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Montreal Cognitive Assessment Performance in Patients with Parkinson's Disease with "Normal" Global Cognition According to Mini-Mental State Examination Score

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Abstract

OBJECTIVES—To examine Montreal Cognitive Assessment (MoCA) performance in patients with Parkinson's disease (PD) with "normal" global cognition according to Mini-Mental State Examination (MMSE) score.

DESIGN—A cross-sectional comparison of the MoCA and the MMSE.

SETTING—Two movement disorders centers at the University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center.

PARTICIPANTS—A convenience sample of 131 patients with idiopathic PD who were screened for cognitive and psychiatric complications.

MEASUREMENTS—Subjects were administered the MoCA and MMSE, and only subjects defined as having a normal age- and education-adjusted MMSE score were included in the analyses (N = 100). As previously recommended in patients without PD, a MoCA score less than 26 was used to indicate the presence of at least mild cognitive impairment (MCI).

RESULTS—Mean MMSE and MoCA scores ± standard deviation were 28.8 ± 1.1 and 24.9 ± 3.1, respectively. More than half (52.0%) of subjects with normal MMSE scores had cognitive impairment according to their MoCA score. Impairments were seen in numerous cognitive domains, including memory, visuospatial and executive abilities, attention, and language. Predictors of cognitive impairment on the MoCA using univariate analyses were male sex, older age, lower

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educational level, and greater disease severity; older age was the only predictor in a multivariate model.

CONCLUSION—Approximately half of patients with PD with a normal MMSE score have cognitive impairment based on the recommended MoCA cutoff score. These results suggest that MCI is common in PD and that the MoCA is a more sensitive instrument than the MMSE for its detection.

Keywords

cognitive impairment; Parkinson's disease; Mini-Mental State Examination; Montreal Cognitive Assessment; neuropsychology

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Cognitive impairment insufficient to meet criteria for dementia (mild cognitive impairment (MCI)) has been reported to occur in 20% to 30% of patients with Parkinson's disease (PD),[1–5] even in newly diagnosed patients.[4,5] Identification of initial impact or MCI in PD is important, because it predicts future cognitive decline, including development of PD dementia (PDD),[2,3,6,7] and deterioration of health-related quality of life.[8]

Impairments in executive function, attention, visuospatial skills, and memory characterize the "typical" cognitive profile in PD, whereas language and praxis are thought to be relatively spared.[3,4,9] The memory impairment associated with PD is classically considered a retrieval deficit (i.e., subcortical memory profile) as opposed to an encoding deficit (i.e., cortical memory profile).

There is substantial overlap in the pattern of observed cognitive deficits in PD without dementia and PDD. Studies enrolling both groups of patients have shown qualitatively similar, but quantitatively greater, impairments in patients with PDD in executive function, visuospatial abilities, attention, and psychomotor skills.[10] In longitudinal studies of patients without dementia at baseline, verbal memory deficits[11] and executive or visuospatial impairments[12] have been shown to predict development of PDD on long-term follow-up.

Given the aforementioned high prevalence of MCI in PD and its association with future development of dementia, it is important that patients with PD, even those with mild disease, be screened regularly for cognitive impairment.[12] An ideal cognitive screening instrument in PD should be brief, assess a range of cognitive domains, simple to administer, sensitive to the initial stage of cognitive impairment, and unaffected by motor impairment.

Few screening instruments have been validated or developed to assess global cognition in PD. The Scales for Outcomes of Parkinson's Disease—Cognition was recently developed and has been shown to be valid and reliable in differentiating patients with PD with and without dementia,[13,14] but its performance, specifically in patients without significant global cognitive impairment, has not been reported. The Cambridge Cognitive Examination—Revised distinguishes between patients with PD with and without dementia and detects cognitive impairment in patients with PD with an MMSE score less than 25,[15] but it takes approximately 60 minutes to administer.

