Updated Criteria for the Diagnostic Procedure for Parkinson's Disease Dementia on Level I and their Validity in Deep Brain Stimulation Cohort

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Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterized by a gradual and progressive onset of motor symptoms, including rigidity, bradykinesia, and resting tremors, which eventually extend to both motor and non-motor impairments (Postuma et al., 2015). Beyond these hallmark features, cognitive decline is a critical aspect of the disease trajectory, culminating in Parkinson's disease dementia (PDD) in a substantial subset of patients.

The diagnostic criteria for PDD, first formalized in 2006, were heavily influenced by frameworks established for Alzheimer's disease (AD) owing to the absence of PD-specific biomarkers that could facilitate a biologically grounded diagnostic system (Dubois et al., 2007; Emre et al., 2007). Although these criteria provided a valuable initial foundation, they lacked the specificity required to capture the distinct pathophysiological and cognitive features of PD-related dementia (Yamashita et al., 2023).

An important feature of the original criteria was the provision of an algorithm that allowed for flexibility in test selection (Dubois et al., 2007). Specifically, clinicians could choose between months reversed or seven backwards for attention assessment, lexical fluency or clock drawing for executive function evaluation, MMSE pentagons for visuospatial ability, and three-word recall for memory assessment. The availability of multiple operationalization options for PDD enhances the ability to examine the psychometric properties of the construct. Agreement across different criteria allows for the parallel computation of inter-rater reliability , which, in turn, facilitates the calculation of construct validity (Conway et al., 1995) further strengthening the diagnostic framework for PDD.

Subsequent advancements have introduced the concept of Parkinson's disease mild cognitive impairment (PD-MCI), refining the understanding of cognitive dysfunction in PD. The PD-MCI criteria, published in 2012, have propelled progress in diverse areas, enabling improvements in clinical characterization, identification of genetic correlates, therapeutic interventions, clinical trial design, and the assessment of progression risk to PDD (Aarsland et

al., 2021; Hoogland et al., 2017, 2019; Litvan et al., 2012).

Currently, efforts are focused on refining the PDD diagnostic framework to improve its consistency and applicability in both research and clinical contexts across multiple centers (Kulisevsky et al., 2024). Our prior investigations have underscored the importance of employing rigorous psychometric methodologies to differentiate PD-MCI from PDD, particularly given that a diagnosis of PDD remains a contraindication for deep brain stimulation (DBS) (Bezdicek et al., 2016; Deuschl et al., 2006).

The present study evaluates the diagnostic concordance between the original Level I PDD criteria, as established by the Movement Disorder Society (MDS) Task Force (Dubois et al., 2007; Emre et al., 2007) and the recently revised criteria (Kulisevsky et al., 2024) within a PD cohort selected for DBS. Specifically, we aimed to:

Compare diagnostic outcomes utilizing the original and revised Level I criteria and assess the agreement of revised Level I criteria with comprehensive neuropsychological assessment at Level II.Compare diagnostic outcomes using the original and revised Level I criteria.

By addressing these objectives, this study seeks to validate the revised PDD criteria and evaluate their relevance in the context of DBS eligibility, thereby contributing to the refinement of cognitive assessment protocols in PD.

Methods

Participants

This study retrospectively analyzed clinical data from patients diagnosed with idiopathic PD by a movement disorder specialist according to the MDS Clinical Diagnostic Criteria for PD (Postuma et al., 2015) Clinical records spanning January 2014 to December 2023 were examined. All participants underwent neuropsychological evaluations conducted by a trained clinical psychologist as part of standard preoperative cognitive assessments for DBS eligibility at the General University Hospital in Prague.

Ethical approval for the study protocol was obtained from the Ethics Committee of the General University Hospital in Prague. Informed consent was secured from all patients prior to their neuropsychological assessments, in adherence to ethical research guidelines.

Neuropsychological Assessment

Cognitive performance was evaluated at Level I using the Mini-Mental State Examination (MMSE) (Folstein et al., 1975; Stepankova et al., 2015) and the Montreal Cognitive Assessment (MoCA) (Kopecek et al., 2016; Nasreddine et al., 2005), both of which provide measures of global cognitive functioning.

