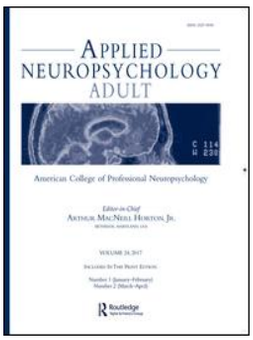

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Validity and reliability of the Persian version of the Montreal Cognitive Assessment (MoCA-P) scale among subjects with Parkinson's disease

Seyedeh Zahra Badrkhahan[a], Hajir Sikaroodi[b], Farshad Sharifi[c,d], Leila Kouti Pharmd[e], and Maryam Noroozian[f]

[a]Department of Geriatric Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; [b]Department of Neurology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; [c]Elderly Health Research Center, Endocrinology and Metabolism Population Sciences Research Institute, Tehran University of Medical Sciences, Tehran, Iran; [d]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran; [e]Clinical Pharmacy Department, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Iran; [f]Cognitive Neurology & Neuropsychiatry Division, Department of Psychiatry, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Parkinson's disease (PD) is a progressive multifactorial degenerative disorder that has both motor and nonmotor features. Among the nonmotor features of PD, cognitive impairment; Mild Cognitive Impairment (MCI) and dementia, poses one of the most significant implications for disability. Because of the high possibility of developing Dementia in PD, it is essential to obtain a reliable cognitive screen. Two commonly used cognitive measures include the Mini Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). The MoCA is a more sensitive tool for the detection of MCI in compared to the MMSE. Because of the cultural differences, in this study, we evaluated the psychometric properties of the Persian version of the MoCA (MoCA-P) in a group of participants with PD in Iran. Participants were assessed by MMSE, Geriatric Depression Scale (GDS), and Functional Assessment Staging Test (FAST). If they met study eligibility, the MoCA-P scale was administered. Receiver Operating Characteristic (ROC) curve analyses showed that the MoCA-P scale produced significant discrimination of PD with Dementia (PDD) from PD with MCI (PD-MCI). It seems that the MoCA-P has adequate psychometric properties as a screening instrument for the detection of PD-MCI and PDD in Iranian patients. As near to 30% of patients with PD go on to develop dementia, the MoCA-P can be useful in the detection of cognitive impairment in patients with PD and is suitable for executive function assessment.

KEYWORDS

Elderly; MoCA; Montreal Cognitive Assessment; older adults; Parkinson's disease; Parkinson disease dementia; reliability; validity

Introduction

Parkinson's disease (PD) is a progressive, multifactorial degenerative disorder that shows an increasing trend in prevalence after age 50. The global number of individuals over the age of 50 with PD in 2005 was approximately 4.3 million and is projected to increase to more than 9 million by 2030 (Dorsey et al., 2007).

The diagnosis of PD is motor disturbance-based (tremor at rest, rigidity, bradykinesia, and postural instability), but PD can also affect cognition, mood, sleep, and autonomic abnormalities (Shulman, De Jager, & Feany, 2011; Zis, Sokolov, & Chaudhuri, 2016). Among the nonmotor features of PD, cognitive impairment, Mild Cognitive Impairment (MCI), and/or dementia, poses one of the most significant implications for disability, the decline in quality of life, and the increase of caregiver burden. Parkinson Disease Dementia (PDD) is associated with higher rates in institutionalization, treatment costs, and mortality rate (Dujardin et al., 2010; Emre et al., 2007). Moreover, PDD is one of the major risk factors of falls (Allcock, 2009; Ashburn, 2001) and, yet, remains an exclusionary criterion for Deep Brain Stimulation (DBS); a surgical procedure used to improve motor symptoms in patients (Aschermann, 2016).

