Screening Mild and Major Neurocognitive Disorders in Parkinson’s Disease

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Introduction. Among the nonmotor features of Parkinson’s disease (PD), cognitive impairment is one of the most troublesome problems. New diagnostic criteria for mild and major neurocognitive disorder (NCD) in PD were established by Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5). The aim of our study was to establish the diagnostic accuracy of widely used screening tests for NCD in PD. Methods. Within the scope of our study we evaluated the sensitivity and specificity of different neuropsychological tests (Addenbrooke’s Cognitive Examination (ACE), Mattis Dementia Rating Scale (MDRS), Mini Mental State Examination (MMSE), and Montreal Cognitive Assessment (MoCA)) in 370 PD patients without depression. Results. MoCA and ACE feature the finest diagnostic accuracy for detecting mild cognitive disorder in PD (DSM-5) at the cut-off scores of 23.5 and 83.5 points, respectively. The diagnostic accuracy of these tests was 0.859 (95% CI: 0.818–0.894, MoCA) and 0.820 (95% CI: 0.774–0.859, ACE). In the detection of major NCD (DSM-5), MoCA and MDRS tests exhibited the best diagnostic accuracy at the cut-off scores of 20.5 and 132.5 points, respectively. The diagnostic accuracy of these tests was 0.863 (95% CI: 0.823–0.897, MoCA) and 0.830 (95% CI: 0.785–0.869, MDRS). Conclusion. Our study demonstrated that the MoCA may be the most suitable test for detecting mild and major NCD in PD.

1. Introduction

Parkinson’s disease (PD) is a neurodegenerative disorder characterized by both motor and nonmotor symptoms including depression, fatigue, and autonomic problems. Among nonmotor features, cognitive impairment has one of the most serious consequences by diminishing the quality of life and requiring an increase in caregiver’s burden [1–4]. Based on the findings of long-term follow-up studies, neurocognitive impairment unavoidably evolves by disease progression [5, 6]. According to some recent studies, the prevalence of dementia in PD is approximately 20–40% [7]; furthermore, patients with PD have a sixfold risk to develop dementia compared to healthy controls [8].

Although detection of neurocognitive impairment is of the utmost clinical importance, this task is difficult to accurately perform [9]. One of the problems is the heterogeneity of definitions. Previously, the Movement Disorders Society (MDS) Task Force created definitions for dementia in PD (PDD) [9] and mild cognitive impairment in PD (PD-MCI) [10–12]. Moreover, the PD-MCI diagnosis can also be based on two assessment levels: abbreviated (Level I) and comprehensive (Level II) [10–12].

Although the MDS criteria for PDD and PD-MCI have been highly recognized by movement disorder specialists, there are some countries where the diagnosis of cognitive impairment has to be determined by psychiatrists. Until the publication of the most recent version of Diagnostic and Statistical Manual of Mental Disorders (5th edition, DSM-5) in 2013 [13], the diagnosis of PD-MCI was impossible from psychiatric point of view due to the lack of appropriate definitions. According to DSM-5, minor and major neurocognitive disorders (NCD) in PD may be diagnosed which can be considered as the equivalent versions for PD-MCI and PDD,
Comparing to the previous version (DSM 4th edition text revision, DSM-IVTR), the establishment of mild and major NCD in PD is an important enhancement, because previously only the dementia in PD was defined. Therefore, a less severe level of cognitive impairment could not be coded and diagnosed by DSM-4TR. The newly recognized term of mild NCD due to PD may facilitate research and change clinical practice (e.g., patient selection for deep brain stimulation surgery).

According to DSM-5 mild and major NCD may be diagnosed if evidence of significant or modest cognitive decline from a previous level of performance in one or more cognitive domains can be established, respectively. This evidence must be supported by both the concern of the individual, a knowledgeable informant, or the examining clinician noting a significant decline in cognitive function, and a substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment. In the case of major NCD the cognitive deficits interfere with independence in everyday activities, whereas in minor NCD the cognitive deficits do not interfere with capacity for independence in everyday activities, but greater effort, compensatory strategies, or accommodation may be required.

