], M.S Siddiqui[9], M. Simu[10], L. Bergmann[11], O. Ladhani[11], T. Gao[11], D.G Standaert[12], N. Kovács[13]

[1]Sapienza University of Rome, Department of Neurological Sciences, Mental Health & Sensory Organs, Rome, Italy, [2]Parkinson's Foundation International Centre of Excellence, King's College Hospital, and King's College Institute of Psychiatry, Biomedical Research Centre, Psychology & Neuroscience, London, United Kingdom, [3]Selkirk Neurology, Spokane, United States, [4]AZ Groeninge, Department of Neurology, Kortrijk, Belgium, [5]Vanderbilt University Medical Center, Department of Neurology, Nashville, United States, [6]Hospital Universitario Burgos, Neurology Department, Burgos, Spain, [7]Edith Wolfson Medical Center, Department of Neurology, Holon, Israel, [8]Kingston Centre, Monash Health, Melbourne, Australia, [9]Wake Forest School of Medicine, Department of Neurology, Winston Salem, United States, [10]Victor Babes University of Medicine and Pharmacy, Department of Neurology, Timisoara, Romania, [11]AbbVie Inc., North Chicago, United States, [12]University of Alabama at Birmingham, Department of Neurology, Birmingham, United States, [13]University of Pécs, Department of Neurology, Pécs, Hungary

Background: Real-world data on the impact of baseline disease severity on efficacy and safety of levodopa-carbidopa intestinal gel (LCIG) are limited. This analysis evaluates the effect of baseline disease severity on long-term effectiveness and safety of LCIG treatment in routine clinical practice.

Methods: DUOGLOBE (NCT02611713) was a prospective, multinational, observational study of LCIG-naïve patients treated in routine clinical practice and 3-year follow-up. Stratified by H&Y scores <3 and ≥3 at baseline, this post hoc analysis assessed change from baseline to month (M) 36 for "Off" time, Unified Dyskinesia Rating Scale (UDysRS), Non-Motor Symptom Scale (NMSS), Unified Parkinson's Disease Rating Scale (UPDRS) II and III, axial symptoms (UPDRS III axial items [sum of 18/22/27–30]), Parkinson's diesease Questionnaire 8 (PDQ-8), and serious adverse events (SAEs).

Results: Of 188 patients with baseline H&Y scores, baseline characteristics in both groups were similar except mean (SD) UPDRS II (<3, 10.7 [6.7]; ≥3, 16.8 [7.6]) and III (<3, 19.3 [9.4]; ≥3, 31.7 [13.0]).Strong, significant improvements were observed in "Off" time through M36 in both groups (<3, P<.01; ≥3, P<.001). In <3, UDysRS total scores improved significantly until M12 (P<.05) and numerically through M36, and significantly improved through M36 (P<.05) in ≥3.

Sustained improvements in NMSS were observed in both groups (both P<.05), with significant improvements in PDQ-8 until M18 (<3, P<.05; ≥3, P<.01). Both groups showed a significant increase in UPDRS II and III scores at M36 (UPDRS II <3, P<.001; ≥3, P<.05; UPDRS III <3, P<.01; ≥3, P<.05). Axial symptoms worsened in <3 (P<.001) but remained generally stable over time in ≥3. SAEs and discontinuation rates were generally similar in both groups.

Conclusions: This first reported long-term analysis in patients who received LCIG in different H&Y stages suggests patients experience important benefits from LCIG treatment independent of H&Y stage. Safety was consistent with the established LCIG safety profile.

P 102 (GPT)
Levodopa-Carbidopa intestinal gel may improve treatment-resistant freezing of gait

M. Shackleford[1,2], V. Mishra[2], Z. Mari[2]
[1]Kirk Kerkorian School of Medicine UNLV, Las Vegas, United States, [2]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States

Background: Freezing of gait (FOG) is a highly disabling symptom in Parkinson's Disease (PD) with varying degree of benefits from oral dopaminergic medications and several subtypes that present with different medication states (e.g., off FOG, on FOG, pseudo-on FOG, supra-on FOG). Levodopa-Carbidopa Intestinal Gel (LCIG) avoids the fluctuations in dopamine levels inherent to oral therapy via continuous jejunal delivery of medication. While the ability of LCIG to treat various motor symptoms of PD is well-characterized, there are few publications specifically addressing its ability to treat FOG. This review examines the literature surrounding LCIG as a therapy for FOG.
Methods: A PubMed search was conducted using the search query "Intestinal AND (Levodopa OR L-dopa) AND Freezing of Gait AND Parkinson." Additional eligibility criteria included articles written in English and currently published journal articles. Articles were excluded if they did not have a clinical design or if they did not yield reportable data on FOG.
Results: The literature search yielded 15 articles, of which we included 10 and excluded 5. Of the 10 studies included, there were 5 retrospective studies, 4 case reports, and 1 chart review (n=449 patients total). 9 of the 10 studies concluded that LCIG has a favorable effect on FOG.
Conclusions: LCIG is a promising treatment for patients with FOG that is poorly controlled with oral therapy because of its ability to reduce fluctuations in dopamine levels. Further research is necessary on LCIG as a therapy for refractory FOG, with particular attention to the different subtypes of FOG.

P 103
ParkinsonGoesDTx – a novel gait monitor concept triggers treatment decisions in Parkinson's disease

T. Gladow[1,2], S. Stallforth[2,1], J. Stiefel[1], J. Jukic[2], B. Eskofier[3], J. Winkler[2], J. Klucken[1,2,4,5,6]
[1]Medical Valley Digital Health Application Center, Bamberg, Germany, [2]University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Molecular Neurology, Erlangen, Germany, [3]Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Machine Learning and Data Analytics Lab, Erlangen, Germany, [4]University of Luxembourg, Digital Medicine Department (LCSB), Luxembourg, Luxembourg, [5]Luxembourg Institute of Health (LIH), Luxembourg, Luxembourg, [6]Centre Hospitalier de Luxembourg (CHL), Luxembourg, Luxembourg

Background: Digital therapeutics (DTx) are patient-centered medical devices with an interventional effect on disease characteristics. The digital healthcare act in Germany (DVG) enables physicians to prescribe DTx to patients after positive care effects have been demonstrated. An innovative digital application for gait

analysis is ParkinsonGo, aiming to monitor the health status of Parkinson's patients using sensor-based and patient-reported outcomes to support clinical decisions. The interventional benefit of ParkinsonGo was evaluated in an intersectoral multicenter trial in Germany.

Methods: ParkinsonGo (Portabiles HCT, Germany) is designed as a digital companion with a smartphone-enabled application, wearable sensors, and a web interface for physicians to capture scripted and free-living gait characteristics, document symptoms and gait-related events, and visualize progress for patients and their treating physicians.

Patients with Parkinson's disease (PD) were enrolled for a 60-day clinical trial. Endpoints include the status of health (motor-symptoms - UPDRS III), quality of life ($PDQ\text{-}39_{mob}$), patient sovereignty (SDM-Q9), and health literacy (ErPDKT) analyzed by repeated measures designs between baseline (day 0) and closeout (day 60).

Results: Twenty-two patients were recruited for the study. An interim analysis was performed with 18 participants (83% male, mean age = 60 years, mean Hoehn & Yahr = 1.8). The UPDRS III motor score decreased (Δ = -2.00) statistically significant ($p < 0.02$) within the intervention period. In 59% of patients (-37 points) the motor score decreased, 12% had a small increase (+3 points). Improvement in mobility-related quality of life (PDQ-39mob Δ = -2.22; $p = 0.275$), patient sovereignty (SDM-Q-9 Δ = 1.75; $p = 0.332$), and health literacy (ErPDKT Δ = 3.12; $p = 0.085$) was observed.

Conclusions: Despite the short observation period and small sample size, significant positive care effects were demonstrated. By monitoring individual gait features using DTx, patients are able to assess their health status and participate in clinical decision-making.

P 104
Impact of injection guidance techniques on the efficacy and safety of incobotulinumtoxinA for sialorrhea

W. Jost[1], F. Pagan[2], O. Michel[3], C. Oehlwein[4], J. Slawek[5], A. Bogucki[6], S. Ochudlo[7], M. Banach[8], B. Flatau-Baqué[9], J. Csikos[9], A. Blitzer[10]

[1]Parkinson-Klinik, Ortenau, Wolfach, Germany, [2]Georgetown University, Washington D.C., United States, [3]University Hospital Brussels, Brussels, Belgium, [4]Neurological Outpatient Clinic for Parkinson Disease and Deep Brain Stimulation, Gera, Germany, [5]Medical University of Gdansk, Gdansk, Poland, [6]Medical University of Łódź, Łódź, Poland, [7]Medical University of Silesia, Katowice, Poland, [8]Collegium Medicum, Jagiellonian University, Krakow, Poland, [9]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [10]Icahn School of Medicine at Mount Sinai, New York, United States

Background: SIAXI (NCT02091739), a double-blind, randomized, placebo-controlled study, assessed the efficacy and safety of incobotulinumtoxinA 75 or 100 U in patients with sialorrhea due to Parkinson's disease (PD), atypical parkinsonism, stroke or traumatic brain injury. This subgroup analysis assessed the impact of injection guidance technique.

Methods: Patients were randomized (2:2:1) to incobotulinumtoxinA 75 or 100 U, or placebo, distributed in bilateral parotid and submandibular glands in a single injection cycle (IC) in the main period (MP). All eligible patients completing the MP received three further incobotulinumtoxinA ICs (75 or 100 U; each 16±2

weeks) in the extension period (EP). Injections were guided by ultrasound (US) or anatomical landmarks (AL). Outcomes included unstimulated salivary flow rate (uSFR) and patients' Global Impression of Change Scale (GICS). The incidence of adverse events (AEs) was reported.

Results: 184 patients received either incobotulinumtoxinA 75 U (n=74) or 100 U (n=74), or placebo (n=36) in the MP; 173 entered the EP. In the MP, injections were guided by US in 56.5% of patients and by AL in 43.5%. Among patients treated with incobotulinumtoxinA in all 4 ICs, mean uSFR decreased with 75 U and 100 U from baseline to 4 weeks post-injection, (mean [SD] change from baseline to end of study: US, –0.15 [0.20] and –0.17 [0.25]; AL, –0.19 [0.22] and –0.17 [0.20]). Patients' GICS also showed improvement at 4 weeks post-injection with both US and AL guidance. The incidence of AEs over all ICs with incobotulinumtoxinA treatment was similar with US and AL guidance (67.0% and 61.0%). The most frequent treatment-related AEs were dry mouth (10.7% and 6.5%) and dysphagia (3.9% and 2.6%).

Conclusions: In contrast to current literature, repeated incobotulinumtoxinA injections under US or AL guidance are similarly effective and well tolerated for sialorrhea in patients with PD or other neurological disorders.

P 105
Apomorphine sublingual film for "OFF" episodes in Parkinson's disease: long-term safety and efficacy

S. Factor[1], W.G. Ondo[2], S. Isaacson[3], I. Zhang[4], B. Navia[4], E. Pappert[4]

[1]Emory University, Atlanta, United States, [2]Methodist Neurological Institute, Houston, United States, [3]Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, United States, [4]Sunovion Pharmaceuticals Inc., Marlborough, United States

Background: Apomorphine sublingual film (APL) was efficacious and well tolerated for treatment of "OFF" episodes in Parkinson's disease (PD) in a pivotal 12-week study.

Methods: Patients with PD and "OFF" episodes on stable PD medications were enrolled in an open-label, Phase 3 study (NCT02542696). In patients who were "OFF," APL was titrated to an effective, tolerable dose (10–35 mg; 5-mg increments) resulting in FULL "ON" within 45 minutes. During the long-term safety phase, patients self-administered their titrated dose for ≤5 "OFF" episodes/day. Endpoints included treatment-emergent adverse events (TEAEs) during long-term treatment (primary), change from predose in MDS-UPDRS Part III score, percentage of patients with self-rated FULL "ON" 30 minutes postdose, and change in Clinical and Patient Global Impression of Improvement (CGI-I, PGI-I) responses.

Results: Patients (n=397) who received ≥1 APL dose (40%, 24%, and 11% for >6, >12, and >24 months, respectively) during long-term treatment were evaluated (data cut 30Sep2020). Most patients (64%) achieved FULL "ON" at 10–20 mg (most common: 15 mg). TEAEs occurred in 84% of patients; most (58%) were mild. Nausea (21%); fall (8%); oral mucosal erythema (7%); somnolence (7%); and dizziness, dyskinesia, fatigue, lip swelling, mouth ulceration, and yawning (6% each) occurred most frequently (>5%). TEAEs led to discontinuation in 35% of patients; most common was nausea (6%). Five deaths occurred during long-term treatment (unrelated to study drug). At week 24, MDS-UPDRS Part III scores at 15, 30, and 60 minutes postdose decreased –13.9, –21.4, and –20.2 points from predose, respectively.

Similar changes occurred at 36 and 48 weeks. Patient-rated FULL "ON" within 30 minutes was achieved by ≥76% of patients (office visits or home diary) at weeks 24–48. Most patients (≥61%) demonstrated improved CGI-I and PGI-I responses.
Conclusions: APL is well tolerated and effective for long-term "on-demand" treatment of "OFF" episodes in PD.

P 106
Apomorphine sublingual film has minimal effect on impulse control disorders in long-term treatment of "OFF" episodes in Parkinson's disease

A. Espay[1], *K. Markopoulou*[2,3], *I. Zhang*[4], *B. Navia*[4], *E. Pappert*[4]
[1]University of Cincinnati, Cincinnati, United States, [2]NorthShore Neurological Institute, Glenview, United States, [3]University of Chicago, Chicago, United States, [4]Sunovion Pharmaceuticals Inc., Marlborough, United States

Background: Dopaminergic agents, including apomorphine, have been associated with impulse control disorders (ICD); however, the effect of apomorphine sublingual film (APL) on ICDs during treatment of "OFF" episodes in Parkinson's disease (PD) remains unclear.
Methods: An open-label, Phase 3 study (NCT02542696) evaluated long-term safety (LTS) and efficacy of APL in patients (new or rollover from prior studies) with PD and "OFF" episodes on stable PD medications. APL dose titration occurred while patients were "OFF" to determine the dose (10–35mg; 5-mg increments) providing FULL "ON" within 45 minutes. During LTS treatment, patients self-administered their titrated APL dose for up to 5 "OFF" episodes/day. ICDs were assessed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease–Rating Scale (QUIP-RS). Treatment-emergent adverse events (TEAE) associated with ICDs were also evaluated. Results were assessed at weeks 24, 36, and 48 and summarized descriptively.
Results: This analysis (data cut 30Sep2020) evaluated 397 patients (median [range] APL exposure was 169 days [1–1181]; 1.8 mean doses/day; highest dose received in the LTS phase, 10/15/20/25/30/35 mg: 18%/23%/23%/18%/11%/7%). Mean (SD) baseline total ICD score was 5.4 (6.6); changes from baseline were –0.2 (6.3), –0.5 (8.2), and –0.5 (7.5) at weeks 24, 36, and 48, respectively. Mean (SD) baseline total QUIP-RS score was 10.0 (12.0); changes from baseline were –1.7 (11.8), –2.9 (15.38), and –2.0 (16.5) at weeks 24, 36, and 48, respectively. Incidences of ICD behaviors decreased or remained similar from baseline to week 48: gambling (14% vs 16%), sex (47% vs 34%), buying (40% vs 30%), eating (54% vs 37%), hobbyism/punding (53% vs 37%), and medication use (41% vs 34%). TEAEs associated with ICDs occurred in <1% of patients during the LTS phase.
Conclusions: APL as "on-demand" treatment for "OFF" episodes in patients with PD had minimal effect on ICDs for up to 48 weeks in the long-term study.

P 107

Apomorphine sublingual film does not worsen dyskinesia in the long-term treatment of "OFF" episodes in Parkinson's disease

K.J. Klos[1], J.S. Hui[2], I. Zhang[3], B. Navia[3], E. Pappert[3]

[1]The Movement Disorder Clinic of Oklahoma, Tulsa, United States, [2]Keck School of Medicine, University of Southern California, Los Angeles, United States, [3]Sunovion Pharmaceuticals Inc., Marlborough, United States

Background: Dopaminergic agents, including apomorphine, have been associated with dyskinesia; however, the effect of apomorphine sublingual film (APL) on dyskinesia during treatment of "OFF" episodes in Parkinson's disease (PD) is unclear.

Methods: Patients with PD and "OFF" episodes on stable PD medications were enrolled in an open-label, Phase 3 study (NCT02542696). APL dose titration occurred while patients were "OFF" to determine the dose (10–35 mg; 5-mg increments) resulting in tolerable FULL "ON" within 45 minutes. In the long-term safety (LTS) phase, patients self-administered their titrated APL dose for ≤5 "OFF" episodes/day. Dyskinesia was assessed using MDS-UPDRS Part IV. Treatment-emergent adverse events of dyskinesia were evaluated. Results were assessed at weeks 24, 36, and 48 and summarized descriptively.

Results: Analyses (data cut 30Sep2020) evaluated 397 patients (median [range] exposure to APL was 169 days [1–1181]; 1.8 mean doses/day; highest dose during LTS phase, 10/15/20/25/30/35 mg: 18%/23%/23%/18%/11%/7%). Mean (SD) percent time with dyskinesia decreased from baseline (12.0 [16.9]) by –1.1 (21.5), –2.0 (19.6), and –3.9 (19.0) at weeks 24, 36, and 48, respectively.

Time spent with dyskinesia was normal to mild severity in 96% of patients at baseline and 98%, 99%, and 99% at weeks 24, 36, and 48, respectively. More patients reported "Improved" or "No change" versus "Worsening" for change from baseline in time spent with dyskinesia at weeks 24 (83% vs 17%), 36 (84% vs 16%), and 48 (83% vs 17%), and functional impact of dyskinesia at weeks 24 (83% vs 17%), 36 (87% vs 13%), and 48 (83% vs 17%).

Conclusions: APL as "on-demand" treatment for "OFF" episodes in patients with PD reduced time with dyskinesia and increased rates of "Improved" or "No change" versus "Worsening" of dyskinesia for ≤48 weeks in the long-term study. Data suggest long-term APL use is not associated with development or worsening of dyskinesia.

P 108

Antiemetics may not be necessary for titration of apomorphine sublingual film for the treatment of "OFF" episodes in Parkinson's disease

R.A. Hauser[1], S.A. Factor[2], W.G. Ondo[3], I. Zhang[4], B. Navia[4], E. Pappert[4]

[1]University of South Florida, Tampa, United States, [2]Emory University, Atlanta, United States, [3]Houston Methodist Neurological Institute, Houston, United States, [4]Sunovion Pharmaceuticals Inc., Marlborough, United States

Background: Antiemetics (eg, trimethobenzamide) have been used prophylactically in clinical trials to prevent nausea and vomiting associated with apomorphine use. The need for antiemetics to achieve an efficacious and tolerable apomorphine sublingual film (APL) dose for patients with Parkinson's disease (PD) and "OFF" episodes remains unclear.

Methods: An open-label, Phase 3 study (NCT02542696) enrolled patients (new [no previous APL exposure] or rollover from prior APL studies) with PD and "OFF" episodes while on stable PD medications. APL dose titration (DT) occurred while "OFF" to determine the dose (10–35 mg; 5-mg increments) resulting in a tolerable FULL "ON" within 45 minutes.

After a protocol amendment, use of antiemetic treatment with trimethobenzamide (300 mg 3 times daily) was permitted only if clinically warranted. Results of a post hoc analysis of nausea and vomiting rates are reported descriptively in new United States (US) patients who received APL (10–30 mg) with or without trimethobenzamide.

Results: This analysis (data cutoff 30 Sep 2020) evaluated 176 new US patients who received ≥1 APL dose during DT, of whom 145 (82%) did not use trimethobenzamide. During DT, 88% (127/145) of patients who did not use trimethobenzamide achieved an efficacious and tolerable dose and enrolled in the long-term safety phase. Nausea (13%), vomiting (1%), and nausea/vomiting (13%) were reported in patients who did not use trimethobenzamide. All events were mild to moderate; none led to discontinuation. Trimethobenzamide was used by 31/176 (18%) patients during DT. Patients who used trimethobenzamide reported nausea (52%), vomiting (13%), and nausea/vomiting (55%). Most events were mild to moderate (≥75%). Nausea and nausea/vomiting each led to discontinuation in 10% of these patients.

Conclusions: This post hoc analysis examining the need for antiemetics during titration of APL suggests most patients with PD and "OFF" episodes can be titrated to an efficacious and tolerable dose without antiemetics.

P 109

Apomorphine sublingual film for "OFF" episodes in Parkinson's disease: analysis of baseline factors

A.P. Nicholas[1], *C. Singer*[2], *I. Zhang*[3], *B. Navia*[3], *E. Pappert*[3]

[1]University of Alabama at Birmingham, Birmingham, United States, [2]University of Miami Health System, Miami, United States, [3]Sunovion Pharmaceuticals Inc., Marlborough, United States

Background: Apomorphine sublingual film (APL) is approved for "on-demand" treatment of "OFF" episodes in Parkinson's disease (PD) in the US and Canada. This analysis determined if baseline factors were associated with the APL dose required to achieve FULL "ON."

Methods: Patients with PD and "OFF" episodes on stable PD medications were enrolled in 2 studies (pivotal: NCT02469090; long-term: NCT02542696). APL dose titration occurred in patients who were "OFF" to determine the effective and tolerable dose (10–35 mg; 5-mg increments) that converted them to FULL "ON" within 45 minutes.

Baseline factors evaluated included age, body mass index, gender, region, predose MDS-UPDRS Part III score, Hoehn and Yahr score when "ON," time since PD diagnosis, baseline daily levodopa dose, length/number of "OFF" episodes, and dopamine agonist use at baseline or monoamine oxidase-B inhibitors any time.

Association between baseline factors and APL dose that achieved FULL "ON" during titration was assessed by Spearman rank correlation and/or other descriptive statistics.

Results: Of 414 patients who completed dose titration across both studies, moderate positive correlations were observed with APL dose resulting in FULL "ON" and predose MDS-UPDRS Part III score (n=414; r=0.233; 95% CI: 0.140, 0.322) and baseline daily levodopa dose (n=400; r=0.240; 95% CI: 0.145, 0.330).

Higher (30-35 mg) versus lower (10-15 mg) APL doses, respectively, were required for patients with predose MDS-UPDRS Part III score ≥44 and <88 (58–61% vs 26–37%), PD diagnosis ≥5 years (87–91% vs 78–81%), baseline levodopa ≥900 mg/d (61–74% vs 44–45%), and baseline dopamine agonist use (74–76% vs 47–54%) to convert from "OFF" to FULL "ON."

Conclusions: Baseline factors (predose MDS-UPDRS Part III score, baseline daily levodopa dose, PD duration, and baseline dopamine agonist use) may predict APL doses required to achieve FULL "ON." Patients with more advanced disease may require higher doses.

P 110

Population pharmacokinetics model of apomorphine (sublingual film or subcutaneous injection) in healthy subjects and patients with Parkinson's disease (updated)

F. Agbo[1], R.L. Crass[2], Y.-Y. Chiu[1], S. Chapel[2], G. Galluppi[1], B. Navia[3]

[1]Sunovion Pharmaceuticals, Inc., Fort Lee, United States, [2]Ann Arbor Pharmacometrics Group, Inc., Ann Arbor, United States, [3]Sunovion Pharmaceuticals, Inc., Marlborough, United States

Background: Apomorphine sublingual film (APL) is approved for "on-demand" treatment of "OFF" episodes in Parkinson's disease (PD) in the US and Canada. Herein, apomorphine and apomorphine sulfate pharmacokinetics (PK) were characterized in healthy subjects and patients with PD after apomorphine treatment (APL or apomorphine subcutaneous injection [SC-APO]) using a population-based PK modeling approach.

Methods: Pooled PK data from 87 healthy Asian subjects and 101 patients with PD (North America, n=55; Europe, n=46) were collected from 10 studies (3333 apomorphine and 1851 apomorphine sulfate samples). Joint parent-metabolite PK analyses were done sequentially with NONMEM® (version 7.3) using first-order conditional estimation method with interaction. Prespecified covariate-parameter relationships were evaluated using a full model approach followed by backward elimination. Candidate models were assessed by standard goodness-of-fit plots, change in objective function value, precision in parameter estimates, and condition number. Predictive performance of the final model was assessed with visual predictive checks.

Results: Using data from 5 Phase 1, 3 Phase 2, and 2 Phase 3 studies, apomorphine and apomorphine sulfate PK was well described by 2- and 1-compartment disposition models, respectively, with transit absorption via both sublingual and subcutaneous routes and linear elimination of both analytes. Bioavailability of APL relative to SC-APO was about 18% (healthy subjects) and 23% (patients with PD) at a 20-mg dose. Additional covariates in the joint parent-metabolite final model included contact time under the tongue on APL absorption rate, as well as creatinine clearance and female sex on apomorphine sulfate clearance and volume, respectively. The effect of these covariates on exposure was marginal and not expected to be clinically meaningful.

Conclusions: A population PK model adequately described comparable and differentiated PK characteristics of apomorphine and apomorphine sulfate after APL and SC-APO administration and supports its administration in patients with PD and "OFF" episodes, regardless of demographic and clinical characteristics.

P 111

Comparison of pharmacokinetics of apomorphine (sublingual film or subcutaneous injection) between patients with Parkinson's disease in Europe and North America

F. Agbo[1], S.J. Brantley[2], J. Hu[2], Y.-Y. Chiu[1], J. Schwarz[3], F. Stocchi[4], B. Navia[5]

[1]Sunovion Pharmaceuticals, Inc., Fort Lee, United States, [2]Nuventra, LLC, Durham, United States, [3]Kliniken Kreis Mühldorf, Oberbayern, Germany, [4]University and Institute for Research and Medical Care San Raffaele, Rome, Italy, [5]Sunovion Pharmaceuticals, Inc., Marlborough, United States

Background: Apomorphine (sublingual film [APL]; subcutaneous injection [SC-APO]) is an approved "on-demand" treatment for Parkinson's disease (PD) "OFF" episodes. Limited data are available comparing European (EU) versus North American (NA) patients. Pooled clinical data were used to assess/compare APL and SC-APO pharmacokinetics (PK) in EU and NA patients.

Methods: Noncompartmental PK parameters were available for 86 APL-treated (EU, n=41; NA, n=45) and 34 SC-APO-treated (EU, n=26; NA, n=8) patients across 4 studies. Regional effect (EU vs NA) was evaluated with a mixed-effects model comparing area under the concentration curve (AUC) from time zero to last quantifiable concentration (AUC_{last}) or extrapolated to infinity (AUC_{inf}), and maximum concentration (C_{max}). Relative bioavailability of APL to SC-APO for AUC_{last}, AUC_{inf}, and C_{max} was evaluated with a mixed-effects model. Dose proportionality was explored using a power model constructed from natural log (Ln)-transformed PK parameters and Ln-transformed dose.

Results: There were no discernable differences in dose-normalized PK between EU and NA patients; geometric least squares mean ratio (90% CI) for AUC_{inf}, AUC_{last}, and C_{max} was 104% (84.6–128%), 100% (82.5–122%), and 122% (95.8–154%), respectively. Relative bioavailability of APL to SC-APO was 22% (AUC) and 15% (C_{max}). With increasing APL dose, apomorphine exposure increased less than dose proportionally (slope estimates: C_{max}, 0.516; AUC_{last}, 0.596), and apomorphine sulfate exposure increased approximately dose proportionally (slope estimates: C_{max}, 1.01; AUC_{last}, 0.951). With increasing SC-APO dose, apomorphine and apomorphine sulfate exposure increased slightly greater than dose proportionally (C_{max}, 1.32 and 1.24; AUC, 1.31 and 1.26, respectively).

Conclusions: Apomorphine and apomorphine sulfate PK post-APL dosing were similar for EU and NA patients. Apomorphine exposure was less than dose proportional with APL and slightly greater than dose proportional with SC-APO. Relative bioavailability of APL to SC-APO was <25%. These data support APL use in patients with PD and "OFF" episodes, regardless of geographical region.

P 112 (GPT)

Effect of istradefylline dosage on unified Parkisons' disease rating scale (UPDRS) III-ON scores: results from four randomized clinical trials

J. Kulisevsky[1], *Y. Nakajima*[2], *N. Kronfeld*[3], *S. King*[4], *A. Mori*[5]

[1]Sant Pau Hospital, Universitat Autònoma de Barcelona, Ciberned, Barcelona, Spain, [2]Kyowa Kirin, Inc., Biometrics, Princeton, United States, [3]Kyowa Kirin, Inc., Medical Affairs, Marlow, United Kingdom, [4]Kyowa Kirin, Inc., Medical Affairs, Bedminster, United States, [5]Kyowa Kirin Co., Ltd., Medical Affairs, Tokyo, Japan

Background: Istradefylline, a non-dopaminergic selective adenosine A_{2A} receptor antagonist, is indicated in the US and Japan as adjunctive treatment to levodopa-containing medication in adults with Parkinson's disease (PD) experiencing OFF-time. This four-trial analysis evaluated impact of istradefylline dosage on UPDRS-III-ON score.

Methods: Data from four randomized phase 2b/3 trials (6002-US-018, 6002-009, 6002-0608, and 6002-014) were analyzed to determine the difference in impact of 20 vs 40mg/day istradefylline on UPDRS-III-ON scores in patients with PD experiencing OFF-time.

For each study, difference in least-squares (LS) mean change from baseline in UPDRS-III-ON scores between the two dosages was assessed by mixed-model repeated-measures analyses; results were combined using a random-effect meta-analysis.

Results: The LS mean change from baseline to week 12 in UPDRS-III-ON score was greater with istradefylline than placebo; in three studies, this effect was greater at the 40mg/day dosage vs 20mg/day (*Figure*).

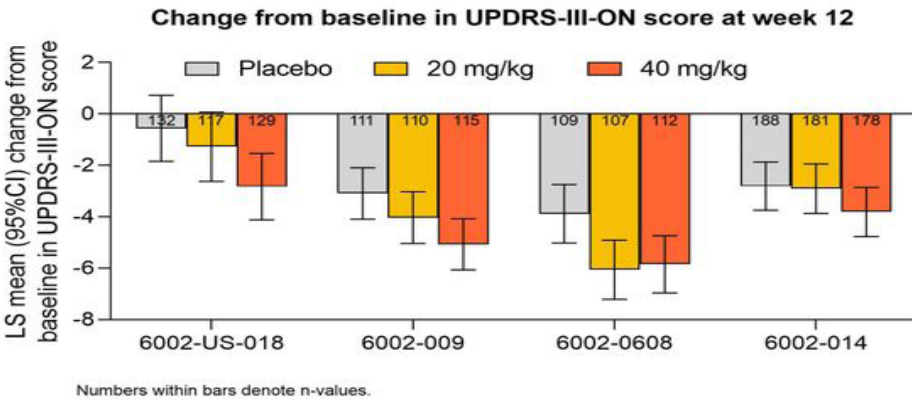


Figure. Change from baseline (CFB) in UPDRS-III-ON score at week 12

In the random-effect meta-analysis, there was a significant difference in LS mean change from baseline between 20 and 40mg/day treatment arms (-0.80 [95%CI, -1.55, -0.04], nominal p=0.038). The rates of treatment-emergent adverse events (TEAEs) from each of the four studies were comparable between the

20 (59-82%) and 40mg/day (59-84%) dosages; the most common TEAE was dyskinesia in three studies (20mg/day, 11-17% vs 40mg/day, 12-26%) and nasopharyngitis in one (6% vs 9%). Impact of baseline UPDRS-III-ON score on improvements at both dosages will be presented.
Conclusions: Regarding motor improvement, these data suggest that 40mg/day istradefylline has greater benefit than 20mg/day. Safety was comparable between the two istradefylline treatment groups.
Supported by: Kyowa Kirin, Inc.

P 113 (GPT)

SAGE-718 in Parkinson's disease mild cognitive impairment: results from the Phase 2 PARADIGM Study

A. Koenig[1], *J. Johannesen*[1], *E. Freitag*[1], *S. Li*[1], *J. Petrillo*[1], *J. Wald*[1], *K. Paumier*[1], *M. Quirk*[1], *J. Doherty*[1]
[1]Sage Therapeutics, Inc., Cambridge, United States

Background: Mild cognitive impairment in patients with Parkinson's disease (PD-MCI) is an area of significant unmet need.
Methods: PARADIGM (NCT04476017) is a Phase 2, open-label trial of SAGE-718 in patients with PD-MCI. Patients (aged 50-75 years) meeting PD-MCI criteria (Movement Disorders Society Task Force), with a baseline Montreal Cognitive Assessment (MoCA) score of 20-25, were administered SAGE-718 3-mg tablets once daily for either 14 days (Part A) or for 28 days (Part B).
The primary endpoint was incidence of treatment-emergent adverse events (TEAEs); plasma pharmacokinetics, cognitive measures, and functional outcomes (patient and caregiver perspective) were also collected.
Results: Part A enrolled 11 patients; mean (standard deviation [SD]) age was 69.1 (6.9) years, mean (SD) MoCA baseline score was 23.8 (2.3), 90.9% Hoehn & Yahr stage 2, 81.8% male, and 100% White. At Day 14, improvements from baseline were observed on multiple tests of executive functioning (Digit Symbol Substitution, Multitasking, One Touch Stockings, Spatial Working Memory, and 2-Back tests).
Results indicate improvement relative to baseline on select tests of learning and memory (Pattern Recognition Memory and Verbal Recognition Memory tests) as well. Importantly, no change was observed on measures of simple attention/psychomotor speed.
No severe/serious adverse events or deaths were reported, and no TEAEs were considered study drug related or resulted in drug discontinuation or study withdrawal. The observed pharmacokinetic profile was consistent with previous studies. Part A is complete; Part B (28-day dosing cohort) will provide additional results to inform clinical development activities.
Conclusions: SAGE-718 was generally safe and well tolerated and associated with improved performance on tests of executive functioning and learning/memory in patients with PD-MCI. These results are consistent with previous exploratory studies in healthy adults and both Alzheimer's and Huntington's patient populations, and support further investigation of SAGE-718 in treating mild cognitive impairment.