It is estimated that the prevalence of Mild Cognitive Impairment (MCI) in patients with a new diagnosis of PD ranges from 10 to 35% (Dujardin et al., 2010; Shulman et al., 2011; Zis et al., 2016). Approximately 30% of patients with PD go on to develop dementia (Dorsey et al., 2007). MCI refers to the impairment in one or more cognitive domains

CONTACT Maryam Noroozian, MD maryam.noroozian.mn@gmail.com Cognitive Neurology & Neuropsychiatry Division, Department of Psychiatry, Tehran University of Medical Sciences, Roozbeh Hospital, 1333795914, South Kargar Avenue, Tehran, Iran

with preservation of independence in functional abilities (Petersen, 2004). MCI is heterogeneous, with amnestic and nonamnestic deficits. MCI patients can evolve into Alzheimer's Dementia (AD) patients. "Amnestic" MCI (aMCI) is used to differentiate isolated memory impairment from impairments of other cognitive domains, while nonamnestic MCI (naMCI) refers to impairments in cognitive domains not including memory. The aMCI is often the prodromal phase of AD, while naMCI may be the early manifestation of other types of dementia, including Parkinson's disease Dementia (PDD). The deficits in patients with Parkinson's disease with Mild Cognitive Impairment (PD-MCI) mostly affected executive and visuospatial functions, rather than memory disturbances typically found in MCI in AD. Patients with PDD often present with impairment in more than one cognitive domain (including memory) and with impairment in functional abilities that impede independence (Emre et al., 2007). Patients with PD-MCI are at a higher risk of developing PDD compare to patients with PD without MCI (Aarsland et al., 2003; Kehagia, Barker, & Robbins, 2010; Litvan et al., 2011; Portin & Rinne, 1987; Williams-Gray, Foltynie, Brayne, Robbins, & Barker, 2007). Given the risk factors associated with developing dementia in PD, it is essential to obtain a reliable cognitive screening, insensitive to motor disturbance and aimed at assessing all cognitive domains (Broeders et al., 2013; Buter et al., 2008). Two commonly used cognitive screening tools include the Mini Mental Status Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). Both tests are 30-point instruments that can be administered in 10 minutes, with higher scores indicating better function. Although the MMSE is the most commonly used screening tool for detecting cognitive impairment, the MoCA is more powerful in screening PD-MCI and PDD and it is a more sensitive tool for the detection of MCI compared to the MMSE (Hobson & Meara, 2015; Pedersen, Larsen, Tysnes, & Alves, 2013). Nasreddine et al. (2005) has reported that the MoCA is more sensitive in detecting MCI in a group of healthy controls, subjects with MCI, and patients with Alzheimer's disease (AD) (sensitivity of 90%) compared to the MMSE (sensitivity of 18%) and a score of $\leq$26 was reported as an optimal cutoff point for the diagnosis of cognitive impairment. Many different studies have confirmed the results and shown the MoCA has acceptable psychometric properties for cognitive assessment in subjects with PD (Dalrymple-Alford et al., 2010; Razali et al., 2014; Kasten et al., 2010; Zadikoff et al., 2008).

There are cultural differences between eastern and western countries; therefore, it is essential to measure the cognitive scales in different cultures (Nasreddine et al., 2005). There are just a few studies on the diagnostic accuracy of the MoCA in the detection of cognitive impairment in Iranian patients. Furthermore, only one study evaluated subjects with PD but there was no comparison between PD-MCI and PDD. Therefore, in this study, we aimed to evaluate the psychometric properties of the Persian version of the MoCA (MoCA-P) and to define the optimal cutoff points in subjects with PD in Iran.

Methods

This was a cross-sectional diagnostic accuracy study to evaluate psychometric properties of the MoCA-P in individuals with PD in Iran. The MoCA is translated into Persian and then back-translated into English by Sikaroodi, Yadegari, and Miri (2013) and this Persian version was published in the formal site of the MoCA that is available from http://www.mocatest.org.

Participants

The participants of this study were recruited from two memory centers; Roozbeh Department of Memory and Behavioral Neurology Division at Tehran University of Medical Sciences (TUMS) & Yaadmaan (a private memory center) and two movement disorders centers Shariati (movement disorders center affiliated to TUMS) & Toos (a referral private movement disorders clinic). The participants without PD were chosen from caregivers of patients with PD who were independent in the activity of daily living without a history of psychiatric, neurological, and medical disorders.

The inclusion criteria were: age $\geq$60, at least having six years formal education, diagnosis of idiopathic PD for at least a year before enrollment, native speaker in Persian, to have no depression (GDS-15 $\leq$ 7) (Malakouti, Fatollahi, Mirabzadeh, Salavati, & Zandi, 2006), to have no delirium, to have no moderate to severe dementia (FAST $\geq$6), to have no severe and uncontrolled hallucinations, to have no uncontrolled motor symptoms, to have no history of abnormalities in thyroid hormone levels, to have no evidence of cortical and subcortical infarct or hemorrhagic stroke in brain MRI, and to have no history of receiving cholinesterase inhibitors or psychoactive treatment.