The problem with the establishment of diagnosis is the lack of appropriate clinical screening testing. An ideal screening test should be brief, fast, and appropriately sensitive and specific for detecting subjects possessing characteristics of cognitive impairment [14].

Detection of minor and major NCD in Parkinson's disease is an important task, because cognitive decline is a frequent and important exclusion criteria for deep brain stimulator implantation [15]. Therefore, the necessity of proper screening for cognitive impairment in PD is highly encouraged in clinical practice.

Currently, Mini Mental State Examination (MMSE) is the most commonly used tool for screening cognitive abilities in Hungary [16, 17]. Although it can evaluate orientation, memory, visual abilities, attention and calculation, language, writing, reading, and constructive capabilities, it is not sensitive enough for identifying frontal and executive deficits, and visuospatial dysfunctions. Moreover, it has a limited poor sensitivity for detecting dementia in early stages [18, 19] and it is also unable to differentiate between major types of dementia if applied alone [20]. Although MMSE has been translated and validated into many languages and used in many countries [21], it remains unsuitable for judging eligibility for deep brain stimulation of the subthalamic nuclei (STN DBS) [14, 22]. Best cut-off value for MMSE is 26 points with the sensitivity of 79.9% and specificity of 74.0% for detecting PDD [14], but for PD-MCI it remains unsuitable for screening [23].

Therefore, other dementia screening tests are needed in clinical practice. Although Addenbrooke's Cognitive Examination (ACE) is able to detect early stages of dementia and differentiate some subtypes, its applicability is limited in PD by the lack of widely applicable normative data [14]. ACE also evaluates the major domains of PDD such as orientation, attention and mental flexibility, episodic and semantic memory, verbal fluency, phonemic and semantic category, aphasia tasks, and visuospatial and constructional ability. However, ACE was initially developed by Mathuranath et al. for differentiating between Alzheimer's disease (AD) and frontotemporal dementia (FTD) [24]. The maximum score on ACE is 100 points. ACE was translated into many languages including Hungarian, but it has mainly been tested in AD and not in PD. ACE was validated in PD in some countries [25]. It has limited (<80%) specificity for detecting PDD (the best cut-off score identifying PDD was 80 points, sensitivity = 74.0%, specificity = 78.1%, positive predictive value = 67.42%, negative predictive value = 83.42%) [14]. Therefore, both the original and the revised version of ACE (ACE-R) must be used cautiously as a screening tool for PD-MCI, with results largely influenced by its fluency subdomain score and patient education levels [26, 27].

Mattis Dementia Rating Scale (MDRS) is also a widely used screening instrument for evaluating dementia. It can measure the domains of attention, initiation and perseveration, construction, conceptualization, and memory. MDRS seems to be sensitive for mediotemporal and frontal pathology [28, 29]. Respectfully, the authors generally agree it is one of the most frequently used screening tools for judging cognitive impairment in European DBS centers [30, 31]. Moreover, it is a recommended scale for PD-MCI and PD-D according to MDS criteria at Level I [II, 32]. Its maximum obtainable score is 144 points, whereas the cut-off scores for dementia in French and Spanish PD population was 130 and 123 points, respectively [30, 33]. For the Hungarian version, MDRS had a good sensitivity and specificity for detecting PDD (sensitivity = 89.8%, specificity = 98.3%) using the cut-off score of 125 point [14]. Because the administration of MDRS requires a lengthy period (approximately 30–45 minutes) in clinical setting, MDRS is not an appropriate tool to identify dementia in PD in all occasions.

