

# Cognitive Profiles Stratified by Education Using Montreal Cognitive Assessment in Parkinson's Disease Patients with Freezing of Gait

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**Purpose:** Parkinson's disease (PD) patients with freezing of gait (FOG) may present with complex and heterogeneous cognitive profiles. Owing to limited access to comprehensive neuropsychological battery in ordinary clinical practice, the Montreal Cognitive Assessment (MoCA) is likely to be easily available cognitive data for comparisons among studies. This study aims to explore the cognitive profiles stratified by education using MoCA in PD patients with FOG.

**Patients and Methods:** PD patients with FOG (FOG+, n = 52) and without FOG (FOG-, n = 71) were included in our study. MoCA items were categorized into five subsections (attention/working memory, executive function, episodic memory, language, and visuospatial function) referring to previously published criteria. Cognitive assessments were compared based on five subsections between groups stratified by three education levels (0–6 years, 7–12 years, and >12 years). The association of cognitive measurements with FOG were analyzed using binary logistic regression models with adjustment for variables.

**Results:** The total scores and subscores of each subsection of MoCA were similar between two groups of each education level. Further detailed analysis showed that a composite measure labeled “Attention/working memory-Composite” (abbreviated to Attention-C), consisting of the scores of four items (target detection task, serial sevens, digit forward and backward, and sentence repetition), were lower significantly in FOG+ group compared with FOG- group in patients with education year  $\leq 6$  years. The significant association of Attention-C with FOG held true when controlling for disease duration, but not for H-Y stage, MDS-UPDRS III, HAMA, and HAMD.

**Conclusion:** Overall, our findings gave a hint that Attention-C derived from MoCA might be a potential factor associated with FOG in PD patients with lower education level (education year  $\leq 6$  years), which will need to be validated in future studies.

**Plain Language Summary:** Parkinson's disease (PD) patients with freezing of gait (FOG) may present with complex and heterogeneous cognitive profiles. Owing to limited access to comprehensive neuropsychological battery in ordinary clinical practice, the Montreal Cognitive Assessment (MoCA) is likely to be easily available cognitive data for comparisons among studies. To the best of our knowledge, our study is the first to investigate the cognitive profiles using MoCA stratified by education in Chinese PD patients with FOG. We proposed a novel composite measure derived from MoCA labeled “Attention/working memory-Composite” (abbreviated to Attention-C), consisting of the scores of four items (target detection task, serial sevens, digit forward and backward, and sentence repetition). We found a significant association of Attention-C with FOG existed in PD patients with education year  $\leq 6$  years when controlling for disease duration, but disappeared for H-Y stage, MDS-UPDRS III, HAMA, and HAMD. It may be attributed to a large extent to the relatively small size of our study population. Our findings gave a hint that Attention-C derived from MoCA might be a potential factor associated with FOG in PD patients with lower education level (education year  $\leq 6$  years), which need to be further explored and validated in expanded studies with different international populations. Thus, the present study could provide critical implications for ordinary clinical practice where comprehensive neuropsychological batteries are not easily accessible to clinicians.

**Keywords:** Parkinson's disease, freezing of gait, Montreal Cognitive Assessment, attention, working memory, executive function

