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Oral Poster Sessions

Session I: Behavior and Cognition, Deep Brain Stimulation

OP-1-01
Freezing of gait in Parkinson’s disease: Is it just a motor problem or more?
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Objective: Deficit in inhibitory control (IC) is considered to be the prime reason for freezing of gait in Parkinson’s Disease (Bisett et al, 2015). The IC mechanism consists of Intention formation of activities, Initiation of ongoing activities, inhibiting current activity and switching to another activity. Attention switching is involved in the third step and its failure will lead to failure of inhibitory control. The current study investigates specifically how failure of attention switching results in Freezing of Gait.

Method: We compared 3 groups: 15 elderly patients of Parkinson’s Disease with Freezing of Gait, 15 patients without freezing of gait and 15 matched healthy controls (55-82yrs) and administered attention switching task which measures the speed and accuracy of how the individual is able to switch from one activity to another. Montreal Cognitive Assessment was performed to rule out dementia and Frontal Assessment Battery was administered to check for overall executive functioning.

Results: Multivariate ANOVA was used for the analysis. The results show that the group having freezing of gait performed significantly poorly on congruent $F(2, 42) = 7.593, p = 0.002$ and incongruent trials $[F(2, 42) = 30.776, p = 0.000]$ and as well as overall AST task performance with respect to accuracy $[F(2, 42) = 34.304, p = 0.000]$ and reaction time. The performance was unaffected among the patients without freezing of gait but they had significantly lower mean reaction time than the healthy control group.

Conclusion: This study suggests a deficit in the attention-switching component among patients with freezing of gait leading to failed switching from concurrent task to another task further leading to a deficient inhibitory control system. The group without freezing of gait experienced overall slowing suggested by the cognitive assessments but their task accuracy was unaffected. The better understanding of this phenomenon will lead to better management of freezing of gait. Therefore, this can help improve the functioning of patients with Parkinson’s disease and their caregivers.
Cognitive stimulation is beneficial for individuals with Parkinson’s disease dementia living in long-term care: A randomized crossover pilot study

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Objective: While the efficacy of cognitive stimulation (CS) has been demonstrated in patients with dementia, no study has included patients with Parkinson’s disease dementia (PDD). For the first time, this randomized crossover pilot study examined the feasibility and potential effects of CS in PDD.

Methods: All residents of a PDD-specific long-term care unit in the Netherlands that were eligible for the study (n = 12) were randomly allocated to group A (n = 6) receiving CS (eight weeks, twice weekly for 60 minutes), or group B (n = 6) receiving usual care (control group, CG). The CG participated in CS afterwards, resulting in an experimental group (EG) consisting of n = 12. Pre- and post-assessments and a six-week follow-up (FU) were conducted for cognition, neuropsychiatric symptoms, quality of life (QoL), and activities of daily living (ADL) outcomes.

Results: Between-group analyses with pre- to post-intervention difference scores showed significant short-term effects favoring the EG for visuoconstruction, and statistical trends for global cognition, clock drawing, and neuropsychiatric symptoms, all with moderate-to-large effect sizes. Within-group analyses demonstrated a significant decline in visuoconstruction and QoL in the CG, but short- and long-term benefits in cognitive and non-cognitive outcomes in the EG. ADL deteriorated at FU in the EG.

Conclusions: Although our data are preliminary due to the small sample size, this study shows that CS is feasible and potentially effective for cognitive and non-cognitive outcomes in PDD patients. Randomized controlled trials with larger sample sizes are needed to confirm these promising results.
OP-01-03
Cognition in subjects with REM sleep behavior disorder and cumulative signs of prodromal Parkinson's disease
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Prodromal signs of Parkinson's disease (PD) include REM Sleep Behavior Disorder (RBD) as the most prominent, followed by hyposmia, constipation and depression. Cognitive dysfunction (CD) is observed early in PD and could thus be added to the list of prodromal PD signs if already observed in subjects with RBD. Therefore we investigate CD in a group of RBD patients without parkinsonism, compared to healthy controls. In the frame of the Luxembourg Parkinson's study, 552 subjects without parkinsonism underwent a deep clinical phenotyping including the RBD Screening Questionnaire (RBDSQ) to identify subjects with probable RBD (pRBDs). In addition we assessed depression (Beck depression inventory), constipation (SCOPA-AUT-item5), hyposmia (sniffin'sticks), motor (MDS-UPDRS 3) and cognitive functions (Table 1).

<table>
<thead>
<tr>
<th>Cognitive function</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global cognition</td>
<td>Montreal Cognitive Assessment (MoCA)</td>
</tr>
<tr>
<td>Executive</td>
<td>Trail Making Test B (TMTB)</td>
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<td></td>
<td>Phonemic fluency (F)</td>
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<td></td>
<td>STROOP-Test</td>
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<tr>
<td>Working memory</td>
<td>Digit and block spans (forward/backward)</td>
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<tr>
<td>Attention</td>
<td>Trail Making Test A (TMTA)</td>
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<tr>
<td>Episodic memory</td>
<td>CERAD word list learning, delayed recall and recognition</td>
</tr>
<tr>
<td>Language</td>
<td>Semantic fluency (animals)</td>
</tr>
<tr>
<td>Visuo-spatial</td>
<td>Benton's Judgment of Line Orientation</td>
</tr>
</tbody>
</table>

(Table 1: List of test used for assessment of cognitive function)

We identified 95 pRBDs with a RBDSQ cut-off of 5, the other 457 subjects were used as control group (CG). With similar age (56.7±14.3 vs. 58.3±12) and gender distribution (m/f 57.5/42.5 vs. 55.8/44.2), we observed higher BDI scores in pRBDs compared to the CG (8±7 vs. 4.9±4.7; p<0.001). All the cognitive assessments showed similar results in both groups. Differences compared to the CG in cognitive assessments appeared when increasing the RBDSQ cut-off to 7, as well as in pRBDs reporting constipation, reduced smell (sniffin' sticks < 10/16) or at least 2 prodromal signs for PD adding to RBD (table 2).
Our results show that global cognition and executive function are impaired in pRBD subjects, depending on the severity of RBD symptoms and presence of additional prodromal signs for PD. As these functions are known to be frequently impaired in early PD, they should be added to the list of prodromal PD signs. Polysomnography and increased sample size are foreseen to confirm our results after completion of recruitment for the Luxembourg Parkinson's Study, as well as 4 years follow-up to evaluate conversion rates to synucleinopathies.

**OP-01-04**

**Visuospatial working memory and executive function deficits in single- versus multiple-domain amnestic mild cognitive impairment: a combined ERP and sLORETA study**

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**Objective:** According to recent classification criteria, amnestic mild cognitive impairment (aMCI) could be divided into two categories: single-domain aMCI (sd-aMCI) and multiple-domain aMCI (md-aMCI). The exact relationship between sd-aMCI and md-aMCI still needs further exploration. The present study aimed to explore deficits in visuospatial working memory (VSWM) and executive function in sd-aMCI versus md-aMCI patients via event-related potentials (ERP) and standardized low-resolution brain electromagnetic tomography analysis (sLORETA).
Methods: ERP were analyzed in 26 sd-aMCI, 13 md-aMCI patients and 46 healthy elderly controls (HEC) during VSWM and Go/Nogo tasks. 

Results: The investigation detected decreased P300 amplitude in md-aMCI patients compared to HEC and sd-aMCI patients during VSWM task. Additionally, sLORETA models suggested that md-aMCI showed a hypoactivation in the right superior parietal lobule and precuneus during the P300 time range compared to HEC and sd-aMCI, respectively. During the Go/Nogo task, sd-aMCI and md-aMCI patients showed reduced N200 amplitude, compared to HEC. In addition, md-aMCI patients had decreased N200 amplitude, with respect to sd-aMCI patients. Md-aMCI patients presented a hypoactivation in the right medial frontal gyrus and superior frontal gyrus during the N200 time range compared to HEC and sd-aMCI, respectively. 

Conclusions: In conclusion, the study revealed that a combined ERP and sLORETA study during VSWM and Go/Nogo tasks distinguished md-aMCI from sd-aMCI.

Significance: These findings added novel insights to deficits in VSWM and executive function in sd-aMCI versus md-aMCI patients with a combined ERP and sLORETA study.

OP-01-05
Cognitive and histopathological phenotypes in new rat models of cortical synucleinopathy
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Objective: Both Parkinson’s disease dementia (PDD) and Dementia with Lewy bodies (DLB) are associated with the formation of intracellular protein inclusions containing alpha-synuclein (α-syn) in the cerebral cortex. However, a causal link between such pathology and cognitive decline remains unproven. To address this question, there is a need to develop animal models where cortical α-syn pathology can be induced under controlled conditions. We therefore aimed to create rat models displaying α-syn pathology in cortical and subcortical regions relevant to PDD/DLB and elucidate the relationship between patterns of pathology and cognitive deficits.

Methods: Two models were evaluated: (1) rats sustaining bilateral injections of adeno-associated viral vectors coding for wild-type human α-syn (AAV-syn) into the medial prefrontal cortex (mPFC); (2) rats sustaining AAV injections as above, shortly followed by inoculation of preformed fibrils of human α-syn (PFF) into the rostromedial striatum. Rats were evaluated in two behavioral tests that probe prefrontal cognitive functions. Neuropathology was studied immunohistochemically using antibodies against human α-syn, Ser129-phosphorylated α-syn, and NeuN.

Results: Rats that received only AAV-syn injections exhibited unchanged performance in the cognitive tasks, while rats with additional PFF inoculation showed significant deficits in both. Human α-syn was highly expressed in somatas and axons of mPFC neurons in both models, resulting in marked immunostaining in both mPFC and its projection targets. Immunostaining for Ser129-phosphorylated α-syn revealed extensive somatic and neuritic inclusions in AAV-syn-PFF-inoculated rats, while only AAV-syn resulted in
somata-localized expression within mPFC. Finally, AAV-syn-PFF-inoculated rats displayed abundant dystrophic dendrites and a marked drop of NeuN positive cells in mPFC. 

**Conclusions:** Our data suggest that cortical overexpression of human α-syn is not sufficient to produce cognitive dysfunction, while a combination of α-syn overexpression and pathology seeding by misfolded α-syn yields both cognitive and histopathological phenotypes that are relevant to PDD/DLB.

**OP-01-06**

**Association between post-operative delirium and Parkinson disease following common US surgical procedures**

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**Objective:** To determine the association of Parkinson disease (PD) and post-operative delirium following common surgical procedures.

**Methods:** A matched sample of patients with and without PD who underwent any of the ten most common surgical procedures in the US were identified between 2005-2014 using the National Inpatient Sample. The primary measure was post-operative delirium for patients with and without PD. The secondary measures included use of life sustaining therapies, discharge disposition, length of stay, and hospital costs.

**Results:** We identified 3,235,866 patients as undergoing any one of the ten most common operative procedures in the US. Among these, 35,743 patients with and without PD were matched based on age, sex, elective admission, Charlson comorbidity index, and presence of dementia. Mean age was 77 ± 6.8 years, mean Charlson comorbidity index score was 1.2 ± 1.5, 46.6% were female, and 46.8% were admitted electively. Post-operative delirium was present in 1,519 patients with PD compared to 828 matched patients without (4.2% vs. 2.3%; \( P < 0.001 \)). The adjusted odds ratio (AOR) of post-operative delirium for PD compared to the matched cohort without PD was 1.88 (95% CI 1.73-2.05). Those undergoing spinal fusion (AOR 2.99, 95% CI 2.06-4.38) had greater adjusted odds than all operative procedures combined. For patients with PD, length of stay (6.2 days vs. 5.3 days, \( P < 0.001 \); Incident Rate Ratio 1.15 [95% CI 1.13-1.17]), hospital costs (Adjusted Mean Difference $1,150 [95% CI $1,092-$1,208]), and odds of post-acute care facility discharge were greater.

**Conclusion:** Patients with PD are more likely to develop post-operative delirium and have a more complicated post-operative course with longer length of stay and greater hospitalization costs. Surgeons, especially those performing spinal fusion, should be aware of these post-operative risks and consider multidisciplinary management of PD patients in coordination with neurologists and/or geriatricians.
Cortical 123I-FP-CIT binding deficits are associated with mild cognitive impairment in Parkinson’s disease

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Objectives: Severe deficits within dopaminergic striatal binding have been associated with early progression to dementia in Parkinson’s disease (PD). The objective of the study was to evaluate the relationship between subcortical and cortical 123I-FP-CIT binding and early cognitive deficits in PD.

Methods: Sixty-seven PD patients (mean age 67.6 ± 10.7 years, mean disease duration 5.1 ± 4.2 years) entered the study and underwent DaTSCAN imaging. An extensive neuropsychological evaluation (level II MDS definition) was performed, allowing the classification of patients into 33 with normal cognition (PDNC) and 34 with mild cognitive impairment (PD-MCI).

The striatal tracer uptake was evaluated using BRASS software (Hermes, Sweden). The correlation between deficits within performances in specific neuropsychological tests and striatal dopaminergic binding were evaluated by multiple regression analyses. The whole-brain analysis was performed with Statistical Parametric Mapping (SPM). All the analyses were adjusted for the effect of age, sex, disease duration and presence of impulsive-compulsive disorders.

Results: No significant striatal binding differences were found between PD-MCI and PDNC patients by using adjusted BRASS analyses. Right caudate and right putamen binding correlated with MMSE and verbal fluency scores, respectively. PD-MCI patients showed a significant reduction of left precuneus tracer uptake compared to PD-NC (125 voxels, adjusted p=0.001, uncorrected, Figure 1).

Discussion: The development of cognitive deficits in PD may be related to early cortical 123I-FP-CIT reduction, even in absence of any difference in striatal binding. This might reflect a selective damage in PD-MCI of precuneus, classically impaired in early Alzheimer’s disease. Alternatively, this might be secondary to a disconnection of bioaminergic striato-cortical projections. Multi-modal imaging and longitudinal studies are warranted in order to clarify this issue.
Subthalamic deep brain stimulation for advanced Parkinson’s disease beyond the 5-year follow-up

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Objective: Subthalamic DBS is a world-wide accepted and effective treatment for levodopa-responsive symptoms and complications of prolonged dopaminergic treatment in advanced Parkinson's disease (PD). Nevertheless, most patients tend to deteriorate over time. Studies describing remote results of STN-DBS are still limited. We aimed to assess efficacy and safety of STN-DBS in long-term follow-up up to seven years postoperatively.

Methods: We evaluated 33 PD-patients undergone STN-DBS with follow-up beyond 5 years. Age at surgery was 53.1±6.8 years, disease duration 11.8±3.3 years, Hoehn&Yahr stage 3.4±0.5. We assessed motor and functional outcome (UPDRS-2,3,4), activities of daily living (Schwab&England scale), quality of life (PDQ-39 questionnaire), and antiparkinsonian medication regimen (levodopa dose and L-dopa equivalent daily dose) preoperatively and annually after STN-DBS. Complications and side effects were noticed.

Results: Following STN-DBS, significant amelioration of PD-symptoms in OFF-medication state and L-dopa therapy complications were observed. At 7-year follow-up, absolute improvements in UPDRS-3 OFF-score remained 25.2±19.1 (42%), in UPDRS-2 OFF-score 6.9±8.9 (24%), in UPDRS-4 5.8±3.8 (58%), and in OFF-Schwab&England score 23%. Motor function in ON-state was relatively stable, however, slight decrease in daily life activities was noticed (-6.5%, UPDRS-2, p< 0.0001). Reduction in L-dopa dose was 41%, and in LEDD 35% (p<0.0001), although, generally deteriorated over time. In three patients, levodopa remained withdrawn. Quality of life was improved to the 7th year by 9%. In the primary years of STN-DBS, extent of PDQ-39 improvement correlated positively with severity of preoperative QoL-impairment (p< 0.01) and Hoehn&Yahr stage (p< 0.05). After 5-year follow-up, PDQ-39 improved more in patients with earlier PD-onset and longer disease duration (p< 0.05).

Conclusions: In advanced PD-patients, STN-DBS could provide significant improvement in OFF-state and diminish dopaminergic medication up to seven postoperative years. Functional activity in the best ON-state tends to decline over time. For long-term quality of life, age of onset, disease duration, and initial disability seem to be important. Overall disease progression remains crucial for outcome.
Deep brain stimulation of the nucleus basalis of Meynert as a treatment for Parkinson’s Disease Dementia: A systematic review of animal studies

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Objectives: To meta-analyse the effect of the electrical stimulation of the nucleus basalis of Meynert (NBM) on cognitive performance in animal studies and to provide more insight in the underlying hypotheses on deep brain stimulation (DBS) of the NBM as an alternative therapy for Parkinson’s Disease Dementia (PDD) and other types of dementia.

Methods: We reviewed systematically all the animal studies investigating the effect of electrical stimulation of the NBM on cognitive performance. Data on the stimulation methods and the results of the cognitive assessments were extracted from the included studies.

Results: Twelve animal studies were included in our review, reporting the effect of electrical stimulation of the NBM on cognitive performance. The overall effect of electrical stimulation of the NBM on cognitive performance was positive (overall z-score= 7.30, p< 0.00001; d=1.02; 95% CI= 0.75-1.30), but substantial discrepancies with the applied clinical methodologies on the stimulation were observed. Firstly, none of the included animal studies applied the electrical stimulation of the NBM bilaterally. Secondly, the stimulation was performed at very short time-period, such as before, during or after the behavioral acquisition phase, as well as just before or during the behavioral assessment phase. Thirdly, all studies except one performed the stimulation in animals with intact NBM cholinergic neurons. Finally, the mode of stimulation proved to be important. Synchronizing electrical pulses with the applied cues overall showed better effects on cognition (z=6.65, p< 0.00001; d=2.17, 95% CI=1.53-2.81) compared to unsynchronized stimulation.

Conclusion: The currently applied methodology in NBM stimulation in PDD and other dementias lacks substantial preclinical evidence, which might be the reason for the overall negative outcomes of NBM stimulation in human.
**Abstracts**

**OP-01-10**

**Long-term effect of subthalamic deep brain stimulation in young- and late-onset Parkinson’s disease: 10-year follow-up study**


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**Objectives:** The efficacy of DBS according to age at onset of Parkinson’s disease (PD) is still unclear. We aimed to investigate the 10-year efficacy and safety of subthalamic (STN) DBS in advanced patients with young-onset PD (YOPD) compared with those with late-onset PD (LOPD).

**Methods:** We retrospectively analyzed 10-year follow-up clinical data of consecutive 51 advanced patients with PD who underwent STN DBS between March 1, 2002 and March 31, 2007 at Asan Medical Center, Seoul, Korea. Twenty-seven patients were excluded during 10-year follow-up period because of death, diagnosis of Parkinson-plus syndrome, and serious adverse effects. Hence, twenty-four patients were finally analyzed in this study. YOPD (N=13) was defined as a patient who developed the first motor symptoms before age 40, and LOPD (N=11) was defined as having age at onset after age 40. Motor symptoms of PD was primarily assessed using Unified Parkinson’s Disease Rating Scale (UPDRS) scores.

**Results:** At baseline, there was no significant difference of baseline clinical motor and non-motor features between two groups. At 10 years after DBS surgery, the reduction of levodopa equivalent dose (LED) from baseline and levodopa-induced dyskinesia (LID) score (Unified Dyskinesia Rating scale items 16-22) were significantly lower in YOPD compared with LOPD (P = 0.023 and P = 0.013, respectively). The improvement of LID remained significant until 5 years after DBS surgery in both groups, but LID severity had significantly increased in LOPD at 10 years after DBS surgery. The improvement of total UPDRS scores, the presence of visual hallucination, and adverse effects were not different between two groups.

**Conclusions:** This study shows that STN DBS showed higher effect on LED reduction in LOPD and LID improvement in YOPD at 10 years after DBS surgery. These results may have clinical implications for tailored application of STN DBS in patients with PD.
OP-01-11
Bilateral GPi DBS improves medically intractable postural and kinetic tremor in patients with Parkinson’s disease

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Patients with Parkinson’s disease (PD) may present with postural and kinetic tremors, the phenotype of which is indistinguishable from essential tremor. Such ET-type tremor in PD patients may occur unilaterally or bilaterally, and in the arm(s), leg(s), or both. It can be very disturbing as it often does not respond to medications for PD and tremors. Thus, the patients with disabling tremor are often referred to neurosurgery for deep brain stimulation (DBS). If the tremor is unilateral or markedly asymmetric, unilateral DBS to the Vim or PSA will resolve the problem. However, if the tremor is bilateral, DBS is performed only unilaterally for the fear of complications of bilateral DBS in Vim or PSA.

Methods: We performed bilateral GPi DBS for 11 PD patients with medically intractable ET-type tremor (4M 7F, age= 66.7 ±6.48 years, mean ±SD). Severity of Parkinsonism and tremor were assessed using UPDRS III and TETRUS respectively at off and on states before DBS and 6 months to one year after DBS. PET scans were performed to all patients before DBS using [18F]FDG and [18F]FP-CIT (ligand for DAT). We compared the binding of [18F]FP-CIT in the globus pallidus between PD patients with marked postural and kinetic tremor and those without tremor.

Results: Before DBS, L-dopa improved parkinsonism, but not the postural and kinetic tremor. After DBS, the postural and kinetic tremor was improved significantly on both sides. The patients’ states were assessed with clinical scales and recorded with video. The analysis of FDG uptake and FP-CIT binding in the basal ganglia will be presented at the congress.

Conclusions: Bilateral GPi DBS improved postural and kinetic tremor in PD patients. Analysis of FP-CIT and FDG PET will provide further insight in the mechanisms of ET-like tremor in PD patients.

OP-01-12
Non-motor symptoms in dystonia patients and influence of deep brain stimulation and botulinum toxin on them

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Objectives: Our aim was to see the prevalence of some non-motor symptoms (pain, cognition, anxiety, depression, sleep problems) in dystonia patients and effect of Deep brain stimulation (DBS) and Botulinum toxin on them.

Background: Nonmotor problems in dystonia patients are often neglected and untreated but affect significantly quality of life.

Methods: We conducted investigation with anamnesis and treatments’ data, Pittsburgh Sleep Quality Index (PSQI), Visual Analogue Scale, McGill questionnaire and Hospital Anxiety and Depression Scale (HADS), Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE). The study involved
randomly selected 100 dystonia patients that came to our out-patients clinic (30 generalized dystonia, 35 cervical dystonia and 35 facial dystonia: blepharospasm, oromandibular dystonia and hemifacial spasm). We did the basal testing before treatment and another investigation after 6 months. 26 of them (25 with generalized dystonia and 1 with cervical dystonia) were treated with DBS and the others with Botulinum toxin and/or medications. 

**Results:** After 6 months the pain was reduced in group treated with Botulinum toxin (from 72% to 20%) but sleep problems were without significant changes (45% vrs 43%). After DBS we observed significant decrease in frequency concerning sleep problems (from 80 % to 10% of patients) and pain (from 90% to 25%) (p< 0.05). The cognition was without any change in all patients (16% vrs 17%). Depression was improved in groups with generalized dystonia and cervical dystonia patients, especially in subgroup treated with DBS.

**Conclusions:** Awareness of non-motor symptoms’ presence is important in management of dystonia patients. DBS helps in relieving of the pain, sleep and mood problems and Botulinum toxin relieves pain and depression in some patients with cervical dystonia. The uniform non-motor symptoms scale for dystonia patients is needed for better outcome evaluation of our dystonia patients.

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**OP-01-13**

**The subthalamic nucleus activity at gait initiation in Parkinson’s disease**


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**Background:** Start hesitation or gait initiation (GI) failure, the inability to successfully transition from a standing position to walking, is a common motor impairment in patients with Parkinson’s disease (PD). GI is a highly challenging task requiring coordinated multiple muscles activations (Anticipatory Postural Adjustments, APAs) that are essential to control the body balance and to generate the propulsive forces necessary to start walking.

The subthalamic nucleus (STN) is a crucial node of the supraspinal locomotor network and can play role in correct APAs execution, but direct evidence is still lacking.

**Methods:** We recruited nine PD patients implanted with the Activa PC+S system (Medtronic, PLC), a deep brain stimulation device that allows on-demand recordings of the Local Field Potentials (LFPs) in the STN months after surgery from the chronically implanted electrodes. APAs were described by kinematic (Smart DX, BTS), dynamic (Kistler force plates) and EMG measurements (FREEEMG 1000, BTS) of the tibialis anterior, soleus and gastrocnemius muscles, bilaterally.

All subjects completed at least three GI trials after overnight suspension of all dopaminergic drugs (medication off state) and one hour after pausing the electrical stimulation (stimulation off state).

**Results:** The main finding was increased beta-oscillations (13-35Hz) in the STN contralateral to the stance limb at APAs onset.
**Conclusion:** We showed a direct involvement of the STN during GI possibly related to the weight support activity of the stance limb. This result advances our understanding of the supraspinal neural mechanism of GI in PD patients and fosters the detection of biomarkers of complex motor tasks towards the development of new treatments such as adaptive deep brain stimulation.

**OP-01-14**

**Long-term clinical outcome of deep brain stimulation for PKAN syndrome**

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**Objective:** To describe long-term clinical outcome after deep brain stimulation (DBS) surgery in a series of patients suffering from PKAN syndrome. PKAN syndrome is an autosomal recessive neurodegenerative disorder secondary to PANK2 gene mutations, manifesting by severe generalized dystonia and spasticity. No pharmacological treatment has yet been approved for this condition. To date, only short-term therapeutic outcome of globus pallidus internus (GPi) and subthalamic (STN) nucleus DBS has been published.

**Methods:** We conducted a retrospective systematic review of patients with documented diagnosis of PKAN syndrome treated with DBS in our center. Clinical outcome was measured with BFMDRS. All patients were implanted with MRI-guided targeting without microelectrode recordings.

**Results:** 18 patients corresponded to inclusion criteria: 5 adults and 13 children (M: F=10:8). Age at the moment of surgery was 28.6±7 years for adults and 11.9±2.6 for children. Median follow-up was 10 years. Disease onset older than 8yr was associated with a better clinical outcome. All patients underwent GPi DBS; several patients were implanted with supplementary ‘rescue leads’ in the follow-up (thalamic Vim/Vop target (n=4), second pair of GPi leads (n=3) and STN (n=4)). Four patients were treated with intrathecal baclofen pump. Six patients developed status dystonicus in the follow-up: GPi DBS led to sustained response in this clinical context for 3 patients. STN DBS showed promising short-term results in 3 patients with severe dystonia. Five subjects required tube feeding for severe dysphagia. Several device-related adverse events complicated postoperative management: lead fracture or dysfunction (7 patients). Five patients died despite intensive care unit management and advanced surgical therapies (2.8±2 yr after surgery).

**Conclusions:** GPi DBS was effective to treat status dystonicus, axial dystonia and dysphagia. Early disease onset (< 8yr) and pallidal atrophy were poor outcome predictors. Device dysfunction or fracture led to rebound worsening with possible status dystonicus in several patients.
Finding ways to improve axial symptoms in patients with chronic STN DBS for Parkinson’s disease

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Objective: To report the outcome of a DBS programming paradigm (PP) aimed at reducing gait, balance and speech impairment after prolonged STN DBS.

Background: DBS of the STN using high frequency (130-185Hz) stimulation (HFS) is more effective for appendicular than axial symptoms. Low frequency stimulation (LFS) of the STN may reduce gait/balance impairment, but often results in worsening of appendicular symptoms. Medtronic DBS offers interleaving that allows delivery of two programs on each DBS lead. We used this to create a PP with a combination of low and high frequencies.

Methods: The novel PP (interlink-interleave, IL-IL) consists of two overlapping LFS programs on each DBS lead, with the overlapping area focused around the optimal contact. This area receives HFS aimed at controlling appendicular symptoms. The non-overlapping areas receives LFS potentially reducing gait/balance impairment and stimulation-induced-dysarthria. The Clinical-Global-Impression-of-Change (CGI-C) was completed retrospectively based on patient/caregiver feedback in patients remaining on IL-IL (at 3 months and current time).

Results: Seventy-six patients were programmed on IL-IL from optimized HFS settings. Fifty-five (72%) of patients remained on IL-IL after an average of 18 months. Patients were separated into three groups (gait, dysarthria, appendicular symptom control) based on chief complaint with some belonging to more than one group. The median (range) CGI-C for gait was 2(1-5) at 3-months and 3(1-4) currently, for dysarthria was 4(1-4) at 3-months and 4(1-5) currently, and for incomplete appendicular control was 2(1-3) at 3-months and 2(1-3) currently. Nine (12%) patients returned to conventional HFS after 5 days because of incomplete appendicular symptom control. Twelve (16%) patients have not returned for follow up.

Conclusion: A significant number of patients chose to remain on IL-IL because of subjective improvements in balance/gait or dysarthria. Formal assessment with objective/quantitative outcome measures is currently ongoing and preliminary data (n=16) will be presented.
OP-01-16

Battery longevity of neurostimulators in Parkinson-disease: A historic cohort study

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Objectives: Deep brain stimulation (DBS) of the sub-thalamic nucleus (STN) is a well-established treatment for motor complications in Parkinson’s disease (PD). Since 2012, the non-rechargeable dual channel neurostimulator available in France seems to have a shorter battery-life longevity compared to the previous model.

The aim of this study is to evaluate battery-life longevity of the older and the more recent neurostimulators and to explore factors associated to battery life variations.

Methods: We retrospectively studied our cohort of PD patients who underwent STN-DBS between 1987 and 2017. We collected data concerning neurostimulators replacements and parameters. We compared the overall survival of the first available one, Kinetra® and the actual one, Activa-PC® (Medtronic Inc.) and estimated factors that impact on battery-life longevity through a Cox logistic regression.

Results: 364 PD patients received a total of 654 DBS-STN neurostimulators: 317 Kinetra® (48.5%) and 337 Activa-PC® (51.5%). The survival analysis, using the Kaplan-Meier estimator, showed a difference between the curves of the two devices (Log-rank test; p< 0.001). The median survival of an Activa-PC® is 1666 days vs. 2379 days for the Kinetra®.

After adjustment, according to the multivariate analysis, the main factors associated to battery lifetime were the neurostimulator type; a high-ranking pose, the total electrical energy delivered (TEED) and the male sex.

Conclusions: Kinetra® neurostimulator lifetime was 2.5 years longer than the Activa-PC®. The type of the device, the high TEED and the high ranking pose mostly influence battery-life longevity. These results have medical and socio-economic implications as the survival of PD patients with DBS increases over years.
Suicide after STN-DBS in Parkinson’s disease: who, when and how to prevent?

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Objectives:
1) To determine the postoperative attempted and completed suicide rates after subthalamic nucleus deep brain stimulation (STN-DBS) in a single center cohort;
2) To determine factors associated with attempted and completed suicide.

Methods: We retrospectively included all Parkinson’s disease (PD) patients who underwent bilateral STN-DBS surgery at the Grenoble University Hospital between 1993 and 2016. Clinical data were collected from medical records. Detailed preoperative and postoperative neuropsychological evaluations, including frontal and Beck depression inventory (BDI) scores, were gathered. For each patient who committed or attempted suicide, two PD patients with STN-DBS without any suicidal behaviors were matched for age (±1 years), sex and year of surgery (±2 years).

Results: A total of 534 PD patients were included (337 males). Completed and attempted suicide percentages were 0.75% (4/534) and 4.11% (22/534), respectively. Observed suicide rate in the first postoperative year (187.20/100000/year, 1/534) was higher than the expected National Observatory on Suicide Risks rate adjusted for age and gender (Standardized Mortality Ratio: SMR=8.1). This rate remained similar over the second and third postoperative year. Comparing the 26 patients completing/attempting suicide with 52 controls, the first group showed:
1) more frequent previous history of suicidal ideation/suicide attempts and psychotic symptoms;
2) higher percentage of familiar psychiatric history (addiction, depression and suicide); 3) higher psychiatric medication use both in the preoperative and postoperative phase;
4) higher preoperative frontal and BDI scores at neuropsychological evaluations.

Conclusions: Suicide and suicide attempts can occur after STN-DBS, especially during the first 3 years, in patients with previous history of psychiatric issues and higher frontal scores. A carefully multidisciplinary assessment and long-term follow-up are recommended to recognize and treat this potentially preventable risk for mortality.
OP-02-02
Frequencies, genetic, clinical and radiologic characterization of spinocerebellar ataxia in Korea
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Background: Spinocerebellar ataxia (SCA) is an autosomal dominant cerebellar ataxia with more than 40 kinds of causative genes. Depending on ethnic background of the patients, frequencies and clinical manifestations of each subtype are various among different ethnic groups. We aimed to describe the relative frequencies of SCAs and compare genetic, clinical and radiologic features of patients with genetically confirmed SCAs in Korean population.

Method: Among the patients who had been seen between November 1994 and February 2016 in our center, 152 patients who had been genetically confirmed as SCA were included. We retrospectively reviewed medical records and organized data to figure out characteristics, including age of onset, presence of family history, the number of trinucleotide repeats, clinical features and radiologic findings.

Result: Frequency analysis revealed that SCA3 was the most prevalent subtype followed by SCA2 and SCA6. 58 patients (38.16%) denied definite family history. There was a prominent inverse relationship between the age of onset and CAG repeat length in SCA7 (r= -0.928), 1 (r= -0.767), 2 (r= -0.637), 6 (r= -0.621) and 3 (r= -0.527). Heterogeneous clinical features were observed with different frequencies depending on subtypes. Hot cross bun signs were the most prominent in SCA2 and middle cerebellar peduncle signs in SCA7.

Conclusion: We explored the unique distribution of SCA subtypes in Korean population. Furthermore, SCAs of Korean population manifested various clinical and radiologic characteristics depending on its subtype. Characterization of these features would help to narrow the scope of candidate genes and eventually lead to cost effective and accurate diagnosis.
Subcortical brain areas correlate genetic characteristics in spinocerebellar ataxia type 2 patients

**Objective:** Spinocerebellar ataxia (SCA) type 2 is the autosomal dominant neurodegenerative disorder having characteristic clinical manifestation of slow saccade along with gait imbalance, ophthalmoplegia, dysarthria, pyramidal and extrapyramidal signs. This clinical dysfunction is the outcome of unstable trinucleotide (CAG) repeat expansion. This in turn, is the cause of neuronal loss in the cerebellum and brain stem as well as degeneration of spinocerebellar tracts as per literature reported. We have also seen the subcortical degeneration beyond cerebellum. Therefore, the present study was planned to know the correlation among the degree of atrophy in subcortical brain areas and genetic characteristics in SCA2 patients.

**Methods:** MRI was performed by using a 3T scanner (Philips, Achieva) to obtain 3D T1-weighted scans of the whole brain and analyzed by FreeSurfer (version 5.3) software in the genetically proven SCA2 (n = 25, age = 33.6 ± 10.7 yrs) patients. MRI parameters used in T1-weighted scans were: Voxel size = 0.6×0.6×1, FOV = 240×240×180 and flip angle = 8°. GeneScan confirmed the average CAG repeats (42.4± 3.9) of SCA2 patients. Clinical severity was assessed by International Cooperative Ataxia Rating Scale (ICARS) in the same patient group. On accordance to the data distribution, Pearson's correlation (for parametric data) and Spearman's rank correlation (for nonparametric data) analyses were done between brain areas and ICARS score and CAG repeats of SCA2 patients by using Graph-Pad Prism Version 5.00 for Windows (GraphPad Software, Inc., USA).

**Results:** In SCA2 patients, CAG repeats showed a significant inverse correlation with subcortical volume of left cerebellar white matter (r = -0.432, p = 0.031), right cerebellar white matter (r = -0.470, p = 0.018), left thalamus (r = -0.506, p = 0.010), right thalamus (r = -0.517, p = 0.008), left hippocampus (r = -0.437, p = 0.029) and right ventral diencephalon (r = -0.439, p = 0.028). Furthermore, CAG repeats were also negatively associated with age (r = -0.752, p < 0.001) and age of onset (r = -0.759, p < 0.001) in the patients. Interestingly, CAG repeats were significantly correlated with clinical severity (r = 0.408, p = 0.043) of SCA2 patients.

**Conclusions:** It has been found a significant correlation between the genetic characteristics and degree of atrophy in cerebellum (noted as the area of motor control) along with certain subcortical brain areas. Also, the length of CAG repeat allele showed a good correlation with the clinical dysfunction in SCA2 patients.
Clinical and genetic aspects of Huntington’s disease in 11 Malian families: The largest cohort genetically confirmed in Sub-Saharan Africa

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Background: Huntington’s disease (HD) is an autosomal dominant disorder characterized by involuntary movements, dementia and behavior problems. Only few studies has been reported in Africa that has the lowest prevalence in the world.

Objective: Describe the clinical and genetic aspects of Huntington’s disease in the Malian population.

Methods: Over a three-year period, patient with HD phenotype with or without family history were enrolled. They were seen in our clinic or referred by other neurologists. After giving their consent, patients were examined and laboratory evaluations were performed. DNA was extracted for genetic testing.

Results: Fourteen patients from 11 families with HD phenotype were seen. A familial history of the disease was found in 85.7% cases, 14.3% of cases being sporadic. Maternal transmission was the most common with 50% of cases. The mean age of onset was 47.4 years (34-62 years). Choreic movements were the most predominant symptoms, found in 100% of our patients, followed by cognitive impairment and psychiatric disorders with 71.4% and 50%, respectively. Genetic testing identified CAG repeat in the IT15 gene in 7 families including 10 patients. The average number of CAG repeats was 43.7 with extremes of 42 and 45. Genetic testing is ongoing in four families.

Conclusion: Our study showed that HD is not so rare in sub-saharan Africa, and the increasing access to genetic testing could elucidate many other cases. Future haplotype studies may shed light in origin of the African mutation.
**Objective:** The efficacy and safety of daxibotulinumtoxinA for injection (DAXI), a 150 kDa botulinum neurotoxin A (BoNTA) formulated with a proprietary stabilizing excipient RTP004, in adults with cervical dystonia (CD) have been described. This report focuses on the immunogenicity of DAXI.

**Methods:** BoNT-naïve or previously treated adults with moderate to severe CD were enrolled and given one treatment of DAXI. Neutralizing antibody (nAB) status was determined before injection at Baseline, Week 4 and Week 24 using a high sensitivity ELISA screening assay, a high specificity ELISA confirmation assay with AB titer quantification and the lethality assay for final confirmation (the mouse protection assay).

**Results:** 34 subjects (mean age: 56 years; 76% female; 67% [20/34] BoNT-naïve and 41% [14/34] were previously treated) enrolled in the study. At baseline, the mean Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-Total score was 44; mean DAXI dose administered (range): 244 (100 - 450) units. Antibody screen on 106 serum samples (Baseline, Week 4, and Week 24): 26% screened positive; 5% confirmed positive; only 3 samples (Baseline, Week 4, and Week 24) from 1 subject had nAB, confirmed by the lethality assay. A subject previously treated with Botox 650 U with a nAB titer of 2 at baseline was given one treatment of DAXI 450 U, and the titers later doubled at Week 4 and Week 24. This subject’s response to DAXI (reduction in TWSTRS-Total score from baseline) was -16.8 (-32%) at Week 4 and -10.8 (-20%) at Week 24. This subject was the only of 14 subjects previously treated with BoNT who had an increase in nAB titer after treatment. Overall, no BoNT-naïve subjects (0/20) developed nAB to DAXI after one treatment.

**Conclusions:** The low rate of DAXI immunogenicity is comparable to other BoNTA products. Longer-term (>2 years) studies are needed to confirm these findings.
**Intero- and exteroceptive mirroring and overflow movements are useful in assessing writer’s cramp**

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**Objective:** Writer’s cramp (involuntary, sustained muscle contractions causing abnormal writing postures) are associated with contralateral overflow movements and mirror movements (i.e. stimulated by the physical task of writing). Both phenomena may distinguish between primary dystonic muscles and secondary compensatory movements of the hand whilst writing, and help in selecting muscles to inject with botulinum toxin. The “external”, physical act of writing to trigger WC is defined as exteroceptive stimuli, whereas “internal” motor imagery, i.e. the imagined task of writing to stimulate dystonic movements, are called interoceptive stimuli. We examined the effects of exteroceptive and interoceptive stimuli on dystonic movements in patients with Writer’s Cramp (WC).

**Methods:** We retrospectively assessed 22 patients with primary WC. They were assessed clinically at rest and on extero- and interoceptive stimuli, writing with both dystonic and non-dystonic hands. Primary dystonic posturing and the presence of contralateral overflow and mirror movements, were analysed.

**Results:** With exteroceptive stimuli, 8 patients had contralateral overflow movements whilst 19 had mirror movements. With the interoceptive stimulus of imagined writing with the affected hand, 15 patients had ipsilateral overflow movements, whilst 5 had contralateral overflow movements. Interoceptive movements only occurred in those with exteroceptive contralateral overflow or mirror movements. Interoceptive movements were consistent with those of exteroceptive movements but were of smaller amplitudes and less obvious.

**Conclusions:** Imagined writing as a stimulus for dystonic movements is a significant and common phenomenon in writer’s cramp. We believe that a combination of interoceptive and exteroceptive stimuli should be used to screen for dystonic movements in the assessment of writer’s cramp to aid us in selecting the primary dystonic muscles for injection with botulinum toxin as treatment. Future studies, which include patient response to botulinum injection identified by interoceptive/exteroceptive movements and presence of interoceptive geste antagoniste, are necessary to add validity to our findings.

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<th>Ipsilateral Overflow</th>
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<th>Mirror Movements</th>
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<tr>
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<td>Interoceptive Stimuli</td>
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*[Table 1: Frequency of dystonic movements using exteroceptive and interoceptive stimuli for 22 patients with Writer’s Cramp]*
Abstracts

OP-02-08
Hyperkinetic movement disorders induced by mirtazapine: unusual case report and clinical analysis of reported cases
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Background: Hyperkinetic movement disorders caused by mirtazapine are very rarely reported, and involuntary severe cervical and truncal dystonia as an initial manifestation of mirtazapine-induced hyperkinetic movement disorder have not yet been reported. This study aimed to report an unusual case and to investigate the clinical pattern of mirtazapine-induced hyperkinetic movement disorder.

Methods: We present a patient with involuntary severe cervical and truncal dystonia as an initial manifestation of mirtazapine-induced hyperkinetic movement disorders. Additionally, we review previously reported cases and analyze the clinical pattern of mirtazapine-induced hyperkinetic movement disorders.

Results: Among 12 cases including our case, the main features of hyperkinetic movement symptoms induced by mirtazapine are akathisia (n=5, 42%) and dystonia (n=4, 33%). The other movement symptoms were dyskinesia (n=2, 17%) and periodic limb movement disorder (PLMD)-like nocturnal movements (n=1, 8%). Major associated conditions were older patients with depression or previous medication history of multiple neuropsychiatric drugs.

Conclusions: The results of this clinically investigative study may provide support for the diagnosis of mirtazapine-induced hyperkinetic movement disorders. In addition, if there are hyperkinetic movement symptoms in older depressive patients taking psychiatric medications, including mirtazapine, a diagnosis of drug-induced hyperkinetic movement disorder caused by mirtazapine should be considered, and cessation of mirtazapine should be implemented as the best treatment of choice.

OP-02-09
Deep brain stimulation parameters for dystonia: A systematic review
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Introduction: Programming of globus pallidus pars interna (GPI) deep brain stimulation (DBS) systems for dystonia is complex because clinical benefits are often gradual. Some groups have advocated starting DBS with higher electrical parameters, whereas others have suggested the opposite. This variability in programming, even within each dystonia subtype, makes it challenging to compare outcomes and program the generators. To determine how variable DBS for dystonia stimulation parameters are, we performed a systematic literature review.

Methods: A comprehensive systematic literature search for GPI DBS stimulation parameters used in dystonia was performed in PubMed/Medline, Embase and Cochrane databases.

Results: Of 813 publications retrieved from individual search engines, 593 were eligible for review and 401 publications were excluded. Data were extracted from 192 publications representing 1505 patients and 2964 electrodes. Stimulation amplitude averaged 3.3 V ± 0.6 V and frequency 131 Hz ± 5 Hz. Three different common pulse widths were identified at 112 ± 31 µs, 203 ± 22 µs, and 446 ± 8 µs.
**Conclusions:** Despite anecdotal reports using low frequencies or pulse widths and variability in DBS stimulation parameters required to treat dystonia, there is consistency in amplitude and frequencies utilized. Some dystonia subtypes may improve with specific pulse widths. This review emphasizes the importance of complete data reporting in the literature and suggests that large prospective controlled blinded studies and international registries are needed to understand and optimize DBS settings for dystonia.

**OP-02-10**

**Approach to health care shaped by Generational Expectations (the AGE study): Patients’ preferences for healthcare providers**

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**Objective:** To determine the preferences of each generational group (i.e. Traditionalists, Baby Boomers, Generation Xers, Millenials) regarding their healthcare provider in a movement disorder clinic.

**Methods:** In this cross-sectional study, we recruited 230 patients who filled a survey with demographic information and healthcare preferences questions. Medical encounter scenarios were used to assess the patient’s view on clinician’s time management and style of care. Descriptive statistics were calculated. A proportional odds model was applied to determine the differences in odds of agreement among generational groups.

**Results:** The sample included 53% female and 92% white patients with an average age of 57.4 (SD 18.2). Regardless of the generation, most patients responded neutrally about their preferences for their clinician’s gender, attire, age, and the presence of a foreign accent. All generations, especially Generation Xers saw their doctor as a friend and an advocate, and also as a figure of authority. Most patients preferred to be included in the clinical decision making. Millennials, Generation Xers and Traditionalists were more likely to prefer a clinician of the same gender and of an older age. All generations, except for Millennials, reported no preferences towards the presence a foreign accent. White coat use was mostly preferred by Traditionalists. Baby Boomers remained mostly neutral when indicating their clinician preferences. When given choices of different case scenarios, most patients, regardless of the generational group, would rather have a “gentle and thorough” clinician as opposed to one with a more “direct and confident” approach.

**Conclusion:** Regardless of the generation, patients prefer a gentle and through clinician who includes them in the clinical decision making. Traditionalist and Milennials tend to have stronger opinions regarding gender, age, use of white coat, or presence of a foreign accent in their doctors. Baby Boomers appeared to be have more flexible preferences regarding their doctor.
OP-02-11
Effects of long-term valbenazine on tardive dyskinesia and patient-reported outcomes: Results from the KINECT 4 study
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Objective: To explore the long-term effects of once-daily valbenazine on tardive dyskinesia (TD).

Background: Valbenazine was approved for TD based on several short-term placebo-controlled trials, a blinded extension study, and the long-term KINECT 4 (NCT02405091) study, presented here.

Methods: Adults with TD received 48 weeks of open-label treatment with valbenazine. Dosing was initiated at 40 mg, with escalation to 80 mg at Week 4 based on efficacy (inadequate/insufficient clinical response per investigator judgment) and tolerability. Dose reduction back to 40 mg was allowed in participants who could not tolerate the 80 mg dose. Change from baseline (CFB) in the Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1-7) was used to assess changes in TD. Additional efficacy assessments included the Patient Global Impression of Change (PGIC) and Clinical Global Impression of Change-TD (CGI-TD) scales. Standard safety methods were applied, including treatment-emergent adverse event (TEAE) reporting.

Results: In the safety population (N=163), 107 participants were escalated to 80 mg and 45 had no dose escalation; 11 were escalated to 80 mg but later required reduction to 40 mg. Mean CFB to Week 48 in AIMS total score indicated TD improvements: 80 mg, -11.0; 40 mg, -10.2. At Week 48, >75% of participants had a PGIC score ≤2 (much improved or very much improved): 80 mg, 89.2%; 40 mg, 90.0%. Mean CGI-TD scores at Week 48 (80 mg, 1.6; 40 mg, 1.7) indicated clinically meaningful long-term improvement for all dose groups. Less than 15% of all participants had a serious TEAE (12.9%) or TEAE leading to discontinuation (14.7%).

Conclusions: Consistent with previous trials, substantial clinician- and patient-reported improvements were observed in adults with TD receiving once-daily valbenazine for 48 weeks. Valbenazine was generally well tolerated and no safety signals were detected.
The neural mechanism of freezing of gait in patients with Parkinson’s disease

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Background: Freezing of gait (FOG) is a common symptom of Parkinson’s disease (PD) that causes paroxysmal inability of effective stepping. FOG severely worsens patients’ quality of life, triggering falls and hospitalization. The treatment of FOG is challenging and limited by its unclear pathophysiology. Recent molecular brain imaging studies showed a supraspinal locomotor circuit impairment in PD patients with FOG, but did not describe the functional alterations causing it. We envisioned a derangement of the locomotor network oscillation dynamics, a mechanism of brain coordination, during gait freezing in patients with PD.

Methods: We investigated the coupling between the cortex and the subthalamic nucleus (STN), two main nodes of the locomotor network, during (effective) walking and gait freezing in three freely-moving PD patients with deep brain stimulation (DBS). Recording were performed with a portable 64-channels EEG system (MOVE, BrainAmp) and novel DBS devices that allow on-demand measurements months after surgery (Activa PC+S®, Medtronic PLC or AlphaDBS, Newronika Srl). Neurophysiological recordings were combined with kinematic and molecular brain imaging studies.

Results: Cortices and STN coupled in low-frequency band (θ-α range, 4-13Hz) during (effective) walking. Gait freezing was selectively characterized by the suppression of this low-frequency coupling in favour of inter-hemispheric subthalamic β-coupling (13-35Hz). This switch anticipated the occurrence of FOG and it was restored with the recovery of an effective walking pattern. This cortical-subthalamic derangement was sustained by a loss of striatal dopaminergic innervation.

Conclusion: These findings show for the first time the neural mechanism underpinning FOG in PD. The cortical-subcortical communication derangement during FOG can prevent the update of the ongoing gait pattern to environmental needs. These results foster the management of FOG with neuromodulation techniques, possibly adaptive DBS.
Session III: Parkinson Disease

OP-03-01
Nilotinib increases dopamine metabolism and reduces oligomeric: total alpha-synuclein ratio in Parkinson’s disease

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Background: Our pre-clinical and open label phase I data indicate that the tyrosine kinase inhibitor (TKI) Nilotinib may improve motor symptoms and cognition, reverse dopamine loss and reduce brain alpha-synuclein.

Methods: This is a phase II, open label, random single dose (RSD) study in mid-stage PD patients with mild cognitive impairment (MCI) to evaluate the effects of Nilotinib on disease biomarkers of PD. Cerebrospinal fluid (CSF) from 75 patients was examined to assess changes in the levels of CSF alpha-synuclein and the dopamine metabolite homovanillic acid (HVA) and 3,4-Dihydroxyphenylacetic acid DOPAC as primary disease biomarkers. A total of 15 patients in each of 5 randomized study groups, including placebo, 150mg, 200mg, 300mg and 400mg Nilotinib had lumbar punctures at 1-4 hours after a single time oral drug administration.

Results: CSF biomarkers analyses showed a statistically significant increase in the level of CSF HVA and DOPAC. No change was detected in total levels of CSF total alpha-synuclein, but lower dose (150mg and 200mg) resulted in a significant decrease of oligomeric;total CSF alpha-synuclein. Further analysis will be performed to compare plasma and CSF levels of these biomarkers between this single time administration and 52-week treatment.