Montreal Cognitive Assessment (MoCA) was developed as a brief, 10-minute bedside assessment tool for detection of mild cognitive impairment and dementia in AD. It measures 7 domains of cognitive functioning, including visuospatial/executive functions, naming, memory, attention, language, abstraction, and orientation [34]. Comparing to MMSE, MoCA is a more sensitive tool for testing executive, visuospatial functions and attention, which areas are most often impaired in PD. MoCA also has high interrater, test-retest reliability [35], and good discriminant validity for assessing dementia in PD [36, 37]. Further studies demonstrate that MoCA is able to assess broader cognitive domains, and it has higher sensitivity for detecting mild cognitive impairment and dementia in PD [38, 39]. Larner demonstrated better sensitivity and specificity of ACE-R and MoCA over MMSE by comparison [40]. MoCA has been translated and validated into several languages [41–44] and has several alternative forms to overcome the potential practice effects [45, 46].

With reference to the authors' awareness none of the above mentioned screening tools were validated against the diagnostic criteria of DSM-5. Therefore, the aim of our study was to establish the diagnostic accuracy of Montreal
Cognitive Assessment (version 7.2) as compared to other widely used screening tests for detecting mild and major neurocognitive disorder in a large sample of Hungarian PD patients.

2. Methods

2.1. Participants. Four hundred and seventy-two consecutive PD patients treated at Department of Neurology, University of Pécs, were recruited for this study. Each patient fulfilled the clinical diagnostic criteria for idiopathic PD [47]. All of the subjects provided a written informed consent according to the approval of the Regional Ethical Board of University of Pécs.

History of cerebrovascular disease, alcoholism, or other conditions known to impair mental status besides PD served as exclusion criteria for participation. Each patient had a routine brain MRI (or brain CT if MRI was contraindicated). Patients with focal abnormalities on neuroimaging studies, abnormalities in thyroid hormone levels, or uncompensated systemic diseases (i.e., diabetes, hypertension, heart failure) were also excluded.

2.2. Patient Evaluation. Patients were evaluated using Hungarian versions of Lille Apathy Scale (LARS) [48], Montgomery-Asberg Depression Rating Scale (MADRS) [49], MMSE [14, 16], ACE [24, 50], MDRS [28], and MoCA [44]. Severity of the Parkinsonian symptoms was assessed by the Hoehn & Yahr (HYS) [51] and the Hungarian validated version of Movement Disorders Society Unified Parkinson’s Disease Rating Scales (MDS-UPDRS) [52, 53]. The administering of the applied tests was alternated one from the other to diminish the potential of sequential effect.

Patients suffering from depression were excluded from clinical investigation (score > 18 on MADRS and/or fulfilling the criteria of DSM-5 for depression) to minimize the impact of affective syndromes on cognitive performance. Subsequently, the nondepressed PD patients were divided into three groups based on the fulfillment of the clinical diagnostic criteria for minor and major NCD in PD: patients with major neurocognitive disorder (major NCD group), patients with minor neurocognitive disorder (minor NCD group), and patients without either minor or major neurocognitive disorder (normal PD group) [13]. To increase reliability, a single experienced investigator (NK) categorized each patient into normal, minor NCD, and major NCD groups.

2.3. Data Analysis. Statistical analyses were performed by The R Project for Statistical Computing (Windows version 3.1.2) [54]. Because most data did not follow the normal distribution, nonparametric tests (Kruskal-Wallis tests) were applied. Since HYS represents an ordinal scale, Chi-square test was applied for analyses involving HYS. The level of significance was set at 0.05.

To measure diagnostic accuracy for neurocognitive batteries, Receiver Operating Characteristic (ROC) curve analysis was obtained [55] to measure sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value, negative predictive value, and diagnostic accuracy.

Because the ideal cut-off is one which selects an immense amount of disease (high sensitivity) but has very few false positives (high specificity), we chose the best cut-off point for balancing the sensitivity and specificity by identifying the point on the curve closest to the (0, 1) point.