## Introduction

Cognitive dysfunction is common in Parkinson's disease (PD), especially as the disease advances. Cognitive profile of PD is complex with heterogeneity in onset timing, spectrum of cognitive domains being affected, progression to dementia, as well as response to treatments.<sup>1,2</sup> A dual syndrome hypothesis have been put forward that the fronto-striatal profile of cognitive deficit (often referring to executive function) in PD patients which generally respond to dopaminergic therapy and spare the progression to dementia, in contrast with a dementia syndrome with prodromal visuospatial impairments which may be sensitive to a greater degree to cholinergic drugs.<sup>3,4</sup> Freezing of gait (FOG) is characterized by brief and episodic absence or evident reduction of forward stepping typically triggered by gait initiation, turning, traversing narrow passages, or dual task, and is a mysterious clinical phenomenon with its own pathophysiology distinct from the cardinal motor features of PD.<sup>5</sup> Recent evidence suggested that FOG patterns could be identified according to motor, cognitive, and limbic impairments.<sup>6</sup> PD patients with FOG seem to present with more enigmatic cognitive profile in view of the predominant involvement of cognitive impairment in underlying neurobiological underpinnings of FOG.<sup>7-9</sup> Attentional set-shifting/executive deficits are widely recognized to be associated with FOG.<sup>10-15</sup> Furthermore, poorer memory and visuospatial deficit, as well as hallucinations, have been reported to be linked to FOG in PD patients.<sup>16-18</sup> However, results are still in debate. Furthermore, no studies to date have stratified education, which is one of the most important factors associated with cognition, in cognition assessments of FOG patients. It is widely recognized that less education correlate with worse performance in cognition assessments. Different education levels in culturally diverse populations lead to the necessity of establishing or adjusting the cutoff points of cognitive scales.<sup>19,20</sup> For example, Lu et al found that the recommended cutoff points of initial version of MoCA was not applicable to elderly Chinese due to low average and broad range in both education level and MoCA score.<sup>21</sup> The heterogeneity in education level of prior studies to some extent influenced the comparability of the results. Thus, it is required to explore the cognitive profiles stratified by education in PD patients with FOG.

The Montreal Cognitive Assessment (MoCA) has been widely used as a screening tool for global cognitive function, and is only used for level I (abbreviated assessment) diagnosis and not domain-specific diagnosis in PD.<sup>22</sup> However, many clinicians and researchers do not have access to the comprehensive neuropsychological battery. Hendershott et al assessed the five domain-specific subsections of MoCA (attention/working memory, executive function, episodic memory, language, and visuospatial function) compared to the full neuropsychology batteries, and found that all MoCA subsections predicted impairment in their respective cognitive domain in PD patients.<sup>23</sup> Therefore, MoCA was applied in our study to analyze the cognitive profile of PD patients with and without FOG, in order to provide useful implications for ordinary clinical practice.

The objective of this study was to compare cognitive function using MoCA between PD patients with and without FOG, and then further analyze the domain-specific cognitive performance stratified by education. Lastly, we sought to examine the association of cognitive measurements with FOG in PD patients.

## Materials and Methods

### Study Design and Patients

We consecutively recruited idiopathic patients with PD from Department of Neurology in Beijing Shijingshan Hospital from January 2020 to August 2022. The inclusion criteria were as follows: (1) age  $\geq 55$  years; (2) patients with the diagnosis of clinical definite PD according to the Movement Disorder Society (MDS) Clinical Diagnostic Criteria. The exclusion criteria were as follows: (1) evidence of secondary, atypical, or hereditary parkinsonism; (2) history of moderate-to-severe stroke, head trauma or tumor; (3) an inability to complete the cognitive and movement assessments, such as severe visual impairment, hearing loss, severe dementia or psychiatric disorders; (4) patients with unclear FOG or gait problems that could not exclude the possibility of being secondary to orthopedic issues, visual defects, ataxia et al. This study was approved by the Ethics Committee of Beijing Shijingshan Hospital, Shijingshan Teaching Hospital of Capital Medical University, and was conducted in accordance with the ethical standards outlined in the Helsinki Declaration. The written informed consent was obtained from the patients or their legal proxies.

## Clinical Assessment

The following socio-demographic and clinical data of patients were collected: age, gender, years of education, past medical history, history of smoking and alcohol use. The severity and stage of PD was evaluated using MDS Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III) and Hoehn and Yahr (H-Y) staging. FOG was assessed with FOG questionnaire (FOGQ) combined with history and examination by two experienced neurologists. FOG was defined as a score of one or more on item 3 of FOGQ (feeling like feet being glued to the floor) and the neurologist would explain and demonstrate freezing if required. Based on this, patients were divided into two groups, FOG+ and FOG-. Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD) were applied to assess patients' anxiety and depression, respectively.