P 114

The effects of once-daily opicapone 50 mg on the pharmacokinetics of levodopa administered as carbidopa/levodopa extended-release capsules: an open-label study

O. Klepitskaya[1], *A. Vijan*[1], *K. Olson*[1], *T. O'Reilly*[2], *G. Liang*[1], *G. Loewen*[1]
[1]Neurocrine Biosciences, Inc., San Diego, United States, [2]Celerion, Inc., Tempe, United States

Background: Opicapone, an oral long-acting catechol-O-methyltransferase (COMT) inhibitor, is an approved once-daily adjunctive treatment to carbidopa/levodopa (CD/LD) in patients with Parkinson's disease (PD) experiencing "OFF" episodes. It has been demonstrated that addition of opicapone to immediate-release CD/LD decreases plasma peak-to-trough fluctuations, thus providing more consistent exposure to LD. We assessed the effects of opicapone 50 mg on the pharmacokinetics (PK) of LD and its metabolite, 3-O-methyldopa (3-OMD),when administered with CD/LD extended-release (ER) capsules in healthy individuals.
Methods: In a Phase 1 open-label study, CD/LD-ER 23.75/95 mg was administered to 18 healthy subjects (9 male, 9 female): 1 capsule 3 times a day (TID) on Days 1 and 16; 2 capsules TID on Days 2-3 and Days 17-18 every 7 hours at 07:00, 14:00, and 21:00. Opicapone 50 mg once-daily was administered at 22:00 on Days 4-18. Blood samples to assess LD and 3-OMD plasma concentrations were collected on Days 3-4 (CD/LD-ER without opicapone) and Days 18-19 (CD/LD-ER with opicapone) every 30 minutes from 07:00 to 21:00, and every 2 hours from 23:00 until 09:00 the next morning. Samples for soluble COMT (S-COMT) activity were collected on Day 1 and Day 19.
Results: Administration of once-daily opicapone with CD/LD-ER resulted in increased trough (+208%), peak (+75%), and overall LD exposure (+122%), and decreased peak-to-trough fluctuation index (-38%). Morning LD trough concentration increased (+167%); 3-OMD levels and S-COMT activity markedly decreased (-82% and -80%, respectively).
Conclusions: Providing more consistent LD levels is a central treatment strategy for the management of motor fluctuations in PD. Administering once-daily opicapone with CD/LD-ER resulted in increased overall LD exposure and improved peak-to-trough fluctuations. The effects of opicapone on this extended-release formulation of CD/LD contributes to more consistent LD exposure throughout the day and nighttime, which continues to be a challenge and goal in treating PD.

P 116 (GPT)

A novel treatment for Apraxia of Eyelid Opening using a pulsating headband: a single-centre pilot study

S. Arjun[1], *H. Singh*[1], *N. Sawal*[2], *M. Matta*[1]

[1]Government Medical College and Hospital, Chandigarh, India, [2]Fortis Mohali, Neurology, Mohali, India

Background: Apraxia of Eyelid Opening (AEO) is characterised by an inability to initiate eyelid opening. It manifests as an isolated condition or along with other neurodegenerative-disorders like Parkinson's Disease (PD) and Progressive Supra-nuclear Palsy. Patients with AEO typically use sensory-tricks (*geste-antagoniste*) like touching the temporal region or elevating eyelids manually to overcome this impairment.

Hirayama et al.(2000) proposed - proprioceptive stimuli to facial-muscles, by wearing skiing/swimming goggles, improved the AEO of patients with PD. Pathogenesis of AEO involves either the Frontalis or the Orbicularis-Oculi muscle. EMG studies showed 80ms-long pulsations stimulated Orbicularis-Oculi and 1000ms stimulated the Frontalis.

In our study, we wanted to evaluate the effectiveness of a vibrating-headband that would provide proprioceptive-stimuli to facial muscles for treatment of AEO and compare the effectiveness of 80ms vs. 1000ms-long vibrations.

Methods: A battery-operated headband with two vibrating-motors was placed just above the patient's eyebrows [*Fig.1*].

Figure 1. Pateint with Apraxia of eyelid opening (left), eyes are open while wearing the Pulsating Headband (right).

A pilot study was performed on 4-patients with AEO, 1-patient having blepharospasm was excluded (n=3). Using the AEO Scoring System(AEOSS) provided by Ferrazzano et al.(2020), severity of AEO was determined:

1. Without headband
2. With headband-OFF
3. Headband-ON pulsating at 80ms
4. Headband-ON pulsating at 1000ms

Results: The mean AEO-score without the headband was 6.0±1.7, with the headband-ON at 80ms was 4.7±1.2 and with the headband-ON at 1000ms was 3.3±1.5. Compared to without the headband, there was a 21.6% reduction in AEOSS ($p>0.05$) with the headband-ON vibrating at 80ms and 45.0% reduction when vibrating at 1000ms ($p<0.05$) [*Table.1*].

Patient Code	Age/Sex	Diagnosis	Apraxia of Eyelid Opening Scoring System (AEOSS) (out of 10)			
			Without the Headband	With Headband Turned **OFF**	With Headband Turned **ON** Duration of Pulsations	
					80ms	1000ms
BR-18	66/F	PD*	8	7	6	5
SB-19	71/F	PSP†	5	5	4	2
BA-19	74/F	PSP†	5	4	4	3

**PD: Parkinson's Disease (with STN DBS), †PSP: Progressive Supranuclear Palsy*

Table 1. Apraxia of Eyelid Opening Score of Patient without the headband compared to with the Headband

Conclusions: There was a statistically-significant reduction in AEO-score with the headband-ON, vibrating with 1000ms-long pulses, compared to baseline.

P 117 (GPT)

Bezoar And Catheter Knotting As Rare Complications Of Levodopa Carbidopa Intestinal Gel Therapy

T. Saltoğlu[1], *Y. SÜCÜLLÜ KARADAĞ*[1]
[1]Ankara City Hospital, Ankara, Turkey

Background: Levodopa-carbidopa intestinal gel (LCIG) is the device-assisted therapy that used in advanced-stage Parkinson's disease. The crucial complications of this treatment are rare and mostly due to percutaneous gastrostomy. In this abstract, we present two rare catheter complications of percutaneous gastrostomy with levodopa-carbidopa intestinal gel therapy.
Methods: Patient one is a 69-year-old female patient with LCIG treatment for one year was admitted to the hospital because of intermittent obstructions during washing the jejunal tube. The bezoars were seen around the bumper of the PEG tube which was not visible on esophagogastroduodenoscopy (EGD).
Patient 2 is a 50-year-old male patient with LCIG treatment was admitted for abdominal pain and obstructions during washing the jejunal tube one year after the procedure. On EGD, the jejunal catheter was located in the jejunum, but on withdrawing it into the stomach, it was observed that its distal part was knotted on itself.
Results: When the first patient was questioned, the recommended traction movements after the procedure were not optimal and the patient was usually given fibrous nutrients although impaired gastrointestinal motility.
For the second patient, it thought to the braid form of the distal catheter part may become knotted around itself due to impaired gastrointestinal motility and pigtail structure.

Figure 1. Bezoars around the bumper of the patient EGD removal

Conclusions: These rare side effects should be considered for the treatment that has highly positive effects, and necessary post-procedure care should be taken and a proper diet for motility should be done for optimal results.

P 120

Long-term safety of continuous levodopa/carbidopa infusion with ND0612: results from the ongoing BeyoND study

W. Poewe[1], *F. Stocchi*[2], *S. Sopromadze*[3], *L. Adar*[3], *N. Sasson*[3], *T. Yardeni*[3], *N. Giladi*[4]

[1]Medical University Innsbruck, Department of Neurology, Innsbruck, Austria, [2]University and Institute for Research and Medical Care IRCCS San Raffaele, Rome, Italy, [3]NeuroDerm, Rehovot, Israel, [4]Neurological Institute, Tel Aviv Medical Center, Sackler School of Medicine, Sagol School of Neurosciences, Tel Aviv, Israel

Background: ND0612 is in development as a continuous, subcutaneous levodopa/carbidopa (LD/CD) delivery system for Parkinson's disease (PD) experiencing motor fluctuations. Primary safety data from the BeyoND study (NCT02726386) showed that subcutaneous LD/CD infusion with ND0612 is generally safe up to one year of treatment. The study has been extended to 102 months, and we report cumulative data beyond the first year of treatment.

Methods: PD patients (aged ≥30 years) taking ≥4 LD doses/day and ≥1 other PD medication and experiencing ≥2 hours of OFF time/day were eligible for this ongoing study. Patients received open-label ND0612 for a regimen of either 16-hours/day or 24-hours/day.

Results: Of the 214 enrolled patients, 120 completed the first year and 114 continued into the extension period. As of December 2021, 58 patients were still in the study, with a treatment duration of up to 5.1 years. Cumulative safety data showed that 74.3% of patients had ≥1 drug-related treatment-emergent adverse event (TEAE).

The most frequent TEAEs were Infusion Site Reactions (ISRs) (e.g., nodules, hematoma, infection, pain, eschar), which accounted for 532/690 related TEAEs and were generally reversible and manageable.

The most common systemic TEAEs were fall (16.8%), urinary tract infection (14.0%), and nausea (10.7%). Only 3 ISRs led to treatment discontinuation in ≥1% of patients over the whole study: infusion site nodule (6.1%), infusion site pain (3.3%) and infusion site hematoma (1.9%).

Conclusions: ND0612 infusion was safe, with generally mild to moderate local TEAEs that were reversible and manageable. Systemic safety was typical for PD patients treated with LD/CD.

P 121

Population pharmacokinetics of levodopa and carbidopa following subcutaneous infusion

T. Birnberg[1], *L. Adar*[1], *G. Smania*[2], *M. Bjornsson*[2], *N. Jonsson*[2], *R. Case*[2], *M.O. Karlsson*[3]
[1]NeuroDerm, Rehovot, Israel, [2]Pharmetheus, Uppsala, Sweden, [3]Uppsala University, Uppsala, Sweden

Background: ND0612 is in development as the first continuous subcutaneous (SC) levodopa/carbidopa delivery system for patients with Parkinson's disease (PD) and motor fluctuations. A population PK model of levodopa and carbidopa following subcutaneous infusion of ND0612 with/without oral therapy was developed.
Methods: Two integrated population PK models (for levodopa and for carbidopa) were developed using data from two phase-1 studies of ND0612 (Studies 004 and 005) in PD patients and healthy volunteers, respectively. The predictive performance of each model was then tested using data from a third phase 1 study in healthy volunteers (Study 114). Model refinement was performed using aggregated data from the three studies and will be updated as sparse PK data from ongoing studies becomes available.
Results: Levodopa and carbidopa population PK models were both adequately described by a one compartment model with sequential zero and first-order SC absorption and first-order oral absorption. Carbidopa had linear elimination from the central compartment.
Levodopa had parallel dopa decarboxylase (DDC) and catechol-O-methyltransferase (COMT) elimination from the central compartment, in which the inhibition of apparent DDC-mediated clearance was driven by carbidopa plasma concentrations.
Exploration of covariates showed age had a significant effect on apparent clearance and apparent volume of distribution for both carbidopa and levodopa, even after accounting for body weight differences; both parameters decreased with increasing age.
Conclusions: Model diagnostics for the carbidopa and levodopa population PK models indicated a satisfactory predictive performance, supporting their usability to derive individual predictions of exposure to be used in future pharmacokinetic-pharmacodynamic analyses.

P 122

Nicotinamide riboside alleviates Parkinson's disease symptoms but downregulates dopamine metabolism

G. Turconi[1], F. Alam[2], T. SenGupta[3], S. Pirnes-Karhu[2], S. Olfat[2], M. Schmidt[4], K. Mätlik[2], A. Montaño-Rodriguez[2], V. Heiskanen[2], P. Piepponen[2], C. Brenner[5], C. Holmberg[2], H. Nilsen[3], J.-O. Andressoo[2,6], E. Pirinen[2]

[1]University of Helsinki, Pharmacology & HiLIFE, Helsinki, Finland, [2]University of Helsinki, Helsinki, Finland, [3]University of Oslo, Oslo, Norway, [4]University of Iowa, Iowa, United States, [5]City of Hope National Medical Center, Duarte, United States, [6]Karolinska Institute, Stockholm, Sweden

Background: Activation of mitochondrial metabolism and proteostasis with the NAD^+ precursor nicotinamide riboside (NR) has emerged as a potential therapeutic approach for neurodegenerative disorders including Parkinson's disease (PD). However, despite recently started clinical trials, studies on NR in animal models of PD are scarce. In this study, we investigated the effect of NR in multiple models of PD.

Methods: We tested the effect of NR supplementation in transgenic *C. elegans* overexpressing alpha-synuclein, a protein of which aggregation is believed to promote PD, and in a lactacystin mouse model of PD. In mice, the extent of the nigral lactacystin lesion was longitudinally evaluated with behavioral tests including cylinder test, elevated body swing test, adhesive removal test, and open field.

Mitochondrial oxygen consumption in the substantia nigra was measured using the Oroboros Oxygraph-2k, and mitochondria were analyzed with the electron microscope. After dissections, total dopamine levels in the striatum and substantia nigra were measured with HPLC and mRNA level of relevant genes with RT-qPCR.

Results: In transgenic *C. elegans* overexpressing alpha-synuclein, NR rescued PD-like phenotypes likely by activating the mitochondrial unfolded protein response (UPR^{mt}). Similarly, in a proteasome inhibitor, lactacystin, -induced mouse model of PD, NR rescued mitochondrial dysfunction and promoted alterations in mitochondrial dynamics in the substantia nigra in lactacystin lesioned side. Moreover, NR alleviated lactacystin-induced behavioral deficits in the cylinder, elevated body swing, and adhesive removal tests that are commonly used to evaluate the severity of the unilateral lesion in PD mouse models.

However, long-term NR supplementation, in conjunction with proteasome inhibition, resulted in decreased dopamine levels in both the lesioned and unlesioned sides of the substantia nigra with concomitant downregulation of key genes in dopamine metabolism. This was accompanied by a decrease in spontaneous locomotor activity in NR supplemented mice measured with the open field test.

Conclusions: Our results suggest specific endpoints that should be monitored in ongoing NR clinical trials and call for further research in various PD models.

P 123

Mode of action of the neurotrophic factor CDNF as a potential drug for Parkinson's disease

V. Kovaleva[1], *O. Shpironok*[1], *L. Ivanova*[2], *L.-Y. Yu*[1], *M. Karelson*[2], *M. Saarma*[1]
[1]University of Helsinki, Institute of Biotechnology, HiLIFE, Helsinki, Finland, [2]University of Tartu, Institute of Chemistry, Tartu, Estonia

Background: Cerebral dopamine neurotrophic factor (CDNF) is an endoplasmic reticulum (ER)-located but also secreted protein promoting the survival of dopamine neurons, degenerating in Parkinson's disease (PD). CDNF was discovered in our laboratory and recently it has successfully passed phase I-II clinical trials for PD treatment.
CDNF is known to regulate unfolded protein response (UPR), signaling machinery aimed to restore cellular homeostasis upon increased loading of ER with misfolded or aggregated proteins, occurring in PD and many other pathological conditions.
The exact mechanism of how CDNF regulates UPR is unknown and ER- or plasma membrane receptors for CDNF have not been found yet.
Methods: Computational modeling, site-directed mutagenesis, and binding studies (microscale thermophoresis, proximity ligation analysis, bimolecular fluorescence complementation assay), neuronal culture and microinjections, primary cultures of midbrain dopamine neurons, receptor oligomerization assay, immunocytochemistry, western blotting, real-time quantitative PCR.
Results: We have identified putative ER-located receptors of CDNF and mapped exact binding sites in CDNF and these receptors. Currently, we are characterizing CDNF interactions with its receptors and studying their physiological meaning.
We have found a few small-molecule compounds, binding putative receptors of CDNF and mimicking its action on UPR, and the *in vitro* screening of these compounds is currently ongoing.
Conclusions: Our results are important for the development of new strategies to treat PD. Based on our results, CDNF can exert its protective effect through regulation of all three UPR pathways, and therefore it can be much more potent as an anti-parkinsonian drug, than specific inhibitors of single UPR pathways shown to be protective in animal models of neurodegeneration.

P 124 (GPT)

Adverse effects of levodopa/carbidopa intrajejunal gel treatment: a single center long-term prospective study

M. Premzl[1], *T. Rus*[1], *M. Trošt*[1,2]

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

Background: Levodopa/carbidopa intrajejunal gel (LCIG) is an efficient therapeutic strategy to overcome motor fluctuation in advanced Parkinson's disease (PD). However, it requires invasive percutaneous endoscopic gastrojejunostomy (PEG) and is associated with several adverse effects (AE).

In this study, we evaluated PEG-related, device-related and other AE in a well-defined prospective cohort of PD patients.

Methods: We followed 106 consecutive PD patients (males/females 61/45, age 70.6±7.6, disease duration 14.8±6.0) that started LCIG treatment at UMC Ljubljana between June 2007 and September 2021. PEG-related AE (local acute/chronic infection, peritonitis, abscess formation, ileus, ulcerations), device-related AE (tube dislocation, disconnection, knotting or device malfunction), polyneuropathy due to vitamin B12 deficiency (polyneuropathy-B12) , neuropsychiatric AE and dyskinesia were studied in time using survival analysis and Cox's model with age, disease duration, gender and recurrent AE as covariates.

Results: Among all PD patients, 20.7% (95%CI 9.1%-35.5%) experienced PEG-related AE within the first month and 50% (95%CI 40.3%-60.6%) within 3.4 years.

Older age was a significant risk factor (p=0.04) in contrast to gender or disease duration. Patients with recurrent PEG-related AE experienced it earlier (p=0.0002). Device-related AE occurred in 3.8% (95%CI 0,1%-29,3%) at 2 months and 50% (95%CI 36,3%-64.6%) before 6.7 years.

Older age was a significant risk factor (p=0.02) as well as early AE for a subsequent one. Polineuropathy-B12 was present in 50% of patients (95%CI 18.0%-76.6%) within 11.9 years with disease duration (p=0.02) as a significant cofactor.

Neuropsychiatric AE occurred in 50% of patients in 11.9 years as well (95%CI 28.3%-76.0%). All the patients evolved dyskinesia before 11.2 years. Studied covariates were not found significant in the later two analyses.

Conclusions: LCIG is an efficient treatment in advanced PD. However, due to the high incidence of serious AE, it is necessary to carefully select and monitor patients, especially those whose side effects occur early.

P 125

GT-02287, a brain-penetrant structurally targeted allosteric regulator for glucocerebrosidase show evidence of pharmacological efficacy in models of Parkinson's disease

B. Guzman[1], N. Perez[2], A.M. Garcia[2], E. Cubero[2], X. Barril[2], M. Bellotto[1], S. Morales[2], A. Ruano[2], A. Delgado[2], C. Poletto[3], G. Forloni[3], R. Maj[1]

[1]Gain Therapeutics, Lugano, Switzerland, [2]Gain Therapeutics, Barcelona, Spain, [3]Istituto di Ricerche Farmacologiche IRCCS, Neuroscience, Milan, Italy

Background: *GBA1* encodes the lysosomal enzyme glucocerebrosidase (GCase), whose deficiency has been linked to increased alpha-synuclein accumulation, phosphorylation, and aggregation, as well as to mitochondrial and endoplasmic reticulum stress, common pathophysiological features in Parkinson's disease (PD). Interestingly, different *GBA1* mutations also increase the risk factor for sporadic PD.

Methods: Gain Therapeutics applies its innovative proprietary drug discovery platform, Site-directed Enzyme Enhancement Therapy (SEE-Tx™), to the development of small-molecule structurally targeted allosteric regulators (STAR^s) that stabilize GCase avoiding its degradation whilst facilitating its maturation and trafficking to the lysosomes. GT-02287 is a small molecule identified in the context of the SEE-Tx platform that enhances GCase activity by inducing its stabilization.

Rotenone-based models are considered relevant for the investigation of PD pathogenesis and development of treatments for the disease. Here, we demonstrate pharmacological chaperone-mediated activity in dopaminergic cells derived from human neuroblastoma SH SY5Y after rotenone injury, and in rats chronically treated with rotenone.

Results: We report *in vitro* and *in vivo* evidence showing that our orally bioavailable and brain penetrant lead, GT-02287, increases expression of brain dopamine levels and promotes the degradation of both phospho and aggregated alpha-synuclein, thus reducing rotenone-induced *neurotoxicity.*

Conclusions: Enhancement of the lysosomal GCase activity by GT-02287 protects against key pathological features of PD, including alpha-synuclein related pathology, ameliorating dopaminergic cells phenotype. Therefore, STAR^s therapy represents a novel pharmacological tool for the treatment of PD, warranting further development towards the clinic.

P 126

Switching and combining device-aided therapies in advanced Parkinson's disease: a double centre retrospective study

S. Delalić[1], D. Georgiev[2,3], N. Zupančič Križnar[2], A. Socher[4], T. Gurevich[4], M. Trošt[2,5]

[1]General Hospital of Isola, Department of Neurology, Isola, Slovenia, [2]University Medical Centre Ljubljana, Department of Neurology, Ljubljana, Slovenia, [3]University of Ljubljana, Faculty of Computer and Information Sciences, Ljubljana, Slovenia, [4]Tel Aviv Sourasky Medical Centre, Movement Disorders Unit, Tel Aviv, Israel, [5]University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

Background: Continuous subcutaneous apomorphine infusion (CSAI), levodopa-carbidopa intestinal gel infusion (LCIG), and deep brain stimulation of the subthalamic nucleus (STN-DBS) have markedly changed the treatment landscape of advanced Parkinson's disease (aPD). Despite a similar outcome of all device-aided therapies (DATs), some patients switch or combine DATs.

The aim of this retrospective study was to explore the frequency and reasons for switching between or combining DATs in two movement disorders centres in Slovenia and Israel.

Methods: We collected and analysed demographic and clinical data from aPD patients who switched between or combined DATs. Motor and non-motor reasons and their frequency for switching/combining were examined, as was the effect of DAT using the Global Improvement subscale of the Clinical Global Impression Scale. Non-parametric tests were used to analyse the data.

Results: Of 505 aPD patients treated with DATs at both centres between January 2009 and June 2021, we identified in total 30 patients (6%), who either switched DAT (N=24: 7 LCIG-to-STN-DBS, 1 LCIG-to-CSAI, 5 CSAI-to STN-DBS, 8 CSAI-to-LCIG, 1 STN-DBS-to-LCIG, 1 LCIG-to-CSAI-to-STN-DBS, and 1 STN-DBS-to-CSAI-to-LCIG) or combined DATs (N=6: 5 STN-DBS+LCIG and 1 STN-DBS+CSAI-to-STN-DBS+LCIG).

In most of these patients, inadequate control of motor symptoms was the main reason for switching or combining DATs, but non-motor reasons (related to the disease and/or DAT) were also identified.

Conclusions: Switching between and combining DATs is uncommon, but in some patients brings substantial clinical improvement and should be considered in those who have either inadequate symptom control on DAT treatment or have developed DAT related complications.

P 127 (GPT)

Setting the TEMPO: A phase 3 program to investigate tavapadon, a selective D1/D5 partial agonist, for Parkinson's disease

H.F. Fernandez[1], S.P. Pfister[2], M. Leoni[2], M. Berry[2], A. Gangadharan[2], S. Duvvuri[2], J. Parker[2], S. Wang[2], R.B. Briscoe[2], R. Sanchez[2]

[1]Cleveland Clinic, Cleveland, United States, [2]Cerevel Therapeutics, Cambridge, United Kingdom

Background: Tavapadon is a first-in-class, highly selective partial agonist at dopamine D1 and D5 receptors. By selectively targeting D1/D5 receptors, tavapadon may improve motor symptoms while minimizing adverse events generally associated with traditional D2/D3 receptor agonists.

Previous phase 1b/2 studies support phase 3 investigation of tavapadon.

The phase 3 TEMPO program will evaluate the efficacy, safety, and tolerability of once-daily (QD) tavapadon in Parkinson's disease (PD).

Methods: TEMPO-1 and TEMPO-2 are phase 3, randomized, placebo-controlled, 27-week studies of tavapadon monotherapy as fixed doses (5 and 15 mg QD) and flexible doses (5-15 mg QD), respectively, in patients with early-stage PD (Movement Disorder Society – Unified Parkinson's Disease Rating Scale [MDS-UPDRS] Part II score ≥2 and Part III score ≥10; modified Hoehn and Yahr stage 1, 1.5, or 2). TEMPO-3 is a randomized, placebo-controlled, 27-week study of tavapadon (flexible dose: 5-15 mg QD) adjunctive to levodopa in patients experiencing motor fluctuations (modified Hoehn and Yahr stage 2, 2.5, or 3 in the "ON" state, minimum 2.5 h of "OFF" time on 2 consecutive days).

Participants who complete TEMPO-1/-2/-3 will be eligible for the open-label, 58-week TEMPO-4 study. COVID-19 mitigation for TEMPO studies includes home health visits, telemedicine, and direct-to-patient delivery of study drug.

Results: Detailed study designs will be presented. Primary endpoints include change from baseline in the MDS-UPDRS Parts II and III combined score (TEMPO-1/-2) and change from baseline in total "ON" time without troublesome dyskinesia based on Hauser diary 2-day average (TEMPO-3). TEMPO-4 will investigate long-term safety, tolerability, and efficacy (change from baseline in MDS-UPDRS Parts I-III, Hauser diary).

Conclusions: There has been no FDA-approved levodopa-adjunct and monotherapy drug in over a decade. The TEMPO program will establish the efficacy and safety profile of tavapadon as a promising next-generation PD treatment.

P 128 (GPT)

Advanced therapies for Parkinson's disease (PD) in the age of telehealth

Z. Mari[1]
[1]Cleveland Clinic, Lou Ruvo Center for Brain Health, Las Vegas, United States

Background: Up until recently, movement disorder experts frequently pointed to advanced therapies, including deep brain stimulation (DBS), as an area highlighting telehealth's limitations. With a number of technological breakthroughs and innovation, however, we are increasingly realizing that DBS care can be reimagined in the age of telehealth, turning a presumed limitation to enhancements in care.
Methods: This is a comprehensive review of 3 main approaches to advanced therapies, especially DBS.
Results: A recent pilot explored the use of home health management in DBS care for PD: (https://jamanetwork.com/journals/jamaneurology/article-abstract/2781464,
see also: https://www.practiceupdate.com/content/home-health-management-of-parkinson-disease-dbs/122580/65/7/1)
and a similar approach can easily be adopted to other forms of advanced therapies, such as infusion pump management, allowing care to take place in the patient's home, as opposed to being dependent on in-person visit requiring travel to academic centers and other brick-and-mortar locations, where movement disorder specialists practice.
Another important area of technological innovation likely to revolutionize DBS care and dramatically reducing the dependence of DBS care on in-person visits is the "closed loop" self-programming concept: (https://pubmed.ncbi.nlm.nih.gov/33941932/).
Finally, remote programming with the use of smart devices, programmers, and broadband connection through the cloud between the patient in their home and the remote DBS programming provider, is already a reality: (https://pubmed.ncbi.nlm.nih.gov/35151948/).
Conclusions: As we are transitioning into the post-pandemic world of neurology care, telehealth regulatory and reimbursement realities continue to shape our views and warrant adjustments globally. This review specifically focuses on how advanced therapies in PD may not only be compatible with telehealth and possible to imagine in the remote setting, but in fact remote options likely will become the norm and a way to improve access, reduce cost, and enhance care.
In such future, the "limitation" is not going to be associated primarily with telehealth and remote care in the conversation about advanced therapies, but rather, the opposite: limitations associated with in-person care (such as having to travel long distance, park, restricted scheduling logistics, limited number and frequency of visits, etc) will be what are going to be more increasingly obvious to providers and patients alike.

P 129
Fears and certainties of chilean neurologists in the therapeutic approach to parkinson's disease

P. Salles[1], *M. Teran-Jimenez*[1,2], *B.-H. Palma*[1], *M. Retamal*[1], *P. Chana-Cuevas*[1,3]
[1]Centro de Trastornos del Movimiento CETRAM, Santiago, Chile, [2]Felix Bulnes Hospital, Movement Disorders Section, Santiago, Chile, [3]University of Santiago de Chile, Faculty of Medical Sciences, Santiago, Chile

Background: The therapeutic approach of Parkinson disease (PD) has evolved. After the emergence of levodopa as the best treatment available, theories on its neurotoxicity found no clinical substrate [1].
Previous guidelines prevented the use of levodopa early in PD by focusing on delaying dyskinesias [2], and supporting the use of drugs with now debatable neuroprotective effect [2,3]. Recent findings do not support this approach [4].
Contemporary opinions are focused on accumulated disability, suggesting, when necessary, an earlier start of levodopa to promote a better quality of life [5].
Methods: An electronic survey with questions about the therapeutic approach in PD was sent to neurologists from different centers and regions in Chile.
Results: Forty-two answered the survey (30 general neurologists and 12 movement disorders specialists), of these >85% finished their residency less than 10 years ago, and >75% attended an update in PD treatment in the last year. The majority report not feeling like they are offering the best possible care.
Most of them indicate physical exercise to patients in the early stage of PD, and rehabilitation when gait and/or balance problems arise. Immediate-release levodopa plus a dopa decarboxylase inhibitor, and immediate-release pramipexole are the most indicated drugs.
Almost half consider anticholinergics to be the most effective in tremor, although dopamine agonists are the most used drugs in tremor-dominant PD. About 21% believe levodopa is potentially neurotoxic, and more than 1/3 avoid prescribing levodopa early for fear of developing motor fluctuations and dyskinesias. On the other hand, about 1/3 avoid prescribing dopamine agonists, and more than 2/3 avoid prescribing anticholinergics for fear of developing adverse effects. More than 80% report being familiar with risk factors for the development of levodopa-associated dyskinesias and impulse control disorders due to dopamine agonists.
Conclusions: Preferences on the management of PD are heterogeneous. "Levodopa phobia" and fear of agonists are current issues among Chilean neurologists. We must continue to debunk myths and establish realities in the therapeutic approach to PD.

P 129-I

Retrospective Analyses Evaluating the Risk of Mortality Associated With Pimavanserin or Other Atypical Antipsychotics in Patients With Parkinson's Disease Psychosis

S. Isaacson[1], F. Pagan[2], D.Truong[3], V.Abler[4], R. Pahwa[5]

[1]Parkinson's Disease and Movement Disorders of Boca Raton, Boca Raton, FL, USA; [2]Department of Neurology, Georgetown University Medical Center, Washington, DC, USA; [3]The Parkinson and Movement Disorder Institute, Fountain Valley, CA and Department of Psychiatry and Neuroscience, University of California Riverside, Riverside, CA, USA; [4]Acadia Pharmaceuticals Inc., San Diego, CA, USA; [5]Department of Neurology, University of Kansas Medical Center, Kansas City, KS, USA

Background: Summarize the available data for the mortality risk associated with Parkinson's disease (PD) psychosis (PDP) and pimavanserin.

PDP is associated with increased mortality compared with PD without psychosis. For PDP, an observed mortality rate of 28.2 per 100 patient-years (95% CI, 27.5–28.8) has been reported. Atypical antipsychotics (AAPs) used off label to treat PDP symptoms can increase the risk of mortality; >2-fold increases in risk have been reported. Pimavanserin is a selective 5-HT_{2A} inverse agonist/antagonist that is currently the only FDA-approved medication for hallucinations and delusions associated with PDP.

Methods: This narrative review describes mortality data of pimavanserin in the treatment of PDP from one open-label extension study, 5 retrospective studies, and postmarketing analysis (based on events reported from April 29, 2016–April 28, 2021).

Results: In the open-label extension study, the observed mortality rate was 6.45 deaths per 100 patient-years. In a retrospective study of PD patients (N=2994), mortality rates were similar for pimavanserin vs untreated patients (odds ratio, 1.2; 95% CI, 0.35– 3.13). A retrospective cohort study of PD patients (N=21,725) found lower all-cause mortality rates with pimavanserin compared with AAPs (hazard ratio, 0.78; 95% CI, 0.67–0.91).

Findings reported in 2 additional retrospective studies were consistent. A retrospective study of PD patients in long-term care (N=20,398) reported increased 90-day mortality with pimavanserin vs nonuse (adjusted hazard, 1.20; 95% CI, 1.02–1.41). In the postmarketing analysis, the overall cumulative mortality rate of pimavanserin was 15.40 per 100 patient-years (95% CI, 14.97–15.85), with a minimum of 41,218 patients (30,426 patient-years) exposed.

Reported causes of death reflect common comorbidities and underlying conditions of an elderly PDP population (eg, PD, disease progression, dementia, pneumonia, and respiratory and cardiac events).

Conclusion: The mortality risk associated with pimavanserin has remained consistent over time, supporting the established benefit/risk profile of pimavanserin for the treatment of PDP.

Study Supported By: Funded by Acadia Pharmaceuticals Inc.

Parkinson Disease: Other topics

P 130 (GPT)
If not insulin resistance so what? Comparison fasting glycaemia in idiopathic Parkinson's disease and atypical parkinsonism

T. Chmiela[1], J. Węgrzynek[2], A. Kasprzyk[2], D. Waksmundzki[2], D. Wilczek[2], A. Gorzkowska[3]
[1]Faculty of Medical Sciences in Katowice, Medical University of Silesia, Department of Neurology, Katowice, Poland, [2]Faculty of Medical Sciences in Katowice, Medical University of Silesia, Students' Scientific Association, Department of Neurorehabilitation, Katowice, Poland, [3]Faculty of Medical Sciences in Katowice, Medical University of Silesia, Department of Neurorehabilitation, Katowice, Poland

Background: Parkinson's disease (PD) is one of the most common neurodegenerative diseases. Besides impaired motor functions, patients with PD present numerous non-motor symptoms. Existing evidence support the interplay between glucose metabolism and neurodegenerations in PD. Some research suggests the existence of different mechanisms of diabetes development in PD, and a.o. autonomic dysfunction which appears commonly in synucleinopathies may contributed to impaired glucose metabolism.
The objective of this study was to determine the prevalence of metabolic disorders with particular emphasis on glucose metabolism in patients with PD and atypical parkinsonism (AP).
Methods: A retrospective study was performed by analyzing 461 clinical data of consecutive patients diagnosed with PD, MSA and PSP hospitalized from 2019 to 2021 in the authors institution. The study group included 350 patients (303 PD, 14 MSA, 33 PSP), aged 65,8±9.7 years (42% were female). Laboratory results (fasting glycaemia, lipid parameters, TSH, homocysteine and vitamin D3 levels) were collected. The patient's clinical condition was assessed in UPDRS p.III, Hoehn-Yahr scale, MMSE and BDI.
Results: Impaired fasting glycaemia (IGF) was more prevalent by PD than in the PSP (43.43% vs. 18.18%; p=0.043). Similarly PD presented a higher level of fasting glycaemia (102.4±16.7 mg/dl vs. 92.2±16.1mg/dl; p=0.042).
According to lipid parameters, patients with PD showed lower LDL cholesterol (92.3±44.3mg/dl vs. 119±61.0mg/dl; p=0.016) and BMI compared to patients with PSP (26.1±4.0kg/m^2 vs. 29.3±4.4 kg/m^2; p=0.024), but there were no statistically significant differences in TG and HDL cholesterol levels.
Males with PD presented greater frequency of IFG (35.05% vs. 50.6%) p=0.042), higher fasting glycaemia (99.1±14.3mg/dl vs. 103.7±14.7mg/dl p=0.006), lower total cholesterol, HDL cholesterol and BMI compared to women with PD.
Conclusions: Our investigation support an association between synucleinopathies and glucose dysregulation. Exact mechanism remains unclear but is presumably related to dysautonomia.

