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ADVANCED PERSPECTIVES FOR THE DIAGNOSIS OF PARKINSON'S AND ALZHEIMER'S DISEASE THROUGH MACHINE LEARNING TECHNIQUES

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Background: A new paradigm called *Neurodegenerative Elderly Syndrome* proposed by Caligiore et al. (2022), conceives Parkinson's disease (PD) and Alzheimer's disease (AD) as different manifestations of a single disease at very early stages. Accordingly, in this study we aim to observe and compare PDs and ADs features importance at baseline, 12-months and 24-months of follow-up, to predict disease conversion and differentiate or classify both pathologies.
Methods: We analyzed 1378 Prodromal-PDs, 1219 PDs, 714 MCIs, 458 ADs and 1202 Healthy Controls from ADNI and PPMI databases. Machine Learning (ML) approaches like Random-Forest Classifier, Features Importance Analysis and K-means Clustering Analysis were used. A combination of six groups of features was selected: demographic, cognitive/neuropsychological, clinical, genetic, neuroimaging and neuropathological.
Results: Classification accuracy of 96%/86% and precision of 92%/87% were obtained for PDs/ADs respectively. At baseline and 24-months, age and gender showed higher importance in predicting PDs classification ($p<0.05$). At baseline, MMSE, MOCA, Clock Drawing Test, Digit Span Backward, and Boston Naming Test are more predictive in PDs classification than in ADs ($p<0.05$). Notably, F-Fluency test has a higher importance in predicting PDs classification than in ADs ($p<0.05$). Clinically, postural instability and right/left hand tremor are important only in predicting PDs categorization at baseline. Interestingly, at 12-months of follow-up, $APOE^{\varepsilon 3\text{-}\varepsilon 4/\varepsilon 4}$ demonstrated higher importance in PDs classification than in ADs.
Conclusions: To our knowledge, this is the first attempt to analyze and compare different AD and PD variables at baseline and during disease progression, based on non-invasively ML approaches. A possible practical implication for clinicians could be having predictive ML models of neurodegeneration curves to consult when PD and AD pathologies are clinically indistinguishable or very similar. Further studies are needed to validate our findings by testing and refining our predictive models on different multi and monocentric cohorts of patients.

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VALIDATION OF THE POLISH VERSION OF THE GASTROINTESTINAL DYSFUNCTION SCALE FOR PARKINSON'S DISEASE

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Background: Gastrointestinal dysfunction is a common non-motor manifestation of Parkinson's disease. Digestive tract symptoms are often debilitating for Parkinson's disease patients and may precede motor symptom onset by many years. Up till now, there was no scale available in Polish that thoroughly assessed gastrointestinal symptoms in patients with Parkinson's disease. The Gastrointestinal Dysfunction Scale for Parkinson's Disease (GIDS-PD) is a disease-specific self-report questionnaire, which is used to quantitatively assess three domains (constipation, bowel irritability, upper gastrointestinal symptoms) of gastrointestinal dysfunction in Parkinson's disease patients. We aim to validate the Polish translation of this scale and compare it to the English language version.
Methods: Developing a Polish translation of the GIDS-PD consisted of four steps: translating and then back-translating the scale, cognitive pretesting, field testing on a representative sample, and full clinimetric testing. The GIDS-PD was translated into Polish by two investigators, then back-translated by a separate team of investigators not involved in the original translation. 10 patients were enrolled for cognitive pretesting, and a subsequent 64 for field testing. 20 of the patients recruited for field testing completed the GIDS-PD a second time after 8-12 weeks.
Results: The GIDS-PD demonstrated overall good consistency (Cronbach's alpha of 0.74, ICC of 0.74). The constipation subscore exhibited good reliability, the bowel irritability subscore – moderate reliability, and the upper GI subscore – poor reliability. Upper GI symptoms seemed to be less severe and more varied in the Polish Parkinson's disease sample than in the English one. The GIDS-PD showed high internal validity and the total score was positively, moderately, and significantly associated with the MDS-NMS item J score.
Conclusions: We present a validated Polish translation of the GIDS-PD questionnaire. It is our recommendation that the GIDS-PD be used for both research purposes and everyday clinical practice in the Polish Parkinson's disease population.

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ASSOCIATION AND SPATIOTEMPORAL PROGRESSION PATTERNS OF DOPAMINE AVAILABILITY AND DEEP GRAY MATTER VOLUME IN PARKINSON'S DISEASE–RELATED COGNITIVE IMPAIRMENT

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Background: In Parkinson's disease (PD), cognitive impairment is common and linked to dopamine depletion and deep gray matter atrophy. We aimed to explore spatiotemporal progression patterns of striatal dopamine availability and regional brain volume based on cognitive status among PD patients.
Methods: A total of 168 patients with newly diagnosed non-medicated PD was enrolled in this study. Patients were classified into normal cognition (PD-NC), mild cognitive impairment (PD-MCI), and PD dementia (PDD) groups using neuropsychological tests. Brain magnetic resonance imaging and positron emission tomography with ^{18}F-N-(3-fluoropropyl)-2beta-carbon ethoxy-3beta-(4-iodophenyl) nortropane were performed. Standardized uptake value ratios (SUVRs) for regional dopamine availability and regional gray matter volumes via automated segmentation were obtained. These metrics were compared across cognitive status groups, and spatiotemporal progression patterns were analyzed using the Subtype and Stage Inference (SuStaIn) machine learning technique.
Results: Sixty-five patients had PD-NC, 65 had PD-MCI, and 38 had PDD. PD-MCI patients exhibited lower SUVRs in the caudate nucleus compared to PD-NC patients but higher SUVRs than those of PDD patients. PD-NC patients had higher thalamic SUVRs than both PD-MCI and PDD patients. Regional deep gray matter volumes of the caudate nucleus, thalamus, and hippocampus were more reduced in PD-MCI or PDD patients compared to PD-NC patients, and the SUVR of the caudate nucleus correlated with caudate volume. Hippocampal atrophy was the initial change influencing cognitive impairment. The reduced dopamine availability of the thalamus preceded reductions in volume across most deep gray matter regions.
Conclusions: Our finding underscores the association between decreased dopamine availability and volume of the caudate nucleus and thalamus with cognitive dysfunction in PD. The dopamine availability of the caudate nucleus and thalamus was reduced before the volume of the caudate