Of the total 103 participants, 73 patients had a clinical diagnosis of idiopathic PD; 37 subjects with normal cognitive status (PD-NC); 22 subjects with PD

and MCI (PD-MCI); and 14 patients with Parkinson Disease Dementia (PDD). The remaining 30 participants did not have a diagnosis of PD and had normal cognitive status: 33.3% of subjects with normal cognition without PD; 40% of subjects with PD-NC; 38.9% of subjects with PD-MCI; and 90% of subjects with PDD were amnestic (delayed recall ≤ 2 in MMSE).

Cognitive and functional assessments

The cognitive status of the participants was determined by the Persian version of the Functional Assessment Staging Test (FAST) instrument[1] and an expert academic neurologist. If there was a discrepancy regarding cognitive status between the diagnostic stage of the expert clinician and the FAST, our reference was the expert opinion. The FAST (Reisberg, 1988; Sabbagh et al., 2007; Sclan & Reisberg, 1992), is used to categorize functional impairment into seven stages, ranging from normal aging to severe dementia (7(f)). The participants with PD-MCI presented with memory complaints but without functional impairment, which were corroborated by the participant's informants and/or caregivers according to the FAST (Reisberg, 1988). They have normal activities of daily living and normal general cognitive function and objective impairment in one area of cognitive function as an abnormal memory function for age according to the Peterson criteria (Petersen, 2004).

The participants with PDD presented with both significant cognitive deficits and impairment in daily functioning as a consequence of their cognitive impairment.

The MMSE was used to assess the impairment in five cognitive domains, including orientation, immediate recall, attention and calculation, delayed recall, language, and executive function (Folstein, Folstein, & McHugh, 1975). The validation study of the Persian version of this tool was performed Seyedian et al., 2008). The MoCA has been designed to measure eight cognitive domains, including visuospatial abilities and executive functioning (cube drawing, clock drawing, trail making B test, a phonemic fluency task, and a two-item abstract thinking), language (naming task with low-familiarity animals, repetition of two syntactically complex sentences and verbal fluency), attention, concentration, and working memory (digits forward and backward, target detection using tapping, serial subtraction), short-term memory (delayed recall), and orientation (time orientation and space orientation).

[1]The article is accepted and will be published

The Geriatric Depression Scale-15 (GDS-15) was used to assess depression. It is a 15-question instrument for depression evaluation provided by Yesavage et al. in 1982. It has been translated into various languages and has been validated in different cultures. The Persian version of GDS-15 has been validated by Malakouti et al. in 2006 and the cutoff point to determine depression has been reported score ≤ 7.

Parkinson's disease diagnosis

The diagnosis of PD was performed by an expert academic neurologist using physical and neurologic examinations, as well as a brain MRI.

Procedure

The participants were assessed by a trained general physician who conducted a clinical interview, neurological evaluation, and administered the MMSE and the FAST scores. The patient also was assessed and examined by a neurologist. The individuals diagnosed with idiopathic PD from the neurologist assessment were referred to a geriatric resident trained in neuropsychological assessment. Once study eligibility was met, the MoCA-P scale was administered. The investigator was blind to the FAST and the MMSE scores to avoid experimental bias. To assess reliability, 10% of subjects were reevaluated by another rater after two weeks. Details of the recruitment process are illustrated in Figure 1.

Validation

The content validity of the MoCA-P was verified by a panel of seven experts on cognitive impairment (two neurologists, two psychiatrists, one geriatrician, one epidemiologist, and one geriatric nurse). The relevance of each item and comprehensiveness of the test were evaluated by a Likert scale (0 = not at all relevant, 1 = relatively not relevant, 2 = relatively relevant, and 3 = completely relevant). A mean score of ≥ 2 was considered as acceptable content validity.

The face validity of the MoCA-P was assessed by eight subjects with PD-NC. Each item clearance was determined using a Likert scale (0 = not at all clear, 1 = relatively not clear, 2 = relatively clear, and 3 = completely clear). The acceptable mean score was ≥ 2 point.