P 131 (GPT)

Burning mouth syndrome to oral cenesthopathy: a spectrum of neuropsychiatric and sensory complications in neurodegenerative parkinsonism

J.R.T. Yu[1], *X.X. Yu*[1], *R. Rajaram*[2], *H. Fernandez*[1], *J. Siddiqui*[1]

[1]Cleveland Clinic, Neurological Institute, Cleveland, United States, [2]Cleveland Clinic, Department of Psychiatry, Cleveland, United States

Background: Burning mouth syndrome (BMS) and oral cenesthopathy (CE) are debilitating conditions that may be difficult to treat. BMS may be a nonmotor manifestation of dopaminergic dysfunction in Parkinson disease (PD). BMS has been associated with hypo- and hyper-dopaminergic states, and co-morbid mood disorders. Oral CE, perhaps a variant of tactile hallucinations, has been reported in patients with schizophrenia, dementia with Lewy bodies (DLB), and PD after deep brain stimulation (DBS) targeting the subthalamic nucleus (STN).

Methods: We report a case of a 71-year-old female with probable PD presenting with gradually progressive LD responsive parkinsonism, psychiatric disturbances, who developed evolving and debilitating sensory disturbances in the oral cavity.

Results: The patient initially presented with burning pain in the tongue, palate and gum which later progressed to a sensation of ants and worms crawling down her throat and eventually to foreign body sensation including hair in her oral cavity. BMS and parkinsonian symptoms worsened with reduction in oral levodopa (LD) and no improvement was noted with dopamine agonist. BMS improved with lidocaine solution, while CE responded to low dose of quetiapine.

Conclusions: BMS evolving to oral CE in a patient with probable PD warrants exploration of dopaminergic mechanisms and understanding of underlying psychiatric comorbidities. BMS and CE may be a continuum of psychosomatic oral sensations and a clue to more significant psychiatric comorbidity in neurodegenerative parkinsonism.

P 132
Possible link between cognition and motor reserve in patients with Parkinson's disease

S.J. Chung[1,2], Y.J. Kim[3], Y.J. Kim[2], M. Yun[4], P.H. Lee[1], Y. Jeong[5], Y.H. Sohn[1]

[1]Yonsei University College of Medicine, Department of Neurology, Seoul, Korea, Republic of, [2]Yongin Severance Hospital, Department of Neurology, Yongin-si, Korea, Republic of, [3]Korea Advanced Institute of Science and Technology, Program of Brain and Cognitive Engineering, Daejeon, Korea, Republic of, [4]Yonsei University College of Medicine, Department of Nuclear Medicine, Seoul, Korea, Republic of, [5]Korea Advanced Institute of Science and Technology, Department of Bio and Brain Engineering, Daejeon, Korea, Republic of

Background: Motor reserve refers to the individual capacity to cope with nigrostriatal dopamine depletion in Parkinson's disease (PD). This study aimed to investigate whether there is a link between cognitive function and motor reserve in patients with newly diagnosed PD.

Methods: A total of 163 patients with early-stage drug-naïve PD who underwent ^{18}F-FP-CIT PET and brain MRI scans and a detailed neuropsychological test at initial assessment were enrolled. We estimated individual motor reserve based on the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) scores and dopamine transporter (DAT) availability in the posterior putamen using a residual model.

We performed correlation analyses between the motor reserve estimate and cognitive composite scores. Diffusion connectometry analysis was performed to map the white matter fiber tracts, the fractional anisotropy (FA) values of which were well-correlated with the motor reserve estimate. Additionally, Cox regression analysis was used to assess the effect of the initial motor reserve on the risk of dementia conversion during the follow-up period.

Results: Correlation analyses demonstrated that the motor reserve estimate was positively correlated with the composite score of the verbal memory function domain and with the years of education. Connectometry analysis showed that FA values in the left fornix were positively correlated with the motor reserve estimate, while no fiber tracts were negatively correlated with the motor reserve estimate. Cox regression analysis demonstrated that the higher motor reserve estimates tended to be associated with a lower risk of dementia conversion.

Conclusions: The present study demonstrated that the motor reserve estimate was well-correlated with verbal memory function and with white matter integrity in the left fornix, suggesting a possible link between cognition and motor reserve in patients with PD.

P 133
Sleep problems in Parkinson's disease: PD patients' survey on common issues and treatments expectations

N. Singer[1], N. Ratcliffe[2], R. Fisher[1], K. Fletcher[2], E. Eyal[1], E. Berkovich[1]
[1]Clexio Biosciences LTD, Petach Tikva, Israel, [2]Parkinson's UK, London, United Kingdom

Background: Sleep problems are common and varied in Parkinson's disease (PD) across all stages of the condition. Medication early wearing off often results in troublesome nocturnal symptoms. CLE-600 is being developed as a night pill for the treatment of nocturnal PD symptoms using the proprietary OLAR® drug delivery platform (see https://www.clexio.com/forpeople/#pipeline).
In order to inform drug development, Clexio conducted a patient survey with support from Parkinson's UK to better understand the nature and impact of sleep problems in Parkinson's.
Methods: The survey included 22 questions (5 demographics, 6 Early Morning OFF and 11 sleep) in addition to open text options.
The survey was disseminated to the Parkinson's UK Research Support Network via email.
Results: 396 PD patients experiencing nocturnal symptoms completed the survey (58% male), 89% between the ages of 55-84 and 66% within 3-10 years from diagnosis. The most common nocturnal complaints having a significant impact on patients' lives were: waking up frequently (52%), difficulty turning in bed (45%) and leg movements (32%).
Over half of respondents (54%) reported experiencing sleep problems every night with the frequency and worsening of problems having increased with time since diagnosis. The most common expectations from a potential drug treatment were to allow longer periods of uninterrupted sleep and better quality sleep, both to enable patients to wake up feeling refreshed and reduce their daytime sleepiness.
Conclusions: Nocturnal symptomology is a high unmet need in PD and among the main reasons for low Quality of Life reported by patients. Motor complications during the night are reflected by the most common complaints of difficulty turning in bed and leg movements leading to frequent waking up and interrupted sleep. CLE-600 is being developed as the first solution dedicated for PD nocturnal problems and morning akinesia, integrating patient input into the development process.

P 134
Optimization of recruitment for movement disorders clinical trials in a pandemic: a single center experience

O. Phillips[1], J. Kosco[1], M. Serrano[1], H. Fernandez[1]
[1]Cleveland Clinic, Center for Neurological Restoration, Cleveland, United States

Background: The COVID-19 pandemic introduced dramatic challenges to many aspects of society, including the sudden halt of clinical trials recruitment. In the wake of this pandemic, Cleveland Clinic's Center for Neurological Restoration (CNR) sought to optimize clinical trials recruitment. We describe implementation of strategies to overcome challenges posed by the COVID-19 pandemic.

Methods: CNR's research infrastructure and clinical faculty established monthly brainstorming sessions to assess clinical trials workflow and determine strategies to safely recommence recruitment. *Provider-facing* and *participant-facing* strategies were developed and implemented. Qualitative and quantitative analyses of these methods were regularly evaluated.
Results: We identified particular challenges in this period including:
1. Hesitancy among providers and participants regarding clinical trials participation; and,
2. Fewer in-person visits in which to recruit participants.
Several *participant-facing* recruitment methods were introduced and found to be particularly effective. Virtual educational events promoted enrollments in a socially distanced manner to large audiences of eligible participants. Research staff expanded pre-screening chart review to deliver targeted telephone, mailed, and electronic messages to eligible participants. Highly visible recruitment posters were mounted in each clinic room with descriptions of active studies.
An internal website accessible to participants (https://my.clevelandclinic.org/departments/neurological/clinical-trials) of ongoing clinical trials increased direct participant-to-coordinator enrollment.
Qualitatively effective *provider-facing* strategies were also implemented. These included monthly research conferences in which researchers pitch projects to clinicians to increase interest and awareness.
Note templates integrated dropdown menus of ongoing studies. In highly trafficked provider spaces, graphical visualizations of recruitment goals were posted with similar visualizations updated weekly via email.
With implementation of these strategies, non-data analysis studies opening enrollment in CNR increased to 18 in 2020-2021 compared to 17 in 2018-2019
Conclusions: Clinical trials recruitment required adaptations in the COVID-19 pandemic. We describe a multifaceted approach to optimize recruitment with pandemic-conscious measures whose implementation enabled successful fulfillment of enrollment goals.

P 135
Obstructive Sleep Apnea (OSA) detection system based on Fast Fourier Transform (FFT) algorithm on electrocardiogram

R. Fajar[1], *N.I. Kurniastuti*[1], *T.H. Wulandari*[1]
[1]Yogyakarta State University, Computational Biology and Medicine Laboratory, Sleman, Indonesia

Background: Sleep apnea is a potentially serious sleep disorder in which breathing repeatedly stops and starts. Although in-laboratory polysomnography represents the gold standard for the diagnosis of OSA, it is costly and time-consuming. In this study, an Obstructive Sleep Apnea (OSA) disease detection system was created using the RR interval parameter. The design of this detection system uses backpropagation Artificial Neural Network (ANN) which is implemented using MATLAB software as a method in the classification of OSA determination.
Methods: The steps taken to design an OSA disease detection system in this study include data collection, feature extraction, ANN training, ANN testing, and performance determination. The feature extraction stage is performed using the Fast Fourier Transform (FFT) mathematical algorithm process. The result

of feature extraction is then carried out ANN training using 10% of the entire data and ANN testing using 90% of the total data. To get the best performance results, variations in segment length features, variations in OSA definition features, and variations in frequency composition features are performed.
Results: The best performance results in this OSA disease detection system design are features that use a combination of frequency components 2, 5, and 6 with an OSA definition of 5% in the 90-segment length. This is shown from the results of ANN performance in the form of specialization, sensitivity, and best accuracy, with successive values of 79.3%, 84.6%, and 81.6%.
Conclusions: A system design has been made to detect OSA which is implemented in MATLAB software. The feature used in this detection system is the RR interval feature that has been transformed using the FFT operation. Based on the results of performance calculations, all values indicate a number exceeding 75% so that a system that can be said to be good in detecting is obtained.

P 136
Correlation analyses of serum cytokine in Parkinson's disease and Parkinsonism-plus syndrome

X. Chen[1], *H. Shang*[1], *J. Liu*[1]
[1]Sichuan University, Chengdu, China

Background: To investigate the correlation between serum inflammatory cytokines and clinical symptoms of Parkinson's disease (PD) and Parkinsonism-plus syndrome (PPS).
Methods: Serum levels of the cytokines were measured in 183 PD patients, 99 PPS patients and 91 cases of healthy controls (HCs). And the PD and PPS patients were assessed with ten different scales to evaluate the conditions of cognitive function, mood, sleep, non-motor symptoms, motor symptoms and disease severity. SPPS 23.0 software was used to analyze the differences of the inflammatory indicators and clinical correlation in the PD and PPS group and the HC group.
Results: Serum levels of TNF-α, IL-6 and IL-8 in the PD and PPS group were higher than those in HC group. In the subgroup analysis, TNF-α level of PD patients in mild anxiety group was lower than that in the moderate anxiety group, and Hs-CRP level in the mild cognitive impairment group was lower than that in the moderate cognitive impairment group.TNF-α level of PPS patients was lower in the middle stage group than in the late stage group.
In the correlation analysis, MOCA was negatively related to IL-6 and Hs-CRP level, FAB was negatively correlated with IL-2R, IL-6, TNF-α and Hs-CRP level, and HAMD was positively related to Hs-CRP level. UPDRS III were positively correlated with IL-6 and Hs-CRP levels. H&Y stage was positively related to serum IL-2R, IL-6 and TNF-α levels in PD patients. HAMD and HAMA were positively correlated with IL-6 and IL-8 levels, and total NMSS score was positively related to Hs-CRP level in PPS patients.
Conclusions: The levels of serum cytokines were higher in the PD and PPS group than those in the HC group. The pro-inflammatory cytokines included in this study were related to the age, motor symptoms, non-motor symptoms and disease severity of the PD and PPS patients.

P 137 (GPT)

Model of virtual communication of the Reference center for invasive methods of treatment of Parkinson's disease during the COVID-19 pandemic

V. Komen[1], *E. Papic*[1,2], *G. Rozmaric*[1], *V. Vuletic*[1,2]

[1]Clinical Hospital Center Rijeka, Clinic of Neurology, Rijeka, Croatia, [2]Faculty of Medicine, University of Rijeka, Department of Neurology, Rijeka, Croatia

Background: Due to the specific situation with our center during the COVID 19 pandemic and lockdown, we developed a sort of telemedicine model that we could implement at that time at our center. In this study, we wanted to see the effectiveness of our model.

Methods: We reviewed data from all Parkinson's disease patients who required in 2021 telemedicine examination. The model used various online platforms like e-mail, Skype, and other applications with videos and cameras available on smartphones. The first conversation with patients was online with application that was most accessible to them.

For patients with milder symptoms, this would usually be enough, and they wouldn't have to come for an additional examination. If the patients presented with more severe symptoms, they would be further processed either in the day hospital or would be hospitalized.

Results: In 2021 we examined 2,000 patients through various online platforms. Out of that, 230 patients needed to come to the day hospital for an additional examination, while 100 patients required hospitalization. The most common symptoms were anxiety and depression (67%). 20% of patients overcame COVID-19 infection and 5% of patients developed post-COVID-19 neurological syndrome that includes sleep disturbances, headache, cognitive impairment, and fatigue.

The occurrence of hallucinations and psychosis was observed in 30% of patients and cognitive impairment in 20% of patients. Motor disorders, most often in the form of stiffness, tremor and dyskinesia were reported by 50% of patients and in 20% of them new sleep disturbances were observed.

Conclusions: The presented model proved to be applicable. Most of the patients avoided coming to hospital but clinical conditions that required coming for further treatment were identified in time. Worsening of motor and non-motor symptoms of Parkinson's disease was observed in patients with COVID-19 infection, which we were able to diagnose and treat in time.

P 138
Assessment of bilirubin levels in Parkinson's disease

E. Kobak Tur[1], *B.C. Ari*[2]
[1]Healthy Science University Istanbul Fatih Sultan Mehmet Training and Research Hospital, Neurology, Istanbul, Turkey, [2]Bahcesehir University School of Medicine, Neurology, Istanbul, Turkey

Background: Excessive generation of the reactive oxygen species (ROS) triggers oxidative stress. Bilirubin suppresses oxidation more powerfully than many other antioxidants. Since it has received significant critical attention on Parkinson's Disease (PD) pathophysiology, researchers have started investigating its impact upon the disease. The correlation between PD and antioxidant status has not been wholly researched.
Therefore, our aim in this study is to assess serum bilirubin levels associated with demographic and clinical features of patients with PD.
Methods: A total of 289 individuals were involved in this study. Their serum total, direct, and indirect bilirubin concentrations were compared with demographic and clinical characteristics. We determined the severity of the disease by the modified Hoehn &Yahr Staging Scale (HYRS) and clinical features by the Unified Parkinson's Disease Rating Scale (UPDRS).
Results: There were 189 patients with PD and 100 healthy controls in the study. The mean UPDRS score was 64.4 ± 21.9 in the patients with PD. Grouping based on H&Y stages as early (≤2) and advanced (>2) revealed an almost similar distribution (50.8% and 49.2%). Comparison of the bilirubin levels between the groups showed no difference. After adjusting age, indirect bilirubin levels were significantly higher in the patients with PD (p=0.024). Male patients had higher levels of bilirubin levels (direct, indirect, and total) than the female patients (p<0.05).
Conclusions: Bilirubin is an essential antioxidant marker indicating a dopaminergic deficiency in Parkinson's disease. Increased bilirubin levels may be an improved response to oxidative stress that occurs during the progression of Parkinson's disease.

P 139
The conjugacy of migraine and parkinsonism, from theory to practice

N. Panoeva[1], *M. Gulova*[1], *M. Sanoeva*[2]
[1]Bukhara State Medicine Institute, Neurology, Bukhara, Uzbekistan, [2]Tashkent Medical Academy, Neurology and Medicine Psychology, Tashkent, Uzbekistan

Background: Parkinson's disease (PD) is a chronic and progressive brain disease with impaired nerve connections, which may be associated with migraine.
Methods: We examined 74 patients with PD (1-gr), aged 67.2±2.32 years (men-42(56.8%), women-32 (43.2%)); 56 patients with migraine (2-gr) aged 41.2±2.02 years (men-18(32.2%), women-38(67.9%)). Among them, 32(57.1%) patients had aura (15(26.8%) men, 17(30.4%) women); and 32 healthy volunteers (3-gr). Clinical and neurological, anamnestic and statistical analysis was carried out.

Results: In 1-gr 38(90.5%) men had a history of headaches, 22(52.4%) of them diagnosed migraine, and 17(40.5%) men had migraine with aura. 28(87.5%) women of the 1-gr suffered from headaches, 23(71.9%) of them were diagnosed migraine, and 18(56.3%) women had aura. In 1-gr. only 8(10.8%) patients had no history of headache.
We observed that men suffering from migraine with aura were 3.4 times, women 3.6 times more likely to develop Parkinson's disease than volunteers, and there were practically no gender differences.
In patients with migraine and aura, 4 out of 6 symptoms of Parkinson's disease were observed 3.8 times more often, and in patients with migraine without aura, they were detected 2.0 times more often compared to healthy volunteers.
In detail, signs of PD were observed in 9(28.1%) patients with migraine and aura, in 4(16.7%) patients with migraine without aura, and only in 2(6.3%) healthy volunteers. It was noted that in patients with migraine and aura, men are 2.5 times more likely, and women are 3.0 times more likely to have a family history of Parkinson's disease, compared with volunteers.
Conclusions: Thus, in patients with migraine with aura, the risk of developing Parkinson's disease is 28.1%, migraines without aura-16.7%, and without headaches-6.3%. However, we do not exclude the presence of vascular and mediator risk factors for the development of Parkinson's disease in migraine, which will be studied further.

P 140
Hippocampal and amygdala atrophy rates correlate with the severity of sleep apnoea in Parkinson's disease

K. Burdová[1], P. Filip[1], K. Šonka[1], P. Dušek[1], J. Nepožitek[1], P. Štofániková[1], S. Dostálová[1], P. Peřinová[1], R. Jech[1]
[1]First Faculty of Medicine, Charles University and General University Hospital, Department of Neurology and Centre of Clinical Neuroscience, Prague, Czech Republic

Background: Sleep disturbances are common non-motor symptoms of Parkinson's disease (PD), manifesting in its preclinical or early stage. These include REM sleep behaviour disorder (RBD) - parasomnia accompanied by loss of muscle atonia during REM sleep leading to abnormal complex movements and vocalisations, which usually progresses to fully expressed synucleinopathy, most often PD. Sleep apnoea (SA) is a sleep-related breathing disorder characterised by repeated pauses or restrictions in breathing. In our study, we searched for the associations between SA and brain morphometric parameters in patients with early PD, and in patients with idiopathic RBD (iRBD).
Methods: The study enrolled 66 PD patients (27 female, age [average ±standard deviation] 59.9 ± 12.3), 58 iRBD (7 female, 66.8 ± 7.8) and 44 control subjects (CON) (13 female, 61.4 ± 9.5). T1- and T2-weighted high-resolution structural brain scans were acquired and SA was assessed using the AHI index (the mean number of apnoeas and hypopnoeas episodes per hour). FreeSurfer v7.1.0 was utilised to segment and estimate the volume of the following structures of interest: hippocampus, amygdala, brainstem, thalamus, cerebellum, caudate with putamen, cortex. General Linear Models (GLM) were used to compare between-group differences in the volumes and the correlation of AHI and volume, with age as covariate of non-interest. Alpha of 0.05 after False Discovery Rate (FDR) was implemented.

Results: There were no inter-group differences in the volumes of segmented structures of interest. However, there was a significant inter-group difference in volume-AHI correlation for hippocampus (p_{FDRcor} = 0.0102) and amygdala (p_{FDRcor} = 0.0219), stemming from differences between PD-CON for hippocampus (z_{obs}= -3.0459) and amygdala (z_{obs}= -2.3918) and PD-iRBD for hippocampus (z_{obs}= -2.3261).
Conclusions: Our findings may point to higher sensitivity of hippocampus and amygdala to SA-related insults in synucleinopathies.
This study was funded under grant AZV: NV19-04-00233.

P 141 (GPT)

A Croatian tertiary center experience on the impact of the COVID-19 pandemic on Parkinson's disease: a cross-sectional telephone study

M. Hero[1,2], G. Rožmarić[3], V. Rački[1,2], V. Vuletić[1,2]
[1]Clinic of Neurology, Clinical Hospital Center Rijeka, Rijeka, Croatia, [2]Faculty of Medicine, University of Rijeka, Department of Neurology, Rijeka, Croatia, [3]Faculty of Medicine of the University of Rijeka, Rijeka, Croatia

Background: The COVID-19 epidemic began in Wuhan, China, in December 2019 and has since drastically altered many facets of human life. People in risk groups were obliged to quickly limit their social lives and minimize the number of contacts due to the more harmful health implications.
Methods: This cross-sectional telephone study involved Parkinson's disease patients who had at least one control examination at the Clinic of Neurology of the Clinical Hospital Center Rijeka in 2020 and were Croatian citizens. The final sample included 87 successfully interviewed patients.
Results: The majority of patients reported subjective worsening of motor symptoms. Patients with PD who lived alone, as opposed to those who lived with a partner, had worse motor scores, indicating that the living situation is an essential component in motor symptom deterioration.
Most of the patients reported worsening of anxiety symptoms. Significant worsening of anxiety symptoms was found in patients who have been living alone, were less educated, had longer disease duration and had avoided check-ups. Compared to motor and anxiety symptoms, fewer patients had problems with depressive symptoms.
Significantly higher HAM-D scores were observed in patients with longer disease duration. Non-motor symptoms were the last analyzed domain, and significant worsening was found in individuals who lived alone, were less educated, had a longer disease duration, and had higher Charlson Comorbidity index scores.
Conclusions: Parkinson's disease patients in Croatia who were living alone, had longer disease duration, were less educated, had been avoiding check-ups and had more comorbidites were more susceptible to the negative effects of social isolation on physical and mental health.

P 142
Impact of telemedicine among Parkinson's disease patients during COVID-19 pandemic in Nepal

R. Ojha[1], R. Karn[1], B.P. Gajurel[1], R. Rajbhandari[1], N. Gautam[1], A. Shrestha[1], J.K. Yadav[2], P. Joshi[2], G. Nepal[2]
[1]Tribhuvan University Institute of Medicine, Maharajgunj Medical Campus, Department of Neurology, Kathmandu, Nepal, [2]Tribhuvan University Institute of Medicine, Maharajgunj Medical Campus, Department of Medicine, Kathmandu, Nepal

Background: The coronavirus pandemic imposed various restrictions on chronic patients including Parkinson's sufferers. With its challenges came new opportunities, such as telemedicine consultation. In this study, we aim to investigate the feasibility of teleconsultations and the impact of the coronavirus pandemic on PD patients in Nepal.
Methods: Between April and August 2021, patients who called the Neurology Department's hotline for follow-up care and possessed smart phones or laptops with video conferencing apps (Viber, Messenger, or WhatsApp) were enrolled. Video conferencing was used to examine baseline demographics and motor and non-motor symptoms. A questionnaire also assessed the survey's effectiveness and patient satisfaction. This study employed descriptive statistics. All the values were expressed in terms of means and standard deviation (for continuous variable) and percentages for categorical variable.
Results: Bradykinesia (92.3%), resting tremor (82.6%), and postural instability (65.3%) were some of the most common motor signs observed during our telemedicine consultation whereas constipation (57.6%) and forgetfulness (42.3%) were most frequently reported non motor signs among the patients. Depression was reported in 25% of our patients. 30.7% patients had mRS score of 0-1, 61.5% patients had score of 2-3 and remaining had score of 4 and above. The average UPDRS motor
Score was 21.63 ±12.867 (min 3 and max 58). 78% patients responded that telemedicine consultation was at par with OPD consultation and all of them were satisfied.
Conclusions: Our study suggests that telemedicine consultation through smartphone is feasible for PD patients. Telemedicine could help rural PD patients in low income countries with geographical obstacles.

P 143 (GPT)
Morbidity and severity of COVID-19 in patients with Parkinson's disease treated with amantadine

J. Sławek[1], F. Przytuła[2], J. Kasprzak[2], J. Dulski[2]
[1]Medical University of Gdańsk, Department of Neurological-Psychiatric Nursing, Gdańsk, Poland,
[2]St. Adalbert Hospital, Neurology&Stroke Dpt., Gdańsk, Poland

Background: After more than 2 years of the pandemic SARS-CoV-2, there is still a lack of a medications with satisfactory efficacy. Amantadine was hypothesized to be a potentially efefctive therapy. A retrospective, observational study was conducted to assess the incidence of COVID-19 in patients with Parkinson's disease (PD) taking amantadine and those who did not.

Methods: An observational, retrospective cohort study was conducted among patients with PD. The questionnaires were filled in during the patient's follow-up visits at the Outpatient Clinic or during hospitalization.
The questionnaire included data on: patient's age, duration of PD, Hoehn-Yahr (HY) stage, comorbidities, all medications taken (both for PD and comorbidities), and whether they had COVID confirmed by reverse transcription polymerase chain reaction (RT-PCR) swab test for SARS-CoV-2.
Results: 542 patients participated in the study.
Out of all patients, 97 patients (18%) had confirmed COVID-19 infection, in 1 patient the result of the RT-PCR test was inconclusive twice. 444 patients did not develop COVID-19 (82%).
Of the COVID-19 positive patients, 47 were amantadine users (48.5% of all COVID-19 (+) patients, 21.8% of all patients taking amantadine).
The remaining 50 COVID-19 positive patients were not taking amantadine (51.5%).
Of the patients who did not have COVID-19, 167 (37.6%) were taking amantadine.
The differences were not statistically significant.
Conclusions: The results of our study indicate that there are no significant differences in the incidence of COVID-19 and the severity of infection between amantadine (+) and (-) groups. The assessment was biased due to the lack of data on the death rates between both groups. Further research is needed to assess the effect of amantadine on COVID-19 infection.

P 144
Comparison of patient preferences for Parkinson's disease treatments and reductions in OFF-time

M. Serbin[1], C. Mansfield[2], C. Leach[2], C. Yonan[1], M. Sheehan[3], A. Donnelly[4], O. Klepitskaya[1]
[1]Neurocrine Biosciences, San Diego, United States, [2]RTI Health Solutions, Research Triangle Park, United States, [3]Ashurst, Washington, United States, [4]Northwestern University, Evanston, United States

Background: This study evaluated preferences of Parkinson's disease (PD) patients for features of two commercially available adjunctive medications. Opicapone is an oral adjunctive medication with similar mechanism of action to entacapone, but it has several distinct attributes of clinical relevance. Little is known about patients' preferences for efficacy and adverse events that differentiate these products.
Methods: 480 United States adults with self-reported PD, treated with levodopa/carbidopa and experiencing OFF-episodes were recruited through the Michael J. Fox Foundation for Parkinson's Research to complete an online discrete-choice experiment (DCE) survey. In the DCE, respondents evaluated pairs of hypothetical adjunct PD treatment profiles with variable additional ON-time, additional troublesome dyskinesia [TD], risk of diarrhea, risk of a change in bodily fluid color, and dosing frequency or "No Additional Medicine."
A fixed choice question between two profiles with attributes corresponding to opicapone and entacapone (using head-to-head clinical trial data [BIPARK I] and FDA labelling) or "No Additional Medicine" was also presented. Percentage of respondents selecting each profile was compared to the modeled probability using the DCE results.

Results: In the fixed choice question, ~ 71% chose an additional medication over "No Additional Medicine", with 84% of those choosing the opicapone profile. The modeled probability of selecting each option using the DCE data yielded similar results. Additional minutes of ON time, no risk of diarrhea and body fluid discoloration, and once daily dosing outweighed five additional minutes of troublesome dyskinesia contributing to patient preference for this profile.
Conclusions: In this study, most PD patients experiencing OFF-episodes expressed interest in adjunctive medication. The majority preferred a product profile similar to opicapone over entacapone. Nuances of safety, efficacy, and administration mode in combination may result in large differences in patients' preference for medications. Patient preference can help inform shared decision making when selecting adjunctive therapies.

P 145
Malnutrition status and cognitive functions correlation in patients with Parkinson's disease and atypical parkinsonisms: a preliminary study

V. Ferri[1], M. Barichella[2], E. Cereda[3], C. Castelli[2], C. Pusani[2], C. Bolliri[1], S. Caronni[1], M.C. Macchione[1], G. Legnani[2], D. Calandrella[1], F. Garri'[1], G. Sacilotto[2], M. Zini[2], F. Del Sorbo[2], V. Cereda[1], B. Pozzi[1], G. Pezzoli[1]
[1]Fondazione Grigioni per il Morbo di Parkinson, Milan, Italy, [2]ASST Pini-CTO, Milan, Italy, [3]IRCCS Policlinico San Matteo, Pavia, Italy

Background: In Parkinson's disease (PD) and atypical parkinsonisms (PKS) changes in nutritional status are observed throughout the duration of the disease, with consequent body weight and muscle mass loss and possible sarcopenia. The objective of this study was to verify how nutritional status and body composition are associated with cognitive functions.
Methods: We enrolled patients with PD or atypical PKS (MSA,PSO and LBD), aged 60 years and over, hospitalized in the Department of Neurology of Asst-Pini-Cto (Milan). We evaluated: anthropometric parameters (weight, height, circumferences, bioimpedance analysis, routine blood tests, nutritional risk and swallowing disturbances (MUST, MNA, SDQ, EAT-10), disease duration, UPDRS, H&Y scale, drug therapy, global cognition tests (MMSE, MOCA). The diagnosis of sarcopenia was conducted according to EWGSOP2 criteria, based on handgrip strength test (HGS), skeletal muscle index (SMI) and 4-meter gait speed test (GST).
Results: We enrolled 100 patients, 64 men and 36 women (mean age, 68 years, DS±6.5). Mean BMI was 23.6 kg/m^2 in women and 27.4 kg/m^2 in men; 5 patients presented underweight, 38 normal weight, 33 overweight, 24 obesity. Low HGS and GST were found in 69% and 100% of patients, respectively. Sarcopenia was diagnosed in 5 women (14%) and 11 men (17.5%). The evaluation of severe sarcopenia was rendered inaccurate by the influence of motor symptoms on GST. Using general linear models to test the association between BMI class, SMI, sarcopenia and HGS with MMSE and MOCA, a significant difference was found in MMSE, correct for age and schooling, only between patients presenting low and normal HGS (F-ratio, 3.9; P=0.049).
Conclusions: HGS shows a widespread reduction in strength, but in this preliminary group of enrolled patients we found only a correlation between the decrease of HGS and the MMSE. Other investigations in larger populations are needed.

P 146
Interaction lead neurotoxicity and Parkinson's disease *In vivo* study

N. Mostefa[1], *N. Djebli*[1]
[1]Pharmacognosy & Api Phytotherapy Laboratory, Mostaganem University, Mostaganem, Algeria

Background: Lead neurotoxicity is a major health problem known as a risk factor for neurodegenerative diseases, including the manifestation of parkinsonism-like disorder. Lead poisoning is a costly and largely preventable public health problem that persists primarily due to the pervasive use of lead in paint throughout much of the 20th century and its continuing presence in housing stock, especially in low-income and minority neighborhoods.
The aim of our study is to investigate the neurophysiological and biochemical correlates of motor deficits induced by sub-chronic injections of lead and Parkinson's disease in rats.
Methods: Twenty Albino mice were selected randomly and assigned into 2 groups:
Control group (N=10), PD group (N=10). The animals were housed in individual cages under identical conditions (22 ± 1 °C, free access to standard chow and water, 12 hours dark/light cycle).
PD was induced by injecting mice with 10 doses of MPTP (25 mg/kg) and probenecid (250 mg/kg) (chemicals were obtained from Sigma Chemical Co. (St. Louis, MO, USA)). Mice in control group were injected by saline (25 mg/kg).
Results: The study findings showed that the expression level of iNOS in control group was 0.125 and this expression level was further increased in Parkinson's disease group, 0.21. This variation in the expression level in study groups was statistically significant (P< 0.001).
Conclusions: The present study confirmed the impact of induction of iNOS in the etiology of Parkinson's disease.

P 147 (GPT)
Violation of motor and non-motor functions in patients with COVID-19 with oral pathology

M. Giyazova[1], *M. Sanoeva*[2]
[1]Bukhara State Medicine Institute, Physiology, Bukhara, Uzbekistan, [2]Tashkent Medical Academy, Neurology and Medicine Psychology, Tashkent, Uzbekistan

Background: COVID-19 causes loss of taste and smell, and SARS-CoV-2 leads to nonspecific damage to the oral mucosa. After undergoing COVID-19, even in the long term, complications may occur in the form of autoimmunization of the body, due to antibodies that aggressively attack cells of organs and tissues.
The main route of transmission of the virus is the oral cavity, its immune state significantly affects the formation of the clinical course of coronavirus infection and complications (Fig. 1).

