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Movement Disorders 1

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Movement Disorders 1
Heterogeneous determinants of quality of life in different phenotypes of Parkinson's disease

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Background: Health-related quality of life (HRQoL) is an important outcome in patients with Parkinson's disease (PD). A broad list of motor and non-motor features affect quality of life, however, there is a dearth of information about the complexity of interrelationships between its determinants in different phenotypes.
Objective: We aimed to find independent determinates and the best structural model for HRQoL, and investigate the heterogeneity between PD patients with different phenotypes regarding onset-age, progression rate and dominant symptom.
Patients and methods: A broad spectrum of demographic, motor and non-motor characteristics were investigated in 157 idiopathic PD patients namely comorbidity profile, nutritional status, UPDRS, psychiatric symptoms, fatigue, psychosocial functioning and PD severity index using Parkinson's Disease Questionnaire-39. Structural equation model and multivariate regressions were applied.
Results: Female sex, anxiety, depression and UPDRS-part II scores were the significant independent determinants of PD severity index. A model consisted of global motor, non-motor and co-morbidity components was able to explain 89% of the variance in HRQoL. In older-onset and slow-progression phenotypes, motor domain showed smaller contribution and the majority of its effects was mediated through non-motor features. Comorbidity component was a significant determinant only among older-onset and non-tremor-dominant patients. Fatigue was not a significant indicator of non-motor component to affect quality of life in rapid-progression PD.
Conclusion: Our findings showed outstanding heterogeneities in the pattern and determinants of HRQoL in different PD phenotypes, which should be considered during the assessments and developing personalized interventions to improve life quality in PD patients with different prominent features.

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Outcome of autosomal recessive early onset Parkinson's disease patients with PINK1 gene-5 year follow-up (2010–2015)

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Background: In 2009 a new complex homozygous large rearrangement of the pink1 gene in a Sudanese family with early onset Parkinson's disease was reported. The members of this family were followed-up for the last 5 years; we here report their clinical progression, management modalities and outcomes
Case report: This family was first seen in 2005 at OPD for adult neurology at Soba University Hospital (one of the Khartoum University hospitals). Four members of the family presented with progressive difficulty in initiating movement, resting tremors and shuffling gait. A provisional diagnosis of early onset Parkinson's disease (EOPD) was made and genetic workup revealed a mutation in the PINK1 gene. Symptoms started as early as 9 years in one patient and at 1–-14 years in others. All family members developed motor symptoms including bradykinesia, resting tremors, postural instability and rigidity. Two patients have severe non motor symptoms including depression, cognitive impairment, and sleep disorders. Two patients had severe side effects to levodopa and in spite of being given small frequent doses they are still suffering from severe rigidity and bradykinesia and getting severe dyskinesia at the onset of medication.
Conclusion and recommendation: For the last 5 years the patients have shown progression in their symptoms and have started developing impaired cognitive functions. Is there any management option that gives hope for these patients to improve their quality life?

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Movement Disorders 1
Neuropsychological assessment in a Chilean cohort of patients with Parkinson's disease

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Background: Cognitive impairment is a great challenge in patients with Parkinson's Disease (PD). We present a neuropsychological assessment in a PD population using a standardized battery based on Movement disorders Society recommendations.
Patients and methods: We evaluated extensively different cognitive domains (attention, memory, language, executive functions and processing speed) and depressive symptoms in a prospective cohort of PD patients in control in our center, using a standardized neuropsychological battery.
Results: Twenty five patients were included. Age (mean+/−SD) was 60.8 ± 11.7 years, 28% were females. PD evolution was between 2 and 15 years. Alterations in at least one neuropsychological test were present in 100% of subjects. Dementia was diagnosed in 18% of patients, whereas mild cognitive impairment was present in 36% of the cases. Dementia was present in 60% of those older than 70 years. MoCA test was affected in 80% of cases (Z: −2.6 ± 1.9). AVLT (Episodic auditive verbal memory) was altered in 84% of subjects (Z: −3,8 ± 2.0). BVMT (Visuospatial memory) was affected in 44% of patients (Z: −1.4 ± 0.9). Boston test (semantic memory) was altered in 40 subjects (Z:−1.1 ± 1.2). TMT-A (visual attention) was altered in 32% of cases (Z: 0.6 ± 2.4). Digit Span (Auditive attention) was affected in 32% of patients (Z: −0.4 ± 1.8). SDMT (Processing speed) was altered in 24% of cases (Z:-0.4 ± 1.0). FAS (cognitive alternancy) was affected in 28% of subjects (Z:−0.5 ± 1.4). The tower test of D-KEFS was altered in 20%, (Z:−0,5 ± 1.4). Depressive symptoms were present in 53% of patients.
Discussion: We found a high percentage of cognitive alterations in our PD population. Both verbal and visual episodic memory were affected in 50% of patients. As previously reported, older patients were more affected by dementia.