Conclusions: These data suggest that a single time oral administration of Nilotinib may increase brain dopamine levels and metabolism. These results suggest Nilotinib, in a dose dependent manner, may have a symptomatic effect through modulation of brain dopamine levels. Additionally, the significant reduction of oligomeric alpha-synuclein, which is expected to increase in the CSF of PD patients as the disease progresses, suggests that Nilotinib may reduce misfolded alpha-synuclein accumulation and have a long-term disease modifying effect. Importantly, the dose response of oligomeric alpha-synuclein and HVA changes to nilotinib suggests that the dose administered may depend on the stage of disease to potentially halt PD progression.
**OP-03-02**

**Clinical subtypes of excessive daytime sleepiness in Parkinson’s disease**

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**Objective:** To examine reasons and associated clinical features of excessive daytime sleepiness (EDS) in patients with Parkinson’s disease (PD).

**Methods:** PD patients [N=63 (35M); 63.8±6.3 years old; 4.6±3.2 (0.3-12) years disease duration, HY range 1-3, mean MoCA score 25.7±1.9 (22-29)] underwent clinical evaluation including Hoehn and Yahr scale, MDS-UPDRS, the scale of autonomic dysfunction in PD, Epworth Sleepiness Scale (ESS), PD sleep scale - 2 (PDSS-2). 33 patients with EDS underwent polysomnography and multiple sleep latency test (MSLT).

**Results:** 68.3% of patients had EDS (PD-EDS). There were male predominance (29M versus 14M, p=0.016), longer therapy duration (4.1±3.3 versus 2.1±2.7 years, p=0.01) and higher levodopa equivalent dose (LED) (621.8±323.2 versus 451.0±199.8 mg, p=0.03) in PD-EDS.

PD-EDS were divided into groups by results of sleep investigation: 1 - pure EDS (n=17), 2 - moderate and severe obstructive sleep apnea syndrome (OSAS) (n=8), 3 - patients with negative MSLT and subjective sleepiness due to orthostatic hypotension (OH) and/or postprandial hypotension (PH) (n=8). The highest ESS scores were in group 2 (14.2±3.7) in comparison with group 1 (10.4±4.1, p=0.02) and group 3 (10.4±3.9, p>0.05). Patients in group 2 had the highest BMI - 33.7±5.3 kg/m² in comparison with group 1 - 27.1±3.3 kg/m² and group 3 - 23.1±2.3 kg/m² (p<0.05). Group 3 had more prominent autonomic dysfunction in comparison with group 1 (p=0.0003), OH was more frequent in this group (p<0.025).

**Conclusions:** EDS was found in 68% of patients. Risk factors for EDS were male sex, therapy duration, high LED and BMI. Pure EDS was found in 51%, OSAS lead to EDS in 24%. Complaints about EDS were related with cardiovascular dysfunction in 24%. High BMI and ESS score were strongly associated with OSAS. OH, high score of the scale of autonomic dysfunction, low BMI were prognostic factors for subjective sleepiness.

**OP-03-03**

**Neuroprotective effects of Ethnodyn Neuro® (SNC-1), a natural product used in ayurvedic traditional medicine, on in vitro models of Parkinson’s disease**

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Motor symptoms in Parkinson’s disease are caused by the loss of the dopaminergic signal in the substantia nigra. The degeneration of dopaminergic neurons is caused by mitochondrial impairments and alpha-synuclein aggregation, which are pathological hallmarks in Parkinson’s disease.
Traditional medicine, based on natural products, is a source of new therapeutic compounds with antioxidant, neuroprotective and anti-inflammatory properties. SNC-1 is a mixture of processed extracts of three plants (Withania somnifera, Emblica officinalis, and Bacopa monnieri) used in ayurvedic medicine. Several lines of evidence suggest that SNC-1 could exert neuroprotective effects in neurodegenerative diseases, such as Parkinson’s disease.

Here, we aimed to study the effects of SNC-1 on two distinct in vitro models of Parkinson’s disease, that recapitulate an alpha-synuclein proteinopathy and a mitochondrial stress. Mesencephalic neurons were intoxicated with oligomers of alpha-synuclein (250 nM, 48 hours) or with the mitochondrial toxin MPP+ (4 μM, 48 hours). Neuronal survival and neurite network of dopaminergic neurons were investigated by immunocytochemistry. Tyrosine hydroxylase synthetises L-DOPA, the precursor of dopamine. The expression level of tyrosine hydroxylase was assessed by quantitative PCR. Our results show that SNC-1 protected dopaminergic neurons from the cell death induced by MPP+ or by alpha-synuclein, on a dose-dependent manner. SNC-1 was also able to promote the expression of tyrosine hydroxylase.

Altogether, these results support that SNC-1 represents a promising therapeutic agent for Parkinson’s disease.

OP-03-04
Propensity of Mucuna Pruriens to offset rotenone-induced biochemical, behavioral and oxidative dysfunctions in mice: Implications for Parkinson’s disease
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Aim & Objectives: The present study was designed in order to explore the possible anti-Parkinson’s potential of methanolic extract of Mucuna Pruriens Seeds (MPM). The neuroprotective role of MPM was explored in rotenone induced behavioural, oxidative and mitochondrial dysfunction in mice model of Parkinson’s disease.

Background: Mucuna Pruriens, is a natural polyphenolic, powerful bioactive compounds used word wide. They exhibited numerous biological and pharmacological activities including potent antioxidant, cardiovascular disease, anticancer, anti-inflammatory effects and neurodegenerative disorders in cell cultures and animal models.

Methods: Chronic administration of rotenone (1 mg/kg i.p.) for a period of three weeks significantly impaired behavioural paradigm (Memory, learning and locomotor activity), oxidative defence (Decreased activity of superoxide dismutase, catalase and reduced glutathione level) and mitochondrial Complex-II-Succinate Dehydrogenase (SDH), Complex III- MTT (3- (4,5-dimethylthiazol-2-yl)-2,5-diphenyl-H-tetrazolium bromide) enzymes activities as compared to normal control group in the brain of mice.

Results: Three weeks of MPM (25, 50 and 100 mg/kg, p.o) treatment significantly improved behaviour parameters (P < 0.001) oxidative damage (P < 0.001) and mitochondrial enzyme complex activities (< 0.05, P < 0.01, P < 0.001) as compared to negative control (rotenone treated) group. We found that MPM restored motor deficits and enhanced the activities of antioxidant enzymes suggesting its antioxidant and neuroprotective potential in vivo.
**Conclusion:** Collectively, these data suggest that *Mucuna Pruriens* therapy may provide neuroprotection primarily by the restoration effect on antioxidant defence and mitochondrial function which lead to improved locomotor phenotype.

**Key words:** *Mucuna Pruriens*; Rotenone; Neuroprotective; Parkinson’s disease; Mitochondrial Dysfunction; Oxidative Stress


**OP-03-05**

**Effect of Tai Chi exercise to reduce falls and improve balance performance in Parkinson’s disease: A meta-analysis**

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**Introduction:** Parkinson’s disease (PD) is a common neurodegenerative disorder that may increase risk of falls, functional limitation and balance deficits. Tai Chi was used as an option for improving balance in people with PD. The aim of this systematic review with meta-analysis is to evaluate the effects of Tai Chi on falls, functional mobility and balance in individuals with PD.

**Method:** The search was conducted in PubMed, Cochrane, CINAHL, PEDro, Medline, Embase, sportDISCUC, Trip, and National Digital Library of Theses and Dissertations in Taiwan databases. Randomized controlled trials (RCTs) analyzing Tai Chi effects in comparison on no intervention or to other physical trainings, on falls, functional mobility and balance of PD patients were selected. The outcome measurements included falling rates, Berg Balance Scale (BBS), Functional Reach (FR), and Timed-Up and Go test (TUG). Two reviewers independently extracted methodological quality and studies data using PEDro scale.

**Result:** Five RCTs with 355 PD patients were included in this review. The grades of evidence quality for these studies were moderate to high. In comparison to no intervention or to other physical training, Tai Chi significantly decreased falling rates (odds ratio=0.47, 95% confidence interval (CI) 0.30 to 0.74, p=0.001), and also significantly improved functional mobility and balance (BBS mean difference (MD)=3.47, 95% CI 2.11 to 4.80, p< 0.001; FR MD=3.55 cm, 95% CI 1.88 to 5.23, p< 0.001; TUG MD=-1.06 s, 95% CI -1.61 to -0.51, p< 0.001) in people with PD.

**Conclusion:** This systematic reviews provides moderate to high evidence from five RCTs that Tai Chi could be a good physical training strategy in individuals with PD.
OP-03-06
Is Parkinson’s disease with history of agent orange exposure different from idiopathic Parkinson’s disease?

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Background and purpose: To elucidate the effects of Agent Orange exposure on PD, we compared the clinical characteristics and radiolabeled 18F-FP-CIT PET uptake between patients with Agent Orange exposure and no-exposure.

Methods: We retrospectively evaluated from our movement clinics database of 143 patients with Agent Orange exposure and 500 patients with Agent Orange no-exposure. The differences between clinical characteristics and pattern of 18F-FP-CIT PET uptake were investigated.

Results: Among UPDRS motor subscales, tremor at rest, rigidity, finger taps, and rapid alternating movement was significantly higher in patients with Agent Orange exposure compared to patients with Agent no-exposure. The facial expression score was significantly lower in patient with Agent Orange exposure compared to patient with Agent Orange no-exposure. Compared to patients with Agent no-exposure, all basal ganglia areas(contra- and ipsilateral caudate nucleus, anterior putamen, posterior putamen) showed a lower 18F-FP-CIT uptake and higher asymmetry index of anterior and posterior putamen was found in patient with Agent Orange exposure. The caudate/putamen ratio were significantly lower in patients with Agent Orange exposure compared to patients with Agent Orange no-exposure.

Conclusions: This study showed a different clinical profile and FP-CIT PET findings between patients with Agent Orange exposure and no-exposure. This suggested the possibility of different pathophysiology of PD in patients with Agent Orange exposure from idiopathic PD.

OP-03-07
α-Synuclein induced dopaminergic neurons mitochondrial dysfunction via cytochrome c oxidase subunit 2

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The misfolded α-Synuclein(α-Syn) transferring from cells to cells as prion protein is an important pathogenesis of Parkinson’s disease(PD). It had been reported that the extraneous α-synuclein could induced the dopaminergic neurons apoptosis by causing mitochondrial dysfunction. However, the mechanism of how α-Syn injure the mitochondrial function is still unclear.

The results of gene microarray and western blot showed that the expression of cytochrome c oxidase subunit 2(MT-CO2,COXII) had increased significantly in SY-SH5Y cells stimulated by α-Syn for 24h. Furthermore, the ATP decline, the decreased mitochondrial membrane potential (MMP) and the enhanced ROS in cells treated by α-Syn had been reversed by inhibiting MT-CO2 gene expression. The following data have illustrated that the up-regulation of MT-CO2 contribute to the release of cytochrome c and the alteration of some mitochondria-localized proteins such as Bcl-2 family proteins.
So we suggested that after being transferred into the dopaminergic neurons, α-synuclein result in mitochondrial injury via activating COXII. This discovery might reveal the initial step of the process by which α-Syn injures the dopaminergic neurons and provide new therapeutic targets of PD.

OP-03-08
Dopaminergic treatment and speech in Parkinson’s disease: acoustic analysis and correlation with motor features and dyskinesia
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Analyse the effects of levodopa on speech and its possible relationship with motor features and dyskinesias in a group of advanced Parkinson’s disease (PD) patients. We retrospectively evaluated data from 25 PD patients admitted to our department for a preoperative evaluation for Subthalamic Nucleus Deep Brain Stimulation. Disease severity was assessed using the Unified Parkinson’s Disease Rating Scale (UPDRS) scores and subscores in the ON-state and OFF-state. L-dopa responsiveness was evaluated with a drug-challenge test and ON-state dyskinesias were assessed with the Clinical Dyskinesia Rating Scale (CDRS). Each patient was evaluated ON and OFF-state and performed the following speech tasks: monologue, diadochokinesis, reading of a passage and sustained phonation. A perceptual and acoustic analysis was performed using a standardized protocol and 13 parameters were evaluated, applying PRAAT, a free software for the analysis of speech, for the acoustical part. Statistical analysis was performed using Pearson correlation coefficient and paired t test. The severity of the disease, expressed by the UPDRS Part III in OFF state, influenced negatively the maximum phonation time (MFT) (p=0.0365). In the ON-state we found a positive correlation between the UPDRS axial subscore and the Shimmer Local dB (p=0.0284). Furthermore, the UPDRS axial subscore correlated negatively with the MFT (p=0.0145) and the mean intensity of sustained phonation (p=0.0136). The total CDRS score and the CDRS subscore related to axial (face, neck and trunk) dyskinesias strongly correlated with the ON-state Shimmer Local dB (p=0.0070 and p=0.0194 respectively). Our data confirm the close relationship between different speech parameters and axial symptoms in PD patients particularly after levodopa intake. Furthermore, the intensity and location of ON-state dyskinesias could negatively influence the ON-state speech quality in PD, with axial dyskinesia that could negatively influence the pneumo-phono-articulatory system.
Video game-based dexterity training in patients with Parkinson’s disease: a pilot feasibility study
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Objectives: Many patients with Parkinson’s disease (PD) suffer from impaired dexterity, which impacts activities of daily living and quality of life (QoL). The Leap Motion Controller (LMC) combines video game-based training with augmented virtual reality. The aim of the present pilot study was to comprehensively evaluate the feasibility of a dexterity training program using the LMC, in patients with PD.

Methods: Ten patients with PD (aged between 55-75 years, Hoehn and Yahr stage II-IV) trained over a period of four weeks, twice a week for 30 minutes. Baseline (T0) and post-intervention (T1) assessments were done. Primary outcomes with respect to feasibility were the compliance rate, open-end questions, the level of participation (Pittsburgh Rehabilitation Participation Scale) and the usability (System Usability Scale). Dexterous function was measured with the Nine Hole Peg Test and the Dexterity Questionnaire 24. Upper limb motor impairment was assessed by a modified version of the Movement Disorders Society Unified Parkinson’s Disease Rating Scale III. Finally, QoL was assessed by the Parkinson’s disease questionnaire 39.

Results: Compliance rate was 99%, motivation increased significantly from 3.9 to 4.8 (PRPS, p=0.03) and system usability of the LMC system was acceptable to very good. Regarding potential efficacy, patients with impaired dexterity at T0, significantly improved in dexterity (Nine Hole Peg Test) and QoL (PDQ-39, both p< 0.05)).

Conclusions: The present pilot study suggests that video game-based LMC dexterity training in PD is feasible and has potential to improve dexterity. Its efficacy should now be investigated in a properly powered randomized controlled trial.

Keywords: Parkinson’s disease; dexterity; Leap Motion Controller; video game-based, feasibility, virtual reality.
OP-03-10
PROtein, LEucine And vitamin D Enhancing Rehabilitation (PRO-LEADER) in patients with Parkinson’s disease or parkinsonism: An RCT
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Objectives: Physical rehabilitation is an important strategy for treating motor disability in patients with Parkinson’s disease (PD) or parkinsonism. Studies in old adults have shown that muscle-targeted nutritional support can positively influence muscle mass and physical performance but no evidence is available in parkinsonian syndrome which are characterized by high rates of muscle dysfunction, particularly muscle weakness. We evaluated the efficacy of a muscle-targeted nutritional support on the functional outcomes of a multidisciplinary intensive rehabilitation treatment (MIRT) in patients with PD or parkinsonism.

Methods: We conducted a randomized (1:1), controlled trial (NCT03124277) in patients suffering from PD or parkinsonism and undergoing a MIRT. Patients (n=150) received a standard hospital diet with or without a vitamin D and leucine-enriched whey protein-based nutritional supplement twice daily for 30 days. The primary efficacy end point was the increase in the distance walked during a 6-minute walking test (6MWT). Secondary outcome variables were changes in: gait speed, timed up and go test (TUG), Berg balance scale, handgrip strength, Self-assessment Parkinson’s Disease Disability Scale, body weight and skeletal muscle mass (SMM).

Results: Nutritional support resulted in a greater increase in the distance walked during a 6MWT (mean, 69.6 meters [95%CI, 60.7-78.6]) than no support (51.8 meters [95%CI, 37.0-66.7]): center-adjusted mean difference, 18.1 meters [95%CI, 0.9-35.3] (P=0.039). Further adjustment for changes in dopaminergic therapy and SMM yielded consistent results: mean difference, 18.0 meters [95%CI, 0.7-35.2] (P=0.043). A significant effect was also found for the following secondary end points: 4-meter walking speed (0.07 m/s [95%CI, 0.01-0.13], P=0.032), TUG test (-1.1 s [95%CI, -2.2-0.0], P=0.046), SMM (0.5 kg [95%CI, 0.0-1.0], P=0.029).

Conclusions: In patients with PD or parkinsonism, the consumption of a whey protein-based nutritional formula enriched with essential amino acids and vitamin D improved the efficacy of a MIRT, particularly lower body physical function.
OP-03-11
Parkinson’s disease: Social determinants of quality of life of patients in the central belt of Ghana
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Objective: The study assessed the social factors that influenced health-related quality of life (HRQoL) of Parkinson’s disease (PD) patients. This was imperative in a developing country such as Ghana, where formal support structures and systems for PD patients are practically absent and where disease awareness is low. The study explained how differences in socio-demographic factors influenced HRQoL of PD patients.

Methodology: Sixty patients were randomly sampled from PD’s database of the Neurology Outpatient Clinic of Komfo Anokye Teaching Hospital, which is the highest referral facility in the Central belt where PD is diagnosed and treatment administered to patients. A socio-demographic questionnaire and Parkinson’ Disease Questionnaire - 39 were administered to patients. Regression analysis was used to assess relative contributions of the socio-demographic factors on HRQoL of PD patients, anova and independent sampled t-test were adopted to analyse differences in HRQoL among patients with different socio-demographic.

Results: The social determinants of HRQoL were gender, level of education, economic status, and years of experiencing PD. Male patients had more support from partners than females. PD patients earning regular incomes had better HRQoL than those without. PD patients with low or without any informal education experienced more stigma and depression than those with tertiary level of education. PD patients within 10 years had better social support than those above. This was attributed to disease fatigue on caregivers. PD patients from the urban areas felt more isolated and lonely than those from rural areas.

Conclusions: Socio-demographic factors have significant influence on HRQoL of PD patients. Many of the factors revolved around ignorance about the disease. The study suggested for the decentralisation of PD counselling, awareness and treatment centres to District Health Centres to intensify awareness creation about the disease.

OP-03-12
Exploration of the regulation of miR-4639-5p expression and its role in the pathogenesis of Parkinson’s disease
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Our previous study had shown that miR-4639-5p could regulate DJ-1 expression, and elevated plasma miR-4639-5p was potential to be an early diagnostic marker for sporadic PD. However, whether the elevated plasma miR-4639-5p level in PD patients reflect its abnormal change in CNS and the molecular mechanism of the abnormal up-regulation of miR-4639 in PD is still obscure. Exosomes were isolated from plasma to analyze the origin of plasma miR-4639-5p, and we found miR-4639-5p in CNS exosomes was the main source of miR-4639-5p level in circulating plasma, which means changes in plasma miR-4639-5p
level could reflect its level changes in the CNS to some extent. To further discover the molecular mechanism regarding abnormal up-regulation of miR-4639-5p in PD patients, we looked into miRNA biogenesis pathways, especially transcriptional regulation. We identified miR-4639 core promoter region by dual-luciferase reporter assay, which is 10kb upstream pre-miR-4639 sequence. CRISPR-Cas9 system was used to knockout miR-4639 promoter region in SH-SY5Y cells for further validation. Endogenous expression level of miR-4639 was dramatically decreased in promoter knockout cells. We further sequenced the promoter region in 308 PD patients and 357 healthy controls, and found T allele in rs760632 showed a higher frequency in PD compared to control group (P=0.015). Dual-luciferase reporter assay also suggested that rs760632 T allele had an increased transcriptional activity compared to C allele, which further validated the functional importance of this region. In conclusion, abnormally up-regulated miR-4639-5p level in plasma could reflect brain changes of sporadic PD patients to some extent, suggesting a promising role of miR-4639-5p as a biomarker for PD early diagnosis. Promoter region of miR-4639 was identified, which may help to discover the mechanism of abnormal up-regulated miR-4639 in PD patients.

OP-03-13

Biochemical studies in the brain of transgenic drosophila as a model of Parkinson’s disease treated by ropinirole silver nanocomposite (RAgNC)

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Objective: Parkinson's disease (PD) is the second most common disease among the other neurodegenerative disease. The symptoms are characterized by a variety of motoric dysfunctions including difficulties in initiating movements, slowed movements (bradykinesia), rigidity, and resting tremor. These signs result from reduction in the level of striatal dopamine, which accompanies progressive degeneration of dopaminergic neurons in the substantia nigra, pars compacta. There is no treatment available for PD but its symptoms can be improved by enhancing dopamine content in the brain. Therefore, the main objective of the current study was to assess the effect of Ropinirole silver nanocomposite (RAgNC) treatment on the brain functions of transgenic Drosophila expressing human alpha synuclein.

Methods: The transgenic flies expressing human αS in the brain were exposed to different doses of synthesized and characterized RAgNC in an established diet for 24 days. After 24 days of exposure the flies were assayed for climbing assay, Drosophila activity pattern, oxidative stress markers, caspase-3 & 9 activity, dopamine content and expression of alpha synuclein in PD flies brain using immunohistochemistry.

Results: The exposure of PD flies to various doses of RAgNC resulted in the reduction of glutathione-S-transferase activity, lipid peroxidation, monoamine oxidase, caspase-3, caspase-9 activity and alpha synuclein expression in a dose-dependent manner.

Conclusion: The results of the present study revealed that RAgNC increased the life span, dopamine content and reduced the oxidative stress as well as apoptosis in transgenic Drosophila model of PD. Thus, RAgNC can be used as potent therapeutic agent for improving symptoms of PD.
Rifampicin inhibits rotenone-induced inflammation by improving lysosomal function and autophagic flux in microglia

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Accumulating evidence suggests that inflammation and the impairment of autophagy-lysosome pathway play a crucial role in Parkinson’s disease (PD). Our previous studies indicated that rifampicin inhibited the release of inflammatory factors in microglia exposed to rotenone, but the precise mechanism has not been fully explored.

The present study was to investigate whether rifampicin pretreatment suppressed rotenone-induced inflammation in microglia via improving lysosomal function and autophagic flux. Human microglia (HM) cells were pretreated for 2 h with rifampicin followed by 0.1 µM rotenone, alone or in combination with chloroquine. Here, we showed that the production of IL-1β in rotenone-treated HM cells was alleviated by rifampicin pretreatment, and this effect was suppressed when autophagy was inhibited by chloroquine. The results also demonstrated that rotenone significantly enhanced the number of yellow LC3 dots with a marginal elevation in red-only dots in RFP-GFP tf-LC3 transfected HM cells, indicating the impairment in autophagic flux. While the autophagic flux was recovered by rifampicin pretreatment as revealed by fewer yellow/red dots staining.

We suggest that the mechanism for rifampicin-mediated anti-inflammatory effect is the improvement of lysosomal function. Indeed, rotenone enhanced lysosome pH as LysoTracker Red fluorescence and LysoSensor fluorescence shift from blue to yellow was markedly decreased. Rifampicin pretreatment could increase the lysosomal acidic fluorescence and promote LysoSensor fluorescence shift from blue to yellow.

In conclusion, the data provide further evidence that rifampicin exerts neuroprotection against rotenone-induced microglia inflammation, partially through improving lysosomal function and autophagic flux. Modulation of lysosomal function by rifampicin is a novel therapeutic strategy for PD.
OP-03-15
Effects of transcranial magnetic stimulation on hypokinetic dysarthria in Parkinson’s disease

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Objectives: The objective of this research project is to identify an optimal protocol for repetitive transcranial magnetic stimulation (rTMS) to improve hypokinetic dysarthria in PD. We investigate both short-term and long-term effects of rTMS using acoustic and perceptive analysis of speech, respectively.

Methods: In exploratory study of short-term effects, we used 1 Hz and 10 Hz rTMS applied over the left orofacial motor area, over the right superior temporal gyrus (STG) and over the vertex (a control stimulation site) in 15 PD patients using a cross-over design. Resting state seed-based functional connectivity (rs-FC) with the seed located in the stimulation site was used to analyze neural correlates of induced behavioral changes. Based on results from exploratory study we investigate long-term effects of 10 repeated sessions of low-frequency rTMS applied over STG in 10 PD patients. This longitudinal study is ongoing and neural correlates of stimulation aftereffects will be assessed.

Results: In the exploratory study, both 1 Hz and 10 Hz rTMS of the right STG induced positive changes on HD. The major impact was observed for 1 Hz rTMS over the STG. The stimulation improved speech rhythmicity and articulation via modulation of the STG rs-FC with the parahippocampal gyrus. The 10 Hz rTMS of the STG improved articulation while enhancing the rs-FC with the inferior parietal lobule. In the ongoing longitudinal study, preliminary perceptual rating by speech therapist shows positive effect of rTMS that lasts 1 month after stimulation.

Conclusions: The exploratory study shows that rTMS applied over the auditory feedback area may lead to improvement of speech in PD through enhanced connectivity among brain regions involved in the dorsal language pathway. Based on preliminary and partial results of the longitudinal study, we assume, that these positive effects could be long-lasting.
Bradykinesia assessment using evolutionary algorithms in Parkinson’s disease: Clinical validation

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Background: Bradykinesia is the prerequisite for PD diagnosis according to MDS diagnostic criteria, and so accurate identification of bradykinesia is important. Unfortunately, bradykinesia-related items have the lowest reliability among all UPDRS items, particularly when the severity is slight or mild. Therefore, there is an important need for developing objective, effective and convenient measurements to help clinicians accurately identify bradykinesia, which could potentially lead to earlier diagnosis of PD. We aim to validate the ability of the evolutionary algorithms to distinguish the early stage of PD and examine whether it could be used to monitor disease progression.

Methods: 107 PD, 41 essential tremor (ET) patients and 49 normal controls (NC) were included. Participants performed finger-taping (FT) task with two sensors at thumb and index finger. Readings from the sensors are transmitted to a tablet device and then analyzed by specialist software employing evolutionary algorithms. During FT tasks, the bradykinesia was rated using MDS-UPDRS 3.4.

Results: A positive correlation was found by comparing the PD-monitor score with MDS-UPDRS FT subjective grade (p< 0.001). PD-monitor score was significantly higher in early PD patients (H-Y=1) compared with NC (p< 0.001). The ROC curves illustrated strong separation, with an AUC of 0.832 (p< 0.0001) and AUC of 0.841 (p< 0.0001) for the right and left affected side, though 21.7% PD patients manifested very slight bradykinesia with MDS-UPDRS FT scored zero. The ROC curve also reflected a separation between the early PD and ET (p< 0.01). Moreover, the PD-monitor score gradually increased as H-Y stage increased. Correlation analysis showed the PD-monitor score was significantly positively correlated with disease duration of PD patients.

Conclusions: A simple device employing classifiers derived from evolutionary algorithms can be used to accurately measure bradykinesia in PD. The device has the potential to make early diagnosis of PD and monitor disease progression.
OP-03-18
Genomic variants associated with cognitive impairment in Parkinson’s disease
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Objectives: Cognitive impairment is a frequent nonmotor symptom in Parkinson’s disease (PD), with significant heterogeneity in onset timing, severity, and outcome. Etiology of cognitive impairment in patients with PD is still unclear and pathological features are highly variable. There is no convincing biomarker to predict the development of cognitive impairment in patients with PD. We aimed to identify the genomic variants that are associated with cognitive impairment in patients with PD.

Methods: Genomic data was produced in patients with PD (N=1,021), using the Korean Chip (K-CHIP), Affymetrix Axiom KORV1.1 (variants number of 827,400), which contains imputation genome-wide association study (GWAS) grid and other GWAS loci, functional variants of nonsynonymous exome, pharmacogenetics variants, variants in genes involved in absorption, distribution, metabolism and excretion (ADME) of drugs, and expression quantitative trait loci (eQTL). Genomic analysis was performed according to the scores of Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA).

Results: One upstream variant in Chromosome 17 (OR=0.54, CI=0.44-0.69, P=1.45×10^-7) and one intronic variant in Chromosome 3 (OR=0.31, CI=0.20-0.50, P=3.77×10^-7) were significantly associated with the lower scores of MMSE (score < 24) after Bonferroni correction. One intronic variant in Chromosome 10 (OR=0.53, CI=0.41-0.70, P=4.56×10^-6) was significantly associated with the lower scores of MoCA (score < 23). Severe other variants showed associations with lower scores of MMSE or MoCA, but they did not remain significant after Bonferroni correction.

Conclusions: This study identified new loci associated with lower scores of cognitive screening tests in patients with PD. Further studies are needed to confirm our findings using more comprehensive cognitive tests.

OP-03-19
Tear proteins as possible biomarkers for Parkinson’s disease
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Objective: To evaluate whether the tear fluid of people with Parkinson’s disease (PD) differs compared to people without PD.

Background: Non-motor features of PD occur years prior to motor dysfunction, and represent a well-suited platform to investigate for a possible biomarker. Lacrimal glands are highly innervated by cholinergic neurons, and tear fluid secreted by lacrimal glands is greatly stimulated by cholinergic neurons. The
production, packaging and secretion of specific proteins into tears may be regulated by changes in nerve function to lacrimal glands. Analysis of alteration in the secretion of proteins into tears may identify a reliable and non-invasive biomarker for PD.

**Design/Methods:** Tear samples from 94 PD patients of varying severity and 60 age- and gender-matched non-PD controls were collected and pooled from both eyes for analysis of alpha synuclein, CC chemokine ligand 2 (CCL-2) and DJ-1 (Park 7) using a Human magnetic Luminex assay kit (R&D systems) and analysis of oligomeric alpha synuclein using an Human alpha-synuclein oligo ELISA kit (MyBioSource), respectively.

**Results:** Total alpha synuclein decreased significantly in PD patients (401.1 ± 41.7 pg/mg tear protein) relative to healthy controls (615.1 ± 81.6 pg/mg tear protein) (p-value = 0.001) in tears from patients acquired from Schirmer’s strips taken during an anesthetized Schirmer’s test. Oligomeric alpha synuclein increased significantly in PD patients (3.43 ± 0.58 ng/mg tear protein) relative to controls (0.84 ± 0.15 ng/mg tear protein) (p-value=.0002 ). The ratio of alpha synuclein oligomeric/ total alpha synuclein (p-value < 0.0001) While detectable in tears, neither CCL-2 nor DJ-1 varied between PD patients and non-PD controls.

**Conclusions:** Total alpha synuclein and oligomeric synuclein may have potential to discriminate between tears of PD patients and healthy controls. To our knowledge this is the first report of tear collection and protein analysis as a possible non-invasive, inexpensive and reliable biomarker for PD.
Objectives: This study aimed to map the differences in altered functional connectivity (FC) of cortico-striatal loops at an early stage of “non-freezing” state between Parkinson’s disease (PD) patients who will develop into freezing of gait (FOG) and those who will not.

Methods: New diagnosed, untreated PD patients who had already conducted an fMRI scan were followed-up. Based on the follow-up assessment, all patients were divided into FOG+ group (patients developed FOG) and FOG- group (patients did not develop FOG). Finally, 17 FOG+ patients, 17 FOG- patients, and 17 sex and age matched healthy controls (HCs) were included in analysis.

Results: Compared to FOG- patients, FOG+ patients showed increased FC between striatum and temporal lobe and cerebellum but decreased FC between striatum and sensorimotor cortex. Compared to controls, FOG+ patients showed increased FC between striatum gyri rectus and cerebellum but decreased FC between striatum and occipital lobe and frontal lobe. Compared to controls, FOG- patients showed increased FC between striatum and sensorimotor cortex but decreased FC between striatum and occipital lobe, cerebellum and precuneus. Compared to patients with FOG- and controls, patients with FOG+ showed higher Z values of FC between striatum and gyri rectus and cerebellum \((P < 0.05)\) as well as lower Z values of FC between striatum and orbitofrontal cortex and frontal lobe \((P < 0.05)\). Compared to controls, both FOG+ and FOG- patients showed higher Z values of FC between striatum and occipital lobe \((P < 0.05)\).

Conclusions: FOG+ patients showed decreased FC in striatal loop at the early “non-freezing” state when compared to FOG- patients and HCs, and this decreased FC may be compensated by the enhanced FC between striatum and temporal lobe and cerebellum.
OP-04-02
Pathway based genetic markers reveals relation between stroke and Parkinson’s disease
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Background: The risk of stroke in patients with Parkinson’s disease (PD) remains controversial. However, link between stroke and PD may be attributed to common pathogenesis pathways. Therefore, identifications of pathways based genetic markers may provide insights into stroke relation with PD.

Aim: To assess expression-pattern of specific gene-sets that share common cellular pathways in stroke and PD, and identification of potential therapeutic targets.

Materials and methods: The dataset GSE22255, comprises mRNA expression of peripheral blood mononuclear cells of 20 controls and 20 stroke patients, was obtained from GEO database. The expression intensity was calculated using bioconductor-package “affy” and significantly (p< 0.01) altered genes were filtered using pair-wise t-test. Further, gene set enrichment analysis was performed on differentially expressed genes and drug targets were screened by Reactome-FI-cytoscape-tool.

Results: A total of 117 genes were found to be deregulated in disease condition. Majority of genes were upregulated (67.5%) and showed high functional-enrichment (68.6%) with stroke-phenotypes (Figure 1A). However, 32.5% genes were upregulated with 31.4% correlation in controls (Figure 1B). The GSEA results suggested two significant pathways, homeostatic process (ES=-0.31; NES=-0.89; NOM p-val=0.602) and cell development pathway (ES=-0.31; NES=-0.75; NOM p-val=0.813), identified as significantly dysregulated (Figure 2B). Three markers (SLC18A2, SLC12A5, RHAG) in homeostatic process and five markers (ETV5, PARVA, SLC12A5, RHAG, BMPR1B, ROBO2) were identified; however, two druggable targets were found as SLC12A5 and RHAG. It is interesting to note that identified markers were also found to be associated with PD such as solute carrier vesicular transporters (SLC18A2, SLC12A5) enhances dopamine release for cellular homeostasis whose deregulation may be linked to PD and stroke.

Conclusions: Pathway based expression and GSEA showed cellular homeostasis and cell development pathways are affected which can be link between stroke and PD. Seven marker and two druggable targets were identified; however, further analysis is required for clinical developments.

[Figure 1: (A) Heat Map of the mRNA expression in controls (n=20) and Ischemic Stroke phenotypes (n=20); (B) Ranked list correlations for Ischemic Stroke]
A novel co-activation pattern analysis of resting-state fMRI networks in Parkinson’s disease reveals reduced network dynamics that correlate with motor symptom severity

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Objectives: An MRI-based method to capture dynamic brain network changes in Parkinson’s Disease (PD) that correlate with symptoms remains elusive. The temporal dynamics of intrinsic brain networks have recently been studied using co-activation pattern (CAP) analysis. In this study, we utilized a novel CAP method to investigate brain network dynamics in PD. The method was applied to resting-state fMRI (rs-fMRI) in Healthy Controls (HC) v. PD, where we hypothesized that 1) reduced network dynamics would be evident in PD, and 2) reduced PD network dynamics would correlate with motor dysfunction.

Methods: The novel CAP analysis is described in detail elsewhere, but briefly a cohort-specific CAP set was determined for HC and PD, and then rs-fMRI networks in each cohort were characterized by spatial similarity to the CAPs. Subsequently, a CAP-based subject-specific network-switching probability was determined to quantify network dynamics. Utilizing this method, rs-fMRI data for 18 HC and 20 de-novo PD obtained from PPMI were analyzed. Seven brain networks were investigated: default mode (DMN), frontal-parietal (FPN), sub-thalamic (STh), striatal (STR), sensorimotor (SMN), executive (ECN), and medial temporal (MTN) networks. CAP sets were determined for each network in PD and HC separately, and then switching probabilities were calculated and used to compare network-based temporal dynamics between the two groups and compared to motor symptom severity in PD as well.

Results: There were fewer CAPs overall in PD in ECN, MTN, STh, and STR, as compared to HCs. Furthermore, between-network switching probability for the PD group was reduced. Lastly, reduced PD network dynamics correlated with increasing motor symptom severity.
Abstracts

Conclusions: The proposed data-driven rs-fMRI-based CAP approach enabled network dynamics to be compared between HC v. PD. As hypothesized, we found reduced network-dynamics in most networks in PD, and importantly these reduced network dynamics correlated with PD symptom severity.

OP-04-04

Early Parkinson’s disease is distinguished by a structural network backbone identified through graph theoretical analysis of diffusion MRI

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Objectives: Neuroimaging that captures the spreading structural pathology of early Parkinson’s Disease (PD) remains elusive. MRI-based graph-theoretical approaches have the ability to characterize structural connectivity backbone networks, as recently demonstrated in Healthy Controls (HC). Thus, we applied hypothesis-free whole-brain graph-theoretical approaches to diffusion-MRI data in early PD to characterize backbone structural networks and determine if this could differentiate PD from HC early in disease.

Methods: Diffusion-MRI from 49 HC and 92 early PD were derived from PPMI for this study. Two atlases were used to generate cortical and subcortical nodes for the networks. Whole brain tractography was performed utilizing only fiber tracts with both ends in nodes. Each internode connection (edge) was weighted by the product of fiber number and average FA. Nonparametric sign test was then performed within each cohort, and edges with a significantly greater chance to be present in each subject were retained as the cohort’s structural backbone network. Global, local, and nodal network properties were then computed.

Results: The majority of cortical-subcortical fibers were retained as internode fibers, and mean connectivity matrix did not reveal qualitative differences between HC v. PD (but variance of structural connectivity from backbone was greater within PD). Network-based-statistics revealed 13 backbone paths where PD had altered structural connectivity v. HC, comprising mostly of PD-relevant subcortical and cortical connections including frontal and SMA cortices, striatum, STN, SN, and pallidum. In addition, aberrant global and local network properties were evident in PD-relevant connections, including loss of striatal nodal architecture in PD with a shift to a precentral nodal structure.

Conclusions: Without a priori assumptions, our hypothesis-free whole-brain graph-theoretical DTI investigation revealed a distinctive structural backbone network in early PD involving connections between brain regions known to be involved in the disease. Furthermore, altered global, local, and nodal network architecture was observed in PD.
OP-04-05
Oligogenic inheritance in Parkinson disease explained by multiple mitochondrial and lysosomal gene mutations
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Introduction: Although mutations in PARK2, PINK1, DJ-1 and VPS13C cause autosomal recessive Parkinson Disease (ARPD), a high prevalence of single heterozygous mutations and the presence of compound mutations in different ARPD genes are frequently observed. Oligogenic inheritance of these genes could be explained by their essential roles in common mitochondrial quality control pathways. Additionally, substantial evidence highlights the importance of lysosomal mechanisms in PD and the crosstalk between lysosomes and mitochondria, including excessive burden of lysosomal storage disorder (LSD) gene variants in PD patients.

Methods: We analyzed whole-exome sequencing (WES) data of 66 PD patients, including 34 patients with a single rare heterozygous mutation in an ARPD gene and 2 related patients, to investigate a role for different genetic factors in disease etiology. Variants in autosomal recessive genes associated with PD, atypical parkinsonian syndromes and LSD were prioritized based on quality, frequency in public databases and impact on protein.

Results: The WES data analysis revealed the presence of oligogenic inheritance through known pathogenic and rare novel heterozygous mutations in multiple genes. We identified 1 patient carrier of compound mutations in PARK2/DJ-1 and 1 patient with compound mutations in PARK2/VPS13C. Coexistence of mitochondrial and lysosomal pathways is established by the observation in 16 patients of multiple mutations in PD and LSD genes, including 7 known pathogenic LSD gene mutations. Of note, the compound mutations PARK2 p.P437L and HEXA p.R247W are both present in an affected mother and daughter. Additionally, we found 4 carriers of compound mutations in different LSD genes.

Conclusions: Our results underpin the potential oligogenic complexity of Mendelian genes in PD etiology and highlight the crosstalk between mitochondria and lysosomes in the pathophysiology of PD. WES of an additional 21 PD patients with one singe heterozygous VPS13C mutation is currently ongoing to expand our findings.
OP-04-06
Distinct between-network functional connectivity changes in Parkinson’s disease: A follow-up study
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Introduction: The frontoparietal control network (FPCN) controls switching between the task-negative network (default mode, DMN) and tasks-positive brain networks (dorsal attentional, DAN; visual, VN), i.e. the main functional networks related to cognition. We explored resting state functional connectivity (rs-FC) between the FPCN and other abovementioned networks in Parkinson’s disease patients with mild cognitive impairment (PD-MCI) or normal cognition (PD-NC) as compared to age-matched healthy controls (HC) using various analytical approaches.

Methods: 51 HC, 17 PD-NC and 24 PD-MCI underwent clinical and MRI examination at baseline and some individuals underwent the follow-up examination after one year. Representative seeds were chosen for the abovementioned networks and the mean internetwork rs-FC was calculated between the FPCN and other networks. Moreover, correlation matrices for each subject were calculated using AAL atlas masks and assessed with graph metrics (GT). Submatrices composed of masks belonging to our networks of interest were evaluated using partial least squares (PLS) analysis.

Results: At baseline assessment, FPCN-DAN, FPCN-VN and FPCN-DMN connectivity was significantly reduced in PD-NC as compared to HC. The connectivities decreased in the order HC > PD-MCI > PD-NC. These results were replicated using the PLS analysis. The GT measures detected a significant decrease in clustering coefficient, node strength, and efficiency and increase in path length in PD-NC compared to HC, with all GT measures showing the same trend HC > PD-MCI > PD-NC. At one-year follow-up as compared to baseline significant increases in FPCN-VN and FPCN-DMN connectivity was observed in the merged PD group (n=23) while no changes were detectable in the HC group (n=37).

Conclusion: The study shows decreased network efficiency and functional connectivity between the FPCN and other cognitive networks in PD-NC, while rs-FC inter-network increases probably reflect compensatory attempts that occur with the disease progression.
Diagnostic utility of a targeted resequencing technique of next generation sequencing in detecting copy number changes in PARK2

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Background & Objective: We investigate feasibility of Next Generation Sequencing (NGS) targeted sequencing technique using Ampliseq® technology by Ion PGM® to detect copy number variation mutation in PARK2 gene. Among causative genes for familial Parkinson’s disease (PD), PARK2 is the most common autosomal recessive gene for familial Parkinson’s disease. In East Asian, while 10% of mutations in PARK2 are single nucleotide variants, 90% of PARK2 mutations are copy number variation (CNV) mutation (i.e., deletion/duplication) caused by exonic rearrangement. Targeted resequencing of a panel of genes using NGS technique has been known to capture single nucleotide variant accurately. However, whether this technique can detect CNV mutation precisely enough to be used in clinical genetics has not been systematically studied.

Methods: Targeted resequencing of five PD-causing genes (PARK2, ATP13A, PLA2G6, PINK1, SNCA) using Ion PGM® was performed in a group of 32 PD patients with early onset PD. Results of copy number change analyses in PARK2 based on depth-based algorithm was compared to those obtained by a gold standard method, real-time PCR (RT-PCR).

Results: An average of 144,767 mapping reads per a sample were on target (99.28%) were obtained with an average coverage depth 1,273X and coverage uniformity of 95.40 %. In unsupervised analyses, the concordances as determined by Cohen’s kappa between depth-based CNV detection and RT-PCR was poor to good (kappa=0.43, 95% CI 0.24-0.63). In a supervised analysis, kappa was higher (kappa=0.77, CI 0.63-0.91), however, results of CNV analyzed by Ampliseq® technology by Ion PGM® using coverage depth-based algorithm were significantly different from those by a gold standard method, RT-PCR (McNemar test, p< 0.05).

Conclusions: Our results suggest that depth-based CNV analysis algorithm using data obtained by Ampliseq® technique of NGS is not comparable to RT-PCR in detecting PARK2 exonic rearrangement.
Investigating glucocerebrosidase (GBA) gene mutations in Parkinson’s disease


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Background: Parkinson Disease (PD) is a chronic progressive disorder that comes with a complex multitude of motor problems such as bradykinesia, stiffness, resting tremors and postural instability, as well as non-motor symptoms such as cognitive impairment, urinary dysfunction and psychological issues. These symptoms vary from patient to patient. Increasingly, evidence suggests that genetic variation could be a relevant risk factor for PD, other than aging and environmental factors. One such risk factor is mutations in GBA gene. GBA gene mutation has been found to contribute to development of PD, which could serve as a potential target for therapeutic approaches to be developed. Identifying the prevalence of GBA gene mutation carriers in the confirmed PD cases locally will therefore be worthwhile.

Objective: The objective of this study is to investigate the prevalence of GBA mutation in Singapore’s population of people with PD.

Methods: A total of 1,896 subjects were recruited into the study. Blood samples were obtained from these subjects and DNA was extracted. Subsequently, L444P type of GBA gene mutation was determined.

Results: Out of the 1,896 subjects, 27 of them were found to carry the GBA gene mutation. Those subjects with the mutation were found to have an earlier age of onset of PD when compared to those without.

Conclusion: In Singapore’s PD population, the frequency of L444P type mutation of GBA gene is 1.42%. The carriers of this type of GBA gene mutation are approximately 4 years younger as compare to non-carriers. PD patients, who are carriers of this GBA gene mutation, are potential candidates for therapeutic studies targeting GBA gene mutation.
**OP-04-09**

**Correlations between white matter lesions and cognitive impairment in Parkinson’s disease**

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**Objective:** White matter lesions (WMLs) have an impact on neuronal connectivity and could affect cognition in both normal aging and disease states. Using a fully automated segmentation algorithm and multimodal images, we estimated WMLs volumes to predict the level of cognitive impairment in a cohort of PD and controls.

**Methodology:** Whole-brain MRI was performed at 1.5 and 3 Tesla on a case-control cohort of 41 subjects (16 PD and 25 controls). Cognitive function was tested using Montreal Cognitive Assessment (MoCA) and Frontal Assessment battery (FAB). WMLs segmentations were assessed using an automated method based on a supervised approach, and refined using a partial volume estimation algorithm, on MPRAGE and 3D FLAIR images.

**Results:** WMLs in frontal, prefrontal and periventricular regions were significantly higher in PD (p < .01) and negatively correlated (p < 0.05) with both MoCA and FAB scores. WMLs volumes were significantly higher in the frontal region (p< 0.05) in PD. Stepwise regression showed that frontal WMLs alone significantly predicted MoCA (b=-905, F(1,32)=30.69, p< .001) and FAB scores (b=-361, F(1,32)=14.07, p=.001).

**Conclusion:** Frontal lobe functions are more severely affected by WMLs in PD, and higher-order brain functions (e.g., executive function) are more vulnerable to WMLs changes that affect the connectivity of parietal and temporal association cortices. Future studies will aim at evaluating the impact of periventricular WMLs on other PD motor subtypes and in other specific cognitive domains.

**OP-04-10**

**Diagnostic utility of acute levodopa challenge test: Beyond levodopa responsiveness**

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**Background:** Acute levodopa challenge test(ALCT) is useful for distinguishing IPD from other parkinsonian syndromes during the early years of parkinsonism, & predicting long-term levodopa responsiveness also. But no other previous studies had addressed the significance of levodopa intolerance or dyskinesia development during ALCT in predicting MSA or LID during chronic levodopa therapy.
89 Patients admitted with parkinsonism were recruited for the study

4 patients develop akinetic rigidity syndrome during anti-parkinsonian drug withdrawal & excluded from the study

Acute levodopa challenge test were performed in 85 parkinsonian patients & the following were observed
1. Looked for improvement in UPDRS3 scoring
2. Development of symptoms of clinical intolerance during acute levodopa challenge test
3. Appearance of any dyskinesia

Followed up over a period of 18 months

10 patients were lost in follow-up and were excluded from the study

75 patients completed 18 months follow up

Patients were again evaluated for 18 months to look for
1. Provisional diagnosis of specific parkinsonian syndrome
2. Long term levodopa responsiveness

[Figure 1: Study design]
## Table 1. Acute levodopa Challenge Test findings among the different Parkinsonian Syndromes

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th>No of Pts</th>
<th>Sex (Female/Male)</th>
<th>Age (years) (SD)</th>
<th>Disease duration (month) (SD)</th>
<th>Acute challenge response (N/Y)</th>
<th>SCI (N/Y)</th>
<th>Dyiskinesia during challenge (N/Y)</th>
<th>LID (N/Y)</th>
<th>Long term levodopa response (N/Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPD</td>
<td>34</td>
<td>14/20</td>
<td>69.2 (7.9)</td>
<td>17.8 (3.8)</td>
<td>14/20</td>
<td>32/2</td>
<td>30/4</td>
<td>21/13</td>
<td>2/32</td>
</tr>
<tr>
<td>MSA</td>
<td>9</td>
<td>5/4</td>
<td>59.8 (7.1)</td>
<td>17 (3.7)</td>
<td>7/2</td>
<td>5/4</td>
<td>5/4</td>
<td>5/4</td>
<td>4/5</td>
</tr>
<tr>
<td>PSP</td>
<td>4</td>
<td>1/3</td>
<td>63 (3.6)</td>
<td>16.2 (3.9)</td>
<td>3/1</td>
<td>4/0</td>
<td>4/0</td>
<td>4/0</td>
<td>4/0</td>
</tr>
<tr>
<td>DLP</td>
<td>2</td>
<td>1/1</td>
<td>64 (8.5)</td>
<td>15 (2.8)</td>
<td>1/1</td>
<td>2/0</td>
<td>2/0</td>
<td>2/0</td>
<td>1/1</td>
</tr>
<tr>
<td>CBD</td>
<td>1</td>
<td>1/0</td>
<td>65</td>
<td>23</td>
<td>1/0</td>
<td>1/0</td>
<td>1/0</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>FTD-P</td>
<td>2</td>
<td>1/1</td>
<td>57.5 (4.9)</td>
<td>16 (4.2)</td>
<td>1/1</td>
<td>2/0</td>
<td>2/0</td>
<td>2/0</td>
<td>2/0</td>
</tr>
<tr>
<td>NPH</td>
<td>7</td>
<td>2/5</td>
<td>67.7 (8.1)</td>
<td>13.4 (4.4)</td>
<td>6/1</td>
<td>7/0</td>
<td>7/0</td>
<td>7/0</td>
<td>7/0</td>
</tr>
<tr>
<td>DIP</td>
<td>1</td>
<td>1/0</td>
<td>63</td>
<td>15</td>
<td>1/0</td>
<td>1/0</td>
<td>1/0</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Vap</td>
<td>2</td>
<td>1/1</td>
<td>66.5 (6.4)</td>
<td>17 (2.8)</td>
<td>1/1</td>
<td>2/0</td>
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<td>58.7 (13.6)</td>
<td>17.2 (4.8)</td>
<td>7/5</td>
<td>11/1</td>
<td>11/1</td>
<td>10/2</td>
<td>7/5</td>
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<tr>
<td>Total</td>
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<td>33/42</td>
<td>65.3 (9.4)</td>
<td>16.9 (4.1)</td>
<td>43/32</td>
<td>68/7</td>
<td>66/9</td>
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[Diagram 3. Comparison of sensitivity & specificity of development of dyskinesia and symptoms of levodopa intolerance in predicting a diagnosis of MSA]
Abstracts

Objectives: This prospective cohort study was conducted to evaluate the sensitivity and specificity of different outcomes of ALCT (motor improvement, levodopa intolerance & dyskinesia) to predict IPD, MSA, long-term levodopa responsiveness & LID during chronic levodopa therapy.

Methods: ALCT was performed on 89 pts with parkinsonism of less than two years & were followed up for 18 months(fig-1), to make a provisional clinical diagnosis of specific parkinsonian syndromes, to look for long-term levodopa responsiveness & LID during chronic levodopa therapy.