3. Results

One hundred and two patients expressed a coexistent depression; therefore, they were excluded from further analyses. Therefore, the data of 370 patients were analyzed subsequently. Out of the 370 evaluated subjects, 257 had normal cognitive profile, 60 had mild neurocognitive disorder, and 53 had major neurocognitive disorder in PD according to DSM-5 classification. The comparison of the demographic and clinical characteristics between normal, mild NC, and major NC groups is presented in Table 1.

Fulfilling our expectations, all the examined dementia screening scales (MDRS, MoCA, MMSE, and ACE) demonstrated significant differences between the normal, mild NC, and major NC groups (Table 1).

Based on ROC analysis, MoCA and ACE had the best diagnostic accuracy for detecting mild NCD in PD at the cut-off scores of 23.5 and 83.5 points, respectively (Table 2, Figure 1). The diagnostic accuracy of these tests was 0.859 (95% confidence interval—CI: 0.818–0.894, MoCA) and 0.820 (95% CI: 0.774–0.859, ACE) meaning 85.9% and 82.0% of true positive and true negative cases are identified. The other variables describing the diagnostic accuracy (specificity, sensitivity, positive and negative predictive values, and positive and negative likelihood ratios) are presented in Table 2 with their 95% CI values. Area under the curve (AUC) values are demonstrated in Figure 1.

For detecting major NCD, MoCA and MDRS tests exhibited the highest diagnostic accuracy at the cut-off scores of 20.5 and 132.5 points, respectively (Table 3 and Figure 2). The diagnostic accuracy of these tests was 0.863 (95% CI: 0.823–0.897, MoCA) and 0.830 (95% CI: 0.785–0.869, MDRS) meaning 86.3% and 83.0% of true positive and true negative cases are identified. The other variables describing the diagnostic accuracy (specificity, sensitivity, positive and negative predictive values, and positive and negative likelihood ratios) are presented in Table 3 with their 95% CI values. AUC values are demonstrated in Figure 2.

4. Discussion

Screening for NCD in Parkinson’s disease is an important clinical necessity for establishing diagnosis and initiating effective and proper treatment. In differentiating between normal cognition from impaired cognitive abilities an easily applicable, reproducible, and validated test battery with high diagnostic accuracy is needed. The aim of our study was to establish the diagnostic accuracy of widely used screening tests for detecting mild and major neurocognitive disorder in PD.
Table 1: Demographic, Parkinson’s disease-(PD-)-related and neurocognitive data of the study population.

<table>
<thead>
<tr>
<th></th>
<th>Normal cognition (n = 257)</th>
<th>Mild neurocognitivedisorder due to PD (n = 60)</th>
<th>Major neurocognitivedisorder due to PD (n = 53)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median 65.4</td>
<td>Percentile 25 53.7</td>
<td>Percentile 75 73.3</td>
<td>Mean 63.7</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>Median 57.6</td>
<td>Percentile 25 48.6</td>
<td>Percentile 75 64.1</td>
<td>Mean 52.0</td>
</tr>
<tr>
<td>Education (years)</td>
<td>Median 12.0</td>
<td>Percentile 25 10.0</td>
<td>Percentile 75 16.0</td>
<td>Mean 12.9</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>51M/157F</td>
<td>12M/48F</td>
<td>9M/39F</td>
<td>0.268</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>Median 6.0</td>
<td>Percentile 25 0.00</td>
<td>Percentile 75 12.0</td>
<td>Mean 7.0</td>
</tr>
<tr>
<td>LED (mg)</td>
<td>Median 400</td>
<td>Percentile 25 143</td>
<td>Percentile 75 560</td>
<td>Mean 499.0</td>
</tr>
<tr>
<td>MDS-UPDRS Part 1</td>
<td>Median 12.0</td>
<td>Percentile 25 9.0</td>
<td>Percentile 75 17.0</td>
<td>Mean 13.7</td>
</tr>
<tr>
<td>MDS-UPDRS Part 2</td>
<td>Median 13.0</td>
<td>Percentile 25 7.0</td>
<td>Percentile 75 19.0</td>
<td>Mean 13.7</td>
</tr>
<tr>
<td>MDS-UPDRS Part 3</td>
<td>Median 37.0</td>
<td>Percentile 25 28.0</td>
<td>Percentile 75 42.0</td>
<td>Mean 37.8</td>
</tr>
</tbody>
</table>
| Parkinson’s disease was defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition criteria. p values are calculated by Kruskal–Wallis test with the exception of Hoehn & Yahr Scale and sex where Chi-square tests were utilized. ACE: Addenbrooke’s Cognitive Examination; F: females; LARS: Lille’s Apathy Scale; M: males; MADRS: Montgomery-Asberg Depression Rating Scale; MDRS: Mattis Dementia Rating Scale; MDS-UPDRS: Movement Disorders Society’s Unified Parkinson’s Disease Rating Scale; MMSE: Mini Mental State Examination; MoCA: Montreal Cognitive Assessment.
Table 2: Diagnostic accuracy of screening tests for detecting mild neurocognitive disorder due to Parkinson's disease.