Concurrent validity was determined using the Spearman's correlation coefficients between the MoCA scores and those of the MMSE and the FAST. The correlation coefficient of ≥ 0.7 was considered

as a strong concurrent validity (Hauke & Kossowski, 2011)

Reliability

The reliability of the MoCA-P was assessed by internal consistencies. It was evaluated by Cronbach's alpha and the value ≥0.8 and over was considered as "good" in internal consistency (Cronbach & Meehl, 1955). Test-retest reliability conducted by using Intraclass Correlation Coefficients (ICC). The agreement between two raters in the scoring of the MoCA-P over two weeks among eight participants was measured and considered as the reliability of The MoCA-P. Two weeks separation between tests was determined to minimize practice effect. ICC ≥ 0.8 considered as good test-retest reliability.

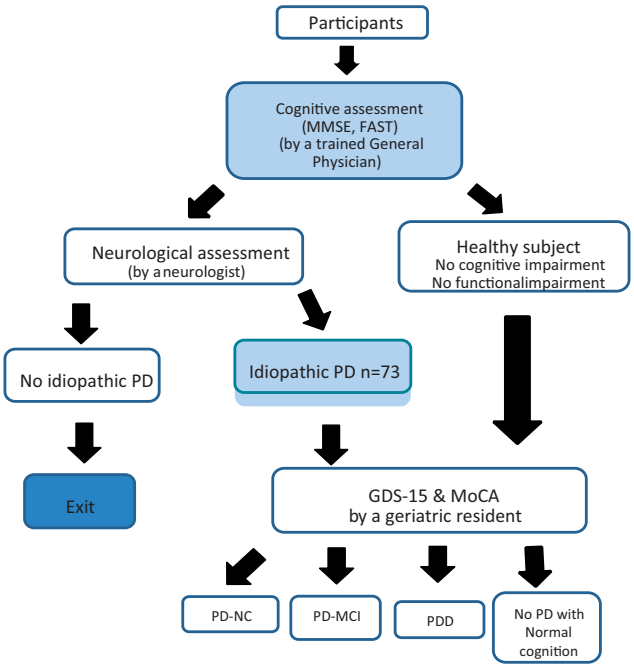

Figure 1. The diagram of the participant's selection. (Total participants $n = 103$, Idiopathic PD $n = 73$; PD-NC $n = 37$; PD-MCI $n = 22$, PDD $n = 14$ and No PD with normal cognition $n = 30$). MMSE = Mini Mental Status Examination; FAST = Functional Assessment Staging Test; PD = Parkinson's disease; GDS-15 = Geriatric Depression Staging-15 items; MoCA = Montreal Cognitive Assessment; PD-NC = Parkinson's disease with Normal Cognition status; PD-MCI = Parkinson's disease with Mild Cognitive Impairment; PDD = Parkinson's disease Dementia.

Statistical analyses

All statistical analyses were performed using SPSS 18 and STATA 12 packages. Comparison between groups in demographic variables, the MoCA-P, the MMSE, the FAST, and the GDS-15 scores was examined using Kruskal-Wallis test.

A nonparametric Receiver Operating Characteristic (ROC) curve analysis was utilized to identify the optimal balance between sensitivity and specificity. The area under the curve (AUC) was used to compare the diagnostic performance of each test. Values of $p < .05$ were considered statistically significant.

Ethical consideration

The study was approved by the Research Ethics Committee of Tehran University of Medical Sciences (TUMS). Written consent informed was obtained from all the participants or their legal guardians (for participants with the MMSE scores ≤21). All results were kept confidential and participants with cognitive impairment were referred to clinicians for treatment.

Results

The median age and years of education for the total sample were 70 years and 12 years, respectively (Table 1). There were not any differences between groups in terms of education levels or gender proportion, but on average, patients with PD-MCI (73.5 years) were younger than those with PDD (78.5 years) and older than normal cognition group subjects (69.5 years) ($p < .001$). The MMSE and the MoCA-P average scores were different between the three groups

Table 1. Demographic and clinical characteristics by cognitive groups.