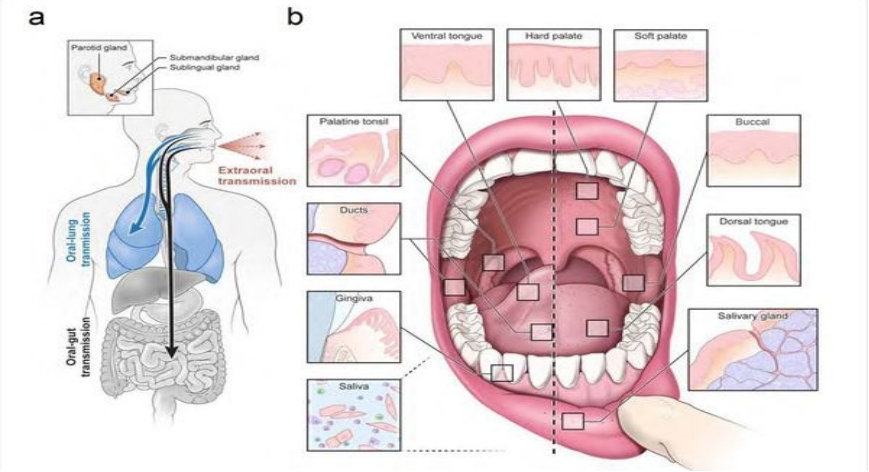


Fig. 1. The rote of transmission of coronavirus infection

Methods: 52 patients with oral pathology who underwent COVID-19 were examined. Used anamnestic data, dental studies, the Bartel scale and the Functional independence measure (FIM) scale to assess motor and non-motor dysfunctions.

Results: The listed symptoms indicated in Table 1 violated the homeostasis and integrity of the oral mucosa, and the disease dragged on, with the formation of complications of varying severity. Among them were motor (walking disorders, gait instability, speech disorders, dizziness, hemihyperreflexia, weakness in the limbs) and non-motor dysfunctions (decreased short-term memory, attention, praxis, tinnitus, headaches, irritability, sleep disorders, neuralgia in the face and neck, anxiety-phobic disorders, depression, bulemia or decreased appetite).

Symptoms	Abs	Percent (%)
ulcers	6	11,5
blisters	18	34,6
necrotising gingivitis	7	13,5
opportunistic coinfections	13	25,0
salivary gland alterations	33	63,5
white and erythematous plaques	11	21,2
necrotic/ulcerative gingiva	19	36,5
oral blisters	18	34,6
oral fungal lesion	21	40,4
recurrent herpetic lesions	12	23,1

Table 1. Common oral symptoms in COVID-19

Conclusions: Thus, SARS-CoV-2 has a tropism to endothelial cells, endotheliitis on the background of Covid-19 leads to inflammation of the oral cavity and the spread of the virus throughout the body, causing severe complications in the long term in the form of motor and non-motor dysfunctions.

P 148
The role of vascular factors in Parkinson's disease and vascular parkinsonism

S.-J. Khamdamov[1], *D. Akramova*[1], *S. Kuranbaeva*[1], *U. Shamsieva*[1], *Y. Musaeva*[1], *S. Kalandarova*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: Purpose: to study the role of vascular factors in Parkinson's disease and vascular parkinsonism.
Methods: Based on this study, the results of a comprehensive clinical examination of 117 patients were analyzed. Research work was carried out on the basis of the Tashkent medical academy clinic in 2019-2022 y. To assess the characteristics of vascular disorders in Parkinson's disease 47 patients with Parkinson's disease(PD), 40 patients with vascular Parkinsonism(VP).
Results: When studying the origin of vascular parkinsonism in patients, 27.5% of patients developed vascular parkinsonism after a stroke, 40% developed on the background of diabetes mellitus, 72.5% of patients developed vascular parkinsonism on the background of chronic cerebral ischemia, 22.5% of patients 22.5% of diabetic patients had a history of myocardial infarction. In patients with VP, the first complaints began with stiffness of the legs in 35% of patients, in 40% of cases the first symptoms of the disease began with a slowdown in movements, only in 10% of cases the first signs of the disease began with tremor.
In PD, the onset of tremor as the first sign of the disease was observed in 86% of patients, unilateral onset was observed, tremor was observed only in the arm in 72% of patients, tremor was also present in the legs in 28%. patients.
In vascular parkinsonism, the disease was observed symmetrically in 68% of cases and started mainly from the foot. The main motor impairments showed similar results in both groups, however, the fact that 89.3% of the resting tremor was expressed in the PD group compared to the VP group confirms that this symptom is mainly specific to PD. In addition, olfactory disorders predominated in PD patients in 57.4%, hypomia in 70.2% of PD patients and in 22.5% of VP patients. General hyperhidrosis was observed in 74.4% of patients in the PD group and 7.5%.
Conclusions: Vascular factors and concomitant diseases play an important role in the pathogenesis of vascular parkinsonism. Tremor in vascular parkinsonism in many cases is symmetrical and is expressed especially in the lower limb.

P 149

Analysis of MRT results in Parkinson's disease, vascular Parkinsonism and chronic ischemia of the brain

A. Umirov[1], *S. Kuranbayeva*[1]
[1]Tashkent Medical Academy, Neurology, Tashkent, Uzbekistan

Background: If Parkinson's disease is the same as vascular parkinsonism, then in the diagnosis of both these two diseases, axillary changes are detected
Objective: to determine the differences in the results of tomography of the brain in Parkinson's disease (Pd), vascular Parkinsonism(VP) and chronic ischemia of the brain.
Methods: The examination was conducted in the Department of Neurology TTA. All patients underwent a clinical neurological examination. The results of MRT in patients were analyzed.
Patients were studied as 3 groups:
1. 68 PCs with Pd
2. 65 PCs with VP
3. 65 patients with chronic ischemia of the brain participated in the examination.
Results: According to the results of a comparative analysis conducted in patients and control group volunteers:
Mild brain atrophy was 64.3±3.3% in the Pd Group, 100% higher in the VP Group, and 37.3% in the chronic ischemia of the brain group, while the alignment of the brain Egas was 16.2±2.1% in the Pd Group, 26.6±1.1% in the VP Group, and BMSI 9.3±3.3% in the BMSI group.
Similar results were recorded mainly in the group of patients with Pd and chronic ischemia of the brain , mild periventricular edema was noted in 49.7±2.1% of Pd, and in 62.4±1.3% of VP in 55.7±3.4% of chronic ischemia of the brain.
Also, in various localizations in the T2 mode in subcortical leukoaraiosis separately and copious capillaries 79,4±3.2 in hyperintensity was observed in 1 group 51,4%, in 2 group 74, in 8%, in the third group 49,3% cases, ischemic changes in the capillaries were observed in the first group 49.2%, in the second group 76,2%, in the third group 38,9% cases.
Conclusions: The results obtained show that the role of tomography of the brain in the course of Pd and VP, in the analysis of its stage, is high. Clinical trials of Pd and VP despite the fact that the symptoms are similar, the etiopathogenesis of the disease in these two pathological cases varied, MRT changes in chronic ischemia of the brain proved to be the same as in mild levels of VP.

P 150

Biomarkers for Parkinson's Disease with Reflex Tears Stratified by Disease Duration

M. Lew[1], S. Janga[2], Y. Ju[2], D. Feigenbaum[1], A. Besharat[1], D. Freire[1], D. Gerke[3], M. Edman[2], W. Mack[4], C. Okamoto[4], S. Hamm-Alvarez[2]

[1]Keck/USC School of Medicine, Neurology, Los Angeles, United States, [2]Keck/USC School of Medicine, Ophthalmology, Los Angeles, United States, [3]Keck/USC School of Medicine, Translational Genomics, Los Angeles, United States, [4]Keck/USC School of Medicine, Population and Public Health Sciences, Los Angeles, United States

Background: We have previously shown that oligomeric alpha synuclein is significantly elevated in both basal tears[1] (anesthetized Schirmer's test) and reflex tears [2](unanesthetized Schirmer's test) versus HC. Our patient sample was homogeneous related to disease duration. We have designed this study to evaluate the efficacy of collecting reflex tears to provide a true biomarker capable of differentiating PD progression compared to HC.

Methods: Reflex tears were collected from 77 male and female early (disease duration 0-4 years), 43 intermediate (5-8 years), and 50 late (greater than 9 years) PD patients and 67 male and female HC using an unanesthetized Schirmer's test. Samples were pooled from both eyes for analysis of oligomeric alpha-synuclein. Values were measured by ELISA and normalized to protein content of the sample.

Results: Oligomeric alpha-synuclein was significantly increased by 5.4-fold in tears of early PD patients (4.28 ± 0.75 ng/mg tear protein, p-value<0.001), 4.0-fold in tears of intermediate PD (3.23 ± 0.54 ng/mg tear protein, p-value<0.001) and 3.1 fold in tears of late PD (2.44 ± 0.40 ng/mg tear protein, p-value<0.001) relative to HC (0.80 ± 0.24 ng/mg tear protein). No significant sex differences were present.

Conclusions: Oligomeric synuclein levels in tear fluid does not enable discrimination between various stages of PD patients based on disease duration compared to HC. The current study is conducted in an independent cohort compared to our previous studies and the results:

1. validate previous findings that oligomeric alpha-synuclein levels are increased in reflex tears of PD patients compared to HC; and,

2. suggest that elevations in oligomeric alpha-synuclein are stable across patients with early stage, intermediate and late stage PD.

This is the first presentation of tear fluid evaluation in PD patients stratified by disease duration.

Other Parkinsonian Disorders

P 152
L-Dopa responsiveness in Perry syndrome (parkinsonism, depression, weight loss, hypoventilation)

J. Dulski[1,2], C. Cerquera-Cleves[3,4], L. Milanowski[5,6,7], J. Kwiatek-Majkusiak[7], D. Koziorowski[7], O.A. Ross[6], J. Pentela-Nowicka[8], J. Slawek[1,2], Z.K. Wszolek[5]

[1]Medical University of Gdansk, Division of Neurological and Psychiatric Nursing, Faculty of Health Sciences, Gdansk, Poland, [2]St. Adalbert Hospital, Copernicus PL, Neurology Department, Gdansk, Poland, [3]Pontificia Universidad Javeriana, San Ignacio Hospital, Neurology Unit, Bogotá, Colombia, [4]Clínica Universitaria Colombia, Movement Disorders Clinic, Bogotá, Colombia, [5]Mayo Clinic, Department of Neurology, Jacksonville, United States, [6]Mayo Clinic, Department of Neuroscience, Jacksonville, United States, [7]Medical University of Warsaw, Department of Neurology, Faculty of Health Science, Warsaw, Poland, [8]Medical University of Lodz, Departement of Neurology, Lodz, Poland

Background: A significant response to L-Dopa (LD) (>30% in UPDRS III) (SLDR), ON/OFF fluctuations (FL), and LD-induced dyskinesia (LID), are supportive criteria for diagnosis of Parkinson's disease (PD). However, these features are occasionally reported in atypical parkinsonism.
This study aims to present Perry syndrome (PS) (parkinsonism, depression, weight loss, hypoventilation) as another possible diagnosis to consider in patients with SLDR, FL, and LID.
Methods: Six patients (4 males and 2 females), 2 from Colombia (no.1-2) and 4 from Poland (no.3-6), with a diagnosis of PS and genetically confirmed *DCTN1* pathogenic mutations (p.G71R in no.1-2, p.G71E in no.3-6) are presented here. The mean age of onset was 51 (36-59), mean age of LD initiation (LDI) was 53 (37-61), mean LD dose was 917 (300-1600) mg, and mean duration of LD treatment was 6 years (0.5-12). Patients no.1 and 5 died after 5 and 9 years from the onset.
Results: Patients no.1-4 displayed SLDR, with mean improvement in no.1,2,4 of 46% (32,4-54,5%) on UPDRS III at mean of 5 years from the onset.
Patient no.3 was severely bradykinetic and could not walk independently; however, he improved significantly after LDI and became ambulatory.
Patients no.1-4 developed LID from a few months (no.3-4) to 2 years (no.1-2) from LDI.
Patients no.1-4 developed FL from a few months (no.3-4) to 2 years (no.1-2) from LDI.
Patients no.5-6 did not display SLDR.
Patient no.5 was started on LD being bedridden with multiple joint contractures at 8 years from the onset.
Patient no.6 was started on LD (up to 300mg/day) only 6 months before the study.
Conclusions: Patients with PS may display SLDR. LID and FL may appear shortly after LDI and resemble PD. Therefore, PS should be included in the differential diagnosis of LD responsive parkinsonism. Higher LD doses may be necessary to obtain SLDR in PS.

P 153 (GPT)

A novel *C19ORF12* mutation in a MPAN family with the treatment of deferiprone

S. Chen[1]
[1]Sichuan University, West Hospital, Chengdu, China

Background: Mitochondrial membrane protein-associated neurodegeneration (MPAN) is a rare and devastating disease caused by *C19orf12* gene mutation. With the application of the whole exome gene sequencing technology, more and more new mutations in *C19orf12* gene have been reported, and the diagnosis of MPAN has made a great breakthrough. However, the therapeutic effect of iron chelation therapy remains controversial.
Methods: Two MPAN patients diagnosed with genetic diagnosis in the Department of Neurology of West China Hospital of Sichuan University in 2017 were collected and the clinical data of the patients in this family were analyzed. The outcomes of the treatment with deferiprone (DFP) were compared during 4 years of long-term follow-up.
Results: Two sisters genetically diagnosed with MPAN responded dramatically different to the treatment of DFP. The proband responded poorly to the iron removal treatment, and exhibited acute deterioration. After two months of iron chelation therapy, she died from severe pulmonary infection. The conditions of the second sister became stable after receiving deferiprone treatment. She was followed up for 4 years, and at the latest follow-up (December 1, 2021), she reported that no new neurological deficit symptoms appeared after the hospital discharge.
Conclusions: The findings of this study enriched the MPAN gene database, and indicated that DFP may delay the progress of MPAN for patients at early stage of the disease, but lead to further aggravation for patient at advanced stage.

P 154

Autonomic nervous system dysfunction in cases of neurodegeneration associated with mutations in *C19orf12*

M. Skowronska[1], *J. Bembenek*[2], *M. Rydzewski*[1], *T. Litwin*[1], *A. Antos*[1], *A. Czlonkowska*[1], *I. Kurkowska Jastrzebska*[1]
[1]Institute of Psychiatry and Neurology, 2nd Department of Neurology, Warsaw, Poland, [2]Institute of Psychiatry and Neurology, Department of Clinical Neurophysiology, Warsaw, Poland

Background: In mitochondrial membrane protein-associated neurodegeneration (MPAN), a subtype of neurodegeneration with brain iron accumulation (NBIA) associated with *C19orf12* mutations, patients suffer from: dystonia, parkinsonism, optic nerve atrophy and dementia. Previous studies showed the decrease in heart rate variability (HRV) in 24-h Holter electrocardiogram, that may reflect an early sign of autonomic nervous system (ANS) dysfunction. Using noninvasive methods for ANS examination we have tested 25 MPAN patients.

Methods: MPAN patients, 8 women, age from 13 to 28, were examined. In all cases sympathetic skin response (SSR) and HRV during normal breathing and hyperventilation were performed. Subjects underwent 24-h ambulatory blood pressure monitoring (ABPM) to screen for nocturnal BP abnormalities.
Results: Twenty three patients had ANS dysfunction. SSR was abnormal in 22 cases, HRV during normal breathing and hyperventilation in 10 cases. The was one case of nocturnal hypertension and 9 cases of nocturnal "non-dippers".
Conclusions: Sympathetic autonomic nervous system is affected in most patients with MPAN. It remains unknown if dysautonomia is due to central damage or peripheral autonomic ganglia dysfunction.

P 155
Progressive Supranuclear Palsy Parkinsonism-Predominant (PSP-P) – a problematic entity in the examination of parkinsonisms

P. Alster[1], M. Nieciecki[2], B. Migda[3], M. Kutyłowski[4], N. Madetko[5], K. Duszyńska-Wąs[6], D. Koziorowski[1], L. Królicki[7], A. Friedman[1]
[1]Medical University of Warsaw, Neurology, Warsawa, Poland, [2]Children's Memorial Health Institute, Nuclear Medicine, Warszawa, Poland, [3]Medical University of Warsaw, Diagnostic Ultrasound Lab, Department of Pediatric Radiology, Warszawa, Poland, [4]Mazovian Brodnowski Hospital, Department of Radiology, Warszawa, Poland, [5]Medical University of Warsaw, Neurology, Warszawa, Poland, [6]Mazovian Brodnowski Hospital, Neurology, Warszawa, Poland, [7]Medical University of Warsaw, Nuclear Medicine, Warszawa, Poland

Background: Progressive Supranuclear Palsy – Parkinsonism Predominant (PSP-P) is related to about 30% of Progressive Supranuclear Palsy Syndrome patients. In primary years the disease may be difficult to differentiate with Parkinson's Disease (PD), in more advanced stages it may present overlaps with other atypical parkinsonisms. The pathophysiology and the reason of its more beneficial course when compared to other atypical parkinsonisms is not fully explored.
Methods: Authors examined 16 patients with PSP-P and 20 patients with Multiple System Atrophy – Parkinsonism Predominant (MSA-P) aged 50 to 81 with 3-6 year duration of symptoms using magnetic resonance imaging (MRI), perfusion Single Photon Emission Computed Tomography (SPECT) and psychological assessment. Measurements concerning third ventricle width, pons, midbrain area, pons/midbrain ratio, Magnetic Resonance Parkinsonism Index (MRPI) and the width of middle and superior cerebellar peduncle (MCP and SCP) were based on assessments performed using MRI Siemens Skyra 3.0 Tesla T2 sequences. The radiotracer used to assess regional cerebral blood flow in SPECT was technetium-99m hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO). The psychological examination consisted of assessment using the Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE).
Results: After statistical analysis using the Bonferroni correction for multiple comparisons, significant differences between PSP-P and MSA-P (pronounced deterioration in PSP-P) were observed in the volume of the mesencephalon, mesencephalon/pons ratio, Magnetic Resonance Parkinsonism Index (MRPI) in MRI and frontal perfusion SPECT. Interestingly no significant differences in the neuropsychological examination were found.

Conclusions: Though PSP-P and MSA-P seem to be clinically different, even among patients with 3-6 year duration of symptoms, significant overlaps can be observed. Additional neuroimaging using MRI and perfusion SPECT should be considered as a feasible in the differential diagnosis.

P 156
Health-related quality of life in multiple system atrophy using EQ-5D-5L: a large cross-sectional study in China

Y. Xiao[1], *L. Zhang*[1], *Q. Wei*[1], *R. Ou*[1], *Y. Hou*[1], *K. Liu*[1], *J. Lin*[1], *T. Yang*[1], *H. Shang*[1]
[1]Sichuan University, Chengdu, China

Background: Multiple system atrophy (MSA) is a Parkinsonism syndrome characterized by autonomic failure and cerebellar ataxia. These symptoms damage the health-related quality of life (HRQoL) of MSA. This study aimed to evaluate the HRQoL of MSA with a preference-based instrument, the five-level EuroQol five-dimensions questionnaire (EQ-5D-5L), for the first time.
Methods: EQ-5D-5L was used to evaluate the HRQoL. The result of HRQoL was displayed as heath utility index and visual analog scale (EQ VAS) score. Specific scales were used to measure the disease severity, cognition, frontal lobe function, anxiety, depression, fatigue, and sleep disorders. The forward logistic model was used to explore the determinants of HRQoL in MSA.
Results: A total of 205 patients with cerebellar variant (MSA-C, 53.9%) and 175 patients with parkinsonian variant (MSA-P, 46.1%) patients were included in the study. The mean scores of the EQ-5D-5L value index and EQ VAS were 0.558 and 59.5, respectively. Problem with mobility was reported by the largest proportion (92.1%) of MSA patients, followed by usual problems with activities (88.7%), self-care (81.3%), anxiety/depression (72.1%), and pain/discomfort (53.9%). The determinants of the lower EQ-5D-5L value index in MSA were female sex, greater total Unified Multiple System Atrophy Rating Scale (UMSARS) scores, fatigue, and Parkinson's disease-related sleep problems (PD-SP). Lower EQ VAS score was associated with greater total UMSARS scores, fatigue, PD-SP, and anxiety symptom. MSA-P patients reported more frequent problems in pain/discomfort than MSA-C patients, while MSA-C patients reported more problems in mobility than MSA-P patients.
Conclusions: Patients with MSA had poor HRQoL evaluated by EQ-5D-5L. The most frequent affected problem is mobility in the Chinese MSA population. Besides the severity of MSA, fatigue, PD-SP and anxiety were determinants for poor HRQoL. Our research provides important information to improve the health status of patients with MSA.

P 157 (GPT)

Lipid profile as a differentiating factor in PSP-Richardson-Steele syndrome and Corticobasal syndrome

N. Madetko[1], *P. Alster*[1], *D. Koziorowski*[1], *A. Friedman*[1]
[1]Medical University of Warsaw, Department of Neurology, Warsaw, Poland

Background: Differential diagnosis of PSP-Richardson-Steele syndrome (PSP-RS) and Corticobasal Syndrome (CBS) remains a difficult issue. The only definite diagnosis is based on the neuropathological evaluation. The aim of this research was to verify whether PSP-RS and CBS show significant differences in the basic biochemical tests performed during routine blood examination.
Methods: 40 patients were included in the study: 21 with clinical diagnosis of PSP-RS (9 females, 12 males) aged 62 to 83; 19 (18 females, 1 males) with CBS aged 57 to 87. The disease duration among all patients varied from 4 to 6 years. The clinical diagnosis was based on the recent criteria.
All of the patients included in the study underwent hematological and biochemical analysis of blood samples. The evaluated parameters – number of neutrophils, lymphocytes, platelets, levels of TSH, vitamin B12, total cholesterol, triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL) were assessed automatically and referred to the hospital database of healthy volunteers.
Additionally, ratios of neutrophils/lymphocytes and platelets/lymphocytes were also examined. The distribution of continuous data was assessed by the W Shapiro-Wilk test. Subgroup analysis was performed with t Student test or U Mann-Whitney test in relation to data distribution. $P < 0.05$ was considered indicative as a statistically significant difference.
Results: CBS patients had significantly higher levels of total cholesterol ($p= 0.0149$) and LDL ($p= 0.0385$). Other analyzed parameters (number of neutrophils, lymphocytes, platelets, levels of TSH, vitamin B12, triglycerides, HDL) did not show statistically significant differences.
Conclusions: The lipid profile turned out to partially show differentiating features between PSP-RS and CBS. LDL and total cholesterol were significantly higher in CBS. The higher incidence of dyslipidemia among CBS patients may be interpreted as consistent with the lately explored issue of vascular pathogenesis of CBS.

P 160 (GPT)

Prediction of disability in multiple system atrophybased on machine learning algorithm

L. Zhang[1], Y. Hou[1], X. Gu[1], B. Cao[1], Q. Wei[1], R. Ou[1], K. Liu[1], J. Lin[1], T. Yang[1], Y. Xiao[1], Y. Chen[1], B. Zhao[1], H. Shang[1]
[1]West China Hospital Sichuan University, Neurology, Chengdu, China

Background: The predictive factors for disability in patients with multiple system atrophy (MSA) are unclear. We aimedto explore the predictive factors for disability in patients with MSA focusing on clinical features and blood biomarkers.
Methods: This prospective cohort study included patients diagnosed with MSA between January 2014 and December 2019. At the deadline of October 2021, patients met the diagnosis of probable MSA were included in the analysis. Random forest (RF) was used to establish a predictive model for disability. Accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) were used to evaluate the performance of the model.
Results: Altogether, 100 patients with MSA including 49 with disability and 51 without disability were enrolled in the RF model. Baseline plasma neurofilament light chain(NFL) levels were higher in patients with disability than in those without disability (P=.037).
According to the Gini index, the five major predictive factors were disease duration, age of onset, Unified MSA Rating Scale(UMSARS)-II score, NFL, and UMSARS-I score, followed byC-reactive protein (CRP) levels, neutrophil-to-lymphocyte ratio (NLR), UMSARS-IV score, symptom onset, orthostatic hypotension, sex, urinary incontinence, and diagnosis subtype. The sensitivity, specificity, accuracy, and AUC of the RF model were 70.82%, 74.55%, 72.29%, and 0.72, respectively.
Conclusions: Besides clinical features, baseline features including NFL, CRP, and NLR were potential predictive biomarkers of disability in MSA. These findings provide new insights into the trials regarding early intervention in MSA.

P 161

Polysomnographic study: characteristics of sleep disturbances in patients with Parkinson's disease

S. Kurbonov[1], *G. Rakhimbaeva*[1], *G. Goyibova*[2]

[1]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan, [2]Tashkent Pediatric Medical Institute, Department of Neurology, Tashkent, Uzbekistan

Background: The study was about improving the diagnosis of sleep breathing disorders, sleep structure disorders, and nocturnal motor activity by analyzing polysomnography in Parkinson's disease.

Methods: Clinical and anamnestic, polysomnography. The material for the study is the data of 93 patients diagnosed with Parkinson's disease, who were admitted for treatment or examination to the neurological department of the Neurology Department of the Tashkent Medical Academy in the period from 2018-2021.

Results: PD is characterized by a predominance of episodes of obstructive and central sleep apnea. Characteristics of motor activity in PD at night is an increase in the Maximum Permissible Concentration (MPC) index in all phases and stages of sleep, as well as the fact that in patients with PD, the most intense episodes of MPC periods of HFS are periods of night wakefulness 82.00 [26.00; 94.00] and period S1/S2 of non-REM sleep stages 43.00 [12.00;58.00]. The median values of the MPC index for HFS in PD correspond to the level of a mild form of RLS 10.5 [4.00;23.5].

It should be especially noted that the complaints of patients with Restless Leg Syndrome (RLS) in PD correspond to the clinical picture of this syndrome, but differ in the polysomnographic pattern. According to the observations obtained, in patients with PD, episodes of MPC are observed throughout the night, and episodes of MPC in patients with PD are observed during the period of nocturnal wakefulness, during the REM phase, during the S1/S2 and S3/S4 stages of non-REM sleep.

Conclusions: Polysomnography is necessary for patients with PD to detect early stages of sleep disorders and SDS and should be included in the algorithm for the diagnostic follow-up of this category of patients in order to select the subsequent therapeutic tactics for managing the patient.

P 162

Clinical and neurophysiological features of sensory dysfunction in Parkinson's disease patients in Uzbekistan

S. Kurbonov[1], *G. Rakhimbaeva*[1], *G. Goyibova*[2]
[1]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan, [2]Tashkent Pediatric Medical Institute, Department of Neurology, Tashkent, Uzbekistan

Background: To investigate the clinical significance and neurophysiological features of multimodal sensory disturbances in PD.
Methods: 295 patients with PD and atypical forms of parkinsonism Atypical Parkinsonism (AP) aged 32 to 70 years were examined.
The 1st group consisted of patients with stages 1–2.5 of PD.
The 2nd group consisted of patients with 3–4 stages of PD.
Persons with AP were included in group 3.
The control group consisted of 100 healthy individuals.
Results: In PD, there is auditory dysfunction at the subclinical level, and in patients with tremulous forms of the disease, the greatest delay in signal conduction throughout the auditory pathway is noted compared to patients who did not have a tremor. A significant violation of the suppression of rotational vertical nystagmus by fixing the gaze in both directions appears already in the early stages of PD and serves as a clinical marker of the disease.
The identified disorders characterize the primary link of vestibular dysfunction in PD and AP and also indicate the important role of adequate interaction between the vestibular and visual sensory systems. In PD, there is a disturbance in the processing of sensory signals, both at the level of the basal ganglia and at the peripheral levels, which is expressed in slowing down the passage of the signal at different levels of organization of the somatosensory system.
Autonomic and emotional disorders in patients with PD have a significant impact on the nature of stem reflexes (in parameters of MR) and also contribute to the development of sensitization from the level of the medulla oblongata to the thalamocortical level, followed by increased activation of the somatosensory cortex, which is a predisposing factor in the development of pain syndromes.
Conclusions: Parkinson's disease is a multisystem degenerative disease, where sensory dysfunction is an integral part of its clinical picture.

P 163
Clinical presentation and diagnosis of a rare brain disease – progressive supranuclear palsy

A. Angelova[1], *G. Novotni*[2], *F. Stojkovska*[3]
[1]University Clinic for Neurology, Skopje, The Republic of North Macedonia, [2]University Clinic for Neurology, Ss Cyril and Methodius University-Faculty of Medicine, Neuroimmunology, Skopje, The Republic of North Macedonia, [3]University Clinic for Neurology, Ss Cyril and Methodius University-Faculty of Medicine, Neuromuscular Disorders, Skopje, The Republic of North Macedonia

Background: Progressive supranuclear palsy is a complex and rare progressive brain disease with marked deterioration of brain cells in few important areas. It affects patient's balance, vision, movement, behavior, cognition, speech and finally swallowing leading to permanent disability and possible life-threatening complications.
Methods: This is a case presentation and medical documentation was used.
Results: We herein report a presentation of progressive supranuclear palsy in a 51-year-old Macedonian woman that had a history of frequent falls and gait difficulties in the last two years which escalated few months prior to hospitalization. Initially they were understood as epileptic seizures and were therefore treated with antiepileptic medication.
Additionally she experienced slurred speech, forgetfulness, and unusual emotional outbursts. Neurological examination on admission showed generalized rigor with axial predominance and bradykinesia, retrocollis, independent gait was impossible, vertical gaze palsy, hypomimia, dysarthria. Deep tendon reflexes were brisk. Primitive reflexes and Babinski were positive.
On mental status examination patient was disoriented and showed emotional incontinence. Magnetic resonance imaging demonstrated typical "hummingbird sign" (midbrain atrophy) and subacute subdural hematoma in the left frontal region. Electroencephalography and neuropsychological testing were also performed. Based on the characteristic neuroimaging and neurologic findings, after eliminating other Parkinson's diseases, diagnosis of supranuclear palsy was proposed.
During hospitalization antiparkinsonian drugs and cholinesterase inhibitors were introduced, and antiepileptic therapy was slowly stopped. Physiotherapy was also started, but there was minimal improvement after two weeks of treatment during hospitalization.
Conclusions: Progressive supranuclear palsy often overlaps with Parkinson's disease and often goes misdiagnosed. Diagnosis is typically made three to four years after onset of symptoms, when the cardinal features such as falls and supranuclear gaze palsy have become unequivocally apparent. Having this in consideration, early and reliable diagnosis remains a big challenge that is demanded by patients and their carers and is important for estimation of prognosis and appropriate multispecialty management.

P 164
Progressive supranuclear palsy

I. Skenderoska[1]
[1]Center for Orthopaedic and Traumatolgy St. Erasmo, Neurology, Ohrid, The Republic of North Macedonia

Background: PSP is an atipical form of parkinsonism with prevalence of 1-5/100000. It appear between 55-70 y and more affect the men in sext decade. PSP(also called Steel Richardson-Olszewski syndrome) is a progressive neurodegenerative disorder and tauopathy due to repeat accumulations of tau proteins in neurons and glia. The characteristic signs and symptoms include early postural instability and falls, vertical supranuclear palsy, problems with speech and swallowing(dysarthria, dysphagia), sleep disturbances anf frontotemporal dementia. Parkinsonian symptoms in PSP are characterized by symmetric bradykinesia, moderate to sever axial rigidity whereas tremor is absent.
A 54 year old man presenting with ataxic gait, supranuclear gaze palsy, instability while walking , early cognitive deteriorations. He had noticed small handwriting. At that time his wife noticed he had some trouble with organising tasks and seemed more irritable. He seemed to have more difficulty with activities of daily living, loss of interest in pleasurable activities.
Methods: - Typical clinical signs (poor verbal fluency, poor attention/concentration, extraocular movements were significant for severely reduced speech of saccades in vertical direction. Tone was increased in neck and billateral upper extremities. He had ataxic gait and postural instabillity on his pull test. He had frequent square -wave jerks.
- Neuropsychological tests
Results: PSP is a rapidly neurodegenerative condition with a poor prognosis. The most common causes of death for patients with PSP are respiratory-related, with the most frequent complication being aspiration pneumonia. Given the high frequency of respiration complications, surgery requiring general anesthesia should be given significant consideration due to the potential for respiratory failure.
Conclusions: There is no pharmacologic therapy for the progression of the disease, and a multidisciplinary team can provide patients and their caretakers with the tools to maximize quality of life and minimize debilitating symptoms.

P 165
Phenotypic spectrum of progressive supranuclear palsy: clinical study and APOE effect

A. Gharbi[1], *S. Mrabet*[1,2], *Y. Abida*[1], *I. Sghaier*[1], *A. Souissi*[1], *A. Gargouri*[1,2], *A. Nasri*[1,2], *I. Kacem*[1,2], *R. Gouider*[1,2]
[1]Razi University Hospital, Department of Neurology, LR18SP03, Manouba, Tunisia, [2]Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

Background: Progressive supranuclear palsy (PSP) is a rare neurodegenerative disorder encompassing several phenotypes with various motor and cognitive deficits. We aimed to study motor and cognitive characteristics across PSP phenotypes, and assess the influence of the Apolipoprotein E (*APOE*) gene variants on PSP phenotypic expression.
Methods: In a cross-sectional study, we retrospectively reviewed the charts of all patients classified as PSP and re-categorized them into phenotypes using the MDS-2017 criteria.
Phenotypes were divided into three subgroups:
Richardson's syndrome (PSP-RS), PSP-cortical (PSP-F +PSP-SL +PSP-CBS) and PSP-subcortical (PSP-P +PSP-PGF +PSP-PI +PSP-OM +PSP-C +PSP-PLS).
Data on clinical and neuropsychological assessments were collected. Genotyping of *APOE* was performed using the RFLP-PCR and verified by Sanger sequencing.
Results: We included 85 PSP patients comprising 10 phenotypes classified into 28 PSP-RS, 30 PSP-cortical (17.6% PSP-CBS, 9.4% PSP-F, 8.2% PSP-SL) and 27 PSP-subcortical (14.1% PSP-P, 9.4% PSP-PI, 3.5% PSP-OM,2.4% PSP-PGF, 1.2% PSP-C, 1.2% PSP-PLS) subgroups.
PSP-RS cases had older age of onset ($p<0.001$) and more akinetic-rigid and levodopa resistant parkinsonism ($p=0.006$), while PSP-cortical cases had more tremor and asymmetric and/or levodopa responsive parkinsonism ($p=0.025$). Cognitive domains were significantly less altered among PSP-subcortical subgroup. Overall, PSP-*APOE*ε4 carriers developed parkinsonism earlier ($p=0.038$), earlier oculomotor dysfunction ($p=0.052$) and had more altered cognitive profile. It was also associated with younger age of parkinsonism onset in PSP-RS phenotype ($p=0.026$).
Conclusions: This study demonstrated the wide phenotypic spectrum of PSP among Tunisians. Later disease onset and akinetic-rigid and levodopa resistant parkinsonism were the hallmarks of PSP-RS phenotype, while milder cognitive impairment was characteristic of PSP-subcortical subgroup. *APOE*ε4 allele was associated to falls and initial oculomotor dysfunction and seemed to play a role in defining a more altered cognitive profile in PSP patients.