A comprehensive neuropsychological battery was administered in accordance with the Level II criteria for Parkinson's Disease Mild Cognitive Impairment (PD-MCI), as outlined by the MDS Task Force (Litvan et al., 2012). The methodology, including the use of a regression-based normative scoring approach, has been detailed in a prior study (Bezdicek et al., 2017). The neuropsychological assessment covered five cognitive domains, each evaluated through specific tests as follows: attention and working memory assessed using Trail Making Test Part A (TMT-A) (Bezdicek et al., 2012; Reitan, 2004), Prague Stroop Test – Dots (PST-D) (Bezdíček et al., 2021), Letter Number Sequencing (LNS) (Wechsler, 1997), WAIS Digit Span Backward (WAIS DSB) (Wechsler, 1997), and WAIS Corsi Block Backward (WAIS CB) (Wechsler, 1997); executive function evaluated via the Tower of London (ToL) ("Specific Impairments of Planning," 1982), Categorical Verbal Fluency (CF) (Benton et al., 1989), Trail Making Test Part B (TMT-B) (Reitan, 2004), subtests from the Prague Stroop Test – Words (PST-W) and Colors (PST-C) (Bezdíček et al., 2021); language measured with the WAIS Similarities subtest (Wechsler, 1997) and the Boston Naming Test (BNT-60) (Kaplan et al., 1983); memory examined using the Rey Auditory Verbal Learning Test (RAVLT) (Frydrychová et al., 2018; Rey, 1964) for immediate and delayed recall (including List B and recognition trials), and the Brief Visual Memory Test–Revised (BVMTR) (Benedict, 1997; Havlík et al., 2020), including delayed recall and forced choice recognition; visuospatial function assessed through the Judgment of Line Orientation Test (JoLO) (Benton et al., 1983), Clock Drawing Test (CLOX) (Royall et al., 1998), and the Grooved Pegboard Test (GPT) (Klove, 1963).

In addition to the core cognitive assessments, tasks such as the Clock Drawing Test (CDT) and Letter Fluency tasks were included to capture domain-specific impairments. The classification of Parkinson's Disease Dementia (PDD) based on Level I criteria was

determined using established scoring thresholds from Dubois et al. (Dubois et al., 2007) with corresponding MoCA equivalents.

To assess functional impairment, the Functional Activities Questionnaire (FAQ)(Bezdicek et al., 2011; Pfeffer et al., 1982) was administered. Additionally, neuropsychiatric status was evaluated using the Beck Depression Inventory-II (BDI) (Beck et al., 1996; Ciharova et al., 2020) and State-Trait Anxiety Inventory (STAI) (Mullner et al., 1980; Spielberger et al., 1983). Psychotic symptoms were assessed through structured psychiatric interviews conducted by a trained psychiatrist.

Insert Table

Operationalization of Parkinson's Disease Dementia

In this study, we applied three distinct sets of diagnostic criteria for PDD at Level I. The first set was based on the original framework (Dubois et al., 2007), which utilized the Mini-Mental State Examination (MMSE) as a global cognitive screening tool, supplemented by assessments of attention, executive function, visuospatial abilities, and memory. The second set of criteria was drawn from the recent call for change of dementia diagnostic guidelines (Kulisevsky et al., 2024), which advocate for more sensitive cognitive domain assessments in the context of Parkinson's disease (PD). This updated approach incorporated specific items from the Montreal Cognitive Assessment (MoCA) to better detect PD-related dementia. The third approach applied the Czech version of the shortened Montreal Cognitive Assessment (sMoCA) (Bezdicek et al., 2020), a time-efficient modification designed to ascertain whether equivalent cognitive impairments could be reliably identified using a reduced testing protocol. Lastly, the fourth approach followed the Level II battery protocol (Bezdicek et al., 2017), which is commonly used in the evaluation of PD-MCI.

For each of these diagnostic approaches, we applied two operationalization strategies based on deficits in Instrumental Activities of Daily Living (IADL). First, we utilized FAQ item 9, which corresponds to the pill questionnaire from the original criteria (Dubois et al., 2007). Second, we applied the entire Functional Activities Questionnaire (FAQ), employing a cut-off score of 7 points or higher as suggested in the call for change (Kulisevsky et al., 2024). These methodologies resulted in a total of 68 operationalisations, which were distributed

across different diagnostic criteria: 4 for MMSE, 60 for MoCA, 2 for sMoCA, and 2 for the Level II battery.

To facilitate a clear and structured comparison of these diagnostic frameworks, a detailed table summarizing the components, scoring thresholds, and applicability of each diagnostic criterion is provided below.

Inser Table

Results

We described continuous variables using mean, standard deviation, median, minimum, and maximum values, while categorical variables were summarized by the number of patients in each category. As presented in Table 3, we reported the prevalence of PDD according to each set of diagnostic criteria. Specifically, the strictest criteria were found in the sMoCA, which was characterized by a lower threshold for cognitive impairment.

For each of the 68 operationalisations, PDD diagnoses were generated for each patient, and the prevalence of PDD in the entire sample was estimated as a percentage based on the given criteria. This approach allowed for a detailed comparison of the different diagnostic frameworks. Table 3 displays the estimated prevalence rates of probable PDD across different sets of diagnostic criteria/To enhance clarity, the results presented in Table 3 offer a detailed summary of these operationalisations, showing how variations in diagnostic criteria lead to different estimates of PDD prevalence:

Insert table 3

These findings underscore the variability in prevalence estimates depending on the diagnostic framework employed. The stricter sMoCA criteria identified the largest cohort of individuals with PDD, while the MMSE-based criteria, identified the least patients. This suggests that different operationalisations of cognitive deficits and functional impairments may yield differing estimates of PDD prevalence within the same sample.

To enhance clarity, the results presented in Table 3 offer a detailed summary of these operationalisations, showing how variations in diagnostic criteria lead to different estimates of PDD prevalence.

Discussion

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