## Assessment of Cognitive Function

Cognitive function was evaluated using the MoCA-Beijing version in the on-medication state. The MoCA has seven cognitive domains, including visuospatial/executive function, naming, attention, language, abstract, recall and orientation. Diagnostic criteria for mild cognitive impairment (MCI) in PD proposed by MDS Task Force Guidelines recommend cognition assessment in five domains, including attention and working memory, executive, language, memory, and visuospatial. According to published criteria,<sup>24</sup> Hendershott et al categorized the MoCA items into five subsections: (1) Attention/Working Memory included target detection task, serial sevens, and digit forward and backward; (2) Executive Function included Trails B task, phonemic fluency, and verbal abstraction; (3) Episodic Memory included recall task; (4) Language included a naming task and sentence repetition; and (5) Visuospatial function included clock drawing and three-dimensional figure copy, and then identified the concordance of the five subsections of MoCA with comprehensive neuropsychological batteries.<sup>23</sup> Therefore, we tried to explore cognitive function in terms of the five subsections of MoCA in PD patients with and without FOG in our study. Due to the strong association of education with cognition, cognitive assessments and comparisons between two groups were carried out based on three education levels, namely 0–6 years, 7–12 years, and >12 years.

## Statistical Analysis

Data were expressed as number and percentage for categorical variables, and mean with standard deviation or median with interquartile range for continuous variables. The Chi-squared test was performed for categorical variables, and two-sample *t*-test and Mann–Whitney test were performed for continuous variables in normal and abnormal distribution, respectively. Binary logistic regression models were performed to explore the cognitive measurements associated with FOG in PD patients, with adjustment for the possible confounders and variables with  $P < 0.05$  in comparisons between PD patients with and without FOG.  $P < 0.05$  was considered statistically significant. Statistical analysis was conducted with SPSS 24.0 (SPSS Inc, Chicago, IL).

## Results

### Patient Demographics and Characteristics

Of 143 participants during the study period, a total of 123 patients were included in the final analysis, after excluding patients with uncertain PD diagnosis or suspicion of atypical parkinsonism (4 patients), a history of stroke with language or physically disabilities (4 patients), an inability to complete the cognitive and movement assessment (3 patients with hearing loss, 1 patient with visual defects, 3 patients with Clinical Dementia Rating  $\geq 2$ ), gait problems with possibility of being secondary to orthopedic issues (5 patients). No one refused to participate in our study. There were 52 PD patients (42.3%) grouped into FOG+ group, with a longer disease duration compared with FOG- group (6.00 [4.25–8.00] vs 4.00 [3.00–6.00],  $p = 0.004$ ). The education levels were matched between two groups. There was also no statistically significant difference between two groups regarding age, gender, prevalence of medical history, H-Y stage, UPDRS-III score, as well as HAMA and HAMD scores. The demographic and clinical characteristics of the patients are listed in [Table 1](#).

**Table 1** The Demographics and Characteristics Between PD Patients with and without FOG

	<b>FOG+ (n = 52)</b>	<b>FOG- (n = 71)</b>	<b>P</b>
Age (years), median (IQR)	71.5 (67.0–75.0)	69.0 (65.0–73.0)	0.183
Male, no. (%)	29 (55.8)	37 (52.1)	0.688
Education level, no. (%)			0.767
0–6 year	20 (38.5%)	23 (32.4%)	
7–12 year	24 (46.2%)	37 (52.1%)	
>12 year	8 (15.3%)	11 (15.5%)	
Medical history, no. (%)			
Hypertension	25 (48.1)	35 (49.3)	0.894
Diabetes mellitus	13 (25.0)	20 (28.2)	0.695
Hyperlipidemia	26 (50.0)	37 (52.1)	0.817
Coronary heart disease	13 (25.0)	21 (29.6)	0.575
Smoking history, no. (%)	14 (26.9)	17 (23.9)	0.707
Drinking history, no. (%)	13 (25.0)	16 (22.5)	0.750
PD disease duration (years), median (IQR)	6.00 (4.25–8.00)	4.00 (3.00–6.00)	<b>0.004</b>
H-Y stage, median (IQR)	3 (3–4)	3 (3–4)	0.173
MDS-UPDRS III (OFF), median (IQR)	63.0 (51.0–70.8)	57.0 (48.0–68.0)	0.217
HAMA score, median (IQR)	9 (6–12)	7 (6–10)	0.188
HAMD score, median (IQR)	7 (5–10)	6 (5–9)	0.624

