

## Original Article

# Neuropsychological profile in Chinese patients with Parkinson's disease and normal global cognition according to Mini-Mental State Examination Score

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**Abstract:** Object: Cognitive impairments have been reported to be more common in non-demented patients with Parkinson's disease (PD) and education levels play an important role in intelligence. The studies on cognitive impairments in Chinese PD patients with higher education levels and normal global cognition according to Mini-Mental State Examination Score (MMSE) have not been reported. Methods: We enrolled 69 consecutive PD patients with over 6 years education levels and a MMSE score above 24 (of 30) and performed a battery of neuropsychological scales. Results: There are extensive cognitive domain impairments in PD patients with "normal" global cognitive according to MMSE. Montreal Cognitive Assessment (MoCA) is a highly sensitive scale to screen cognitive impairments in PD. Conclusion: The cutoff score of 28 on the MMSE screening for cognitive impairment in Chinese PD patients with high education levels may be more appropriate.

**Keywords:** Parkinson's disease, cognitive impairment, neuropsychology, montreal cognitive assessment scale, mini-mental state examination

## Introduction

Parkinson's disease (PD) is one of the most common slowly progressive neurodegenerative disorders, affecting approximately 1.7% of population aged over 65 years in mainland China [1]. PD affects not only the motor system but also the cognitive domains. Cognitive impairment in mainly visuospatial executive dysfunction and mnemonic disturbances is a common and functionally severe problem in PD patients. It can be identified in PD from the very beginning of the disease. Clinical manifestations range from slight deficits, PD without dementia, only detectable by means of neuropsychological test, to dementia, PD with dementia (PDD). There are evidences showing that cognitive impairment is much more common than dementia in PD. The prevalence of cognitive impairment in non-demented patients was estimated to be about 20%-40% [2, 3]. Early cognitive impairment is a significant feature in many PD patients and can have a profound effect on

the life quality of both patients and caregivers [4]. Most longitudinal studies on PD conclude that dementia is an inevitable outcome if patients are followed up long enough [5, 6].

So far, there are few effective therapeutic options to treat dementia of PD (PDD). Due to the heterogeneous nature of the cognitive deficits in PD, it is also difficult to predict when a patient will develop PDD. Thus, the exact nature of the cognitive impairments occurring at the early stages of PD and their relationship to the evolution of a later dementia should be explored. It is critical to further study the effective screening scales for early cognitive impairment in different PD populations, such as different race and different education levels. A systematic review and meta-analysis revealed that higher levels of education was associated with better cognitive performance while a small but significant slowness in cognitive decline was not associated with a reduction in long-term dementia in PD [7]. Mini-Mental State Ex-

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**Table 1.** Demographic and clinical features of the PD patients

	MoCA<26	MoCA≥26	t/Chi square	P values
No. (%)	45 (65.2)	24 (34.8)		
Gender (M/F)	28/17	17/7	2.887	0.591
Age (yr)	63.89±14.31	64.23±8.58	0.081	0.936
Onset age(yr)	60.90±10.02	60.46±9.28	-0.142	0.888
Education (yr)	11.34±3.14	12.46±3.41	1.072	0.289
Disease duration (yr)	5.29±5.08	3.77±2.86	-0.917	0.364
UPDRS-III	24.49±13.04	13.31±8.17	-2.877	0.006
Hoehn-Yahr stage				
1	9	5	1.955	0.925
1.5	5	3		
2	13	9		
2.5	10	4		
3	4	2		
4	2	1		
5	2	0		

Abbreviation used: PD: Parkinson's disease; MoCA: Montreal Cognitive Assessment; UPDRS-III: Unified Rating Scale; part III.

amination Score (MMSE) and other neuropsychological scales were generally used to screen cognitive impairment in Chinese patient with dementia, especially in Alzheimer's disease [8]. Montreal Cognitive Assessment (MoCA) scale has been shown to be more sensitive than the MMSE for the detection of mild cognitive impairment (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 [9]. Meanwhile, a MMSE score less than 26 was used to classify PD patients to cognitive impairment. However, this cutoff has not been validated for all PD patients [10].