	Total	Normal cognition without PD	PD-N	PD-MCI	PDD	*p*-value[a]
Year of Age median (IQR)	70.0 (13.0)	63.0 (8.5)	69.5 (10.5)	73.5 (8.0)	78.5 (10.8)	<.01
Female No (%)	39 (47.0)	15 (60.0)	13 (43.3)	8 (44.4)	3 (30.0)	.38
Years of Schooling median (IQR)	12 (10.0)	14 (4.0)	12 (11.25)	13 (10.0)	12 (8.5)	.47
Years of PD duration median (IQR)	6.0 (6)	–	4.0 (3)	6.0 (4)	9.0 (3)	<.01
MMSE median (IQR)	28.0 (5)	29.0 (3)	29 (3)	27 (4)	21(14)	<.01
MoCA median (IQR)	25 (5)	26 (3)	26 (4)	22 (4)	14 (11)	<.01
GDS median (IQR)	4.0 (2)	2.0 (1)	2 (2)	4 (2)	3 (5)	<.01
FAST median (IQR)	1.0 (2.0)	1.0 (0)	1.0 (0)	3 (0)	4 (0)	<.01

PD = Parkinson's Disease; PD-N = Parkinson's disease with normal cognition; PD- MCI = Parkinson's Disease with Mild Cognitive Impairment; PDD = Parkinson's Disease Dementia; MMSE = Mini Mental Status Examination; MoCA = Montreal Cognitive Assessment; GDS = Geriatric Depression Scale; FAST = Functional Assessment Staging Test; IQR = Inter Quartile Range, CI = Confidence Interval. [a]Kurskal-Wallis test.

Table 2. Differences in full correct answers in the different groups by different domains of MoCA-P.

	Normal cognition without PD	PD-N	PD-MCI	PDD
Orientation	0.100	0.967	0.830	0.30
Naming	0.880	0.833	0.556	0.60
Visuospatial abilities and executive functioning	0.600	0.560	16.700	0.00
Language	0.720	46.700	38.900	0.00
Abstract thinking	0.920	86.700	66.700	0.00
Attention	0.600	0.730	0.330	0.10
Delayed recall	0.800	0.670	0.000	0.00

MoCA-P = The Persian Version of Montreal Cognitive Assessment.

significantly. The median scores of the MMSE and the MoCA-P had a descending trend in PD-NC, PD-MCI, and PDD groups. The median of the GDS-15 score in PD-MCI was more than PDD and PD-NC. Gender was not related to the MMSE or the MoCA-P scores. Differences in the answers in different domains of MoCA-P are described in Table 2. The Cronbach's alpha of MoCA-P was 0.808 (95% confidence interval [CI] = 0.742–0.853, $p < .001$) (Cronbach & Meehl, 1955). The interclass correlation coefficient between the baseline and repeated measurement of the MoCA-P scores was 0.993 (95% Confidence Interval [CI] = 0.971–0.999, $p < .001$). Spearman's correlation coefficients between the MMSE and the MoCA-P was 0.738 (CI: 0.62 – 0.823) and between the FAST and the MoCA-P determined as −0.701 (CI: −0.572–0.796). The MoCA-P has acceptable content validity and face validity. (Mean score: 2.92 and 2.98, respectively). The ROC curve analyses showed that the MoCA produced discrimination of PDD from PD-MCI (AUC: 0.99) and PD-MCI from PD-NC patients (AUC: 0.90). The optimal MoCA-P screening cutoffs were 19/30 for PDD (sensitivity 90%; specificity 97.9%) and 24/30 for PD-MCI (sensitivity 75%; specificity 76.7%) (Table 3 and Figures 2 and 3). The MoCA screening cutoff regardless of PD was also 24/30 (sensitivity 85.5%; specificity 75%). Therefore, there are not any differences between cutoffs for MCI detection in PD-NC and normal cognition subjects without PD.

The responses to the items of the MoCA-P were compared between subjects with normal cognition without and with PD, PD with MCI, and PDD. Only 16% in normal cognition subjects without PD, 20% in PD-NC, 50% in PD-MCI, and 100% in PDD had a problem in trail making item.

Table 3. Psychometric properties of MoCA-P.

Psychometric Properties	PD with mild cognitive impairment (MoCA ≤ 24)	PD with dementia (MoCA ≤ 19)
Sensitivity (%)	75.00	90.00
Specificity (%)	76.70	97.90
Area Under Curve	0.90	0.99
Positive Predicting Value (%)	75.0	90.0
Negative Predicting Value (%)	76.6	97.9

MoCA-P = The Persian Version of Montreal Cognitive Assessment; PD: Parkinson's disease.