**Note:** Significant results are highlighted in bold (p<0.05).

**Abbreviations:** PD, Parkinson’s disease; FOG, freezing of gait; IQR, interquartile range; H-Y, Hoehn and Yahr; MDS-UPDRS III, Movement Disorder Society Unified Parkinson’s Disease Rating Scale Part III; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale.

### Cognitive Assessments Stratified by Education

Based on the education stratification, comparisons of cognitive assessments in five domain-specific subsections of MoCA between PD patients with and without FOG are presented in Table 2 and Figure 1. There were no significant differences

**Table 2** Cognitive Function Between PD Patients with and without FOG

	<b>FOG+</b>	<b>FOG-</b>	<b>P</b>
All participants			
MoCA total score	21.87 ±3.799	22.62 ±3.173	0.233
Attention/Working memory	5.25 ±0.764	5.46 ±0.581	0.079
Executive function	2.35 ±1.153	2.51 ±1.170	0.450
Episodic memory	2.10 ±0.913	2.30 ±0.885	0.225
Language	3.77 ±0.783	3.93 ±0.704	0.244
Visuospatial	2.35 ±1.170	2.46 ±1.205	0.586
0–6 year			
MoCA total score	18.25 ±2.149	19.43 ±2.519	0.108
Attention/Working memory	4.85 ±0.875	5.30 ±0.703	0.066
Executive function	1.15 ±0.489	1.30 ±0.703	0.404
Episodic memory	1.65 ±0.671	1.91 ±0.848	0.271
Language	3.35 ±0.587	3.74 ±0.752	0.069
Visuospatial	1.25 ±0.639	1.17 ±0.650	0.702
7–12 year			
MoCA total score	23.54 ±2.553	23.73 ±2.104	0.755
Attention/Working memory	5.46 ±0.588	5.51 ±0.507	0.698
Executive function	3.00±0.722	2.95 ±0.911	0.807
Episodic memory	2.21 ±0.932	2.41 ±0.865	0.402
Language	3.96±0.806	3.97 ±0.763	0.832
Visuospatial	2.88 ±0.850	2.95 ±0.911	0.762