<table>
<thead>
<tr>
<th></th>
<th>MoCA</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>ACE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>Diagnostic accuracy</th>
<th>MMSE</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>MDRS</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
</tr>
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<tbody>
<tr>
<td><strong>Best cut-off score</strong></td>
<td>23.5</td>
<td>85.5</td>
<td></td>
<td></td>
<td>275</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>0.915</td>
<td>0.848</td>
<td>0.958</td>
<td>0.871</td>
<td>0.790</td>
<td>0.930</td>
<td></td>
<td></td>
<td>0.602</td>
<td>0.540</td>
<td></td>
<td>0.939</td>
<td>0.873</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>0.831</td>
<td>0.777</td>
<td>0.877</td>
<td>0.797</td>
<td>0.741</td>
<td>0.847</td>
<td></td>
<td></td>
<td>0.706</td>
<td>0.652</td>
<td></td>
<td>0.723</td>
<td>0.670</td>
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<tr>
<td><strong>Positive predictive value</strong></td>
<td>0.733</td>
<td>0.653</td>
<td>0.803</td>
<td>0.647</td>
<td>0.568</td>
<td>0.727</td>
<td></td>
<td></td>
<td>0.623</td>
<td>0.534</td>
<td></td>
<td>0.707</td>
<td>0.550</td>
</tr>
<tr>
<td><strong>Negative predictive value</strong></td>
<td>0.950</td>
<td>0.911</td>
<td>0.976</td>
<td>0.936</td>
<td>0.892</td>
<td>0.965</td>
<td></td>
<td></td>
<td>0.650</td>
<td>0.598</td>
<td></td>
<td>0.793</td>
<td>0.962</td>
</tr>
<tr>
<td><strong>Diagnostic accuracy</strong></td>
<td>0.859</td>
<td>0.818</td>
<td>0.894</td>
<td>0.820</td>
<td>0.774</td>
<td>0.859</td>
<td></td>
<td></td>
<td>0.624</td>
<td>0.712</td>
<td></td>
<td>0.738</td>
<td>0.700</td>
</tr>
<tr>
<td><strong>Likelihood ratio of a positive test</strong></td>
<td>5.417</td>
<td>4.047</td>
<td>7.250</td>
<td>4.302</td>
<td>3.305</td>
<td>5.599</td>
<td></td>
<td></td>
<td>2.575</td>
<td>1.804</td>
<td></td>
<td>3.125</td>
<td>2.843</td>
</tr>
<tr>
<td><strong>Likelihood ratio of a negative test</strong></td>
<td>0.103</td>
<td>0.037</td>
<td>0.187</td>
<td>0.161</td>
<td>0.097</td>
<td>0.269</td>
<td></td>
<td></td>
<td>0.312</td>
<td>0.259</td>
<td></td>
<td>0.484</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Mild neurocognitive disorder because Parkinson’s disease was defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition criteria.