Discussion

With the growth of the aging population, the prevalence and incidence of age-related cognitive disorders are increased. Neuropsychological tools for early detection of cognitive decline may be beneficial to the appropriate management of these disorders. Recently cognitive assessment is considered in different diseases including coronary heart diseases, chronic kidney diseases, and rheumatic diseases. Given the risk of cognitive impairment in PD, it is essential to assess cognition in all patients with PD (Williams-Gray et al., 2007).

The MoCA is an important tool for the evaluation of cognition in patients with PD (Dalrymple-Alford et al., 2010; Hoops et al., 2009; Kasten et al., 2010; McColgan et al., 2012; Ozdilek & Kenangil, 2014; Zadikoff et al., 2008). In this study, psychometric properties of the MoCA-P were evaluated in a sample of the elderly individuals with PD in Iran. The MoCA-P scores were strongly associated with both the MMSE scores and the FAST stages. The results are compatible with other studies. Costa et al. (2012), Emsaki (2012), and Sweet et al. (2011) reported strong associations between the MoCA and the MMSE.

The MoCA-P has also high face validity, content validity, and internal consistency in our study. Similarly, Emsaki (2012) reported acceptable internal consistency in their study in 2012.

The "Trail making" subscale evaluates the integrity of some executive functions such as planning, attention and somehow inhibition. They are related to either frontal lobe impairment or fronto-subcortical connectivity. Moreover, the prefrontal cortex is a key determinant of executive function. Many studies have shown that subjects with PD are characterized by executive dysfunction which is early presented in the course of the disorder when the pathology is confined to basal ganglia. This problem is more seen in patients who are not on treatment than those are on

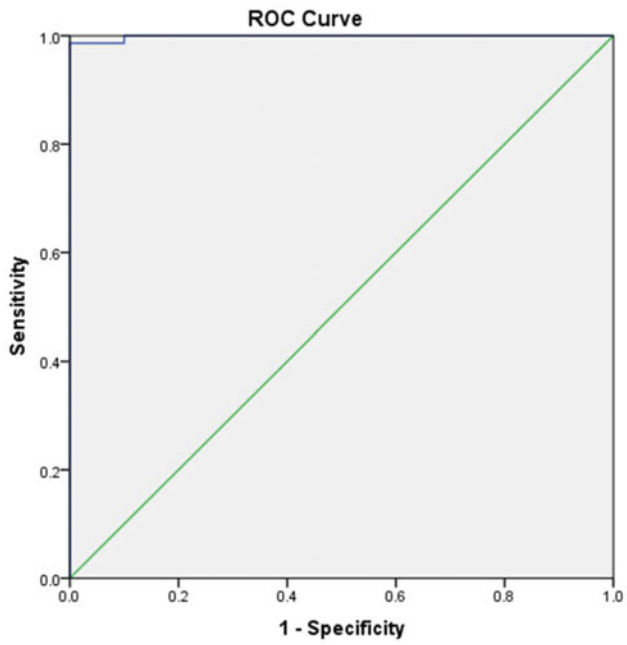

Figure 2. Receiver Operating Characteristic (ROC) curve of the MoCA-P according to the FAST scale differentiation between NC-PD and PD-MCI. NC-PD = Parkinson's disease with normal cognition; PD- MCI = Parkinson's disease with Mild Cognitive Impairment; MoCA-P = The Persian version of the Montreal Cognitive Assessment; FAST = Functional Assessment Staging Test.