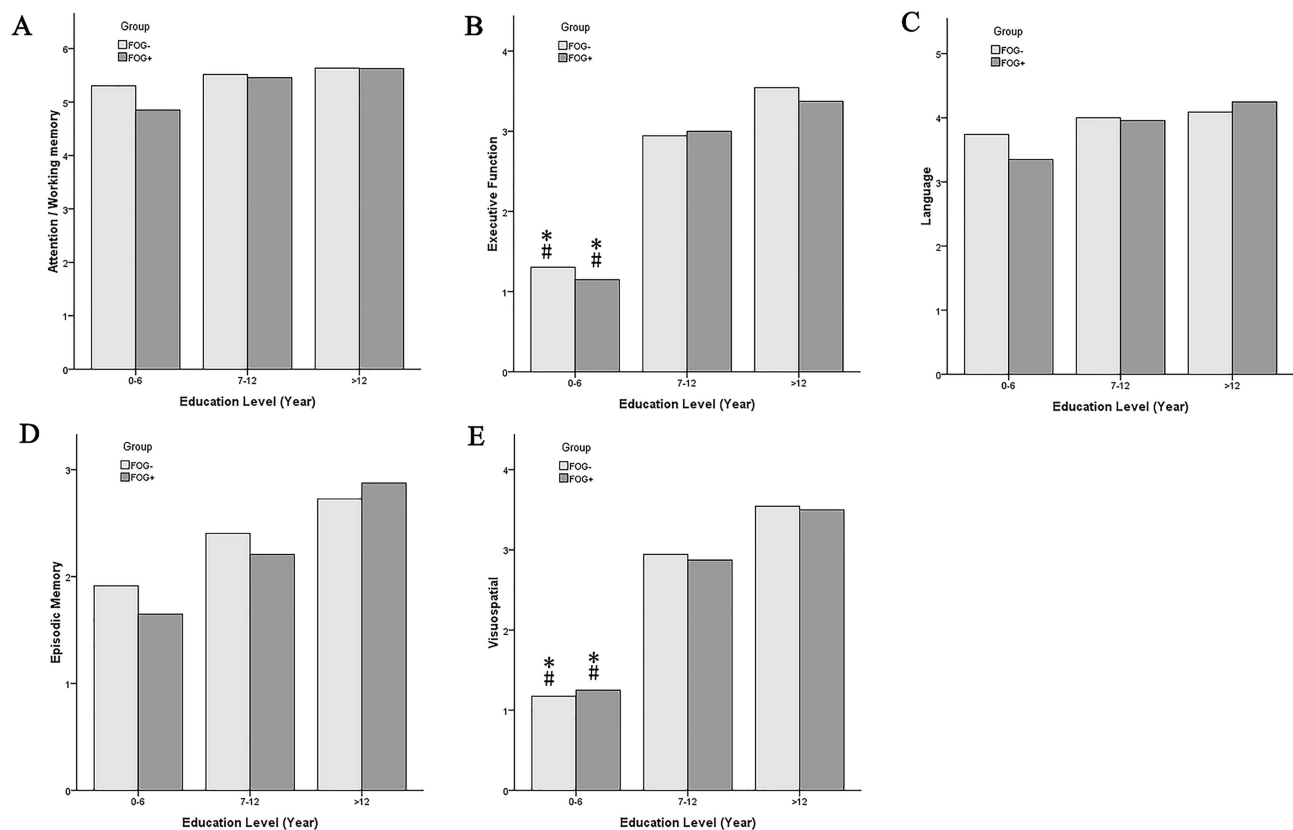
(Continued)

Table 2 (Continued).

	FOG+	FOG-	P
>12 year			
MoCA total score	25.75 ±2.493	25.55 ±1.809	0.838
Attention/Working memory	5.63 ±0.518	5.64 ±0.505	0.962
Executive function	3.38 ±0.744	3.55 ±0.522	0.564
Episodic memory	2.88 ±0.835	2.73±0.786	0.698
Language	4.13 ±0.991	4.09 ±0.539	0.924
Visuospatial	3.50 ±0.756	3.55 ±0.522	0.878

**Abbreviations:** PD, Parkinson's disease; FOG, freezing of gait; MoCA, Montreal Cognitive Assessment.

in neither the total scores nor subscores of each subsection between the two groups of the three education levels. However, it was noted that FOG+ patients were likely to present poorer performance in the attention/working memory and language subsections of MoCA compared to the FOG- group in patients with education year  $\leq 6$  years ( $4.85 \pm 0.875$  vs  $5.30 \pm 0.703$ ,  $p = 0.066$ ;  $3.35 \pm 0.587$  vs  $3.74 \pm 0.752$ ,  $p = 0.069$ , respectively). Moreover, Figure 1 showed that the scores of executive (Figure 1B) and visuospatial function (Figure 1E) subsections were obviously lower in patients with education year  $\leq 6$  years than those with other two higher education levels in both FOG+ and FOG- groups.