ACE: Addenbrooke’s Cognitive Examination; CI: confidence interval; MDRS: Mattis Dementia Rating Scale; MMSE: Mini Mental State Examination; MoCA: Montreal Cognitive Assessment.
### Table 3: Diagnostic accuracy of screening tests for detecting major neurocognitive disorder due to Parkinson’s disease.

<table>
<thead>
<tr>
<th></th>
<th>MoCA</th>
<th>ACE</th>
<th>MMSE</th>
<th>MDRS</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Estimation</td>
<td>Lower 95% CI</td>
<td>Upper 95% CI</td>
<td>Lower 95% CI</td>
</tr>
<tr>
<td><strong>Best cut-off score</strong></td>
<td>20.5</td>
<td>80.5</td>
<td>26.5</td>
<td>132.5</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>0.921</td>
<td>0.860</td>
<td>0.962</td>
<td>0.869</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>0.801</td>
<td>0.738</td>
<td>0.859</td>
<td>0.790</td>
</tr>
<tr>
<td><strong>Positive predictive value</strong></td>
<td>0.750</td>
<td>0.674</td>
<td>0.816</td>
<td>0.640</td>
</tr>
<tr>
<td><strong>Negative predictive value</strong></td>
<td>0.953</td>
<td>0.917</td>
<td>0.980</td>
<td>0.921</td>
</tr>
<tr>
<td><strong>Diagnostic accuracy</strong></td>
<td>0.863</td>
<td>0.823</td>
<td>0.897</td>
<td>0.814</td>
</tr>
<tr>
<td><strong>Likelihood ratio of a negative test</strong></td>
<td>0.095</td>
<td>0.052</td>
<td>0.172</td>
<td>0.162</td>
</tr>
</tbody>
</table>

Major neurocognitive disorder due to Parkinson’s disease was defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition criteria.

ACE: Addenbrooke’s Cognitive Examination; CI: confidence interval; MDRS: Mattis Dementia Rating Scale; MMSE: Mini Mental State Examination; MoCA: Montreal Cognitive Assessment.
Although some major demographic and PD-related properties (e.g., education, sex, disease duration, and anti-Parkinson medication expressed in levodopa equivalent dosage and severity of depressive symptom measured by MADRS) were comparable, patients with either minor or major neurocognitive disorder were older and had higher age at disease onset and more severe Parkinsonian symptoms (MDS-UPDRS and HYS). This is not a surprising factor, because age and age of disease onset are significant factors for developing major neurocognitive disorder, and the presence of cognitive impairment is associated with more severe gait and postural instability resulting in higher HYS and MDS-UPDRS Part 3 (Motor Examination) values [56].

To the best of the author's knowledge, this study is the first validating the most popular screening tests against the recently developed mild and major NCD due to PD established by the DSM-5. Based on our results, MoCA had better diagnostic accuracy for detecting mild NCD in PD based on the DSM-5 criteria. Scores <139.5 on MDRS or <83.5 on ACE or <23.5 on MoCA can suggest the presence of mild NCD in PD (DSM-5). Recent studies revealed similar cut-off values for MDRS. Villeneuve et al. suggested a normality cut-off of 138 on the MDRS having the sensitivity of 72% and specificity of 86% with a correct classification of 80% for detecting PD-MCI (MDS Task Force criteria) [57]. One of the limitations of their study was, however, the relatively low number of PD patients involved (n = 40). Pirogovsky et al. published a different study on MDRS having the sample of 30 patients diagnosed with PD-MCI based on Level II MDS criteria and 68 PD patients with normal cognition. They suggested that a total score of ≤139 for screening purposes yielded a better balance between sensitivity (77%) and specificity (63%) [58].