The Mini-Mental State Examination (MMSE)[16] remains the most commonly used screening instrument for global cognition. The MMSE is used extensively in PD, but its use in this population has been questioned,[17,18] in part because the MMSE primarily assesses memory and language skills and also may not be sensitive to detect many cases of MCI.

The Montreal Cognitive Assessment (MoCA)[19] is a new cognitive screening instrument that was designed to address some of the limitations of the MMSE. It assesses a broader range of cognitive domains than the MMSE and is more challenging from a cognitive standpoint overall.

The MoCA and the MMSE both have items that require motor skills that core PD symptoms potentially affect (5/30 points on the MoCA and MMSE).

The MoCA has been shown to be more sensitive than the MMSE for the detection of MCI and mild Alzheimer's disease in the general population, and a score less than 26 was found to be the optimal cutoff point for a diagnosis of cognitive impairment.[19] There have been two studies using the MoCA in PD, and in one, the MoCA was found to be more sensitive than the MMSE in detecting cognitive impairment in this population,[17] although a MMSE score less than 26 was used to classify patients as having cognitive impairment, and this cutoff has not been validated for PD. In addition, the authors did not examine differences in MoCA subscores in impaired and unimpaired groups or examine correlates of MoCA performance. In the other study, the MoCA was found to have good test–retest reliability, interrater reliability, and convergent validity with a neuropsychological battery in a small sample of patients with PD.[20]

This study presents results on the frequency and correlates of cognitive impairment using the MoCA in patients with PD. These patients were a priori defined as not meeting criteria for global cognitive impairment when evaluated with the MMSE. It was hypothesized that a substantial proportion of patients with PD would be impaired (score <26) on the MoCA in spite of having a normal MMSE score and that cognitive impairment would occur in a range of domains, including visuospatial and executive abilities, attention, and memory.

METHODS

Subjects

Subjects were a convenience sample of patients in routine clinical care with a diagnosis of at least possible idiopathic PD[21] confirmed by a movement disorders specialist at the Parkinson's Disease and Movement Disorders Center at the University of Pennsylvania or the Parkinson's Disease Research, Education and Clinical Center at the Philadelphia Veterans Affairs (VA) Medical Center. The institutional review boards at both institutions approved the study, and subjects provided written informed consent before study participation.

Over a 14-month period, 131 patients were administered the MMSE (specifically the version used to establish normative data[22]) and the MoCA as part of the screening process of a study examining the frequency and correlates of psychiatric and cognitive complications in PD. Because of the inclusion of a VA site with nearly all male patients, screening was continued until women constituted 30% of a sample of 100 subjects.

For the purposes of these analyses, only subjects with a population-based age- and education-adjusted MMSE score in the top 75th percentile[23] were included, because this cutoff has previously been used to characterize individuals with normal MMSE scores (having "intact cognition"[24] or being the "best performing" in a cohort,[25] including in PD[7]).

Procedures

Trained research staff administered the MMSE and the MoCA in a systematically counter-balanced fashion. As part of training, staff were instructed not to deduct points simply for motor impairment (e.g., uneven or small writing); a secondary review of all the MoCAs before data analysis verified this. Subscores for the MoCA are presented two ways. The first, called "subscores," is based on the categories named on the MoCA instrument itself: visuospatial and executive, naming, attention, language, abstraction, delayed recall, and orientation. The second, called "domains," is based on how data was presented in the original MoCA manuscript,[19] and includes visuospatial, executive, attention, language, delayed recall, and orientation domains.

In addition, the 15-item Geriatric Depression Scale (GDS-15)[26] was administered to measure severity of depression symptomatology (scores ranging from 0 to 15, higher scores indicating greater depression severity). Basic demographic and clinical information, including Unified Parkinson's Disease Rating Scale (UPDRS) motor scores and disease severity as measured according to Hoehn and Yahr stage (scores ranging from 1 to 5, higher scores indicating greater disease severity),[27] was obtained from the subjects or chart review. Patients were encouraged to take their regularly scheduled PD medications during the study visit so that they would be evaluated in their "on" state.