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Impulsivity, but not dopamine agonists, explains severity of impulse control disorders in PD

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Background: Impulse control disorders (ICDs) are frequently found in patients with PD treated with dopamine agonists. Despite their name, their relation with impulsivity is not well established.
Objetive: To analyze the relationship between the presence and severity of impulse control disorders (ICDs) in PD and impulsivity.
Methods: Prospective study of 93 consecutive non-demented PD patients. ICDs were assessed using the Questionnaire for Impulsive-Compulsive Disorders (QUIP) and Minnesota Impulsive Disorders Interview (MIDI), and impulsivity using the Barratt Impulsiveness Scale (BIS-11) and commision errors in Conners' Continuous Performance Test II (CCPT).
Results: Thirty-five percent of patients (33/93) presented ICD. Younger age ($p < 0.05$) and dopamine agonists use ($p < 0.05$) were associated with presence of ICD but not to severity ($p = 0.61$ and $p = 0.72$ respectively). Impulsivity, either self-reported (BIS-11) or estimated by CCPT, did not differ between patients with ICD and without. However, in patients presenting ICD impulsivity measures correlated with ICD severity ($p < 0.01$ for both measures). There was no relation between impulsivity and dopaminergic medication use. Dose of dopamine agonist was not associated with ICD. Other PD medications were also not associated. Multivariate analysis confirmed significant association between ICD severity and impulsivity ($p < 0.001$).
Conclusion: Age and dopamine agonist were associated with the presence of ICD, but not with their severity. Conversely, impulsivity was not associated with ICD presence but correlated with severity. This suggests a double dissociation, showing impulsivity as an independent variable explaining ICD severity in patients on treatment with dopamine agonists.

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Movement Disorders 1
Comparison between odor discrimination, substantia nigra echogenicity and nigrostriatal dopaminergic activity measured by 18F.PR04 pet in Parkinsonian syndromes

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Objective: To evaluate the relationship between odor discrimination, substantia nigra echogenicity and nigrostriatal dopaminergic activity in patients with Parkinson's disease.
Background: Positron emission tomography for imaging dopaminergic pathways, transcranial substantia nigra (SN) echogenicity and odor discrimination are used as complementary tools for the diagnosis of PD. However there is a lack of information about the relationship between these three diagnostic methods for helping in the diagnosis of PD.
Methods: Twelve patients with PD according to established criteria were prospectively included. All subjects underwent a dynamic PET scan (Siemens mCT) for a duration of 2 h after bolus injection of 165 ± 15 MBq (mean ± SD) [18F]PR04.MZ. Data analysis using noninvasive Simplified Reference Tissue Model (SRTM) method and Cerebellum as reference was performed for estimation of binding potential in different brain regions. Odor discrimination was evaluated by using sniffing stick test (hyposmia < 7 detections) and transcranial sonography of the SN was also conducted. Pathological echogenicity was considered as SN area more than 0.20 cm^2.

Study was approved by local and governmental authorities and participants signed informed consent.
Results: Age (mean +/− SD) was 56.8 +/− 13.9 years. Substantia nigra hyperechogenicity was found in 10 patients (SN area: 28.8 +/− 14.2). Hyposmia was observed in 6 cases (7.5 +/− 3 odors). PET analyses showed dopaminergic depletion in 11 patients. Percentage of Posterior putamen depletion was 66.0 +/− 29.2. Nine subjects with Dopaminergic depletion also exhibited SN hyperechogenicity. There was no relationship between SN area or olfaction detection and magnitude of dopaminergic depletion.
Conclusions: Evaluation of SN echogenicity and dopaminergic activity by 18FPR04.MZ PET are valuable tools in the diagnosis of PD. Larger studies are required to confirm these findings. SUPPORTED BY FONDECYT No. 11130534.