Results: ALCT was positive in 39(52%) cases and negative in 36(48%) cases out of 85 pts who completed the test. At the end of 18 months follow-up, out of 75 pts, 34(45.3%) were diagnosed as IPD & 41(54.7%) as non-IPD parkinsonism(tab-1). The sensitivity and specificity of positive ALCT to predict a clinical diagnosis of IPD was 79.4% and 70.7%, respectively. The predictive nature of ALCT concerning chronic levodopa responsiveness differed somewhat from making a diagnosis of IPD with both sensitivity and specificity being 60% in predicting long-term levodopa responsiveness. Development of dyskinesia during ALCT could not significantly predict LID during chronic levodopa therapy with a poor sensitivity of 14.3%. Rather appearance of dyskinesia during ALCT can significantly predict a diagnosis of MSA with high specificity (91%) & low sensitivity (37.5%). The appearance of symptoms of levodopa intolerance(SLI) during ALCT can significantly predict a clinical diagnosis of MSA with high specificity (95.5%) & moderate sensitivity (50%)(diag-3).

Conclusion: To conclude positive ALCT was more useful in predicting a clinical diagnosis of IPD, compared to its efficacy in predicting long-term dopaminergic responsiveness. Though the development of dyskinesia during the test performance could not correctly predict the development of LID during chronic dopaminergic therapy, it can predict a diagnosis of MSA, as also the appearance of SLI during the ALCT correctly predicting MSA.

OP-04-11
Onset and progression of pathologic atrophy in patients with Huntington disease in Uzbekistan
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Objective: We aimed to study how caudate and global volumes change as HD progresses from premanifest to early disease.

Patients and methods: 32 HD gene-positive individuals and 14 controls underwent serial volumetric MR imaging (baseline, 12 and 24 months; 2 or 3 scans per person). At baseline, 2 patients with HD were premanifest but developed overt motor features during the study, and 30 had early HD. All had dates of motor onset recorded. Caudates, lateral ventricles, and TIVs were measured using semiautomated procedures. Linear mixed models were used to investigate differences between patients with HD and controls in relation to motor onset, controlling for TIV, sex, and age.

Results: Extrapolating backwards in time, we found that differences in caudate and ventricular volumes between patients with HD and controls were evident 14 and 5 years, respectively, before motor onset (P < .05). At onset, caudate volume was 2.56 mL smaller than that in controls (P < .0001); ventricular volume was 9.23 mL larger (P < .0001). HD caudate atrophy rates were linear, showed low variability between sub-
jects, and were approximately 10-fold higher than those in controls (P < .001). HD ventricular enlargement rates were variable between subjects, were approximately 4-fold higher than those in controls at onset (P < .001), and accelerated with disease duration (P = .02).

**Conclusions:** We provide evidence of acceleration of global atrophy in HD with disproportionate caudate involvement. Both caudate and global measures may be of use as early markers of HD pathology.

**OP-04-12**

**Frontal intermittent rhythmic delta activity (FIRDA) as a marker of Dementia with Lewy Body (DLB). A resting state conventional EEG study**

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**Background:** The search for a neurophysiological marker in the diagnostic workup of degenerative dementias, capable to differentiate DLB from Alzheimer disease (AD) and Parkinson’s disease-Dementia (PD-D), is needed. In the recently revised diagnostic criteria of DLB a “prominent posterior slow wave EEG activity with periodic fluctuations in the pre-alpha/theta range” has been included among the supportive biomarkers that “helps the diagnostic evaluation, but without clear diagnostic specificity”. Quantitative EEG may offer advantages in terms of diagnostic accuracy but this technique allows mainly an intergroups discrimination, whereas conventional EEG might detect abnormalities more useful in diagnosing individual patients.

**Patients and Methods:** We retrospectively revised conventional EEG recordings of 20 patients with clinically diagnosed LBD (17 “probable” and 3 “possible”), 20 patients with clinically diagnosed AD and 20 with PD-D. The median age was 72.5, 77.5 and 77.5 years, the median duration of cognitive impairment was 3, 2 and 2 years and the median MMSE was 19, 14 and 20.5 in DLB, AD and PD-D patients, respectively. EEGs were recorded according to the international 10-20 system with a bipolar montage.

**Results:** 60% of DLB patients showed FIRDA as compared to 5% for both AD and PD-D patients. The median frequency of background activity was lower in DLB and PD-D patients than in AD patients (7 c/s, 7.2 c/s and 8.2 c/s, respectively). Aspecific theta and delta activity was detected in most of the AD and PD-D patients and in 8 DLB patients.

**Conclusions:** FIRDA has been reported in 2.7 to 22% of a wide spectrum of encephalopathies and structural brain lesions, mainly involving the subcortical areas, so being regarded as a non-specific abnormal EEG pattern. The high occurrence of FIRDA found in DLB supports its potential role as a candidate marker suitable to be included among supportive diagnostic criteria of the disease.
**OP-04-13**  
**Comparison of dystonia between Parkinson’s disease and atypical parkinsonism: The clinical usefulness of dystonia distribution and characteristics in the differential diagnosis of parkinsonism**  
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*Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Neurology, Seoul, Republic of Korea*

**Objective:** Dystonia is occasionally found in patients with Parkinson’s disease (PD) and atypical parkinsonisms. However, systematic comparative analysis of the association between dystonia and parkinsonism have seldom been reported. The goals of this study are to compare the clinical characteristics and distributions of dystonia between PD, multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD).

**Methods:** We prospectively enrolled 176 patients who presented with dystonia and parkinsonism out of 1,278 patients with parkinsonism. We analyzed the clinical features of dystonia and parkinsonism.

**Results:** The frequencies of dystonia were 11.0% in PD, 20.9% in MSA, 40.7% in PSP and 66.7% in CBD. Dystonia symptoms were most frequent in CBD and relatively more frequent in PSP and MSA (p< 0.001). Moreover, multiple types of dystonia occurred most frequently in MSA (p=0.034). According to the distribution of dystonia, cranio-facial dystonia (CFD) and cervical dystonia (CD) were more frequently observed in atypical parkinsonism (p=0.001). In contrast, limb dystonia (LD) was more frequently observed in both PD and CBD, and truncal dystonia (TD) was more frequently detected in PD (p< 0.001). Levodopa medication related dystonia was markedly more frequent in PD than in atypical parkinsonism (p=0.030).

**Conclusions:** In this long-term, observational, prospective study, we concluded that levodopa medication related LD and TD were more frequently observed in PD than in atypical parkinsonism. Conversely, levodopa medication non-related CFD and CD were more frequently observed in atypical parkinsonism, and coexisting of some types of multiple dystonia may be unique features of atypical parkinsonism. TD or multiple types of LD, might be representative of PD rather than atypical parkinsonism.

**OP-04-14**  
**Striato-nigral and Cortical 123I-FP-CIT dopaminergic deficits in dementia with Lewy bodies and Parkinson’s disease**  
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**Objectives:** Several studies suggested more symmetrical and extensive nigrostriatal dopaminergic deficits in dementia with Lewy bodies (DLB) compared to Parkinson’s disease (PD). The objective of the study was to evaluate the differences in both nigrostriatal and cortical 123I-FP-CIT binding between PD and DLB patients.
**Methods:** fifty-six early PD (mean age 64.9 ± 10.0 years, mean disease duration 2.2 ± 2.1 years) and 28 DLB patients (mean age 72.3 ± 6.3 years, mean disease duration 2.2 ± 1.4 years) entered the study and underwent 123I-FP-CIT imaging. The striatal tracer uptake and regional cortical binding were evaluated at single-subject levels using standardized region of interest (ROI) after normalization. A whole-brain analysis was performed with Statistical Parametric Mapping (SPM). All the analyses were adjusted for the effect of age, sex and disease duration.

**Results:** No significant striatal binding differences were found between DLB and PD patients at single-subject level. DLB showed significant frontal (mean binding 0.65 ± 0.46 vs 1.9 ± 2.6 p=0.04) and parietal (0.75 ± 0.4 vs 2.0 ± 2.4 p=0.02) 123I-FP-CIT adjusted-binding reduction compared to PD patient. Whole brain SPM group-analyses confirmed the presence of several clusters of dopaminergic deficits in DLB compared to PD patients, adjusting for the effect of age, sex and disease duration.

**Conclusions:** a widespread cortical 123I-FP-CIT reduction differentiate early DLB from PD patients. Further studies are needed in order to understand the mechanisms underlying the differences in striato-cortical dopaminergic deficits in alpha-synucleinopathies.
Abstracts
Session V: Parkinson Disease

OP-05-01
Subcortical steps of visual processing are altered in de novo Parkinson’s disease patients
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1Inserm U1216, Grenoble, France, 2Grenoble Institute of Neurosciences, Grenoble Alpes University, Grenoble, France, 3Division of Neurology, CHU de Grenoble, Grenoble, France

Objective: To evaluate the functional responses of visual structures in de novo Parkinson’s patients (PD).
Methods: Twenty-two untreated PD (F/M=5/15, age 57±10y., stage I or II at HY scale) and twenty-two age-matched healthy controls (CT) (F/M=5/15, age 58±9y.) with normal or corrected-to-normal vision were recruited. Additionally, patients (n=8) were screened at 2 and 6 months after the introduction of a dopaminergic treatment. We used a 3-Tesla MR scanner. Achromatic checkerboards varying in luminance contrast (1-9%), flashing at 4 Hz were alternately presented in each visual hemi-field. MRI preprocessing and a region-of-interest analysis in SC, LGN and V1 individually defined, were performed using SPM12 (see(1)).

[Figure 1: Bold responses in three structures. Left column: Controls vs de novo Parkinson’s patients.]
Results: For CT, SC response was modulated by luminance contrast ($p < 10^{-4}$) (fig.1A). This was not the case in PD ($p = 0.10$) (fig.1A). After two or six months of treatment, this modulation was not restored ($p = 0.16$ and $p = 0.7$ respectively) (fig.1B). PD had a higher response at 1% ($p < 0.01$) and lower response at 9% ($p < 10^{-4}$). LGN response in CT showed a modulation ($p < 10^{-4}$) (fig.1C), which was slightly observed in PD (5-9%: $p < 0.02$) (fig.1C) and altered by the treatment (fig.1D). LGN responses were higher in PD at 1% ($p < 0.01$) and lower at 9% ($p < 0.01$). In PD, V1, unlike SC and LGN, presented a similar modulation ($p < 10^{-4}$) (fig.1E) compared to CT ($p < 10^{-4}$), which was preserved after 2 and 6 months of treatment (fig.1F). PD presented higher level of activity at 3% ($p < 10^{-2}$) corrected by treatment (fig.1F). Analysis of the number of saccades showed no statistical difference between groups.

Conclusions: SC and LGN are altered in de novo PD patients, supporting their potential role as early biomarkers. V1 is preserved. Dopaminergic treatment does not restore a normal functioning of these subcortical structures at 6 months.


OP-05-02
Recommendations for the organization of team care in Parkinson’s disease: Practice-based evidence from 20 expert centers around the world
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Objectives: Optimal management in Parkinson’s disease (PD) involves pharmacological and non-pharmacological treatment, delivered through a multidisciplinary approach. However, the nature of multidisciplinary team care varies widely and there is no guideline available that clarifies how a certain approach should be organized. Therefore, we aim to provide a practice-based guideline for the organization of team care in PD, describing achievable ‘must haves’ and ‘nice to haves’.

Methods: Twenty expert centers in the field of multidisciplinary care in PD participated. Their leading neurologists completed a survey with propositions regarding the organization of care in PD, addressing seven themes (Table 1). Outcomes were discussed and adjusted when needed during a consensus meeting. Subsequently, we drafted a set of concept recommendations and considerations, which were discussed in the multidisciplinary team of each participating center. Finally, three patient organizations reviewed the concept recommendations and prioritized the most important recommendations according to patient opinion. Based on this feedback, the final set of Recommendations & Considerations was developed.

Results: We developed 26 Recommendations and 10 Considerations. The patient organizations considered the following recommendations as the most important: I) care is organized in a patient-centered way; II) there is a core care team available for every newly diagnosed PD patient; and III) the patient’s care team has a team coordinator. A spin-off Quick Reference Card was created to facilitate the practicability of the Recommendations & Considerations.
**Conclusions:** We have provided a practical tool to improve team care for people with PD and their caregivers in an optimal patient-centered way. Future studies should focus on the implementation of these recommendations, to evaluate the effectiveness of this practice-based approach. These recommendations may be applicable to other chronic or complex conditions that also benefit from multidisciplinary care.

<table>
<thead>
<tr>
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<th>Elements for optimal multidisciplinary care</th>
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<tr>
<td>2</td>
<td>Members of the team</td>
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<td>3</td>
<td>The role of patient and caregiver</td>
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<td>4</td>
<td>Coordination of the team</td>
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<td>5</td>
<td>Team meetings</td>
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<td>6</td>
<td>Inpatient or outpatient care</td>
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<td>Telehealth</td>
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[Themes addressed in the survey]

**OP-05-03**

**Effect of istradefylline on non-motor symptoms of Parkinson’s disease: A sub-analysis of a 1-year observational study in Japan (J-FIRST)**

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1 Juntendo University School of Medicine, Department of Neurology, Tokyo, Japan, 2 Iwate Medical University, Morioka, Japan, 3 Research Institute for Brain and Blood Vessels-Akita, Akita, Japan, 4 Tohoku University Graduate School of Medicine, Sendai, Japan, 5 Okayama Kyokuto Hospital, Okayama, Japan, 6 Fukuoka University, Fukuoka, Japan, 7 Ehime University Graduate School of Medicine, Ehime, Japan, 8 Nagoya University, Nagoya, Japan, 9 The Tazuke Kofukai Medical Research Institute, Osaka, Japan

**Objective:** To evaluate effect of istradefylline on non-motor symptoms (NMSs) in istradefylline-naïve Japanese patients with Parkinson’s disease (PD).

**Methods:** In J-FIRST, 996 PD patients with ≥1 NMS and wearing off under anti-parkinsonian treatment were observed for up to 52 weeks to clarify the clinical manifestations of NMSs and identify factors affecting NMSs and quality of life. This sub-analysis was conducted on patients who were istradefylline-naïve before the study. The effect of istradefylline on NMSs was measured by changes in MDS-UPDRS Part I total and individual sub-items scores.

**Results:** Overall, 732 patients were istradefylline-naïve prior to the study; 171 were treated with istradefylline for ≥8 weeks during the 1-year study period. At baseline, patients who received istradefylline (n=171) were more likely to have a caregiver (63.7% vs. 50.0%) and dyskinesia (49.7% vs 40.8%), and received a higher daily dose of levodopa (462.79 mg vs 413.01 mg), than those who did not (n=561). MDS-UPDRS Part I total score at the end of the 52-week observational period increased in both those who received istradefylline and those who did not (0.49±0.41 vs 0.07±0.15, P=0.36, estimated by marginal structural
model). At week 52, the scores for the following sub-items in the istryadefylline-treated group were marginally better than for patients who did not receive istryadefylline: anxious mood (item 4); apathy (item 5); sleep problems (item 7); pain and other sensations (item 9); urinary problems (item 10); and fatigue (item 13). For cognitive impairment (item 1) and hallucinations and psychosis (item 2), patients who did not receive istryadefylline had somewhat more favorable changes; however, none of the above differences were statistically significant.

**Conclusions:** NMSs remained generally controlled in istryadefylline-treated Japanese patients who had wearing off under anti-parkinsonian treatment. Istradefylline could be a feasible and safe treatment option for advanced PD patients that will not worsen existing NMSs.

The authors represent a study group (J-FIRST group).

**OP-05-04**

**Pain: A marker of prodromal Parkinsons disease?**

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**Introduction:** The disease-related changes of PD can start decades before the appearance of cardinal motor symptoms, manifesting certain nonmotor abnormalities among which pain is one of the most important. In this study, we have tried to elicit whether pain can be an early clinical marker of the future development of PD, in the absence of motor signs.

**Methods:** In this combined hospital and community based observational study, 500 persons(>50yrs) from an urban community were assessed regarding the presence of different pain syndromes by verbal questionnaire and review of medical records. The likelihood ratio (LR) of prodromal PD (MDS research criteria for prodromal PD) were estimated in these subjects divided into 2 groups: control group (LR< 80%), & prodromal PD group (LR>80%). Prevalence of different pain syndromes was assessed in 95 PD patients (< 2 yrs disease duration) attending neurology OPD (clinical PD group) by interviewing patients and relatives and reviewing past medical records. ICD-9-CM diagnostic codes were used to classify different pain syndromes.

**Results:** Among the 500 subjects (314 males,186 female), 32 (6.4%) showed an LR>80%. Pain was significantly more the prodromal PD group [23(71.8%)] compared to control group [144(30.76%)]. In the clinical PD group, pain prevalence is 63.15%, which was comparable to prodromal PD group. Clinical PD and prodromal PD group were significantly more associated with cervicalgia, shoulder pain, pain in the pelvic region & thigh joint, backache & low back pain compared to the control group. Clinical PD & prodromal PD group were also significantly more associated with frozen shoulder, RLS & nocturnal leg cramp compared to control group.

**Conclusion:** Different pain syndromes were significantly more in prodromal group compared to the control group, while the prodromal PD and clinical PD group were comparable regarding the presence & distribution of pain. This is an indirect evidence that pain can be an important early clinical marker of PD, but longitudinal studies are indicated to evaluate the predictive value of pain for development of PD.
500 individual without any known neurological disease were recruited from the community. 95 Early Parkinson’s disease (<2 yrs. duration) patient attending neurology OPD were recruited.

Likelihood Ratio (LR) for prodromal PD (MDS research criteria for prodromal PD) were estimated.

Prevalence of different pain syndromes was assessed by verbal questionnaire (interviewing patients and relatives) and reviewing past medical records.

<table>
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<th>Types of different regional pain syndromes</th>
<th>Control group</th>
<th>Prodromal PD group</th>
<th>Clinical PD group</th>
<th>P value</th>
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<td>Total no of patients</td>
<td>468</td>
<td>32</td>
<td>95</td>
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<tr>
<td>Frequency of pain prevalence (%)</td>
<td>144 (30)</td>
<td>23 (71)</td>
<td>60 (63.15)</td>
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<td>Cervicalgia (%)</td>
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<td>8 (25)</td>
<td>28 (29.5)</td>
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<td>Shoulder pain (%)</td>
<td>15 (3.2)</td>
<td>14 (43.75)</td>
<td>31 (32.6)</td>
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<td>Upper arm pain (%)</td>
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<td>6 (18.75)</td>
<td>9 (9.5)</td>
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<td>Forearm pain (%)</td>
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<td>2 (6.25)</td>
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<td>Hand joint pain (%)</td>
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<td>1 (3.125)</td>
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<td>Myalgia/Myositis (%)</td>
<td>32 (6.8)</td>
<td>9 (28.125)</td>
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<td>Lower leg joint pain (%)</td>
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<td>2 (6.25)</td>
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<td>Ankle &amp; foot joint pain (%)</td>
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<td>2 (6.25)</td>
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<td>Limb pain (%)</td>
<td>25 (5.3)</td>
<td>9 (28.125)</td>
<td>15 (15.8)</td>
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<td>Pelvic region / Thigh joint pain (%)</td>
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<td>6 (18.75)</td>
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<td>Low back pain (%)</td>
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<td>13 (40.625)</td>
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<td>5 (15.625)</td>
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<td>Back pain (%)</td>
<td>15 (3.2)</td>
<td>11 (34.375)</td>
<td>30 (31.6)</td>
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</table>

[Prevalence of different regional pain syndromes in the three groups]
OP-05-05
A randomized controlled trial of DA-9701 on gastric motility in patients with Parkinson’s disease
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Objectives: To evaluate the effect of DA-9701, a novel prokinetic drug, on gastric motility evaluated by magnetic resonance imaging in patients with Parkinson’s disease (PD).

Methods: Forty PD patients were randomly allocated to receive either domperidone or DA-9701. Their gastric functions were evaluated using magnetic resonance imaging before and after 4-week treatment period. Information on levodopa daily dose, disease duration, and Unified PD Rating Scale scores was collected. In 18 patients (domperidone: 9, DA-9701: 9), plasma levodopa concentrations were determined. Primary outcome was assessed by a one-sided 95% confidence interval (CI) to show non-inferiority of DA-9701 vs. domperidone with a pre-determined non-inferiority margin of -10 %

Results: Thirty-eight participants (19 men and 19 women; mean age, 67.1 years) completed the study protocol (domperidone: DA-9701 = 19:19). Gastric emptying rate at 120 minutes (2-hr GER) was comparable between the 2 groups; it was not correlated with levodopa daily dose or disease duration or Unified PD Rating Scale scores (all \( p > 0.05 \)). DA-9701 was not inferior to domperidone in changes of 2-hr GERs before and after the treatment (absolute difference, 4.0 %; one-sided 95% CI, - 3.7 to infinity). However, a significant increase in 2-hr GER was observed only in DA-9701 group (54.5 % and 63.8 %, before and after treatment, respectively, \( p < 0.05 \)). Plasma L-dopa concentration showed an insignificant but increasing trend in DA-9701 group. There were neither adverse reactions nor deteriorations of parkinsonian symptoms observed in the study participants.

Conclusion: DA-9701 can be used for the patients with PD to enhance gastric motility without aggravating PD symptoms.
OP-05-06
Promoter identification and transcriptional regulation of the anti-inflammation gene CD200R1 in Parkinson’s disease
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Recent researches have been shown that abnormal activation of microglia plays an important role in pathogenesis of Parkinson’s disease (PD). Microglia are normally inhibited in a stationary state almost by the contact inhibition between neuron and microglia. This contact inhibition recently has been found closely related to the interaction between CD200 (located in neuron) and its receptor CD200R (located in microglia). Normally, CD200R1 upregulates to increase CD200-CD200R inhibit signaling thus preventing microglia from overactivating when brain being attacked.

Our previous studies showed, however, expression of CD200R could not increase in PD when received inflammation stimulation, which means abnormal regulation of CD200R expression happens in PD. However, no information about the regulatory element of the CD200R gene and its transcriptional regulation has been reported so far. Here we identified the CD200R promoter using a promoter luciferase construct that directs transcription of CD200R.

Our results show that the region from -485 to -267 (first base of CDS is +1) constitutes the core promoter and harbors motifs for the binding of NFkB1 as validated by analysis websites JARSPAR and P-MATCH. Knock down of NFkB1 dropped the promoter activity of CD200R. Using chromatin immunoprecipitation assay and EMSA, we demonstrated the physical interaction of NFkB1 to the CD200R core promoter sequence. In human PBMC, expression levels of NFkB1 correlated significantly to CD200R (P< 0.001). Knock down of NFkB1 reduced CD200R expression in PBMC (P < 0.001). Importantly, LPS stimulation led to increase expression of CD200R which was prevented when knock down of NFkB1 in human PBMC. Meanwhile, levels of NFkB1 showed a decrease in PD patients (P< 0.001).

This is the first study identifying the CD200R promoter and its transcriptional regulation by NFkB1. Knowledge of the transcriptional regulation of the CD200R gene will implicate in enhanced understanding of its role in pathogenesis of PD.
OP-05-07

Long-term efficacy and safety of incobotulinumtoxinA treatment for sialorrhoea in Parkinson’s disease and other neurologic conditions

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Objective: SIAXI (NCT02091739), a pivotal, double-blind, randomised, placebo-controlled study with a 48-week extension period (EP), assessed the efficacy and safety of incobotulinumtoxinA 75U and 100U in patients with sialorrhoea due to neurological causes. Here, we present data from the complete study.

Methods: MP patients were randomised (2:2:1) to incobotulinumtoxinA 75 or 100U (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 75U or 100U. Placebo recipients were randomised 1:1 to either 75U or 100U incobotulinumtoxinA in the EP. Outcomes included: unstimulated salivary flow rate (uSFR), patients’ Global Impression of Change Scale (GICS), Drooling Severity and Frequency Scale (DSFS), modified Radboud Oral Motor Inventory for Parkinson’s Disease (mROMP) (Kalf JG, Arch Phys Med Rehabil 2011), EuroQol 5-dimensions visual analogue scale (EQ-5D VAS) and adverse events (AEs).

Results: Of 184 patients randomised, 173 (mean [SD] age 65.2 [11.4] years; 71.7% male; 71.1% with sialorrhoea due to PD) completed the MP and entered the EP. Among 68 and 72 patients treated with 75U or 100U incobotulinumtoxinA, respectively, in all 4 ICs, mean (SD) uSFR decreased continuously from study baseline with repeated ICs [figure 1]. Patients’ GICS showed improvements at all visits; mean (SD) improvements at IC4 end, 1.29 (1.18) and 1.41 (1.18). DSFS, mROMP drooling scores and EQ-5D VAS also improved from study baseline to 4 weeks post-injection in each IC. mROMP speech and swallowing symptom scores remained stable. The most common treatment-related AEs were dry mouth (4.4% and 11.1%) and dysphagia (1.5% and 4.2%). Serious treatment-related AEs were speech disorder (1/68 [1.5%] incobotulinumtoxinA 75U recipient) and dysphagia (1/72 [1.4%] 100U recipient).

Conclusions: These data support the long-term efficacy and safety of repeated incobotulinumtoxinA treatment for sialorrhoea of neurological origin.
OP-05-08
Long-term prognosis and survival of new Parkinson’s disease subtypes
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Objectives: To provide validation and long-term prognosis data on new Parkinson’s disease (PD) subtypes using a large group of pathology-confirmed PD cases.

Methods: Retrospective review of clinical records of consecutive autopsy-confirmed PD cases from the Queen Square Brain Bank. Severity of motor signs (bradykinesia, tremor, rigidity and postural instability), autonomic dysfunction, REM sleep behaviour disorder and cognitive impairment were graded (absent, mild, moderate, severe) at time of diagnosis. Classification criteria were adapted from Fereshtehnejad as follows:

- Mild motor predominant: motor and non-motor scores < 75th percentile
- Intermediate
- Diffuse malignant: motor score >75th percentile and 1 non-motor score >75th percentile or all non-motor scores >75th percentile

SD, standard deviation; uSFR, unstimulated salivary flow rate

[Figure 1. Change from study baseline in uSFR (g/min)]
Time from diagnosis to disease milestones (recurrent falls, wheelchair dependence, dementia, care home placement) and death were compared between subtypes and their risks were estimated using Cox hazard regression models.

**Results:** 117 PD patients were included (61.5% male; age at diagnosis 62.3 ± 11.5 years). Mild-motor predominant patients (67.5%) were younger and had better levodopa response while diffuse-malignant patients (11.1%) were older, almost all male, more commonly misdiagnosed with atypical parkinsonism and had a poorer response to levodopa ($P < 0.001$ for all comparisons). Intermediate and diffuse malignant subtypes had a faster progression of the disease (earlier development of disease milestones) and reduced survival than the mild-motor subtype (all $P < 0.05$). The risk of any disease milestone was 12 times higher (HR 12.58 (5.94-26.65); $P < 0.001$) and the risk of death was 4 times higher (HR 4.01 (2.02-7.98); $P < 0.001$) in the diffuse malignant group compared to the mild-motor predominant.

**Conclusions:**
- New PD subtype classification is applicable in clinical practice using retrospective clinical data.
- PD subtyping shows accurate long-term prognosis prediction of disease progression and survival.

**OP-05-09**

**Acute dopaminergic neurotoxicity of alpha-synuclein oligomers is mediated by microglial cells**

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The loss of dopaminergic neurons is caused by mitochondrial impairments and alpha-synuclein aggregation, which are pathological hallmarks in Parkinson’s disease. It is currently admitted that alpha-synuclein oligomers are one of the main toxic factors triggering the death of TH expressing cells and contribute to the progression of symptoms in Parkinson’s disease. Multiple lines of evidence suggest that microglial cells are involved in the pathophysiology of this disease. The uptake of released alpha-synuclein by microglia has been evidenced in Parkinson’s disease and interpreted as a defensive mechanism at early disease stage. On the other hand, activated microglia cause neuroinflammation and neuronal cells death in the later stages of the disease.

Here, we investigated the alpha-synuclein oligomer toxicity on TH expressing neurons and the role of microglial cells in the neuronal death. Mesencephalic TH expressing neurons were cultured, in presence or absence of microglial cells, and injured by a solution of alpha-synuclein (250 nM, containing oligomers) for 24 hours or 48 hours. Neuronal survival and neurite network of dopaminergic neurons was assessed by immunocytochemistry, the activation of microglia and the cytokine release were also studied. We showed that in absence of microglia, the application of alpha-synuclein oligomers did not induce any acute neurotoxicity (in the 48h after application). We showed that acute toxicity of alpha-synuclein oligomers on TH expressing neurons is mediated by activated microglial cells and by the production of pro-inflammatory cytokines (TNFa, IL 1). Altogether, these results reinforce the role of microglia in the neurotoxic process occurring in Parkinson’s disease and potentially in other synucleinopathies.
Nonlinearities in outcome-specific hazard of motor and nonmotor long-term complications of Parkinson’s disease

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Objectives: To estimate the specific hazard of motor and nonmotor milestones of Parkinson’s disease (PD) progression in the long term.

Methods: We conducted a retrospective cohort study of PD-outpatients visiting Lyon’s university hospital-based movement disorders center. Seven clinical milestones of PD progression were analyzed encompassing four domains: (1) motor (motor fluctuations, dyskinesias); (2) axial (postural instability and falls, freezing of gait); (3) neuropsychiatric (impulse control disorders, hallucinations) and (4) cognitive (dementia) complications. We estimated the outcome-specific hazard rate for each complication independently using parsimonious smooth parametric Poisson regression models, so as to evaluate the specific contribution of timescales and their interaction.

Results: A total of 1232 PD-patients experienced 1527 disease-related complications in up to 12 years follow-up. Outcome-specific baseline hazard dramatically increased with disease duration for all complications. Hazard rates at 5-years were greatest for motor fluctuations and lowest for dementia in patients aged 65 at diagnosis, ranging from 124.8 [95% CI, 95.1-163.9] per 1.000 person-years in men and 166.7 [95% CI, 125.7-221.2] in women for motor fluctuations, to 8.1 [95% CI, 5.2-12.4] in men and 7.6 [95% CI, 4.6-12.9] in women for dementia. Nonlinear patterns in hazard were found for age at diagnosis, predicting dramatic increase in hazard for axial complications after 70 years, and for motor fluctuations, dyskinesias and impulse control disorders before 60 years. Increasing age at diagnosis also predicted hallucinations (HR, 1.03 [95% CI, 1.01-1.04]) and dementia (HR, 1.1 [95% CI, 1.07-1.14]). Disease duration and age at diagnosis statistically interacted for postural instability and falls, suggesting age-related accelerated pathological processes linked to postural instability in PD.

Conclusions: Progression to motor and nonmotor milestones in PD is determined by disease duration and age at diagnosis in nonlinear patterns. This strongly suggests disease duration- and age-specific thresholds in the multiple neurodegenerative processes accumulating in PD at different paces.
OP-05-11
Early serotonergic lesion promotes the emergence and severity of motor symptoms in monkeys

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Objective: Serotonergic (5-HT) neurons degenerate in Parkinson’s disease (PD). We and others have highlighted strong relationships between the alteration of the serotonergic (5-HT) system and the expression of motor and non-motor symptoms on both parkinsonian patients and monkeys. It is therefore crucial to investigate the precise implication of 5-HT besides dopamine (DA) in the parkinsonian symptomatology. We want to assess the impact of an early serotonergic (5-HT) lesion on the development and severity of motor symptoms induced by a dopaminergic lesion in non-human primates.

Methods: 5-HT fibers (not somas) were lesioned by using 3,4-methylenedioxyn-N-methamphetamine (MDMA) while DA neurons were lesioned by using 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in two groups of macaque monkeys (MDMA/MPTP and MPTP alone). Lesions were assessed by positron emission tomography (PET) imaging using the following tracers: [11C]DASB for the 5-HT transporter (SERT), [11C]P2I for the DA transporter and [11C]Raclopride for DA D2/D3 receptors. Lesions were also assessed by immunohistochemistry using tyrosine hydroxylase, tryptophan hydroxylase 2 and SERT antibodies. The severity of parkinsonian symptoms was assessed longitudinally using the rating scale of Schneider and Kovelowski. The higher the score, the more symptomatic the monkey.

Results: As expected, MDMA led to a decrease of [11C]DASB binding around 40% in the brain, except in the raphe. MPTP led a strong decrease of [11C]P2I binding in the striatum, independently of the groups. More surprisingly, a strong increase of [11C]Raclopride was evidenced in the striatum after MPTP in MDMA/MPTP lesioned monkeys compared to MPTP lesioned ones. Assessment of motor symptoms showed that MDMA/MPTP monkeys exhibited more rapidly and severely rigidity, tremor and postural abnormality compared to MPTP ones.

Conclusion: All together, these results demonstrate that the early lesion of serotonergic fibers promotes the emergence and severity of parkinsonism in response to MPTP in macaque monkeys.
Safety of sublingual apomorphine film (APL-130277) for the treatment of OFF episodes in patients with Parkinson’s disease: Results from a phase 3 double-blind, placebo-controlled trial

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Objective: To evaluate the safety of APL-130277 (APL) in the double-blind, placebo-controlled trial.

Background: OFF episodes are a common complication of Parkinson’s Disease (PD). APL is a sublingual formulation of apomorphine being developed for the acute treatment of OFF episodes.

Methods: A 12-week, well-controlled, double-blind trial was conducted, in patients with PD receiving levodopa who were experiencing motor fluctuations, to evaluate the efficacy of APL for the acute treatment of OFF episodes. The APL dose (10-35 mg) to produce a FULL ON response was determined. Patients were then randomized at the titrated dose to APL or placebo for 12 weeks, dosing up to 5x/day. Safety assessments included adverse events (AE), vital signs, ECG and laboratory and were collected during the titration and maintenance phases.

Results: 141 patients were enrolled in the study. The most common AEs in the titration phase were nausea (20.6%), yawning (12.1%), somnolence (11.3%), and dizziness (11.3%). 109 subjects (placebo-55 and APL-54) were randomized in the maintenance phase. Fifteen (27.8%) and 5 (9.1%) subjects discontinued treatment due an AE in the APL and placebo groups, respectively. The most common AEs that led to discontinuation in the APL group during the maintenance phase were lip swelling (n=2), oral mucosal erythema (n=2) and oropharyngeal swelling (n=2). The most frequently reported AEs during the maintenance phase for APL and placebo, respectively, were nausea: 27.8% and 3.6%; somnolence: 13% and 1.8%; and, dizziness: 9.3% and 0%. Most TEAEs were mild to moderate in severity. Oral AEs occurred in 31.5% of APL- and 7.3% of placebo-treated patients, respectively. These events were generally mild to moderate and reversible, with study drug discontinuation. Orthostatic hypotension, hallucinations and dyskinesias were rare.

Conclusion: In this study of PD patients with OFF episodes, APL was generally well-tolerated over the 12-week study period.
**OP-05-13**

**Therapeutic potential of a prolyl hydroxylase Inhibitor FG-4592 for Parkinson’s diseases**

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As the main transcription factor that regulates the cellular responses to hypoxia, Hypoxia-inducible factor-1a (HIF-1a) plays an important role in the pathogenesis of Parkinson’s disease (PD). HIF-1a is normally degraded through ubiquitination after hydroxylation by prolyl hydroxylases (PHD). Emerging evidence has suggested that HIF PHD inhibitors (HIF-PHI) may have neuroprotective effects on PD through increasing HIF-1a expression.

However, the therapeutic potential of HIF-PHI for PD remain poorly explored due to the lack of proper clinical compounds and understanding of the underlying molecular mechanisms. In this study, we examined the therapeutic benefit in PD models using a new HIF-PHI, FG-4592, which is currently in phase 3 clinical trials to treat anemia in patients with chronic kidney diseases (CKD). FG-4592 attenuated MPPC-induced apoptosis and loss of tyrosine hydroxylase (TH) in SH-SY5Y cells.

Pretreatment with FG-4592 mitigated MPPC-induced loss of mitochondrial membrane potential (MMP), mitochondrial oxygen consumption rate (OCR), production of reactive oxygen species (ROS) and ATP. Furthermore, FG-4592 counterbalanced the oxidative stress through up-regulating nuclear factor erythroid 2 p45-related factor 2 (Nrf-2), heme oxygenase-1 (HO-1) and superoxide dismutase 2 (SOD2). FG-4592 treatment also induced the expression of Peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α) through increasing the phosphorylation of AMP-activated protein kinase (AMPK). In MPTP-treated mice, FG-4592 protected against MPTP-induced loss of TH-positive neurons of substantia nigra and attenuated behavioral impairments.

Collectively, our study demonstrates that FG-4592 is a promising therapeutic strategy for PD through improving the mitochondrial function under oxidative stress.

**OP-05-14**

**Sodium oxybate for excessive daytime sleepiness and sleep disturbance in Parkinson’s disease: A randomized clinical trial**


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**Objective:** Sleep-wake disorders are a common and debilitating non-motor manifestation of Parkinson’s disease (PD) but treatment options are scarce. We tested whether nocturnal sodium oxybate (SO), a first-line treatment in narcolepsy, is effective and safe for excessive daytime sleepiness (EDS) and disturbed nighttime sleep.
Methods: In this randomized double-blind placebo-controlled crossover phase 2a study, 12 patients were randomized to a treatment sequence (SO/placebo or placebo/SO, ratio 1:1) and 11 completed the study. Two patients developed obstructive sleep apnea under SO (one was the drop-out) and were excluded from the per-protocol (n=10) but included in the intention-to-treat analysis (n=12).

Nocturnal sodium oxybate and placebo were taken at bedtime and 2.5-4h later with an individually titrated dose between 3-9g/night for a duration of 6 weeks with a 2-4-week washout period interposed. Primary outcome measure was change of objective EDS as electrophysiologically measured by mean sleep latency in the Multiple Sleep Latency Test. Secondary outcome measures included measures of subjective EDS, sleep quality and objective parameters of nighttime sleep (polysomnography).

Results: Among 12 patients in the intention-to-treat population, SO substantially improved EDS as measured objectively (mean sleep latency +2.9 min, P=.002) and subjectively (-4.2 points Epworth score, P=.001). It significantly enhanced subjective sleep quality and objectively measured slow wave sleep duration (+72.7 min, P<.001).

Differences were more pronounced in the per-protocol analysis. SO was well tolerated under dose adjustments, but induced de novo obstructive sleep apnea in 2 patients and parasomnia in one, as detected by polysomnography, all of whom did not benefit from SO treatment.

Conclusion and Relevance: This study provides class I evidence for the efficacy of sodium oxybate in treating EDS and nocturnal sleep disturbance in PD. Special monitoring with follow-up polysomnography is necessary to rule out treatment-related complications and larger follow-up trials with longer treatment durations are warranted for validation.

OP-05-15
A novel adenosine A2A receptor antagonist KW-6356 in early Parkinson’s disease: A randomized controlled trial for efficacy and safety
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Objective: To evaluate the efficacy and the safety of KW-6356 as monotherapy in early Parkinson’s disease (PD) (NCT02939391).

Methods: This was a multicenter, double-blind, phase 2a proof of concept study. The inclusion criteria were age from 20 to 80 years, diagnosis of PD by the United Kingdom PD Society Brain Bank clinical diagnostic criteria, modified Hoehn and Yahr stage 1 to 3, Movement Disorder Society version Unified PD Rating Scale (MDS-UPDRS) part III more than 14.

Patients were randomized into high dose, low dose or placebo. KW-6356 was orally administered once a day for 12 weeks. The primary endpoint was the least squares means of change from baseline in MDS-UPDRS part III. Secondary endpoints were MDS-UPDRS (total, part I and II), clinical global impression of improvement and treatment emergent adverse event. All values were analyzed statistically.
Results: Total of 168 patients could be enrolled and assigned into 3 groups as equal (high dose: low dose: placebo=58: 55: 55). Baseline clinical characteristics among these groups showed no significant difference such as male ratio (44.4%: 55.1%: 59.6%) and mean age (66.5: 66.6: 66.7). In the primary endpoint, changes from baseline of MDS-UPDRS part III were -4.76 (95% CI, -6.55 to -2.96) for high dose, -5.37 (95% CI, -7.25 to -3.48) for low dose and -3.14 (95% CI, -4.97 to -1.30) for placebo. Both doses of KW-6356 groups showed more reduction than placebo group. No notable differences of safety issues were observed among groups.

Conclusion: KW-6356 monotherapy is well tolerated and more effective than placebo in patients with early PD.

OP-05-16
A novel mGlu4 compound displays anti-parkinsonian and anti-dyskinetic activity in primate models of Parkinson’s disease
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Objective: Levodopa remains the gold standard treatment for Parkinson’s Disease (PD). However, as the disease progresses, dopaminergic treatments become less effective and produce debilitating side effects, including motor fluctuations and levodopa-induced dyskinesia (LID). Over the past decade, modulation of presynaptic metabotropic glutamate receptor 4 (mGlu4) has been proposed as a promising approach to normalize the basal ganglia circuitry in PD but it has never been demonstrated in primates so far. Objective of the study was to assess the therapeutic potential of our novel mGlu4 positive allosteric modulator (PAM), foliglurax, as an anti-parkinsonian treatment in non-human primate models.

Methods: Foliglurax (PXT002331) was tested in various models of MPTP-induced parkinsonism in macaques, modeling different stages of the disease: early stage, advanced parkinsonism and LID. Brain penetration of the compound has also been assessed using PET imaging in macaques.

Results: Foliglurax demonstrated consistent anti-parkinsonian efficacy in all models. Co-administration of foliglurax and levodopa resulted in a robust and dose-dependent reversal of parkinsonian motor symptoms in macaques. Moreover, foliglurax strongly decreased dyskinesia induced by levodopa, thus having therapeutic efficacy on both aspects: parkinsonian motor symptoms and LID.

Conclusion: This is the first demonstration that a mGlu4 PAM can alleviate the motor symptoms of PD and the motor complications induced by levodopa in primates. Supported by its unique preclinical profile, foliglurax has been the first mGlu4 PAM entering the clinics and is now being tested in a Phase IIa study.
Efficacy and safety of incobotulinumtoxinA for upper-limb essential tremor in a randomised, double-blind, placebo-controlled trial using kinematics-guided clinical decision support

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Objective: To assess the efficacy and safety of a single, kinematics-guided intramuscular injection of incobotulinumtoxinA compared with placebo, for moderate-to-marked essential tremor (ET) of the upper limb, in a multicentre, randomised, double-blind, Phase II study (NCT02207946).

Methods: Patients with ET were randomised 2:1 to receive incobotulinumtoxinA (total dose ≤195U) or placebo in a single treatment cycle. Muscle selection was individualised according to patterns of wrist, elbow and shoulder tremor, and doses per muscle based on TremorTek™ analysis (providing kinematics-guided, clinical-decision support to guide the injection protocol). Kinematics and clinical-outcome metrics (including Fahn-Tolosa-Marin [FTM] and grip strength) were assessed over 24 weeks. From baseline, differences between incobotulinumtoxinA and placebo were assessed at Weeks 4 and 8 for the maximum angular wrist-tremor amplitude and FTM Part B motor performance score.

Results: In total, 30 patients were randomised (incobotulinumtoxinA, n=19; placebo, n=11). There was a trend towards decreased wrist-tremor amplitude with incobotulinumtoxinA versus placebo at Week 4 (95% CI -1.108, 0.039) and a significant improvement at Week 8 (95% CI -0.806, -0.070). Sensitivity analysis by ANCOVA: Week 4, p=0.144; Week 8, p=0.005. Kinematic outputs also showed persistent anti-tremor effects ≤24 weeks after a single injection of incobotulinumtoxinA. FTM Part B showed significant improvement in the incobotulinumtoxinA group versus placebo at Week 4 (95% CI -3.4, -0.6). Sensitivity analysis by ANCOVA yielded significant results: Week 4 (p=0.003); Week 8 (p=0.031). Maximum grip strength in the treated arm decreased by 20%, with no notable change using placebo. Two patients (incobotulinumtoxinA group) reported localised finger-muscle weakness. There were no muscle weakness-related premature discontinuations.

Conclusions: Kinematics-guided incobotulinumtoxinA administration significantly decreased tremor severity and improved hand motor function versus placebo in patients with ET of the upper limb. Individualised dosing was well-tolerated, with no muscle weakness-related premature discontinuations.
OP-05-18
Comparison of botulinum toxin injections in forearm FLexor plus EXtensor muscles versus flexor muscles alone for the treatment of Essential hand Tremor (FLEX ET)
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We conducted a double blind, randomized, parallel double dummy, pilot single center trial on 2 types of abobotulinumtoxinA (BTX) injection patterns for treatment of essential tremor (ET).

Patients were randomized to receive either injections of 75 units of BTX in flexor compartment (flexor carpi radialis (FCR) and flexor carpi ulnaris (FCU) of dominant arm along with placebo in extensor carpi radialis (ECR) and extensor carpi ulnaris (ECU) or 75 units in FCR and FCU and 25 units in ECR and ECU (F + E group).

Patients were seen in follow up at 6 weeks and again at 12 weeks. At 6 weeks we repeated all baseline measures (i.e. Tremor Rating Scale (TRS), Task-Specific Improvement Scale (TSIS), QUEST, PHQ-9 and GAD7) and patients evaluated treatment response using a patient and clinician global impact scale ranging from -4 (severely worse) to +4 (no more tremor) with 0 meaning no change as well as rate improvement in carrying out task that was most bothersome for patient prior to injection.

Grip strength was measured prior to injections as well as at each followup visit.

As a whole (without considering treatment type), the group significantly improved in TRS (p < .001) but displayed a mild significant decline in grip strength (p < .001). There was no significant change on any other measure.

The F+E group scored significantly higher on the clinician global improvement scale, with a median score of 3 (IQR 1-3), compared to a median score of 1 in the Flexors group (IQR 0-2) (p = .025).

From our small pilot study, it does appear that the group who received flexor and extensor BTX injections (3:1 ratio) experienced greater benefit without additional worsening of grip strength, as compared to those who had flexor only injections.

OP-05-19
Beyond cerebellar involvement: Abnormal subcortical volumes in essential tremor
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Objectives: The spectrum of symptoms observed in patients with essential tremor (ET) extends beyond the classical upper limb postural tremor, and several non-motor symptoms have been reported. The cerebellum has been most commonly implicated in the pathogenesis of ET and although several neuroimaging studies have suggested the involvement of brain regions apart from the cerebellum, the exact macro-
structural differences in volumes of subcortical nuclei have not been reported. This study aims to compare the volumes of subcortical nuclei in patients with ET in order to ascertain neuroimaging correlates of motor and non-motor features of ET.

**Methods:** Forty patients of ET and forty age and gender matched healthy controls (HC) were enrolled in this study. Tremor severity was quantified with the Fahn-Tolosa-Marin tremor rating scale (FTMRS). Structural imaging was performed on a 3T scanner, and volumes of subcortical structures were obtained using FIRST in FSL.

**Results:** There were no difference in total brain volume between ET and HC. Significant volume loss was observed in bilateral thalamus, hippocampus, and ventral diencephalon, in patients with ET when compared to HC. A significant increase in volume was observed in the right caudate nucleus, pallidum, amygdala, and bilateral putamen, and nucleus accumbens. Negative correlations were observed between the FTMRS scores and volumes of bilateral putamen and hippocampus.

**Conclusion:** Patients with essential tremor have significant alterations in volumes of subcortical nuclei, which are not limited to the motor domain and include structures involved in cognitive and behavioral functions. These results add to the growing concept of the pathophysiology of essential tremor extending beyond the cerebellum.
POSTER EXHIBITION

Topic: Basic Neuroscience

P 001
Drug-Induced Parkinsonism as a risk factor for Parkinson’s disease: A cohort review from Uzbekistan
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We aimed to study whether subjects who experienced a reversible episode of drug-induced parkinsonism have an increased risk of subsequent Parkinson’s disease. We provide a cohort review in history materials of 24 patients with Parkinson’s disease (PD) for the period from 2008 to 2015y. All observed cases of PD were compared to the control group including practical healthy population whose age and gender status matches to 1st group. From all cases in the 1st group with PD only two patients with drug-induced parkinsonism, Parkinson’s disease later developed. A comparison with the cases in the 2nd group with practical healthy population (0.08) yielded a relative risk of 23.7 (94% confidence interval, 2.8 to 87.5; \( P=0.005 \)). We revealed that drug-induced parkinsonism is associated with a high risk of PD. Clarification of the mechanisms of this association may have preventive implications.

P 002
Lead acute intoxication alters dopaminergic system and locomotor performance in Meriones shawi
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Objectives: Lead induces several developmental, neurological, behavioral impairments; and affects neurotransmitter systems in the brain. In the present study, we investigated effects of acute lead exposure on the dopaminergic system in Meriones shawi.

Methods: Adult male Meriones shawi were injected intraperitoneally with 25mg/Kg of lead acetate for three consecutive days. Locomotor behavior was assessed using the open field test and meriones were sacrificed for an immunohistochemical analysis of tyrosine hydroxylase, in Substantia Nigra compacta (SNc),
**Abstracts**

**Results:** we reported, in acute Pb intoxicated meriones, an increased TH expression within SNC, those alterations were correlated to behavioral abnormalities such as a severe loss of locomotor performance in the intoxicated animal compared to controls.

**Conclusions:** this data supports the possible implication of Pb, as a risk factor for Parkinson’s disease (PD) and may let us to more understand the pathophysiology of the PD.

**P 003**

**Assessment of antiparkinsonian activity by experimental way**

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**Objective:** Assessment of antiparkinsonian activity by experimental methods.

**Methods:** Methods for assessing antiparkinsonian activity, based on the oppression of dopaminergic transmission. Methods based on the inhibition of DA transmission include tests simulating development catalepsy and other extrapyramidal disorders administration of dopaminergic agents, as well as the model SS-induced neurotoxin 1-methyl-4-phenyl-1, 2, 3, 6-tetra gidopiridinom (MPTP) causing selective damage to DA neurons.

**Results:** Catalepsy caused usually by administration of various doses, of which the most commonly used and haloperidol triflazin. Typical antipsychotics cause blockade of DA receptors, and their appointment in large doses, even if there is a single application of extrapyramidal disorders.

**Conclusions:** It should be noted that this model has several drawbacks. Under the action of neuroleptics degenerative changes in DA neurons and their terminals are not developed, while at the PS celebrated the death of at least 70-80% of DA neurons in the compact part of the substantianigra. However, these methods expressed catalepsy model and allow us to establish the presence of DA level in the mechanism of action of the test compound and is therefore widely used for the evaluation of anti-money. Furthermore, to create extrapyramidal disorders using reserpine causing DA-deficient state by exhaust of catecholamines of CNS. The most adequate model of the PS is now recognized method using a neurotoxin MPTP, which causes neurodegenerative changes in DA neurons in the substantianigra.
P 004
Experimental model of Parkinson’s syndrome in animals
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Objective: To asses Rotenone model of of parkinsonian syndrome in rats .
Background: Rotenone is of highly lipophilic substances that can freely enter hematoencephalic barrier through and biological membranes. The mechanism of action of rotenone as mechanism MPTP actions associated with mitochondrial respiratory chain. Rotenone to provoke dopaminergic neurodegeneration, most similar in its symptoms.

Methods: Rotenone is used primarily on cellular structures and embryological studies. In adult animals, primarily rats, rotenone used less frequently because of its low chemical stability in animal tissues and body fluids.