Previously our team also validated MDRS against the PDD criteria (MDS Task Force criteria) [14]. In this former study we suggested the usage of 125 points as a cut-off score for diagnosing PDD. However, in the present study we recommended the cut-off of 132.5 points to diagnose major NCD in PD. This apparent difference might be due to the larger sample size (370 versus 73), the difference between the applied diagnostic criteria (major NCD according to DSM-5 versus PDD established by MDS Task Force), and the discrepancies between the mean educational levels (11.9 ± 4.4 versus 13.0 ± 3.8 years).

Although MMSE is still one of the most frequently used screening tests, it is generally considered unsuitable for reliable NCD identification in PD [22]. Despite the MoCA and MMSE scores which can be converted [59], MoCA, MDRS, and ACE tests appear to be generally superior for screening NCD in PD [14, 23, 37, 57]. PD subjects with normal range MMSE but abnormal MoCA scores had evidence of caudate nucleus dopaminergic denervation and mild cognitive changes, predominantly in executive function [60]. PD patients with borderline cognitive impairment have impairments in their decisional capacity. The MoCA may be useful to identify the patients at risk of impaired capacity [61].
The Parkinson Study Group Cognitive/Psychiatric Working Group recommended MoCA as a minimum cognitive screening measure in clinical trials of PD where cognitive performance is not the primary outcome measure [22]. The commonly recommended cut-off screening score for dementia of 26 on the MoCA is too high for PD patients and most studies suggest the utilization 23-24 points for cut-off [62].

However, the application of MoCA in PD-MCI remains controversial. A recent study [63] demonstrated that MoCA is suitable for screening large population for Parkinson's disease dementia (PDD, according to MDS Task Force criteria [9]). On the contrary, other studies showed that when decline from estimated premorbid levels was considered evidence of cognitive impairment (Level 2 criteria for PD-MCI), both MoCA and MMSE had poor diagnostic accuracy for PD-MCI (65.3%) [60]. At the lowest cut-off levels that provided at least 80% sensitivity, specificity was low (44%) for the Montreal Cognitive Assessment [23]. Therefore the authors concluded that MoCA may be able to preferentially detect executive dysfunction compared to the MMSE, but the MoCA has limited diagnostic accuracy for PD-MCI and should not solely be used to substantiate this diagnosis.

The MoCA may be more sensitive than the MMSE in detecting early baseline and longitudinal cognitive impairment in PD. Based on the analysis of 95 patients, a MoCA score of ≤26 provided a sensitivity of 93.1% for the diagnosis of PD-MCI [64]. In the longitudinal cohort, baseline MoCA was useful in predicting cognitive decline over 2 years [64]. A baseline MoCA ≤26 was highly predictive of progressive cognitive decline (HR 3.47, 95% CI 2.38–5.07; p < 0.01) over 2 years. This finding was also confirmed by another study [65]. The longitudinal data from 155 patients with PD over 18 months showed significant reductions in MoCA scores, but not in MMSE scores, with 21.3% of patients moving from normal cognition to MCI and 4.5% moving from MCI to dementia.

5. Conclusions

DSM-5 criteria for diagnosing mild and major NCD in PD are clinically feasible. Although most popular screening tests including MoCA, MDRS, and ACE are proven useful for screening patients, in the risk population the accurate diagnosis should be based on appropriate neuropsychological evaluation.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ACE</td>
<td>Addenbrooke’s Cognitive Examination</td>
</tr>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>AUC</td>
<td>Area under curve</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>DSM-5</td>
<td>Diagnostic and Statistical Manual of Mental Disorders 5th edition</td>
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<tr>
<td>HYS</td>
<td>Hoehn &amp; Yahr Scale</td>
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<tr>
<td>LARS</td>
<td>Lille’s Apathy Scale</td>
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<td>Neurocognitive disorder</td>
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<td>Parkinson’s disease</td>
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<tr>
<td>ROC</td>
<td>Receiver Operating Characteristic</td>
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References