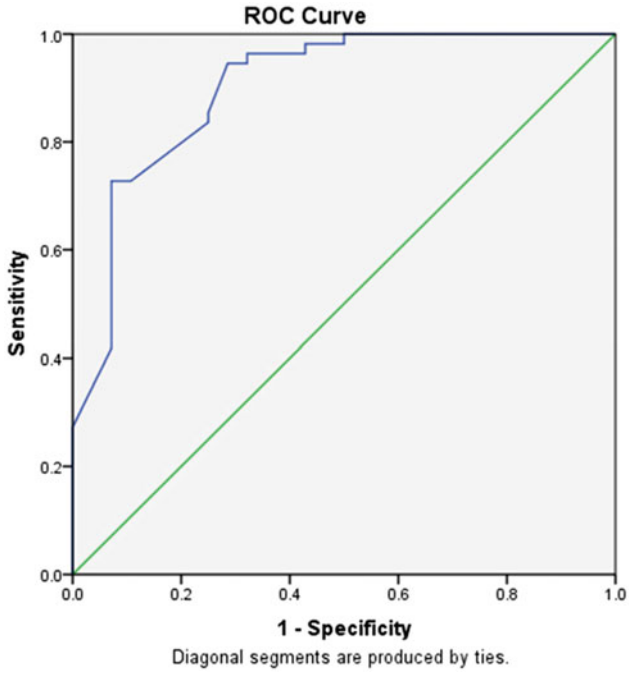

Figure 3. Receiver Operating Characteristic (ROC) curve of the MoCA-P according to the FAST scale differentiation between PD-MCI and PDD. PD-MCI = Parkinson's disease with Mild Cognitive Impairment; PDD = Parkinson's Disease Dementia; MoCA-P = The Persian version of the Montreal Cognitive Assessment; FAST = Functional Assessment Staging Test.

medications. In the study of Aarsland et al. (2010), the most common cognitive impairment in PD-MCI was nonamnestic MCI. In the study of Hobson and Meara (2015) and Sollinger (2010), executive dysfunction was the most common impairment in PD. In the same directions, our findings indicate that the most common deficits in cognitive function in patients with PD were related to executive function. The correct answers to different domains were different in four groups and they become limited by worsening of cognitive function. The optimal MoCA-P screening cutoffs were 19/30 for PDD and 24/30 for PD-MCI. Dalrymple-Alford et al. (2010), in New Zealand, reported a cutoff of <21/30 for separating PDD from PD-MCI and a cutoff of <26/30 for separating PD-MCI from NC-PD. Brown et al. (2016) have reported a cutoff of <25/30 for the detection of PD-MCI. Lucza et al. (2015) determined a cutoff of <26/30 for the detection of PD-MCI and a cutoff of<23/30 for the detection of PDD. The cutoff of <26/30 was recommended by the original MoCA, but decreased cutoff scores lower than 26 similar to our study are reported in various studies (Gil et al., 2015; Lee et al., 2008; Tsai et al., 2012). Luis et al., (2009) and Gil et al., (2015) have shown that age and education have significant effects on the MoCA score. Moreover, the differences in cutoff scores between this study and other studies may be due to differences in cultural context and socioeconomic status.

We indicated concurrent validity between the MMSE and the MoCA-P scores with Spearman's correlation coefficients >0.7, which was reported as a strong correlation in methodological studies (e.g., Hauke & Kossowski, 2011). Furthermore, for the assessment of test-retest validity, we used the Intraclass Correlation Coefficient (ICC) >0.8 that was considered by another researcher (Weir, 2005).

Some cultural differences were present in our study. The first issue we came across regarding the "Similarity part" of the test was that in almost all cases, the NC-PD subjects were not able to accumulate any points. In the first question, when asked what the similarities between a train and a bicycle are, they answered that they both have wheels. In the second part when asked what the similarities between a clock and a ruler are, they answered that they both have dials. Therefore, the result of the aforementioned answers would be zero based on the original MoCA, as we believe that these subjects could understand the core of the answers. These were common findings in the current elderly population in Iran. The second issue was regarding the "Trail making" subscale,

which was difficult to capture. This finding may be related to the practice defect in this population. The third one was regarding one of the Naming subscales, the "Rhinoceros part," in which a small proportion of the elderly population answered that may be due to the natural geography of Iran and also limited general information.

The strength of our study was the use of an expert clinical diagnosis as a golden standard reference for the determination of optimum cutoffs grades of the MoCA-P. There were multiple conditions in exclusion criteria; therefore, the results could not be generalized to all patients with PD. Even though recent research has proposed the criteria for PD-MCI, it should be considered that these criteria were not in the literature when we started to work on MCI in patients with PD.

Conclusions

The MoCA-P has adequate psychometric properties as a screening instrument for the detection of Iranian patients with PD-MCI and PDD. It can be effective for detecting cognitive impairment and is suitable in the assessment of executive function in patients with PD. This instrument provides a valuable opportunity to detect cognitive decline in early detection of PD and, thus, provides for early pharmacological and nonpharmacological interventions. Allotting enough time is an important difficulty of the MoCA especially in patients with PDD, because of slower motor functions in these patients; therefore, validation of the short form in other studies could be useful.

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