P 166
Orthostatic hypotension - insidious onset of MCA-C

F. Stojkovska[1], *Z. Chanakovski*[2]
[1]University Clinic of Neurology, neurology, Skopje, The Republic of North Macedonia, [2]Military Medical Center, Neurology, Skopje, The Republic of North Macedonia

Background: Multiple system atrophy (MSA) is defined as an adult onset, sporadic, multisystem, rapidly progressive neurodegenerative disease of unknown etiology. The disease is characterized clinically with parkinsonian features, cerebellar, autonomic and urogenital dysfunction and involve the extrapyramidal, pyramidal system, the cerebellum and the autonomic nerves. Neuropathological hallmarks of MSA are cell loss in the striatonigral and olivopontocerebellar parts in the brain and spinal cord accompanied by profuse glia cytoplasmic inclusions which is formed by fibrillized alpha-synuclein proteins (synucleinopathy). There are two subtypes of MSA: MSA-P (predominant parkinsonism), MSA-C (predominant cerebellar signs).
Methods: This report describes case of a 65-year old man who has dizziness for 7-8 month 2 times followed with syncope and rapidly develop MSA-C.
Results: Eight month ago, patient starting experienced repeated episodes of dizziness,all of them when he was standing from recumbent position. In two times he developed syncope, fall to the ground, exhibit no response to others,for a few seconds each time. He reported light-headedness, dimming of vision, palpitations, weakness and tingling of the limbs, without limb convulsion, lip or tongue bites. He reported long-term constipation, urinary incontinence and sometimes gait instability.
After his first syncope, neurologist made some tests which were all good likewise neurological examination. He was discharged with therapy, which improved circulation and advice for diet with salt and fluid intake.
After second syncope, he came again to another neurologist, said that he did not feel better with medications. He had a healthy status, did not consume tobacco or alcohol and did not report any history of genetic disease in his family. His vital signs were normal, likewise heart, lung and abdomen. With regard to his neurological examination, he was conscious, with minor slurring of speech. He had horizontal nystagmus. Cranial nerves were normal. He had symmetric minor rigidity of the limbs. His left knee-jerk reflex was brisk and Babinski sign on the left was positive. The finger-to-nose test shows dysmetria and the heel-to-shin test also. Romberg was positive. He had gait ataxia occasionally.
Cranial MRI and DWI shows mild cerebellar atrophy, hot cross bun sign and no other abnormalities on the brain. The standing and lying blood pressures differed by 38/21mmHg. Other blood test were not significantly abnormal. Patient's medical history, combined with physical signs and auxiliary examinations, MSA-C was considered.
Conclusions: This study examines a 65-year old male who presented with insidious onset od MSA-C. We report a MSA-C patient who has developed light rigidity and cerebellar ataxia after diagnosed with orthostatic hypotension. This case may suggest that the diagnosis of MSA could not be excluded by the presence of orthostatic hypotension and syncope.

P 167 (GPT)

Can restless legs syndrome be a predictor of parkinsonism in patients with migraine comorbid with hypertension?

M. Gulova[1], *M. Sanoeva*[2], *N. Panoeva*[1]

[1]Bukhara State Medical Institute, Neurology, Bukhara, Uzbekistan, [2]Tashkent Medical Academy, Neurology and Medicine Psychology, Tashkent, Uzbekistan

Background: Up to 34% of migraines are accompanied by restless legs syndrome (RLS), due to damage to the dopaminergic system, as in Parkinson's disease (PD). We have studied whether RLS is a predictor of PD in migraine with concomitant hypertension.

Methods: 78 patients were examined: 47(60.3%) patients with migraine and hypertension (MHT), 31(39.7%) patients with PD. We used Hen and Yar scale, statistical analyses, diagnostic criteria of the Brain Bank of the PD Society. RLS determined with Johns Hopkins Restless Legs Severity Scale (JHRLSS). The distribution of patients was as follows (Table 1):

Patient groups	Quantity	women	men	middle age
MHT	47 (60,3%)	34 (72,3%)	13 (27,7%)	43,8±2,32
PD	31 (39,7%)	16 (51,6%)	15 (48,4%)	58,9±3,24

Table 1. Distribution of patients by gender and age

Signs	MHT (n=47)		PD (n=31)	
	абс	%	абс	%
Sleep disorder	22	46,8	27	87,1
Sensory symptoms	18	38,3	14	45,2
Motor symptoms	16	34,0	8	25,8
Remitting current	22	46,8	3	9,7
Progressive course	12	25,5	19	61,3
Genetic background	12	25,5	3	9,7
Family history	28	59,6	4	12,9
Evening anxiety	27	57,4	16	51,6
Daytime anxiety	7	14,9	6	19,4
Very severe degree	2	4,3	4	12,9
Severe degree	5	10,6	7	22,6
Moderate degree	18	38,3	5	16,1
Light degree	9	19,2	6	19,4

Table 2. Clinical signs of RLS

Results: 16(58.1%) patients with PD had headaches, 9(29.1%) of them were treated for migraines. 36(76.6%) patients with MHT had 4 out of 6 symptoms of PD. 34(72.3%) patients with MHT and 22(71.0%) patients with PD was detected RLS. There were somnological, sensory and motor symptom complexes of

RLS were observed in both groups. The severity of RLS was almost the same and was assessed as - very severe (36.7±1.26), severe (26.1±1.22), moderate (18.2±1.01), and mild (7.8±0.86) (Table 2). Additional symptoms with a predominance of one or another sign were detected in patients of both groups.
Conclusions: Thus, RLS may be a predictor of parkinsonism in patients with migraine, concomitant hypertension.

P 168
Features of the specific clinical manifestations of vascular disorders in Parkinson's disease and vascular parkinsonism

D. Akramova[1], *G. Rakhimbaeva*[1], *T. Bobomuratov*[1], *U. Shamsieva*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: The clinical features of Parkinson's disease and vascular parkinsonism, cognitive disorders associated with the disease, neuroimaging in Parkinson's disease and vascular parkinsonism, as well as intracranial vascular lesions are therefore discussed.
Methods: Based on this study, the results of a comprehensive clinical examination of 117 patients were analyzed. Research work was carried out on the basis of the TMA clinic in 2019-2022. To assess the characteristics of vascular disorders in Parkinson's disease 47 patients with Parkinson's disease(PD), 40 patients with vascular Parkinsonism(VP) and 30 patients with Cerebral chronic ischemia(CCI). All patients underwent angiography MRI and the results were statistically analyzed
Results: On neuroimaging examination, moderate periventricular oedema was reported in 49.7 ± 2.4% ($p<0.05$) for PD, 62.4 ± 2.3% for VP ($p < 0.05$) and 55.7 ± 3.4% ($p < 0.05$) for CCI. Also subcortical leukoareosis separately and with multihyperintensity in different localisation in T2 mode in 51.4% ($p<0.05$) in group 1, 74.8% ($p<0.01$) in group 2, 49.3% in group 3. Ischemic changes of subcortical nuclei were observed in 49.2% ($p<0.05$) in group 1, 76.2% ($p<0.01$) in group 2 and 38.9% in group 3. Results of fMRI analysis showed a correlation between periventricular edema and height and postural disturbance $r = -0.31$, a correlation between coordination impairment $r = 0.71$, memory impairment $r = 0.31$ and an association with emotional lability $r = -0.31$.
Angiographic data showed more damage to the middle cerebral artery, mainly in patients with vascular parkinsonism. A correlation between vascular stenosis and neurological abnormalities was found. On MR angiography, the correlation between middle cerebral artery narrowing and motor retardation was $r = 0.31$ ($p < 0.05$), similarly the correlation between height and postural abnormalities and middle cerebral artery narrowing was $r = 0.31$ ($p < 0.05$). The correlation between vertebral artery narrowing and movement retardation was $r = 0.30$ ($p < 0.05$) and the correlation between coordination disorders was $r = 0.77$ ($p < 0.01$). The correlation between constriction of the anterior and spinal artery and impaired coordination was $r = 0.77$ ($p < 0.01$), with vertigo $r = 0.31$ ($p < 0.05$) and insomnia $r = 0.48$ ($p < 0.05$).
Conclusions: The process of long-term cerebral vascular disorders in vascular parkinsonism changes the morphological structure of the brain tissue. In particular, vascular changes are clinically significant in terms of their effect on the pathophysiological form of vascular parkinsonism, the appearance of neuroimaging and the clinical form of the disease.

P 169
Development of osteomyelitis after COVID 19 in patients with vascular parkinsonism

D. Bobamuratova[1,1], *T. Bobomuratov*[1], *D. Akramova*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: An increase in blood coagulation in patients vascular parkinsonism undergoing COVID-19 against the background of diabetes mellitus is most often complicated by thrombosis of the cavernous sinus. In addition to coagulopathy, inflammatory diseases of the sinuses, face also lead to these pathologies.
Methods: Pathological examination was carried out in the IPSUM clinic in the resected palate and upper jaw as a result of osteonecrosis, necrotic biopsies from the mucous membrane of the nose and palate, obtained 200 total operations such as sequestrectomy (resection) of the upper jaw, FESS (functional endoscopic sinus surgery) and inoculation eyes held in the multidisciplinary clinic of the Tashkent medical academy in patients with a diagnosis of cavernous sinus thrombosis, maxillofacial osteonecrosis.
Results: Clinical bone tissue in pathological foci (areas of its exposure, especially the palate) has a dirty gray, dull, dull, or yellow-brown color. Bone tissue looks "eaten away" in the absence of granulation tissue in the area of the pathological focus.
Histological in all foci of necrotic masses, small clusters, thickened mycelium with clavate thickened edges. Meet separate large nerve trunks and endings with necrobiosis or necrosis. Blood vessels of the predominantly microcirculatory bed in a state of sharp expansion and overflow with blood, microthrombi are detected. Numerous disordered or palisade-like clusters of thin, segmented, straight, or curved mucorale mycelium with globular nubs at the ends. Neuro and angioinvasion of the mycelium are observed, which is the cause of thrombosis and neuropathy.
Conclusions: Most likely, zygomycetes mucorale cause osteonecrosis of face bones and thrombosis of the cavernous sinus patients with vascular parkinsonism. Angio and neuroinvasion affects the severity of the clinical course.

P 170
Cavernous sinus thrombosis in patients after coronavirus disease patients with vascular parkinsonism in Uzbekistan

D. Bobamuratova[1], *S. Boymuradov*[1], *T. Bobomuratov*[1], *D. Akramova*[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: Severe and life-threatening cases of blood vessel thrombosis in the brain and face increased dramatically over the next 2 years after Covid-19. In addition to coagulopathy, the addition of infection to the adjacent oral and nasal cavities, the spread of infection to the lungs through the blood vessels leads to the development of septic thrombosis of the cavernous sinus.
Our goal is to analyze the clinical course of facial and maxillary complications in patients with coronavirus disease patients with vascular parkinsonism.

Methods: Scientific analysis was carried out in 256 patients treated at the TTA multidisciplinary clinic with a diagnosis of postcovid syndrome, cavernous sinus thrombosis, osteomyelitis of the upper jaw. The age of the patients was from 18 to 76 years, the average age was 52.5 ± 3.9 years in 148 men (57.8%) and 108 women (42.2%).

Results: Almost the bulk of the primary referrals of patients fell on the warm months of the year. Most patients have bilateral pneumonia, type II diabetes mellitus. In the polysyndromic course of cavernous sinus thrombosis, inflammation of the maxillofacial region and osteonecrosis, ophthalmological, neurological pathologies, and inflammation of the ENT organs prevailed (table 1). Circumstances causing disability and death, such as vision loss, cerebrovascular disorders and inflammation, stroke, soft tissue and bone necrosis, have been confirmed in these patients.

Conclusions: Cavernous sinus thrombosis is characterized by ischemic, necrotic and inflammatory types, as well as neurological pathology in areas associated with angiopathy and neuropathy III, IV, V, VI pairs of brain nerves. In the early and late stages of the Covid-19 disease, it is necessary to strictly control the coagulogram and other metabolic parameters, rehabilitation foci of oral cavity infection and nasal cavities.

Dystonia

P 171 (GPT)
Effects of botulinum toxin type A in Meige's syndrome

A. Duarte[1], *H.A. Ghizoni Teive*[1]
[1]Universidade Federal do Paraná, Curitiba, Brazil

Background: Meige's syndrome (MS) is a type of facial dystonia characterized by the simultaneous occurrence of blepharospasm and oromandibular dystonia. It was first described in 1910, by dr. Henri Meige, a French neurologist. Since then, MS physiopathology was not completely identified. It is known that genetic factors, as well as environmental triggers, are involved in changes in the dopaminergic system modulation, causing hyperactivation of certain regions of the nervous system, such as the hypothalamus and basal ganglia. Botulinum toxin, especially the botulinum toxin type A (TBA), has been used since the eighties as a treatment for facial dystonia.
However, there is a lack of studies about its effects in MS. The aim of our study was to evaluate the effects of the TBA application in patients with Meige's syndrome.
Methods: Patients that apply botulinum toxin type A (TBA) as a treatment for Meige's syndrome at Hospital de Clínicas da Universidade Federal do Paraná were questioned about the occurrence of dystonia before and after the application of TBA, using the Burke-Fahn-Marsden Dystonia Scale (BFMDS) to quantify the symptoms improvement. They were also questioned about the occurrence of side effects. Those data were noted in an Excel sheet and statistical analysis was performed.
Results: The study had 41 participants (mean age: 67.6; 9 men : 32 women). The mean total BFMDS score before the TBA application was 13.1, and after, 4.41 ($p < 0.001$).
Without considering the weight, the mean eyes BFMDS score was 9.41 before the TBA application, and after was 2,66, while the mouth score was 8.37 before and 3.10 after ($p < 0.001$). Side effects occurrence was 18.92%, and ptosis was the most frequent.
Conclusions: TBA application is an effective and safe therapeutic to MS. Blepharospasm showed a better response to the treatment than oromandibular dystonia.

P 172

A multimodal meta-analysis of structural and functional brain changes in idiopathic blepharospasm

M. Zhang[1], *X. Huang*[1], *H. Shang*[1], *J. Yang*[1]
[1]West China Hospital of Sichuan University, Neurology, Chengdu, China

Background: Neuroimaging studies have shown structural and functional alterations in patients with idiopathic blepharospasm (iBSP); however, these findings are variable and inconsistent, and no systematic information is available relating these two domains. In this study, we investigate the specific and common neurostructural/functional abnormalities in iBSP patients comparing with healthy controls by conducting separate and multimodal meta-analysis of structural and functional imaging studies.
Methods: A systematic literature search from PubMed, Web of Science and Embase was conducted to identify relevant publications. We conducted separate meta-analysis for whole-brain voxel-based morphometry (VBM) studies and for functional imaging studies, and a multimodal meta-analysis across VBM and functional studies in iBSP, using anisotropic effect size-based signed differential mapping.
Results: Eighteen studies met the inclusion criteria. The structural database comprised 129 iBSP patients and 144 healthy controls whilst the functional database included 183 iBSP patients and 253 healthy controls.
The meta-analysis of VBM studies showed increased gray matter in bilateral precentral and postcentral gyri, right supplementary motor area and bilateral paracentral lobules, while decreased gray matter in right superior and inferior parietal gyri, left inferior parietal gyrus, left inferior temporal gyrus, left fusiform and parahippocampal gyrus.
The meta-analysis of functional studies revealed hyperactivity in right dorsolateral superior frontal gyrus, left thalamus and right fusiform gyrus, while hypoactivity in left temporal pole, left insula, left precentral gyrus, bilateral precuneus and paracentral lobules, right supplementary motor area and middle frontal gyrus.
The multimodal meta-analysis identified conjoint anatomic and functional changes in left precentral gyrus, right supplementary motor area, bilateral paracentral lobules, right inferior occipital gyrus and fusiform gyrus.
Conclusions: This meta-analyses identified complicated patterns of conjoint and dissociated brain alterations in iBSP, which may help provide new insight into the neuropathology of iBSP.

P 173

IncobotulinumtoxinA injections at intervals <10 weeks are effective and safe for cervical dystonia patients with inadequate benefit from standard intervals

C. Comella[1], R. Hauser[2], S. Isaacson[3], D. Truong[4], O. Oguh[5], J. Hui[6], E. Molho[7], M. Brodsky[8], E. Furr-Stimming[9], G. Comes[10], M. Hast[11], D. Charles[12]

[1]Rush University Medical Center, Chicago, United States, [2]University of South Florida Health Byrd Institute, Tampa, United States, [3]Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, United States, [4]UC Riverside, Riverside, United States, [5]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States, [6]University of Southern California, Los Angeles, United States, [7]Albany Medical Center Neurosciences Institute, Albany, United States, [8]Oregon Health & Science University, Portland, United States, [9]The University of Texas Health Science Center at Houston, Houston, United States, [10]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [11]Merz Pharmaceuticals, LLC, Raleigh, United States, [12]Vanderbilt University Medical Center, Nashville, United States

Background: Efficacy and safety of two incobotulinumtoxinA injection schedules for treating cervical dystonia (CD) were compared. Some CD patients receiving long-term botulinum toxin (BoNT) therapy report early waning of treatment effect (even after favorable peak response) before a typical 3-month reinjection interval. This study addresses the safety and efficacy of incobotulinumtoxinA injection intervals <10 weeks.

Methods: CD Flex (NCT01486264) was a phase IV, open-label, randomized, noninferiority study comparing 2 incobotulinumtoxinA injection schedules (short-flex: 8±2 weeks; long-flex: 14±2 weeks) in CD subjects. BoNT-responsive subjects (≥2 prior successful injections) reporting acceptable clinical benefit lasting <10 weeks were recruited. Efficacy and safety were evaluated after 8 injection cycles.

Primary endpoint: change in the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) severity subscale (blinded rater) 4 weeks post-injection 8.

Secondary endpoints: TWSTRS total and other subscale scores. Immunogenicity was assessed in a subset of patients at baseline/post-injection 8. Safety was monitored throughout.

Results: 282 CD subjects were randomized (short-flex, N=142; long-flex, N=140); 207 completed the study. Mean dosing was similar in the short-flex (272U) and long-flex (268U); mean intervals were 54 days (short-flex) and 86 days (long-flex). Significant improvements in TWSTRS-severity from study baseline to 4 weeks after cycle 8 were observed in both the short-flex (4.1 patients; $P<0.0001$) and long-flex (2.4 patients; $P=0.002$). Short-flex was noninferior to long-flex (LS mean difference=1.4 pts; $P=0.0693$). Responder rates (≥20% improvement in TWSTRS-severity) post-injection 8 did not differ significantly between groups. Adverse events (AEs) were comparable between groups. There was no secondary loss of treatment effect due to neutralizing antibodies after 8 cycles among those tested.

Conclusions: IncobotulinumtoxinA injection cycles <10 weeks are effective and noninferior to longer intervals for treating CD patients with early waning of clinical benefit. Shorter intervals did not increase AEs or lead to loss of treatment effect due to neutralizing antibodies.

P 174

Cervical dystonia with cerebellar ataxia in *KCNA1* mutation: a phenotypic expansion

R. Mahale[1], *S Jayanth*[1], *D. Dutta*[1], *H. Padmanabha*[1], *P. Mailankody*[1]
[1]NIMHANS, Bangalore, India

Background: The *KCNA1* gene encodes the voltage-gated potassium (K^+) channel Kv1.1 α-subunits and the mutation have been primarily linked to episodic ataxia type 1 (EA1). However, persistent cerebellar ataxia with dystonia as a phenotype of *KCNA1* gene mutation has not been described. Hereby we report a 20-year-old lady who presented with cervical dystonia followed by persistent cerebellar ataxia. Genetic analysis showed heterozygous missense mutation in the *KCNA1* gene.

Methods: NA

Results: A 23-year-old lady born out of consanguineous parentage with normal milestones had presented with history of abnormal posturing of head in the form of head turn to the right for 3 years. There was no diurnal variation.

After 1 month, patient developed walking difficulty in the form of imbalance and tremulousness of both hand on target-oriented activities. Family history was non-contributory. Systemic examination was unremarkable. Neurological examination showed normal cognition. There was bilateral horizontal gaze-evoked nystagmus. She had anterior sagittal shift (combination of anterocollis and retrocaput), left horizontal shift of head, right laterocaput and left laterocollis with dystonic tremors both during rest and worsening on walking **(***video 1***)**.

There was no null point. There was bilateral impaired finger-nose-finger co-ordination, heel-knee co-ordination, dysdiadochokinesia and impaired tandem gait with gait ataxia **(***video 2***)**.

Brain magnetic resonance imaging (MRI) was normal. Genetic analysis showed a novel heterozygous missense variant (p.Arg295Cys) in exon 2 of *KCNA1* gene (NM_000217.3). The missense variant KCNA1(NM_000217.3):c.883C>T (p.Arg295Cys) has not been reported previously as a benign variant, to our knowledge.

As the clinical phenotype of the proband almost matches with that of the disorder caused by pathogenic variants in the gene *KCNA1*, this variant was classified as likely pathogenic. She was treated with tetrabenazine (75mg/day), trihexyphenidyl (10 mg/day) and acetazolamide (750mg/day). There was no improvement in gait ataxia.

Conclusions: This case reports an expansion in the clinical phenotype of *KCNA1* channelopathy.

P 175 (GPT)

Biopsychosocial aspect of patients with X-Linked Dystonia-Parkinsonism: Its implications on quality of life

A. Alcachupas[1,2], K. Bellosillo[1], W.R. Catolico[1], M.C. Davis[1], A. Diaz[1], Y.K. Doyongan[1], R. Eduarte[1], E. Gersava[1], M.B. Intrepido[1], M.G.K. Laluma[1], C.C. Lavalle[1], J.J. Millan[1]

[1]West Visayas State University, College of Medicine, Iloilo City, Philippines, [2]Liverpool University Hospitals NHS Foundation Trust, Liverpool, United Kingdom

Background: This study aims to describe the demographic profile in terms of age, marital status, annual family income, and educational attainment; to describe the physical, psychological, and social manifestations; to determine and describe coping mechanisms; to determine the goals, aspirations, and needs; and, to determine the interaction and impact of the lived experiences to the quality of life of XDP (X-Linked Dystonia-Parkinsonism) patients.

Methods: This qualitative-phenomenological study was conducted in the island of Panay. Purposive sampling was utilized. The researchers utilized in-depth interview, observation, and triangulation as part of the data collection methods. The data was transcribed verbatim, kept for content analysis, and coded in their appropriate cell categories after themes were identified.

Results: Ten male patients who were residents of Panay, aged 30-65 years old participated in this study. Disease manifestations included limb dystonia, blepharospasm, truncal torsion, oromandibular symptoms, torticollis and dysphonia, contributing to limitations to performing activities of daily living.

Denial was the most common initial reaction after being diagnosed with XDP. Social manifestations were greatly affected by family and community. Money and medications were the primary needs identified by the patients with hopes of a better future for their families. There was an overall deterioration in the quality of life of the patients.

Conclusions: XDP patients had individualized experiences with the disease. The patient's quality of life was affected by different interlocking chain of factors. The multidimensional aspects of the quality of life should be placed under constant check and balance; the family and health workers alike should be the accountants.

Finding meaning to their quality of life did not only rely on physical relief of symptoms, but in gaining social acceptance, independence, and life-long support and love.

P 176 (GPT)

Depression impact on subjective and objective severity of cervical and segmental dystonia

V. Meļņikova[1], *R. Valante*[1], *S. Valtiņa-Briģe*[1]
[1]Pauls Stradiņš Clinical Univerity Hospital, Department of Neurology, Rīga, Latvia

Background: Dystonia is highly disabling and disfiguring disease. Therefore, depressive symptoms are one of the most common nonmotor feature in these patients.
The aim of this study was to investigate depression impact on the severity of dystonia.
Methods: Patients with cervical and segmental dystonia were interviewed during outpatient visit at Movement disorder clinic in P. Stradiņš clinical university hospital. Patients were divided in two groups, based on the PHQ-9 questionnaire: with no depression or mild depressive features and those with moderate, moderately severe, severe depression.
Severity of dystonia was assessed with modified TSUI scale and Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) - physical findings part. Self-assessment of dystonia severity was possible choosing one option of three proposed: mild, moderate, severe. Objective and self-assessment of dystonia severity was calculated and compared in both depression groups.
Results: The total of 32 patients were included in the research. There were 24 patients without depressive signs and with mild depression (first group) and 8 patients with moderate, moderately severe, or severe depressive disorder (second group).
The modified TSUI score was slightly higher in the patient group with clinically significant depressive signs, than in the group without or mild depressive symptoms (8,8 and 7,8 accordingly), but difference did not have statistical significance (P=0,428). The TWSTRS (physical findings part) scale score had tendency to be higher in the second group than in first (14,0 and 12,0 accordingly; P=0,07).
Self-assessment did not differ statistically significantly between the two groups (P=0,123), although nobody in the second group admitted having mild dystonia.
Conclusions: Dystonia patients suffering from clinically significant depression have more negative self-assessment of the disease. Also, patients with clinically significant depressive signs scored higher on both measuring tools. TWSTRS (physical findings part) scale showing more significant cervical dystonia severity difference between both patient groups than TSUI scale.

P 177 (GPT)

Clinical aspects of patients with blepharospasm in Latvia: one center study

M. Kalniņa[1,2], *R. Valante*[1], *K. Lazdovska*[1]

[1]Pauls Stradiņš Clinical University Hospital, Department of Neurology, Riga, Latvia, [2]Rīga Stradiņš University, Faculty of Residency, Riga, Latvia

Background: Blepharospasm, a spontaneous eyelid closure, is a common dystonia, that can occur for few days and disappear without treatment, or become persistent, causing discomfort and disrupting daily life.

Methods: A total of 80 patients with blepharospasm were identified at Pauls Stradiņš Clinical University Hospital outpatient clinic who had their first examination in time period from 2006 to 2020 and recieved botulinum toxin injections. 24 were not enrolled due to various exclusion criteria (18 could not be contacted, 5 were deceased, 1 had other diagnosis). 56 patients were contacted by telephone in 2021 and interviewed about disease characteristics and overall health.

Results: Patients sought medical help on average 5,4 years after symptom onset. 23,2% were male (N=13), 76,8% female (N=43), with average age of symptom onset - 57,5 years. Involuntary blinking as the main symptom was present in 21,4% patients (N=12), 58,9% (N=33) had spasms of the orbicularis oculi muscles, while in 19,6% (N=11) had combination of aforementioned symptoms.

At the time of diagnosis unilateral involvement was observed in 29 cases, while 27 patients had bilateral asymmetrical blepharospasm. 12,5% (N=7) patients reported burning sensation in the eye before blepharospasm, 26,7% (N=15) had dry eye, 57,1% (N=32) noted photophobia. 41% (N=23) of patients could identify the trigger event – passing of a relative (N=9), trauma (N=3), cataract operation (N=3), emotional stress in general (N=8).

On average it took 5,7 months for symptoms to develop following the triggering event. 7,1% of patients (N=7) had a positive family history. Comorbidities included hypertension (58,9%, N=33), insomnia (46%, N=26), depression (30%, N=17) and anxiety (19,6%, N=11). Sensory tricks were used successfully by 57,1% (N=32) of patients.

Conclusions: Overall sex distribution and clinical features are similar as described in literature. Majority of patients link their onset of blepharospasm with emotional trigger.

P 178 (GPT)

Data of P. Stradins Clinical University Hospital Dystonia Register: time from symptoms to diagnosis and treatment of blepharospasm

M. Kalniņa[1,2], *R. Valante*[1], *K. Lazdovska*[1]

[1]Pauls Stradiņš Clinical University Hospital, Department of Neurology, Riga, Latvia, [2]Rīga Stradiņš University, Faculty of Residency, Riga, Latvia

Background: Blepharospasm, a form of dystonia that causes eyelid closure due to involuntary muscle contractions of the orbicularis oculi muscles, is underdiagnosed and therefore mismanaged disorder in Latvian population.

Methods: 56 patients with blepharospasm were interviewed following treatment with botulinum toxin injections at Pauls Stradiņš Clinical University Hospital outpatient clinic during the period of 2006 to 2020.

Results: Period from symptom onset to diagnosis took 5,4 years on average. Patients were divided in three groups (A, B, C) based on time period from symptom onset to diagnosis: A – less than 2 years (46,4%, N=26), B - 2-5 years (28,6%, N=16), C – more than 5 years (25%, N=14).

There was no statistical difference in treatment efficacy and side effect incidence in aforementioned groups. Time period on average from diagnosis till first course of treatment (injections of botulinum toxin) was 3,5 years. Botulinum injections were repeated 2,6 times a year on average.

Following botulinum toxin injections patient exacerbation was observed in 7,1% (N=4) of cases, 10,7% (N=6) had none or minimal effect, 8,9% (N=5) noticed diminishing of the blepharospasms, while majority of patients (78,5%, N=44) had a noticeable clinical improvement.

Mean effect from injections lasted for 5,8 months and improvement was observed on 7th day after treatment. 48,2% (N=27) of patients never experienced side effects, while the remaining patients (51,8%, N=29) had various unwanted reactions – 41% ptosis (N=23), 5,3% double vision (N=3), 3,5% facial asymmetry (N=2), 3,5% eyelid edema (N=2).

Conclusions: More than 25% of patients with blepharospasm had delayed diagnosis and therefore did not receive specific treatment early on. Patient and primary physician education would shorten the time of diagnosis and provide better treatment options. Additional research is needed to cognize the impact of delayed diagnosis and quality of life for patients with blepharospasm.

P 179 (GPT)
Comparing the features of cervical dystonia subtypes: a retrospective study in Pakistan

A. Fatima[1]
[1]Fatima Jinnah Medical University/Sir Gangaram Hospital, Neurology, Lahore, Pakistan

Background: Cervical dystonia (CD) being the most comman are characterised by abnormal twisted postures of head and neck. Although they differ phenotypically but one hallmark feature of CD is the heterogeneity and variability of the clinical signs of these patients. We aim to find out the how different subgroups of cervical dystonia differ in terms of sensorimotor features as they usually differ clinically in terms of onset and spread.
Methods: Clinical and demographic data of 600 patients was collected. Motor features (head tremor and tremor elsewhere) and sensory features (sensory trick and neck pain) were investigated. We analyzed possible associations between motor and sensory features in CD subgroups [focal neck onset, no spread (FNO-NS); focal neck onset, segmental spread (FNO-SS); focal onset elsewhere with segmental spread to neck (FOE-SS); segmental neck involvement without spread (SNI)].
Results: Neck pain was present in 61.3% of patients. Head tremor was present in 54.43% and tremor elsewhere was present in 16% of CD. In FNO-NS, FOE-SS, and SNI subgroups, head tremor was associated with the presence of tremor elsewhere. Sensory trick was associated with pain in patients with FNO-NS and with head tremor in patients with FNO-SS.
Conclusions: The frequent association between head tremor and tremor elsewhere may suggest a common pathophysiological mechanism. For sensory trick in FNO-NS and FNO-SS it may be hypothesised that theres a gating mechanism attempting to reduce pain and a sensorimotor mechanism attempting to control tremor.

P 180
Non-motor symptoms in cervical dystonia

E. Kobak Tur[1], *K.I. Carus*[1], *E. Gözke*[1]
[1]Healthy Science University Istanbul Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey

Background: Cervical dystonia (CD) is a movement disorder characterized by cranial muscle overactivity leading to an abnormal head posture. The patients with CD experience motor and various types of non-motor symptoms (NMSs), which significantly contribute to disability and decrease quality of life. This study investigated the frequency of NMSs and their relation to CD severity.
Methods: Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Standardized Mini-Mental State Examination (SMMSE), Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS) were used to evaluate NMSs in 26 patients with CD and 26 healthy controls (HCs). Motor symptoms of CD patients were assessed by the Toronto Western Spasmodic Torticollis Rating Scale-severity scale (TWSTRSS).

Results: The mean BDI and BAI scores were significantly higher in the patient group (p=0,006 and p=0,001, respectively). The mean score of SMMSE was considerably lower in the patient group than that in HCs (p=0,014). The frequency of excessive daytime sleepiness did not differ between groups (p>0,05). The patients with CD had worse sleep quality than HCs (p=0,001), (Table 1).

	Patient (n:26) Mean ±SD (Median)	***Control (n:26) Mean ±SD (Median)***	***p-value***
Age	49,96±13,8 (50)	48,69±11,3(48,5)	0,647
BDI	11,96±7,97 (10)	5,92±3,7 (6,5	***0,006****
BAI	13,15±7,12 (12,5)	5,46±3,47 (4)	***0,001****
ESS	3,62±3,46(3,5)	5,15±3,45 (4,5)	0,065
SMMSE	26,27±2,18 (26)	27,85±2,19 (28)	***0,014****
PSQI global score	6,15±4,26 (5)	2,65±1,06 (3)	***0,001****

*Mann Whitney U Test *p<0,05 **p<0,01*
BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory,
ESS: Epworth Sleepiness Scale, SMMSE: Standardized Mini-Mental State Examination,PSQI: Pittsburgh Sleep Quality Index

Table 1. Prevalence of NMSs among patients and controls

PSQI sleep onset latency and PSQI sleep disturbance were significantly higher in the patient group (p=0,001 and p=0,012, respectively). Also, PSQI sleep duration and PSQI sleep efficiency were significantly lower in the patient group (p=0,001 and p=0,001, respectively). No significant correlation was found between NMSs and disease severity, age, duration of disease in the patients with CD (p>0,05).

Conclusions: Cervical dystonia causes functional impairment in many patients and leads to difficulties in activities such as lack of self-confidence, timidity, avoidance of social movements, and depressive mood. Therefore, it is crucial to evaluate the patient thoroughly by observing the NMSs of the patients diagnosed with CD.