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Movement Disorders 1
Prevalence, recognition and treatment of parkinsonism, dementia and depression in the assisted living population of Slovakia

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Background: Cognitive decline, Parkinsonism and depression are frequent accompaniments of aging. Prevalence of these disorders rises together with age. Among residents of assisted living facilities there is presumption of higher occurrence of these disorders.
Objective: To obtain a direct estimate of the prevalence of dementia, Parkinsonism and depression among residents of assisted living facilities in Slovakia and their rates of recognition and treatment, we carried out this study.
Patients and methods: 821 people living in assisted living facilities (mean age 75.9 years) were examined in order to review the occurrence of parkinsonism, cognitive deficit and depression. Patients were evaluated by neurologists professionally focused on movement disorders and dementias. We have obtained patient and/or Institutional Review Board (IRB) approval, as necessary.
Results: Out of the total there were 113 residents (13%) with Parkinsonism. 73.5% of Parkinsonian patients (83) suffered from dementia and 59% of these patients suffered from depression. The most frequent cause of Parkinsonism was Parkinson disease, (67 patients, 59.2%), followed by vascular Parkinsonism, (46 patients, 40.7%), Lewy body disease, drug induced Parkinsonism, frontotemporal dementia with Parkinsonism and Fahr disease. Only 51% of these patients were admitted in the assisted living facility with the diagnosis of Parkinsonism. Only 55% of Parkinsonian patients were treated with anti-Parkinson medications.
Conclusion: Parkinsonism is significantly under-diagnosed and under-treated in assisted living facilities setting. This finding emphasizes the need for accurate detection and treatment of movement disorders also in assisted living facilities and nursing homes.

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Movement Disorders 1
Dysfunctional motor and cognitive networks in Parkinson's disease detected by resting state fMRI

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Objective: The impact of dopaminergic treatment on motor and cognitive networks in Parkinson's Disease (PD) is not fully understood. In our study we focused on brain connectivity change derived from low frequency fluctuations of the blood oxygenation level-dependent signal. We used eigenvector centrality (EC) mapping which automatically detects all brain areas serving as strong communication hubs.
Participants and methods: Twenty-nine PD patients (aged 64.7 ± (SD) 8.0 years, PD duration 11.0 ± 3.6 years) were assessed with the Unified Parkinson's disease rating scale motor score (UPDRS-III) and the Montreal Cognitive Assessment (MoCA). Patients were instructed to watch a cross while lying motionless in the supine position for 10 min during 3 T-fMRI acquisition in off and on medication states. The EC analysis was conducted with Lipsia software (Leipzig, Germany). The 2nd level analysis of general connectivity was based on voxel-wise correlations of the EC maps with the UPDRS-III and MoCA, respectively ($P < 0.05$ corrected).
Results: The UPDRS-III score positively correlated with the EC values in the premotor, primary sensorimotor and associative parietal cortices bilaterally regardless of medication state ($r = 0.83$, $P < 0.001$). In addition, the EC value correlated positively with the MoCA score in the right prefrontal cortex ($r = 0.66$, $P < 0.001$) only in the off medication state.
Conclusions: Our data driven approach enabled an automatic separation of resting state networks of PD patients into motor and cognitive domains. While the motor network showed increased global connectivity with the worsening of motor symptoms, the lower global connectivity of the frontal cognitive network potentially limited cognitive performance. Supported by IGA-NT12282-5-2011; PRVOUK-P26/LF1/4.

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Movement Disorders 1
Anxiety and salivary cortisol changes in Parkinson's disease are related to global connectivity of the ventromedial prefrontal network

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Objective: Anxiety and chronic stress are common symptoms of Parkinson's disease (PD) influencing the quality of life. To identify brain regions associated with these symptoms we compared resting brain connectivity to actual anxiety and to the cortisol awakening response.
Participants and methods: Using the resting state-fMRI (3 T, TR = 2 s, 300 scans) we analyzed spontaneous low frequency blood oxygenation-level dependent signal fluctuations in 25 PD patients (66.7 ± (SD)7.4 years) in their OFF and ON medication states. The State-Trait Anxiety Inventory (STAI) was used to assess the severity of anxiety immediately before each fMRI session. Cortisol salivary levels were measured at awakening and 30, 60 and 90 min later. We calculated the area under the curve with respect to the ground (AUCg). To evaluate brain connectivity we used Eigenvector centrality (EC) mapping, which automatically detects all brain areas serving as strong communication hubs.
Results: The STAI state anxiety increased during OFF compared to ON condition ($p < 0.01$) and positively correlated with the EC values in the dorsal part of the right ventromedial prefrontal cortex (VMPFC) and in both caudates ($P < 0.05$ corrected). Cortisol salivary levels did not change significantly between the sessions, however, the AUCg showed a negative correlation with EC values in the ventral part of the VMPFC.
Conclusions: The state anxiety and the cortisol awakening response during OFF and ON sessions are accompanied by inverse changes of the functional connectivity in the distinct regions of the VMPFC network. Supported by IGA-NT12282-5-2011; PRVOUK-P26/LF1/4.

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