For formation of experimental parkinsonism it requires a long period of chronic administration of rotenone (from 1 week to 3 months). When administered subcutaneously rotenone was dissolved in a vegetable oil, and administered at a dose (2 mg / kg / day) for 4 weeks. In animals developed bradykinesia, postural non stability and / or rigidity, which abolished the introduction of apomorphine.

Results: Behavior of animals studied at 3, 6 and 9 days of the experiment. Used a series of tests for the detection of extrapyramidal disorders, as well as test apomorphine verticalization. Apomorphine is administered at a dose of 1 mg / kg subcutaneously 5 min assess vertical activity, and after 10 min - postural instability. Also used unilateral introduction of rotenone (12 .mu.g in 0.5 .mu.l with Dimexidum a rate of 0.1 .mu.l / min.) in «medial forebrain bundle» by coordinates (AP: +0,2; L: ± 1,8; DV: 8 mm) stereotactic atlas.

Conclusion: Intrinigralnoe single unilateral introduction of rotenone in small doses on today is available as one of the adequate models of parcinsonian syndrome of rats, which reproduces lengthy neurochemical and neuropathological changes similar to the changes in Parkinson diseases in the nigrostriatal system.

P 005
Tremorin model of Parkinson disease
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Objective: To evaluation of muscarinic agonist by using model of tremor caused by active metabolite of tremorin - oxotremorine

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

Conclusion: Points received in the assessment of the average value for the group. The results allow us to know about the quality of the experiment and the whole study drug.


P 006
Methodical recommendation for experimental modeling of parkinsonian syndrome
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Objective: Despite of differences in etiology, pathogenetic basis of all forms of Parkinson's syndrome (PS) is same. Aim is evaluate of quality of experimental modeling of parkinsonian syndrome in laboratory animals.

Background: PS is considered a progressive multisystem disorder.

Methods: In this research analyzed existing methods of experimental modeling of parkinsonian syndrome in laboratory animals. Obtained data is processed by means of modern statistical methods and also Two types of these models differ in the dynamics of the process and its manifestations and it’s considered as reproducing, respectively, akinetic-rigidity and tremor form of PS. When oppression of DA transmission PS is occurs slowly, lasts a few days, begins with oligokinesia; prevails akinetic-rigidity form.

Results: Reduction of symptoms begins with rigidity, and their severity depends on the age of the animals. PS develops quickly when activation of cholinergic system, lasts a few hours, begins with tremor predominant form of rigid-trembling, the reduction begins with symptoms of tremor, age of experimental animals significantly irrelevant.

The results of an research of new drug must contain materials that prove the presence of a pronounced antiparkinsonian activity and has advantages over conventional means.

For each test substance study at least three doses. They should be used in at least two ways of administration, one of which it corresponds to the intended clinical route of administration. Not less her than one of the main test is necessary to examine dose-response curve and to determine the effect of duration of effect using the route, relevance of the proposed clinic.

Conclusion: Research antiparkinsonian active substance must be conducted in comparison with the most «standard» drugs of the same type of action. Analysis showed that in literature there are no data available about specific assessment of the most effective methods.
P 007
The experimental model of extrapyramidal disorders caused by reserpine
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Objective: To evaluate extrapyramidal disorders caused by reserpine.

Methods: The effect of drugs on extrapyramidal disorders caused by reserpine is evaluated in white mongrel mice by administering a 2.5 mg/kg dose intraperitoneally in suspension with Tween-80.

Results: Reserpine causes the depletion of catecholamine stocks in the central nervous system and, in connection with this, allows to model the DA deficiency state observed in the PS. In rats, reserpine causes a decrease in motor activity - oligokinesia and catalepsy. The test substances are injected 30 minutes after the injection of reserpine. Depending on the age of the animals, PS manifestations differ significantly.

Assessment of motor activity is carried out after 10 minutes 2 hours after the injection of reserpine. An animal group is placed in the actometer. Usually take into account the overall indicator for the group, while the control and receiving groups should contain an equal number of animals.

Assessment of autonomic disorders. Ptosis is recorded in points according to the size of the eye gap: 3 - complete closure of the eyes, 2 - a gap to 1 mm, 1 - a gap to 2 mm, 0 - the eyes are completely open.

Salivation is estimated by the size of a wet spot on the neck: 3 to 2 cm, 2 to 1 cm, 1 to 0.5 cm, 0 - no effect.

Diarrhea is recorded. The body temperature is measured by an electrothermometer with a rectal sensor when the electrode is immersed to a depth of 1.5-1.8 cm.

Conclusions: This model has a number of shortcomings. However, these methods model the expressed oligokinesia and allow to establish the presence of DA link in the mechanism of action of the test compound and therefore are widely used for the evaluation of antiparkinsonian agents.

P 009
L-theanine recues quinolinic acid induced motor dysfunction and striatal neurotoxicity: Reduction in oxido-nitrosative stress and restoration of striatal neurotransmitters level
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L-theanine has been documented to possess anti-oxidant, anti-inflammatory and neuroprotective potential in various animal models of neurological disorders. The study was anticipated to investigate the effect of L-theanine against quinolinic acid induced motor deficits, oxido-nitrosative stress, neuro-inflammation and neurotransmitters alteration in rats. Rats were stereotaxically injected QA (200 nmol/2µl saline; intra-striatal); bilaterally on 0 day and L-theanine (25 & 50 mg/kg; p.o.) was administered for 21 days starting from day 1 of QA injection. Either, L-NAME (10 mg/kg; i.p.), a nitric oxide synthase inhibitor and L-arginine
(50 mg/kg; i.p.), a nitric oxide synthase precursor were administered with L-theanine in respective groups. Behavioral observations were evaluated on weekly basis using rota-rod, grip strength, narrow beam walking and open field test. QA treatment induces significant alteration in body weight, motor coordination, oxidative defense, pro-inflammatory cytokines and striatal neurotransmitters level. L-theanine treatment alone, at both the tested doses, significantly attenuated QA induced alterations. In addition, treatment of L-theanine with L-NAME significantly enhances the protective effect of L-theanine whereas treatment of L-theanine with L-arginine significantly ameliorated the protective effect of L-theanine. The protective effect of L-theanine is attributed to its anti-oxidant, anti-inflammatory and modulatory effect on nitric oxide pathway and neurotransmitters level in striatum. This suggests use of L-theanine in the clinical settings of HD.

P 010
Intranigral inoculation of Parkinson’s disease linked mutation G51D alpha-synuclein fibrils induces Lewy-like pathology in mice
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Parkinson’s disease (PD) is a neurodegenerative disease characterized by movement disorder and its pathological features include progressive neuronal loss in the substantia nigra (SN) and Lewy body (LB) formation. α-synuclein (α-syn) is the main component of LB, and its genetic mutation causes familial PD. Among these mutations, G51D mutation exhibits most severe clinical symptoms. In vitro findings of G51D mutation being rather mild in cytotoxicity and aggregate-forming ability are not well correlated with the clinical symptoms. Therefore, we performed pathological analysis of G51D mutation using in vivo inoculation model of α-syn fibrils into mouse SN. G51D α-syn fibrils induces robust phosphorylated α-syn inclusions in inoculation side at 12 weeks, which further spread to the contralateral side at 24 weeks. Moreover, mice inoculated with G51D α-syn fibrils showed nigral neuronal loss and motor impairment at 24 weeks. These results are consistent with PD pathology, suggesting that this mouse model can be effective tool for developing new PD therapies.
P 011

Role of metformin in diabetic aging female rat brain: a future therapy for neurodegenerative diseases
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Background: The emerging view is that diabetic brain features many symptoms that are best described as accelerated brain aging. Metformin is the most frequently used oral anti-diabetic drug, which apart from hypoglycaemic activity, improves serum lipid profiles, positively influences the process of haemostasis, and possesses anti-inflammatory properties.

Objective: The objective of this study was to investigate effects of metformin on glucose transporter (GLUT1, GLUT3) expression, intracellular calcium levels, expression of synaptic molecules synaptophysin and synapsin I, biomarkers of oxidative stress such as antioxidant capacity (FRAP), malondialdehyde (MDA), reduced glutathione (GSH), protein carbonyl (PCO), reactive oxygen species (ROS) and neurolipofuscin in diabetic aging brain of female rats.

Methods: Young (3 months) adult (12 months) and aged (24 months) rats will be diabetic by using alloxan monohydrate. Metformin was administered i.p. at a dose of 200 mg/kg/day for 30 days to both control and diabetic aging rats. A detailed study was carried on expression of glucose transporter, calcium levels, biomarkers of oxidative stress. Morris water maze with expression of synaptic molecules synaptophysin and synapsin I and ultrastructural studies of brain region by magnetic resonance imaging.

Results: Present study shows that there was a similar pattern of increased intracellular calcium levels, neurolipofuscin, MDA, PCO, and ROS levels, and a decrease in levels of FRAP, GSH and (GLUT1, GLUT3) expression in brain of both aging and diabetes. On the other hand, metformin treated groups exhibited significant reduction in helped to reverse the age related changes studied, to normal levels. Metformin treatments improved attention and memory functions with enhanced the levels of synaptic molecules synaptophysin and synapsin I. Our data showed that exogenous administration of Metformin brought these changes to near normalcy in diabetic aging female rats.

Conclusions: The results of this study will be useful for pharmacological modification of the aging process and applying new strategies for control of age related disorders including metabolic syndrome and neurodegenerative diseases.
**P 012**

*Aloe arborescens* and *Curcuma longa* protect against acute copper exposure induced the neurobehavioral characteristics of Parkinson's disease in rats

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**Objectives:** Parkinson's disease (PD) is a chronic neurodegenerative pathology implying a primary motor dysfunction and classic clinical features including rigidity, difficulty with walking and bradykinesia, which are the consequence of progressive death of dopaminergic neurons in the substantia nigra. Numerous findings sustain the implication of heavy metals, as an environmental risk factor such as copper (Cu), in the neuropathology of PD. We aimed herein to describe the neuroprotective potential of *Aloe arborescens* and *Curcuma longa* against of acute Cu intoxication on dopaminergic system and locomotor performance in rat.

**Methods:** Adult male rats were injected intraperitonially with 10mg/Kg for three consecutive days together with the oral administration of curcumin I (30mg/kg B.W.) or *Aloe arborescens* extract (200mg/kg B.W) to Cu intoxicated rats. Locomotor behavior was evaluated by the open field test and rats were scarified for an immunohistochemical analysis of tyrosine hydroxylase, in Substantia Nigra compacta (SNc), in the ventral tegmental area (VTA) and in the subsequent striatal outputs.

**Results:** we reported, in acute Cu intoxicated rats, a loss of TH expression within SNc, VTA and the subsequent striatal outputs, those alterations were correlated severe loss of locomotor performance. Aloe arborescens or curcumin I co-treatment reversed these changes and exhibited a clear protective effect; manifested by a complete recovery of TH immunoreactivity and locomotor performance observed in the intoxicated rats.

**Conclusions:** The present study shows, on the one hand, an altered dopaminergic innervations following acute Cu intoxication and strengthens the probable implication of Cu, in the pathophysiology of PD. On the other hand, new therapeutic potential of aloe arborescens and curcumin-I against Cu-induced dopaminergic dysfunction and therefore, preventing heavy metals induced Parkinsonism.

**P 013**

Impaired dopaminergic and serotonergic innervations in thioacetamide induced acute hepatic encephalopathy may be linked to hypolocomotion

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**Objective:** Hepatic encephalopathy (HE) is a progressive and complex neuropsychiatric disorder resulting from acute as well as chronic hepatic failures and may impact negatively on the quality of life of HE patients. Advanced HE is generally accompanied with extrapyramidal symptoms including rigidity and
tremor, which may reflect alterations of several neurotransmitters including dopamine, GABA, glutamate or serotonin. The present investigation aimed the assessment the dopaminergic and serotonergic responses and the possible correlation to locomotion in an animal model of acute hepatic encephalopathy in rat.

**Methods:** Acute HE was induced by repetitive i.p administrations of thioacetamide (TAA) (300 mg/kg), 1 injection/day during 3 consecutive days. While controls received physiological saline buffer (NaCl 0.9%). Using immunohistochemistry and open field test, we assessed respectively the expression of tyrosine hydroxylase (TH) in substantia nigra pars compacta and serotonin level in the dorsal Raphe nucleus and locomotor activity 12 hours following the last TAA administration.

**Results:** Our data showed a significant loss of TH level within substantia nigra pars compacta and decreased serotonin immunoreactivity in the dorsal Raphe nucleus, and this was concomitant with hypoactvity in TAA rats compared to controls.

**Conclusion:** the present finding seems to involve the loss of brain dopamine innervations as well as serotonin as a possible neuronal basis of hypolocomotion, known to occur in acute hepatic encephalopathy.

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**P 014**

**Study on the operation time of deep brain stimulation for Parkinson’s disease**

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**Objectives:** To explore whether STN DBS has better efficacy in early PD rats than in late PD rats.

**Methods:**
1. Establish hemi-parkinsonian rat model by injecting the toxin 6-OHDA into the right medial forebrain bundle (MFB).
2. Implant the concentric bipolar electrodes into the right STN of rats and perform 18F-AV133-VMAT2 imaging and behavior tests on these rats after surgery.
3. Repeat the 18F-AV133-VMAT2 imaging and behavior tests after two weeks' stimulation.
4. Confirm the implantation site by Nissl staining and calculate the remaining nigral cells by immunohistochemistry.

**Results:**
1. Compared with PD rats without stimulation, AV133-VMAT2 imaging didn't show any difference between the early stimulation and late stimulation of PD rats.
2. There was no significant difference in APO test between PD rats without stimulation and those received stimulation, neither early stimulation nor late stimulation of PD rats.
3. Early stimulation and late stimulation showed better efficacy in the Cylinder task than PD rats without stimulation (P < 0.05).
4. TH immunohistochemistry showed significantly reduced more than 90% TH-positive cells in substantia nigra in the lesion side (right side) in PD rat models. Compare with the PD rats without stimulation, early stimulation present less neuronal loss(68.3%) than late stimulation(83.3%). But there was no significant change of TH immunohistochemistry between early and late stimulation in PD rat models.
Conclusions: STN DBS can improve motor behavior in PD rats. The early and late stimulation of PD rats had no effect on their VMAT2 binding rate whereas early stimulation shows better neuronal protection.

P 015
2014-2016 worldwide bibliometric snapshot of the scientific literature on Parkinson’s disease

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We investigated the scientific publications on Parkinson's disease (PD) from 2014-2016 to provide various global quantitative characteristics of the literature. Using the WoS SCI-expanded database all articles and reviews (or papers) related to PD were retrieved and analyzed. In the most recent 2014-2016 period, 92 countries participated in the publication of 8,483 PD-related papers, almost all written in English. The top-5 productive countries were: USA (n=2,415), China (n=1,056), UK (n=980), Italy (n=812), and Germany (n=805). Conversely 41 (≈45%) countries published under 2% (n=134) of the papers. Of the EU-28, all but one member country contributed 3,758 (44%) papers, and 17 EU countries (≈63%) published more than 50 papers. Besides China (ranked 2nd), three Asian countries ranked within the top-15 productive countries: Japan 11th (n=367), South Korea 12th (n=363), and India 14th (n=246). The BRICS (Brazil, Russia, India, China, and South Africa) published 1,615 (19%) papers. Fourteen African countries participated in only 96 (1%) papers and most published fewer than 10 papers. The 8,483 papers on PD were published in 1,254 journals with the five most productive journals concentrating nearly 26% of the papers: Parkinsonism & Related Disorders (n=730), Movement Disorders (n=706), PLOS One (n=312), Journal of Parkinson's Disease (n=254), and Parkinson's Disease (n=193). Conversely, nearly 90% (n=1,119) of the journals published ≤ 10 papers. Nine of the top-10 journals were in Clinical Neurology and/or Neurosciences WoS categories and Movement Disorders had the highest impact factor (7.072). The publishing profile of the top-5 countries revealed China's overall different preferences: lower percentage of review-type papers (10% versus 14%-18%); lower number of collaborative countries (35 versus 54-75); highest percentage of papers authored by nationals only (75% versus 33%-55%); lowest percentage of papers with international collaborators (25% versus 45%-67%); and preference for more general versus specific PD journals.
P 017
Clinical correlations between Parkinson’s disease and vascular parkinsonism: New retrospective review from Uzbekistan
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Objectives: 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 to 2 groups (VP and PD), and compared the clinical features.

Results: The 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 effect (P< .05).

Conclusions: These differences in clinical features suggest a 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 020
The role of apoproteins in the development of Parkinson’s disease
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A group of American scientists undertook a study of potential biomarkers of the risk of Parkinson’s (PD) disease in the blood plasma.

Using a multiplex immunoassay, a cohort of 152 PD patients was examined, while 96 plasma concentrations were measured in the plasma. Finally, the plasma levels of the most probable biomarkers of the PD were studied in the third cohort, which consisted of 134 asymptomatic individuals with a high risk of developing PD, participating in the PARS study (Parkinson’s Associated Risk Study). To assess the relationship between the plasma concentration of proteins and the integrity of the dopaminergic system, isotope neuroimaging with a dopamine transporter (single photon emission computed tomography) was used.

According to the results of the first screening study, one of the most suitable candidates for the role of the biomarker was the level of plasma apolipoprotein A1 (ApoA1, p = 0.001). The low level of ApoA1 correlated with the earlier onset of PD, with the transition of ApoA1 upward for each subsequent tertile, the risk of PD development decreased by 26% (according to the Cox proportional hazard model, p < 0.001, risk ratio 0.742).
The relationship between the plasma level of ApoA1 and the age of onset of PD was reproduced in an independent sample of patients with PD (p < 0.001). In a cohort of asymptomatic individuals with a high PD risk from the PARS study, a low level of ApoA1 was associated with a large stratum dopaminergic deficiency (p = 0.037).

It was concluded that a low level of ApoA1 correlates with the inconsistency of the dopaminergic system in symptomatic patients with PD and asymptomatic individuals with a reduced density of the dopamine transporter reflecting the prodromal phase of PD. Thus, ApoA1 can be considered as a new biomarker for PD risk.

**P 021**

Combined administration of an A<sub>2A</sub> receptor antagonist and a 5-HT<sub>1A/1B</sub> receptor agonist reverses neuroinflammation in the 6-OHDA model of Parkinson’s disease

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A previous study of our laboratory demonstrated an improved motor performance in 6-hydroxydopamine (6-OHDA) unilaterally lesioned rats, a model of Parkinson’s disease (PD), that were treated with the combination of L-dopa, the serotonin 5-HT<sub>1A/1B</sub> receptor agonist eltoprazine, and the adenosine A<sub>2A</sub> receptor antagonist preladenant. Starting from these findings, and from evidences that implicates neuroinflammation in PD progression, the present study investigated whether counteraction of neuroinflammation participated in the motor effects of the L-dopa+eltoprazine+preladenant combination.

6-OHDA-lesioned rats were chronically treated with L-dopa+eltoprazine+preladenant. Then, we evaluated in the denervated caudate-putamen (CPu) and substantia nigra pars compacta (SNc) the immunoreactivity (IR) for the glial fibrillary acidic protein (GFAP), and the co-localization of the ionized calcium binding adaptor molecule 1 (IBA1), with interleukin (IL)-1β, tumor necrosis factor-α (TNF-α) and IL-10. Finally, the IR for tyrosine hydroxylase (TH) and the dopamine (DA) transporter (DAT) was quantified.

Combined treatment with L-dopa+eltoprazine+preladenant induced a reduction of basal GFAP and IBA1 IR in both CPu and SNc. Moreover, a reduction of IL-1β in IBA1-positive cells both in CPu and SNc and of TNF-α in IBA1-positive cells in SNc was observed. Besides, a significant increase in IL-10 in IBA1-positive cells was also observed in SNc. Finally, a significant reduction of DAT and TH IRs was found in all the experimental groups.

The present findings indicate that the combined administration of L-dopa+eltoprazine+preladenant reduced the inflammatory and neurodegenerative responses in the nigrostriatal system of 6-OHDA-lesioned rats.
**P 022**

**Prevention of Parkinson's disease using natural biological additives**

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The leading place among the causes of stroke and the subsequent development of Parkinson's disease, occupies atherosclerosis (AC) - one of the most common and socially significant diseases in the world.

The traditional strategy for primary prevention of diseases, associated with atherosclerosis, is the impact on its factors risk.

The medication tactics of combating one of the key links of atherogenesis - dyslipidemia (DLP) - are prescribed by means of synthetic origin: statins, fibrates, nicotinic acid, bile acid sequestrants. However, a number of side effects and contraindications limit their wide clinical application. Every year the number of studies increases, aimed at finding alternative lipid-lowering drugs.

Among them, the leading place is occupied by preparations of natural origin.

A number of clinical and experimental studies have shown antihyperlipidemic effect of garlic. The positive effect on the lipid metabolism of plant oils.

In recent years, significantly increased interest in complex preparations of natural origin, affecting the various links of the pathogenetic process.

The objects of the study were white mongrel rat males. Study of hypolipidemic properties natural substances was carried out in accordance with the guidelines on preclinical study of medicines with using appropriate methods of statistical processing data. The consumption of phytosterols in mice with apo-E deficiency reduced the number of platelets, the sensitivity of erythrocytes to hemolysis, plasma fibrinogen. All this led to reduce the formation of atherosclerotic lesions.

In a comparative study of the lipid-lowering properties of the powder garlic, it was found that the garlic powder was statistically significantly lowered TG (-23.6%, -22.8%). Given the biological properties of amaranth oil, it seems extremely promising its further inclusion in the complex drug, having hypolipidemic, hypotriglyceridemic and antisclerotic actions.
Cerebral microbleeds in dementia with Lewy bodies is not characteristic.

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It is proved that the budget of CMB (cerebral microbleeds) correlates with the severity of cerebral vascular changes. First of all, the severity of leukoarosis and the number of lacunar infarcts. As a rule, vascular changes in the brain are not characteristic of DLB (dementia with Lewy bodies). Nevertheless, there are publications on the frontal localization of CMB in DLB.

The aim of the study was to study the dynamics of the MRI data, neurological and neuropsychological profile in DLB.

Methods: We studied 16 patients with DLB with cognitive decline older than 65 years during 24±4 months. MRI was performed on MR tomograph with a magnetic field of 1.5 Tesla «Signa Excite». Neuropsychological battery included Montreal Cognitive Assessment scale (MoCA), Addenbrooke’s Cognitive Examination (ACE-R), MMSE.

Results: Initially, single changes were found resembling subcortical CMB in 3 patients. We have excluded the deposits of calcium with the help of a computer tomography. After 2 years, two patients had multiple (2-5) cortical CMB (temporal and occipital) and a more pronounced cognitive decline (6±2 MMSE scores per years). The appearance of CMB was accompanied by a more pronounced leukoarosis, there was no difference in the degree of atrophy.

Conclusions: CMB in dementia with Lewy bodies is not characteristic. CMB might be an indicator of the clinical significance of leukoaraiosis. Isolated cases of multiple cortical CMB in DLB might be considered as sporadic cerebral amyloid angiopathy. In the case of a combination of vascular changes with DLB and sporadic cerebral amyloid angiopathy, Alzheimer’s component take place. The presence of CMB contribute to the cognitive decline. Specifically, CMB were associated with worse memory and visuospatial domains and the total ACE-R score in especially in DLB which had AD sings (p< 0.05). Multiple CMBs might represent an independent factor of cognitive decline.
P 024
Assessment of clinic-biochemical features of Parkinson’s disease
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Objective: To study the features of the cytokine status under different forms and variants of PD course.

Methods: The study included 100 patients - 52 women (52%) and 48 men (48%) aged 41 to 82 years with PD 2.0-4.0 on the Hoehn and Yahr scale. Blood samples were obtained in all patients, samples of CSF in 20 males and 8 females in 1st Republic Immunology Clinic. The content of interleukin (IL) -1β, IL-1 receptor antagonist IL-1RA, IL -10, tumor necrosis factor (TNF) α, IL-6 in the blood serum and CSF was determined by the method enzyme immunoassay.

Results: The study showed that differences in the cytokine profile of the akinetic-rigid and tremor forms increase with the progression of the disease, at the 3rd and 4th stages of the PD, in addition to the differences in the content of IL-10 in the serum, there is a difference in the level of IL-6 and IL-1PA: these the rates are lower by 64% and 72% in patients with akinetic- rigid form of PD respectively. For patients with predominantly right-sided clinical lateralization of the PD, the level of TNFα in the blood is increased by 38%. The relationship between serum TNF-α and the clinical BP lateralization was revealed: in patients with predominantly right-sided clinical symptoms, the level of TNFα in the blood was higher (3.1 (1.4-5.6) pg / ml) than in patients with predominantly left-sided symptoms (1.6 (0-3.1) pg / ml) (p = 0.04).

Conclusion: Following this approach, it is possible to identify “new” PD subtypes, which is especially important for the identification of previously unknown links in pathogenesis, determining the features of the course of the disease in each subgroup of patients and, as a consequence, to create modern therapeutic strategies.

P 026
Evaluation of the 70 kDa heat shock protein (Hsp70) plasma level in Parkinson’s disease and GBA-associated Parkinson’s disease patients
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Objectives: The analysis of association between Hsp70 plasma level in sporadic Parkinson disease (sPD) and GBA-associated PD (GBA-PD) patients and disease progression.

Methods: For the study we enrolled 92 participants: 48 PD patients (from two medical centers First Pavlov State Medical University of St. Petersburg and Institute of Experimental Medicine Clinic), 14 GBA-PD patients and 30 healthy individuals. All patients had undergone clinical examination with evaluation of
Hoehn and Yahr scale and cognitive examination (MMSE, MoCA, FAB). Screening of two known GBA mutations (N370S, L444P) as well as two polymorphic variants (E326K, T369M) was performed in both groups of patients and controls using the primers and specific restriction enzymes as previously described. Collected plasma samples were analyzed for the Hsp70 content (pg/ml) employing ELISA assay according to the manufacturer’s protocol (Invitrogen, USA).

**Results:** The detected Hsp70 plasma level in sPD patients was significantly lower as compared to healthy individuals, constituting 2382.5 ± 127.8 and 3298.8 ± 191.5 pg/ml correspondingly ($P < 0.0001$). Hsp70 plasma content in GBA-PD patients was not statistically different from that of sPD patients and healthy controls, constituting 2814.8 ± 221.8 pg/ml ($P=0.189$ and $P=0.089$, correspondingly). Subgroup analysis of the GBA-PD patients (i.e., mutation (L444P and N370S) carriers and polymorphic variants carriers (E326K and T369M)) did not reveal any statistical significance as compared to control group ($P=0.322$ and $P=0.34$, correspondingly). No significant correlation between stage of disease, cognitive status (MoCA, MMSE, FAB) and the plasma levels of Hsp70 was found.

**Conclusions:** The present study ascertains that lower levels of Hsp70 may contribute to the development of Parkinson disease.

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**P 027**

**A rare fatal Familial parkinsonism in elderly with early respiratory failure**

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**Objective:** To detail the first report from India of a rare fatal autosomal dominant syndrome of parkinsonism with early respiratory failure with onset in the elderly.

**Case summary:** A 62 year old doctor presented with acute encephalopathy, hypercapnia, central hypoventilation and seizures and required ventilatory support thereafter for persistent respiratory failure despite resolution of encephalopathy. He had orthostatic hypotension, snoring, episodes of shallow breathing, unsteadiness and weight loss for the last 2 years and had received treatment for anxiety and depression. His mother and elder brother had died of a similar illness at a similar age. A younger brother had progressive muscle disease with muscle biopsy showing inclusion bodies and mild inflammation. He did not respond to immunomodulation.

Similar inclusions were noted in the patient. Investigations for neuromuscular disease including myasthenia were negative. Genetic tests for a panel of muscular dystrophies and myopathies were negative. Evaluation for infectious, autoimmune and para-neoplastic encephalitis were negative. Pompes disease was excluded. Neuroimaging and electrophysiological studies were unremarkable. Empirical Intravenous immunoglobulin therapy was ineffective. During his hospital stay he developed marked rigidity, bradykinesia along with mild ptosis.

In view of a combination of early onset respiratory failure, parkinsonism, unexplained weight loss and positive family history, genetic test for Perrys syndrome was done. A heterozygous missense variation in Exon 2 of the DCTN1 gene (chr2:74605273;C>C/G;g.133G>G/C) that results in the substitution of Proline
for Alanine at codon 45 (p.A45P) was detected. This variation was not detected in his surviving asymptomatic elder brother. The clinical presentation and genetic test was consistent with Perry syndrome, which has never been reported from India. Patient is currently at home, on ventilator support and his parkinsonian symptoms have improved with Levodopa.

**Conclusion:** Perry syndrome should be considered in elderly patients with early onset respiratory failure, parkinsonism, weight loss and behavioral symptoms.

**P 029**

**Application of convolutional neural networks in the diagnosis of Parkinson’s disease dementia based on magnetic resonance imaging**

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Cognitive impairment is one of the most common non-motor symptoms in Parkinson’s disease (PD). Identification of PD patients at risk for the development of dementia is crucial for early intervention.

**Aim** - to verify the usefulness of convolutional neural networks (CNNs) in identification of damaged brain areas visualised with magnetic resonance (MRI) in PD patients with different severity of cognitive impairment.

A CNNs model was build to estimate parameters used in the process of creating activation maps of the neuronal layers classification. Those maps were used as an input signal in the identification process of different brain areas.

T1&T2 MRI brain images of 12 PD patients (6 normal cognition, 2 MCI, 4 demented) were used to train CNNs. In those 3 subgroups, 3 independent CNNs were trained using both MRI sequences simultaneously, and each one separately. For individual experiments, medium and differential activation maps were generated. The prepared average activation maps for each subgroup represented elements of the MRI image that were the most involved in the classification process.

The differential activation maps were created, and showed areas potentially significant in the diagnosis of cognitive impairment severity. The results have demonstrated, that the most active areas were located in the cerberellum, temporal and frontal cortex and cerebral ventricles. Furthermore, cerberellum was automatically segmented with the use of MiMSeg algorithm (doi.org/10.1016/j.ins.2016.07.052). The significant changes in cerberellum volume (p=0.0063) and folding (p=0.0132) were identified in the 3 subgroups of patients, showing volume and folding decrease with cognitive impairment progression.

Our analysis proved the usefulness of CNNs for the detection of areas of MRI images important in the diagnosis of cognitive impairment severity in patients with PD. The proposed methodology uses MRI sequences only and is able to detect changes, for which more sophisticated and expensive methods (DTI or DatScan) are being used.
P 030
DAT scan abnormalities in juvenile Westphal variant of Huntington’s disease
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Huntington’s disease (HD) is an autosomal dominantly inherited neurodegenerative disorder leading to motor, mood and cognitive deficits. Manifestations of Huntington’s disease include chorea, dementia, and psychiatric disturbance. It is caused by a genetic defect mapped to the short arm of chromosome 4 (4p16.3), with 40 or more “CAG” repeats in the coding sequence associated with disease manifestation. The age of onset correlates with number of CAG repeats showing anticipation.

When the onset of HD occurs before age 20, in most cases, the principle movement disorder is not chorea, but an akinetic-rigid syndrome with parkinsonian features known as the Westphal variant of HD (W-HD). W-HD is characterized by early onset parkinsonism and later presentation of chorea, if any. W-HD accounts for 85% of childhood onset HD and only 6% of patients with adult onset Huntington’s disease. This rare form of HD has associated findings of bradykinesia, rigidity, dystonia, cerebellar ataxia, eye movement abnormalities, action, intention tremor and catatonia.

There are no current guidelines for treatment of W-HD. Limited case reports have touched upon the potential benefits of L-dopa as well as dopamine agonists in providing symptomatic relief in W-HD variant with parkinsonian features.

We aim to present 3 cases of W-HD. There have been limited case reports documenting response to dopamine agonists. However, the exact mechanism of dopaminergic agents in W-HD remains unknown. We conducted DAT Scans in all our subjects prior to trial of dopaminergic agents. The results of DAT Scans in W-HD patients paralleled the DAT Scans of patients with parkinsonism with hypo-metabolism of striato-nigral pathways. These findings further illustrate a link of W-HD to dysregulation of neurotransmitters in the striatocortical and corticocortical pathways, as seen in parkinsonism which may account for the efficacy of dopaminergic medications in these cases.

P 031
Influence of alpha-synuclein promoter (Rep1) polymorphism on cognition, disability and plasma alpha-synuclein levels in Parkinson’s disease
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The association between alpha-synuclein gene (SNCA) promoter region (Rep1) polymorphism and Parkinson’s disease (PD) is well-established, with longer Rep1 allele carriers displaying increased PD risk and greater motor decline in multiple studies than short allele carriers. The association of Rep1 polymorphism with cognition and plasma alpha-synuclein levels remains unknown.
We investigated Rep1 allele length with cognitive and disability scores, and plasma alpha-synuclein levels in 129 subjects (37 age- and gender-matched controls and 92 PD patients). Subjects were grouped according to Rep1 allele length: 0/1 (short), 0/1-1/2 (medium) and 2/3 (long). Plasma alpha-synuclein levels were significantly higher in PD than controls (14976.4 vs 10845.0 pg/ml, p=0.002) but did not differ significantly according to Rep1 length. MMSE scores were significantly lower in PD than controls (p< 0.001) with a trend towards lower MMSE in PD patients with longer vs shorter alleles (24.1 vs 25.4, p=0.40). While UPDRS motor scores did not vary according to Rep1 length, there was a higher frequency of short allele carriers (48%) than longer allele carriers (10%) amongst patients with milder disease (Hoehn & Yahr, H&Y≤2).

Our findings suggest that patients with longer SNCA Rep1 alleles may display worse global cognition and disability scores compared to shorter allele carriers.

P 032
The role of 18F-FP-CIT PET in differentiation of progressive supranuclear palsy and frontotemporal dementia in the early stage
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Purpose: To evaluate whether the pattern of striatal dopamine transporter (DAT) availability could differentiate between progressive supranuclear palsy (PSP) and frontotemporal dementia (FTD) in the first few years of the disease.

Methods: We enrolled patients who had parkinsonism and frontal dysfunction and/or language deficit, visited the clinic within 2 years of the onset of symptoms, and had been followed-up for longer than 5 years, thus consisting of 26 patients with PSP and 24 FTD patients. By quantitatively analyzing N-(3-[18F]fluoropropyl)-2β-carbon ethoxy-3β-(4-iodophenyl) nortropane PET, we compared the pattern of DAT availability at the time of the baseline evaluation between the two groups. The discriminatory power of variables including DAT activity and clinical parameters was investigated by receiver operating characteristics (ROC) analyses. Additionally, we analyzed the correlation between striatal subregional DAT availability and cognitive profiles.

Results: Patients with PSP and FTD had significantly lower DAT availability than normal controls in the whole striatum and in each striatal subregion. When comparing the two groups, DAT availability was significantly lower in patients with PSP than those with FTD in all striatal subregions. The PSP and FTD groups had generally similar subregional patterns of DAT activity in terms of the anteroposterior and ventrodorsal gradients and asymmetry, except for a different preferential involvement in the caudate. The ROC analysis showed that the DAT activity of the whole striatum had an excellent discriminatory power relative to parkinsonism or neurocognitive profiles. Correlation analysis showed that verbal memory was significantly correlated with DAT availability in the whole striatum and the putaminal subregion only in patients with PSP.

Conclusions: DAT scans have prognostic value in determining whether patients with parkinsonism and behavioral and/or language dysfunction will develop features of PSP or FTD later in the disease course.
Association analysis of DRD2 rs2283265 and DRD1 rs4532 with Parkinson’s disease and Multiple system atrophy in a large Chinese population
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Background: Parkinson’s disease (PD) is a progressive neurodegenerative disorder associated with dopaminergic system dysfunction in the brain. Dopamine replacement therapy (DRT) is an established treatment for PD. However, there remains variability in drug response among PD patients. Studies have shown that some genetic polymorphisms in dopamine receptors (DR) are associated with the risk of PD, the response to treatment and motor complications of PD, such as DRD2 rs2283265 and DRD1 rs4532. Multiple system atrophy (MSA) is another neurodegenerative disease shares clinical and pathological characteristics with PD.

Objective: To explore the relationship between two polymorphisms of DR: DRD2 rs2283265 and DRD1 rs4532 and two neurodegenerative diseases (PD and MSA) in a large Chinese population.

Methods: A total of 1504 PD patients, 487 MSA patients, and 894 Healthy Controls (HCs) were directly sequenced for DRD2 rs2283265 and DRD1 rs4532.

Results: Significant differences were found in the genotype distributions and MAF of DRD2 rs2283265 between PD patients and HC and between MSA patients and HC when sex and age were controlled. Analyzing the recessive genetic model revealed that PD patients who carry the minor allele “A” (AA) exhibited an increased risk compared to patients who carry the major allele (CC+AC). In the subgroup analysis, the minor allele of DRD2 rs2283265 has the tendency to increase the risk for developing PD in female, early onset PD and the occurrence of freezing of gait (FOG). However, no association was found between DRD1 rs4532 and PD as well as MSA.

Conclusion: DRD2 rs2283265 is associated with the increased risk for PD and MSA. The minor allele is likely to increase the risk for developing PD in female, early onset PD and the occurrence of FOG. More studies in different ethnic are needed to verify these results.

Key words: Parkinson’s disease; multiple system atrophy; dopamine receptor; single nucleotide polymorphisms
P 035
Early brain metabolic changes in patients with Parkinson’s disease and its correlation to the risk of falling
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Background: The risk of falls is one of the main concerns in people with Parkinson’s disease (PD) leading to poor quality of life and increased mortality. Presently, there is no single measurement or test able to efficiently detect subjects at risk of falling.

Methods: We retrospectively collected clinical and 18F-fluorodeoxyglucose PET data of 33 PD patients without history of falls (24 M; age: 62±8.6 years) and 12 healthy controls (HC, 7 M; 62±14.2 years). Between 8 to 12 months after PET, 11 patients (8 M; age 64±8.6 years; disease duration: 7±4.2 years; age at onset: 57±11.1 years; UPDRS-III: 37.4±14.1; LEDD: 829±405 [baseline]) reported the occurrence of two or more falls; whereas 22 patients never experience any falls (16 M; age: 61±9.0 years; disease duration: 8±4.5 years; age at onset: 54±8.7 years; UPDRS-III: 28.2±14.6; LEDD: 753±373 [baseline]). Brain metabolic differences between fallers, non-fallers and HC were tested by Statistical Parametric Mapping (SPM) with age and disease duration as covariates, and a post hoc volume-of-interest (VOI) analysis.

Results: At baseline, clinical data did not differ between PD fallers and non-fallers. In PD fallers (vs. non-fallers), SPM analysis revealed a lower FDG uptake in the left parietal cortex (inferior and superior parietal lobules; pFWEcorr< 0.05) and a higher bilateral cerebellar FDG uptake (posterior lobes; pFWEcorr< 0.05). Fallers also showed a significant hypometabolism in the left parietal cortex compared to healthy controls (p< 0.01). These results were confirmed by the VOI analysis (p< 0.001).

Conclusion: We described an altered brain metabolism in PD patients 8-12 months before the first fall episode. Subjects with PD and a high risk of falling showed a metabolic impairment in sensorimotor cortical areas, combined with an increased -possibly compensatory- cerebellar activity.

P 036
Spg 11 gene mutation associated autosomal recessive hereditary spastic paraplegia presenting with partially levodopa responsive parkinsonism, stereotypy and cognitive decline
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Background: Hereditary Spastic Paraplegia (HSP) is neurodegenerative disorder affecting primarily the long axonal fibers of the corticospinal tracts. Clinically they are classified into pure or complicated HSPs which have multiple accompanied features. The exact clinical profile of SPG11 gene mutation associated
complex HSP is still being described in literature. Majority of SPG11 gene mutation patients present with spastic paraplegia with cognitive involvement. Only three other case reports with associated partially levodopa responsive parkinsonism in patients with complex HSP associated with SPG11 mutation have been reported in literature.

**Case:** A 33 year old male presented with history of regression with onset in second decade of life. He had normal birth and developmental milestones. At 15 years he developed gradually progressive spastic paraparesis associated with slowness and rigidity, followed by cognitive impairment with stereotypical movements and complex motor tics and became wheelchair bound by 25 years of age. There was no family history of similar symptoms or consanguinity. All the metabolic workup and ophthalmologic evaluation was normal. MRI brain revealed mild thinning of corpus callosum and mild periventricular white matter changes. He was partially responsive to levodopa at doses of up to 475 mg/day. The diagnosis of hereditary spastic paraplegia was confirmed by genome sequencing which showed mutation in exon 11 of SPG11 gene.

**Results:** All the metabolic workup and ophthalmologic evaluation was normal. MRI brain revealed mild thinning of corpus callosum and mild periventricular white matter changes. He was partially responsive to levodopa at doses of up to 475 mg/day. The diagnosis of hereditary spastic paraplegia was confirmed by genome sequencing which showed mutation in exon 11 of SPG11 gene.

**Conclusions:** Complex HSP due to SPG11 mutation should also be considered in differential diagnosis of patients with young onset levodopa responsive Parkinsonism with spasticity and cognitive decline.

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**P 037**

**Gene-lifestyle interactions in Parkinson’s disease**

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**Objective:** Current information on lifestyle-gene interactions in Parkinson’s disease (PD) is limited. Caffeine intake reduces PD risk, but its potential interaction with genes is unclear. The leucine-rich repeat kinase 2 (LRRK2) gene has been linked to the autosomal dominant familial form of PD, and the S1647T variant is a risk factor for PD in the Chinese population.

**Methodology:** Patients who satisfied the UK PD Brain Bank criteria and controls without neurological disorders were recruited (1790 PD, 2698 controls). Caffeine intake was assessed using a validated clinical tool. Genotyping of LRRK2 S1647T variant was carried out.

**Results:** Non-caffeine consumers with high genetic susceptibility had almost four times increased risk of PD compared to caffeine consumers with low genetic susceptibility [OR 4.01 (1.99, 8.09) p< 0.001; AP=0.55].

**Conclusion:** There is evidence that caffeine consumption significantly reduces the risk of PD in cases with high genetic susceptibility compared to those with low genetic susceptibility at the LRRK2 S1647T variant. Future studies can investigate the interactions with other genetic risk variants of PD.

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**Abstracts**
P 040

Improvement of apraxia of eyelid opening in a patient with Parkinson’s disease following the change of the directional lead for subthalamic nucleus deep brain stimulation.

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Objectives: To report a patient with Parkinson’s disease (PD) in whom apraxia of eyelid opening (ALO) improved after the change of another lead for subthalamic nucleus deep brain stimulation (STN-DBS).

Methods: A 61-year-old woman with a 21-year history of PD received bilateral STN-DBS surgery at the age of 49, because of motor fluctuations and dyskinesia. She underwent the surgery to replace the right electrode lead at the age of 55, because of akinesia. A half year after the surgery, akinesia emerged again. Thus, the left electrode lead was exchanged. Then akinesia somewhat improved, but ALO appeared. Four years after the last operation, she visited to our hospital. We changed to another IPG with Multiple Independent Current Control (MICC), because the voltage of right-side IPG could not be maintained. By adjusting the IPG with MICC, ALO and akinesia significantly improved. But she didn’t satisfy with the improvement of AOL. We decided to replace the new directional lead.

Results: Directional lead technology was suitable with her AOL. The AOL completely disappeared. She satisfied with this replacement. Several studies have reported the incidence of ALO between 6.1 to 11.3% after STN-DBS, but the precise mechanism of ALO is not well understood. It is difficult to treat ALO by adjusting stimulation of STN-DBS.

Conclusions: Directional lead technology could be useful for the adverse effect of DBS, such as AOL.
P 041
Toe dystonia in Parkinson’s disease: impact of subthalamic nucleus deep brain stimulation
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Objective: Off state toe dystonia (TD) is a symptom frequently encountered in Parkinson’s disease (PD), but little is known about its evolution after subthalamic nucleus deep brain stimulation (STN-DBS). Our objective was to analyze the prevalence and the evolution of TD in PD patients candidate to STN-DBS.

Methods: Individual data of consecutive 130 PD patients who underwent STN-DBS between 2010 and 2015 were collected. The presence of TD before and/or after surgery and the delay of appearance of TD after DBS for patients free of this symptom before were assessed retrospectively by medical records analysis and patients’ interviews as such information could have been missing in the files.

Results: Data were successfully collected in 95 patients. TD was present in 32.7% of patients before surgery and was alleviated by STN-DBS in 48% of the cases. TD was more frequently encountered in female patients. Motor improvement provided by STN-DBS, levodopa-equivalent treatment diminution after surgery, disease duration or age at the time of surgery were not predictive of TD evolution. A younger age at PD diagnosis was significantly associated with TD resolution.

Conclusion: STN-DBS is partially efficient for TD but its evolution seems independent of significant predictive factors. Therefore, one has to remain cautious about patients’ expectations regarding the evolution of this symptom after STN DBS.

P 042
Long term outcome of the subthalamic nucleus DBS for advanced Parkinson’s disease: An eight years follow-up study in China
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Background: Parkinson’s disease (PD) is a neurodegenerative disease. With the progression of the disease, the symptoms gradually worsen and levodopa-induced motor complications arose. Deep brain stimulation (DBS) is an effective treatment for advanced PD. But its long term efficacy has been little reported in China.

Objective: To investigate the long term efficacy and its safety of STN DBS on PD patients in China with eight years follow-up.

Methods: Patients with PD who had received bilateral STN DBS, was assessed preoperatively (baseline) and 1, 3, 5 and 8 years postoperatively on medication (med-on) and off (med-off) medication, using the Unified Parkinson’s disease Rating Scale (UPDRS) and a series of neuropsychological assessment. At the same time, the levodopa equivalent daily dose (LEDD) and stimulating parameters were also recorded.
Results: Compared with preoperative med-off state, motor symptom improved by 37.3% (P = 0.002) 8 years postoperation. Rigidity and tremor showed the most prominent improvement, followed by bradykinesia, and then axial symptom. At the med-on state, motor symptom did not show significant change. The quality of life improved by 39.7%, 56.1%, 18.8% (P < 0.001) at 1, 3, and 5 years separately, but deteriorated at 8 years (-4.1%). Sleep, cognition, and emotion were mostly unchanged. Levodopa equivalent daily dose was reduced from 708.1 ± 172.5 mg at baseline to 330 ± 207.8 mg at 8 years (by 53.4%, P < 0.001). The stimulating parameters gradually increased and their stimulating pattern has changed from monopolar to bipolar and interleaving.

Conclusions: STN DBS showed a positive efficacy on advanced PD, appearing as improving motor symptoms and reducing more than half of the dosage of anti-PD medication. Patients’ quality of life showed an improvement till 5 years postoperatively. Compared with other studies, patients in our study received diverse stimulating setting which can control patients’ symptoms better and have less severe adverse events (AEs).

P 043
The long-term development of excessive daytime sleepiness after subthalamic deep brain stimulation in patients with Parkinson’s disease
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Objectives: Subthalamic nucleus deep brain stimulation (STN DBS) has a positive effect on overall sleep quality, but its effect on wake functions are controversial. We aimed to assess the longitudinal changes of the quality of sleep and EDS in PD patients undergoing STN DBS and identify which factors are highly associated with the presence of EDS before and after STN DBS.

Methods: A total of 45 PD patients who underwent bilateral STN DBS between July 2011 and October 2015 were recruited. We evaluated subjective sleep quality assessed by Parkinson’s Disease Sleep Scale (PDSS) and EDS using Epworth Sleepiness Scale (ESS) preoperatively and 6 months, 1 year, and 2 years postoperatively. A cut-off ESS score of ≥11 was applied.

Results: There is a significant improvement in PDSS, and a noticeable change occurs immediately after the surgery. After DBS, the number of patients with persistent EDS gradually decreased, but new patients with worsening of EDS were developed. Consequently, there seemed to be no significant change in the prevalence of EDS before and after DBS. At baseline, there was no significant difference between the patients with and without EDS in the demographic or clinical variables, as well as no meaningful risk factors associated with EDS. Postoperative worsening EDS was more correlated with an increase of dopamine agonist dose than the severity of PD. Baseline ESS score is highly correlated with EDS at 6 months postoperatively, and use of dopamine agonist is a main risk factor for EDS 1 and 2 years after DBS.
Conclusions: Bilateral STN DBS improves the subjective sleep quality, but EDS may improve or worsen. In the long term after surgery, the increase in dose of dopaminergic agonists is thought to have the greatest effect on EDS, and the disease progression might also be partially affected.

P 044
Usefulness of directional deep brain stimulation in patients with movement disorders

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Introduction: Deep brain stimulation (DBS) is effective in the treatment of several movement disorders. Directional DBS (D-DBS) has been recently reported to increase side effects thresholds by steering the energy to a particular anatomical area. The possibility of adverse effects (AE) could be theoretically reduced achieving a similar clinical efficacy. The aim of the present study was to analyze the usefulness of D-DBS in the clinical practice.

Methods: This was a prospective study in 10 patients in whom directional electrodes had been recently implanted. In successive sessions monopolar review was done to select the best contact. Current intensity using circular stimulation (non-directional) was progressively increased until obtaining a good clinical effect or AE. In consecutive follow-up visits were evaluated for the presence of subacute AE or suboptimal clinical results. In that case D-DBS was initiated based on the clinical findings, AE, and their anatomical correlation.

Results: Ten patients were included: five with Parkinson disease (STN), four with dystonia (GPi) and one with Tourette syndrome (GPi). Mean age was 52 (73-22), and disease duration was 19 years (47-5). Seven patients received D-DBS due to insufficient clinical improvement or AE. Follow-up ranged from 8 to 3 months. The AE were dysarthria (5), muscular twitching (5), parkinsonism (1) and behavioral changes (2). D-DBS allowed an increase of the therapeutic window leading to clinical amelioration and avoiding the presence of AE.

Conclusions: D-DBS is a useful tool in the clinical practice since allows increasing the therapeutic window favoring a better clinical outcome without AE.
P 045

Predicting patient discharge disposition subsequent to deep brain stimulation surgery: A pilot study
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Background: Research has shown that surgeons are not able to accurately predict the clinical status of a patient after deep brain stimulation surgery. Furthermore, clinical decision making is susceptible to biases based on individual experience. Clinical decision making can be improved with the application of predictive models and decision support tools. The purpose of this study was to develop a predictive risk stratification model and decision support system that could accurately predict whether a patient is likely to be of high- or low-acuity discharge disposition status after deep brain stimulation surgery, based on routinely measured preoperative variables.

Methods: Preoperative and postoperative data were collected for 135 deep brain stimulation patients by reviewing medical records. Logistic regression analysis was applied to develop the predictive algorithm based on patient demographic parameters (e.g., age and BMI) and co-morbidities (e.g., hypertension, depression and COPD). We additionally developed a decision support system tool that could estimate the likelihood of an individual patient experiencing high-acuity discharge disposition status postoperatively.

Results: Two predictive models were significant. They both showed good fit, and were calibrated by using area under the receiver operating characteristics (AUROC) curve analysis. The model predicting discharge disposition in all patients (n=135) yielded a predictive accuracy of 91.9% (AUROC = 0.825, p< .001). The model predicting discharge disposition in Parkinson’s Disease patients (n=91) yielded a predictive accuracy of 89.0% (AUROC = 0.853, p< .001). No significant multivariate model could be constructed to predict complications in DBS patients.

Conclusions: It is possible to accurately predict the discharge disposition of DBS patients using routinely collected preoperative clinical variables. The resulting predictive algorithms can be applied in the form of a model-driven decision support systems to assist in improving clinical decision making, healthcare resource planning and patient safety.