P 181
Dystonia 23: first report of a Colombian case

D. García-Orjuela[1], *X. García*[2]
[1]Pontificia Universidad Javeriana, Neuroscience, Bogotá, Colombia, [2]C.I.F.E.L., Movement Disorders, Bogotá, Colombia

Background: In the movement disorders field, the number of genetic entities has been increasing, several genetic causes have been associated with dystonia-related disorders. Mutations in CACNA1B gene, located at 9q34, has been causally related with adult-onset cervical dystonia, part of Dystonia 23 (DYT 23). This disease has a very few reports. We present a case report of a Colombian patient.
Methods: A 33 -year-old Colombian male without any relevant medical history, developed sudden abnormal cervical posture, he consulted an orthopedist that diagnosed acute mechanical cervicalgia and treated with muscle relaxant and NSAIDs without improvement, he was sent to a psychiatrist who discarded psychogenic cause, lately, a movement disorders specialist diagnosed isolated focal early adulthood onset dystonia.
Results: Genetic evaluation showed a heterozygous c.4166G-A transition in the CACNA1B gene, that results in an arg1389-to-his (R1389H). The CACNA1B mutation gene was linked to hyperexcitability in structures such as basal ganglia, and abnormal calcium metabolism is well document in the pathophysiology of early adulthood onset dystonia, however, the medical literature was no conclusive, CACNA1B mutation is considered a variant of unknown significance regarding dystonia.
Conclusions: The presented case could correspond to the first Colombian report of DYT 23. Authors consider this possibility very likely, given the fact that phenotype of patient (young adult onset cervical dystonia) was reported previously as part of the spectrum of DYT 23, and no other ascribable cause was identified.

P 182
Clinical characteristic of hemifacial spasm patients in Latvian population

A. Dubra[1,2]
[1]Riga Stradiņš University, Neurology, Riga, Latvia, [2]Pauls Stradins Clinical University Hospital, Neurology, Riga, Latvia

Background: Hemifacial spasm (HFS) is a condition which characterized by nonpainful, involuntary twitching or contraction of the facial muscles on one side of the face and in rare cases has bilateral facial muscles involvement. Aim of study investigate and compare most characteristic features of patients with hemifacial spasm in Latvia.
Methods: This was a retrospective, descriptive study carried out in Pauls Stradins Clinical University Hospital Botulin toxin outpatient clinic from January 2020 to December 2021. Data was collected by questionnaire requesting information on sex, the age of HFS onset, the treatment duration, provocative factors, distribution of facial spasm, the time elapsing between the first symptoms and the correct diagnosis of HFS, the treatment duration of local injections of botulinum toxin.

Results: The data of 60 patients with hemifacial spasm were analyzed. Most of the patients were female 80% (n=48). Mean age of patients with hemifacial spasm was 58,8± 11,8 years (32-79 years), the average age at onset of HFS was 49,4 ± 8,8 years (22-70 years), and the disease duration was 10,7 ± 15,8 years (0.3-49.0 years). Hemifacial spasm was left-sided in patients 36 (60.0%), right-sided in 23 (38.3%), and bilateral in 1 patient.

Average time from the first symptoms till the correct diagnosis of HFS was 1.9± years (0-3 years), of all patients 10 patients average time till the correct diagnosis 1.6± 2.2 years. Patients were receiving treatment with botulinum toxin, the treatment duration was 5.8 ± 4.5 years, and the duration of the beneficial effect was about 3 months.

Conclusions: Our data shows that common in Latvian population sex distribution, age of onset and affected side do not differ from other studies. But the time of diagnosis and receiving therapy is still to long.

P 183
Generalized dystonia of early onset associated with a homozygous loss-of-function variant in the *AOPEP* gene

C. Fevga[1], *F. Ferraro*[1], *G.J. Breedveld*[1], *C. Savant Sankhla*[2], *V. Bonifati*[1]
[1]Erasmus MC, University Medical Center Rotterdam, Clinical Genetics, Rotterdam, Netherlands,
[2]P D Hinduja National Hospital, Neurology, Mahim, Mumbai, Maharashtra, India

Background: Biallelic loss-of-function variants in the *AOPEP* gene were recently identified in European cases with generalized/multifocal dystonia. We describe a patient born to consanguineous parents of Indian ancestry with generalized dystonia, carrying a novel homozygous loss-of-function *AOPEP* variant.

Methods: We performed high-density SNP genome-wide genotyping in all available family members and whole exome sequencing (WES) in the patient. We carried out linkage analysis under an autosomal recessive mode of inheritance, which yielded a list of candidate genomic regions. We then inspected these regions for rare homozygous variants by means of copy number variant (CNV) and WES analyses. Sanger sequencing and agarose gel electrophoresis were performed to test the presence and state of the resulting variants in the family.

Results: A 31-year-old male presented with dystonia in the upper limbs since 20 years of age, which progressively involved the cervical and truncal segments. His family history was negative for neurological disorders, while perinatal and past medical history were unremarkable. Upon examination, we found dysarthria, laryngeal dysphonia, kyphoscoliosis, retrocollis, truncal and bilateral hand dystonia. Hypertonia was evident in both upper and lower limbs.

The patient was able to walk without support but with extensor trunk posture. The rest of the neurological examination as well as brain and cervical spine MRI were normal. Our genetic analysis revealed a homozygous 70-nucleotide duplication in exon 2 of *AOPEP* (NM_001193329.1), leading to premature termination in the encoded protein: c.333_402dup (p.Gly135*), which we regarded as the disease-causing variant in this patient.

Conclusions: Our data support the contention that biallelic loss-of-function variants in *AOPEP* are causative for early-onset, generalized dystonia. Additional work remains ahead to characterize the full genetic and clinical spectrum, as well as to decipher the disease molecular mechanisms in patients with *AOPEP* variants.

P 184
Health-related quality of life in cervical dystoniausing EQ-5D-5L: a large cross-sectional study in China

J. Lin[1], *Y. Liang*[1], *R. Ou*[1], *Q. Wei*[1], *Y. Hou*[1], *L. Zhang*[1], *C. Li*[1], *K. Liu*[1], *Z. Jiang*[1], *T. Yang*[1], *J. Yang*[1], *M. Zhang*[1], *S. Kang*[1], *Y. Xiao*[1], *Q. Jiang*[1], *X. Gu*[1], *J. Yang*[1], *W. Song*[1], *X. Chen*[1], *B. Zhao*[1], *Y. Wu*[1], *H. Shang*[1]
[1]West China Hospital, Sichuan University, Chengdu, China

Background: The study aimed to evaluatethe health-related quality of life (HRQoL) measured by the five-level EuroQol-5 dimensions (EQ-5D-5L) in cervical dystonia, and to explore the determinants of HRQoL in patients with cervical dystonia.
Methods: EQ-5D-5L health state profile were converted into a single aggregated "health utility" score. A calibrated visual analog scale (EQVAS) was used for self-rating of current health status. Multiple linearregressionanalysis was used to explore the factors associated with HRQoL in cervical dystonia.
Results: A total of 333 patients with cervical dystonia were enrolled in the analysis, with an average age of 44.3 years old. The most common impaired dimensions of health was anxiety/depression (73.6%), followed by pain/discomfort (68.2%) and usual activities (48.0%). The median health utility score was 0.80 and the median EQVAS score was 70.
Multivariate linear regression analysis indicated that disease duration and the scores of the Hamilton Depression Rating Scale (HDRS), Pittsburgh sleep quality index (PSQI), Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) Part I, andTWSTRS Part IIIwere associated with the health utility scores. After adjusting other parameters, TWSTRS Part III score and HDRS score were significantly associated with the EQVAS scores ($P < 0.05$).
Conclusions: This study evaluated HRQoL in patients with cervical dystoniausing the Chinese version of the EQ-5D-5L scale. We found that besides motor symptoms, non-motor symptoms including depression, pain and sleep quality were could be greater determinants of HRQoL in patients with cervical dystonia. Management of non-motor symptoms therefore may help improve HRQoL in patients with cervical dystonia.

P 185 (GPT)

Mutation screening and burden analysis of *IMPDH2* in dystonia in a Chinese population

J. Lin[1], *C. Li*[1], *X. Gu*[1], *Y. Cui*[1], *Y. Hou*[1], *L. Zhang*[1], *R. Ou*[1], *Q. Wei*[1], *B. Cao*[1], *K. Liu*[1], *Z. Jiang*[1], *T. Yang*[1], *J. Yang*[1], *M. Zhang*[1], *S. Kang*[1], *Y. Xiao*[1], *Q. Jiang*[1], *W. Song*[1], *B. Zhao*[1], *J. Yang*[1], *X. Chen*[1], *Y. Wu*[1], *H. Shang*[1]
[1]West China Hospital, Sichuan University, Chengdu, China

Background: Recently, co-segregation analysis in a Finnish family with dystonia identified that deleterious heterozygous truncating variant p. (Tyr32MetfsTer19) in IMPDH2might be the disease cause.However, no further replication study has been conducted in dystonia cohorts. We aimed to systematically evaluate the genetic associations of *IMPDH2* with dystonia in a dystonia cohort.
Methods: We analyzed rare variants of *IMPDH2* in 399 Chinese dystonia patientswith whole exome sequencing. The over-representation of rare variants in patients was examined with Fisher's exact test at allele and gene levels.
Results: The variant reported in the original study was not identified in our dataset. Only one rare missense mutation (minor allele frequency < 0.01) p.A396T was identified. At allele level, this variant was associated with dystonia with summary data from both gnomAD and ChinaMAP as control. However, gene-based burden analysis did not detect enrichment of rare variants of *IMPDH2* in dystonia.
Conclusions: After comprehensively analyzing the genetic involvement of *IMPDH2* in dystonia, we found that variants of *IMPDH2* were rare in Chinese dystonia patients, which paved way for future research.

P 186

Whole exome sequencing of familial, combined or complex dystonia

E. Kafantari[1], *A. Puschmann*[1]
[1]Lund University, Skåne University Hospital, Neurology, Lund, Sweden

Background: To determine the usefulness of whole exome sequencing (WES) in the diagnostic evaluation of patients and small families with familial, combined and/or complex forms of dystonia identified from an adult neurology clinic at a tertiary center, and to set up a computational pathway for the bioinformatics analyses.
Methods: By mail, we contacted all 347 patients from our department who during a 4-year period had an ICD-10 diagnosis of dystonia. Of these, 122 were re-examined within our research study. Patients who had combined and/or complex dystonia phenotypes and patients who reported close family members with dystonia were examined by WES. Different computational approaches followed (co-segregation or trio analysis, filtering variants based on an *in-house* gene list with more than 500 dystonia nuclear and mitochondrial genes etc.). Copy number variants (CNVs) were also detected by using *in-silico* tools.
Results: Re-examination revealed that 11 of 122 (9.0%) of patients had other disorders. Of the remaining 111 patients, fourteen had familial, combined or complex dystonia phenotypes starting at mean 37.6 (SD 14.9) years and were analysed by WES. For 5 of these, a definite or candidate monogenic disease cause was identified (table).

ID	Sex	Age at onset	Phenomenology	Variant(s) identified	Family analyses	Comments
P 120	Female	27 years	Paroxysmal dystonia, startle	***KCNMA1*** missense heterozygous	Affected mother-proband pair. Asymptomatic sibling carries the variant	Incomplete penetrance
P 746	Female	38 years	Dystonia, myoclonic jerks	**New candidate gene** missense heterozygous	Affected proband-son pair. Unaffected sibling and two proband's half siblings	Co-segregation analysis. Gene product interacts with TorsinA.
P 765	Female	8 years	Tremor, ataxia, dystonia, ADHD symptoms	***STXBP1*** missense heterozygous	Mother with the same genotype and similar phenotype	Novel variant located in a conserved mutational hotspot
P 858	Female	From birth	Dystonia, epilepsy, tremor, Parkinsonism, myoclonus, intellectual disability	***WARS2*** missense compound heterozygous	Parents heterozygous for one of the variants each. Trio analysis.	Variants described previously in PMID:35074316 and a 2nd Swedish family
P 1005	Male	16 years	Dystonia, ataxia, mild intellectual disability, ichtyosis	**Deletion on Xp22.31** (*PUDP* [or *HDHD1*], *VCX*, *STS*, *PNPLA4*) hemizygous	Patient had no copies of the genes. Unaffected sister also carries the deletion. Mother had blepharo-spasm since age 50.	Clinical phenotype in line with previous description of a deletion of these 4 genes (ClinVar 813270)

The diagnostic yield in this project was 35,7% with positive or likely positive findings. Two of 5 patients had variants that had been described previously (40%) and the remaining 3 carried putatively pathogenic variants (60%).

Conclusions: Candidate disease-causing variants were identified in 5 out of 14 cases investigated, all these had combined or complex dystonia and relatively young onset (mean 22.3, SD 11.3 years). CNV analysis is relevant in the genetic workup of familial/combined/complex dystonia.

P 187 (GPT)

Leigh-like syndrome as a presentation of biallelic variants in *DNAJC30* gene with predominant putamen degeneration and limb dystonia

M. Krygier[1], M. Zawadzka[1], K. Rutkowska[2], J. Sławek[3,4], M. Vernet Machado Bressan Wilke[5], E.W. Klee[5], L.A. Schimmenti[6], R. Płoski[2], M. Mazurkiewicz-Bełdzińska[1]

[1]Medical University of Gdansk, Department of Developmental Neurology, Gdansk, Poland, [2]Medical University of Warsaw, Department of Medical Genetics, Warsaw, Poland, [3]Medical University of Gdansk, Department of Neurological and Psychiatric Nursing, Faculty of Health Sciences, Gdansk, Poland, [4]St Adalbert Hospital, Neurology Department, Gdańsk, Poland, [5]Mayo Clinic, Center for Individualized Medicine, Rochester, United States, [6]Mayo Clinic, Department of Clinical Genomics, Rochester, United States

Background: Leigh syndrome (LS) is a progressive neurodegenerative disease, characterized by extensive clinical, biochemical and genetic heterogeneity. The hallmark of LS is the presence of bilateral symmetric T2-weighted hyperintense basal ganglia and/or brain stem lesions on brain magnetic resonance imaging (MRI). To date, mutations in over 80 genes have been found to cause LS and LS-like phenotypes.
Recently, a novel gene *DNAJC30* was described to be crucial for the efficient repair of mitochondrial complex I subunits. Pathogenic variants in this gene were identified in patients with Leber hereditary optic neuropathy.
Methods: Three individuals from two unrelated Polish families with clinical manifestations of LS underwent extensive clinical, biochemical and molecular investigations. Two siblings, a 16-year-old female and a 11-year-old male presented with gradually progressing hypertonic-hypokinetic syndrome, paroxysmal upper limb dyskinesia and limb dystonia, in the absence of ocular nerve damage. Brain MRI revealed bilateral symmetric necrosis of putamen and nuclei caudate.
The third individual, a nine-year-old boy exhibited progressive gait ataxia, limb dystonia and spastic paraparesis, T2-weighted hiperintense lesions in the putamen, right thalamus and midbrain, and signs of bilateral optic nerve atrophy.
The results of laboratory investigations were suggestive for mitochondrial dysfunction. Whole exome sequencing (WES) was performed to identify the cause of the disease.
Results: In the siblings two *DNAJC30* variants were identified: NM_032317.3: c.152A>G p. (Tyr51Cys) and c.130_131delTC p.(Ser44ValfsTer8) in a compound heterozygous state. The third patient was found to be homozygous for a *DNAJC30* variant NM_032317.3: c.152A>G p.(Tyr51Cys).
Conclusions: According to the literature, there is a strong evidence that biallelic *DNAJC30* variants lead to Leigh-like syndrome in our cases. This indicates that *DNAJC30* mutations cause LS with predominant basal ganglia degeneration and moderate elevation of lactate in peripheral blood and central nervous system. It is important to emphasize that *DNAJC30* alterations should be suspected in patients with LS even without optic nerve involvement.

P 188

Structural Cerebellar Lobules Correlates of Dystonic Head Rotation in Idiopathic Cervical Dystonia

m. Qiu[1], *l. Feng*[1], *l. Jin*[2]

[1]Shanghai Tongji University, Neurotoxin Research center of Key Laboratory of Spine and Spinal Cord Injury Repair and Regeneration of Ministry of Education, Neurological Department of Tongji Hospital, School of Mediceine, Tongji University, Shanghai, China, Shanghai, China, [2]Shanghai Tongji University, Department of Neurology and Neurological Rehabilitation, Shanghai YangZhi Rehabilitation Hospital (Shanghai Sunshine Rehabilitation Center), School of Medicine, Tongji University, Shanghai 201619, China, Shanghai, China

Background: Idiopathic cervical dystonia (ICD) is among the most common types of adult-onset focal dystonia. There is mounting evidence that cerebellar abnormalities may involve in the pathophysiology of dystonia. In this study, we used a novel multi-atlas cerebellar segmentation method to investigate the presence of cerebellar structural modifications in ICD and their clinical relevance.

Methods: Structural MRI scans of 80 patients with ICD and 42 healthy controls were segmented wih automated CEREbellum Segmentation pipeline. Volumetry as well as cortical thickness of the 26 cerebellar lobules were compared between the two groups. Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) was used to assess dystonia severity. Then the correlation between the volume and grey matter volume of cerebellar lobule and the severity of symptoms was studied.

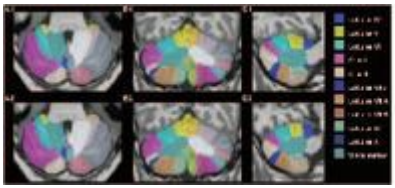


Figure 1. Two representative labeled segmentation of T1-weighted magnetic resonance imaging scans of one 63-year-old healthy man control (A1, B1, C1) and one 60-year-old man with ICD (A2, B2, C2) from our study, as determined by volBrain/CEREbs Segmentation pipeline. A. Axial, B. coronal, and C. sagittal segmented lobules.

Results: ICD patients showed a significantly reduced volume and GM volume of cerebellar lobule V compared to controls ($p = 0.003$ and $p = 0.005$), regardless of the directions of head turned, and lower lobule V volume and GM volume was associated with the presence of ICD (odds ratio = 0.54, $p = 0.003$; odds ratio = 0.5, $p = 0.005$). Multivariate linear regression analysis revealed that both volume and GM volume of cerebellar lobule V were negatively correlated with Torticollis severity scores (odds ratio = 0.932, $p = 0.018$; odds ratio = 0.948, $p = 0.018$).

Conclusions: ICD patients appeared to a reduced grey matter volume of cerebellar lobule V compared with healthy controls, and the degree of volume reduction tended to be positively associated with severity scores of ICD.

Chorea, Athetosis, Ballism, Tics

P 189 (GPT)

Functional chorea diagnosed in a patient with schizophrenia treated with paliperidone: extrapyramidal side effect or functional?

F. Erdogan Kucukdagli[1], *T. Saltoglu*[1], *Y. Sucullu Karadag*[1]
[1]Ankara City Hospital, Department of Neurology, Ankara, Turkey

Background: Functional movement disorders are conditions in which affected patients develop abnormal movements that are incongruous with known, organic, movement disorders, often associated with psychological stressors. Psychogenic choreiform movements and vocal tics are unusual part of the functional movement disorders. The objective of this case report is to highlight this rare condition and the differential diagnosis.
We present a 27-year-old male patient who came to the outpatient clinic due to involuntary choreiform movements of his head, neck and right arm. He was diagnosed with schizophrenia 2 years ago and was on paliperidone treatment for 1 year. He was admitted to the psychiatry inpatient service for a close follow-up. After the patient was evaluated by the Neurology department, other related causes of chorea and tic were investigated in order to make the differential diagnosis.
Methods: The patient was evaluated for neuroacanthocystosis, however no acanthocyte was observed in the peripheral smear and other findings were also inconsistent. Urine copper and serum ceruloplasmin levels revealed no abnormality in terms of Wilson's disease. A series of videos were taken demonstrating the choreiform movements of the patient's head, neck, and right arm, as well as the patient's speech disorder, trembling voice, and later the patient's recovery. The patient's prior written consent to release the videos has been received.
Results: The patient, who was thought to have functional chorea according to both Neurology and Psychiatry evaluations, was followed up with anxiolytic (diazepam) and SSRI (escitalopram). Antipsychotic treatment was changed to aripiprazole. On day 10, involuntary movements were significantly improved.
Conclusions: Functional chorea is a rare and unique disorder as a functional movement disorder. The clinician's experience of recognizing this condition is crucial. Differentiating movement disorders, providing clear explanations and addressing underlying conditions with a multidisciplinary approach are essential to successful treatment, especially in the follow-up of patients receiving antipsychotic treatment.

P 190
Heat-induced tic reduction in Gilles de la Tourette syndrome

A. Durbin[1], *J. Brasic*[1]
[1]Johns Hopkins University, Baltimore, United States

Background: Patients with Gilles de la Tourette syndrome (GTS) may exhibit decrements or increments of tics with heat.
Methods: A 25 year old male presented for evaluation. Since 7 years of age, he experienced motor and phonic tics. At age 23 year, 5 months, he had his baseline evaluation. For the baseline evaluation please refer to Table 1 for objective assessments.
Family history: His mother had TS. His sister has obsessive-compulsive disorder. He is married with one child. At age 3 and a half years, his 5-year-old son began to display motor tics, including eye blinks and simultaneous head movements to the shoulder along with shoulder shrugs, and a phonic tic, exaggerated coughing, similar to the proband.

Axis I Clinical Disorders	**307.23 Tourette's Disorder**	
Axis II Personality Disorders, Mental Retardation	No diagnosis on Axis II	
Axis III General Medical Conditions	Status post concussion	Status post tonsillectomy
Axis IV Psychosocial and Environmental Problems	Occupational problems	Seeking full-time employment
Axis V Global Assessment of Functioning Scale	Current	Highest past year
Possible Range of Scores: 0-100 (higher score indicates better functioning)	81	83

Results:

Instrument	Range of scores	Seven months before remission
Compulsion checklist	(0, 111)	10
Dental pain/fear/anxiety	(0, 112)	4
Dental pain/fear/anxiety Mid	(0, 112)	4
Dental pain/fear/anxiety Post	(0, 112)	1
Dental pain/fear/anxiety 1 months follow-up	(0, 112)	0
Dental pain/fear/anxiety 3 months follow-up	(0, 112)	0
Fear Questionaire	(0, 192)	8
Social Situations Questionnaire	(0, 192)	13
Questionnaire for tic disorders	(0, 23)	21
Tic Symptom Self Report Motor	(0, 60)	24
Tic Symptom Self Report Vocal	(0, 60)	11
University of Miami Modified Maudsley Obsessive-Compulsive Inventory	(0, 60)	11
Wender Utah Rating Scale (WURS) Behaviors	(0, 168)	46
Wender Utah Rating Scale (WURS) Medical problems	(0, 28)	1
Wender Utah Rating Scale (WURS) School	(0, 48)	11
Wender Utah Rating Scale (WURS) Attention-Deficit/Hyperactivity Disorder (ADHD items	(0, 100)	39

Instrument	Range of scores	Six months before remission	One month after remission	Eleven months after remission
Urine drug toxicology for tetrahydrocannabis	Negative or positive	Negative	Positive	Positive
Abnormal Involuntary Movement Scale (AIMS)	(0, 40)	9	0	1
Clinical Global Impression (CGI) Severity Index (SI)	(0, 7)	4 Moderately mentally ill	3 Mildly ill	2 Borderline mentally ill
Clinical Global Impression (CGI) Global Improvement (GI)	(0, 7)	4 No Change	2 Much improved	1 Very much improved
Clinical Global Impression (CGI) Efficacy Index (EI)	(0, 16)	13	5	13
Clinical Global Impression (CGI) Therapeutic effect	Not applicable	Unchanged or worse	Moderate	Unchanged or worse
Clinical Global Impression (CGI) Side effects	Not applicable	None	None	None
Clinical Global Impression (CGI) Attention Deficit Disorder (ADD)	(0,6)	1 Borderline	0	1 Borderline
Clinical Global Impression (CGI) Obsessive-Compulsive disorder (OCD)	(0,6)	3 Moderate	2	2 Mild
Clinical Global Impression (CGI) Tourette syndrome (TS)	(0,6)	3 Moderate	1	1 Borderline
Clinical Global Improvement (CGI) Rater Global Evaluation (RGE)	(1,7)	4 Unchanged	2 Much improved	1 Very much improved
Hillside Akathisia Scale (HAS) Subjective items	(0, 8)	0	0	0
Hillside Akathisia Scale (HAS) Objective items	(0, 12)	6	0	0
Hillside Akathisia Scale (HAS) Clinical Global Impression (CGI) Severity of Akathisia (SA)	(0, 7)	3 Mildly akathisic	11 Normal, not akathisic	1 Normal, not akathisic
Hillside Akathisia Scale (HAS) Clinical Global Impression (CGI) Global Improvement (GI)	(0, 7)	4 No change	1 Very much improved	1 Very much improved
Brief Psychiatric Rating Scale (BPRS) Anchors	(20, 140)	26	21	21
Movement Disorders checklist	(0, 23)	14	8	0
Myoclonus versus tic checklist	(-2, 6)	6	3	0
National Institutes of Mental Health (NIMH) Obsessive-compulsive scale (OCS)	(0, 15)	5	2	1
Rating Scale for Acute Drug-Induced Akathisia (RSADIA) Subjective	(0,9)	0	0	0
Rating Scale for Acute Drug-Induced Akathisia (RSADIA) Objective	(0, 21)	1	0	0
Rating Scale for Acute Drug-Induced Akathisia (RSADIA) Global Rating	(0, 3)	0	0	0
Rating Scale for Drug-Induced Akathisia (RSDIA) Subjective	(0, 6)	0	0	0
Rating Scale for Drug-Induced Akathisia (RSDIA) Objective	(0, 3)	1	0	0
Rating Scale for Drug-Induced Akathisia (RSDIA) Global Clinical Assessment of Akathisia (GCAA)	(0, 5)	1	0	0
Rating Scale for Tardive Dyskinesia (RSTD) Face	(16, 96)	26	17	18
Rating Scale for Tardive Dyskinesia (RSTD) Neck and trunk	(8, 48)	11	8	8
Rating Scale for Tardive Dyskinesia (RSTD) Extremities (upper)	(8, 48)	11	8	8
Rating Scale for Tardive Dyskinesia (RSTD) Extremities (lower)	(8, 48)	8	8	8
Rating Scale for Tardive Dyskinesia (RSTD) Entire body	(4, 24)	4	4	4
Times Stereotypies Rating Scale	(0, 1000)	27	2	1
Tourette Syndrome Diagnostic Confidence Index (TSDCI)	(0, 100)	61	missing	82
Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)	(0, 40)	4	10	4
Obsessive-Compulsive Disorder* through the application of the current criteria[40] to the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)	(0, 1)	0	1	0
Yale Global Tic Severity Scale (YGTSS)	(0, 25)	19	13	12
Yale Global Tic Severity Scale (YGTSS) Phonic	(0, 25)	9	0	11
Yale Global Tic Severity Scale (YGTSS) Impairment	(0, 50)	27	0	9

Conclusions: A 25 year-old man with TS underwent heat-induced dehydration and underwent a profound remission for 2 years. After a tetanus immunization, he had an exacerbation.

P 191 (GPT)

Fingolimod-responsive complex hyperkinetic movement disorder in neuromyelitis optica spectrum disorder

R.E. Cortes[1], *J.A. Vatanagul*[1], *G. Saranza*[2]

[1]Perpetual Succour Hospital of Cebu, Inc., Internal Medicine, Cebu City, Philippines, [2]Chong Hua Hospital, Neurology, Cebu City, Philippines

Background: Neuromyelitis optica spectrum disorder (NMOSD) can present with hyperkinetic movement disorders, such as dystonia, myoclonus, and chorea/ballism. Occasionally, the movements are complex, posing a diagnostic and therapeutic challenge.

Methods: A 57-year-old woman diagnosed with seronegative NMOSD of three years duration presented with involuntary, nonrhythmic, non-suppressible, purposeless movements affecting the right upper extremities, accompanied by weakness, numbness, and impaired proprioception. The hyperkinetic movements were noted more with postural maintenance and varied in speed and amplitude. The movements were seemingly complex and did not meet the classic definition of tremor, myoclonus, chorea, or dystonia.

Results: Cranial MRI and electroencephalogram were unremarkable. Cervical MRI showed an ill-defined hyperintense intramedullary lesion at the level of C1-C6. Given the current extent of the spine lesion, which previously just affected the C1-C2 levels, a relapse of her NMOSD was considered. Initial treatment with anti-epileptic medications, haloperidol, and muscle relaxants did control her abnormal movements. High dose methylprednisolone was given for five days but with no signs of improvement. Second-line therapy with fingolimod for 30 days afforded complete remission of the hyperkinetic movements and sensory loss.

Conclusions: This case report highlights the importance of recognizing movement disorders as a presenting symptom of NMOSD exacerbation. The hyperkinetic movements can be complex and are vaguely termed "spinal movement disorders" associated with NMOSD. Voluntary compensation for weakness and a consequence of sensory deafferentation of proprioceptive feedback are the purported mechanism behind these disabling abnormal movements.

To date, available therapeutic options for these movements are scarce. Herein, we have demonstrated the potential use of fingolimod as a treatment option for movement disorders in NMOSD, stressing the need for immunosuppression when dealing with these involuntary movements.

P 192 (GPT)

Characteristics of tics in follow-up study of community-based high risk cohort of 2511 children

N. Szejko[1,1], P. Macul Ferreira de Barros[2], M. Panczyk[1], P.M. Pan[2], P. Gomez de Alvarenga[2], M. Hoextra[2], K. Timpano[3], J. Leckman[4], E. Miguel[2]

[1]Medical University of Warsaw, Warsaw, Poland, [2]Institute of Psychiatry, Sao Paulo, Brazil, [3]University of Miami, Miami, United States, [4]Yale University, New Haven, United States

Background: Although several studies have aimed to investigate risk factors for occurrence of tics as well as determinants of tic remission or exacerbation, previous findings regarding this research questions were conflicting. Moreover, all of these studies were done in cohort of patients examined in centers specialized in tics and, therefore, in patients with more severe phenotype.

Methods: Our analysis was based on the High-Risk Cohort Study for the Development of Childhood Psychiatric Disorders (HRC). It is an ongoing multicentric follow up study of 2511 children and adolescents who were born between the years of 1998 and 2004, and who live in the cities of Porto Alegre and São Paulo (Brazil).

Results: Our baseline cohort included 2511 participants (1375 males, 54.8%). Lifetime history of tics was reported by 289 participants (1.2%). The mean age of tic onset was 6.83 (3.01 SD). When comparing baseline and follow up data, the incidence of tics decreased from 23.2% to 10.4% (p=0.08), this trend was significant for motor tics (p<0.001). When analyzing variety of prenatal and perinatal factors and their influence on tic persistence lack of parent's support during their offspring's childhood (p=0.012) influenced tic perseverance.

Other factors influencing tic persistence when comparing baseline and follow up assessments were the history of bullying (p=0.035), smoking at very young age (p=0.034), history of behavioral treatment (p=0.038), history of school suspension (p=0.024) and referral to custody council (p=0.040) and higher results in the Dimensional Yale-Brown Obsessive-Compulsive Scale (p=0.025).

Conclusions: To summarize, as expected, the incidence of tics decreased with age. Importantly, several sociopsychological risk factors, such as lack of parent's support, history of bullying or behavioral problems, were found to have impact on tic persistence.

P 193

Klazomania in Gilles de la Tourette syndrome

J. Kaczyńska[1], P. Janik[1]

[1]Medical University of Warsaw, Department of Neurology, Warsaw, Poland

Background: Klazomania is defined as compulsive, paroxysmal, loud shouting and usually recognized as a vocal tic. However, there is no systematic studies on klazomania in GTS. We aimed to assess if clinical associations of klazomania include tic-related variables, or whether its occurrence is associated rather with co-morbid psychiatric disorders.

Methods: We performed a one-time registration study in a cohort of 133 consecutive GTS patients aged 4-50 years (mean age 14.7±8.8; 39 females, 29.3%; 37 adults, 27.8%; mean disease duration 7.5±7.1 years). All patients were personally interviewed and examined.
Results: Klazomania occurred at some point in the lifetime of 31 patients (23.3%) with a mean age of onset of 10.3±4.4 years. Statistical analysis showed a significant correlation between the occurrence of klazomania and Yale Global Tic Severity Scale score (p-value = 0.003) and worst tic severity a patient has ever experienced (p-value = 0.005). There was no significant correlation between the occurrence of klazomania and Attention-Deficit/Hyperactivity Disorder, Obsessive-Compulsive Disorder, Anxiety Disorder, Depression, Autism Spectrum Disorder, Oppositional Defiant Disorder.
Conclusions: Klazomania belongs to the tic spectrum, is fairly common symptom of GTS, and occurs in patients with more severe tics.

P 194
EEG findings in Gilles de la Tourette syndrome

C. Rajczewska-Oleszkiewicz[1], *J. Kaczyńska*[1], *P. Janik*[1]
[1]Medical University of Warsaw, Department of Neurology, Warszawa, Poland

Background: Patients with Gilles de la Tourette Syndrome (GTS) have an 18-fold increased risk of epilepsy. On the other hand, first presentation of tic disorder may mimic epilepsy, especially focal seizures. Epileptiform discharges found on EEG in patients with tic disorders may lead to the unnecessary introduction of antiepileptic medications.
The aim of this work was to show the incidence and characteristics of EEG abnormalities in patients with diagnosed GTS who do not have epilepsy as a comorbidity.
Methods: We analyzed retrospectively the database of 441 patients (330 males, mean age: 16.0±9.5, range 4-66) with GTS who were treated in outpatient clinic Four patients with GTS who had been diagnosed also with epilepsy were excluded from the analysis. EEG recordings were analyzed by clinicians who were licensed in EEG.
Four groups of EEG results were distinguished:
i. normal;
ii. generalized epileptiform discharge (sharp waves, polyspikes, sharp-and-slow wave complex);
iii. focal epileptiform discharge;
iv. abnormal findings without epileptiform discharge (slow waves e.g. theta and delta waves).
The statistical analysis was made in MS Excel.
Results: EEG results were available at evaluation in 34% of patients (n=154), 90 children (up to 11 years old), 37 adolescents (aged 12 to 17) and 27 adults. The abnormal findings were recorded in 44% of individuals (n=67). In 17% (n=26) we observed generalized epileptiform discharge, in 10% (n=15) focal epileptiform discharge, and in 17% (n=26) abnormal EEG without epileptiform discharge.
Conclusions: Nearly half of the GTS patients with no evidence of epilepsy had abnormal EEG and one-fourth showed EEG recordings typical for epilepsy. Clinicians should be aware of these abnormalities in differentiating tics from epileptic seizures.