Analyses

All statistical procedures were performed with SPSS 15.0 for Windows (SPSS Inc., Chicago, IL). Cognitive impairment was defined as a total score less than 26 on the MoCA and no cognitive impairment a total score of 26 or greater, as recommended for the general population.[19] Between-group comparisons between impaired and unimpaired samples on MoCA subscores and domains were made using a two-sample *t*-test or Mann-Whitney *U*-test. Correlates of cognitive impairment variables were determined using logistic regression models. Two sets of analyses are presented. First, each demographic and clinical variable was analyzed for a marginal association with cognitive impairment using univariate logistic regression. Second, factors that exhibited a significant marginal association based on a *P*-value ≤.10 were entered into a single, multivariate, logistic regression model with a forward stepwise entry method, and results were verified using a forced-entry method. For all other analyses, a Bonferroni correction for multiple comparisons was used to maintain at least a .05 Type I error level.

RESULTS

Subject Characteristics

Of the original sample of 131 patients, 31 (23.7%) did not meet the MMSE criterion for intact global cognition, leaving a final study sample of 100 patients. Of the patients excluded based on their MMSE score, only four (12.9%) scored 26 or higher on the MoCA.

The final sample was predominately male (70.0%) and white (96.0%), and the mean age and formal education level ± standard deviation of the cohort was 65.3 ± 11.5 and 15.7 ± 3.6 years, respectively. Overall patients were representative of patients with PD in specialty care settings, with mean disease duration of 7.7 ± 6.4 years and PD of mild to moderate severity (median Hoehn & Yahr Stage 2.0, mean levodopa dosage 493.3 ± 398.4mg/d, and dopamine agonist use by 50.0% of subjects). Nineteen percent of patients had undergone deep brain stimulation surgery. The mean GDS-15 score was 3.4 ± 3.8, with 26.0% of patients having a score suggesting clinically significant depression based on a previously validated cutoff point in PD.[28]

Comparison of MoCA and MMSE Performance

The mean MMSE and MoCA scores of the final cohort were 28.8 ± 1.1 and 24.9 ± 3.1, respectively. In spite of normal MMSE scores as part of the eligibility criteria, 52.0% met criteria for cognitive impairment based on their MoCA score (<26).

The average administration time for the MoCA was less than 10 minutes. Order of administration did not affect test performance ($t = -0.3$, degrees of freedom *(df)* = 98, $P = .79$ for the MMSE, $t = 1.8$, $df = 98$, $P = .07$ for the MoCA).

Pattern of Cognitive Impairment on the MoCA

Impaired patients scored worse than unimpaired patients on five of seven MoCA subscores, specifically the visuospatial and executive, naming, attention, language, and delayed recall subscores (Table 1). When using broader cognitive domains identified in the original MoCA article,[19] significant differences were found on five of six domains, specifically visuosopatial, executive, attention, language, and delayed recall (Table 2).

Correlates of Cognitive Impairment

Older age, male sex, lower level of education, and greater disease severity (by Hoehn and Yahr stage and UPDRS score) were all associated at the $P < .05$ level with cognitive impairment on univariate analyses (Table 3). Entering these variables (Hoehn and Yahr stage for disease severity because of its stronger association with cognitive impairment than UPDRS score) into a multivariate model, only age remained an independent predictor of cognitive impairment in both the forward stepwise and forced entry multivariate logistic regression models adjusted for multiple comparisons.

To examine the direct effect of motor impairment on MoCA performance, the association between UPDRS motor score and performance was determined on those parts of the MoCA that require motor skills: the visuospatial and executive subscore and the visuospatial domain. There was not a significant association between UPDRS motor score and the visuospatial and executive subscore (Pearson correlation coefficient *(r)* = −0.14, $P = .16$) or the visuospatial domain (Pearson $r = -0.14$, $P = .17$).