P 046

Meta-analysis of mortality following subthalamic and pallidal deep brain stimulation for patients with Parkinson’s disease
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Introduction: Subthalamic nucleus (STN) and Globus Pallidus internus (GPI) are two common targets for deep brain stimulation (DBS) in PD patients. This meta-analysis aims at comparing mortality after STN- and GPI- DBS for patients with Parkinson’s disease (PD).
Methods: We searched PubMed through February, 2018 for prospective controlled studies comparing STN DBS and GPi DBS for PD patients. Records were screened for prospective controlled trials comparing STN DBS and GPi DBS for PD patients. Frequency of mortality in both groups were pooled as risk ration between the two groups in a fixed effect model meta-analysis. We introduced subgroup analysis according to the follow up duration to investigate whether the mortality rate was affected by the follow up period. Heterogeneity was assessed by visual inspection of the forest plots and measured by I-square and Chi-Square tests. We used RevMan 5.3 for windows.

Results: Four studies (7 full text articles) were included in the final analysis with a total of 479 patients (STN 253 patients, and GPi 226 patients). Follow up duration ranged from 6 months in COMPARE trial to 6 years in the study of DBS group 2001. The overall risk ratio favored GPi DBS than STN DBS with RR 3.64, 95% CI (1.68 to 7.87). Pooled studies were not heterogeneous. This results suggests more than 3-fold increase in mortality following STN DBS than GPi DBS.

Conclusion: Death was more common after STN DBS than GPi DBS in PD patients. But most of death cases were due to postoperative complications and were not related directly to stimulation. Our results highlight the importance of considering postoperative complication while choosing surgical target for PD patients.
Objective: To assess the clinical feature of genetic changes in PARK1 (α-synuclein) and PARK2 with the help of PCR in patients with Parkinson’s disease and study its association with PD course.

Methods: The study involved 50 patients with PD (28 men and 22 women with an average age of 56.6 ± 2.8 years, the average duration of the disease 6.9 ± 2.5 years, 3.0 on the Hoehn and Yahr scale (2.0-4.0). Blood samples were obtained in all patients. Rapid polymerase chain reaction (PCR) was performed with primers and fluorochrome-labeled probes on a Light Cycler.

Results: The study showed that mutations in PARK1 in 30% of patients with PD while 25% in PARK2. It was also noted that mutations in α-synuclein gene and in addition to genomic triplications of a region of α-synuclein gene are associated with autosomal dominant PD. Patients with mutation in PARK 1 consisted of 48 % men and 52% women respectively. Patients with PARK 2 mutations comprised 53% men and 47% women. Mutations in the parkin gene are a major cause of autosomal recessive early onset PD. Heterozygous pathogenic variants for a few genes were analyzed in autosomal dominant forms of Parkinson disease in which the onset of disease is typically later than autosomal recessive forms of Parkinson disease.

Conclusion: Thus PCR allowed rapid production and mutation in short pieces of DNA in patients with PD at an early stage, even when not more than the sequence of the two primers is known.
**P 050**

**Influence of the stage in Parkinson’s Disease on the level of cognitive impairment in people over 65 years of age**

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**Objectives:** Parkinson’s Disease (PD) is the second most prevalent neurodegenerative disease in the world and its origin is still unknown. Its symptoms are multisystemic, in which you can find motor and non-motor symptoms. In non-motor symptoms is cognitive impairment, which is characterized by a predominance dysexecutive be accompanied by deficits in visuospatial domain, attentional domain and processing speed. The aim of the present study is to identify the existence of associations between the degree of Parkinson’s disease affection and cognitive impairment.

**Methods:** A total of 35 (48.6% female) Parkinsonians of 69.06 ± 9.87 years, belonging to the Parkinson’s Association of the Province of Pontevedra, participated in the study. To assess cognitive impairment, the Mini-mental test (MMSE) and the Montreal Cognitive Assessment (MoCA) were used. The degree of Parkinson’s disease was evaluated with the Hoehn and Yahr scale.

**Results:** A tendency has been obtained (Figure 1) towards a greater degree of involvement of cognitive impairment proportional to the progress of the disease as can be seen in Table 1, although these results have not been significant.

**Conclusions:** Therefore, the cognitive deterioration and the degree of involvement of Parkinson’s disease are related and are directly proportional, to a greater degree of affectionation of the disease, greater cognitive deterioration.

<table>
<thead>
<tr>
<th></th>
<th>MMSE</th>
<th>MoCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HY I</td>
<td>27.50±6.36</td>
<td>27.50±2.12</td>
</tr>
<tr>
<td>HY II</td>
<td>24.76±4.80</td>
<td>17.88±7.29</td>
</tr>
<tr>
<td>HY III</td>
<td>22.73±5.64</td>
<td>18.36±8.78</td>
</tr>
<tr>
<td>HY IV</td>
<td>21.00±5.66</td>
<td>11.00±2.83</td>
</tr>
</tbody>
</table>

(Table 1. Influence of the stage in Parkinson’s Disease on the level of Cognitive Impairment)
P 051
A case report of psychosis in Parkinson disease treated with anticholinesterase drug
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Case report: We present a 68-year-old male, retired civil servant who was seen in the neurology clinic at Barau Dikko Teaching hospital, Kaduna-Nigeria with a complaint of abnormal movements of upper and lower limbs for one year, and difficulty in walking for two months. The abnormal movement started on the distal part of both upper limbs simultaneously. It was noticed more at rest and got aggravated during movements. He was diagnosed with PD and was treated with L-dopa and Artane. However, six weeks after the commencement of his therapy he started developing a visual hallucination that subsequently became so intense that he started isolating himself and became suspicious of the wife conniving with strange people to kill him. His psychosis was initially treated with clozapine which controlled the hallucination to some extent but made his dyskinesia worse. This prompted us to stop the clozapine and to decrease the L-dopa, while introducing an anticholinesterase pyridostigmine which helped ameliorating the psychotic episode.

Discussion: The use of psychotropic medication may control the psychotic features but will aggravate the PD. A trial with anticholinesterases has been found to be effective in the control of psychosis in PD.

Keywords: Parkinson’s disease; Psychosis; L-dopa; Anticholinesterases

P 056
Use of safinamide in Parkinson’s disease patients over 70 years with dyskinesias and pharmacological psychosis
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Objectives: The aim of this study is to assess the safety and efficacy of Safinamide in patients over 70 years with long-standing PD who present psychotic symptoms and dyskinesias related to dopaminergic treatment.

Methods: Observational study that included patients older than 70 years with PD of more than 10 years of evolution not meeting criteria of dementia. All developed disabling dyskinesias, visual hallucinations and delusions related to dopaminergic treatment. We analyzed demographic data, disease duration, equivalent dose of levodopa (EDL), Hoehn and Yahr scale (HY), UPDRS-III scale, Dyskinesia Scale (DS) and visual hallucinations and delusions.

Results: Three patients were included, 2 women and 1 man. Average age: 80 years (SD 7.2). Mean disease duration: 12 years. The following clinical aspects were observed at each visit:

Visit 1: The three patients had visual hallucinations and psychomotor agitation. Two of them also showed severe dyskinesias and delusions and one very disabling dyskinesias. Regarding pharmacological treatment, average EDL was 575 mg per day, all patients took Entacapone and Rasagiline and 2 patients took Pramipexole 1.05 mg per day.
Visit 2: A medication adjustment was performed discontinuing Entacapone, Rasagiline and Pramipexole. EDL was reduced to 567 mg per day. After adjustment, visual hallucinations, delusions and psychomotor agitation disappeared and dyskinesias improved but modestly. In one patient Amantadine was added. Motor symptoms worsened presenting greater bradykinesia and muscle rigidity. Visit 3: Safinamide 100 mg per day was added with motor symptoms improving enough to make possible walking again. Dyskinesias disappeared in one patient and remained mild in two. After introducing Safinamide, no visual hallucinations or delusions reappeared.

Conclusion: In our experience, the use of Safinamide in elderly patients with pharmacological psychosis is safe. Safinamide 100 mg improves disabling dyskinesias without triggering psychotic symptoms in patients older than 70 years with long-standing Parkinson’s disease.

P 058
A non-motor symptom unheard of? Hearing loss in Mexican patients with Parkinson’s disease

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Objective: To evaluate the presence of sensorineural hearing loss in a mexican population of Parkinson’s disease (PD) patients, and describe the clinical characteristics of such population.

Methods: We recruited 16 patients. Bilateral pure tone audiometry, frequencies ranging from 125kHz to 8000kHz was performed, and hearing loss defined as present when above 21 dB. Severity was evaluated with MDS-UPDRS motor score, and non-motor symptom scale (NMSS).

Results: Prevalence of sensorineural hearing loss was 87%, baseline characteristics are described in table 1. Laterality and symmetry of hearing loss are shown in figure 1. Tremor-dominant was the most common subtype across all frequencies, and no difference was seen in years with Parkinson’s Disease. MDS-UPDRS and NMSS Scores showed a tendency to decrease with hearing loss at higher frequencies.

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Hearing Loss [n (%)]</th>
<th>Age (years)</th>
<th>Years with Parkinson’s Disease</th>
<th>Tremor Dominant PD [n (%)]</th>
<th>MDS-UPDRS</th>
<th>NMSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>14 (87.5%)</td>
<td>64.6 ± 10.3</td>
<td>7.0 (2.0-20.0)</td>
<td>11 (69)</td>
<td>51.0 (23.0-106.0)</td>
<td>44.5 (4.0-198.0)</td>
</tr>
<tr>
<td>125 kHz</td>
<td>4 (25%)</td>
<td>71.3 ± 4.9</td>
<td>6.0 (4.0-20.0)</td>
<td>3 (75%)</td>
<td>56.5 (31.0-106.0)</td>
<td>57.0 (22.0-118.0)</td>
</tr>
<tr>
<td>250 kHz</td>
<td>4 (25%)</td>
<td>67.8 ± 7.5</td>
<td>5.5 (4.0-20.0)</td>
<td>2 (50%)</td>
<td>35.5 (25.0-106.0)</td>
<td>40.0 (4.0-118.0)</td>
</tr>
<tr>
<td>500 kHz</td>
<td>6 (37.5%)</td>
<td>70.3 ± 7.3</td>
<td>6.0 (4.0-20.0)</td>
<td>4 (66.7%)</td>
<td>56.5 (25.0-106.0)</td>
<td>57.0 (4.0-158.0)</td>
</tr>
<tr>
<td>1000 kHz</td>
<td>7 (43.8%)</td>
<td>68.0 ± 9.2</td>
<td>6.0 (2.0-14.0)</td>
<td>5 (71.4%)</td>
<td>50.0 (25.0-106.0)</td>
<td>30.0 (4.0-158.0)</td>
</tr>
<tr>
<td>2000 kHz</td>
<td>12 (75%)</td>
<td>65.7 ± 10.6</td>
<td>6.0 (2.0-20.0)</td>
<td>9 (75%)</td>
<td>45.0 (23.0-106.0)</td>
<td>31.5 (4.0-198.0)</td>
</tr>
<tr>
<td>4000 kHz</td>
<td>14 (87.5%)</td>
<td>60.4 ± 12.2</td>
<td>6.0 (2.0-20.0)</td>
<td>10 (71.4%)</td>
<td>46.0 (23.0-106.0)</td>
<td>31.5 (4.0-198.0)</td>
</tr>
<tr>
<td>8000 kHz</td>
<td>14 (87.5%)</td>
<td>55.2 ± 12.9</td>
<td>6.0 (2.0-20.0)</td>
<td>10 (71.4%)</td>
<td>46.0 (23.0-106.0)</td>
<td>31.5 (4.0-198.0)</td>
</tr>
</tbody>
</table>

[Baseline Characteristics]
Conclusion: Hearing loss is common in PD. Hearing loss was more prevalent (and at higher frequencies) as age increased; interestingly we found lower motor and non-motor scores among patients with hearing loss at higher frequencies.

P 059
Development of anti-Parkinsonism poly herbal sustained release formulation composed of potential traditional plant extracts
Jain A., Jain S., Bhargav S.

Background: Various allopathic drugs such as Carbidopa, Levodopa, Benzeraside, are used in the management of Parkinson disease but have serious side effects and also they are very costly as compared to herbal medicines which has very less side effects so we choose herbal drug for the management of Parkinson disease.
**Objective:** Parkinsonism is one of the commonest neurodegenerative diseases, which is characterized by a selective and progressive degeneration of dopaminergic neurons, causing a series of symptoms which might ultimately induce programmed cell death. In present study Floating tablets of alcoholic extracts of *Mucuna pruriens*, *Bacopa monniera*, *Centella asiatica* and *Curcuma longa* were developed with an aim to prolong its gastric residence time and increase the bioavailability of drug.

**Method:** Direct compression technique was used for the formulation of polyherbal floating tablets which consists of different compositions of Hydroxy Propyl Methyl Cellulose Micro Crystalline Cellulose (MCC) and Sodium bicarbonate (NaHCO3). Formulation was optimized on the basis of floating time and in vitro drug release. Parkinson’s disease was induced by administering haloperidol (1 mg/kg i.p. daily x 1 week). The mice of either sex were divided into different group (n =6). First group received distilled water (orally), 2nd group were administered haloperidol (20 mg/kg i.p.). The 3rd groups were administered optimized formulation respectively, along with haloperidol. Group 4th received Levodopa (30mg/kg, i.p,) along with haloperidol. Behavioural changes caused by haloperidol were studied by rotarod test, grip strength test and locomotor activity by actophotometer.

**Results:** The buoyancy time of all tablet formulations were found to be less than 10 min and remained in floating condition throughout the study, maximum till 12 hours. The optimized formulation was found to be f3 which was having buoyancy time of 4.2 min. The increased cataleptic scores (induced by haloperidol) were significantly (p< 0.001) found to be more reduced with the f4 formulation as compared to negative control and standard treated group.

**Conclusion:** The optimized formulation shows sustained release of herbal constituents for more than 12 hours and In Vivo studies also showed its potential for the treatment of parkinsonism.

P 060

**Microarray analysis upon a synthetic α-synuclein induced model reveals some susceptibility genes in Parkinson’s disease**

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To uncover new disease-associated genes and their relevant mechanisms in the pathogenetic process of neurodegenerative disorders, we carried out a gene microarray analysis based on a Parkinson’s disease (PD) in vitro model induced by α-synuclein oligomers. This cellular model induced by 25 mol/L α-synuclein oligomers has been confirmed to show the stable, transmissible neurotoxicity of α-synuclein, a typical PD pathological marker.

A significant differentially expressed lncRNAs, G069488, were chosen as a breakthrough point for the further research because it was located to the gene NEED9, which is relative to the axon growth and neurodevelopment closely. Subsequent verified qPCR experiment determined the same variation trend as the result of microarray analysis showed.

The results of the present study widen our horizon of PD susceptibility genes and provide new pathways towards efficient diagnostic biomarkers and therapeutic targets for PD.
P 061
Postural instability in patients with Parkinson Disease and its correction by balance therapy
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Objective: To study the features of postural instability in Parkinson Disease (PD) and its correction by the method of biocontrol over statokinesigramme.

Materials and methods: 82 patients with PD (female - 36, male - 46), average age - 54.5 ± 9.3 years, average stage of the disease on the scale Hoehn and Yahr - 2.71 ± 0.47, duration - 5.8 ± 2.5 years.

Results: Stabilographic examination revealed features of postural control in different forms of PD. It was shown that in clinically more stable patients with trembling forms of PD increased (compared with the norm) area of the statokinesigram at calm standing due to the presence of a tremor of rest, and this increase should not be regarded as a manifestation of postural instability.

At the same time, in clinically unstable patients with akinetic-rigid form of PD with calm standing, parameters of the statokinesigram area were registered within the limits of the norm, however, correlation analysis revealed a reliable level of dependence between propensity to fall and the area of the statokinesgram.

Statistically significant improvement in the stability of the vertical posture according to clinical studies using special scales was observed. Significant changes were noted also in the study of dynamic stability - with an arbitrary displacement of the body in each of the four directions: forward, backward, right and left. Credible increase in the length of the deviation in different directions was noted in practically all patients.

Conclusion: Improvement of individual parameters posture control in the process of training in patients even with progressive forms of PD is possible. Of course, we can not argue that training, for example, arbitrary control of the posture will significantly affect the recovery postural automatisms, but that it will expand the motor repertoire of patients and thus facilitate the conditions of their life, absolutely obvious.

P 062
Insomnia due to restlessness restricted to the perianal region in a patient with Parkinson’s disease
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Background: Restless legs syndrome (RLS) typically involves the legs, and the involvement of other body parts have been reported as RLS variants. We here first to report dopamine-agonist responsive restlessness restricted to the perianal region in a patient with PD.

Case report: An 83-year-old woman with a 2-year history of PD developed difficulty in initiating asleep due to abnormal sensations and restlessness restricted to the perianal region over 10 months. The patient had been treated for PD with 100 mg L-dopa with peripheral decarboxylase inhibitor three times daily. The patient was in Hoehn and Yahr stage 2. The laboratory findings were unremarkable except for decreased...
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ferritin levels. The abnormal sensations fulfilled the 4 essential features for RLS, when applied to the perianal region. Following administration of a low dose of pramipexole (0.125mg) at bedtime, her abnormal sensation in the perianal region and insomnia completely disappeared.

Conclusion: We should be aware of RLS variants involving any body parts in PD patients, which can result in insomnia.

P 063
Worsening of dyskinesia following the change of peptic ulcer treatment in a patient with Parkinson’s disease under the Levodopa-Carbidopa Intestinal Gel infusion therapy

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Objectives: To report a patient with Parkinson’s disease (PD) in whom dyskinesia worsened after the change of peptic ulcer treatment under the Levodopa-Carbidopa Intestinal Gel (LCIG) infusion therapy.

Methods: A 72-year-old woman with a 6-year history of PD received LCIG therapy, because of motor fluctuations, dyskinesia and deglutition disorder. She was administrated with a proton pump inhibitor (PPI) before introducing gastrostomy for LCIG therapy. After LCIG, her symptoms of PD were improved.

Results: Because she had no abdominal symptoms, after her discharge, we exchanged the PPI to a medicine of Histamine H2 receptor antagonist (H2). Then, troublesome dyskinesia appeared. We exchanged the H2 to PPI again. After that, the troublesome dyskinesia disappeared. Because of LCIG is basically direct intestinal absorption therapy, gastric acid will not affect with the absorption. But in this case, we suspected that increase gastric acid induced troublesome dyskinesia after the change of peptic ulcer treatment.

Conclusions: The results of this case suggest that we should consider the gastric acid influence even though LCIG therapy.

P 064
Investigation of sleep duration, sedentary behavior, and physical activity in idiopathic Parkinson Disease

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1Dokuz Eylül University School of Physical Therapy and Rehabilitation, Izmir, Turkey, 2Dokuz Eylül University, Department of Neurology, Izmir, Turkey

Objective: To investigate the sleep duration, sedentary behavior and physical activity in Idiopathic Parkinson Disease (PD) and healthy controls (HC).

Methods: The functional disabilities of PD were classified according to Hoehn&Yahr (H&Y). Sleep duration (hours/day), sedentary behavior (hours/day), number of steps (steps/day) and daily energy expenditure (DEE, joules/day) belong to the whole-day activity behavior of Idiopathic PD and HC were evaluated.
with SenseWear Armband (SWA) accelerometer. SWA had worn continuously for 7 days by participants. Schwab&England Activities of Daily Living (S&E ADL) scale for PD was used to assess functional independency in daily living. The Mann-Whitney U test was used for two independent quantitative variables. Spearman’s rank correlation test was used to evaluate correlations between parameters in PD.

**Results:** There were 51 PD (19 female, 32 male) and 49 HC (20 female, 29 male). The median of H&Y was 2.00 (2.00-2.50). Differences in terms of sleep duration, sedentary behavior, number of steps and DEE were significant between two groups (p < 0.05).

<table>
<thead>
<tr>
<th></th>
<th>Parkinson Disease Group (Median-Interquartile Range)</th>
<th>Healthy Controls Group (Median-Interquartile Range)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.00 (58.00-72.00)</td>
<td>63.00 (57.00-68.00)</td>
<td>0.304</td>
</tr>
<tr>
<td>Sleep duration (hour/day)</td>
<td>5.97 (4.57-6.90)</td>
<td>6.49 (5.88-7.58)</td>
<td>0.022*</td>
</tr>
<tr>
<td>Sedentary behavior (hour/day)</td>
<td>7.21 (5.82-8.27)</td>
<td>8.20 (7.39-8.85)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Number of steps (steps/day)</td>
<td>5024.71 (3445.71-8159.00)</td>
<td>7499.71 (5324.50-9413.57)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Daily energy expenditure (joules/day)</td>
<td>10637.57 (9116.28-12483.71)</td>
<td>9745.00 (8411.07-10831.57)</td>
<td>0.030*</td>
</tr>
</tbody>
</table>

There was a negative correlation between S&E ADL and sleep duration (weak; rho=-0.370, p=0.008), sedentary behavior (moderate; rho=-0.428, p=0.002). There was a positive correlation between S&E ADL and number of steps (moderate; rho=0.450, p=0.001), DEE (moderate; rho=0.444, p=0.001) in PD.

**Conclusions:** We are thought that Parkinson patients have more energy expenditure due to lower sleep duration and decreased sedentary behavior than HC. But, it wouldn’t mean that patients are more active than HC. Because, the number of steps in PD is lower than HC. The high energy expenditure could be associated with medication or disease specific. This situation which deteriorates the physical activity and functional independency of Parkinson patients could be improved by appropriate medication and exercise program.
P 069
Measurement of Parkinson’s disease patients functional ability before and after physiotherapy: a case series
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1Warwick Medical School, Coventry, United Kingdom, 2University Hospital Coventry and Warwickshire, Coventry, United Kingdom

Aims/Objectives: This study aimed to investigate the outcomes of physiotherapy for patients with Parkinson’s disease.

Methods: To assess patients outcomes following physiotherapy we retrospectively looked at measurements of patients functional ability at admission to the physiotherapy service and on discharge. These measurements included Lindop scale scores and tragus to Wall measurements. Data was collected from the physiotherapy service at University Hospital Coventry and Warwickshire. Data was analysed using Excel. Outcomes were compared for statistical significance using a two tail T test.

Results: 46 patients patients had Lindop scores calculated pre and post physiotherapy. The average Lindop scale score for patients first appointment was 26. The average score at patients final appointment was 28.02 (p< 0.01).

46 patients had tragus to wall measurement completed before and after physiotherapy. The average score prior to physiotherapy was 16.9cm and after physiotherapy 15.3cm (p< 0.01).

Conclusions/Outcomes: This study shows that physiotherapy had statistically significant benefits for patients when measured against both the Lindop Scale score and tragus to wall.

P 070
Rotenone induced Parkinson’s disease model: Analysis of PARK2 and PINK1 genes expression
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Objective: Parkinson’s disease (PD) a chronic progressive neurodegenerative disorder. The molecular pathway involves the oxidative stress induce deactivation of mitochondria due to reduced performance of electron transport complexes (complex 1) and elevated ROS formation due to stress. PINK1-1 (PTEN Induce putative kinase1) act as recruit of PARK2 gene (Parkin protein) which is a part of E3 complex of ubiquitin system and dysfunction of mitochondria. Treatments are available for PD but they are restricted to symptomatic relief only. The aim of this study is to target the progressive symptoms of Parkinson’s disease and halt the death of dopaminergic neuron.

Methods: In this study, in vivo mice model of PD was developed by intra peritoneal administration of three doses (i) low dose (ii) median dose (iii) high dose rotenone. Hind limb clasping test and Grip strength test were conducted to analysed symptoms progression. Animals were sacrificed, mid brain and striatum were isolated and processed for expression of PARK2 and PINK1 gene by Real time PCR. Neurotransmitter
analysis was done by High Performance Liquid Chromatography (HPLC) to quantify the Dopamine turn over and DOPAC turn over in striatum of brain.

**Results and conclusion:** Based on the preliminary findings we conclude that the median dose of rotenone drastically kill the dopaminergic neurons as compare to other doses, this was confirmed by comparing the turn out number of Dopamine with its metabolite DOPAC. Gene expression of PINK1 and PARK2 was confirmed by RT PCR shows that decrease level of PINK1 gene provides ineffective protection due to mitochondrial dysfunction expression of PARK2 gene is also decreases. The accumulation of degraded protein caused the death of dopaminergic neuron, for future study we will screen the novel peptides to find the lead compound that can be used as a potential therapeutic agent or Parkinson's disease.

**P 071**

**The late effects of traumatic brain injury- leading to Parkinson disease - A prospective study**

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**Background:** Over the last century, traumatic brain injury is considered a risk factor for Parkinson disease.

**Objective:** We aim to analyse the huge proportion of traumatic brain injuries occurring in lower middle income countries like Pakistan which lead to Parkinson disease. The study also targets to provide surgeons, health planners, nurses and hospital managers with the useful information which may help for the further workup of head injuries. The main aim is to investigate and prevent the burden of head injuries leading to Parkinson disease.

**Patients and Methods / Material and methods:** The study was done in Sir Ganga Ram Hospital from May 2015 to May 2016. We included patients and divided them into 2 groups TBI and non TBI respectively. Informed consent was obtained. Epidemiological, clinical and management data were collected for the study.

**Results:** TBI patients were significantly more likely to be diagnosed with Parkinson disease than non TBI. Out of 100 patients, 76 were males. The median age was 50.0 years (SD=13.3). Fights (n=20, 38.5%) and road traffic accidents (n=19, 52.4%) were the most common causes of head injury. Half of the patients sustained mild and 52.4% sustained severe head injury. Assessment by TBI severity (mild TBI: HR = 1.24, 95% CI = 1.04-1.48; moderate/severe TBI: HR = 1.50, 95% CI = 1.35-1.66) and TBI frequency (1 TBI: HR = 1.45, 95% CI = 1.30-1.60; >1 TBI: HR = 1.87, 95% CI = 1.58-2.21) revealed a dose response.

**Conclusion:** We concluded that mTBI is associated with 56% increased risk of PD, even after adjusting for demographics and medical/psychiatric comorbidities. This study highlights the importance of traumatic brain injury prevention, long-term follow-up, and the need to determine mechanisms and modifiable risk factors to prevent the traumatic brain injury.
Is restless legs syndrome (RLS), a prodromal feature of Parkinson’s disease (PD), associated to small fiber pathology?

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**Background:** About one third of RLS co-morbid with PD develops in the pre-motor phase of the latter, suggesting that RLS could be an early feature of the neurodegenerative disease. Although the determinants of RLS in this setting remains unknown, based upon recent findings of small fiber neuropathy in early PD and in RBD, it may be hypothesized that a dysfunction of epidermal small fibers may underlie also the RLS emerging in pre-motor phase.

**Methods:** Three-mm punch skin biopsies were carried out in the proximal and distal sites of the lower limbs in four patients with PD, 2 male and 2 female, aged 53-71 years, in which RLS had developed 1.5 to 13 years before the onset of motor signs of PD. The skin specimens were processed with PGP 9.5 as primary antibody according to the EFNS recommendations.

**Results:** The somato-sensory epidermal small fiber density, expressed as the number of fibers per millimeter of epidermal length, was found reduced mainly in the proximal sites, as compared to normative values, in the four patients. Autonomic sweat glands and erector pili muscles innervations were spared in all patients.

**Conclusion:** The finding of a non-length dependent small fiber pathology in the lower limbs suggests a possible involvement of small neurons in the somato-sensory root ganglia as the underlying substrate of the RLS in these patients. The lack of secondary causes of the axonopathy supports the view of a process intrinsic to PD and likewise the lack of coexistent conditions known to be associated to RLS suggests a link between the sensory-motor disorder and the somato-sensory small fiber pathology. Our findings are preliminary requiring further confirmations on a larger number of patients in order the RLS may be regarded as a prodromal feature of PD as an epiphenomenon of small fiber pathology.
**P 073**

**Does the side of onset of motor symptoms in parkinsonian patients have an impact on the global clinical phenotype?**

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**Objectives:** To describe demographic and clinical characteristics of a cohort of 285 consecutive PD patients and to understand the phenotypic differences of right onset (RPD) and left onset PD (LPD).

**Methods:** In this retrospective study, 285 consecutive PD patients visited by a movement disorders specialist between 2013 and 2018 at Ospedale Maggiore Policlinico, Milan, were enrolled. Their data were collected from all available clinical records and grouped into 5 thematic areas: demographic characteristics and disease history, motor complications, cognitive or behavioral disturbances, non-motor symptoms (NMS), dopaminergic therapy.

We analyzed the data of the total cohort, and afterwards of the two subgroups.

**Results:** The demographic characteristics of our cohort are in line with previous reports, with a slight predominance of male gender (57.2%) and a median age at disease onset of 62 years. The presence of familial history is slightly higher than expected: 38.6% of patients have at least one case of PD among their relatives.

After comparing RPD and LPD, demographic and disease history aspects do not suggest significant differences, except for longer disease duration in LPD (median: 8 years vs 6 years, p 0.029). Cognitive, behavioral and NMS seem all to be more frequent in LPD, but only ICD reached statistical significance (30.7% vs 16.2%, p 0.007). Similarly, dopaminergic drugs side effects were significantly more common in LPD (motor fluctuations: 63.7% vs 48%, p 0.013; dyskinesia: 52.5% vs 39.8%, p 0.045).

**Conclusions:** The higher frequency of many phenotypic aspects of LPD patients may be due to a physioanatomic reason, related to the asymmetry of dopaminergic circuits involved in the two subgroups of patients. Nevertheless, a significant impact of the longer disease duration and the higher dopaminergic drugs dosage in this subgroup cannot be excluded. It is our aim to investigate this finding by means of a prospective study.
**P 074**  
**Instrumental evaluation of autonomic nervous system disfunction in idiopathic Parkinson’s disease**  
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**Objective:** Autonomic nervous system (ANS) dysfunction in idiopathic Parkinson's disease (PD) correlated with dementia, depression and falls. Adequately diagnostics of non-motor symptoms could be a clue in phenotyping PD patients or helps with differentiation diagnosis. The aim of the study was instrumental evaluation of the occurrence and intensity autonomic disturbance in patients with idiopathic PD.  

**Methods:** 36 patients with idiopathic PD and 20 sex and age matched healthy control have been examined. Five minutes resting heart rate variability (HRV) using BiopacSystem have been conducted. Two components were assessed: LF (component of the low-frequency range, modulated by sympathetic and parasympathetic nervous system and associated with baroreceptor activity) and HF (component of the high-frequency range, modulated by the parasympathetic nervous system).  
In tilt test blood pressure in horizontal position, and in 1ᵗʰ, 3ᵗʰ and 5ᵗʰ minutes after tilting to 60° have been measured.  
The result was presumed as positive and the orthostatic hypotension (OH) have been diagnosed when systolic blood pressure fell >20 mmHg, and diastolic blood pressure fell >10mmHg. Subjective evaluation of autonomic disfunction were made with COMPASS31 questionnaire.  

**Results:** Compared to healthy control in PD patients both components - LF and HF were significantly lower (p< 0,05) - what is the evidence for sympathetic and parasympathetic impairment. Compared to PD patients without OH in cases of PD patients with OH HRV component of low-frequency range was significantly lower (p< 0,05) - what means that OH is the result of advanced sympathetic degeneration. OH patients was older, had more severe motor symptoms in UPDRS-III and took higher daily doses of levodopa (LEDD) (p>0,05). In COMPASS31 questionnaire dysautonomia intense corelated with time of disease duration and LEDD and was significantly higher than in control group.  

**Conclusion:** HRV analysis, tilt test and subjective dysautonomia questionnaire are objective and sensitive instruments for evaluation of ANS disfunction in PD patients.

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**P 075**  
**Effective rehabilitation program for Parkinson’s disease - from National Hospital Organization Japan**  
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**Objective:** We developed new programs for mild and advanced stage of Parkinson’s disease (PD) patients, because the limited number of established PD program is available now. The programs, TSPDM for mild to moderate and TSPDA for advanced stage of PD were applied to PD patients.
**Background:** Programs of physiotherapy for PD are needed for the most of the patients with moderate to advanced stage of the disease.

**Patients:** Multicenter trial registered 67 PD patients with mild to moderate stage and assigned randomly for TSPDM (23), Nordic Walking (22) and static exercise (22). Advanced 38 patients, with longer disease period than in TSPDM, were divided randomly for TSPDA and conventional ROM exercise. After 4 weeks, main efficiency was measured by MDS-UPDRS score change from baseline. Student t test was employed for analysis.

**Results:** Significant reduction of MDS-UPDRS total and motor score obtained only in TSPDM against static exercise in TSPDM study: p< 0.01 and p< 0.05, respectively. Motor score reduction is 20% of original score. In TSPDA study, reduction of MDS-UPDRS score is significant in total and motor, p< 0.005 in both. Reduction of motor score in TSPDA was 20% more than in ROM exercise.

**Conclusion:** New effective physiotherapy programs for the range of mild to advanced stage of PD is established.

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**P 076**  
Interrelation between chronic pain syndrome and cognitive and affective disturbances in patients with Parkinson’s disease  
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**Objective:** To study interrelation of chronic pain syndrome and cognitive and affective disorders in patients with PD.

**Methods:** 109 patients (ages 65.8±8.5) with PD were examined.  
Two groups: 1st (75 pers.) - patients with chronic pain syndrome, 2nd (34 pers.) - patients without pain were formed. Assessment of movement disorders (UPDRS), of pain (VAS, presalgometry), of cognitive functions (MMSE), of attention (Wechsler Adult Intelligence Scale - WAIS), of visual-spatial functions («drawing hours» test (Manos, 1994)), of memory (visual memory test of SKT scale (H.Lehbeld, H.Erzigkeit, 1980)), of speech (test on the availability and directional association (AR Luria, 1969)), of affective disorders (Beck Depression Inventory, Scale obsessive-compulsive syndrome (Goodman et al, 1984)) were performed.

**Results:** Assessment of the general state of patients’ cognitive functions on MMSE ranged from 27 to 30 points (averaged 28,8 points). The group of patients with pain had lower indicators of neuropsychological functions than patients without pain (p< 0,05). Patients with pain had more pronounced disturbances than patients without pain at performance of clock drawing test (7,5±1,1 versus 9,2±0,7), «coding» test (26,8±11,5 versus 34,1±8,2), on speech activity test (10,9±6,7 versus 14,7±3,5), visual memory test (6,9±2,2 versus 9,6±2,5), (p< 0,05).

However, patients with pain did not differ from patients without pain on the overall level of cognitive function and abstract thinking. Depressive symptoms were observed in 49 (69%) patients with pain syndrome (17,3±7,6 points) and in 11 (28%) patients without pain (12,6±6,8 points). Intensity of pain assessed by the VAS correlated with the
severity of depressive symptoms ($R=0.51; p<0.001$). Intensity of pain in patients from 1st group was higher ($53.8 \pm 23.2$ points) than in patients without pain ($43.6 \pm 19.1$ points), ($P=0.03$).

**Conclusion:** The development of chronic pain in patients with PD is associated with depressive, obsessive-compulsive symptoms and neurodynamic and regulatory cognitive impairment.

P 078
**Effect of ventricle size on development of freezing of gait in Parkinson’s disease**
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**Background and purpose:** A freezing of gait (FOG) is a disabling motor symptom in Parkinson’s disease (PD) which is hardly understood so far. There have been neither effective treatment nor known certain risk factor for occurrence of this mysterious phenomenon. We sought to investigate the enlarged intracranial ventricle could predict the development of FOG in patients with PD.

**Methods:** This study included 16 PD subjects who have encountered a symptom of FOG in spite of standard treatment over follow-up period. Quantitative parameters for intracranial ventricle include Evans’ ratio, thickness of corpus callosum, and coronal angle of corpus callosum.

**Results:** The PD with FOG group showed more increased Evans’ ratio ($0.33 \pm 0.14$ vs $0.26 \pm 0.09$, $p = 0.015$) and thinner thickness of corpus callosum ($5.31 \pm 2.37$ vs $7.81 \pm 3.62$ mm, $p < 0.001$) than those of the PD without FOG group. A thinner corpus callosum was strongly implicated to occurrence of FOG (Odds ratio (OR), 0.897; standard error(SE), 0.007; $p = 0.014$), while a trend without significance was observed on Evans’ ratio (OR, 1.125; SE, 0.248; $p = 0.074$).

**Conclusions:** The enlarged ventricle might contribute to occurrence of FOG in PD. A thorough assessment of ventricle parameters at early stage of PD is likely to predict the presence or absence of future FOG.

P 079
**Non-motor symptoms of Parkinson’s disease: evaluation of urinary disorders**
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**Objectives:** Violation of urination, as a manifestation of autonomic failure is common to many patients with Parkinson’s disease (PD) and is a very actual. This is important that determining the type of clinical manifestations of violation of urination will increase the level of social adaptation and significantly improve the quality of life at patients with Parkinson’s disease.

**Methods:** Author examined 78 patients with Parkinson’s disease (45 men and 33 women), mean age - 64.09 years. Urological examination: physical exam, general urinalysis, bladder diary and bladder scan by ultrasound. The severity of Parkinson’s disease was evaluated by UPDRS scale.
**Results:** The main clinical manifestation of urinary disorders in patients with PD was overactive bladder syndrome and diagnosed in 38 patients. The classic triad of symptoms of overactive bladder was observed in 29 (76.3%) patients, and the mean UPDRS scale was 65.47 (p<0.01*). Urgency with incontinence were observed in 6 (15.8%) and the median on the scale -72.14; urinate frequently with urgency in 3 (7.9%) patients, the median - 58.81. In patients with akinetic-rigid form of expression of overactive bladder syndrome was significantly more than the patients with resting tremor forms of PD.

**Conclusions:** The expression violations urination depends on the severity, the clinical form of PD. The presence of urinary disorders significantly reduces the quality of life and daily activities of patients with PD. Timely diagnosis of various types of urological disorders will improve the quality of life of patients.

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**P 082**

**The impact of levodopa induced dyskinesia on the quality of life in Parkinson’s disease patients**

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**Aims:** To investigate the impact of levodopa-induced dyskinesia on patient’s quality of life in Parkinson’s disease (PD) in Singapore.

**Methods:** A cross-sectional study was conducted on 240 idiopathic PD patients. Patients were evaluated for their (i) motor abilities using Unified Parkinson’s Disease Rating Scale (UPDRS) III, modified Hoehn and Yahr Staging Scale (H&Y) and Schwab England Activities of Daily Living (ADL); (ii) levodopa-induced motor complications using UPDRS IV and (iii) quality of life (QoL) using Parkinson Disease Questionnaire (PDQ-39). Socio-demographic and other clinical variables were also noted. Multivariate linear models and correlation analyses were performed.

**Results:** 12.92% of the patients reported to have dyskinesia. Of which, 7.08% had 1-25% of their waking day while 5.42% had 26-50% of their waking day. For the dyskinesia experienced, a small percentage of patients complained it of being slight (2.08%) or moderately (1.25%) painful. Also, 32.26% of the patients found the dyskinesia experienced to be non-disabling and 48.39% found it to be mildly disabling. Significant positive correlation was found between dyskinesia and all PDQ-39 domains except for social support.

**Conclusion:** Levodopa-induced dyskinesias impact PD patient’s QoL in Singapore. Clinical strategies that target the management or even the prevention of it is therefore important.
P 083
Prevalence and associations for depression in patients with Parkinson’s disease: a Sri Lankan experience
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Objectives: (a) Estimate the prevalence of depression (or depressive symptoms) among patients with Parkinson disease presenting to a tertiary neurology clinic in Sri Lanka, (b) identify any significant clinical or demographic associations for presence of depression in this patient sample and (c) forward recommendations and suggestions for providing optimal care for patients with a dual diagnosis of Parkinson disease and depression.

Methods: We conducted this cross sectional study at the Institute of Neurology, National Hospital of Sri Lanka. 75 patients with a diagnosis of idiopathic Parkinson disease were enrolled. The patients were interviewed by investigators (medical practitioners) with an interviewer-administered questionnaire. Symptoms of depression were assessed with Hamilton rating scale for depression.

Results: We enrolled 75 patients [males; 54 (75%), mean age; 63.6 years, SD ± 6.8]. Forty-six (61.3%) patients had depressions and 17 of them (36%) were formally diagnosed with depression and were on treatment. (Table 1) 40% of them still had evidence of depression despite treatment. Other 29 (64%) showed evidence of depression and were undiagnosed at the time of evaluation. Majority of patients with depression had mild depression (83%) and only one had severe depression. Bradykinesia, being currently employed, having an income below average per capita income and having a family history of depression in a first degree relative were significantly associated with depression.

Gender, marital status, current age or age at diagnosis, level of education, concurrent chronic medical problems, presence of tremor or rigidity, side of onset of symptoms were not associated with the incidence of depression.

Conclusion: Given the potential benefit in treatment, all patients with Parkinson’s disease should be screened for depression regularly. HAM-D would be a good tool for this purpose as it has good reliability, validity and can be administered within a reasonable time limit.

P 084
Contribution of insomnia to the quality of life of patients in Parkinson’s disease
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Objective: Evaluation of the incidence of insomnia, its association with motor, neuropsychiatric disorders.

Methods: The study involved 100 patients 60 men and 40 women diagnosed with PD without dementia, the average age was 60.34 ± 0.6 years, the stage was 2.24 ± 0.5, and the PD duration was 5.6 ± 3.4 years. Hoehn-Yahr stage evaluation, the unified PD assessment scale, Beck depression questionnaires, Spielberger anxiety, Parkinson’s Disease Sleep Scale (PDSS), Euphoria sleepiness - Excessive Sleep Scale
Results: Sleep disturbances were noted in 36% of patients, night awakenings with sleep fragmentation in 82%, early awakenings in 41% of patients. A greater frequency of disturbances of sleep, night awakenings, unpleasant dreams were noted in women. There was a tendency to intensify insomnia as the severity increased and the duration of PD increased. Patients with the onset of insomnia in the “premotor” stage of PD were statistically significant (p < 0.05) differed from patients in other groups more low self-esteem of the quality of sleep, the severity of sleep disturbances, the greater frequency of nocturnal awakenings. Patients with sleep fragmentation statistically significant (p < 0.05) were characterized by a greater severity of sleep disturbances and the frequency of early awakenings, lower sleep quality, akathisia, nocturia, morning drowsiness, the presence of unpredictable daily fluctuations.

Conclusion: Sleep disorders in patients with BP are heterogeneous - partly due to the age factor, motor and non-motor disorders. Based on the multifactority of insomnia in PD, effective therapy of patients with sleep disorders should be individualized taking into account the nature of motor disorders, concomitant emotional disorders.

P 085

Metabolic and functional changes in the eye as a manifestation of the systemic neurodegeneration of parkinsonism

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Objective: Parkinson's disease (PD) is a systemic neurodegenerative disorder that is diagnosed after the loss of most nigrostriatal dopaminergic neurons, which explains the low efficiency of treatment. Therefore the development of early (prodromal) diagnosis of PD is a high priority. Since visual impairment is among manifestations of PD, this study was aimed to search for metabolic and functional changes in the eye and eyelid as potential prodromal markers, in MPTP-treated mice at the presymptomatic of PD.

Methods: 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine(MPTP)-treated mice at presymptomatic and symptomatic stages of parkinsonism were used to evaluate (i) the monoamine content in the eye and eyelid with HPLC; (ii) intraocular pressure.

Results: We found a decrease in the content of norepinephrine, dopamine and serotonin in the eye in mice at both studied stages of parkinsonism, which indicates that pathological changes in the monoaminergic systems of the eye precede the onset of motor disorders. Moreover, mice at both stages of parkinsonism are characterized by unidirectional changes in the intraocular pressure, suggesting that this functional marker can be used for early diagnosis of PD. In contrast to the eye, serotonin level in the eyelids of MPTP-treated mice was increased, in presymptomatic mice more than in symptomatic mice. Given
Abstracts

that serotonin is involved in the regulation of eyelid lacrimal glands, such an increase in serotonin level in parkinsonian mice can induce a change in the tear fluid, which may be a potential diagnostic marker of the early stage of PD.

Conclusions: Changes in the metabolism of monoamines in the eye / eyelid and of the corresponding functions observed in presymptomatic mice can be considered as potential markers for early diagnosis of PD.

P 086

Acute lethargic state after abrupt apomorphine withdrawal in Parkinson’s disease

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Continuous apomorphine subcutaneous infusion represents an established treatment for motor complications in Parkinson’s disease (PD). Abrupt interruptions of apomorphine infusion may occur, mainly related to technical issues, and result in quick worsening of motor condition. We repeatedly observed acute lethargic states following abrupt apomorphine withdrawal.

We assessed the behaviour of a PD patient during acute apomorphine withdrawal in different occasions related to deep brain stimulation (DBS) surgery and programming.

A 55-year-old man with advanced PD was started on 24-hour continuous apomorphine infusion because of severe fluctuations. Two years later the patient underwent bilateral subthalamic nucleus (STN) DBS. Few hours before surgery, apomorphine treatment was discontinued leading to a progressive reduction of arousal one hour later. Resuming apomorphine infusion allowed recovering of arousal. During the first STN-DBS programming, dopaminergic medication withdrawal (including apomorphine) led to progressive alteration of consciousness. Resuming apomorphine again allowed recovering of arousal. Subsequently, apomorphine treatment was gradually reduced and discontinued, without any arousal change. One month after the surgery, the patient developed an infection of the internal pulse generator (IPG), with subsequent removal of the IPG. Apomorphine continuous treatment was resumed and IPG was repositioned 6 months later. When resuming stimulation, although keeping oral dopaminergic medication, the abrupt withdrawal of apomorphine provoked again a progressive alteration of consciousness. After resuming apomorphine the patient recovered alertness.

This is the first description of a lethargic state after abrupt apomorphine withdrawal. Since its first applications, dopaminergic medication has been described to increase arousal in never treated PD patients, as reported by O.Sacks in Awakenings. The lethargic state induced by apomorphine withdrawal reminds that of addiction to amphetamine, a potent inhibitor of dopamine transporter after drug withdrawal. The occurrence of a lethargic state as a result from abrupt apomorphine withdrawal should be taken into account in the management of PD patients.
P 089
Evaluations of additive effect of two indigenous medicinal plants Cedrus Deodara and Mucuna pruriens towards the treatment of Parkinson's disease
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Objective: Parkinson’s disease is the second most common neurodegenerative disease ranking next to Alzheimer’s disease. Recently, the focus of PD’s treatment has shifted towards herbal medicines. In this Study we evaluated additive effect of combined powder extract of Mucuna pruriens and Cedrus deodara. Mucuna Pruriens (Mp) is traditional herbal medicines known to have neuro-protective effects due to the L-DOPA while Cedrus deodara is used traditionally as a neuro-protective drug.

Methods: Parkinson’s disease was induced by administering haloperidol (2.0 mg/kg i.p.) Daily for a week. The mice were divided into 5 group (n=6). Group I received haloperidol (2mg/kg body weight).Group II received combination of levodopa and carbidopa (100mg+ 10mg/kg by i.p along with haloperidol) and Group III received combined powder extract of Mucuna pruriens (Seed) and Cedrus deodara (Stem bark) (MPCD) of (400mg/kg by p.o), Group IV received extract of Mucuna pruriens (Seed) alone at a dose of 500 mg/kg (p.o.), respectively for 15 days along with haloperidol. Behavioural changes caused by haloperidol were studied by rotarod test, grip strength test and locomotor activity by actophotometer.

Results: The increased cataleptic scores (induced by haloperidol) were significantly (P< 0.001) found to be more reduced with the combined powder extract of Mucuna pruriens (Seed) and Cedrus deodara (Stem bark) at a dose of 400 mg/kg (p.o.) as compared to Mucuna pruriens (Seed) extract alone at a dose of 500 mg/kg (p.o.).

Conclusion: From the findings of the performed models we can conclude that combined powder extract of Mucuna pruriens (Seed) and Cedrus deodara (Stem bark) shows better anti-parkinson activity as compared to Mucuna pruriens (Seed) extract and might be useful as a better and safer herbal alternate for management of Parkinsonism.

Keywords: Mucuna pruriens, Cedrus deodara, Parkinsonism, Additive
ON is not always ON: When non-motor fluctuations do not match motor fluctuation conditions

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Objective: To study the correlations between non-motor neuropsychological fluctuations and motor fluctuations in Parkinson’s disease (PD) patients.

Methods: The Parkinson’s Kinetigraph (Global Kinetics Corporation: PKG) system was used to objectively detect motor fluctuations and dyskinesia for three consecutive days in non-demented PD patients with motor fluctuations. Bradykinesia score (BKS) and dyskinesia score (DKS) were obtained using specific algorithms. The Neuropsychiatric Fluctuations Scale (NFS) is a self-administered questionnaire developed by the Grenoble team that can be applied in acute settings to detect neuropsychiatric fluctuations. It is composed of 20 items, ten for the ON and ten for the OFF neuropsychiatric states. Patients were instructed to use the PKG and to fill the NFS for three consecutive days. Patients were divided in two groups: group A filled the NFS 4 times/day in previously identified ON and OFF motor periods, whereas group B filled the scale 4 times/day when they felt to be in the OFF and ON motor conditions. Data for BKS and DKS was collected at the time of filling the NFS, and ten minutes before and after.

Results: Eighteen patients were enrolled (8 in group A and 10 in group B). A direct correlation was found between the OFF-motor periods identified with BKS and the OFF NFS item in both groups, (r=0.364, p<0.0001, group A; r=0.281, p=0.010, group B). In group A the correlation was also present with BKS ten minute before filling the scale (r=0.259, p=0.003). A correlation was found between DKS score and the ON NFS items in group A at the time of filling the scale (r=0.210, p=0.016) and ten minutes before (p=0.023, r=0.201).

Conclusions: Our findings suggest that PD patients can better perceive the OFF-motor condition compared to the ON-motor condition, and stress the importance of using specific tools to evaluate and treat non-motor fluctuating symptoms.

Trunk exercise program for Parkinson’s disease

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Background: Axial symptoms in Parkinson’s disease (PD) is resistant to conventional treatment and disabling in daily life of patients, as shown as abnormal posture, postural instability or gait disturbance. Mobility and strength of trunk have significant impacts on those axial symptoms, but there have been limited attention and efforts targeting trunk mobility. The purpose of this pilot study is development and verification of trunk exercise program for PD.
Methods: Mobile PD patients in mild to moderate stage of disease were consecutively recruited from out-patients clinic. Trunk exercise program was developed and consist of stretching and strengthening exercise for trunk muscles, and conducted 3 times a week for 12 weeks. Each session was performed for 60 minutes, and the intensity of exercise was increased based on rating of perceived exertion of patients at every 3 weeks. The effects of trunk exercise program were evaluated using trunk mobility scale (TMS) for PD and senior fitness test. Demographic and disease characteristics of patient were also evaluated and compared with control patients.

Results: Nineteen patients participated, and exercise group enrolled 10 patients. Two patient in control group withdrew consents, so results of 17 patients were compared. There was no difference in demographic and clinical characteristics between exercise and control groups. Exercise program conducted safely and finished without serious adverse event. Trunk mobility improved significantly in exercise group only (TMS score; pre-exercise 5.75±2.75 vs. post-exercise 4.21±2.64). Exercise group also showed improvement in functional fitness tasks requiring trunk mobility, such as timed up and go test, sit to stand test, and 2 minutes walking test. Control group showed no difference but deteriorating tendency during 12 week period.

Conclusion: The results of this pilot study demonstrated feasibility and efficacy of trunk exercise program, and could support the rationale for the exercise program targeting resistant symptoms of PD.