We hypothesized that a substantial proportion of PD patients would be detected as cognitive impairment (score <26) based on the MoCA in spite of having a normal MMSE score. Although there are many studies addressing the issue of cognition and risk factors in PD [11-15], an investigation on cognitive impairment in Chinese PD patients with higher education levels and normal global cognition according to MMSE has not been reported. The aim of this study was to explore characteristics of cognitive impairments by the MoCA in Chinese PD patients with higher education levels and normal global cognition according to MMSE. This

study will be very helpful for the prevention and treatment of cognitive impairment in patients with PD.

### Patients and methods

#### Participants

A cohort of 69 consecutive PD patients (45 male and 24 female) were admitted at the First Affiliated Hospital of Xi'an Jiaotong University from March 2010 to December 2013. This study was approved and registered in the First Affiliated Hospital of Xi'an Jiaotong University, all patients signed the informed consent, and their demographic data were listed in **Table 1**.

The diagnosis of PD was established by an expert neurologist in movement disorders according to the UK Brain Bank criteria [16]. Only PD patients who were educated to middle

school and above (more than 6 years) were consecutively enrolled in this study. All other patients including Lewy body dementia, symptomatic Parkinson's syndrome and Parkinson's plus syndrome with different diagnosis were excluded. All patients were recruited in this study when their MMSE scores were more than 24 (of 30), where the cutoff point for participants who had more than 6 years of education (middle or high school) was adopted to screen dementia in China [16]. Although the Movement Disorder Society Task Force (MDS-TF) recommend that PD patients with decreased global cognitive were identified by a MMSE score under 26, the recommended cut off is appropriate for patients below the age of 80 and for those with at least 10 years of formal education [17]. Patients were enrolled based on the cutoff MMSE score 24 as a normal cognitive function standard in order to exclude the patients with apparent dementia.

#### Neurological and neuropsychological assessment

A neurologic examination was performed on all patients to confirm the diagnosis of PD. The following data were collected: gender, age, onset age, educational years, disease duration, medical history and medicine usage. The duration of

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**Table 2.** Neuropsychological assessment in PD patients with (MoCA<26) or without cognitive impairment (MoCA≥26)

	MoCA<26 (n=45)	MoCA ≥26 (n=24)	T value	P value
FOM	15.66±2.47	17.38±1.26	3.170	0.003
RVR	33.89±7.98	48.23±8.27	5.475	0.000
BD	25.66±11.18	43.38±7.55	5.269	0.000
DS	11.20±1.92	13.23±2.01	3.216	0.002
MMSE	27.31±1.38	29.23±1.01	4.536	0.000

Abbreviation used: PD: Parkinson's disease; FOM: Fuld Object Memory; RVR: Rapid Verbal Retrieve; BD: Block Design; DS: Digit Span; MoCA: Montreal Cognitive Assessment; MMSE: Mini-Mental State Examination Score.

disease was defined as the time between the appearance of the first motor symptom as reported by the patient, and the disease severity which was determined using the Hoehn-yahr staging rating scale and the Unified Parkinson's Disease Rating Scale part III (UPDRS-III) [18]. Each participant was interviewed by a licensed neuropsychologist. A battery of the neuropsychological tests [8, 19, 20] was administered to assess multiple cognitive domains, which included: the Chinese version of MMSE and Montreal Cognitive Assessment Scale (MoCA) were used to evaluate the total cognition function; Fuld Object Memory evaluation (FOM) was used to evaluate delay memory function; Rapid Verbal Retrieve (RVR) was used to evaluate language fluency; Block Design (BD) in Wechsler Intelligence Scale for Children (WISC) was used to evaluate visuospatial function; Digit Span (DS) in Wechsler Adult Intelligence Scale-Revised Chinese (WAIS-RC) was used to evaluate immediate memory function and attention. The above neuropsychological tests were performed to all PD patients.