**Figure 1** Cognitive profiles in PD patients with and without FOG stratified by education.

**Notes:** The cognitive assessments in five domain-specific subsection of MoCA (A) attention/working memory; (B) executive function; (C) language; (D) episodic memory; (E) visuospatial function between PD patients with and without FOG are compared among the three education levels. \*Denotes a significant difference ( $p < 0.001$ ) in comparison between patients with education year  $\leq 6$  years and 7–12 years. #Denotes a significant difference ( $p < 0.001$ ) in comparison between patients with education year  $\leq 6$  years and  $>12$  years.

## Comparisons of Each Item of Attention/Working Memory and Language Between FOG+ and FOG- Patients with Education Year $\leq 6$ Years

Further detailed comparisons revealed that patients with educational year  $\leq 6$  years, in both FOG+ and FOG- groups, gained full points in the naming task of language subsection, which hinted that the sentence repetition rather than naming was the component contributing to the difference of language subsection. Thus, we tried to get a composite measure consisting of the scores of four items (target detection task, serial sevens, digit forward and backward, and sentence repetition). The composite measure was lower significantly in FOG+ group compared with FOG- group in PD patients with education year  $\leq 6$  years ( $5.20 \pm 1.240$  vs  $6.04 \pm 1.261$ ,  $p = 0.033$ ) (Table 3). The other two groups with higher education level did not present significant difference between PD patients with and without FOG (Supplemental Table 1).

## The Association of the Composite Cognitive Measure with FOG in PD Patients with Educational Year $\leq 6$ Years

The binary logistic regression analyses were conducted in PD patients with educational year  $\leq 6$  years (Table 4). We used variables and controlled for them in different models in order to show their contribution to the association of the

**Table 3** Comparison of Each Item of Attention/Working Memory and Language Between FOG+ and FOG- Patients with Education Year  $\leq 6$  Years

	FOG+	FOG-	P
Attention/Working memory			
Target detection task	0.85 $\pm$ 0.366	0.96 $\pm$ 0.209	0.260
Serial sevens	2.20 $\pm$ 0.616	2.39 $\pm$ 0.583	0.302
Digit forward/backward	1.80 $\pm$ 0.410	1.96 $\pm$ 0.209	0.135
Language			
Naming	3 $\pm$ 0	3 $\pm$ 0	N/A
Sentence repetition	0.35 $\pm$ 0.587	0.74 $\pm$ 0.752	0.069
Composite measure	5.20 $\pm$ 1.240	6.04 $\pm$ 1.261	<b>0.033</b>

**Note:** Significant results are highlighted in bold ( $p < 0.05$ ).

**Abbreviations:** FOG, freezing of gait; N/A, not applicable.

**Table 4** Logistic Regression Analysis for the Association of the Composite Cognitive Measure with FOG in PD Patients with Education Year  $\leq 6$  Years

	OR (95% CI)	P
Model 1	0.575 (0.338–0.979)	<b>0.042</b>
Model 2	0.570 (0.317–1.027)	0.061
Model 3	0.600 (0.350–1.030)	0.064

**Notes:** Significant results are highlighted in bold ( $p < 0.05$ ). Model 1: disease duration and Attention-C were included as co-variables. Model 2: disease duration, H-Y stage, MDS-UPDRS III score, and Attention-C were included as co-variables. Model 3: disease duration, HAMA score, HAMD score, and Attention-C were included as co-variables.

**Abbreviations:** FOG, freezing of gait; PD, Parkinson's disease; OR, odds ratio; CI, confidence interval; H-Y, Hoehn and Yahr; MDS-UPDRS III, Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale.

composite cognitive measure with FOG. The composite measure was associated with FOG independent of disease duration (odds ratio [OR], 0.575; 95% confidence interval [CI], 0.338–0.979;  $p = 0.042$ ), but the significance was disappeared when adjusting for disease duration, H-Y stage, and MDS-UPDRS III score simultaneously (OR, 0.570; CI, 0.317–1.027;  $p = 0.061$ ) and for disease duration, HAMA score, and HAMD score simultaneously (OR, 0.600; CI, 0.350–1.030;  $p = 0.064$ ). The data of logistic regression analyses for all participants and subgroup based on education level was shown in [Supplemental Table 2](#). The other two group with higher education level did not present significant association of the composite cognitive measure with FOG.