P 092
The neuropsychiatric fluctuations scale for Parkinson’s disease: A pilot study
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Background: Non-motor fluctuations represent a main source of disability in Parkinson’s disease (PD), including neuropsychiatric fluctuations. Anxiety, sadness, lack of energy and motivation, fatigue and pain are common during the off-medication condition, whereas euphoria, well-being, impulse control disorders and behavioral addictions, mania, and psychosis might occur during the on-medication condition. These neuropsychiatric fluctuations might hasten the development of addiction to dopaminergic medication. Early diagnosis of these non-motor neuropsychiatric fluctuations is crucial for a holistic management of the disease. Unfortunately, neuropsychiatric fluctuations are often under-recognized by patients and physicians. One of the main reasons of under-recognition or misdiagnosis is the lack of specific tools for the assessment of neuropsychiatric fluctuations.

Objective: To develop a scale for detecting and evaluating the presence and the severity of neuropsychiatric symptoms during the ON and OFF phases of non-motor fluctuations.

Methods: Neuropsychiatric symptoms reported by PD patients in the OFF- and the ON-medication condition were collected using different neuropsychiatric scales (BDI-II, BAI, Young, VAS, etc.). Subsequently, a pilot study was performed for cognitive pretesting, identification of ambiguous or redundant items (item reduction), and to obtain preliminary data of acceptability of the new scale. For the pilot study, the scale was applied in both the OFF and ON condition during a levodopa challenge.
Results: Twenty items were selected for the final version of the neuropsychiatric fluctuation scale (NFS): ten items measured the ON neuropsychological symptoms and ten items the OFF neuropsychological manifestations. Each item rated from 0-3, providing respective subscores from 0 to 30.

Conclusions: Once validated, our NFS can be used to identify and quantify neuropsychiatric fluctuations during motor fluctuations. The main novelty is that it could be used in acute settings. As such, the NFS can assess the neuropsychiatric state of the patient at the time of examination.

P 093
The impact of impulsivity on quality of life in drug-naive Parkinson’s disease
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We sought to investigate how much impulsivity affects on quality of life (QOL) in drug-naïve Parkinson’s disease (PD), compared with other clinical characteristics and motor symptom. Although impulse control disorder are related with dopamine replacement therapy (DRT), some drug naïve PD patients also experience impulsivity. Impulsivity makes patients hesitate to treat with DRT and influence on poor QOL. We included consecutive 73 patients with De novo PD who met the clinical PD criteria and presented dopamine transporter defects on FP-CIT PET scan.

We performed multivariable-adjusted linear regression analysis of Parkinson’s Disease Questionnaire-39 (PDQ-39) with age, sex, BMI, diabetes mellitus, hypertension, smoking, disease duration, family history of PD, The United Parkinson Disease Rating Scale (UPDRS) part III scores and Questionnaire for Impulsive-compulsive disorders in Parkinson’s disease-Rating Scale (QUIP-RS). 29 patients (39.73%) were experienced impulsivity on QUIP-RS and 4 patients (5.48%) were diagnosed as combined ICD. Age ($\beta=0.600 \pm 0.284$) and UPDRS motor score ($\beta=1.103 \pm 0.289$) were significantly correlated with PDQ-39. Male sex ($\beta=1.984 \pm 0.908$) and QUIP-RS score ($\beta=1.169 \pm 0.082$) was correlated with communication. Though, BMI, DM, HTN, cigarette history and family history were not correlated with PDQ-39 and sub-scores.

Our study showed that older age and more severe motor symptoms were associated with lower QOL in drug naive PD patients. Considering that correlation between impulsivity and total QOL was not significant, treatment strategy have to target the improvement of motor symptoms in PD.
The cost-effectiveness of specialized nursing interventions for people with Parkinson’s disease: protocol of a randomized controlled trial

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Objective: The Dutch Multidisciplinary Guideline for Parkinson’s disease (PD) recommends that each patient should have access to Parkinson’s Disease Nurse Specialist (PDNS) care. However, this is mainly based on expert opinion, with little supporting scientific evidence. Currently PDNS care is only partially implemented, creating unequal access to care and presumably avoidable disability and costs. Therefore, we aim to study the cost-effectiveness of specialized PDNS care as compared to no PDNS care for people with PD. We hypothesize that, by offering more patients access to PDNS care, quality of life will increase with equal healthcare costs. Increasing direct medical costs (for nurse staffing) will be offset by a reduced number of general practitioner and neurologist consultations. In the longer term, we expect healthcare costs to decrease.

Methods: We will perform an 18-month, single-blind, randomized controlled trial in 8 community hospitals in the Netherlands. A total of 240 people with idiopathic PD that have not been treated by a PDNS over the past two years will be included, independent of disease severity or duration. In each hospital, 30 patients will randomly be allocated in a 1:1 ratio to either PDNS care according to the Dutch Guideline on PDNS care, or no nursing intervention (continuing usual care). We will use two co-primary outcomes: quality of life (PDQ-39) and motor symptoms (MDS-UPDRS-III). Secondary outcomes include non-motor symptoms, experienced quality of care, health-related quality of life, self-management, medication adherence and caregiver burden. Data will be collected after 12 months and after 18 months. A healthcare utilization and cost questionnaire will be completed every 3 months.

Conclusions: The results of this trial will have an immediate impact on the current treatment of people with PD. When the intervention group shows increased quality of life and equal costs, as expected, wide implementation of PDNS care is warranted.
Clinical features of Parkinson's disease with and without rapid eye movement sleep behavior disorder


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Background: Rapid eye movement sleep behavior disorder (RBD) and Parkinson's disease (PD) are two distinct clinical diseases but they share some common pathological and anatomical characteristics. This study aims to confirm the clinical features of RBD in Chinese PD patients.

Objective: Study the relationship between RBD and other symptoms of PD.

Methods: 150 PD patients were enrolled from the Department of Neurology, Shanghai First People's Hospital from January 2013 to August 2014. This study examined PD patients with or without RBD as determined by the REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ), assessed motor subtype by Unified PD Rating Scale (UPDRS) III at “on” state, and compared the sub-scale scores representing tremor, rigidity, appendicular and axial. Investigators also assessed the Hamilton Anxiety Scale (HAMA), Hamilton Depression Scale (HAMD), Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR), and Parkinson’s disease Sleep Scale (PDSS).

Results: 141 PD patients entered the final study. 30 (21.28%) PD patients had probable RBD (pRBD) diagnosed with a RBDSQ score of 6 or above. There were no significant differences for age, including age of PD onset and PD duration, gender, smoking status, alcohol or coffee use, presence of anosmia or freezing, UPDRS III, and H-Y stages between the pRBD+ and pRBD- groups. pRBD+ group had lower MMSE scores, higher PDSS scores, and pRBD+ PD patients had more prominent proportion in anxiety, depression, constipation, hallucination and a greater prevalence of orthostatic hypotension.

Conclusion: pRBD+ PD patients exhibited greater changes in non-motor symptoms. However, there was no increase in motor deficits.
**P 096**

**Investigation to expand application sites of rotigotine transdermal patch**

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**Objective:** Rotigotine transdermal patch (RTP) is a dopamine agonist for the treatment of Parkinson’s disease (PD). However, some patients with PD cannot continue to use RTP due to application site reactions such as severe itching, redness, and swelling in application sites (shoulder, upper arm, abdomen, etc). In this study, we examined to see whether to expand the application sites of RTP.

**Methods:** Thirty patients with PD (76 years of age, 12 men) who use RTP with some application site reactions are included in this study. When sticking RTP on the application sites or the frontal part of the crus for 2 to 4 weeks, skin reactions, itching, motor symptoms, and plasma concentration of rotigotine were separately examined.

**Results:** There was no significant difference of MDS-UPDRS part 3 (34.5 on the approval sites and 32.7 in the frontal part of the crus). However, the sticking sites itching sensation using VAS score and the skin irritation score were significantly reduced from 43.9 and 0.7 on the application sites to 9.6 (P < 0.05) and 0.3 (P < 0.01) on the anterior part of the crus, respectively. Plasma concentration of rotigotine (n=3) were 103824, 1220124, 172898 and 3363537 cps on the application sites to 113042, 806971, 154286 and 1974688 cps on the anterior part of the crus, respectively.

**Conclusions:** Although there was no difference of the motor symptoms when sticking RTP on the application sites and the frontal part of the crus, there was a significant reduction of the skin reactions in the frontal part of the crus. Plasma concentration of rotigotine in the frontal part of the crus seems to be decreased. These results suggest that RTP can be stuck on the frontal part of the crus as well as the application sites already applied.

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**P 097**

**The Polymorphism of SREBF1 Gene rs11868035 G/A is associated with susceptibility to Parkinson’s disease in a Chinese population**

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**Objective:** The potential association between the single-nucleotide polymorphism of two functional genes (SREBF1 gene rs11868035 and USP25 gene rs2823357) and susceptibility to Parkinson’s disease (PD) in people of Northeast China was examined in the present study.

**Background:** Recently, genome-wide association studies have successfully identified single-nucleotide polymorphism rs11868035 near sterol regulatory element binding transcription factor 1 (SREBF1) and SNP rs2823357 near Ubiquitin specific peptidase 25 (USP25) as susceptibility loci for PD. SNP rs11868035 lies in an intron of SREBF1 gene on Chr17, which is a modifier of low density lipoprotein receptor and some
genes involved in sterol biosynthesis. Recent study demonstrated that SREBF1 links lipogenesis to mitophagy, and also found carriers of the USP25 rs2823357 variant had progressed to α-synucleinopathies of PD faster than others. However, this has not been confirmed in Chinese population. In the present study we examined the association of the polymorphism of both two genes with susceptibility of PD using a case control study.

Methods: 649 cases of Parkinson's disease from consecutive outpatient and inpatient ward of our hospital were included in this retrospective study, and 355 healthy people were also included as control group. The technique of Kompetitive Allele Specific PCR was applied to determine the frequency distribution of genotype and allele gene of rs11868035 and rs2823357 in both groups.

Results: The significant association was observed for SREBF1 gene rs11868035 in G carriers in PD patients. The frequency of GA+GG genotype and G allele in PD group is significantly higher than in control group of SREBF1 gene rs11868035 (P< 0.0001). As for USP25, there was no significant difference in the distributions of genotypes and alleles of rs2823357 between PD patients and controls (P>0.05). PD patients with G/A variant have higher UPDRS II + III score and lower MMSE score than non-carriers. The results were statistically different (P=0.017, P=0.003, respective).

Conclusion: Polymorphism of SREBF1 gene rs11868035 may increase susceptibility to Parkinson's disease in northeastern Chinese population. USP25 gene rs2823357 variants may have no association with susceptibility to Parkinson's disease in northeastern Chinese. PD patients with G/A variant have worsened motor and cognitive function.

P 098
Quantitative keyboard measurement correlates with changes in subthalamic nucleus LFPs of Parkinson’s disease patients treated with dopaminergic medication better than UPDRS subscores
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Objective: Reliable and objective assessments of the symptoms of patients with Parkinson's disease (PD) and the correlation of the measures with neural patterns is important for the development novel closed-loop therapies. To this end, we employed an objective computerized keyboard task alongside UPDRS, in order to quantify the bradykinesia severity and correlated both modalities with the modulations in the subband powers of the local field potentials (LFPs) recorded from the subthalamic nucleus (STN).

Methods: LFPs were recorded from nine patients with externalized lead (#3389, Medtronic) implantation for three medication intake cycles over 24 hours. The motor performance in the unmedicated (OFF) and medicated (ON) states were assessed separately for each trial by UPDRS items 22, 23-26 and a 30-second alternating keyboard task. The band powers of theta-alpha (4-12Hz), beta (13-30Hz), gamma (70-90Hz), and high frequency oscillations (HFOs, 200-400Hz) were computed using 10 minute data from both states. HFO change was represented as the ratio of 200-300Hz and 300-400Hz bands since they were mutually exclusive in each state. Due to the repeated samples, a mixed-model was used to find the correlations.
Results: Table 1 summarizes the correlations between the improvement of symptoms and the changes in the LFP patterns. The improvement in keyboard always correlated better than bradykinesia for all markers. Additionally, the correlation between bradykinesia and keyboard was $r = 0.65$ ($p < 0.001$).

<table>
<thead>
<tr>
<th></th>
<th>Keyboard Score</th>
<th>Bradykinesia Score</th>
<th>Bradykinesia+Rigididy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theta-alpha power</td>
<td>$r=0.43$, $p=0.04$</td>
<td>$r=0.34$, $p=0.1$</td>
<td>$r=0.29$, $p=0.16$</td>
</tr>
<tr>
<td>Beta power</td>
<td>$r=-0.51$, $p=0.01$</td>
<td>$r=-0.28$, $p=0.19$</td>
<td>$r=-0.54$, $p=0.01$</td>
</tr>
<tr>
<td>Gamma power</td>
<td>$r=0.68$, $p=4e-4$</td>
<td>$r=0.27$, $p=0.22$</td>
<td>$r=0.44$, $p=0.04$</td>
</tr>
<tr>
<td>HFO ratio</td>
<td>$r=-0.62$, $p=0.002$</td>
<td>$r=-0.43$, $p=0.04$</td>
<td>$r=-0.4$, $p=0.06$</td>
</tr>
</tbody>
</table>

[Table 1. The correlations between symptom measures (columns) and electrophysiological modulations (rows)]

Conclusions: The moderate correlation between bradykinesia and keyboard shows that they do not completely agree. Although not comprehensive and conclusive, keyboard always explained the changes in the neural data better, compared to bradykinesia. This might be because the rater knew the patient’s state but was blinded to neural data. In short, the superior correlations obtained from keyboard indicates that well-designed tasks can help determining the symptoms in a more reliable and standardized fashion.

P 100
Brain-derived neutrophic factor and lipid profile in Parkinson’s disease
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Background: Parkinson’s disease (PD) is a neurodegenerative disorder that affects many body systems, including cardiometabolic function. Brain-derived neutrophic factor (BDNF) is altered in PD and has also been implicated in cardiometabolic function. However, few studies examined the effect altered BDNF on lipid profile among PD. Therefore, the current study examined the relationship of BDNF with lipid profile in PD.

Methods: Serum BDNF and lipid profile were determined in 28 PD and 28 age/gender matching control.

Results: The comparisons show that BDNF and lipid profile are altered ($p < 0.05$) in PD as compared to the control. Additionally, simple linear regression in the patients only, showed that BDNF predicted 11.9% of total cholesterol ($p=0.05$), 3.0% of HDL ($p=0.003$), 27.3% of LDL ($p=0.006$), 16.6% of triglyceride ($p=0.04$), 15.8% of total cholesterol/HDL ($p=0.06$), 22.1% of total cholesterol/LDL ($p=0.01$), and 35.1% of triglyceride/HDL ($p=0.001$). However, after including these variables in a stepwise regression, BDNF predicted only 50.0% triglyceride ($p=0.0001$) and 35.1% of triglyceride/HDL ($p=0.001$).

Conclusions: The results indicate that BDNF is positively related to “desired” lipid profile, especially triglyceride and triglyceride/HDL in PD. Therefore, strategies aiming at improving BDNF levels are warranted.
**P 101**

**Fatigue in Parkinson’s disease: Correlates and its effects on ability of daily living**

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**Objectives:** Fatigue is a common complaint in patients with Parkinson’s disease (PD). The purpose of this study was to investigate the correlates of fatigue in PD and its effect on performance of activities of daily living (ADL).

**Methods:** One hundred and thirty-one patients with PD were recruited and completed a series of comprehensive assessments. The severity of symptoms of PD was measured with the unified Parkinson’s disease rating scale III (UPDRS-III) subscore, together with fatigue assessed by the Fatigue Severity Scale (FSS) and depressive symptoms by the Hamilton Depression Rating Scale (HDRS). The Mini-mental Status Examination (MMSE) was performed to measure the global cognitive function. The performance of ADL were evaluated using the Schwab and England Ability of Daily Livings Scale (SEADL).

**Results:** The included patients had a mean age of 67.8 (8.7) years old, 73.8% of them were male. In binary correlation analyse, FSS significantly correlated with age, dosage of levedopa, presence of motor fluctuation, UPDRS-III subscore, Hoehn-Yahr stages, MMSE and HDRS scores \((P<0.05)\). Multiple linear regressions showed that older age and higher HDRS score were significant associated factors of higher FSS score, accounting for 24.4% of the variance of it. FSS correlated with physical anxiety \((r=0.388, P<0.001)\), cognition \((r=0.256, P=0.004)\), retardation \((r=0.256, P<0.001)\), sleep \((r=0.224, P=0.013)\) and disappointment \((r=0.382, P<0.001)\) subscore of the HRDS. FSS did not correlate with SEADL after adjusted for age, duration of disease, Hoehn-Yahr stages and UPDRS-III subscore, although they had a significant association in binary correlation \((r=0.332, P<0.001)\).

**Conclusion:** Depressive symptoms and older age were the major correlates of fatigue in PD. Fatigue remains a comprehensive and complicated symptom in PD and appears not to affect their performance of ADL.

**P 103**

**Thai bamboo dance: Improvements in gait, balance and foot clearance for Parkinson’s disease**

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**Objective:** To investigate the effects of a Thai bamboo dance training program on gait, balance, foot clearance and quality of life in people with Parkinson’s Disease (PD).

**Methods:** Twenty-four people with PD (stage 1.5-3 Hohn and Yahr) were matched by duration of disease and Schwab and England Activities of Daily Living Scale to receive either 1 hour dancing classes using the modified Thai bamboo dance for Parkinson’s Disease model for 10 weeks \((n=13)\) or a usual care control
group (n = 11). Improvements were examined after the training by using the GAITRite electronic Walkway, balance platform, digital motion analysis software and the Parkinson’s Disease Questionnaire (PDQ 8).

**Results:** Comparing the groups, statistically significant improvements were found in gait velocity, stride length, Mean sway medio-lateral (ML), Mean sway antero-posterior (AP), Mean velocity medio-lateral (ML), Mean velocity antero-posterior (AP) and Maximum Ground Clearance in dance group. No adverse effects were detected. Patients expressed enjoyment, satisfaction and interest in continuing Thai Bamboo dance classes.

**Conclusions:** These findings suggest Thai bamboo dance may be used as an exercise program to promote gait, balance and foot clearance because it naturally combines cognitive movement strategies, cueing techniques (Visual and auditory), balance exercises, gait training, normalizing body posture and physical activity while focusing on the enjoyment of moving across the bamboos with music.

**P 104**

**Effectiveness and safety of continuous infusion of levodopa-carbidopa intestinal therapy for patients with advanced Parkinson’s disease: a single center experience**

**Vuletic V.**

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**Introduction:** Patients with advanced Parkinson’s disease (PD) with unsatisfactory effect of oral medications need invasive therapy due to development of motor complications including fluctuations and involuntary movements (dyskinesias) and low quality of life (QoL). Continuous administration of levodopa-carbidopa intestinal therapy (LCIG) through intestinal infusion is a therapeutic invasive option for advanced PD. Our aim was to see effect, benefit and safety of LCIG treatment on 14 PD patients (7 female, 7 male, mean age 68 years) treated in our center during last 3 years.

**Methods:** We followed patients before treatment, 1 month after and 3 months after treatment by using Functional Independence Measure (FIM) instrument, Unified Parkinson Disease Rating Scale (especially motor score and activities of daily living) (UPDRS), number of medications and quality of life scale (PDQ-39) as main outcome instruments. We also use the patients’ self-evaluation of their QoL and satisfactory before and after LCIG therapy measured using the 10-point Visual Analog Scale (VAS).

**Results:** The mean duration from the time of clinical diagnosis of Parkinson’s disease until LCIG therapy initiation was 14 years. The mean duration of LCIG therapy was 1.4 years. We found good outcome results concerning motor improvement, disability improvement, reducing a number of medications, safety, quality of life perception and patients’ satisfactory in PD patients due to significant (p< 0.05) improvement in FIM scores, UPDRS, QoL and VAS scores.

**Conclusion:** This study has shown that PD patients after treatment with continuous infusion of levodopa-carbidopa intestinal therapy have a good benefit, safety, tolerability and effectiveness in maximizing patients’ functional improvement.
**P 106**

**Russian validation study of the Berg Balance Scale**

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**Objective:** Instability is one of the significant symptoms of the Parkinson’s disease (PD). There is a need for the standardized objective approach in the assessment of stability of PD patients in Russia and Russian-speaking countries as there is not validated scale for this purpose. Meanwhile in Europe and USA Berg Balance Scale (BBS) is widely used for assessment stability of PD patients (Qutubuddin A. et al., 2005). The aim was to perform a validation study of Russian version of BBS.

**Methods:** Fifty-five PD patients included in the study had mild to moderate disability and could walk unassisted. The entire BBS validation procedure included translation by two independent medical translators and back translation by a native English speaker with fluent Russian, cultural adaptation and finally, assessment of psychometric parameters: Internal and Test-retest consistency, Inter-rater reliability, concurrent validity, and sensitivity. To test concurrent validity of the translated scale, Romberg Balance Test was performed in stabilometric platform Stabilan-01-2 (JSC Rhythm, Russia).

**Results:** Internal consistency of Russian version of the BBS assessed by Cronbach’s alpha was 0.82 (p<0.001) that was higher than critical threshold (0.80). Inter-rater reliability of the scale evaluated by the Cohen’s kappa was 0.91 (p<0.001). Test-retest consistency was also high with the Pearson’s correlation coefficient r=0.94 (p< 0.0001), indicating the stability of patient’s assessment during the observation period. The BBS scores correlated significantly (r=0.78, p< 0.05) with Romberg Balance Test, indicating acceptable concurrent validity. Finally, it was revealed high enough level of sensitivity as Student’s t-test showed a significant difference (p=0.047) between scores before and after rehabilitation treatment.

**Conclusions:** Russian version of the BBS is a valid and sensitive scale for clinical assessment of rehabilitation progress. It is also a useful tool for entire neurological examination of a PD patient.

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**P 107**

**Assessing Tele-Health Outcomes in Multiyear Extensions of Parkinson’s Disease trials (AT-HOME PD): Design of a long-term observational study**

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**Objective:** The objective of this study is to develop, implement, and evaluate a model for the remote, long-term observation of Parkinson’s disease (PD) clinical research cohorts using smartphone-based assessments, web-based surveys, and virtual research visits (tele-visits). The use of mobile and remote technologies that enable frequent data collection and objective assessment in a realistic setting will permit long-term observation, reduce barriers to participation, and enable the development of digital biomark-
ers of disease progression, potentially improving clinical trial efficiency. We will 1) implement the infrastructure for a new research model, 2) compare smartphone outcomes against tele-visit outcomes, and 3) develop novel biomarkers of PD disability and progression.

**Methods:** STEADY-PD3 and SURE-PD3 are active NINDS-funded phase 3 interventional studies of potential disease-modifying therapeutics for PD. An estimated 420 individuals completing either STEADY-PD3 or SURE-PD3 will enroll into a remote observational study (AT-HOME PD). Participants will be followed for 24-months through tele-visits, smartphone-based assessments, and web-based surveys. Centralized movement disorders specialists will conduct annual tele-visits, which will include standard motor and cognitive assessments. On a quarterly basis, participants will complete two-week sessions of smartphone-based motor and cognitive tasks. For consented participants, the smartphone application will collect GPS and accelerometer data on movement and activity. Participants will be asked to enroll in a companion online study, Fox Insight, to complete web-based surveys on a quarterly basis. Data from the three platforms will be integrated with data from the parent studies and transferred to the Parkinson’s Disease Biomarkers Program’s Data Management Resource for use by the broader research community.

**Results:** Protocol development and study planning has begun ahead of a planned launch of AT-HOME PD in the summer of 2018.

**Conclusions:** We will use novel tele-health metrics to enable the remote, long-term follow-up of PD clinical research cohorts and develop digital biomarkers of disease progression.

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**P 108**

**Neuroprotective effect of Naringin loaded solid lipid nanoparticles via induction of GDNF in MPP+ induced Parkinson’s disease in animal model**

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**Backgrounds:** Naringin is a flavonoid majorly founds in grapefruit and citrus fruits. The administration of a neurotoxin in Parkinson’s disease (PD) animal model resulted degeneration of the nigrostriatal dopaminergic (DA) neuron. Further induction of glia-derived neurotrophic factor (GDNF) observed by administration of naringin loaded solid lipid nanoparticle (SLN), which involving in the preventions of DA neuron degenerations.

**Material and methods:** 1-Methyl-4-phenylpyridinium (MPP+) is a neurotoxin, which injected into the medial forebrain bundle of rat brains for a PD in the presence or absence of naringin solution and naringin SLN by intraperitoneal injection/day. To make sure of whether naringin SLN induced GDNF to neuroprotection in the MPP+ rat model of PD.

**Result and discussion:** Our finding demonstrates that Naringin loaded SLNs enhances the level of GDNF in DA neurons and protected neuron in MPP+ rat model of PD along with activation of mammalian target of rapamycin complex 1. Moreover, the neurotoxicity in substantia nigra resulted due to increased level
of tumour necrosis factor-α by MPP+. After administration of Naringin-SLN, it much reduces the level of TNF-α and protected the substantia nigral neuron as compared to Naringin solution. Moreover, it also produces GDNF as a therapeutic agent and imparts anti-inflammatory effects to DA neuron against PD.

**Conclusion:** Collectively, we can conclude that naringin loaded solid lipid nanoparticles is an effective therapeutic carrier over conventional carrier for the prevention of DA degeneration in the animal model of PD.

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**P 109**

**Decreased striatal dopamine and neuropsychiatric symptoms in patients with Parkinson’s disease**

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**Backgrounds:** Neuropsychiatric symptoms such as depression and anxiety are common in Parkinson’s disease (PD). Previous studies showed that an alteration in dopamine metabolism was found in neuropsychiatric symptoms in PD. The aim of this study was to investigate the association between neuropsychiatric symptoms and striatal dopamine in patients with PD.

**Patients and Methods:** Consecutive patients newly diagnosed with PD who visited the movement disorder clinic of Seoul St. Mary’s hospital and Yeouido St. Mary’s Hospital in Seoul, Korea, between March 2013 and December 2014 were enrolled. To assess neuropsychiatric symptoms, the Neuropsychiatric Inventory (NPI) was used and patients were categorized to three groups. Fluorinated N-3-fluoropropyl-2-α-carboxymethoxy-3-α-(4-iodophenyl) nortropane (FP-CIT) PET imaging was performed and quantitative analyses with standard set of regions of interest (ROIs) was used to take the average standardized uptake values of the striatum.

**Results:** Of the 133 PD patients, 27 was mild group, 81 was mood/apathy group, and 25 were agitation/psychosis group. Striatal FP-CIT uptake was decreased in mood/apathy group than in mild group. Average standardized uptake ratio for left caudate to occipitum in mild group was higher than both mood/apathy and agitation/psychosis groups. Linear regression analyses showed that decreased caudate uptake was associated with agitation, depression, anxiety, apathy, and nighttime behavior disorders. Decreased uptake in putamen was associated with anxiety and nighttime behavior disorders.

**Conclusion:** The severity of neuropsychiatric symptoms in PD was generally associated with decreased striatal dopamine uptake. In mood/apathy group, striatal dopamine uptake was reduced than in mild neuropsychiatric symptoms group, which supports that dopaminergic dysfunction was related to affective symptoms in PD. Dopamine loss in the caudate nucleus was associated with depression, anxiety, and nighttime behavior disorders.
Patterns of movement disorders among HIV/AIDS patients: a cross sectional study

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There is limited information on the prevalence of neurological disorders in general and movement disorders in specific among HIV/AIDS patients. Most cases are seen by general practitioners in Africa. Resources cannot be allocated to improve care unless reliable data are collected.

We performed a cross sectional point prevalence study of all HIV/AIDS patients seen at Ethiopian Federal Police Commission Referral Hospital in Addis Ababa, Ethiopia, over 24-month period to determine the frequency of movement disorders seen, disease characteristics, diagnostic evaluations, and treatment options.

A total of 2,543 patients were seen during the study period. 25.4 % were seen for neurological disorders. 16.1% of the neurological patients were seen for movement disorders. Of these, most were for parkinsonism (50.5%), followed by different ataxias (15.9%), dystonia (9.1%), chorea (6.8%), essential tremor (6.3%), and others (11.4%). Diagnostic evaluations and treatment were available, although expensive. Only 28.2 % of the patients feel their symptoms were controlled adequately. 73.9% of the patients endorse they faced some kind of stigmas because of the movement disorder they have. Most (83.6%) were seen by general practitioners. Only 15.9% had regular follow-ups.

Despite limited resources, HIV/AIDS patients with movement disorders require comprehensive care. It makes the patient care more crucial hence patients with HIV/AIDS and movement disorders are prone to significant stigma among the general public. Only a segment of patients was seen a neurologist. This finding implies the need for adequate training in movement disorders for physicians and neurologists in Africa.

Unraveling gut microbiota in Parkinson’s disease and atypical parkinsonism

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Objectives: Recent evidences support the hypothesis that dysfunction in the brain-gut microbiota axis may play a critical role in the pathogenesis of Parkinson’s disease (PD). However, findings are heterogeneous probably due to the presence of several confounders. We evaluated the differences in gut micro-
biota among PD, atypical parkinsonism (i.e. multiple system atrophy [MSA] and progressive supranuclear palsy [PSP]) and healthy controls (HC) and whether microbiota may act as modulator of disease progression and clinical phenotype.

**Methods:** We recruited patients with idiopathic PD (n=193, of whom 39 were de-novo), PSP (n=22), MSA (n=22), and HC (n=113). Several confounders were taken into account, including pharmacological therapy, dietary habits and genetic status. Information on the type of lactation were also recorded.

**Results:** Despite simple non-parametric comparison of PD patients and HC showed several differences in relative taxa abundances, the number of significant comparisons was reduced after adjusting for multiple confounders. We observed a constant effect of age on almost all abundances. The use of COMT inhibitors appeared to influence the level of several taxa. Overall, PD patients had increased *Verrucomicrobia*, *Christensenellaceae*, *Lactobacillaceae*, and decreased *Lachnospiraceae* and *Ruminococcaceae* than HC. Reduced level of *Lachnospiraceae* was significant in all PD duration strata, while many of these differences were associated with disease progression. De-novo PD differed from HC only by lower abundance in *Lachnospiraceae*. Compared to PD, *Lachnospiraceae* and *Ruminococcaceae* were not significantly lower in MSA, while in PSP cases other genera of *Ruminococcaceae* and *Lactobacillaceae* were higher and comparable, respectively. Increased *Lactobacillaceae*, *Christensenellaceae*, *Verrucomicrobia* and decreased *Lachnospiraceae* were associated with worse disease severity, including intellectual impairment, axial features (gait disturbances and postural instability) and other non-motor symptoms.

**Conclusions:** Gut microbiota may play a role in the pathogenesis of PD and act as modulators of individual differences in disease severity, especially non-dopaminergic features (cognition and axial symptoms).

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A phase 2A study of nilotinib in patients with advanced and early Parkinson’s disease study design


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To assess the safety and tolerability of nilotinib (150-300 mg QD) in moderate/advanced and early/de novo Parkinson disease (PD) participants.

We have initiated a Phase 2a randomized, double-blind, placebo-controlled, parallel group, two cohort study. See Figure 1 for study design. The study will enroll 75 participants with moderate to advanced PD in Cohort 1. The participants will be randomized 1:1:1 to a once daily dose of nilotinib or placebo (150 mg : 300 mg : placebo) for 6 months. Assuming one or more doses are determined to be safe in Cohort 1,
Cohort 2 will enroll 60 de novo PD participants randomized 2:1 to a once daily dose of nilotinib or placebo (the highest tolerated and safe dose from cohort 1: placebo) for 12 months. The primary outcome for both cohorts is safety and tolerability. A key secondary objective for Cohort 1 is a futility analysis of the change in the MDS-UPDRS part III score, based on the magnitude of the change observed in the previously completed pilot study (ClinicalTrials.gov NCT02281474). Additional secondary and exploratory outcomes include assessment of symptomatic effect of nilotinib; impact of nilotinib on progression of PD disability (MDS-UPDRS OFF/ON); cognitive function (DRS-2); and quality of life measures. The study also includes a comprehensive battery of serum and spinal fluid biomarkers, measures of serum pharmacokinetics and levels of nilotinib in cerebrospinal fluid. The study is conducted at 25 Parkinson Study Group (PSG) sites in US. The first participant was recruited November 2017. Recruitment for Cohort 1 is expected to be completed in fall 2018, with follow-up continuing through late 2018.

This study will provide further information on safety/tolerability, dose selection and biomarkers profile of Nilotinib as a potential novel therapy to slow PD progression and determine if it is warranted to proceed with the future efficacy studies.

**P 113**

**The comparison of gut biogeography of the gut bacterial microbiota in Parkinson’s disease**

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**Background:** In PD patients, the frequency of constipation is higher than control. People who received total vagotomy for the purpose of treating duodenal ulcers in the past have a 50% reduction in the incidence of PD. These facts suggest that the changes in intestinal environment may be involved in the development of PD. Compositional changes of intestinal bacteria in PD have been reported in many countries. The 16 rRNA analysis and the shotgun metagenome analysis in our cohort were compared with 5 previous reports by others.

**Method:** In the 16s rRNA analysis, the V3-V4 regions were amplified by PCR and 300-bp pair-ends were sequenced with Illumina MiSeq. The obtained data were analyzed by Qiime 2. In the shotgun metagenome analysis, 150-bp pair-ends of the whole metagenome were sequenced with Illumina HiSeq 2500. The obtained data were analyzed by MetaPhlAn 2. We also obtained raw sequencing datasets in the past reports from the GEO database and others. For each downloaded dataset, 16S rRNA analysis and the shotgun metagenome analysis were performed using Qiime 2 and MetaPhlAn 2, respectively.

**Results:** The compositions of microbiota varied widely between countries. The difference in controls between countries was larger than the difference between healthy and PD individuals in each country. In Finland, *Prevotella* was the major intestinal bacterial species. However, in Germany, Japan, and the USA, the ratio of *Prevotella* was small. In Japan, the ratio of *Bifidobacterium* was higher than those in other countries.
**Conclusion:** Differences in microbiota compositions between healthy and PD individuals have been reported in many countries. However, since the microbiota composition in controls in each country varies greatly, it is unlikely that specific bacteria are uniquely changed in PD. In the future, functional analysis, not taxonomic analysis, of shotgun metagenome datasets will elucidate intestinal dysbiosis that is unique to PD.

**P 114**

**Clinical correlation of serum insulin-like growth factor-1 levels in patients with Parkinson’s disease and related disorders**

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**Background:** Insulin-like growth factor-1 (IGF-1) participates in brain growth, development, plasticity and neuronal survival. IGF-1 may have a role in the pathophysiology of neurological disorders. We investigated serum IGF-1 levels in patients with Parkinson’s disease (PD) and related disorders.

**Methods:** This study included 82 patients with PD-related disorders. Serum IGF-1 levels were determined an immunoradiometric assay. Patients were evaluated with Hoehn and Yahr staging. Mini-Mental State Examination (MMSE) was used to assess cognitive function. A card-type odor identification test, Open Essence (Wako, Japan), was used for olfactory function assessment. Cardiac 123I-metaiodobenzylguanidine (MIBG) scintigraphy and 123I-ioflupane SPECT (DAT scan) were performed.

**Results:** Serum IGF-1 levels among the diseases were as follows: PD (n=53), 113.3±43.8 ng/ml; progressive supranuclear palsy (n=14), 105.6±31.6 ng/ml; multiple system atrophy (n=10), 107.7±21.4 ng/ml; dementia with Lewy bodies (n=3), 79.0±14.7 ng/ml; corticobasal degeneration (n=2), 118.0±19.8 ng/ml. In patients with PD, serum IGF-1 levels were inversely correlated with age and positively correlated with the specific binding ratio in the striatum on DAT scan and MMSE score. There was no correlation of serum IGF-1 levels with disease duration, HY stage, cardiac MIBG scintigraphy uptake or open essence score. In patients with other parkinsonian disorders, there was no significant correlation between IGF-1 levels and clinical parameters including striatal DAT binding and uptake of cardiac MIBG scintigraphy.

**Conclusion:** In our study, serum IGF-1 levels were correlated with striatal dopaminergic function and cognitive function in patients with PD.
P 115
Serum uric acid is associated with cognitive decline in de novo patients with Parkinson’s disease

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Objective: To determine whether serum uric acid (UA) level is related to the cognitive impairment in de novo Parkinson’s disease (PD) patients.

Background: Olfactory dysfunction is considered as a biomarker of cognitive decline and dementia in PD. However, there is limited information on the relationship between serum UA and cognition in de novo PD patients. There have been significant questions whether UA is neuroprotective as an antioxidant or neurotoxic as a pro-oxidant.

Methods: The study included 196 de novo Parkinson’s disease patients. The score of Mini-Mental Status Examination (MMSE) and Montreal Cognitive Assessments (MOCA) were used to evaluate cognitive abilities. Receiver-operating characteristic (ROC) curve analysis was performed to determine the cutoff value of the serum UA. The area under the ROC curve (AUC) and the confidence interval (CI) were also assessed.

Results: A total of 196 participants were enrolled in this study. The mean age was 67 years, and 58% were women. The mean serum UA was 4.7 mg/dL and significantly lower in woman than men (4.3 vs 5.2 mg/dL, p< 0.0001). The MMSE and MoCA score was also lower in women (MMSE 25 vs 27, p< 0.0001 and MoCA 20 vs 23, p< 0.0001), suggesting that serum UA level was related with the cognitive function. Correlation analysis clearly demonstrated that the serum UA level was positively related with the cognitive function (MMSE, r=0.222, p=0.003 and MoCA r=0.215, p=0.004). The cutoff value of the serum UA for MMSE >24 was 4.9 mg/dL (sensitivity, 42.2%; specificity, 71.4%) and AUC was 0.603 (95% CI, 0.510-0.695, p=0.035). The cutoff value of the serum UA for MoCA >24 was 4.9 mg/dL (sensitivity, 50.0%; specificity, 67.8%) and AUC was 0.595 (95% CI, 0.508-0.681, p=0.038).

Conclusions: This study showed that lower serum UA was associated with cognitive impairment in de novo PD patients.

P 116
Home mobility system for monitoring patients with Parkinson’s disease: validation with actigraphy

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Introduction: Assessment of daily living of patients with Parkinson’s disease (PD) is important in clinical practice. Technical advances made it feasible to monitor PD patients continuously in free-living environment, which ensures better assessment and provision of quality care. This study is to validate the home mobility system with an actigraphy device to confirm whether the system could monitor the activity of PD patients well or not.
Methods: The participants were recruited from the department of neurology in the Kyung Hee University Hospital. Patients with PD and healthy controls who live alone were eligible for this study. The 24-hour mobility monitoring system were installed at home, and the participants wore an actigraphy device during monitoring period. The parameters of activity from the system and device were compared between two groups.

Results: Total 26 participants were initially enrolled to the study. Eight subjects in control group were excluded due to inconvenience of wearing the actigraphy device. Finally, 8 PD patients and 6 controls were included in the analysis. The overall correlation between the home monitoring device and actigraphy in all participants showed a significant positive correlation ($R = 0.487$, $p <0.001$). This positive correlation was also confirmed in the data of each patient. When the clinical features and activity parameters of PD patients and controls were compared, the home mobility parameter was significantly lower in PD patients.

Conclusion: The home mobility system is a relatively accurate and useful tool for recording the activity of PD patients when compared with a wearable actigraphy device.

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Can coenzyme Q10 and creatine slow the progress of Parkinson’s disease?

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Background: Coenzyme Q10 (CoQ10) and creatine are two antioxidants that showed neuroprotective effects in animal models of Parkinson’s disease (PD). Both drugs were selected by the National Institute of Neurological Disorders and Stroke as possible disease modifying agents for PD and subjected to evaluation in phase III clinical trials. However, clinical trials on both drugs showed controversial results regarding their efficacy.

Objectives: This meta-analysis of randomized controlled trials (RCTs) analysis aims at providing class one evidence about the efficacy of CoQ10 and creatine for neuroprotection against PD.

Methods: We followed the guidelines of PRISMA statement and Cochrane handbook guidelines during the preparation of this meta-analysis. A computer literature search was performed through October, 2016 to identify relevant RCTs. Outcomes of total Unified Parkinson's Disease Rating Scale (UPDRS), UPDRS I, UPDRS II, and UPDRS III were pooled as standardized mean difference (SMD) or mean difference (MD) between two groups from baseline to the endpoint. Statistical heterogeneity was assessed by visual inspection of the forest plot and measured by chi-square and I-square tests.

Results: Eight RCTS (CoQ10: five RCTs, n=981; and Creatine: three RCTs, n=1935) were included in this study. Neither CoQ10 nor creatine was superior to placebo in terms of: UPDRS total score (CoQ10: SMD -0.05, 95% CI [-0.10 to 0.15]; creatine: MD 1.07, 95% CI [3.38 to 1.25]), UPDRS III (CoQ10: SMD -0.05, 95% CI [-0.07, 0.17]; creatine: MD 0.62, 95% CI [2.27 to 1.02]), UPDRS II (CoQ10: SMD -0.10, 95% CI [-0.35, 0.15]; creatine: MD 0.03, 95% CI [0.81 to 0.86]), and UPDRS I (CoQ10: SMD -0.05, 95% CI [-0.10, 0.15]; Creatine: MD 0.03, 95% CI [0.33 to 0.28]).

Conclusion: This meta-analysis provides class one evidence that neither Coenzyme Q10 nor Creatine can slow the progress of PD or provide any symptomatic benefit for PD patients.
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Carrier mediated delivery system bearing dopamine for effective management of parkinsonism

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Parkinson is a Neurodegenerative disease in which there is dopamine deficiency in Basal ganglia. The delivery of drug and sustaining it in effective concentration in brain is challenging due to blood brain barrier (BBB). In the present investigation, amino acid coupled liposomes bearing dopamine-HCl were prepared to deliver drug to the brain utilizing receptor-mediated transcytosis for effective management of parkinsonism.

L-lysine stearylamine conjugate (LSC) was synthesized & LSC coupled liposomes bearing dopamine HCl was prepared by lipid cast film method. Formulations were analyzed for average vesicle size measured through Laser diffraction particle analyser (CILAS 1064 L, France), shape through Transmission Electron Microscopy, drug entrapment determined using Sephadex G- 75 minicolumn centrifugation method, in-vitro drug release and in-vivo efficacy of the formulations was assessed by measuring the reduction in the degree of drug induced catatonia in albino rats.

Average particle size was found in the range of 1.92-0.80 mm. There was increase in the size for coupled liposomes due to the inclusion of LSC in liposomal bilayers. The percent encapsulation efficiency decreased from 46.82±2.17% in uncoupled to 38.13±1.18% in coupled liposomes. The in-vitro drug release after 24hrs was 58.9±2.94% with uncoupled while the coupled liposomes showed 43.7±2.18% drug release. The lower value for coupled formulation could be due to the retardation of drug release caused due to the incorporation of LSC in the liposomal bilayers, which enhanced the structural integrity of the bilayer. In-vivo study reveals that the animals receiving uncoupled liposomes showed partial reduction and animals that received coupled liposomes showed almost complete reduction in catatonia.

Fluorescence study clearly indicates the uptake of 6-CF in blood vessels and accumulated in brain. This could be due to enhanced uptake of Lysine coupled liposomes through amino acid transporters present at BBB surface.
A Phase 3 study of isradipine as a disease modifying agent in patients with early Parkinson’s disease (STEADY-PD III): Baseline characteristics and study update

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Objective: The NINDS funded STEADY-PD III trial is a 36 month, Phase 3, parallel group, placebo-controlled study evaluating the efficacy of isradipine 10mg daily as a disease-modifying agent in early PD. Enrollment of 336 participants was 6-months ahead of schedule and participant retention has been excellent. The main objective is to provide a study update in preparation for study close out and dissemination of results.

Methods: The first study participant enrolled in November 2014 and the last subject is anticipated to complete the study in November 2018. The primary outcome is the change in the Unified Parkinson Disease Rating Scale (UPDRS) Part I-III score as measured in the ON state at month 36, in the active arm compared to placebo. Secondary outcome measures include:
1) Time to initiation and utilization of dopaminergic therapy;
2) Time to onset of motor complications;
3) Change in non-motor disability and a spectrum of other PD motor and non-motor outcome measures.

Results: As of April 30, 2018 of the 336 total participants enrolled, 191 are active in the study; (98% retention) and 181 are on study drug. There have been 13 premature withdrawals and 64 serious adverse events, 5 possibly related to study drug, 2 deaths (unrelated), 289 (86%) participants started PD symptomatic therapy.

Conclusion: STEADY-PD III is fully enrolled and maintains high retention despite 3-year duration of intervention. Final study results are expected winter 2019. This study represents a unique opportunity to evaluate the potential impact of a novel therapy to slow progression of PD disability and provide clinically meaningful benefits.

Study supported by the NINDS U01NS080818 and U01NS080840
Neuropsychiatric and behavior changes in Parkinson’s disease patients with impulse control disorder after switching-off dopamine agonist by levodopa/carbidopa slow-release formulations

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Objective: This is a multi-center open-label trial to compare behavioral and neuropsychiatric symptoms in Parkinson’s disease (PD) patients with impulse control disorders (ICD) who were taking dopamine agonists before and 12 weeks after switching-off dopamine agonists by equivalent dose of levodopa/carbidopa slow-release formulation.

Methods: Baseline characteristics in 50 PD patients with ICD were compared with those in 60 medicated- and 40 drug-naïve PD control groups. Neuropsychiatric trait changes in PD-ICD group were investigated 12 weeks after the intervention. ICD behaviors were assessed by modified Minnesota Impulsive Disorders Interview (mMIDI) whereas parkinsonian severity and neuropsychiatric characters were systematically assessed by the Unified PD Rating Scale (UPDRS) and using a predefined neuropsychological assessment battery.

Results: At baseline, ICD patients showed higher scores in the Neuropsychiatric inventories and had anxiety, anger expression, and obsessive-compulsive traits than both PD control groups whereas the three PD groups showed indifference in the impulsivity scales. At 12-weeks after intervention, ICD behaviors significantly improved (p < 0.001) and so did the UPDRS II daily activity scores (p = 0.02). Disinhibitory behaviors tended to improve (p = 0.06), but otherwise no significant change was noted in the Neuropsychiatric Inventory and personality trait scores. Dopamine agonist withdrawal syndrome developed in 5.3% of PD-ICD group.

Conclusions: This study provides Class IV evidence that switching-off dopamine agonists by levodopa/carbidopa slow-release formulations can alleviate ICD behaviors in PD patients leading to improvement in daily activities whereas neuropsychiatric traits associated with ICD persisted by 12-weeks' therapy.
P 122
Microstructural changes in white and grey matter related to apathy, depression and anxiety in de novo Parkinson’s disease patients
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Objectives: To study microstructural changes in grey and white matter in early drug-naïve Parkinson’s disease (PD) patients and correlate these changes with neuropsychological manifestations and known functional serotoninergic and dopaminergic presynaptic alterations in de novo PD-patients with apathy, depression and anxiety.

Methods: We conducted a case-control-control study enrolling 13 de novo PD-patients with apathy (Lille Apathy Rating Scale (LARS) scores ≥ -21), 14 de novo PD-patients without apathy and 15 age-matched healthy controls. Neuropsychological and neurological examination was performed to assess severity of motor and nonmotor symptoms using MDS-UPDRS-III, LARS, BDI-II and STAI-YB scales. All participants underwent anatomical and diffusion 1.5T MR imaging and Positron Emission Tomography (PET) imaging of presynaptic DA and 5-HT transporters using [11C]-PE2I and [11C]-DASB respectively. Fractional anisotropy (FA) and mean diffusivity (MD) were fitted using DTI for grey matter in limbic areas and for white matter in study-specific white matter tracts skeleton using TBSS. Microstructural metrics were compared using voxel-wise permutation-based statistics with GLM and between-groups ANCOVA adjusted for age and sex.

Results: Increased mean diffusivity correlated with greater severity of apathy in grey matter located in the anterior caudate nuclei, subgenual and dorsal anterior cingulate cortex bilaterally for PD-patients, as well as for depression. Moreover, decreased fractional anisotropy in ventral striatum, subgenual and dorsal anterior cingulate cortex and medial orbito-frontal cortex grey matter correlated with greater severity of apathy in PD-patients. Additionally, white matter FA changes indicated decreased directionality in the bilateral forceps minor, uncinate fasciculus, cingulum, anterior limb of the internal capsule and its radiations, and corpus callosum for greater severity of apathy.

Conclusions: Apathy in de novo PD-patients is related to microstructural changes in the limbic system, indicating increased disarray in grey and white matter overlapping with the functional alteration of serotoninergic terminals observed in PET.
P 123
Gait patterns in Parkinson’s disease with or without cognitive impairment
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Background: Cognitive and gait disturbance are common symptoms in Parkinson’s disease (PD). Although the relationship between cognitive impairment and gait dysfunction in PD has been suggested, the specific gait patterns according to cognition are no fully demonstrated. Therefore, the aim of this study was to investigate the gait patterns in patients affected by PD with or without cognitive impairment.

Methods: We studied 88 patients at an average of 4.7 years after the diagnosis of PD. Cognitive impairment was defined as scoring two standard deviation below age- and education-specific means on the Korean Mini-Mental State Examination (MMSE). Three dimensional gait analysis was conducted for all patients and quantified gait parameters of temporal-spatial, kinematic, and kinetic data were used. The relationship among cognition, demographic characteristics, clinical features and gait pattern was evaluated.

Results: Cognitive impairment was observed in 40 patients (45.5%). Compared with patients without cognitive impairment, patients with cognitive impairment displayed reduced gait speed, step length and stride length. Among MMSE subcategories, “attention and calculation” was significantly associated with speed, step length and stride length. However, age, disease duration, Hoehn-Yahr (HY) Stage and Unified Parkinson’s Disease Rating Scale (UPDRS) motor score were not significantly related to any gait analysis parameter.

Conclusion: Our present study findings show that cognitive impairment is associated with slow, short-stepped gait, regardless of HY stage or UPDRS motor score. This suggest that cognitive impairment especially attention deficit may serve as a surrogate marker of gait disturbance in PD patients.

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Effect of striatal dopamine depletion on cognition in de novo Parkinson’s disease
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Objective: To investigate the relationship between the sub-regional pattern of striatal dopamine depletion and cognitive impairment in early-stage Parkinson’s disease (PD), and determine the effect of striatal dopamine density on cognitive prognosis.

Methods: Patients with drug-naïve non-demented PD were divided into mild cognitive impairment (PD-MCI; n = 129) and cognitively normal (PD-CogN; n = 182) groups. Using quantification of the dopamine transporter (DAT) availability in each striatal sub-region with 18F-FP-CIT PET scans, we performed inter-group comparative analysis of DAT availability and multivariate linear regression analysis to assess the
association between DAT availability and cognitive performance. Additionally, the effect of baseline DAT availability on the cognitive decline across time as well as on changes in the cognitive status was estimated.

**Results:** The PD-MCI group exhibited more severely decreased DAT availability in all the striatal sub-regions compared to the PD-CogN group, although there was no significant difference in PD duration. The DAT availability in the caudate, anterior putamen, and ventral striatum was directly associated with attention/working memory, frontal/executive, and visuospatial functions, while the DAT availability of the posterior putamen was not. However, the baseline DAT availability of the striatal sub-regions did not influence the cognitive decline or cognitive status in the longitudinal cognitive assessment.

**Conclusions:** Our results suggest that striatal DAT availability may determine MCI in patients with de novo PD. Dopamine loss in the associative and limbic striatum is closely linked to cognitive deficits in early-stage PD, although it does not affect cognitive prognosis.