DISCUSSION

The primary finding was that cognitive impairment, defined according to the recommended score of less than 26 on the MoCA, is common in patients with PD without evidence of global cognitive impairment based on MMSE performance. In addition, it was found that the earliest cognitive impairment in PD occurs in a range of cognitive domains.

To the authors' knowledge, this is the first report on the use of a cognitive screening instrument in a cohort of patients with PD that was defined as having normal global cognition based on the results of a commonly used standardized cognitive screening test (the MMSE). Using a well-standardized cognitive screening instrument and a conservative cutoff point (excluding patients in the bottom 25th percentile based on their age- and education-adjusted score) helped ensure that the population did not have global cognitive impairment beyond the earliest stage.

In spite of having normal MMSE scores, approximately half of the patients met predefined criteria for cognitive impairment based on their MoCA score. These findings demonstrate that, even when defining a PD population as cognitively intact according to the most widely used bedside or office screening instrument (the MMSE), the majority of patients will show some degree of impairment on more-extensive and -sensitive neuropsychological testing. Because the MMSE remains the most commonly used screening instrument of cognitive impairment in general, these results also suggest that the earliest stages of cognitive impairment in PD often go unrecognized in routine clinical care.

These findings suggest that initial cognitive impairment in PD occurs in a broad range of cognitive domains, including visuospatial and executive abilities, language, memory, and attention, confirming previous research on patients without dementia with PD.[1,3,29,30] Thus, these results underscore the importance of a careful evaluation of cognitive function with a simple but sensitive neuropsychological test even at the earliest stage of illness.

Male sex, older age, lower formal education, and greater disease severity were factors associated with a low MoCA score on univariate analyses. These same variables have also been reported as risk factors for the development of dementia in PD,[31] suggesting that patients identified as having early cognitive impairment based on their MoCA score are at greater risk of developing dementia later in the course of illness and might be good candidates for trials of cognition-enhancing therapies or neuroprotective agents.

Two possible explanations can be offered for why the MoCA is more sensitive than the MMSE in detecting MCI in PD. First, the MMSE tests primarily memory and language abilities, whereas the MoCA equally assesses a broader range of cognitive domains. Therefore, the MoCA is likely to be more sensitive to the particular cognitive impairments that occur in PD. Second, the MoCA overall is more difficult than the MMSE, so it may be more sensitive to changes within a particular domain. For instance, on the MMSE, a subject receives 3 points (10% of total score) for simply registering and repeating the three words for the memory test, whereas on the MoCA no points are given for completion of this relatively easy task. In addition, severity of motor impairment was not associated with performance specifically on those parts of the MoCA requiring motor skills, suggesting that core PD symptoms (tremor, rigidity, and bradykinesia) do not confound MoCA performance.

Although this study demonstrated a clear advantage of the MoCA over the MMSE, it has limitations. First, the results may not be generalizable, because the majority of the patients were male, white, and highly educated, and all were from specialty care centers. There already is a 1-point adjustment made to the total MoCA score for patients with less than 12 years of formal education, but the results of the current study suggest that it may be helpful to have age- and education-normed scores for the MoCA, as exist for the MMSE. Second, formal criteria or a comprehensive neuropsychological battery was not used to provide a criterion standard diagnosis of MCI and dementia, so the criterion validity of the MoCA (i.e., whether a MoCA cutoff point of 26 is optimal in PD) cannot be reported on, only how it relates to MMSE performance. Third, there was no control group, so it cannot be said whether a non-PD cohort of elderly individuals with normal MMSE scores would have demonstrated similar levels of impairment on the MoCA, although in the original MoCA article,[19] only 13% of healthy elderly controls with a “normal” MMSE score demonstrated cognitive impairment on the MoCA.