## Discussion

To the best of our knowledge, this is the first study to investigate the cognitive profiles using MoCA stratified by education in PD patients with FOG. We found a novel composite cognitive measure consisting of the scores of four items in MoCA (target detection task, serial sevens, digit forward and backward, and sentence repetition), which was likely to be associated with FOG in PD patients with education year  $\leq 6$  years.

The diagnostic criteria for PD-associated cognitive impairments from the MDS task force guideline recommended MoCA as a screening test for level I diagnosis and neuropsychological batteries to measure at least five cognitive domains (attention and working memory, executive functions, language, memory, and visuospatial function) for level II diagnosis.<sup>22</sup> However, the neuropsychological batteries are not easily accessible to most clinicians, and the comprehensive cognition assessment is a time-demanding process. Referring to the published criteria, MoCA items were categorized into five domain-specific subsections just in line with MDS task force guideline recommendation, with a concordance with the respective neuropsychological batteries. MoCA, as a promptly applicable and less time-consuming scale, therefore, was applied for cognition assessment of patients in our study.

In present study, no significant difference was found in the total score of MoCA between PD patients with and without FOG, which was in agreement with a previous study.<sup>25</sup> The failure of MoCA to uncover the difference between groups could be partially attributed to the limitation of MoCA, especially the total score, as a screening measure reflecting the global cognitive function, not domain-specific function. However, the study by Scholl et al<sup>26</sup> demonstrated, paradoxically, that PD patients with FOG exhibited lower score of MoCA than those without FOG with significant difference even after adjusting for covariates including age, education, and disease duration. This discrepancy may result from the heterogeneity in study participants and effect of medication “on” or “off” state when assessments were performed. Besides, longer disease duration was observed in FOG+ group compared with FOG- group in PD patients in current study, in line with our previous study.<sup>27</sup> A meta-analysis discovered higher FOG prevalence rate in PD patients with longer disease duration, especially in those with disease duration  $\geq 10$  years.<sup>28</sup> In contrast, no obvious difference in disease duration were observed when comparing FOG+ and FOG- groups, which could be ascribed to too much shorter disease duration of PD patients recruited in Scholl’s study for the emergence of significant difference. Therefore, more studies with larger sample size and more homogeneous study methods are required to further clarify this question.

Cognitive assessments can be affected strikingly by education level. Lu’s team have established the MoCA norms for Chinese elderly individuals,<sup>21</sup> which proposed the different cutoff points corresponding to education levels for screening cognitive decline, unlike the original version of MoCA by Nasreddine et al.<sup>24</sup> Hence, we further explored the cognitive performance by stratifying patients based on education years as well as categorizing the MoCA items into domain-specific subsections. In PD patients with education year  $\leq 6$  years, the attention/working memory and language subsections indicated a tendency toward a significant difference in comparisons between two groups. The following detailed comparisons revealed that sentence repetition rather than naming was the component contributing to the difference of language subsection. This thus prompted us to combine the scores of attention/working memory subsection and sentence repetition item to form a new composite measure, which was consequently found remarkably lower in FOG+ group than FOG- group in patients with education year  $\leq 6$  years. Vogel et al observed that the sentence repetition score of MoCA was strongly associated with the attention factor emerged in the principal component analysis (PCA), suggesting that sentence repetition task requires basic attention demand.<sup>29</sup> We therefore proposed that the composite measure, consisting of the scores of four items (target detection task, serial sevens, digit forward and backward, as well as sentence repetition), is labeled “Attention/working memory-Composite” (abbreviated to Attention-C).