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**P 125**

**Socio-biological cues and saccade generation in Parkinson’s disease**

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**Objective:** Patients with Parkinson’s disease (PD) have abnormalities in the cognitive control of saccadic eye movements. Studies showed that the direction of a centrally presented socio-biological cues (e.g. a face looking to the left or right) influences saccade reaction times (SRTs). However, it is not known if such cue congruency effects are normal in PD. In this study, we investigated the effects of socio-biological cues on both reflexive and voluntary saccades in PD.

**Methods:** 19 PD patients and 15 controls were tested using modified pro- and antisaccade tasks in which target onsets to the left or right were preceded by presentation of cue images depicting either eyes, an arrow or a finger pointing in either a congruent or incongruent direction to the target. Eye movements were recorded using an Eyelink 1000 eye tracker. SRTs, amplitude and errors were measured. The following tests were also used: UPDRS, Hoehn and Yahr stage and MMSE.

**Results:** SRT was significantly increased in PD for both pro- (F(1,14)=4.89, p=0.04) and antisaccades (F(1,14)=4.96, p=0.04), but this effect did not interact with cue type. Antisaccade errors were also significantly increased for PDs (F(1,41)=16.1, p< 0.01) and this difference interacted significantly with cue type (F(2,82)=4.01, p=0.02) such that PDs were seen to make more errors for trials in which Eyes looking to the left or right were presented at fixation.

**Conclusions:** We show that PDs are significantly impaired in terms of saccade response times and errors in a socio-biological cueing task. The effect of Eye cues on error rates in PDs suggest they may find Eye gaze cues particularly distracting or difficult to inhibit responses to.
P 126
Waking-day patterns of motor complications in Parkinson’s disease and the effect of ADS-5102
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Objective: To assess disease patterns of motor complications throughout the day, the transition between each ‘episode’ of these PD-diary states, and the effect of ADS-5102 in this patient population.

Background: Patients with Parkinson’s disease (PD) commonly experience a variety of clinical states, with further variability arising from PD-related perturbations of circadian rhythms. In two Phase 3 trials of ADS-5102 (amantadine) extended release capsules, patients maintained diaries specifying their clinical status each half-hour.

Methods: Patients experiencing ≥1 hr/day of troublesome dyskinesia took double-blind ADS-5102 or placebo once daily at bedtime. At baseline and 12 weeks, diary data for 17-hour time spans following wake-up were assessed descriptively including a summary of the number and duration of ‘episodes’ in each PD-diary state (OFF, ON with troublesome dyskinesia, ON without troublesome dyskinesia) and number of transitions from one motor state to another. In addition, further details on the pooled safety analyses were performed, especially to look at the time to onset and resolution of certain adverse events.

Results: At baseline, 20% to 40% of 138 patients reported troublesome dyskinesia at any given half-hour, and 10% to 15% reported OFF time. Overall, patients experienced on average, 8.0 transitions between PD-diary states throughout the day, including a 3.0 episodes of troublesome dyskinesia, each lasting a 2.0 hours, and 2.1 episodes of OFF time, each lasting a 1.1 hours. For both these states, the total duration, number of episodes, average duration of episodes, and duration of the longest episode showed greater improvement at 12 weeks for ADS-5102 than for placebo. Lastly, individuals treated with ADS-5102 experienced on average a placebo adjusted reduction of 4 transitions between states in their day, and an increase in their first ON time without troublesome dyskinesia episode by approximately 3 hours. Time to onset of AEs of interest were as expected.

Conclusions: In this population, troublesome dyskinesia and OFF time occurred throughout the waking day, suggesting a continuous impact on patients daily living. ADS-5102 treated patients experienced less transitions between states and longer ON time without troublesome dyskinesia, suggested a morning and day with less disruptions. Looking at a PD patient’s entire day and assessing each PD episode, especially the first part of the day, for impact and improvement could lead to be clinical management and patient satisfaction throughout their day.
Effective diagnostic and treatment methods in vascular parkinsonism and Parkinson’s disease: Temporhythmal correction

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Methods of research: in order to early and effective differential diagnostics, also to properly treat of tremor and short steps in vascular parkinsonism (VP) and Parkinson’s disease (PD) it is used method of temporhythmal correction (TRC).

Eighty patients participated in our research and the mean age of them was 62.4±4.7 years.

1st group—patients who have VP and they have received both medicamentous treatment and TRC.

In the 2nd group were patients with PD, they have also received both medicamentous treatment and TRC.

First of all, there is measured height, weight and body mass index. Patients were observed during 10 days: was selected quiet music and have measured amount of steps and length of passed distance for 3 times during the 10 days. Patients walked in the morning under quiet music, on the midday under quickened and on the evening under fast rhythm music.

The results were recorded while there were walking. All patients were evaluated by the Parkinson’s Disease Questionnaire (PDQ-39) scale.

In normal people the average length of step is 40% of the height, in the first days of TRC in all patients this index was 25 or 28% and 30 or 32% on the last day of correction. In patients of 2nd group according to PQD-39 the maximal positive outcome was on “vital activity” and is 2.23±1.16.

The average length of steps in patients with PD was 21 or 23% on the first day of the TRC, and 22,24% in the last days of the TRC.

Conclusion: we can say that TRC is method of treatment and rehabilitation, which is effective in each type of VP and PD also in economical aspect that patient can use both in the hospital and in the home. The average length of steps in PD is more shorter than in the VP. TRC is an effective and cost-effective method of differential diagnosis of VP and PD.

New clinical research: The role of OncoMarkers in Parkinson’s disease and Vascular Parkinsonism

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As we know the Vascular Parkinsonism (VP) and Symptomatic Parkinson’s Disease (PD) is very similar, but both the etiology and pathogenesis of the disease is different. VP and PD had to be separated from each other with different techniques and special diagnostic scales, however, now VP and PD are being diagnosed difficultly.

Objective: We aimed to analyze the PD related VP cancerogenic factors.
Material and methods: We chose the to study the Alpha-fetoprotein concentration to analyze the Oncomarkers factors; we conducted this research A total of 87 patients were participated in our investigation, 44 patients of them are suffering from VP, whereas 43 patients are with PD. All patients were tested anamnestic, neurological and neuropsychological examination. We used the MMSE and Khachinskiy scale methods; moreover we studied the concentration of Alpha-fetoprotein in blood serum in the morning using with immunofluorescence methods.

Results: The Alpha-fetoprotein levels were higher in 23 (52.27%) patients total number of patients with VP n=43, with VP: 8 female (34.7%) and 15 male (65.2%), but in 21 patients (47.72%) it was not determined: 10 female (47.6%) and (52.4%). Finally, the Alpha-fetoprotein levels were higher in 13 (29.51%) patients with PD: 4 female (30.7%) and 9 male (69.2%).

The concentration of Alpha-fetoprotein is higher in blood serum in patients with PD.

Conclusion: The concentration of alphaphetoprotein not only determines the carcinogenic significance in patients with Parkinson's disease and Vascular Parkinsonism, in our opinion the concentration of alphaphetoprotien is increased due to the endothelial factor and this method can correctly differentiate Parkinson's disease from Vascular Parkinsonism.

P 134
A randomized, double blind, placebo controlled, single ascending dose, safety and pharmacokinetic/pharmacodynamic study of INP103 in the presence of benserazide, to L-dopa responsive Parkinson’s patients

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Objectives:
Primary: Compare the safety and tolerability of intranasal INP103 to placebo in patients in the presence of benserazide with PD during an OFF episode.
Secondary: Characterize the PK of single ascending doses of INP103; Explore the effect of single ascending doses of INP103 versus placebo on motor function and PK/pharmacodynamic relationship of INP103 and motor function.

Background: PD is a degenerative disorder characterised by motor symptoms linked to depleted basal ganglia dopamine. Initial management of PD has been oral L-dopa since 1961, but 4 limitations persist:
(1) An enzymatic blood-brain barrier;
(2) Peripheral decarboxylation of dopamine requiring co-administration of a decarboxylase inhibitor (DDI: benserazide or carbidopa);
(3) Progressive decline in L-dopa responsiveness leading to switches between mobility and immobility (ON and OFF periods, respectively) in >50%;
(4) Slow gastric transit
The Precision Olfactory Delivery (POD) device aims to deliver drugs to the vascular rich upper nasal space consistently and efficiently. PD patients suffering OFF episodes would benefit from rapid delivery of L-dopa.
**Methods:** Subjects must demonstrate 30% dopamine responsiveness by UPDRS Part III to their usual anti-OFF medication. All Parkinson medication from 22:00 hrs the evening before dosing will be stopped. The following morning OFF state confirmed, benserazide 25 mg orally given then 60 minutes later they will receive treatment by POD and observed for 4 hours. At 2 hours, subjects will receive their missed morning dose of L-dopa based medication and usual OFF medication if required. Dyskinesia rating and blood draws for PK of L-dopa and benserazide will be conducted and routine safety assessments for 7 days post dosing. **Conclusions:** This study, administering L-dopa to the vascular-rich upper nasal space with the novel POD device should guide further clinical development for an easily, self or care-giver administered, rapidly effective treatment to abort OFF episodes in PD.

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**P 135**  
**Spectral fingerprints of impulse control disorders in Parkinson’s disease**  
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**Objectives:** Impulse control disorders (ICDs) in medicated Parkinson’s disease (PD) patients are disabling and have no satisfying therapeutic option. Because impulsivity is multifaceted, it is unclear which aspect of cognitive impulsivity leads to ICDs. It is also unclear whether ICDs involve motor impulsivity. One origin of the problem is the difficulty to isolate each single neural process with specific experimental tasks. Another one is the inherent limitation of rCBF studies to discriminate multiple concurrent excitatory and inhibitory mechanisms. The present work focuses on the second point by using Electroencephalography (EEG) to probe the functional integrity of the main cortical circuits at rest in PD with ICDs with respect to PD without ICDs.

**Methods:** EEG offers the opportunity to discriminate separate neural processes on the basis of their spectral signature, with good spatial resolution after advanced blind source separation. Twenty-seven PD patients with ICDs (23M/4F; mean age=61.9±6.7), screened for ICDs using the Questionnaire for Impulsive-Compulsive Disorders in PD (QUIP=2.48 ±1.45), were compared to 22 PD patients without ICDs (18M/4F; mean age=58.2±7.6; QUIP=0). Blind analyses of resting state spectral activity (i.e., with no a priori about anatomical sources or frequency bands) were performed.

**Results:** ICDs are characterized by a significant increase in relative alpha power (associated with local inhibition) and a decrease in gamma power (associated with central command control) in three sources located in the dorsal anterior cingulate cortex and in the medial prefrontal cortex (which are parts of the motor inhibition network).

**Conclusion:** Our data strongly suggest that motor, executive dysfunctions related to action control might play a substantial role in ICDs, in addition to more cognitive dysfunctions associated with decisional impulsivity.
Treatment approaches to pain in Parkinson disease: A systematic review

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Objective: Parkinson Disease (PD) diagnosis comprised of the cardinal symptoms, which include tremor at rest, rigidity and akinesia. Relevant to its diagnosis and follow-up assessment is evaluation of non-motor impairments. In patients suspected or diagnosed with PD, autonomic dysfunctions, cognitive or neuro-behavioral disorders, sensory disturbances and/or pain, and sleep abnormalities, must be assessed with utmost thoroughness. The experienced ‘primary pain’ was noted to be associated with worse quality of life. This present review aims to highlight treatment approaches for pain as a non-motor symptom of PD.

Methods: The computer-based literature search was conducted systematically to locate all studies published from 1990 to 2017. Scientific databases utilized included Pubmed/MEDLINE, CINAHL, EMBASE, Cochrane Library and PsycINFO. The search process involved the use of the Medial Subject Headings and Clinical Queries. The terms used were (“Parkinson Disease” OR “Parkinson”) AND (“Pain” OR “Pain Treatment”) AND (“Therapy OR “Therapeutics” OR “Treatment”).

Results: The study selection process included 17 studies in this review. Three controlled trials, 2 post hoc analysis of randomized controlled trials, 9 observational studies, 2 case reports, and 1 case series, were reviewed. A total of 973 subjects were included in the said studies. Levodopa and dopamine agonists showed promising results in terms of various pain subtypes which are indeed PD-related. Results of the reviewed studies have shown the efficacy of levodopa and dopamine agonists in patients who have pain symptoms during “off periods”, as well as, botulinum toxin. Furthermore, opioids, as represented by oxycodone in this report, have shown significant improvement in the pain scores however, the adverse effects of long-term use are undeniable. Surgical interventions, likewise, showed best improvement in the pain severity scores. Although the results are well-reported, the drawback of such interventions being invasive, needed to recruit patients who are good surgical candidates. Hence, the relevance of having pharmacological alternatives for different subtypes of PD-related pain must be kept in value.

Conclusion: Pain symptoms in PD can be a non-motor manifestation, even before the motor phenomenology arises. The pain may increase in intensity and frequency during the progression of the disease state, affecting the quality of life of the patient. It is important to differentiate the PD-related and non-PD related pain, as well as their temporal profile, since the management will be based on that approach. This present review has presented treatment approaches, pharmacotherapy and surgical therapy, for specific pain domains in PD. Further studies, which may conduct sub-analyses of treatment strategies based on pain subtypes is recommended and may report treatment effectiveness. Moreover, studies that will investigate on the effect of combination treatment, both pharmacologic and surgical treatments, are warranted.
P 137
REM sleep behavior disorder in Parkinson disease: Association with blunted heart rate variability on standing
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Objective: While few studies showed impaired heart rate variability (HRV) in REM sleep behavior disorder (RBD), there have been no studies about short-term heart rate variability (HRV) on standing. We examined autonomic response to the head-up tilt table test (HUT) including heart rate variability (HRV) in patients with Parkinson’s Disease (PD) with or without REM sleep behavior disorder (RBD)

Methods: Sixty-one PD patients with RBD (PD+RBD) and an equal number of age and sex- matched PD patients without RBD (PD-RBD) were included. We analyzed the HRV responses at supine rest and during HUT in the time and frequency domain.

Results: PD+RBD patient showed no difference in all HRV parameters at supine rest than PD-RBD. In response to HUT, PD+RBD patients showed a blunted response in the low- (LF) (-120.6 vs. -84.6, p < 0.05) and high-frequency (HF) (-128.3 vs. -54.9, p < 0.05) components than PD-RBD patients.

Conclusions: PD+RBD patients showed the reduced amplitude of both sympathetic and parasympathetic responses at HUT compared to PD-RBD. These findings might support the central autonomic involvement in PD+RBD.

P 138
Efficacy of incobotulinumtoxinA in patients with sialorrhoea, as assessed using the modified Radboud Oral Motor Inventory for Parkinson’s disease (mROMP)
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Objective: The pivotal double-blind, randomised Phase III SIAXI study (NCT02091739), assessed the efficacy and safety of incobotulinumtoxinA 75 and 100U for sialorrhoea. Co-primary endpoints of the placebo-controlled main period (MP) are presented elsewhere. Here we report MP data from the modified Radboud Oral Motor Inventory for Parkinson’s disease (mROMP) subscales.
Methods: Adults with chronic, troublesome sialorrhoea due to Parkinson’s disease (PD), atypical parkinsonism, stroke or traumatic brain injury were randomised (2:2:1) to receive incobotulinumtoxinA 75 or 100U, or placebo distributed in bilateral parotid and submandibular glands in a single injection cycle (16±2 weeks' duration). The change from baseline in three domains (drooling, speech and swallowing symptoms) was assessed using the mROMP. At screening, baseline, 4, 8, 12 and 16 weeks post-treatment, patients 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, Arch Phys Med Rehabil 2011).

Results: 184 patients (mean [SD] age 65.2 [11.4] years; 70.7% male; 70.7% with sialorrhoea due to PD) were randomised and received either incobotulinumtoxinA 75U (n=74), 100U (n=74) or placebo (n=36); 173 patients completed the MP. Baseline demographics were similar in all groups. mROMP drooling scores improved from baseline to all post-treatment visits to a greater extent in both active treatment groups versus placebo. In the incobotulinumtoxinA 75U, 100U and placebo groups, respectively, the greatest mean [SD] 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 slightly 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 patients with sialorrhoea due to neurological causes.

Impact of injection guidance techniques on the efficacy and safety of incobotulinumtoxinA for sialorrhoea


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Objective: SIAXI (NCT02091739), a pivotal, double-blind, randomised, placebo-controlled study with an extension period (EP), assessed the efficacy and safety of incobotulinumtoxinA 75 and 100U in patients with sialorrhoea 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 100U, or placebo, distributed in bilateral parotid and submandibular glands in a single injection cycle (IC) in the main period (MP). Eligible patients completing the MP received three further incobotulinumtoxinA ICs (75 or 100U; each 16±2
weeks) in the EP. Injections were consistently guided by ultrasound (US) or anatomical landmarks (AL) at investigators’ discretion. 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 were randomised to incobotulinumtoxinA 75U (n=74) or 100U (n=74), or placebo (n=36) in the MP; 173 completed the MP and entered the EP. In the MP, injections were guided by US in 56.5% of patients and AL in 43.5%. Among patients treated with incobotulinumtoxinA in all 4 ICs, mean uSFR decreased with incobotulinumtoxinA 75U and 100U from study baseline to 4 weeks post-injection in all ICs with both US and AL guidance. 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%). No new safety concerns with respect to guidance technique were reported.

**Conclusions:** Repeated incobotulinumtoxinA injections under either US or AL guidance are similarly effective and well tolerated for sialorrhoea in patients with PD or other neurological disorders.

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**P 140**

**Efficacy of sublingual apomorphine film (APL-130277) for the treatment of OFF episodes in patients with Parkinson’s disease: Results from the phase 3 double-blind, placebo-controlled trial**

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**Objective:** To evaluate the efficacy of APL-130277 (APL), a sublingual formulation of apomorphine.

**Methods:** A 12-week, double-blind trial was conducted in patients with PD, experiencing motor fluctuations, to evaluate the efficacy of APL for the acute treatment of OFF episodes. The APL dose (10-35 mg) to produce a FULL ON was determined. Patients were randomized at the titrated dose to APL or placebo for 12 weeks. MDS-UPDRS-III score was determined pre-dose and 15, 30, 45, 60, 90 min post-dose at monthly visits. The primary endpoint was the change in MDS-UPDRS-III score at 30 mins post-dose after 12-weeks. The key secondary endpoint was the % of patients who rated themselves as FULL ON at 30 min at 12 weeks.

**Results:** 109 patients who completed the titration phase were randomized. 80 patients completed the study (placebo-46 and APL-34). The LS Mean (SE) change from pre-dose to 30 min post-dose for the MDS-UPDRS-III score at 12 weeks was -11.1 (1.5) and -3.5 (1.3) for the APL and placebo groups, respectively (mean difference = -7.6; p=0.0002). Similar results were observed at day 1, weeks 4 and 8. Separation from placebo was observed as early as 15 min, persisting up to 90 min. There was also a significant difference favoring APL over placebo in the % of patients who rated themselves as FULL ON at 30 min at 12-weeks. Additional supportive findings
focusing APL included % of patients ON within 30 min who remained ON for at least 30 min, CGI/PGI and Home Diaries which showed a larger % of APL-treated patients turned ON within 30 min post-dose versus placebo (LS mean 78.7% vs. 31.10%, respectively).

**Conclusions:** The results of this study demonstrated a clinically meaningful benefit of APL treatment in patients with PD experiencing OFF episodes.

**P 141**

**Opicapone as adjunctive therapy to levodopa in patients with Parkinson’s disease and motor fluctuations: global impressions of change compared to placebo and entacapone**


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**Objective:** Evaluate the subject’s and investigator’s global assessments of change in overall condition after opicapone (OPC) treatment compared to placebo and entacapone (ENT).

**Background:** OPC, a novel once-daily peripheral catechol-O-methyltransferase (COMT) inhibitor, has shown to be safe and effective in reducing OFF-time in patients with Parkinson’s disease (PD) who have motor fluctuations. The subject’s and investigator’s global assessment of change (SGAC and IGAC) are commonly used instruments in clinical trials that provide means for evaluating perceptions about the change in overall condition with treatment.

**Methods:** In this multinational, multicenter, double-blind, 14- to 15-week, placebo- and active-controlled study (BIPARK I), SGAC and IGAC were secondary efficacy endpoints. The SGAC and IGAC were performed in comparison to prior enrollment in the study (“very much improved” to “very much worse”). Both were analyzed with a non-parametric van Elteren’s test stratified by region.

**Results:** The analysis set included 590 subjects: placebo (n=120), 5mg-OPC (n=119), 25mg-OPC (n=116), 50mg-OPC (n=115), and ENT (n=120). For SGAC ratings, the proportion of subjects reporting to have “minimally”, “much,” or “very much improved” ranged between 63.7% to 72.1% for OPC groups versus 50.9% for placebo and 52.5% for ENT. The improvement tendency was significant for both 25mg-OPC (p=0.0055; p=0.0370) and 50mg-OPC (p=0.0008; p=0.0091) compared to placebo and ENT, respectively. The proportion of subjects assessed by investigators (IGAC) as having improved ranged between 60.3% to 73.0% for OPC groups versus 49.9% for placebo and 50.9% for ENT. The improvement tendency was significant for 50mg-OPC (p=0.0005 and p=0.0070 versus placebo and ENT, respectively). No tendency was apparent for ENT when compared to placebo.

**Conclusions:** OPC was associated with favorable ratings in subject’s and clinician’s global impressions of change, in contrast to essentially no difference for ENT compared to placebo in either of these assessments.
Progressive supranuclear palsy (PSP) and Corticobasal degeneration (CBD) are both sporadic disorders with tau pathology, but overlap is not uncommon.

We report the case of a 61-year-old right-handed man who presented initially with subtle postural tremor. Then, after 3 years, he noticed slowness on the left arm, accompanied by inability to coordinate his hand movements and, later, he accused muscle weakness.

Over the course of 1 year, he presented with progressive asymmetric parkinsonism. The examination revealed dysarthria, dysphagia, vertical gaze palsy, slow velocity of horizontal saccades. He had imbalance, myoclonus and grasp reflex, severe ideomotor apraxia on the left upper extremity and a profound inability to execute simple movements with the left arm. He also had bilateral slowness of fine finger movements and foot tapping, left side more than right.

Other important non-motor symptoms include neuropsychiatric and sexual symptoms, gastrointestinal and bladder dysfunction and other symptoms like: diurnal somnolence, fatigue, musculoskeletal pain.

His motor symptoms were partially responsive to levodopa therapy.

The patients MRI revealed asymmetrical (right-lateralization) posterior-frontal and posterior cortical atrophy, with absence of frontopolar temporal atrophy; there were no particular brainstem alterations.

Although clinical consensus criteria are available, an atypical presentation with overlap between PSP and CBD make it difficult to diagnose between probable PSP with Corticobasal syndrome phenotype (PSP-CBS) and CBD with Richardson's syndrome.
P 144
Effects of green tea extract on Parkinsonism and related disorders; neuroleptic anxiety syndrome, growth & pain
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Dopamine receptor antagonists have been shown to induce c-Fos responsiveness in a distributed anxiety-related neural scheme, with a selected neuronal population of nucleus accumbens in the ventral striatum, therefore elicit neuroleptic anxiety syndrome (NAS).

Studies show that mood deficits by haloperidol (HAL) metabolically effect via diet restriction that reduced body weight. Components of green tea extract (GTE) are known to control appetite and body weight while exerting anxiolytic, amnesic effects.

Objectives of the current study was designed to testify the hypothesis that GTE may control NAS elicitation during HAL treatment.

Method: Rats (n=6) were treated with one of the four treatments; oral fluid [water /GTE (1gm/ liter)] plus saline; or oral fluid plus HAL (1mg/kg/day) intraperitoneal administration. Behavioral assessments were preformed weekly following six weeks of treatments in the context of hypothesis.

Results: indicate that HAL induced decreases in fluid and food intake and growth rate were greater in GTE treated animals. GTE was shown to induce anxiogenic behavior examined in light dark box transitional test but not in fear-like exploratory behavior on elevated plus maze (EPM) and no effects on exploratory locomotor behavior was observed in open-field behavioral tests. HAL induced locomotor activity was significantly suppressed, innate aversive and fear-like exploratory behaviors were greater in GTE than water drinking animals. Potential mechanism involved in the greater anorexiogenic and anxiogeneic effects of HAL in green tea treated animals will be discussed.

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Features of the course of Parkinson’s disease in congenital anomalies of cerebral vessels
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Background: Vascular parkinsonism can be caused by various cerebrovasulr diseases: - damage of small cerebral arteries-microangiopathy, damage of large cerebral arteries, cardiogen brain lesions, and others. Angiodysplasia is one of them.

Objective: To determine the features of the course of parkinsonism in congenital anomalies of cerebral vessels.

Methods: Analysis of the study of neurological status, multispiral computer tomography (MSCT) data with angiography, with the diagnosis of congenital abnormalities of cerebral vessels.
Results: We observed 40 patients with cerebral vascular anomalies (25 women and 15 men) aged 42-57 years (mean age 45 ±2.2) Angiodysplasia was found in all the examined subjects 100%, dizziness 86%, postural instability 65% and 45% of cases long before the first symptoms of the disease smell disturbance, sleep disturbance 37.7%, increased sweating 23.9%. In the neurostatus 95% of the cases prevailed stiffness and shuffling gait 45% lack of physiological synkinesis, 37.1% rest tremor and diffuse neurological symptoms.

Analysis of multispiral computer tomography with angiography showed the presence of changes in 100% of cases and pathological tortuosities in hippocampus, lack of key elements of the Willis circle kinking and coiling occurred more in women 53% then in men 47% and more in the internal carotid artery 72.3% rather than in vertebral arteries 28.7%. In the group of patients with changes in the vertebral arteries structural changes in the cervical spine were found.

In addition, 47.3% of the patients underwent hypoplasia of the vertebral artery, 25.5% of the middle cerebral artery and 13.5% of the posterior connective arteries which indicated the hereditary etiology of angiodysplasia.

Conclusion: Based on the results of current investigation, Angiodysplasia of cerebral vessels can be a factor in the risk of Vascular parkinsonism.

Key words: Vascular parkinsonism, angiodysplasia, congenital anomalies, carotid artery, postural instability, hypoplasia, kinking and coiling.

P 147
Pharmacologic approaches in dementia with Lewy bodies: Lessons learned from a case series
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Objective: The pharmacologic approach to psychosis and motor function in Dementia with Lewy bodies (DLB) is challenging due to the lack of clinical trial evidence to support the efficacy of medications and concerns regarding risks and increased susceptibility to side effects. In addition to the increased morbidity and mortality risks associated with the use of antipsychotics in elderly patients with dementia, those with DLB may have reduced tolerability to these agents. Dopaminergic medications used for parkinsonism could worsen psychosis and orthostasis and reports in the literature suggest they may have less impact on motor function. The use of acetylcholinesterase inhibitors (AChIs) has been shown to help with both cognitive function and hallucinations with low risk for worsening parkinsonism. Here, we describe a case series of ten patients with DLB treated with varying pharmacologic approaches and highlight lessons learned.

Methods: We abstracted demographics, clinical characteristics, and pharmacologic approaches among ten patients seen over the past year who met diagnostic criteria of probable DLB by current consensus.

Results: Of the ten patients, six were male with mean age of 78. Visual hallucinations were present in all, accompanied by paranoid delusions in four. Two patients received antipsychotics (quetiapine, tolerated with modest effect in one; neither quetiapine nor pimavanserin tolerated in the other). Five patients were treated with ACHIs (rivastigmine, donepezil) and memantine was added in one. Two of those on ACHIs
had an improvement in psychotic symptoms. Six patients were managed with carbidopa/levodopa for parkinsonism with reported benefit in three; dosages were limited due to intolerability (orthostasis, worsening psychosis) in two.

**Conclusions:** Our findings reflect the variability in approaches currently used in treating psychosis and parkinsonism in DLB and support the potential role of ACHIs for management of psychosis. They also suggest that, in some patients, levodopa may be effective and well-tolerated.

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**P 148**

**Levosulpride induced persistent movement disorders: case series**

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**Background:** Levosulpride is a substituted benzamide which block D2 receptors in the central and enteric nervous system. It can lead to a variety of movement disorders which are more common in elderly females.

**Presentation:** We report three patients of Levosulpride induced movement disorders who presented to our department from May 2017- March 2018.

**Case 1:** 45-year-old female presented with symmetrical onset of bradykinesia and rigidity one and a half months prior to presentation. She was a diabetic and hypertensive and recently diagnosed case of diabetic nephropathy (creatinine 2.5 mg/dl). MRI brain and FDOPA PET were normal. On probing medical records, she was taking 75 mg/day of levosulpride for the last 2 years. Levosulpride was stopped and she improved to some extent, however, was lost to follow up.

**Case 2:** 47-year-old diabetic female presented with oro-lingual movements 8 months prior to presentation. Examination was non-contributory except for the movement disorder. All her investigations including MRI brain and FDOPA PET was normal. She was taking levosulpride 75 mg per day for the last one and a half years. She had partial response to stoppage of levosulpride and is presently on periodic botulinum toxin injections.

**Case 3:** 67-year-old diabetic female presented with symmetrical bradykinesia and camptocormia one year prior to presentation. She had no history of autonomic dysfunction. All her investigations including MRI brain and FDOPA PET were normal. She was on 75 mg/day of levosulpride for the last 18 months and had minimal improvement on stopping the drug.

**Discussion:** Firstly, all our three patients were diabetic females and had a subacute to chronic presentation. It could be possible that they had a sub clinical nigrostriatal dysfunction which was unmasked by Levosulpride. However, both MRI and dopaminergic imaging was normal in all three patients. Secondly, all three had persistent movement disorder despite stopping the drug at variable follow up.

**Conclusion:** To conclude, we suggest that Levosulpride induced movement disorders are not always reversible. Clinicians should avoid continuous exposure of this drug through drug free periods to prevent these disabling movement disorders.
Abstracts

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Single photon emission computer tomography in the differentiation of progressive supranuclear palsy, corticobasal syndrome and multiple system atrophy

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Objective: Parkinson’s Disease (PD), multiple system atrophy are synucleinopathies while corticobasal syndrome and progressive supranuclear palsy are tauopathies. The distinguishing of these diseases due to their similar symptomatology may be difficult. Contemporary literature reveals growing interest in the context of diagnosing CBD-PSP or PSP-CBS. The aim of the study is to assess the association between the changes in neuroimaging and clinical manifestations of CBS, PSP and MSA-P.

Methods: The examination was conducted among patients with most likely PSP (n=10), MSA-P (n=6) and CBS (n=7). All patients underwent neuropsychological examination assessing their cognitive abilities and possible affective deficits. The examination was extended using magnetic resonance imaging (MRI) and assessment of cerebral blood flow using SPECT-CT after administration of ⁹⁹mTc-HM-PAO. The aim of MRI was to exclude other possible diseases causing clinical manifestations. The examination of blood flow was assessed using perfusion analysis of certain structures in the central nervous system - basal ganglia, thalamus, cerebellum and frontal lobe. The distribution of ⁹⁹Tc-HM-PAO was assessed using program comparing radioactivity in certain regions of the brain and data gained from healthy volunteers. Differences between results of patients and reference data was presented as standard deviations. The results of patients were processed using Kruskal-Wallis test and analyzed in the aftermath using post-hoc.

Results: The test indicated statistically significant differences within the left thalamus and right hemisphere of cerebellum. In the aftermath those regions were assessed using post-hoc analysis. In order to indicate how certain regions of the brain differentiate two diseases. The results of the post-hoc analysis presented sufficient differentiation (p<0.05) of PSP and CBS within the left thalamus and between PSP and MSA-P within the right hemisphere of cerebellum

Conclusions: SPECT may be interpreted as a possible supplementary tool in differentiating atypical parkinsonian diseases. This study requires further analysis.

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Movement disorders in bilateral striatopallidodentate calcinosis (Fahr’s syndrome): an analysis of 9 patients

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Background: Bilateral striatopallidodentate calcinosis or Fahr’s syndrome/disease is rare neurodegenerative disorders, characterized by bilateral calcifications of basal ganglia, cerebellar dentate nuclei and white matter, with subsequent brain atrophy, usually associated with neuropsychiatric dysfunctions, seizures
and movement disorders. It can be primary - primary familial (autosomal dominant or recessive) brain calcification or "Fahr’s disease" or secondary "Fahr’s syndrome" due to a specific underlying cause. Here we report the study of movement disorders in 9 patients with non-familial Fahr's syndrome (FS).

**Objective:** To characterize movement disorders associated with bilateral striatopallidodentate calcinosis (Fahr's syndrome).

**Methods:** We retrospectively reviewed medical records, clinical investigations, neuroimaging, and available videos of 9 FS patients: 6 females and 3 males; age range: 38-66 years. 5 patient was diagnosed with FS probably secondary to hypoparathyroidism, 1 patient had previous head injury and 3 patient present with idiopathic bilateral striatopallidodentate calcinosis, they were unable to perform molecular genetic testing, but there were no family history of any movement disorders, seizures, cognitive impairment or psychiatric disorders. Patient were rated for the prevalence and severity of different types of movement disorders.

**Results:** Variety of hypo- and hyperkinetic movement disorders were detected. Parkinsonism was detected in 4 patients (2 with resting tremor), ataxia with kinetic tremor in 2 patients, resting-kinetic tremor of hands in 1 patient, 1 patient presented with multifocal (arm and leg) dystonia and 1 with choreoathetosis. Postural and gait instability were detected in 6 patients. 4 patients had mild and 5 patients had severe cognitive impairment and 4 patients presented with psychotic symptoms.

**Conclusions:** non-familial bilateral striatopallidodentate calcinosis (Fahr's syndrome) can present in variety types of movement disorders such as: parkinsonism, tremor, dystonia, choreoathetosis and ataxia. Our result suggest high incidence of parkinsonism as a presentation of Fahr's syndrome.

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**P 153**

**Memory enhancing effect of combined alcoholic extract of cedrus ceodara loud. and Vitex Nirgundi in scopolamine-induced cognitive impairment in mice**

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**Objective:** Epidemiological studies of Indian population reveal that dementia is largely a hidden problem in India. Ayurveda claims several plants are beneficial in cognitive disorders. Pharmacoepidemiological studies reveal that herbal and allopathic learning and memory enhancing medicines are becoming very popular among Indian population.

The objective of study was to we evaluated the effect Combined Alcoholic Extract of *Cedrus deodara* (Wood) Loud. and *Vitex Nirgundi* (Leaf) in scopolamine-induced cognitive impairment in mice. Current research effort focuses on the development of safer natural compounds with multipronged mechanisms of action that could be used to ameliorate memory deficits in patients. In this study, we evaluated the effect Combined Alcoholic Extract of *Cedrus deodara* (Wood) Loud. and *Vitex Nirgundi* (Leaf) an Indian medicinal plant with significant neuro-pharmacological property on scopolamine-induced cognitive impairment in mice.
Method: Memory impairment was produced by administration of scopolamine (1mg/kg i. p) in rats. The alcoholic extract of Cedrus deodara (Wood) Loud. and Vitex nirgundi (Leaf) (30, 40 and 50 mg/kg, p.o.) was also administered to one group of animals. Passive avoidance paradigms, elevated plus maze and social learning task was used to assess learning and memory.

Result: Cedrus deodara (Wood) Loud. and Vitex nirgundi (Leaf) 50 mg/kg alcoholic extract treated group decreased transfer latency in elevated plus maze model paradigm which is an indicative of cognition improvement. In case of passive avoidance paradigm extract treated group exhibited pronounced effect in reversal of scopolamine induced amnesia which was revealed by increase in step down latency. Social learning task also revealed the memory enhancing activity of combined extract.

Conclusion: The present findings indicate that the combined alcoholic extract of C. deodara and Vitex nirgundi has the best memory-enhancing effect due to its strong antioxidant properties from compounds like terpenoids and flavonoids. The study provides a scientific rationale for the traditional use of C. deodara and Vitex nirgundi in the management of memory dysfunction and related disorders.

Characterization of constipation in multiple system atrophy using Rome III diagnostic criteria
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Objective: Constipation is a common feature of multiple system atrophy (MSA) as well as Parkinson's disease (PD); however, characterization of constipation in MSA patients has not been fully evaluated. Rome III criteria are widely used to detect gastrointestinal disorders. We evaluated characteristics of constipation in MSA patients using Rome III criteria.

Methods: Sixteen patients with MSA (11 female) treated at Fukuoka University Hospital between April 2017 and April 2018 were included in this study. Questionnaires of Rome III criteria were applied to evaluate constipation and irritable bowel syndrome (IBS).

Results: Constipation and IBS were detected in 3 patients (18.8%) and 0 patient (0%), respectively. The most common symptoms related to constipation were sensation of incomplete evacuation and sensation of anorectal obstruction (53.8%).

Conclusions: The most common symptom related to constipation in PD is straining during defecation (77.1%) as we previously reported. Thus, the characteristics of constipation seen in MSA may be different from that of PD. Further studies are required to prospectively compare the characterization of constipation between PD and MSA using Rome criteria.
Risk of Parkinson disease associated with prokinetics from Korean National Health Insurance service claims data

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Benzamide derivatives such as levosulpride, clobopride, and itopride are widely used in enhancing Gastrointestinal motility in South Korea. Benzamide derivatives are well known as offending drugs of drug induced Parkinsonism. The aim of this study was to define the risk of Parkinson’s disease associated with prokinetics.

We evaluate the risk of Parkinson’s disease associated with prokinetics exposure especially benzamide derivatives from Korean National Health Insurance Service Claims Data (NHISCD) National Health Insurance database (2010-2016) was used to set up cohort study including population who had prescription of offending drugs more than 60 days. Patients who had a neuro-degenerative diseases, younger than 45 years and concomitant anti-dopaminergic drug users were excluded. Control (benzamide non-exposure) group is selected as no exposure history of benzamide derivatives before and during follow up period. Follow up period was from 2010 ~ to 2013 (3 years)

From 2010 to 2013, the number of DIP patients related to benzamide derivatives exposure was 1,072. The control number was 4,288. The mean prescription days of benzamide derivatives was 239 days. During the 3 years follow up period after benzamide exposure, 122 person developed parkinson’s disease. (11.4%) In non-exposure group, 23 person developed Parkinson’s disease (0.53%) (p< 0.001) Adjusted hazard ratio is 17.9 in benzamide exposure group. The longer the duration of drug use, the more PD developed (up to 2.2 HR).

This study is retrospective cohort analysis using national health insurance data. The long term use of benzamide derivatives should be restricted with caution especially aged person.

Levodopa-induced dyskinesias impact patient’s quality of life in Parkinson’s disease in Singapore

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Objectives: To investigate the impact of levodopa-induced dyskinesia on patient’s quality of life in Parkinson’s disease (PD) in Singapore.

Methods: A cross-sectional study was conducted on 240 idiopathic PD patients. Patients were evaluated for their (i) motor abilities using Unified Parkinson’s Disease Rating Scale (UPDRS) III, modified Hoehn and Yahr Staging Scale (H&Y) and Schwab England Activities of Daily Living (ADL); (ii) levodopa-induced motor
complications using UPDRS IV and (iii) quality of life (QoL) using Parkinson Disease Questionnaire (PDQ-39). Socio-demographic and other clinical variables were also noted. Multivariate linear models and correlation analyses were performed.

**Results:** 12.92% of the patients reported to have dyskinesia. Of which, 7.08% had 1-25% of their waking day and 5.42% had 26-50% of their waking day. For the dyskinesia experienced, a small percentage of patients complained it of being slight (2.08%) or moderately (1.25%) painful. Additionally, 32.26% of the patients found the dyskinesia experienced to be non-disabling and 48.39% found it to be mildly disabling. Significant positive correlation was found between dyskinesia and all PDQ-39 domains except for social support.

**Conclusion:** Levodopa-induced dyskinesias impact PD patient’s QoL in Singapore. Clinical strategies that target the management or even the prevention of it is therefore important.
Introduction: Dementia is a syndrome characterized by progressive cognitive deterioration that causes disability and dependence. The most common form is Alzheimer’s disease (AD). Mild cognitive impairment (MCI) is a condition between normal aging and dementia. Social cognition, consists of 4 components: 1: Theory of mind (ToM), 2: Executive function (EF) 3: self-awareness and 4: social perception. The ToM is the ability that allows the understanding and interpretation of the behaviors, desires and intentions of others. The EFs are involved in the control of other functions, and intervene in new, conflictive or complex situations. The practical judgment (PJ) serves to evaluate situations and draw conclusions after evaluating the context and its possible consequences.

Objective: Analyze the association between the performance of PJ with EF and ToM, in a group of 30 older adults (OA) and classified into three groups: AD, MCI and controls.

Material and methods: We included 3 groups, with 10 participants each: I) AD; II) MCI and III) cognitively healthy OA. Battery applied: Stroop, (ST) Trail making test B, (TMTb), verbal semantic and phonetic fluency (VFs, VFf); for ToM: reading the mind in the eyes (RME) and pictures of facial affect (POFA) and for the judgment evaluation, the practical judgment test (TOP-J)

Results: When analyzing the associations between the performance of the TOP-J with the EF and ToM tests in all the participants, we found significant associations between TOP-J with FVs and TMTb. As well as the TOP-J with POFA and the RME.

Conclusions: The performance in the 2 EF tests as well as in the ToM shows a statistically significant association with the performance in the TOP-J, with which we can say that the early alterations in the EF can directly impact the capacity of practical judgment in patients with both MCI and patients with Alzheimer’s.
Neuroprotective role of 17β estradiol against amyloid beta neurotoxicity in synaptosomes of aging female rats
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Objectives: Alzheimer’s disease (AD) is characterized by the presence of amyloid plaques which are formed from deposits of β-amyloid protein. The aim of the present study was to determine the effects of neuropeptide, neurokinin B (NKB) and amyloid beta fragment Aβ (25-35) on 17β estradiol (E2) treated aging female rat brain 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 17β estradiol (0.1 µg/g body weight) daily for one month. Synaptosomes were incubated with NKB, Aβ (25-35) and NKB+ Aβ (25-35) in a microfuge tubes at 37 °C for 60 min in a shaking water bath with 0.1, 1 and 5 µM concentration of each of the peptides in all age groups of control and estradiol treated rats. Aging brain function were assayed by measuring the activities of antioxidant enzymes, monoamine oxidase (MAO), membrane bound ATPases, intracellular calcium levels and lipid peroxidation in presence of neuropeptides.

Results: The present results revealed that increased activities of antioxidant enzymes, membrane bound ATPases and decrease in level of calcium levels, MAO activity and lipid peroxidation in presence of NKB and combined NKB and Aβ in vivo E2 treated aging rat brain. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain. An in vitro incubation of E2 treated synaptosomes with Aβ showed toxic effects on all the parameters, while NKB showed stimulating effects and the combined NKB and Aβ showed a partial effects as compared to Aβ (25-35) and NKB alone.

Conclusions: Present study elucidates an antioxidant, neuromodulatory and neuroprotective role of tachykinin peptide NKB against the beta amyloid induced toxicity in E2 treated female rats. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain.

Principles of non-pharmacological therapy in patients with Parkinson’s diseases
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Purpose: To study Principles of non-pharmacological therapy in patients with Parkinson’s diseases.

Materials and methods: The study involved 22 patients 8 of them women, 14 men. The average age of patients 55 ± 6.5 years. The patients were divided into two groups: Main group: 12 patients with basic therapy conducted psychotherapy; The control group of 10 patients who received only basic therapy. To investigate the psycho-emotional spectrum we used Tsung scale to determine depression and Spielberger State-Trait Anxiety Inventory.
The study included patients with Parkinson's disease at 1-2 degree and with complaints on psycho-emotional sphere. In goal of non-pharmacological therapy we used psychodynamic method of psychotherapy. **Results:** To study the psycho-emotional sphere in both groups showed following results. According to the Tsung scale 6 (27.3%) patients had mild depression (50-59 points); 12 (54.5%) had the average level (60-69); and 4 (18.2%) - high degree (70) \((p < 0.01)\). According to the Spielberger State-Trait Anxiety Inventory the level of personal anxiety equals to 31-45 score was observed at 8 (36.4%) patients; 46 and higher scores marked 14 (63.6%).

After the psychodynamic therapy (10 sessions) data of psychometric tests were as follows: depressive status in main group improved by 1.5 times; in turn, anxiety disorders improved by 2 times in compare with control group \((p < 0.01)\).

**Conclusion:** The present psycho-emotional disorder leads to the deterioration of the lifestyle of the patients with Parkinson's disease. With the help of basic therapy in psychopharmacological care can lead to more effective treatment of Parkinson's diseases.

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**Identifying the association of depression and distress in Pakistani patients diagnosed with parkinsonism syndrome**

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**Background and aims:** Depression plays an important role among patients diagnosed with Parkinsonism syndrome. It is believed that diabetes distress is recognised as major psychological issue in Pakistan. Our study aims to identify depression and distress among Pakistani patients diagnosed with Parkinsonism syndrome. We also aim to find out the relationship among depression, distress caused Parkinsonism syndrome.

**Materials and methods:** A cross-sectional study was conducted in Sir Ganga Ram Hospital Lahore during June 2016 to October 2017. Total 80 patients diagnosed with Parkinsonism syndrome were included in the study. Blood levels were collected via venous puncture. A personalized health questionnaire was used to classify depression among patients. A depression scale was used to identify factors such as social distress, interpersonal distress, movement disorder distress, physician related distress, emotional distress and regimen related distress.

**Results:** The rate of depression was 39% among patients diagnosed with Parkinsonism syndrome. 8% were categorised as mild depression, 14% moderate depression and 17% with severe depression. Parkinsonism syndrome associated depression was found in 71% of the selected population. Rates of social distress, interpersonal distress, physician related distress, emotional distress, regimen related distress were 23%, 33.5%, 17.8%, 73.4% and 42.6 respectively.

**Conclusion:** Our study concludes that depression associated with Parkinsonism syndrome is very common among and this is an alarming condition for Pakistani population. We need to develop and modify our management plans in order to combat this deadly distress. Mass media should be involved in order to raise awareness about depression.
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**Features of cognitive functions in parkinsonism**

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**Purpose of the study:** To give a comparative description of neuropsychological features in primary and secondary parkinsonism.

**Materials and methods of research:** Patients with primary parkinsonism - 15 people and with secondary parkinsonism - 14 were examined. For the study of cognitive functions in patients with Parkinsonism, the MMSE scale was used, affective disorders were the hospital scale of anxiety and depression of HADS, the nonspecific SF-36 questionnaire.

**Results of the study:** When assessing the level of cognitive functions, it was revealed that the total indices of the physical and psychological components of health were significantly (p < 0.05) higher in the comparison group (48.1 ± 3.23 and 51.1 ± 2.98 points, respectively) than in basic (31.2 ± 0.53 and 32.8 ± 0.8 points, respectively), and the difference between them was minimal in both groups. A similar situation is found in most scales of cognitive functions, except for BP (pain intensity) and SF (social functioning). Role function due to physical (RP) and psychological (RE) condition, suffered more significantly in patients with Parkinsonism than in persons of the comparison group (p < 0.05). Meanwhile, the index of role functioning due to the psychological component (RE) in men was significantly higher (p < 0.05), and the indicator of pain intensity (BP) in women was significantly lower (p < 0.05). The level of anxiety-depressive disorders in patients with primary parkinsonism was significantly (p < 0.05) higher than in patients with secondary and comparison groups. Trender analysis of anxiety and depression showed their statistically significant (p < 0.05) increase in women compared with men.

**Conclusions:** Neuropsychological characteristics of patients with Parkinsonism depends on the etiologic factor. The degree of cognitive deficits in secondary parkinsonism is more pronounced than in the primary parkinsonism and does not have sex differences.

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**The views of adults with Huntington’s disease on assisted dying in Uzbekistan: A qualitative exploration**

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**Background:** Assisted dying is frequently debated publicly and research often includes the views of health professionals on this issue. However, the views of people with life-limiting conditions, for whom this issue is likely to have a different resonance, are less well represented.

**Aim:** The purpose of this study was to explore the views of people who live with the inevitability of developing Huntington's disease, a genetically transmitted disease which significantly limits life, on assisted dying.

**Methods:** Using thematic analysis methodology, individual semi-structured interviews were conducted. Seven participants (five women and two men) who were gene positive for Huntington's disease took part in the study.
Results: Four themes were extracted: (1) autonomy and kindness in assisted dying: the importance of moral principles; (2) Huntington’s disease threatens life and emphasises issues relating to death; (3) dilemmas in decision-making on assisted dying: “There are no winners” and (4) the absence of explicit discussion on dying and Huntington’s disease: “Elephants in the room”.

Conclusions: Our findings suggest that talking to patients about assisted death may not cause harm and may even be invited by many patients with Huntington’s disease. The perspectives of those who live with Huntington’s disease, especially given its extended effects within families, add significant clinical and theoretical insights.

P 167
Cognitive dysfunction in multiple system atrophy-C
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Objectives: Multiple system atrophy (MSA) is a neurodegenerative disorder involving basal ganglia and frontal-subcortical circuits. Dementia represents an exclusion criterion for the diagnosis of multiple system atrophy (MSA), but there have been reports of fronto-executive dysfunction in patients with MSA of the striatonigral type (MSA-P). To study the cognitive profile of MSA, 20 patients with MSA of the cerebellar type (MSA-C) were subjected to an extensive neuropsychological test battery comprising tests for attention, verbal and visuospatial memory, as well as executive function.

Methods: We assessed 20 patients affected by probable MSA-C according to the criteria of Cilman et al (Mean age: 59.8±7.2; mean disease duration: 8.5±2.3; M/F=13/7) using a neuropsychological battery which included general cognitive assessment (MMSE), executive and attentive functions test (Alternating square & triangle, Luria loop, COWAT), verbal long and short term memory (SVLT, Digit span) and visual-spatial short term memory (RCFT test). We also evaluated depression and neuropsychiatric symptoms using GDS.

Results: Mean MMSE was 26.8±2.1. All patients had pathological score in Alternating square & triangle, Luria loop, COWAT. All patients had borderline scores in visual-spatial short-term memory test. All patients had depression as showed by GDS.

Conclusions: MSA-C patients were shown to have impaired verbal memory and executive function. There was evidence for impaired verbal memory and verbal fluency. Regarding the similar cognitive syndrome of MSA-P, the otherwise subclinical problems in MSA-C result from subcortical rather than from cerebellar dysfunction. Depressive thoughts occur more frequently than PD. One possible explanation for the cognitive deficits in MSA-C is to assume that parts of the cerebral cortex undergo degeneration in parallel to the pontocerebellar system.
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Assessment of cognitive disorders in Parkinson’s disease (PD)

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**Purpose of the study:** Assess the impact of cognitive impairment on the daily activity of patients with BP.

**Results of the research:** The use of the UPDRS scale showed, characterizing the daily activity of patients, the total score was 11.9 ± 0.6 in women, 11.8 ± 0.5 in men (p> 0.05), an average of 11.7 ± 0.4. According to the UPDRS section assessing impairments, the sum of scores in female subjects was 21.2 ± 0.9, in males - 25.1 ± 1.2 (p> 0.05), an average of 22.9 ± 0.7. When examining patients with BP using the cumulative index scale characterizing the level of comorbidity, this indicator averaged 2.4 ± 0.1. He was significantly higher in males compared with females (3.1 ± 0.3 vs. 2.1 ± 0.3, p < 0.02); In general, respiratory diseases, pathology of the genitourinary system were detected. The level of education also did not differ significantly in women and men, respectively 13.1 ± 0.5 years and 12.3 ± 0.5, p> 0.05. At the same time, the total score in female patients was 23.3 ± 0.7 for men with MMSE, 21.9 ± 1.1 for men, and no significant difference (p> 0.05); this indicator for the group was 22.8 ± 0.3.