The cutoff of MoCA score was 26 and the cutoff score for FOM RVR, BD, DS was 11, 25, 20, and 7, respectively. Neuropsychological evaluation was administered by the same neuropsychologist with the patient on the best condition. Brain magnetic resonance imaging (MRI) was performed for all patients to exclude other disease. The diagnosis of cognitive impairment was based on the cutoff MoCA score.

### Statistical analysis

Continuous variables were demonstrate as means ± standard deviations (SD). The Chi square test was used to analyze differences in

the frequency of categorical variables. Differences in the means of continuous measurements were determined with t-test. The demographic, clinical characteristics and cognitive domain of PD patients were classified into two groups (i.e. those screened as positive or negative for cognitive impairment using the MoCA) and compared. Independent factors which indicated an association ( $P \leq 0.10$ ) of PD with cognitive impairment were entered into a binary logistic regression model (i.e., gender, age, onset age, education years, disease duration, Hoehn-Yahr stage, UPDRS III and MMSE, FOM, RVR, BD, DS), with the incident cognitive impairment as the dependent verity. The prediction accuracy of different potential cutoff scores of MMSE screening for PD patients with and without cognitive impairment (classified using the MoCA) was assessed using the area under the receiver operating curve (AUC). For each possible cutoff score, the sensitivity and specificity were computed. The score with the highest Youden Index score was identified as the optimal cutoff score. The relative 95% confidence intervals were also estimated. Statistical analyses were made by using SPSS13.0 for Windows program. A *P*-value of less than 0.05 was considered as a statistically significant difference.

## Results

### *The demographic and clinical basic data from PD patients*

The demographic and clinical features of the 69 PD cases invited to participate in this study were showed in **Table 1**. There were 45 (65.2%) patients reaching this criterion if the cognitive impairment of PD patients was diagnosed as the cutoff score of MoCA was less than 26. That is to say, among the Chinese PD patients who had middle school (or higher) education levels and normal global cognition according to MMSE score, about 65.2% patients have cognitive impairment based on the score of MoCA. Apart from the scores on Part III of the UPDRS, there were no significant difference between PD patients with and without cognitive impairment in other factors including age, onset age, gender, education years and disease duration.

### *Neuropsychological and cognitive domain assessment in PD patients*

As we diagnosed cognitive impairment according to the cutoff score of MoCA, patients with a

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**Table 3.** Cognitive domain assessment in patients with PD according to MoCA

	MoCA<26 (n=45)	MoCA≥26 (n=24)	T value	P value
Visuospatial and executive	3.00±1.43	4.69±0.63	5.660	0.000
Naming	2.40±0.60	2.92±0.28	4.091	0.000
Attention	5.11±0.80	5.92±0.28	5.219	0.000
Language	1.34±0.84	2.15±0.38	4.612	0.000
Abstraction	1.06±0.76	2.00±0.00	7.296	0.000
Delayed recall	1.17±1.51	3.85±1.14	5.802	0.000
Orientation	5.69±0.63	5.92±0.28	1.805	0.078

Abbreviation used: PD: Parkinson's disease; MoCA: Montreal Cognitive Assessment.

**Table 4.** Logistic regression analysis result of the relationship between the cognition and neuropsychological tests and clinical features

	B coefficient	OR	95% CI	P value
UPDRS-III	0.097	1.112	10.21-1.189	0.013
RVR	-0.209	0.866	0.763-0.983	0.026
BD	-0.256	0.775	0.623-0.694	0.021

Abbreviation used: UPDRS-III: Unified Parkinson's Disease Rating Scale part III; RVR: Rapid Verbal Retrieve; BD: Block Design.