The following analyses of our study demonstrated significant association of Attention-C with FOG in PD patients with education year  $\leq 6$  years that held true when controlling for disease duration, but not for H-Y stage, MDS-UPDRS III, HAMA, and HAMD, which may be due to a large extent to the relatively small size of our study population. Similar to our study, Scholl et al<sup>26</sup> found the difference in attention/executive function using Dimensional Change Card Sort test (DCCS) between PD patients with and without FOG, and the difference remained significant after adjusting for disease duration but not when adding disease severity (UPDRS-III) to other covariate adjustments in ANCOVA model. Another previous study by Morris et al<sup>25</sup> identified significant differences in attention/executive function, reflecting by the time to complete Trail Making Test (TMT) Part B minus Part A, the time to complete the Stroop color condition, and the Flankers test, between FOG+ and FOG- in PD patients when not adjusting for covariate, but the difference were no longer significant when controlling for UPDRS-III and other factors. Besides, earlier researches, most of which did not take disease severity into account, have shown that the attention/executive function were worse in PD patients with FOG compared to those without FOG.<sup>10,13,14,16,30</sup> Therefore, the association among attention/executive function, disease severity, and FOG is difficult to disentangle. In addition, the mood problems such as anxiety and depression have also been indicated to associate with attention/executive function and FOG in PD patients,<sup>31,32</sup> which may explain the negative results after controlling for HAMA and HAMD in our study. Notably, our study showed that there was only significant association of Attention-C with FOG in PD patients with education year  $\leq 6$  years, not in other two groups. We conjectured that the items from MoCA might be too simple for patients with higher education level to find significant difference and association between FOG+ and FOG- groups, and it would possibly present different results if alternative comprehensive tests were applied. It is also noteworthy that so far there have been no other studies like ours to analyze the attention/working memory by extracting items from MoCA; therefore, our results may be inappropriate to compare to those studies. Nevertheless, the possibility that the new measure “Attention-C” derived from MoCA may be a potential factor associated with FOG in PD patients with lower education level could not be fully ruled out, which merit further study with larger sample size and better homogeneity.

In fact, most cognitive tasks, such as TMT and DCCS, measure cognitive components embodying attention and executive function, both of which mirror the frontal lobe functions and are indissociable from each other.<sup>33–35</sup> In the present study, as to executive function reflected by items of MoCA including Trails B task, semantic fluency, and verbal abstraction, we failed to find difference between PD patients with and without FOG regardless of education level. Again, the aforementioned studies from Morris’s team and Scholl’s team showed contradictory results regarding executive function. Miyake et al<sup>36</sup> proposed that executive function was a broad term encompassing three components: Inhibition of Prepotent Responses (Inhibition), Mental Set Shifting (Shifting), and Information Monitoring and Updating (Updating). Cohen and colleagues declared that FOG was associated with a specific deficit of inhibition control, rather than with a general executive impairment. Thus, it can be seen that the association of executive function with FOG is highly complex and this deserves further clarification.

Several limitations of our study also should be noted. First, the sample size was relatively small, especially when participants were stratified by education level, and the convincingness of our results is somewhat weakened. Second, it was a cross-sectional and single-center study, thus the causality between attention cognition and FOG cannot be identified, and the sample population may fail to represent the general population. Third, cognitive assessments using MoCA, as most of cognitive scales, is influenced by culture and race, therefore, our findings from a Chinese sample are required to be verified in different international populations.

## Conclusions

In conclusion, the present study proposed a composite measure derived from MoCA labeled “Attention-C” including four items (target detection task, serial sevens, digit forward and backward, and sentence repetition), and gave a hint that Attention-C might be a potential factor associated with FOG in PD patients with lower education level (education year  $\leq 6$  years). Thus, our findings are likely to provide implications for ordinary clinical practice where comprehensive neuropsychological batteries are not easily accessible to clinicians. However, additional researches are warranted to validate our findings.



## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

## Institutional Review Board Statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Beijing Shijingshan Hospital, Shijingshan Teaching Hospital of Capital Medical University. All procedures followed the declaration of Helsinki.

## Informed Consent Statement

The patients/participants provided their written informed consent to participate in this study.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no conflict of interest.

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