P 195 (GPT)

Moving toes in 28-year-old woman: a video case report

C. Rajczewska-Oleszkiewicz[1], *P. Janik*[1]
[1]Medical University of Warsaw, Department of Neurology, Warszawa, Poland

Background: Oral contraception [OC], mainly estrogen component but also progesterone, is a known, but a rare cause of drug-induced chorea. These are mainly generalized chorea and hemichorea.
Methods: We present a video case report of a 28-year-old woman with involuntary movements of the toes induced by binary OC.
Results: The patient had hypothyroidism and polycystic ovaries syndrome, but no history of Sydenham's chorea, recent streptococcal infection, chorea gravidarum, systemic lupus erythematosus [SLE] or antiphospholipid syndrome [APS]. She used binary OC for 5 years. The movements started in the form of abduction/adduction/flexion/circumduction of the 5th left toe.
After six months similar movements started in other toes of the same foot, after next five months in the right foot. The medium frequency of the movements was calculated from 1.3 Hz to 2.0 Hz. They lasted for several hours during a day, were present during a sleep, at rest, while holding the legs in mid-air, aggravated by movement and stress, were painless. They were defined as multifocal chorea/choreoathetosis. Head and spinal cord MRI, cerebrospinal fluid, electroneurography, SLE and APS antibodies, serum copper level, ophthalmologic examination were normal.
After withdrawal of OC involuntary movements gradually decreased in the first month till the total disappearance in three months. The choreic movements were reappearing in the case of OC and were not present during the pregnancy and breastfeeding.
We prepared two films presenting the chorea of the toes of both feet at rest/while moving the lower limbs and the disappearance of involuntary movements after the withdrawal of OC.
Conclusions: We show a clear dependence of involuntary movements with hormonal therapy, both progesterone with estrogen and progesterone itself. These symptoms started not until the few years of medication use and had relapsing-remitting course related to OC use. Phenomenology of drug-induced involuntary movements included distal lower limb, multifocal chorea/choreoathetosis.

P 196
Correlation-gender features in patients with Huntington's disease in Uzbekistan

A. Umarov[1], *G. Rahimbaeva*[1], *G. Goyibova*[2]
[1]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan, [2]Tashkent Pediatric Medical Institute, Department of Neurology, Tashkent, Uzbekistan

Background: It is important to assess the epidemiological features of Huntington's disease (HD) according to the Center for Extrapyramidal Pathology and Botulinum Therapy of the Republic of Uzbekistan in the region.
Methods: We examined 44 manifest patients with HD (37 families in total), of which 26 (59%) were female patients and 18 (41%) male patients according to the Center for Extrapyramidal Pathology and Botulinum Therapy of the Republic of Tatarstan. All patients were divided into 3 groups: 1st - general group (44 people), 2nd - female patients (26 people), 3rd - male patients (18 people);
The design of the study included the identification and analysis of clinical data, genealogical and epidemiological information, and laboratory parameters. The clinical condition was determined using the Unified Huntington's Disease Rating Scale (UHDRS) and the TFC (Total functional capacity) scale.
Results: A higher prevalence of HD was found in the northwestern region of the Republic of Uzbekistan and the Fergana valley of the Republic (46% and 32% of the total number of cases, respectively), even taking into account 11.4% of patients after migration from other regions of the Russian Federation.
A weak correlation (-0.29) was found between the age of onset and the number of CAG repeats in male HD patients, i.e., the higher the expansion of trinucleotide repeats, the earlier the onset of the disease. Mental manifestations prevailed in 75% at the onset of HD, regardless of gender and inheritance.
A moderate correlation was found between the severity of motor symptoms and the number of CAG repeats in paternal HD patients (0.35) and a weak correlation of these parameters in female HD patients. There was no significant difference in the severity of clinical manifestations in patients with HD on the paternal and female lines.
Conclusions: A high prevalence of HD is observed in the northwestern and northeastern regions of the Republic of Tajikistan, with a probable phenomenon of anticipation when the disease is inherited from the paternal line.

P 197 (GPT)

Common pitfalls in recognition of an age old malady: edentulous stereotypy

S. Desai[1], *D. Desai*[2]

[1]Shree Krishna Hospital and Pramukhswami Medical College Bhaikaka University, Neurology, Anand, India, [2]Shree Krishna Hospital and Pramukhswami Medical College Bhaikaka University, Medicine, Anand, India

Background: Different oro-mandibular dyskinesias can often afflict elderly patients. Edentulous stereotypy is well-characterized abnormal movement of the jaw and mouth, which occur in elderly edentulous persons. Though quite common, they are often associated with pitfalls in recognition and management.

Methods: In this descriptive study, we collected series of patients with edentulous stereotypy in which there were pitfalls in recognition leading to inappropriate investigations and management prior to reference to us. We collected series of cases between Jan 2010 to Dec 2021, who presented with edentulous stereotypy. We analyzed the cases where a pitfall in recognition and/or management had happened.

Results: Amongst the 27 patients with edentulous stereotypy [ES] seen during this period, 11 were referred to us as oromandibular dystonia [OMD], 5 referred as functional disorder, 7 were referred to as focal seizures, 2 were referred to as Parkinson's disease and 2 were referred to as autoimmune encephalitis.

The patients had received initial consultation by general physician [15], psychiatrist [7] , general neurologist [5]. The major pitfall for the consideration of OMD was the intermittent movement of jaw. The reason for the pitfall was that the detailed history and examination was not done.

The important features of ES which were missed were: absence of tongue movements, movement occurring only in edentulous patients, having a poor denture satisfaction index, the movement being only "unvoluntary" [occurring passively when patient not paying attention, which is very much controllable by the patient, and the control not causing any sensory "discomfort"]. 8 of the patients misdiagnosed as OMD prior to our consultation were prescribed tetrabenazine, clonazepam, haloperidol, leading to adverse events like somnolence, confusion and imbalance.

The patients misdiagnosed as focal seizures also were treated with anti seizure medicines, with adverse events without benefit. All the patients did not have a major discomfort due to movements, rather their relatives had consulted doctors for the abnormal movement.

All the patients improved with stopping the unneeded medicines, counselling about the diagnosis, lifestyle management like sugar candy or dry berry sucking or wearing proper dentures. 11 of the patients could not adjust to 2 trials of different denture sets and were happy without any dentures and could learn to control the stereotypy voluntarily.

Conclusions: It is important that physicians and neurologists are well aware of the diagnosis and recognition of edentulous stereotypy in order to avoid common pitfalls in its recognition and management.

P 198

Early onset hemichorea-parkinsonism with POLG mutation without external ophthalmoplegia responsive to pallidal DBS

F. Garrì[1], D. Calandrella[1], F. Del Sorbo[2], G. Sacilotto[2], M. Zini[2], C. Bolliri[1], V. Cereda[1], V. Ferri[1], M. Barichella[1,2], G. Pezzoli[1]

[1]Fondazione Grigioni per il Morbo di Parkinson, Milan, Italy, [2]Parkinson Institute, ASST G. Pini-CTO, Milan, Italy

Background: POLG gene have been associated with a wide phenotypic spectrum, including parkinsonism, usually in combination with external ophthalmoplegia. We present a case of subacute onset of left hemichorea-parkinsonism with POLG mutation without external ophthalmoplegia, successfully treated with DBS.

Methods: Case report.

Results: A previously healthy 36-year-old female presented subacute involuntary movements in the left upper limb and, to a lesser extent, in the lower limb and mouth, associated with left mild parkinsonism. Her family history was notable for severe depression. All possible causes of acute/subacute hemichorea, including infectious, paraneoplastic, autoimmune, metabolic, toxic and vascular etiology have been excluded. Brain-MRI showed a significant atrophy in the right striatum. DaTSCAN showed asymmetric striatal hypocaptation, mainly in the right.

Genetic panel for Huntington-Disease (HD) and HD-like syndromes resulted negative, while panel for Parkinson disease showed two mutations in POLG gene: c.2492 A>G (p.Y831C) and c.3708G>T (p.Q1236H), former associated with ophthalmoplegia. Dopaminergic and tetrabenazine treatment were ineffective.

At the age of 38, she underwent right Gpi-DBS with immediate improvement and sustained long-term benefit (4 years-follow-up). After 4 years the patient underwent a sudden clinical worsening with reappearance of left hemichorea due to battery failure, promptly managed with battery replacement.

Repeated DaTSCAN confirmed the bilateral striatal hypocaptation showing a slight increase in tracer uptake in the left caudate and striatum overall.

Conclusions: We described a patient with POLG mutation presenting with a subacute onset of left hemichorea-parkinsonism without external ophthalmoplegia, completely responsive to DBS. Changes in DaTSCAN imaging after DBS remain elusive. We should be aware of recent advances in genetics which have made increasingly common to find genes not always easily interpretable in clinical context, especially in the field of Movement Disorders.

P 200

Study of the difficulties of late diagnostics in patients with Huntington's disease in Uzbekistan

A. Ismatov[1], *D. Tolibov*[1], *A. Umarov*[1]
[1]Tashkent Medical Academy, Neurology, Tashkent, Uzbekistan

Background: To identify the causes that lead to late diagnosis of Huntington's disease.
Methods: To this study was included 17 patients with a confirmed molecular genetic diagnosis, followed up with us from 2019 to the present.
Results: According to our observations, the disease often debuts with mental disorders (3 families), and therefore these patients are observed in psychiatric hospitals and examined by neurologists and geneticists out of time or do not receive consultations from these specialists at all. We have described a patient with Huntington's disease, in whom the disease debuted with cranial dystonia.
In 2 families, the debut of the disease in the son is observed earlier (at the age of 35 years) and more severe than in the father (at the age of over 70 years) - the phenomenon of anticipation. An allele with incomplete penetrance (36–38 repeats) was identified in 2 families.
Conclusions: The main reasons leading to late diagnosis of Huntington's disease are identified:
1. The possibility of disease manifestation with cranial dystonia or other atypical neurological symptoms;
2. The presence in the population of alleles with incomplete penetrance, which complicates the early diagnosis of the disease due to the frequent absence of a family history, in some cases - the minimum severity of choreic hyperkinesis and intact intelligence;
3. The phenomenon of anticipation, leading to diagnostic errors, since the disease debuts in parents later than in children, and has an erased clinic;
4. Manifestation of the disease with mental disorders and frequent cases of suicide in the family before the start of a typical clinic, which leads to long-term observation by psychiatrists.

P 201
"Levine-Critchley syndrome" - obsolete

A. Danek[1], N. Krstić[2], M.T. Hayes[3], R.C. Green[3], C. Westhoff[4], S. Vege[4], R.H. Walker[5]
[1]Ludwig-Maximilians-Universität, Munich, Germany, [2]USF Health-Morsani College of Medicine, Tampa, United States, [3]Harvard Medical School, Boston, United States, [4]New York Blood Center, New York, United States, [5]Mount Sinai School of Medicine, New York, United States

Background: In the 1960s, families of patients with neurological features and red blood cell acanthocytosis in the absence of lipoprotein abnormalities were described independently by Irving Levine and Edmund Critchley (PMID 5677189; 5636069). The condition was later summarized under their names (OMIM #200150), alternatively as "neuroacanthocytosis", "chorea-acanthocytosis/choreoacanthocytosis", "familial tic disorder, parkinsonism, motor neuron disease, and acanthocytosis" and "amyotrophic chorea with acanthocytosis". In 2011, we showed that Critchley´s original family from Kentucky was affected by mutations in the autosomal VPS13A gene (PMID 21987550).
Methods: DNA from the asymptomatic daughter of Levine´s index case (one of a pair of brothers) was analysed.
Results: We confirmed the presence of a mutation in X-chromosomal gene XK, that was previously found in a distant, asymptomatic female relative who had contacted us for advice on her family´s condition.
Conclusions: We conclude that the term "Levine-Critchley syndrome" applies to genetically diverse conditions and is no longer of medical value. It must be replaced by proper molecular diagnoses of "VPS13A disease" or "XK disease", respectively. It is not surprising that the similarity (and thus confusion) of these ultra-rare syndromes results from molecular interaction of the two respective proteins (PMID 32845802). Clinically, the distinct genetic conditions may be distinguished on the basis of Kell blood group typing (McLeod phenotype in XK disease), heart exam (XK: severe involvement), recessive (VPS13A) or X-linked (XK) inheritance, and less so on different ages of onset (VPS13A: young adult males and females, often siblings; XK: elderly males, often brothers or nephew-uncle pairs, but only exceptionally manifesting in females).

Ataxias, hereditary spastic paraparesis

P 202
Late-onset cerebellar ataxia: case report of a new CNV on *TTBK2* gene as possible cause of SCA-11

I. Rodriguez[1], *A. Bochm*[2], *E. Davila*[2], *D. Martinez*[1]
[1]Instituto Tecnologico y de Estudios Superiores de Monterrey, Neurología, Monterrey, Mexico, [2]Instituto Tecnologico y de Estudios Superiores de Monterrey, Escuela de Medicina, Monterrey, Mexico

Background: The spinocerebellar ataxias (SCAs) are a group of neurodegenerative diseases that affect not only the cerebellum but also other nervous system structures such as brainstem, spinal cord, or peripheral nerves. According to Harding's classification, SCAs are classified into three types. Type 3 of SCAs include pure autosomal dominant cerebellar ataxias, the most common group of inherited ataxias.
However, in some cases, this type of pure ataxia could coexist with other clinical signs such as tremors, abnormal eye movements, or pyramidal signs. The main cause is a trinucleotide expansion which encodes polyglutamine proteins; however, others can be caused by missense mutations or small insertion/deletion variants. SCA-11 is included in type 3 of SCAs and accounts for less than 1% of autosomal dominant ataxia in Europe. The pathogenic variant involved, is the *TTBK2 g*ene.
Methods: We present a case of an adult patient with a SCA, followed by a genetic analysis.
Results: A 68-year-old woman presented with a 10-year history of imbalance and abnormal gait. The patient was previously healthy, and her medical and familiar history was irrelevant. On the physical exam, she showed signs of cerebellar ataxia and hyperreflexia in lower extremities.
An approach to exclude acquired causes of cerebellar ataxia was performed, including complete serum blood count, metabolic panel, liver function test, thyroid function tests, vitamin B12 and B1, anti-GAD, antigliadin, anti-endomysial and anti-transglutaminase antibodies, autoimmune panel, all of them without any abnormality. The brain MRI showed brainstem and cerebellar atrophy. Exome sequencing, copy number variants, and mitochondrial genome tests were performed. A copy number variant 43008859_43075833 on the *TKKB2* gene was detected on chromosome 15 in the genomic location of GRCh37.
Conclusions: We report a case of a copy of number variant not previously reported as pathogenic on *TKKB2* gene that can be the cause of spinocerebellar ataxia in our patient.

P 203

Spastic ataxic phenotype of Fatty acid 2-hydroxylase associated neurodegeneration: a case series from India

V.V Holla[1], *N. Sriram*[1], *R. Kumari*[2], *N. Kamble*[1], *R. Yadav*[1], *B. Muthusamy*[2], *P.K. Pal*[1]
[1]National Institute of Mental Health and Neurosciences, Neurology, Bengaluru, India, [2]Institute of Bioinformatics, Bengaluru, India

Background: Fatty acyl 2-hydroxylase (FA2H) neurodegeneration (FAHN) is a type of neurodegeneration with brain iron accumulation (NBIA) that presents with pyramidal, extrapyramidal, cerebellar features and cognitive decline and seizures in later stage. White matter hyperintensity, Hypointense globus pallidi interna, Atrophy of cerebellum and Thin corpus callosum ("WHAT" acronym) is commonly observed radiologically. This study aims to describe clinical, radiological and genetic profile of five cases of hereditary spastic paraplegic (SPG35) presentation of FAHN.
Methods: A retrospective chart review.
Results: Five cases (4 females) with median age at onset of 5 years (range: 4-10 years) and median age at presentation of 10 years (range: 7-29 years) were studied. While 4 had consanguineous parentage, none had positive family history. Walking difficulty (5/5) was the most common presenting symptom with additional dysarthria seen in 4 cases. Spasticity with normal power, brisk reflexes, extensor plantar and normal sensation was seen in all with cerebellar signs in 3 patients.
In addition, 2 patients had mild optic atrophy, and one patient had dystonia. Only one patient was wheel chair bound at the time of presentation. Visual evoked potential was prolonged in the two patients with optic atrophy. MRI Brain revealed callosal atrophy, cerebellar atrophy, periventricular hyperintensity in all and optic atrophy in four cases. GPi mineralization was seen in only 3 cases.
Clinical exome sequencing revealed a different homozygous pathogenic/likely pathogenic variants in *FA2H* in all 5 cases of which four were previously unreported (c.200_202del;p.His67del, c.130C>A;p.Pro44Thr, c.536delT;p.Leu79ArgfsTer62, c.83G>C;p.Arg28Pro) and one previously reported (c.379C>T;p.Ar127Ter). All patients were managed with anti spastic medication and physiotherapy.
Conclusions: FAHN should be considered in cases of pediatric onset progressive spastic paraplegia with or without ataxia. Despite being a type of NBIA, mineralization is not universal. Cerebellar, callosal, optic atrophy with periventricular white matter hyperintensity are the other classical MRI features.

P 204

A Swedish SCA34 family with late onset ataxia, cerebellar atrophy and ocular movement abnormalities with a novel mutation in *ELOVL4*

S. Dobloug[1], *S. Gorcenco*[2], *H. Ehrencrona*[3], *A. Puschmann*[2]

[1]Helsingborg General Hospital, Department of Neurology, Helsingborg, Sweden, [2]Lund University, Skane University Hospital, Department of Neurology, Lund, Sweden, [3]Lund University, Skane University Hospital, Department of Clinical Genetics, Lund, Sweden

Background: To investigate the clinical and radiological presentation of a new *ELOVL4* mutation in a Swedish family.

Methods: We compiled information on a Swedish family with 6 affected members. Four of these had undergone neurological and radiological examinations. Two patients were independently analysed genetically by whole exome or whole genome sequencing.

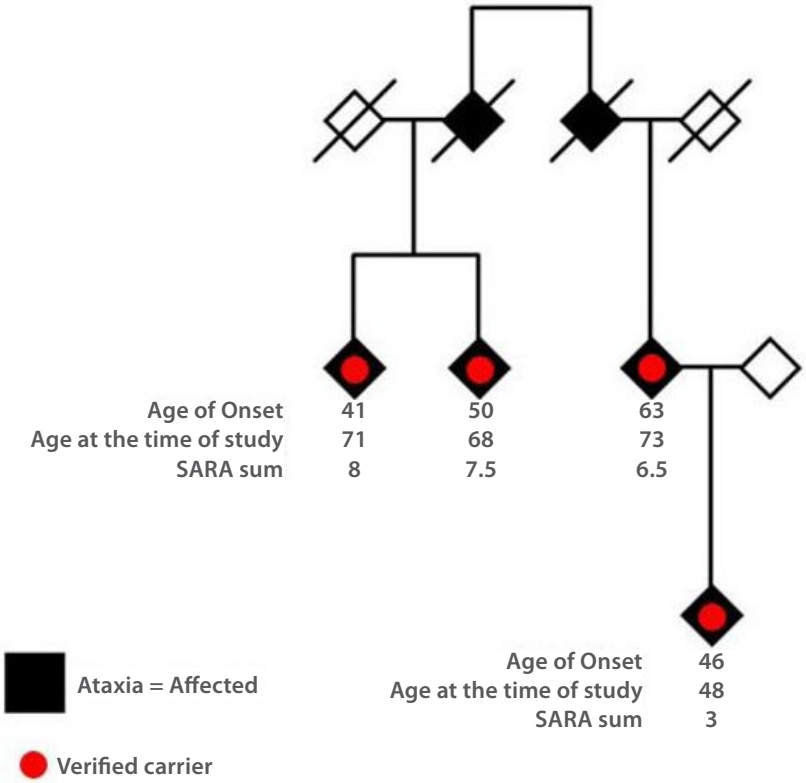


Figure.

Results: All examined affected family members showed slowly progressive cerebellar ataxia with balance impairment starting at between 42 and 70 years, ocular movement disturbances with nystagmus, hypermetric saccades or vertical gaze palsy, and cerebellar atrophy on imaging. None of the affected family members had erytrokeratodermia variabilis, but three had dry skin or psoriasis. Two members had seizures, one had intermittent muscular cramps. One deceased obligate carrier had dementia and one of the members examined had mild cognitive dysfunction (MMSE 23/30). One individual had poor night vision. One individual had a diagnosis of schizophrenia since age 25 years.
We identified a novel heterozygous variant *ELOVL4* c.511A>C, p.(Ile171Leu) (NM_022726.4) in affected individuals. When this was discovered in the first family member it was reported as a variant of uncertain significance (VUS). However, after segregation analysis and detailed clinical information for the entire family, the variant could be reclassified as likely pathogenic according to the ACMG classification system (PMID: 25741868) and Jarvik et al (PMID: 27236918).
Conclusions: So far, including the present report, eight different *ELOVL4* variants have been described in SCA34 patients. Our examinations provide additional knowledge to the presentation of this rare neurodegenerative disorder.

P 206 (GPT)
A comprehensive study of the association between autonomic and clinical severity in spinocerebellar ataxia type 3 patients

D. Tamuli[1], *K.K. Deepak*[2], *A.K. Srivastava*[3]
[1]Nalbari College, Zoology, Nalbari, India, [2]All India Institute of Medical Sciences, Physiology, New Delhi, India, [3]All India Institute of Medical Sciences, Neurology, New Delhi, India

Background: Spinocerebellar ataxia (SCA) type 3 is a neurodegenerative disorder characterized by autonomic abnormalities. There is paucity of literature for quantification of autonomic failure and then correlates with clinical severity in SCA3. Therefore, we evaluated the correlation between autonomic severity and clinical scoring in SCA3 patients.
Methods: For the assessment of autonomic function, continuous HR and BP were recorded in genetically confirmed SCA3 (n=9, age=37.11±9.21 years) patients. Autonomic reactivity tests were performed and analyzed using composite autonomic severity score (CASS). CASS ranges from 0 to 10 and constitutes of sudomotor (0–3), cardiovagal (0–3), and adrenergic (0–4) subscores. The analysis of CASS was done by MATLAB (R2015a). Additionally, the International Cooperative Ataxia Rating Scale (ICARS) was used for measuring clinical severity in SCA3 patients.
Results: The autonomic abnormality was found in SCA3 patients as quantified by CASS, the value was 4 (3 - 4). On the frequency analysis, 55.55% (5/9) autonomic failure was moderate while 44.44% (4/9) was mild in the patients of SCA3. The clinical severity score of SCA3 patients was 21.33 ± 10.06, assessed by ICARS. Correlation analysis showed a significant association between ICARS and CASS (0.730, p=0.025).
Conclusions: There is autonomic dysfunction in SCA3 patients. However, a characteristic association is found between autonomic severity and clinical scoring in SCA3 patients. This may help in clinico-physiological insight.

P 207

Prevalence and clinical correlations of Non-Motor Symptoms in patients with Ataxia: Study in a cohort of Mexican patients

H. Pacheco[1], *H.R. Martinez Hernandez*[2]

[1]Universidad Nacional Autonoma de Mexico, Mexico City, Mexico, [2]Instituto Nacional de Neurologia y Neurocirugia, Mexico City, Mexico

Background: Ataxias are neurological conditions related to alterations in motor coordination and are a heterogeneous group of diseases. They are divided into sporadic, idiopathic or hereditary and can present from childhood to adult life, with a variable clinical course with insidious onset, where symptoms develop slowly, progressively and chronically; or may have an acute onset with rapid progression. Clinical manifestations vary from oculomotor, vestibular, speech alterations, dysmetria and dysdiadochokinesia of the extremities with loss of manual dexterity and coordination, truncal ataxia, alteration in balance and gait. Many aetiologies include the presence of non-motor symptoms such as dysautonomia, affective, cognitive or sleep symptoms.

Methods: Descriptive and retrospective study of a cohort of 130 consecutive patients from the Parkinsons Disease and Movement Disorders Clinic of the National Institute of Neurology and Neurosurgery in Mexico between 2014 and 2020. As part of their initial clinical evaluation, scales for ataxia (SARA and ICARS) and for non-motor symptoms (NMSS). For the statistical analysis, variables were classified according to their distribution. Frequency tables and central dispersion means were used for descriptive analysis and a correlation between motor and non-motor symptoms was performed using Pearson's and ANOVA tests for comparison between groups for continuous variables.

Results: 130 individuals with a mean age of 39.4 ± 14.8 years with different diagnoses were included. We found differences in the diagnosis and the total score on the non-motor symptom scale (NMSS). Tests performed (Pearson's r), found a correlation between the non-motor symptom scale (NMSS) and the age of onset r=0.076 (p=0.391), the duration of the disease r=-0.058 (p= 0.511) and the severity of motor symptoms measured by ICARS r=0.075 (p=0.419), or by SARA scale r=0.075 (p=0.322).

Comparing the different diagnosis groups with the ANOVA test, we observed significant differences between the diagnosis groups, onset age (F 4.823, p=0.000) and total result of the NMSS scale for non-motor symptoms (F=1.952, p=0.045). We found no differences in the disease duration and the total scores of the motor scales.

Conclusions: Presence of non-motor symptoms in ataxias differs in the etiological groups. This is the first study that uses a validated instrument to measure non-motor symptoms in ataxias. Although we didn't found a correlation between severity and non-motor symptoms in ataxia; we observed significant differences between the diagnostic groups and severity of non-motor symptoms. These results allow us to consider the recognition and measurement of non-motor symptoms play a role in the diagnosis of this complex group of patients.

Tremors, Myoclonus

P 208 (GPT)
Prevalence of essential tremor in rural Gujarat, India

S. Desai[1], *A. Chin*[2], *S. Raithatha*[3], *S. Roy*[4], *U. Shah*[3], *D. Desai*[5], *A. Deb*[2]
[1]Shree Krishna Hospital and Pramukhswami Medical College Bhaikaka University, Neurology, Anand, India, [2]University Massachusets Chen Medical School, Neurology, Worcester, United States, [3]Shree Krishna Hospital and Pramukhswami Medical College Bhaikaka University, Community Medicine, Anand, India, [4]Shree Krishna Hospital and Pramukhswami Medical College Bhaikaka University, Central Research, Anand, India, [5]Shree Krishna Hospital and Pramukhswami Medical College Bhaikaka University, Medicine, Anand, India

Background: Worldwide prevalence of essential tremor (ET) ranges from 0.4-8.6%, affecting about 1% of the general population and 4-5% of individuals over 65 years old. However, studies estimating prevalence of ET are few, with no previous studies amongst rural Indian communities. India's diverse population makes data extrapolation inaccurate, presenting a need for population-based surveys. Here, we assess the prevalence of ET in 10 selected villages of Anand district in rural Gujarat, India.
Methods: We utilized a pre-validated modified screening questionnaire for parkinsonism and movement disorders, including ET. Participants who screened positive underwent videography and a detailed clinical examination by a neurologist to confirm the ET diagnosis based on the 2018 MDS Tremor Task Force criteria.
Results: Of 18,896 individuals screened, 54 participants screened positive and underwent formal neurologic evaluation; 17 were diagnosed with ET. The crude prevalence of ET was calculated as 89.96 per 100,000 (0.09%), based on 2018 MDS criteria gathered from survey screening, video recordings and clinical evaluation.
Conclusions: Our study demonstrates a crude prevalence rate of 0.09%, low in comparison to other ET prevalence studies. One reason may be utilization of the updated criteria to diagnose ET and excluding patients with ET plus syndromes.
This study is the only prevalence assessment conducted in a villagebased Indian population. Further studies of prevalence utilizing the MDS diagnostic criteria will help improve awareness, diagnosis, and treatment of ET for the rural Indian population and generate more understanding of ET prevalence throughout India and globally.

P 209

Clinical tremor-study with gender features in patients with essential tremor in Uzbekistan

G. Goyibova[1], *A. Umarov*[2], *A. Ismatov*[2], *D. Tolibov*[2]

[1]Tashkent Pediatric Medical Institute, Department of Neurology, Tashkent, Uzbekistan, [2]Tashkent Medical Academy, Department of Neurology, Tashkent, Uzbekistan

Background: During the diagnosis of essential tremor (ET), it is important to follow strict criteria of inclusion and exception to exclude a reasonable number of neurodegenerative diseases and metabolic disorders that have similar symptoms. We investigated the clinical features of ET in patients from the region of Uzbekistan admitted to the neurology center with long-term complaints of tremor.

Methods: This study was included 32 patients with a verified diagnosis of ET.

Results: By gender, there was a predominance of females: 65.6% (21 people) versus 34.4% (11 people) of males. The mean age of patients with ET was 67.3 ± 1.83 years (range 43 to 85 years). The distribution of patients by age groups showed that the largest number of them falls on the age group of 70-79 years (12 people, 37.5%) and the group of 60-69 years (9 people, 28.1%).

According to the time of manifestation of symptoms, 43.8% (14 people) of patients had a late onset of the disease (over 60 years), 28.1% (9 people) of patients had an early onset (at 20-30 years). In 62.5% (20 people), a combination of postural-kinetic tremor with head tremor was detected; in 12.5% of patients (4 people) - isolated postural hand tremor; isolated head tremor of the "no-no" or "yes-yes" type was observed in 21.9% of patients (7 people); rest tremor was noted in 1 (3.1%) patient. Medium-amplitude tremor was detected in 68.8% (in 22 people), large-amplitude - in 3.1% (in 1 person), small-amplitude - in 28.1% (in 9 people) of cases.

Conclusions: During the analyzing ET cases, it was revealed that female patients predominate among patients, the largest number of patients falls in the age group of 60-79 years. The clinical picture of patients corresponds to the classical phenotype, the severity and amplitude of tremor, mean-amplitude tremor was much more pronounced in patients with ET.

Gait Disturbances and Other Movement Disorders

P 210
Pain reduction in adult patients with limb spasticity following single incobotulinumtoxinA injection: analysis of pooled data from phase 2/3 studies

J. Wissel[1], *A. Camões-Barbosa*[2], *G. Comes*[3], *M. Althaus*[3], *A. Scheschonka*[3], *D.M. Simpson*[4]
[1]Vivantes Hospital Spandau, Department of Neurorehabilitation and Physical Therapy, Berlin, Germany, [2]Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal, [3]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [4]Icahn School of Medicine at Mount Sinai, New York, United States

Background: IncobotulinumtoxinA (incoA) has shown pain-relieving benefits in patients (pts) with limb spasticity in individual studies; data from sizeable pt cohorts are lacking. Pain relief in a large cohort of incoA-treated pts with spasticity-associated pain (SAP) using pooled data from mostly placebo-controlled phase 2/3 studies was assessed.
Methods: Pain severity was assessed with the Disability Assessment Scale (DAS; 0–3) in adults with upper limb SAP. A ≥1 point reduction in the DAS pain score from baseline [BL] to 4 weeks was defined as response. Between-treatment group response rates (overall and by BL pain severity – DAS mild, moderate, severe) and the proportion of pts with complete pain relief (DAS pain score=0) at 4 weeks after 1 injection of incoA or placebo were analyzed using χ^2 test. Overall between-group response rate differences were analyzed using logistic regression (presented as odds ratio [OR] and 95% confidence interval [CI]).
Results: 544 (incoA: 415, placebo: 129) pts reported SAP at BL. At 4 weeks, a significantly higher proportion of incoA- vs placebo-treated pts achieved a response (52.1% vs 28.7%; p<0.0001). IncoA-treated pts were more likely to achieve pain response vs placebo-treated pts (OR 2.6 [95% CI:1.6–4.2]; p<0.0001). Irrespective of BL pain severity, significantly higher response rates were observed with incoA vs placebo at 4 weeks (p<0.02 all comparisons). Complete pain relief was achieved by significantly more incoA- vs placebo-treated pts at 4 weeks (27.1% vs 12.4%; p=0.0006).
Conclusions: Pts receiving incoA vs placebo are significantly, by 2.6 times, more likely to achieve reduced upper limb SAP, irrespective of baseline pain severity, at 4 weeks post-injection thus supporting use of incoA in this setting.

P 211

The need to include functional movement disorders in the differential diagnosis of children presenting to emergency departments

J. Brasic[1]

[1]Johns Hopkins University School of Medicine, The Russell H. Morgan Department of Radiology and Radiological Science, Baltimore, United States

Background: Providers in emergency departments can be challenged by the captious presentation of a child with movements suggesting neurological disorders without a source for history and other information. While providers may experience a sense of urgency to administer diagnostic and therapeutic interventions with serious potential adverse effects, caution is desirable before making major decisions about the optimal course of action.

We report a case to demonstrate that the possible presence of functional neurological symptom disorder (conversion disorder) merits consideration by providers when facing uncertain movements in girls with a history of physical and sexual abuse and a family history of functional neurological symptom disorders.

Methods: A five-year-old girl was shot in her left arm and her chest by an unknown assailant. After a delay of four hours she was taken to an emergency room where she was admitted for a thoracotomy. She then experience nightmares about strangers.

The day before her ninth birthday she was taken to an emergency room with the chief complaint of "I can't hear or see" for the past day.

Results: On examination she shook hands with the examiner, maintained eye contact, and responded to questions despite the din of the environment. She underwent regular outpatient psychotherapy sessions and regained function with encouragement by her providers, teacher, and parents. A few weeks later she was raped on the school bus. When she presented to an emergency room with mouth movements, neck twisting, and frothing followed by confusion, she was begun on phenobarbital 100 mg by mouth twice daily. Her mother had been treated with phenobarbital for a seizure disorder beginning at age 13 that suddenly resolved after a religious experience at age 23.

Conclusions: Children with family histories of functional neurological symptom disorders who experience physical and sexual abuse and neglect are vulnerable to develop functional movement disorders.