MoCA >26 perform better on the neuropsychological scales than do patients with a MoCA <26 (**Table 2**). In addition, by comparing cognitive domain assessments by patients with MoCA score cutoff of 26, it was revealed that differences of cognitive dysfunction existed in visuospatial and executive, naming, attention, language, abstraction and delayed recall disturbances, but not in orientation impairment (**Table 3**).

### Factors associated with cognitive impairment in PD patients

The logistic regression results that identified the demographic, clinical varieties and neuropsychological scales of PD patients were independently associated with positive cognitive impairment (i.e., a score of less than 26 based on the MoCA) are shown in **Table 4**. Only more severe motor symptoms (i.e., higher scores on Part III of the UPDRS) was independently associated with positive cognitive impairment. Somehow surprisingly, apart from RVR and BD, other neuropsychological measures that were significant in the univariate analysis did not remain in the final multivariate model, which

may due to the reason that all of the neuropsychological scales were strongly correlated with the severity of PD motor symptoms (correlation of the five scales with the score on Part III of UPDRS ranged from 0.352 to 0.531).

### Optimal cutoff score for cognitive impairment of the MMSE in Chinese PD patients educated to middle school education or higher

The discriminatory validity of MMSE for screening cognitive impairment (according to MoCA cutoff) in PD patients was examined using receiver operating characteristics curves (ROC). As shown in **Figure 1**, the area under the curve (AUC) was 0.863 (95% CI=0.749-0.978). The biggest Youden Index was 0.523, and the optimal cutoff score was 27.5 (27/28). The sensitivity and specificity of this cutoff were 76.9% and 74.3%, respectively.

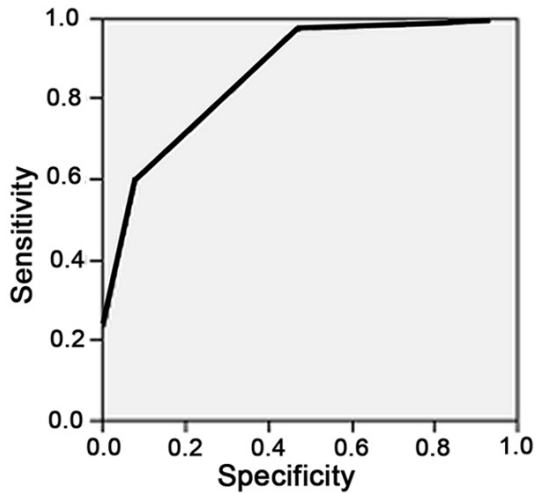
## Discussion

Cognitive impairment is an important clinical feature of PD with the spectrum of deficits ranges from none to severe dementia. It is also even common in early-stage PD patients [21-23]. In this study, among the Chinese PD patients with middle school education and normal global cognition according to MMSE, 65.2% patients have cognitive impairment based on the recommended cutoff score 26 of the MoCA. MoCA evaluation demonstrated more errors than MMSE in these PD patients in cognitive domains such as visuospatial performance, executive function, attention, language, abstraction and delayed recall. This suggests that MoCA will be more sensitive than MMSE to identify early cognitive impairment in PD, which is in accordance with previous conclusion [10].

In this study, we also found that 28 was the optimal cutoff score of the MMSE screening for cognitive impairment in Chinese patients with middle school education or higher, although the sensitivity and specificity of this cutoff were 76.9% and 74.3%, respectively. The MMSE is influenced by the factors such as age and the education level. MDS-TF recommend a MMSE score of under 26 as the cutoff value for global cognitive impairment in PD patients below the



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**Figure 1.** Receiver operating curves (ROC) of MMSE for screening cognitive impairment (defined by MoCA) in PD patients.

age of 80 and those with at least 10 years of formal education [17].