It was found that in 21% of patients with BP the total score for MMSE ranged from 28-30 points, which indicates the absence of cognitive impairment. The magnitude of the total score of MMSE from 24 to 27 points was revealed in 20% of patients, on the average - 25.3 ± 0.2 points. In 25% of patients with BP, the total score for MMSE ranged from 23 to 11, indicating the presence of dementia.

**Conclusions:** When performing a differential diagnosis between BP and vascular parkinsonism, the results of the neuropsychological examination should be taken into account.

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New assessments of cognitive disorders in patients with parkinsonism in Uzbekistan

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**Background:** Parkinsonism-neurologic syndrome is a disorderly degenerative disease of the nervous system, characterized by akinesia, rigidity, tremor in calmness and postural insufficiency. One of the pressing problems in the world of medicine. In the last 20 years, cerebral hemorrhages and atherosclerosis have been associated with Parkinson’s syndrome. Loss of cerebral blood vessels is one of the main causes of Parkinsonism development. The first symptoms of the disease appear in the 50’s and 60’s of the patient’s life.

**Aim:** Study the principle of cognitive impairment in Parkinson’s syndrome (brain cerebral circulation disorder, backdrop of atherosclerosis).

**Patients and methods:** Neurology Department presented 24 patients with cognitive impairment in Parkinson’s syndrome. 46% of them (11) had cerebral (75% male, 25% female) atherosclerosis, 37% (9) hypertension (40% in men, 60% in women), 17% (4) (75% in men and 25% in women). Both patients have
an average age of 58 and 10 for men and 14 males. Cognitive functions were evaluated in a total 30-point scale in the MMSE scale. The scale was inspected at 9 stages. 23 points (19-27) for women in the MMSE scale; in men with 25 points (18-28).

**Results:** Cognitive disorders are mainly: Memory - 85% (20) (80% of men), (100% of women); Attention concentration and calculation: 57% (14 (40% men), 100% women; 100% female (100% female); 100% (100% of men), (100% for women), disorientation with time - 17% (4) (50% men, 50% women; disorientation to the place - 0%; perception - 0%; execution - 14%) (100% for women), speech abilities - 0% in patients.

**Conclusion:** In conclusion, it can be said that Vasculus develops due to parkinsonismal-cerebrovascular disorders. In this type of Parkinsonism, there are primarily pyramidal and neuropsychological disorders. Cerebral microcirculation and metabolic enhancer drugs in cognitive impairment have a positive effect.
Objective: Generalized dystonias are frequently a therapeutic challenge, with poor responses to pharmacological treatment. GPi (globus pallidus internus) pallidotomies for Parkinson’s disease ameliorate all kinds of dyskinesias/dystonia, and recent studies reported a marked improvement of refractory dystonias with this procedure. We aimed to evaluate the efficacy and safety of bilateral pallidotomies in five patients with generalized dystonia.

Methods: Six patients with generalized dystonias refractory to medical treatment were selected; one post-traumatic and four idiopathic. The decision to perform bilateral procedures was based on the predominant axial involvement in these patients. Dystonia severity was assessed with the Burke-Fahn-Marsden Dystonia Scale (BFM). Simultaneous procedures were performed in all but one patient, who had a staged procedure. They were reevaluated with the same scale (BFM) by an unblinded rater at 1, 2, 3, 30, 60, 90, 120 and 180 days post-operatively.

Results: The five patients with idiopathic dystonia showed a progressive improvement up to three months; the patient with posttraumatic dystonia relapsed at three months. One patient had a marked improvement, being able to discontinue all the medications. A mean decrease in the BFM scores of 52.58% was noted. One patient had a trans-operative motor seizure followed by a transient hemiparesis secondary to rack hemorrhage; other was lethargic up to three days after the procedure.

Conclusions: Our results show that bilateral GPi pallidotomies may be a safe and effective approach to medically refractory generalized dystonias; it can also be speculated that the posttraumatic subgroup may not benefit with this procedure.
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Sensorimotor plasticity in writer’s cramp parallels clinical improvement after botulinum toxin injections

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Introduction: Writer’s cramp (WC) is a task specific focal hand dystonia occurring when writing. The physiopathology is still not well known. A central dysfunction appears to characterize the disease. TMS studies have showed enhanced cortical excitability in the hand’s motor cortex (MC). Moreover, patients have sensitive abnormalities. Some studies revealed an overlap in motor and sensitive cortex cartographies. Botulinum toxin injections (BTX) can improve the motor symptoms for 3 months. We have hypothesized that BTX modulate sensorimotor adaptive plasticity. By modifying sensitive inputs, BTX could restore normal cortical excitability in the hand’s primary MC, through a reinforcement of defective short afferent inhibition (SAI) from sensitive inputs to primary MC.

Methods: Adult patients with WC treated by BTX every 3 months were selected. Visits occurred before, 1 week, 1 and 3 months after BTX. Assessments included the Writer’s Cramp Rating Scale for severity, spatial and sensory discrimination skills for sensory disturbances, and robotized and neuronavigated transcranial magnetic stimulation in the affected side (resting motor threshold, sensory and motor cartography, SAI from the primary sensitive to primary MC).

Results: will be fully presented in August 2018. Six patients have been included. Expected results are:
1) patients exhibit an overlap between their first dorsal interosseus and adductor digiti minimi’s motor cartography, and between their IIn d and Vth finger sensitive cartography, which are restored at 1 month, as clinical parameters improve, and worsen at 3 months, as clinical parameters worsen;
2) SAI abnormalities shrink at 1 month, especially in patients undergoing clinical parameters improvement, and worsen with clinical parameters at 3 months.

Conclusion: WC’s clinical improvement after BTX is associated with enhanced motor and sensitive hand cartography and enhanced SAI from the sensitive to the primary hand MC, indicating that WC’s physiopathology deals with maladaptive sensorimotor plasticity and that BTX acts by modulating this plasticity.
Ultrasound echogenicity of the nuclei raphe as marker of depressive disorders in the cervical dystonia

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Dystonia according Dystonia Medical Research Foundation is movement disorders, in which there are persistent muscle cramps that often cause abnormal twisting movements or incorrect posture. Apart from pathological movements, there are also non-motor symptoms, including depressive disorders and pain, which impair the quality of life of patients.

The aim of the study was to analyze the possible relationship between abnormal echogenicity of the nuclei raphe in patients with cervical dystonia correlated with the age, duration of the disease, its severity, pain, and accompanying of depressive disorders.

The study included 76 patients with cervical dystonia, among whom patients taking SSRIs, SNRIs, MAO inhibitors during the last year and patients with cervical dystonia with other psychiatric disorders were also excluded from the Study.

Thus, 64 patient meet criteria were analyzed statistically. Patients were divided into three groups according to severity of depressive disorder at Beck and MADRAS Scale: patients without depression, with moderate depression and severe depressive disorders.

The clinical condition of the patients was assessed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). The nuclei raphe (RN) were localized using ultrasound in the transverse plane of the midbrain. The normal RN is hyperechogenic (RN+) on the TCS when it showed as an uninterrupted relatively echo-intense structure. The abnormal RN is hypo-echogenic (RN−) when this structure was interrupted or had a reduced echogenicity compared to the surrounding brain structures.

Result:

The analyzed patients were aged 22-83 years (mean 52.56), with duration of disease about 9.3 years (SD 8.63). In older patients abnormal RN was more often observed (p = 0.04). There was no statistically significant correlation between the abnormal RN and the duration of cervical dystonia (p = 0.47).

The severity of torticollis (TWSTRS total and part I), the presence of dystonic tremor had no related to ultrasound structure of RN. There was a slight advantage abnormal RN for patient with higher values in the TWSTRS part III (Pain Scale) p> 0.05, there was no correlation between the reported pain and ultrasound image of RN. The Patients with higher total TWSTRS had a higher score on the scale of depression according to Beck’s scale p = 0.047 (r = 0.31).

At higher values in both the depressive scales : Beck and MADRAS scale were related with abnormal ultrasound image of RN. This relationship was shown mainly for depressive disorders of moderate intensity (Beck’s scale p = 0.004, MADRAS scale p = 0.02).
Orthostatic tremor complicated by spinal cord schwannoma

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**Introduction:** Since orthostatic tremor (OT) was described as a tremor of the lower body that occurs upon standing, is absent when seated or lying, and is alleviated by walking or leaning, it still remains one of the relatively unknown and infrequent hyperkinetic movement disorders. Most cases of OT are idiopathic, however, secondary cases have been described uncommonly; causative structural lesions including cerebellar degeneration, non-tumoral aqueduct stenosis, pontine and midbrain lesions, spinal cord lesion. We report an OT case complicated by intradural, extramedullary schwannoma, which turns out to be a coincidental finding.

**Case:** A 60-year-old Korean woman presented with bilateral leg tremor for 1.5 years. Leg tremor occurred exclusively while standing and she also reported arm tremor on standing, however there was no other parkinsonian feature on examination. There was a sense of weakness, stiffness, coldness on bilateral legs, and hypoesthesia on left lateral foot area. Nerve conduction study and lumbar spine CT were performed and sensory polyneuropathy, spinal stenosis and Lt neural foraminal stenosis at L4-5 level were identified. Brain MRI showed multiple white matter ischemic changes and FP-CIT PET/CT showed normal finding. During following 8 months, OT markedly alleviated by clonazepam 0.75mg, primidone 125mg and arotinolol 15mg, however, leg weakness and hypoesthesia had been aggravated. Spine MRI was performed and about 1.4 x 0.9 x 3.3cm sized ovoid intradural extramedullary schwannoma was found in the left posterolateral aspect at T11 level. Despite 1.5 years of follow-up after successful removal of tumor, OT reappears when discontinuation of the medications.

**Conclusion:** This case shows OT complicated with several associated conditions including structural spinal lesion, and long term observation suggests idiopathic rather than secondary cause.
Topic: Chorea, Athetosis and Ballism

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Case report: Chorea gravidarum persisting after delivery
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Objective: To present a case of recurrent, persistent, chorea gravidarum (CG).

Background: CG occurs in pregnancy secondary to an underlying pathology. The mean onset is 22.4 years of age and the chorea usually starts during the first or second trimesters. Lupus, collagen vascular diseases, drug-induced chorea, and history of rheumatic disease are the most common causes. One in five women experience CG recurrence with subsequent pregnancies.

Case: 27 year-old right handed female presents with 9 year history of chorea. She reports that the chorea started during the first trimester of her first pregnancy at 19 years of age. The movements subsided two months after delivery and reemerged 2 years later with her second pregnancy, again starting in the first trimester. The chorea subsided two months after delivery. Two years later she was started on oral contraceptives (OC). She developed the chorea again while on OC. Within the next year she became pregnant despite the use of OC. The chorea has persisted since this time. She denies a history of strep throat, rheumatic fever, and substance abuse. She also denies having ever taken dopaminergic agonists or antagonists, lithium, phenytoin, stimulants, or isoniazid.

On exam, the movements are continuous, jerky, and involve the left arm, left leg, and mouth greater than right arm. Neurologic exam is otherwise normal.

Results / Discussion: This presentation of recurrent CG persisting several years after pregnancy, not on OC, is atypical. CG is considered a “hormone-induced chorea” syndrome that occurs after activation of a previous subclinical lesion in the basal ganglia. Animal studies have shown that estrogen can influence dopamine levels. Finally, the patient has no obvious risk factors for CG. There is no explanation for why the chorea persists. That the chorea recurred with use of OC confirms the hormonal nature of CG.
Neuroprotective role of cinnamaldehyde against 3-nitropropionic acid-induced oxidative stress in a rat model of Huntington’s disease

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Objectives: Huntington’s disease (HD) is a neurodegenerative disorder characterized by symptoms like chorea and dementia, results from the destruction of neurons in the basal ganglia, and oxidative stress has been implicated in its pathogenesis. Cinnamaldehyde (CA) is a diterpene with a wide range of anti-inflammatory, cognitive enhancer, neuroprotective, anti-diabetic effects thus may be advantageous in the treatment of neurological disease. The present study examined the potential therapeutic effects of CA against 3-nitropropionic acid (3-NP)-induced oxidative stress in a rat model of HD and explored the mechanisms of action.

Methods: 50 Male SD rats were pretreated with CA (20 and 40 mg/kg b.w.) orally prior to the intraperitoneally (i.p.) administration of 3-NP (12 mg/kg b.w.) for 15 days. Nimodipine (12 mg/kg, po) was used as positive control drugs. The body weight, grip strength and behavior were monitored within 5th, 10th and 15th day after 3-NP treatment. Then the animals were sacrificed, neuronal damage in striatum was estimated using Nissl staining. Hsp70 expression was detected with immunohistochemistry. Reactive oxygen species (ROS) generation was measured using dihydroethidium (DHE) staining. Memory (Morris water maze), antioxidants enzymes and lipid peroxides were analyzed in rat model of HD.

Results: Present results shown that administration of 3-NP resulted in a marked reduction in the body weight, memory, grip strength locomotion activity and significantly increased lipid peroxidation and depleted antioxidant enzyme accompanied by progressive striatal dysfunction. CA (20 and 40 mg/kg) treated animals exhibited a significant (p < 0.01) improvement in behavioural, biochemical, histological alterations and oxidative stress parameters in comparison to only 3-NP treated animals. Present results shown dose-dependently improved 3-NP-induced behavioral, biochemical, and enzymatic changes (P < 0.001). Similar effects were obtained with the positive control drugs nimodipine.

Conclusions: CA exerts a protective action against 3-NP-induced oxidative stress in the rat model of HD, which is associated with its anti-oxidant activity, and consequently improves behavioral deficits.
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Psychosocial impact of African families structure among patients with Huntington’s disease


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Background: Huntington’s disease (HD) is a rare autosomal dominant neurodegenerative disease caused by an expanded CAG repeats in IT15 with a heavy motor and psychosocial burden. Although widely studied elsewhere, the psychosocial aspect in African populations has not been reported.

Objectives: Determine the psychosocial impact of HD on patients and their families.

Methods: Participants were consented to participate in this study and went through a neurological and laboratory examination. Questionnaires on the motor (MST of UHDRS), cognitive (MMS) and psychosocial impact of the disease were administered.

Preliminary results: Twenty seven participants including fourteen patients from ten families were enrolled. Mean ages of onset and diagnosis were 45.9 and 51.7 years, respectively. The mean motor score 58.8 (N: 0), and MMS was 25 (N: 30); suggesting more motor and less cognitive impairment. The mean CAG repeat length in patients was 43.7. One patient had marital problems and was blamed by a sister, leading to frequent wandering impulsions, and an affected brother of one patient probably committed suicide. Three relatives developed anxiety or anxio-depressive syndrome related to the disease in the family. However, overall, patients had no sentiment of reject.

Conclusion: Beyond the important physical disability, HD can considerably affect the psychosocial life of the patient and his entourage. However, socio-cultural specificities can influence the behavior of patients and their entourage with this disease. Our study has shown fewer negative impact of the disease in the family compared to other populations. A larger cohort might shed light in this preliminary conclusion.

Keywords: Huntington disease, cognitive, psychosocial, cultural, Mali
Taking a step back to reframe the approach - an interesting case of tardive tourettism

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PL, a 51-year-old Asian American with chronic history of schizophrenia, developed tardive tourettism secondary to chronic treatment with a dopamine receptor blocking agent, olanzapine.

PL was brought into the emergency psychiatry department multiple times over several months due to disorganization and involuntary, uncontrollable vocalizations. The symptoms led to frequent inpatient psychiatric hospitalizations. During the first admission process, the patient and family confirmed a twenty-year history of chronic schizophrenia, stable on olanzapine with no history of motor or phonic tics. The family and patient validated the recent development of involuntary vocalizations within the last year.

Initially, the treatment team contributed these vocalizations to the patient’s disorganization. During each inpatient admission, the patient had been non-compliant with olanzapine at home, leading to worsening involuntary vocalizations.

Subsequently, patient was restarted on his home medication of olanzapine during hospitalization, which brought about improvement in the frequency of his involuntary vocalizations. However, due to the patient’s continued presentation and medication noncompliance, the patient was switched to risperidone and transitioned to a long acting injectable of paliperidone.

Unfortunately, the switch to a different antipsychotic worsened the patient’s involuntary vocalizations, leading to an extended stay in the inpatient setting. Once the paliperidone had metabolized out of the patient’s body, titration to original dose of olanzapine was initiated. With the combination of restarting olanzapine and removal of paliperidone from the patient’s system, there once again was remarkable improvement in his involuntary vocalizations. At this stage, the patient was diagnosed with tardive tourettism and his involuntary vocalizations were properly identified as phonic tics.
Incidence of oculopalatal myoclonus in post-stroke patients
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Background: OPM are rare movement disorders connected with the injury in Guillain-Mollaret triangle, especially with hypertrophy of inferior olivary nucleus. The imbalance between inferior olivary nucleus and cerebellum activity is the most crucial in pathophysiology of OPM.

Methods: Patients who developed the OPM in the several months' time after brain injury and who were hospitalized in the Neurorehabilitation Ward of Institute of Psychiatry and Neurology in Warsaw in 2012-2014 were analyzed. The etiology, clinical status, the area of injury in the brain, the functional status and the response to the treatment were taken into account.

Objective: Analysis of clinical course of oculopalatal myoclonus (OPM) and MRI images of the brain.

Results: There were 4 patients who developed the OPM (0.84% of all hospitalized stroke patients). In three cases, the brain injury were caused by ischemic stroke in posterior circulation area, whereas the fourth case was caused by bleeding from ruptured arteriovenous malformations in brainstem and resection of the malformations. In all the cases, myoclonus of the face, the tongue, the pharynx and/or the diaphragm beside the OPM were developed. In all the cases the MRI images revealed lesions in the region of Guillain-Mollaret triangle. Neurological and functional status of the patients was severe (mRS 5-4). Unsatisfactory improvement after applied pharmacological therapy such as valproic acid, levetiracetam, botulinum toxin in all the cases was achieved.

Conclusions: The OPM are rare, treatment-resistant movement disorders, most often connected with vascular injury of the brain.

Clinical manifestations of SYNE1 mutation related cerebellar ataxia from Korea
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Introduction: SYNE1 related autosomal recessive cerebellar ataxia type 1 (ARCA1) is a late-onset cerebellar ataxia with slow progression originally demonstrated in French-Canadian populations of Quebec, Canada. However, recent studies revealed that SYNE1 mutation is not uncommon outside the French-Canadian founder population, and that it commonly presents with multisystemic neurodegenerative disease. Herein, we describe two cases with SYNE1 related ataxia from Korea.

Methods: To determine the underlying genetic cause of the ataxia phenotype in cases from Korea presenting with very slow progressive cerebellar symptoms including dysarthria, dysmetria, and gait ataxia, we performed Whole exome sequencing.
**Results:** We identified compound heterozygous variants in SYNE1 gene from two patients. The phenotype was mainly pure cerebellar ataxia in both cases. However, axonal neuropathy, mild frontal dysfunction and autonomic dysfunction were revealed. Age of onset was relatively late and disease course was rarely progressed.

**Conclusion:** Our results indicate SYNE1 mutations are not an uncommon cause of recessive ataxia with or without additional clinical features in Korean population. This study alerts neurologists to request SYNE1 testing for undetermined adult-onset ataxia in Korean population.

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**The prevalence of restless legs syndrome in Edirne and its districts concomitant comorbid conditions and secondary complications**

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We aimed to determine the prevalence and risk factors of restless legs syndrome in Edirne and its districts, located in Western Thrace, which is the most western part of Turkey. In this study, 4003 individuals who could communicate and agreed to participate in the study were evaluated. To obtain the data from the applicants in 30 Family Health Centres in Edirne and its districts, a face-to-face questionnaire that consisted of 54 questions was prepared by the researchers.

The questionnaire included general information, questions to evaluate potential concomitant comorbid conditions and questions regarding the symptomatology used in restless legs syndrome (RLS) diagnosis, as well as questions to evaluate insomnia and tension-type headache secondary to insomnia according to the ICD-II Criteria (International Classification of Sleep Disorders-II Criteria).

Of 4003 individuals, 282 were diagnosed with RLS according to the questionnaire results from Edirne and its districts, and the prevalence of RLS was 7%. Approximately, 47.9% of the patients with RLS were male, and 52.1% were female, which was not significantly different (p > 0.05). Anaemia was identified in 41.1% of the cases and control group was detected in 19.4%, which was significantly different (p < 0.001). Secondary insomnia was identified in 64.2% of the cases with RLS and was not detected in 35.8%, which was significantly different (p < 0.001). RLS prevalence studies will increase the awareness of the community and provide early diagnosis and treatment, as well as serve as a basis to reduce morbidity and improve the quality of life.
A case of propriospinal myoclonus: secondary form or a sleep disorder?
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Propriospinal myoclonus (PSM) is a rare type of spinal myoclonus with a slow propagation up and down the spinal cord producing a jerky arrhythmic flexion of the trunk, hips, knees and neck. PSM has been seen in cases of restless legs syndrome (RLS) with a tendency to occur during relaxed wakefulness prior to sleep onset. PSM has also been reported to affect the ability to sleep. Secondary PSM has been found to occur in cases with spinal cord lesions. Additionally, over 50% of PSM cases have been diagnosed as functional in origin.

We present an interesting case of PSM in the setting of RLS which began following an acquired thoracic spinal lesion and paraplegia. Interestingly, the RLS which initially involved only the legs began to involve the arms following the onset of paraplegia. The onset of PSM did not present until after the spinal lesion occurred and it has gradually increased in frequency. Symptoms of PSM develop during relaxed wakefulness, when lying down or tilted back in the wheelchair. They do not appear to occur when sitting up or fully awake. Frequencies of symptoms are typically a few times per month rather than every night and result in alteration of sleep patterns. They do not respond to treatment with pramipexole. He was unable to tolerate levetiracetam, however felt symptoms improved with that medication.

This case illustrates propriospinal myoclonus in two ways as a secondary form following thoracic spinal cord lesion and in association with RLS as a parasomnia.

Effects of different training programs on postural control and beta event-related desynchronization in individuals with Parkinson's disease: A pilot study
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Introduction: The purpose of this study was to compare the effects of different exercise programs on postural control and cortical activity in individuals with PD.

Methods: Eighteen PD subjects were recruited and randomly assigned to the specific exercise group (SE), turning-based treadmill training group (TT) or control exercise (CE) group to received 12 sessions training that focused on balance and strengthening, turning-based treadmill training, and general exercise training, respectively, for 30 min followed by 10 minutes of over-ground walking in each session for 4 to 6 weeks. The primary outcomes included sensory organization test (SOT), postural instability and gait disorder, and beta event-related desynchronization (ERD). All measurements were assessed at baseline and after training.
Results: The results (n=6 for each group) showed that both the SE and TT group improved SOT total score, PIGD, and beta ERD over central area comparing with the CE group. For the secondary outcomes, the SE group and TT group showed greater improvements in turn time of the SQT test when compared with CE group. Besides, the PIGD and turn time were positively correlated with beta ERD. However, there were no significant correlation between SOT total score and beta ERD.

Conclusion: This pilot study shows that postural control and beta ERD over central area can be improved after SE training and TT training. These results demonstrated that exercises with intensity are not only resulting in positive effects of physical activity but also may change brain activity in individuals with PD.

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Delayed onset progressive spastic cerebellar ataxia and cerebellar atrophy as a delayed complication of heat stroke
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Objective: To describe a rare case of delayed progressive spastic cerebellar ataxia after survival from an episode of heat stroke.

Case details: A 35 year male farm labourer presented with insidious onset chronic progressive symmetric spastic cerebellar ataxia with frontal subcortical executive dysfunction for 3 years. There was no exposure to drugs / toxins, or having metabolic / endocrinal/ systemic disease or positive family history. He had bilateral pancerebellar ataxia with dysarthric speech, limb, gait and truncal ataxia with increased tone in all 4 limbs, with preserved power, with hyper-reflexia in all 4 limbs and extensor plantars. Bladder bowel functions were normal. He had a history of admission in our hospital 4 years back with history of being found unconscious in the farm in summer with hyperthermia. He had improved after cooling, hydration and intensive care and subsequently recovered.

A review of all old records of past admission revealed that he was diagnosed as heat stroke based on Hyperthermia [Temperature 107 F] , Leukocytosis, raised CPK, pre-renal azotemia with normal MRI brain, CSF stud, negative blood culture with a history of being found in the field in summer. He had improved after cooling, hydration and intensive care and subsequently recovered with rehabilitation.

However, subsequently, he developed gradually progressive spastic cerebellar ataxia. His repeat MRI brain at 3 years revealed severe pancerebellar atrophy with Normal hemogram, liver, renal, thyroid function, electrolytes, Anti-nuclear Ab, Anti-gliadin Ab and normal SCA genetic testing.

A diagnosis of delayed onset progressive cerebellar ataxia post episode of heat stroke was made. This phenomenon is rare but described in literature and is believed to be related to Purkinjee cell degeneration post hyperthermia.

Conclusion: Delayed onset spastic cerebellar ataxia post heat stroke can be a rare preventable cause of ataxia in tropical countries.
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Influence of the level of cognitive impairment on gait parameters in older adults and diagnosed with Parkinson’s disease

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Objectives: Gait disorder in Parkinson’s disease (PD) is common and is one of the main causes of disability. This disease may present with signs of cognitive impairment as its stage progresses. Therefore, the aim of the study is to analyze the gait parameters in the PD population over 65 years of age based on cognitive impairment.

Methods: A total of 35 (48.6% female; 69.06±9.87 years; 5.7% HY I, 51.4% HY II, 37.1% HY III, 5.7% HY IV) parkinsonians of whom 43.7% had signs of cognitive impairment (34.4% mild, 3.1% moderate y el 6.3% severe) have participated in the study. Cognitive impairment was evaluated by means of the minimental test (MMSE), while for gait assessment, a set of wireless inertial detection devices placed in the L4-L5 spinal segment, called Wiva® that include an accelerometer, a magnetometer and a gyroscope (Figure 1).

Results: After the analysis, significant differences were found (p < 0.05) in the study of gait parameters, for parkinsonians without cognitive impairment (WOCI) and with cognitive impairment (WCI) for the variables walking speed (WOCI 103.06 ± 0.32 vs WCI 76.50 ± 0.29 m/s), the cadence (WOCI 90.00 ± 16.16 vs WCI 75.52 ± 28.38 steps/min), average length of passage (WOCI 60.42 ± 6.61 vs WCI 53.00 ± 10.19 cm), reaching higher values the Parkinsonian WOCI, and for the variables of the duration of the gait cycle (WOCI 1.40 ± 0.36 vs WCI 3.02 ± 0.51 s), with lower values for parkinsonian WOCI.

Conclusions: The presence of signs of cognitive impairment in the parkinsonian population is related to a major gait disorder compared to parkinsonians who do not presents signs of cognitive impairment.
The prevalence of essential tremor in Edirne and its districts concomitant comorbid conditions

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Objective: ET has negative impacts on the quality of life in patients. This condition is the subject of an increasing number of epidemiological studies [1,2]. Therefore, it is extremely important to determine the prevalence of ET, which is common but less known, as well as to determine the quality of life and other concomitant chronic processes. While it is recognized that genes play a major role in ET with $\geq$50% of the affected individuals having a positive family history [3,4].

Method: To assess the prevalence of ET in Edirne and its districts, 3008 volunteers, including 1518 men and 1470 women, were included in the study. To account for the possibility of missing cases of ET in our study population, we added an additional 10% to the estimated number of individuals needed, for a total of 3367. However, ultimately, only 3008 individuals were included.

Results: The study population consisted of 3008 participants, including 50.8% men ($n=1518$) and 49.2% women ($n=1490$). The ET prevalence was 7.4% and 226 participants were evaluated as ET positive. One hundred thirty-five (47.9%) of the ET patients were men, and 147 (52.1%) were women. There was a statis-
tically significant relationship between the duration of the disease and the severity of the positive tremor in people who had an essential tremor diagnosis (p=0.000). There was a statistically significant correlation between family history of ET patients and those who did not (p=0.000). There was a statistically significant difference in the presence of thyroid disease between those who received ET and those who did not (p=0.000).

Conclusion: As a result, in many countries and regions, despite many efforts and studies regarding the prevalence, epidemiology, mechanisms and treatment of the disease, ET has not been sufficiently elucidated. We determined family history of ET high frequency of positive. The field of essential tremor (ET) genetics remains extremely challenging. Thus, for the determination of the prevalence and mechanisms of the disease, additional detailed and comprehensive studies are needed.

P 197
A male patient showing abnormal gait, dysarthria and psychotic symptoms followed by genetic diagnosis

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Pantothenate kinase-associated neurodegeneration (PKAN) which was called Hallervorden-Spatz disease (HSD), is a rare degenerative, autosomal-recessive, neurologic disorder associated with progressive motor impairment and mental deterioration. The diagnosis of PKAN is consisted of clinical features and magnetic resonance imaging evidence of iron accumulation in the brain as well as to mutations in the PANK2 gene. The typical clinical features show motor symptoms including dystonia, involuntary movement rigidity as well as dysarthria, and psychiatric symptoms like anxiety, depression and mental retardation. However, psychosis in PKAN has not been reported often and this case presented anxiety, startling and rapidly deteriorated memory impairment. In this patient, we checked T2-weighted magnetic resonance imaging (MRI) of his brain indicating a specific pattern of hyperintensity within the hypointense medial globus pallidus with mutation in the gene encoding pantothenate kinase 2 (PANK2). Interestingly, in schizophrenia, the basal ganglia play a key role on motor symptoms, cognition and affect or mood. Also, PKAN is affected by abnormal iron deposition in the globus pallidus and substantia nigra pars reticulate. Thus, these lesions are able to aggravate various psychotic symptoms, cognitive function impairment and mood disorders.
P 199

Approaching health care shaped by Generational Expectations (The AGE Study): Generational perspective related to time

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Objective: To investigate the preferences different generational groups (i.e. Traditionalists, Baby Boomers, Generation X-ers, and Millennials) have towards healthcare with regards to time management.

Method: A cross-sectional survey was completed by 230 patients from various generations in a movement disorders clinic regardless of diagnosis. The survey consisted of a questionnaire that inquired about basic demographic information and various healthcare preferences which were measured on a five-point Likert scale. A series of proportional odds models was used to evaluate the generational differences in odds of agreement with survey items.

Results: The sample included 53% female and 92% white subjects, with an average age of 57.4 (SD 18.2). The majority of patients preferred their physicians to respond to messages in a timely fashion, with patients in Generation X having 2.5 times the odds of reporting stronger preference over Traditionalists (95% CI 1.07-5.71, p = .034). Only a small subset of patients (< 6%) indicated strongly their understanding when their doctor arrives late to their scheduled appointment. However, no clear generational differences were observed in the survey responses. The majority of respondents appreciated their doctors spending at least 30 minutes to explain treatment options, but also showed preference for concise explanations with regards to illnesses and treatment plans. Neither aspect showed generational differences.

Conclusions: Regarding patients’ preferences on time in health care setting, Generation Xers exhibited a stronger preference for timely response to messages compared to Traditionalists. More importantly, regardless of generation, patients did not appreciate their doctors arriving late to their scheduled appointments, and most preferred their clinicians to be concise in their explanations of diagnosis and treatment options.

P 200

A study of correlation between screening tools for cognitive decline and gait status using three-dimensional gait analysis

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Objective: The objective of this study is to evaluate the correlation between screening tool for dementia and gait status.

Background: Gait impairment in patient with cognitive decline has been much focused in last decades. However, gait disturbance in dementia is usually underdiagnosed clinically. Mini-mental state examination (MMSE) is the most widely used for screening test of dementia. Montreal Cognitive Assessment (MOCA) has been developed for more detail assessment of mild cognitive impairment (MCI). The purpose of our study is to investigate the correlation between gait status and screening test for dementia.
Methods: We recruited 24 patients diagnosed with MCI, 22 patients diagnosed with early stage of dementia. All participants were examined by Korean version MMSE, MOCA test for screening and neuropsychological test for estimating cognitive function. All participants were also performed three-dimensional motion captures for objective measurement of gait. We evaluated the correlation between score of screening tool and gait parameters.

Results: MOCA significantly correlated with walking speed (r=0.33, p<0.05) and stride length (r=0.40, p<0.05). However, MMSE did not correlated with walking speed (r=0.26, p=0.11) and stride length (r=0.21, p=0.22). In neuropsychological test, stride length and walking speed were significantly correlated with memory and frontal lobe function.

Conclusions: We found that MOCA can more reflect gait status than MMSE in patient with cognitive decline. We postulate the reason is that MOCA is more sensitive tool than MMSE and contain frontal lobe function. Our result is support that MOCA is more useful screening tool for assessing MCI as well as gait status.

P 201
A validity study of wearable accelerometer for estimating gait in Parkinson’s disease
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Objectives: Gait disturbance presenting as hypokinetic, short step gait and freezing of gait is major symptoms in Parkinson’s disease (PD). Till now, it is difficult to measure gait disturbance objectively. Recently development of wearable device can enable quantification of gait. However, there were few reports of validation of wearable accelerometer for gait in PD. The purpose of our study is to evaluate the validity of tri-axial wearable accelerometer in gait performance in PD.

Methods: Fifty patients with PD were enrolled in our study. All participants were performed three-dimensional (3D) motion capture, while walking with three-axial accelerometer. We look for the peaks called a minimum that represents the initial contact of the leg and maxima that represents the final contact by using integration and differentiation. We evaluate the correlation between 3D motion capture and wearable accelerometer. We also calculate the mean error rate of wearable accelerometer compared to 3D motion capture.

Results: All gait parameters from wearable accelerometer were highly correlated with 3D motion capture. The mean error rate of wearable accelerometer for step time, stride time, stride length and walking speed were 3.87±14.38, 5.64±4.41, 4.46±4.79 and 4.96±4.83.

Conclusions: Our results proved that wearable accelerometer showed the highly valid tool for estimating gait in PD. Mean error rate of accelerometer revealed less than 10 percent based on 3D motion capture. Wearable accelerometer can enable long-term monitoring of gait and assessing gait state in free living environments.
Approaching health care shaped by Generational Expectations (The AGE Study): A perspective on technology and research


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Objective: To determine if different generational groups (Traditionalists, Baby Boomers, Generation Xers, and Millennials) have different preferences regarding healthcare system and providers, particularly their perspectives on technology and research.

Method: This is a cross-sectional survey study. Patients from the movement disorders clinic were recruited to complete a survey assessing demographic information and a series of healthcare preference questionnaires measured on a five-point Likert scale. A proportional odds model was used to evaluate generational differences in odds of agreement with survey items.

Result: Total of 230 patients were recruited. The sample consisted of 53% female and 92% white, with an average age of 57.4 (SD 18.2). Patients among all generations, especially Millennials and the Generation Xers, were willing to learn new technologies to track their health (e.g. Using an online video call for a follow up appointment, communicating with providers through an online message, or using smart phone applications). Most patients, especially the Generation Xers and the Millennials, were likely to use the internet to search for further information regarding their clinicians and their illness. Regarding their opinion on participating in research, the Generation Xers and Millennials were more agreeable to participate in the newest cutting-edge research, while the traditionalists were more likely to participate in research or clinical trials only after they found the standard of care ineffective.

Conclusion: While the younger generations tended to use technology and internet to track their health, communicate with providers, and search for information, the majority of the older generations were also open and willing to learn to use technology for their health care. Generation Xers and Millennials tended to consider clinical research as one of the treatment options, while the Traditionalist and Baby Boomers tended to view research or clinical trial as a last resort.
Abstracts

P 206
Global improvement and patient satisfaction: Results from a long-term, open-label, rollover study of valbenazine in tardive dyskinesia

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Objective: To assess global improvement and patient satisfaction in participants with tardive dyskinesia (TD) who received long-term treatment with once-daily valbenazine.

Background: Valbenazine has been evaluated in 2 long-term studies (KINECT 3, KINECT 4) in which participants received valbenazine (40 or 80 mg) for 48 weeks. This rollover study (NCT02736955) is the first to include a Patient Satisfaction Questionnaire (PSQ) that evaluates valbenazine as a TD treatment.

Methods: Adults with TD who completed KINECT 3 or KINECT 4 were re-initiated at 40 mg following washout of prior valbenazine treatment. Dose was escalated after 4 weeks to 80 mg based on tolerability and clinical assessment of TD; reduction to 40 mg was allowed if 80 mg was not tolerated. Participants received open-label valbenazine for up to 72 weeks or until commercial availability. Assessments included the Clinical Global Impression of Severity-TD (CGIS-TD: range, 1 [normal/not ill] to 7 [extremely ill]) and PSQ (range, 1 [very satisfied] to 5 [very dissatisfied]).

Results: Of 160 participants included in analyses, 56 (35.0%) reached Week 48 (40 mg, n=12; 80 mg, n=39; 80/40 mg [dose reduction], n=5). Few reached Week 60 (n=4) or Week 72 (n=0) due to commercial availability of valbenazine and study termination. The percentage of participants with CGIS-TD score ≤2 (normal/not ill or borderline ill) increased from baseline (before restarting valbenazine) (40 mg, 5.7%; 80 mg, 18.1%) to Week 48 (40 mg, 41.7%; 80 mg, 74.4%). At baseline, 100% (40 mg) and 99.1% (80 mg) of participants were very or somewhat satisfied with their prior valbenazine experience (PSQ ≤2). At Week 48, most continued to express satisfaction with valbenazine (40 mg, 100%; 80 mg 97.4%).

Conclusions: A clinician-based global assessment indicated ongoing, meaningful TD improvements in adults receiving valbenazine. Patient satisfaction rates remained high, even in patients treated for up to 2 years.
P 207
Efficacy of opicapone in Parkinson’s disease patients with motor fluctuations: Results from the BIPARK I study
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Objective: Investigate the efficacy and tolerability of 3 different opicapone (OPC) doses (5, 25, and 50 mg) compared with entacapone (ENT) and placebo, in levodopa-treated patients with Parkinson’s disease (PD) and motor fluctuations.

Background: Opicapone (OPC) is a novel, once-daily, potent, and long-acting peripheral catechol-O-methyltransferase (COMT) inhibitor.

Methods: BIPARK I was a multinational study that included 14-15 weeks of double-blind placebo- and active-controlled treatment. The primary efficacy variable was the change from baseline in absolute OFF-time based on patient diaries. The key secondary efficacy endpoint was the proportion of OFF- and ON-responders (≥1-hour improvement). Tolerability was assessed by adverse event (AEs), laboratory tests, vital signs, electrocardiogram, and physical and neurological examinations.

Results: A total of 600 subjects were randomized to placebo (n=121), 5mg-OPC (n=122), 25mg-OPC (n=119), 50mg-OPC (n=116) or ENT (n=122). Both 50mg-OPC and ENT significantly reduced the OFF-time (50mg-OPC: -1.95 hours [p=0.0015]; ENT: -1.61 hours [p=0.0131]) versus placebo (-0.93 h) and increased the ON-time without troublesome dyskinesia (50mg-OPC: 1.82 hours [p=0.0016]; ENT: 1.57 hours [p=0.0150]) versus placebo (0.78 h). Significantly more subjects receiving 25mg- or 50mg-OPC achieved the OFF-responder endpoint (25mg-OPC: 60.3% [p=0.0464]; 50mg-OPC: 69.6% [p=0.0011]) versus placebo (47.5%). Both 5mg-OPC and ENT missed statistical significance for OFF-time responders. A significantly higher proportion of ON-responders was also found for the 50mg-OPC group (65.2% [p=0.0028]). OPC and ENT were generally safe and well tolerated.

Conclusions: Opicapone, particularly 50mg-OPC, was effective in reducing OFF-time in PD subjects with a favorable profile compared to ENT.
Switch of double-blind opicapone, entacapone, or placebo to open-label opicapone: efficacy results of the 1-year extension of study BIPARK I

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Objective: Evaluate the efficacy of once-daily opicapone (OPC) as add-on to levodopa over 1 year of treatment in subjects with Parkinson’s disease (PD) and motor fluctuations.

Background: Levodopa still remains the most effective symptomatic treatment for PD. However, following oral administration, levodopa is extensively metabolized in the periphery by dopa decarboxylase and catechol-O-methyltransferase (COMT). OPC is a novel COMT inhibitor that has demonstrated safety and efficacy in two pivotal trials (BIPARK I, BIPARK II). Subjects completing these trials could enroll into a 1-year open-label (OL) extension study. Results from the BIPARK I extension study are presented here.

Methods: After 14-15 weeks of placebo- and active-controlled double-blind (DB) treatment in BIPARK I, adults with PD and end-of-dose motor fluctuations received OL OPC 25 mg for 1 week in addition to levodopa therapy. After Week 1, OPC dosing was adjusted (5, 25, or 50 mg) based on individual response. Efficacy variables included the change in the OFF/ON-time, based on patient diaries.

Results: At the OL endpoint (1 year), mean OFF-time was decreased by -34 min relative to the OL extension baseline, corresponding to a reduction of more than 2 hours (-127 min) relative to the DB baseline. In subjects who received placebo or entacapone (ENT) in the DB period, the switch to OPC resulted in a statistically significant decrease in OFF-time (placebo switch: -65 min [p< 0.0001]; ENT switch: -39 min [p=0.0060]) and increase in ON-time without dyskinesia (placebo switch: 43 min [p=0.0247]; ENT switch: 46 min [p=0.0148]). In participants who received OPC during the DB period, further improvements in OFF- and ON-time were observed, but with no statistical significance.

Conclusions: The switching of ENT to OPC led to a significant reduction in OFF-time and increase in ON-time without dyskinesia. OPC maintained its efficacy over the 1-year OL treatment period.
P 209
Screening of SCN11A in patients with essential tremor
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Essential tremor (ET) is among the most prevalent movement disorders, affecting millions of people worldwide. Although a positive family history is one of the most important risk factors for ET, the genetic architecture of ET remains elusive. Through whole-exome sequencing, a gain-of-function mutation in SCN11A (c.673C>T) was recently discovered in a four-generation Chinese family with adult onset familial ET. Functional analysis of the mutant SCN11A expression in mouse dorsal root ganglion neurons suggests that higher electrical activities of the mutant SCN11A may significantly alter membrane potentials leading to the opening of other sodium channels that cause neurons to be hyper-excitability, contributing to the pathogenesis of ET. To take these findings further, we conducted a case control association study for the variant in our Singaporean population. We included 382 subjects including 193 patients with ET (age 53. ± 19.7 years, 120 Males and 72 Females) and 189 controls (age 61.6 ± 11.6 years, 137 Males and 53 Females) who were recruited from movement disorder outpatient clinics in National Neuroscience Institute (Singapore General Hospital).

The patients were diagnosed by movement disorder specialists according to the Movement Disorder Society (MDS) consensus diagnostic criteria (Deuschl et al., 1998). The genotype of rs138607170 were determined by TaqMan-based probe on a 7500 RT-PCR system (Life Technologies). Five per cent of results were randomly selected and validated by Sanger sequencing. Ethnic background and family history was obtained by interview or a self-report questionnaire for all subjects.

Our results showed that none of our patients harbored the mutation of this gene. We therefore conclude that although of great interest, the SCN11A (c.673C>T) mutation is not relevant for the pathogenesis of ET in our Singaporean cohort.
Generation of isogenic human G2019S Parkinson’s model

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Studying Parkinson’s disease (PD) progression is difficult due to multifactorial nature of the disease causes and the lack of access to diseased dopaminergic (DA) neurons. Mutations in leucine rich repeat kinase 2 (LRRK2) is one of the known causes for PD. Various studies have shown LRRK2 mutation, G2019S, causes phenotypic defects in DA neuron. However, the exact mechanism is not clearly understood. Patient-derived induced pluripotent stem cells carrying G2019S mutation were used to study phenotypic signs of diseased DA neurons but does not account for the varied genetic background of the individual patient. Here, we generate an isogenic stem cell line of G2019S based on H9 human ES cell line using CRISPR technology. Sanger sequencing was performed to check the off-target effects of CRISPR gene editing technique. Validations of the stemness of isogenic lines were performed with various methods: immunofluorescence, RT-PCR, teratoma formation and karyotyping.

Our results showed that the isogenic line retain the stemness and can be differentiated into various neurons. Functional analysis of DA neurons derived from this isogenic line will be carried out to examine the effects of the mutation and understand the mechanism of the PD disease.

Is there any difference between essential and dystonic head tremor?

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Objective: Head tremor is a common clinical feature of essential tremor (ET). If head tremor is the predominant symptom, differentiation between ET and dystonic head tremor (DT) in cervical dystonia can be difficult. We thus aimed to find out if simple clinical tests can be helpful, such as relief of head tremor in the supine compared to sitting position, previously reported in ET but not DT.

Methods: 63 patients with head tremor were included: 25 patients with ET (13M, 12F, mean age 65, SD 11.0) and 38 patients with cervical dystonia (11M, 27F, mean age 59y., SD 9.8). The severity of tremor was rated with the activities of daily living (ADL) and performance subscale (PS) of the ET Rating Assessment Scale (TETRAS). Cervical dystonia was evaluated using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and cerebellar dysfunction with the Scale for the Assessment and Rating of Ataxia (SARA). Head tremor in sitting and supine position was assessed with accelerometer and tremor amplitudes were calculated.
**Results:** In general, patients with ET differed from DT by a significantly higher TETRAS total and ADL subscore, SARA score and a lower TWSTRS total and severity subscore (Tab.1). Decrease of the average head tremor amplitude in the supine (AmpSup) compared to sitting position (AmpSit) was found in both groups, without any significant difference between both groups (Tab.2).

**Conclusion:** Higher scores of tremor were demonstrated in patients with head tremor due to ET and higher dystonia scores were found in DT patients. In addition, ET patients show more signs of cerebellar dysfunction than DT patients. However, no differences between ET and DT were found in the accelerometric measures of change in head tremor in the supine vs. sitting position.

**Acknowledgments:** Grant support by the Czech Ministry of Health, AZV 16-28119A and Charles University, GAUK 580218.

<table>
<thead>
<tr>
<th></th>
<th>ET</th>
<th>DT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive family history</td>
<td>16/25 (64%)</td>
<td>12/38 (32%)</td>
<td>NS</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>36.5 (18.4)</td>
<td>37.1 (15.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Effect of alcohol</td>
<td>11/25 (44%)</td>
<td>17/38 (45%)</td>
<td>NS</td>
</tr>
<tr>
<td>TETRAS ADL</td>
<td>19.6 (10.4)</td>
<td>11.3 (10.9)</td>
<td>p = 0.009</td>
</tr>
<tr>
<td>TETRAS PS</td>
<td>15.3 (6.3)</td>
<td>9.4 (7.3)</td>
<td>NS</td>
</tr>
<tr>
<td>TETRAS total score</td>
<td>34.9 (15.9)</td>
<td>20.8 (17.5)</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>TWSTRS part 1A</td>
<td>0.9 (0.8)</td>
<td>3.1 (1.8)</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>TWSTRS total score</td>
<td>6.7 (7.6)</td>
<td>22.7 (11.2)</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>SARA</td>
<td>5.0 (3.2)</td>
<td>2.47 (3.0)</td>
<td>p &lt;0.001</td>
</tr>
</tbody>
</table>

All parameters are shown as mean (SD), except for family history and effect of alcohol. Statistical analysis was performed by Mann-Whitney test with Bonferroni correction. 

p = statistical significance level; NS = non-significant

[Table 1. Comparison between patients with ET and DT]

<table>
<thead>
<tr>
<th></th>
<th>ET</th>
<th>DT</th>
<th>NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AmpSit (mm)</td>
<td>1.0652 (2.2243)</td>
<td>0.7298 (0.6671)</td>
<td>NS</td>
</tr>
<tr>
<td>AmpSup (mm)</td>
<td>0.3094 (0.4163)</td>
<td>0.3788 (0.4897)</td>
<td>NS</td>
</tr>
<tr>
<td>AmpSit - AmpSup</td>
<td>0.7256 (1.99840)</td>
<td>0.3510 (0.4226)</td>
<td>NS</td>
</tr>
</tbody>
</table>

All parameters are shown as mean (SD), NS = non-significant
Statistical comparison between ET and DT was performed by Wilcoxon-Signed-Rank Test

[Table 2. Difference in head tremor in the sitting and supine position]
**P 212**

**LRP10 subcellular localization in human iPS-derived dopaminergic neurons: Implications for LRP10 dysfunction in synucleinopathies**

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**Background:** We have recently nominated LRP10, as a novel candidate gene in the pathogenesis of late-onset inherited forms of synucleinopathies: Parkinson's disease (PD), Parkinson's Disease Dementia (PDD), and Dementia with Lewy Bodies (DLB). Nevertheless, mechanistic insights into LRP10 protein function are limited, and it is unknown how LRP10 mutations lead to the development of these synucleinopathies.

**Objectives:** The aim of this study is to investigate LRP10 protein function and subcellular localization in dopaminergic (DA) neurons derived from human induced pluripotent stem-like (iPS) cells.

**Methods:** We have differentiated DA neurons from human iPS cells according to established protocols. We have carried out functional protein studies by overexpressing N-terminally V5-tagged LRP10 wild type protein in transfected iPS-derived DA neurons. Localization of LRP10 was assessed by performing immunocytochemistry, using specific protein markers for endosomes, retromer and trans-Golgi network.

**Results:** In 12-week-old human DA neuronal cultures, both in the cell soma and neurites, V5-tagged LRP10 strongly co-localized with the trans-Golgi marker TGOLN2 and GGA1. Furthermore, in the soma, V5-tagged LRP10 also partly co-localized with the early endosomal marker EEA1 and retromer marker VPS35.

**Conclusion:** We show that LRP10 is localized to vesicular structures associated with proteins involved in trafficking between the trans-Golgi network, retromer, endosomes, and plasma membrane (e.g. VPS35 and GGA1) in iPS-derived DA neurons. This is in line with observations by others. Interestingly, a missense mutation in the VPS35 is associated with autosomal dominant PD. Furthermore, GGA proteins as well as VPS35 have been shown to affect a-synuclein oligomerization and secretion. Collectively, these observations, together with the strong Lewy Body pathology detected in PD and DLB patients carrying LRP10 mutations as previously reported by us, suggest an intriguing link between LRP10, VPS35, and GGA proteins in a pathological pathway that contributes to the development of synucleinopathies.

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PTRHD1 loss-of-function mutation in an African family with parkinsonism and intellectual disability

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Background: The genetic bases of Parkinson’s disease (PD) in Sub-Saharan African (SSA) populations remain poorly characterized, and analysis of SSA families with PD might lead to the discovery of novel disease-related genes.

Objectives: To investigate the clinical features and identify the disease-causing gene in a black South African family with three members affected by juvenile-onset parkinsonism and intellectual disability.

Methods: Clinical evaluation, neuroimaging studies, whole-exome sequencing, homozygosity mapping, two-point linkage analysis, Sanger sequencing of selected candidate variants.

Result: A homozygous 28-nucleotides frameshift deletion in the PTRHD1 coding region was identified in the three affected family members, and linked to the disease with genome-wide significant evidence. PTRHD1 was recently nominated as the disease-causing gene in two Iranian families, each containing two siblings with similar phenotypes and homozygous missense mutations.

Conclusion: We provide conclusive evidence that loss-of-function mutations in PTRHD1 cause this novel form of autosomal recessive juvenile parkinsonism and intellectual disability.

First and second author contributed equally to this work and should be considered as joint first authors.