There is increasing evidence that dementia is common in advancing PD, affecting up to 78% of patients followed long term.[32] Because MCI almost always precedes the onset of dementia, the cumulative prevalence of MCI at some point during the course of PD is at least as high. Recognition of cognitive impairment at its initial stage will enable clinicians to educate patients and family members about prognosis and to allow informed decisions about the risks and benefits of therapeutic interventions. Therefore, beginning at time of initial diagnosis, routine cognitive screening with a sensitive instrument, such as the MoCA, may aid in the comprehensive management of all patients with PD.

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Table 1

Performance on Montreal Cognitive Assessment (MoCA) Subtests Based on Cognitive Impairment Status

MoCA Subtest	Cognitively Impaired (MoCA<26) (n = 52) Mean ± Standard Deviation	Cognitively Unimpaired (MoCA ≥26) (n = 48) Mean ± Standard Deviation	*Z* Score*	*P*-Value
Visuospatial and executive	3.5 ± 1.0	4.3 ± 0.8	−4.1	<.001†
Naming	2.7 ± 0.5	3.0 ± 0.2	−3.6	<.001†
Attention	5.3 ± 1.0	5.9 ± 0.4	−3.9	<.001†
Language	1.5 ± 1.0	2.7 ± 0.5	−5.9	<.001†
Abstraction	1.4 ± 0.7	1.7 ± 0.6	−2.1	.04
Delayed recall	1.8 ± 1.5	3.8 ± 1.0	−6.2	<.001†
Orientation	5.9 ± 0.3	6.0 ± 0.1	−1.8	.07

*Mann-Whitney *U*-test.

†Significant ater Bonferroni correction for multiple comparisons.

Table 2

Performance on Montreal Cognitive Assessment (MoCA) Domains Based on Cognitive Impairment Status

MoCA Domain	Cognitively Impaired (MoCA<26) (n = 52) Mean ± Standard Deviation	Cognitively Unimpaired (MoCA ≥26) (N = 48) Mean ± Standard Deviation	*t* (Degrees of Freedom) or *Z* Score	*P*-Value
Visuospatial	2.9 ± 0.9	3.6 ± 0.6	4.5 (98)*	<.001‡
Executive	2.4 ± 1.0	3.4 ± 0.7	5.4 (98)*	<.001‡
Attention	5.3 ± 1.0	5.9 ± 0.4	−3.9†	<.001‡
Language	4.2 ± 1.1	5.6 ± 0.5	−6.6†	<.001‡
Delayed recall	1.8 ± 1.5	3.8 ± 1.0	−6.2†	<.001‡
Orientation	5.9 ± 0.3	6.0 ± 0.1	−1.8†	.07

*
t-test.

†
Mann-Whitney *U*-test.

‡
Significant after Bonferroni correction for multiple comparisons.

Table 3

Correlates of Cognitive Impairment Based on MoCA Score <26

Variable	Odds Ratio (95% Confidence Interval) *P*-Value	
	Univariate Analyses	Multivariate Analysis
Age*	1.75 (1.36–2.25) <.001	1.60 (1.24–2.07) <.001†
Sex	4.65 (1.81–11.95) .001	3.77 (1.21–11.73) .02
Education	0.87 (0.77–0.98) .02	0.85 (0.74–0.98) .03
Hoehn and Yahr‡	3.13 (1.46–6.71) .003	2.58 (1.03–6.50) .04
Unified Parkinson's Disease Rating Scale§	1.07 (1.02–1.11) .006	—
Marital status	1.78 (0.68–4.63) .24	—
Dopamine agonist use	0.52 (0.24–1.16) .11	—
Geriatric Depression Scale score	0.96 (0.86–1.06) .40	—
Levodopa dosage//	1.06 (0.95–1.17) .31	—
Deep brain stimulation	0.80 (0.29–2.16) .65	—
Duration of Parkinson's disease	0.99 (0.93–1.05) .76	—

*Odds ratios for age calculated for 5-year increments.

†Significant after Bonferroni correction for multiple comparisons.

‡Hoehn and Yahr stage included as measure of disease severity.

§N = 98.

//Odds ratio for levodopa dosage calculated for 100-mg increments.