It has been demonstrated that different conclusions will be made due to a different diagnostic standard and measures in the same specific research objects. Thus, the drawing up of standard diagnostic criteria and rating scales for cognitive impairment in PD are very important in clinic research. The properties of the Chinese version of the MoCA have been evaluated in elder Chinese people. It recommended a cutoff score of 26 for the diagnosis of mild cognitive impairment (MCI) and Alzheimer's disease (AD) [19]. However, an appropriate cutoff score of MoCA for screening dementia in PD patients has been argued. In fact, some researchers have recommended that the optimal cutoff score of MoCA for diagnosing cognitive deficit or dementia should be lower than 26 [10, 24]. One study using a score of 26 of MoCA as the cutoff, had showed that PD patients who screened positive for dementia performed worse on only five out of seven MoCA subtests and the subscale scores for attention and abstraction were not significantly different between PD patients who were screened as positive dementia and negative dementia [25]. Another study had found that a cutoff MoCA score of 23 was significantly differed regarding the screening of dementia whether in PD patients or in normal controls [20]. So it is necessary to further study the validity of MoCA in different PD patients.

It is undeniable that PD has a common cognitive impairment in patients without dementia. Our study showed that cognitive dysfunction existed in extensive domains including visuospatial and executive, naming, attention, language, abstraction and delayed recall. The scores of UPDRS-III, RVR and BD were independent predictors for cognitive damage. In addition, we found that the occurrence of cognitive impairment in PD patients was not associated with age, onset age, gender, disease duration, educational years and Hoehn-Yahr stages especially, while the scores of FOM and DS were. It was possible that neuropsychological scales were strongly correlated with the severity of PD motor symptoms. On the other hand, it may not be excluded to the sample size and characteristics of the research objects.

It is showed that many patients have relatively subtle cognitive defects, which is only demonstrable by means of neuropsychological test and may not evolve to dementia in a range of many years of follow-up. Timing to develop dementia has shown highly variable: some develop PD dementia after diagnosis 2-3 years and others remain non-demented for decades [26]. Historically, based on the measurable presence of cognitive dysfunctions in single or multiple cognitive domains without concurring disabilities on activities of daily living [27], mild cognitive impairment (MCI) has been considered as the transitional stage between normality and dementia. The MCI concept has recently been applied to PD patients with subtle cognitive impairment but with short of the diagnostic criteria for dementia. To date, it is still ambiguous regarding the diagnostic criteria for PD-MCI, without universally accepted standard in clinic. There is uncertainty about the appropriate of neuropsychological scales. In fact, whether all cognitive impairment seen in PD should be classified as PD-MCI is still a contentious issue. This term lacks clinical utility and remains a target for scientific research [13, 28]. It should be recognized that cognitive function will decline over time leading to dementia within a relatively short period in some PD patients, while in others, deficits may appear early in the disease but remain unchanged or even improve over time [29]. One study found that there are distinct cognitive phenotypes in PD: one consists of frontostriatal executive deficits that are common but not progressive and another has more

posterior cortical deficits, which indicates that global cognitive declines and eventually develops dementia [30]. However, another study reported that a significant global cognitive decline was heralded and dominated by deficits in the visuospatial function and memory domains, but not in executive function [31]. As such, the cognitive impairment definition of PD and phenotypes of cognitive impairment should take these into account. The heterogeneity of cognitive damage of PD should be defined in the future longitudinal studies.

This retrospective analysis involved 69 consecutive PD patients, probably more cases are needed to justify our findings from large-scale studies. Overall, we believe that the MoCA provides considerably more sensitivity scale for the cognitive status of patients with PD than other clinical screening tools such as the MMSE. The MoCA would be a better choice as a cognitive screening instrument in PD patients no matter whether to have dementia.

In conclusion, there are extensive cognitive domain impairments in PD patients with normal global cognitive according to MMSE. MoCA is a more sensitive scale to screen cognitive impairments in PD. The cutoff score of 28 on MMSE may be more appropriate for screening cognitive impairment in Chinese PD patients with more education levels.

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### Disclosure of conflict of interest

None.

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