P 212
Predictors of early neurological deterioration in Wilson's disease

T. Litwin[1], T. Ziemssen[2], K. Akgun[2], A. Członkowska[1], A. Antos[1], J. Bembenek[3], A. Przybyłkowski[4], M. Skowrońska[1], Ł. Smoliński[1], I. Kurkowska-Jastrzębska[1]

[1]Institute Psychiatry and Neurology, 2nd Department of Neurology, Warsaw, Poland, [2]University Clinic Carl Gustav Carus & Dresden University of Technology, Center of Clinical Neuroscience, Department of Neurology, Dresden, Germany, [3]Institute Psychiatry and Neurology, Department of Neurophysiology, Warsaw, Poland, [4]Medical University of Warsaw, Department of Gastroenterology and Internal Medicine, Warsaw, Poland

Background: Early neurological deterioration in Wilson's disease (WD) after treatment initiation is still one of the main challenges of WD treatment and often predicts its outcome. The available evidence on this phenomenon is conflicting, with a lack of reliable biomarkers. The aim of our study was to investigate risk factors of early neurological deterioration in WD.

Methods: We analyzed 61 drug-naive patients with WD diagnosed between 2017 and 2021. An early neurological deterioration was ascertained based on the change in the Unified Wilson's Disease Rating Scale (UWDRS) scores from baseline to 6 months later. The baseline laboratory (including serum neurofilament light chain (sNfl) concentrations), clinical (UWDRS scores) and neuroradiological variables, duration of disease and kind of treatment were analyzed as a potential risk factors.

Results: Early neurological deterioration was observed in 16.3% (10/61) of patients. Baseline sNfL concentrations were significantly greater in patients who deteriorated (33.2±23.5 pg/mL) than in those who did not (27.6±62.7 pg/mL; $p<0.01$).

Additionally, patients who deteriorated had a more severe baseline neurological impairment scored on UWDRS parts II and III (part II, 4.3±5.0 vs. 2.0±5.9, $p<0.05$; part III, 21.5±14.1 vs. 9.3±16.4, $p<0.01$) and a greater baseline brain injury scored on a semiquantitative MRI scale in total brain MRI score (6.5±4.3 vs. 3.0±4.1, $p<0.01$). Disease duration, type of treatment, and baseline copper metabolism had no impact on early neurological deterioration.

Conclusions: sNf, neurological deficits scored in UWDRS and brain MRI abnormalities scored on a semiquantitative scale could be used as complementary predictors of early neurological deterioration in WD. These measures could pinpoint patients with WD at risk of deterioration who should be observed and treated more carefully.

P 213
Refractory progressive catatonia in autism spectrum disorder

J. Brasic[1]
[1]Johns Hopkins University School of Medicine, The Russell H. Morgan Department of Radiology and Radiological Science, Baltimore, United States

Background: People with autism spectrum disorder (ASD) and other neurodevelopmental disorders may develop catatonia that is refractory to benzodiazepines and electroconvulsive treatments and benefit from the application of precision medicine to create an optimal treatment plan.
Methods: In childhood a boy exhibited difficulties of communication and speech and an unusual scope of interests in childhood.
At 13, he stopped talking after his teacher told him that he would not be promoted from eighth grade.
At 14 his performance intelligence quotient was 63. He was treated with 1 mg benztropine mesylate twice daily and 1 mg haloperidol each morning and 3 mg at bedtime for a month. The medications were discontinued due to lack of improvement.
At 45 he required assistance with activities of daily living.
Results:

Age									
Years	16	17	17	17	17	18	18	19	19
Months	8	4	8	8.5	10	3	7	1	2
Medications	None	None	None	None	D	A, D	D	D	D
General dyskinesias - Abnormal Involuntary Movement Scale									
	1	17	15	16	8	13	13	19	19
TDRS Face	20	21	31	28	27	28	31	27	28
TDRS Neck & Trunk	8	8	11	11	8	11	14	17	13
TDRS Upper extemity	8	8	13	14	8	8	8	8	8
TDRS Lower extemity	8	8	8	8	8	8	8	8	8
TDRS Entire Body	4	4	4	4	4	4	4	4	4
TDRS Total	48	49	67	65	55	59	65	64	61
Akathisia - Hillside Akathisia Scale									
OI	0	0	0	0	0	0	0	0	0
CGISA	1	1	1	1	1	1	1	1	1
CGIGI	3	4	4	5	4	4	4	5	5
Parkinsonism									
UPDRS MBM	3	4	4	4	4	4	4	4	4
UPDRS Activities of Daily Living	5	6	10	6	16	21	19	17	14
UPDRS Motor examination	13	11	11	20	21	22	22	21	17
UPDRS Complications of Therapy	0	0	0	0	0	0	0	0	0
UPDRS MHYS	0	0	0	0	0	0	0	0	0
UPDRS SEADLS	76%	71%	71%	56%	10%	11%	10%	16%	19%
UPDRS Total	21	21	25	30	41	47	45	42	35

Figure 1. Movement ratings of a man with refractory progressive catatonia and autism spectrum disorder

Stereotypes - Timed Stereotypes Rating Scale									
31	20	50	51	40	81	44	60	59	
Tics - TSCGIS									
0	3	3	3	3	3	3	4	4	
Yale Global Tic Severity Scale									
8	13	16	13	14	14	14	16	20	
General psychiatric symptomatology - Brief Psychiatric Rating Scale									
22	25	29	27	31	26	27	28	29	
BPRSC									
22	20	30	33	30	30	33	32	35	
Children's Psychiatric Rating Scale A									
32	41	44	57	47	53	50	50	52	
Children's Psychiatric Rating Scale B									
9	6	12	12	11	9	10	10	18	
Children's Psychiatric Rating Scale Total									
41	47	56	69	58	62	60	60	70	
Overall psychiatric functioning Children's Global Assessment Scale*									
42	36	31	28	9	9	9	9	14	
CGIRGE									
4	4	5	6	4	4	4	6	6	
CGI Severity of Illness									
6	6	6	6	6	6	6	6	6	
CGIGI									
4	5	5	5	4	4	4	6	6	
CGI Efficacy Index									
13	13	13	13	13	13	13	13	13	

A 250 mg amoxicillin by mouth daily
D 240 mg diltiazem by mouth daily
ADDCGIS Attention Deficit Disorder Clinical Global Impression Scale
BPRSC Brief Psychiatric Rating Scale for Children
CGIRGE Clinical Global Improvement Rater Global Evaluation
CGISA Clinical Global Impression Severity of Akathisia
CGI Clinical Global Impressions

CGIGI Clinical Global Impression(s), Global Improvement
MBM Mentation, Behaviour and Mood
MHYS Modified Hoehn and Yahr Staging

OCDCGIS Obsessive Compulsive Disorder Clinical Global Impression Scale
OI Objective Items
SEADLS Schwab and England Activities of Daily Living Scale
TDRS Tardive Dyskinesia Rating Scale
TSCGIS Tourette Syndrome Clinical GLobal Impression Scale
UPDRS Unified Parkinson's Disease Rating Scale
*On this scale only a higher score indicates better functioning.

Conclusions: Environmental stress and treatment with dopamine-receptor blocking drugs may precipitate refractory progressive catatonia in people with ASD.

P 214

Benefit of multiple incobotulinumtoxinA injections for pain reduction in adult patients with limb spasticity: pooled analysis of phase 2/3 studies

J. Wissel[1], *A. Camões-Barbosa*[2], *G. Comes*[3], *M. Althaus*[3], *A. Scheschonka*[3], *D.M. Simpson*[4]

[1]Vivantes Hospital Spandau, Berlin, Germany, [2]Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal, [3]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [4]Icahn School of Medicine at Mount Sinai, New York, United States

Background: Repeated treatment with incobotulinumtoxinA (incoA) has shown pain-relieving benefits in patients (pts) with limb spasticity in individual studies. Pain relief after multiple incoA injections in a large sample of pts with limb spasticity-associated pain (SAP) using pooled data from six phase 2/3 studies (four placebo-controlled) was assessed.

Methods: Adults with upper limb SAP received up to 4 incoA injections administered at 12- to 14-week intervals (injection cycles [ICs] 1–4; total observation period up to 56 weeks). Only IC 1 was placebo-controlled. Pain severity was assessed at control visits (CVs; 4 weeks after each injection) using the Disability Assessment Scale (DAS; pain scores ranging from 0 [no pain] to 3 [severe pain]). The proportions of pts with a response (defined as a reduction by ≥1 point in the DAS score from baseline to each CV) and with a complete response (DAS pain score=0) were assessed at every CV. Data were descriptively analyzed. As placebo-treated pts in IC 1 received incoA in subsequent cycles, they contributed data to the appropriate incoA CVs 1–4.

Results: 517 pts with SAP at baseline were included in this analysis (517, 389, 347, and 184 pts at CVs 1–4, respectively). Response rates increased over time, being 53.0%, 62.7%, 66.9%, and 71.7% at CVs 1–4, respectively. Likewise, the proportion of pts with complete response increased over time, being 27.7%, 37.8%, 41.5%, and 42.9% at CVs 1–4, respectively.

Conclusions: In pts with upper limb SAP, treatment response rates were sustained and showed a cumulative effect over 56 weeks after multiple incoA injections, with a complete pain relief in >40.0% of pts. Results support the use of incoA in reducing upper limb SAP in affected adults.

P 215

Treatment of cervical dystonia using shorter incobotulinumtoxinA injection intervals improves patient-reported outcomes in those with inadequate benefits from standard intervals

C. Comella[1], S. Isaacson[2], D. Charles[3], D. Truong[4], O. Oguh[5], J. Hui[6], E. Molho[7], M. Brodsky[8], E. Furr-Stimming[9], G. Comes[10], M. Hast[11], R. Hauser[12]

[1]Rush University Medical Center, Chicago, United States, [2]Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, United States, [3]Vanderbilt University Medical Center, Nashville, United States, [4]UC Riverside, Riverside, United States, [5]Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, United States, [6]University of Southern California, Los Angeles, United States, [7]Albany Medical Center Neurosciences Institute, Albany, United States, [8]Oregon Health & Science University, Portland, United States, [9]The University of Texas Health Science Center at Houston, Houston, United States, [10]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany, [11]Merz Pharmaceuticals, LLC, Raleigh, United States, [12]University of South Florida Health Byrd Institute, Tampa, United States

Background: The impact of 2 different injection schedules of incobotulinumtoxinA on patient-reported assessments in cervical dystonia (CD) was assessed. There is individual variation in the reported waning of botulinum toxin (BoNT) treatment benefit in patients with CD, even among patients who experience a favorable peak response. Thus, some patients prefer injection intervals shorter than the standard 12 weeks. This study assesses whether individualized treatment intervals can improve patient experience without compromising safety.

Methods: An open-label, randomized, phase IV study (CD Flex; NCT01486264) was designed to compare 2 incobotulinumtoxinA injection intervals (short-flex: 8±2 weeks [N=142]; long-flex: 14±2 weeks [N=140]) in BoNT-responsive subjects with CD who report waning of clinical benefit at <10 weeks. Subjects received 8 injections over a period of up to 2 years. Patient-reported outcomes (4 weeks' post-injection 8) included satisfaction (10-point scale), patient-reported global response (9-point Likert scale), and the CD impact profile (CDIP-58). Additional endpoints included a physician-assessed global response and a clinical global impression of severity.

Results: Subject satisfaction was significantly improved vs study baseline over 8 cycles in the short-flex group (mean change=1.2 points, *P*=0.0007), but not in the long-flex group. A significant improvement was also observed in the short-flex group in the physician-assessed global impression of severity 4 weeks post-injection 8. Most domains of the CDIP-58 analysis (pain/discomfort, sleep, annoyance) demonstrated numerical trends favoring the short-flex group. At 4 weeks' post-injection 8, a similar distribution of scores was observed for both groups on the subject- and physician-rated global response assessments. No differences in safety profile were noted.

Conclusions: Subjects with shorter incobotulinumtoxinA injection intervals reported improved satisfaction after 8 injections. Trends favoring short-flex were observed in both the CDIP-58 analysis and physician-rated clinical global impression of severity. Evidence suggests that individualizing injection intervals to treat CD may improve patient-reported outcomes without compromising safety.

P 216 (GPT)

Detection of Parkinson's disease using a deep neural network based on gait analysis

A. Bajpai[1], *G. Bajpai*[2]
[1]Rajkiya Engineering College, Kannuaj, India, [2]CSJM University, Kanpur, India

Background: In this study, we designed and implemented a deep neural network model based on a body sensor network to diagnose Parkinson's disease in the early stage. The proposed method focuses heavily on detecting abnormal walking patterns. To test our novel model data was collected using a body sensor network. After that, the deep neural model will categorise the data as either Parkinson suffering (PS) patients or healthy. This strategy can aid medical personnel in detecting PS individuals at an early stage. The key advantage of this model is that it can predict a healthy person's future even if only minor symptoms are present in the gait analysis.
Methods: We trained our model using data from an open repository and tested it in a real-world scenario. With this method, we were able to improve the model's accuracy by optimising feature selection. To train our model, we chose a data sample of people under the age of thirty-five to focus on youngers. The main benefit of this model is that it can forecast the future of a healthy younger person to early-stage treatment.
Results: In comparison to prior efforts that used simple neuron models, the innovative model based on deep neural networks performs better. When we used this unique technique to sensor data, the model was able to classify healthy persons and people who are suffering from Parkinson's disease more accurately. Furthermore, we can further classify the data of persons who have minor symptoms of healthy people with relation to Parkinson's disease.
Conclusions: The novel methodology improves previous existing methods, according to performance evaluations based on various parameters. While the findings are still early, this study is based on a small sample size of 50 people from an Asian country to test our approach. Further refinement of this technology could result in a promising clinical benefit.

P 217

Phenotypical and treatment response heterogeneity in a cohort of normal pressure hydrocephalus patients

A. Di Maio[1]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

Background: Normal-pressure hydrocephalus (NPH) is a late-onset neurological syndrome characterized by cerebral ventricles enlargement associated with motor, urinary, and cognitive symptoms. This is a potentially reversible condition, but the diagnostic process presents several challenges. Thus, this study aims to clinically characterize a cohort of patients with NPH in an attempt to identify possible clinical and humoral biomarkers that are able to predict the response to the treatment.

Methods: This retrospective study was conducted in the Neurology Department of the Policlinico Hospital in Milan enrolling 57 patients with clinical and/or neuroradiological suspect of NPH. Epidemiological, clinical, neuroradiological, neuropsychological, and CSF proteins data were collected, as well as clinical response to tap test (TT) and ventriculoperitoneal shunt (VPS) surgery.
Results: The mean age of enrolled patients was 72,5 ± 6,6 years. 73.7% of them displayed motor symptoms at onset, 29.8% falls, 36.8% urinary dysfunction, and 56.1% cognitive impairment. The median volume of collected cerebrospinal fluid (CSF) was 37.5 ml (30.0-40.0) and 49 (86.0%) patients improved after tap test (responders). The mean CSF beta-amyloid level was 562.5 ± 211.6 pg/ml. 20 patients (35.1%) underwent VPS surgery and 89.5% of them showed an improvement in motor, 43.8% in urinary, and 46.2% in cognitive symptoms. Responders showed an earlier age of onset compared to non-responders (71.7 *vs* 76.8 years, p=0.047), in addition to lower instability prevalence at onset (24.5 *vs* 62.5%, p=0.043), higher CSF collected volume (40 *vs* 25ml, p=0.016), and a lower CSF beta-amyloid level (531.9 *vs* 723.7 pg/ml, p=0.026). Patients that didn't undergo VPS surgery showed lower scores at Mini Mental State Examination (MMSE).
Conclusions: This study supports the evidence of a strong heterogeneity in NPH clinical features and therapeutical response, and highlights some of the key aspects that may help clinician during the diagnostic process, such as TT volume standardization, CSF beta-amyloid levels, and comorbidity screening.

P 218
Optimizing CNS-Delivery by Lactyl Stearate-Coupled Liposomes

M. Bhargava[1], *S. Bhargava*[2]
[1]GTB Hospital, R&D, Kanpur, India, [2]Himalayan University, Pharmacy, Kanpur, India

Background: Meningitis is inflammation of tissues which covers brain & spinal cord. Brain drug targeting brings a healthy skepticism to the study of BBB, which is the most frustrating obstacle for pharmacologists wishing to find treatments for brain disorders. The BBB restricts brain uptake of many valuable hydrophilic drugs and limits their efficacy in the treatment of brain diseases. Thus Lactyl stearate(LS) coupled liposomes bearing rifampicin is used for effective management of meningitis.
Methods: LS(synthesized) was used to prepare liposomes bearing rifampicin by Lipid cast film method. Formulations were characterized for vesicle shape by Transmission Electron Microscopy (TEM), average vesicle size, drug entrapment efficiency, in-vitro drug release. In in-vivo studies drug distribution in various organs and blood of albino rats was assessed after I.V. administration. The quantitative uptake by brain in albino rats was assessed by fluorescent microscopy. Brain uptake was increased about 2-3 times in case of uncoupled liposomes and plain drug. Accumulation was increased about 6-8 times with coupled liposomes in comparison to uncoupled and about 10-12 times higher compared to drug solution.
Results: Higher uptake of lactyl stearate coupled liposomes can be explained as, the mono carboxylic acid transporters present on brain endothelial cells, cross the BBB by carrier mediated transport mechanism. Fluorescence study indicates that preparation is crossing basal carotid system & accessing nervous system. 6-CF was distributed in blood vessels and accumulated in cerebellum and cerebrum. This delivery system not only increased brain uptake of drug but it also reduces the administered dose and toxic effect of drug.

Conclusions: Hence it proves great potential in delivery of drug into brain for treatment of diseases associated with brain where very limited drug are available for those diseases. Thus, Lactyl stearate coupled liposomes effectively delivers the drug to brain and has great potential for brain targeting.

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

P 219 (GPT)
Physical interventions for people with Parkinson's disease: results from a Cochrane systematic review and network meta-analysis

M. Ernst[1], A.-K. Folkerts[2], M. Roheger[3], D. Chakraverty[2], F. Krohm[2], J. Caro-Valenzuela[1], R. Gollan[2], E. Lieker[2], A. Adams[4], C. Eggers[5], I. Monsef[1], A. Dresen[6], N. Skoetz[1], E. Kalbe[2]

[1]Cochrane Haematology, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf, Faculty of Medicine and University Hospital, University of Cologne, Cologne, Germany, [2]Medical Psychology | Neuropsychology and Gender Studies & Centre for Neuropsychological Diagnostics and Intervention (CeNDI), Faculty of Medicine and University Hospital, University of Cologne, Cologne, Germany, [3]Department of Neurology, University Medicine Greifswald, Greifswald, Germany, [4]Institute of Medical Statistics and Computational Biology, Faculty of Medicine and University Hospital, University of Cologne, Cologne, Germany, [5]Clinic for Neurology, University Hospital Marburg, Marburg, Germany, [6]Institute of Medical Sociology, Health Services Research and Rehabilitation Science, Faculty of Human Sciences and Faculty of Medicine and University Hospital, University of Cologne, Cologne, Germany

Background: Physical interventions are effective in managing Parkinson's disease. However, the relative benefit of different types of exercise remains unclear.

Methods: We conducted a systematic review of randomized controlled trials (RCTs) on physical interventions for Parkinson's disease. We categorized the interventions and analyzed their effects on motor functions and quality of life (QoL) using a network meta-analysis (NMA). We assessed the quality of studies using the Risk of Bias 2.0 tool and rated our confidence in the evidence following the CINeMA approach.

Results: We included 156 RCTs. The NMA on motor functions and QoL included data from 71 (n=3196), and 55 (n=3283) trials, respectively. The mean number of participants per trial arm was small (M=20.7). Most study results had a high risk of bias (motor functions: 71%; QoL: 100% due to self-reporting).

For motor functions, significant small to moderate effects were found for most types of physical intervention compared to a passive control group (moderate effects: dance [high confidence], aqua-based, gait-balance-functional, and multi-domain trainings [low confidence]; small effects: mind-body, and endurance trainings [low confidence]).

For QoL, we observed a large effect of aqua-based trainings [moderate confidence], a moderate effect of endurance trainings [low confidence], and small effects of gait-balance-functional, and multi-domain trainings [low confidence].

The remaining effects on both outcomes are uncertain [very low confidence].

The most common limitations to our confidence in the effects were a large proportion of high-risk-of-bias-studies and large prediction intervals.

Conclusions: For most physical interventions, we found evidence for beneficial effects on motor functions and QoL. We found very little evidence for differences between the interventions. Thus, while the exact type of exercise might be secondary, our systematic review highlights the importance of physical interventions for people with Parkinson's disease. Larger, well-conducted studies are needed to increase the confidence in the evidence.

P 220
Using Non-Exercise-Physical-Activity to preserve post-Physical Therapy gains in Parkinson's disease: a feasibility study

M. van Emde Boas[1], *U. Marusic*[1], *M. Muller*[1], *N. Bohnen*[1]
[1]University of Michigan, Functional Neuroimaging, Cognitive & Mobility Lab, Ann Arbor, United States

Background: Gains made during Physical Therapy (PT) sessions (ADL, mobility, gait, balance) are lost over time in Parkinson's Disease (PD) Patients. The goal of this study was to conduct a 4-month trial of post-PT in-home facilitation of **Non-Exercise-Physical-Activity (NEPA)** with a novel device: a "dynamic standing desk" or "MoveDesk".
Methods: A randomized single-blind controlled clinical trial. Patients completed 12 sessions of PT followed by randomization. The control group participated in a weekly exercise group (standard of care). The intervention group received a MoveDesk desk at home + participation in a weekly exercise group. 24 patients were recruited. 19 participants were enrolled into the study. 9 participants were randomized to the MoveDesk group and 10 to the control group. 14 participants fully completed the study. The main outcome parameter was the Timed Up and Go test (Tug).
Results: Everyone had significant improvement of TuG times after completion of 12 PT sessions compared to pre-PT levels ($P<0.001$). Average in-home use of the MoveDesk was at least 2.2±0.4 hours per day, 5 days/week. Statistical analysis of the post-PT intervention groups show a near significant effect ($P=0.07$) in favor of maintaining the post-PT effects in the MoveDesk group compared to the controls. (Controls returned to pre-PT values.) Quality of life scores were significantly better in the MoveDesk group ($P< 0.01$). There were no significant side-effects of the in-home MoveDesk and exit interviews showed substantial enthusiasm for the new device.
Conclusions: In-home use of the MoveDesk as a post-PT NEPA program is feasible. Using NEPA (**decreasing sedentary time**) to maintain post-PT gains could be a promising concept.

P 221

Development of a voice and motor speech assessment protocol across an academic health center

C. Rountrey[1], M. Molett[1], B. Kralik[1], A. Spotts[1], M. Mateja[1], N. Mccarthy[1]
[1]University of Cincinnati, Communication Sciences and Disorders, Cincinnati, United States

Background: Speech assessment protocols utilize reading or repetition tasks to evaluate overall speech intelligibility for motor speech disorders (MSDs), including dysarthria caused by Parkinson's Disease (PD) and related disorders. However, the characteristic signs for MSDs may not occur consistently across speaking tasks. Clinical outcomes noting intelligibility solely on reading or repetition tasks may lead to overestimating conversational intelligibility.

This project aims to create an efficient, evidence-based clinical assessment protocol for voice and MSDs including both elicited and spontaneous speech tasks. This assessment protocol will be used at multiple sites across an academic health center, for multiple MSD etiologies and in various levels of patient care. It will probe longstanding research questions regarding how perceptual notations of intelligibility align with quantifiable outcomes measures, using the same samples.

Methods: Researchers developed an assessment for voice and MSDs in collaboration with clinicians across an academic health center. It includes a mini-protocol option and clinician- and client- friendly visual display. Researchers provide calibrated equipment for recording speech samples, and a data management plan with training to make retrospective studies of clinical encounters feasible. This allows for inquiry of important clinical research questions and enhances clinician-researcher collaborations across the academic health center.

Results: In February-March 2022, this protocol will be implemented at Cincinnati VAMC, Gardner Institute, Daniel Drake Center, and University of Cincinnati Speech & Hearing Clinic. We will share preliminary results to the following questions:

1. How do perceptual notations of intelligibility compare to acoustic measures from the same clinical encounter?
2. What are the challenges and opportunities in our collaborations?

Conclusions: Researchers aim to bridge research and clinical practice in a meaningful way while exploring voice and speech outcome measures in clients with MSDs, including those resulting from PD. Future directions for similar collaborations will be shared.

P 222
Vestibular dysfunction: which is the effects of virtual reality?

B. Simone Zeigelboim[1], M.I. Rodrigues Severiano[2], G.J. Bueno dos Santos[2], H.A. Ghizoni Teive[3], J. Stechman-Neto[1], R. Sampaio Santos[1], C. Miranda de Araújo[1], B. Cavalcante-Leão[1]
[1]Universidade Tuiuti do Paraná, Curitiba, Brazil, [2]Instituto Federal do Paraná, Curitiba, Brazil, [3]Universidade Federal do Paraná, Curitiba, Brazil

Background: Effects of vestibular rehabilitation with virtual reality in adults with vestibular disorders are still uncertain. The aim was answer the following question: "What are the effects of vestibular rehabilitation with virtual reality in adults with vestibular disorders?"
Methods: Word combinations were selected and tailored for each electronic database. Studies that met the following criteria were included: adults with vestibular disorders (P); use of virtual reality as treatment (I); comparison between pre- and post-therapy moments (C); assessment of vestibular dysfunction using validated tests or questionnaires (O); randomized, quasi-randomized, non-randomized clinical trials and cohort studies (S). A random-effects meta-analysis comparing the mean difference between pre- and post-therapy time points was performed. The risk of bias was assessed using the Cochrane Collaboration tool for assessing the risk of bias, Risk Of Bias In Non-randomised Studies and Meta-Analysis of Statistics Assessment and Review Instrument. The certainty of the evidence was assessed using the GRADE tool.
Results: Total of 12 articles were included for the meta-analysis. There was an improvement in the level of confidence in balance, with a mean difference in scores between baseline and post-intervention of 10.62 [95%CI = 7.55 – 13.69; I2 = 25%]. An improvement in disabling effects caused by dizziness was also observed, with a difference between means in relation to two periods of -19.87 [95%CI = -28.57 – -10.84; I2 = 91%]. There was no statistical significance for Dynamic Gait Index and Sensory Organization Test. No study had more than 50% of domains at high risk of bias, however two studies did not provide enough information for the full judgment.
Conclusions: Vestibular rehabilitation with virtual reality improved balance confidence, disabling effects caused by dizziness, and postural stability. However, lack of sufficient information to analyze the methodological quality, inconsistency and inaccuracy observed resulted in a low certainty of evidence for this outcome.

P 223 (GPT)

Impact of COVID-19 pandemic on eating behavior and body mass index in patients with Parkinson's disease of Northeastern México

C.K. Lopez-Botello[1], *S.A. Castillo-Torres*[1], *I. Estrada-Bellmann*[1], *B.E. Chávez-Luévanos*[1]
[1]Autonomous University of Nuevo León/ University Hospital "Dr. José Eleuterio González", Neurology, Monterrey, Mexico

Background: The psychological impact of Covid-19 on patients nutrition with Parkinson's disease (PD) has not been thoroughly evaluated. We aimed to assess the impact of psychological stress on eating behavior and body mass index (BMI) of patients with PD.
Methods: From August to October 2021, patients with PD answer an online survey consisting of a validated questionnaire of psychological impact on Covid-19 and three-factor eating questionnaire-R18, (TFEQ), including three eating behaviors: restrained (RE), uncontrolled (UE) and emotional (EE). Body Mass Index (BMI) was calculated from patient-reported weight and height (previous to Pandemic) and at the moment of the survey.
Results: We recruited 50 patients (54% male, mean age 61.6±13.1 years), who experienced weight loss (-1.4±12.9 kg), with higher normal weight during pandemic (46% vs 36%, p<0.001) (Table 1).
Psychological impact of Covid-19 was reported, less motivation (74%), more stress (70%), less energy (68%), mental exhaustion (66%), and sleep problems (56%). We found significant correlation between BMI and stress (r=-0.40; p<0.001) and sleep problems (r=-0.40; p<0.001).
Regarding eating behaviors, patients reported less emotional (62%), uncontrolled (58%), and restrained (52%) eating. We found significant correlation between RE and age (r=-0.46, p<0.001). Women had the lowest score in uncontrolled (55.2%) and emotional eating (48.4%), and men in restrained eating (57.7%).

	Before Pandemic	During Pandemic	p-value
Total kg/m2, mean ± SD	26.4 ± 4.6 kg/m^2	26.2 ± 8.4 kg/m^2	0.001
Categories			
- Overweight	22 (44%)	18 (36%)	
- Obese	9 (18%)	7 (14%)	
- Normal	18 (36%)	23 (46%)	
- Low	1 (2%)	2 (4%)	

Table 1. BMI after and during COVID-19 pandemic.

Conclusions: Despite the considerable psychological distress imposed by the pandemic, patients with PD reported an improvement in eating behaviors and decrease in weight during COVID-19. Nevertheless, patients reported stress and sleep problems were associated with higher BMI progression, whereas female patients had worse eating behaviors.

P 224

Disease severity and gait velocity are predictive of fear of falling avoidance behavior in people with parkinsonisms

M.R. Landers[1], J.V. Rider[2], K. Eckhard[1], R. Hammar[1], F. Vukojevic[1], J. Campbell[3], J.K. Longhurst[4]
[1]University of Nevada, Las Vegas, Physical Therapy, Las Vegas, United States, [2]Touro University Nevada, Occupational Therapy, Henderson, United States, [3]Baylor Scott and White Institute for Rehabilitation, Dallas, United States, [4]Saint Louis University, Physical Therapy, St. Louis, United States

Background: Fear of falling avoidance behavior (FFAB) is common in people with parkinsonisms (PwP) and can result in several negative downstream consequences including sedentary behavior, physical deconditioning, and weakened balance systems, which can further increase fall risk and precipitate functional declines. Identifying which characteristics (e.g., demographics, disease severity, and gait/balance function) are most associated with FFAB in PwP can help facilitate a greater understanding of disease progression and provide preliminary evidence for the development of effective treatment approaches addressing FFAB and associated downstream consequences.
Methods: A retrospective, cross-sectional study was conducted from medical records data of 142 PwP. These data included: demographics (age, sex), disease characteristics (Movement Disorders Society – Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III), years since diagnosis), fall history (number of fall injuries in previous year), and gait and balance function (five times sit to stand (5STS), MiniBESTest, Timed Up and Go (TUG), dual-task TUG, ten-meter walk test (10MWT), observed freezing of gait (FOG) (MDS-UPDRS III item 11)). Multiple imputation was used to handle missing data and hierarchical regression was used to examine the association of the predictor variables with the modified FFAB Questionnaire (mFFABQ). Disease severity (years since diagnosis and MDS-UPDRS III) were entered in Block 1, followed by the number of fall injuries in the last year in Block 2, and, lastly, followed by the gait and balance measures (5STS, MiniBESTest, TUG, dual-task TUG, 10MWT, and FOG).
Results: The model was statistically significant, ($p<.001$) and accounted for 52.4% ($R^2=.524$) of the variability in mFFABQ. Blocks 1 and 3 were statistically significant (ps<.001), accounting for 16.3% and 33.5% of variability, respectively. Disease duration (b=.402, p=.046), UPDRS III (b=.182, p=.029), 10MWT (b=-24.134, p<.001), and UPDRS 3.11 (b=-5.636, p=.014) were found to be significant predictors of mFFABQ.
Conclusions: While disease severity and freezing of gait explained a significant portion of the variability of FFAB, the largest portion of variability in FFAB was explained by gait velocity (10MWT) after controlling for disease severity. Thus, as the parkinsonisms advance, the impact of fear of falling results in more avoidance behavior which may potentiate more negative downstream consequences.
Also, consistent with other studies, we found that fall history was not associated with FFAB. This finding provides further evidence that as one avoids more risky activities, their fall risk exposure decreases, and they fall less, supporting the notion that the relationship between falls and FFAB is likely non-linear.

P 225 (GPT)

Addressing fear of falling avoidance behavior in Parkinson's disease: a theoretical framework to inform clinical practice

M.R. Landers[1], *M.H. Nilsson*[2,3,4]

[1]University of Nevada, Las Vegas, Physical Therapy, Las Vegas, United States, [2]Lund University, Health Sciences, Lund, Sweden, [3]Skåne University Hospital, Memory Clinic (VE minnessjukdomar), Malmö, Sweden, [4]Lund University, Skånes Universitetssjukhus, Clinical Memory Research Unit, Clinical Sciences Malmö, Malmö, Sweden

Background: Postural instability in Parkinson's disease (PD) often results in negative downstream consequences that may increase the risk of falling. Among the prominent downstream consequences is fear of falling (FOF), which can lead to a vicious cycle of avoidance behavior that results in more sedentary behavior and physical deconditioning. This, in turn, may worsen already impaired postural instability and increase the susceptibility to a future fall. While FOF activity avoidance can be adaptive (appropriate), it can also be exaggerated or maladaptive (inappropriate). When this avoidance behavior is contextualized to gait/balance performance, it provides a theoretical framework that can be used by clinicians to match patterns of behavior to a concordant treatment approach.

Methods: FOF avoidance behavior and balance performance were contextualized together using the cut-point of 20 on the Fear of Falling Avoidance Behavior Questionnaire (FFABQ) with the cut -point of 43.5 on the Berg Balance Scale (BBS). This resulted in four quadrants or patterns which were labelled as: appropriate avoiders, appropriate non-avoiders, inappropriate avoiders, and inappropriate non-avoiders.

Data from a previously published study of 63 participants with PD were plotted into the framework.

Results: Of the 63 participants, 45 were in the "appropriate" response quadrants with only 18 in the "inappropriate" quadrants. Fallers were found in each quadrant which supports our hypothesis that fall history in isolation gives an incomplete picture of fall risk.

Those in the two low avoidance quadrants had higher daily step counts and spend more time stepping per day than those in the two avoider quadrants. Those in the two avoider quadrants reported more general anxiety and more fall-related anxiety which supports our hypothesis that FOF is impacted by psychological factors that might trigger avoidance behavior.

Conclusions: Preliminary evidence for the construct validity of this theoretical framework supports the notion that contextualizing FOF avoidance behavior with gait/balance performance in PD offers value from a clinical perspective. Moreover, it suggests that each of the four quadrants or patterns have a unique blend of physical and psychological problems that warrant different treatment approaches to address the underlying physical and psychological issues.

While the main components of this theoretical framework are supported by the literature, the framework itself and the treatment recommendations and considerations are based on face validity and preliminary data. However, establishing validity is an iterative process and, subsequently, more research is needed to support this theoretical framework.