

Rehabilitation training improves subjective cognitive decline in Parkinson's disease patients: A prospective analysis

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Research

Keywords: Parkinson's disease, subjective cognitive decline(SCD), Mild cognitive impairment (MCI), semantic fluency, rehabilitation training

Posted Date: November 18th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-108134/v1>

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Abstract

Background: The predictive value of subjective cognitive decline in Parkinson's disease (PD-SCD) remains controversial. However, there is growing evidence that individuals with subjective cognitive decline (SCD) are associated with Alzheimer's disease pathology and are a higher risk for cognitive decline. The aim of the present study is to characterize PD-SCD and its progression, assess the effects of rehabilitation training programs on cognitive function in PD patients.

Methods: Forty-two PD patients were evaluated with a neuropsychological protocol, and classified depending on the presence (PD-SCD⁺, n=22) or absence of SCD (PD-SCD⁻, n=20). After a mean follow-up of 3.0 years (2.0-4.0 years), we repeated the cognitive assessments with the same subjects. The rehabilitation training for individuals with PD for six months after the re-assessment.

Results: The clinical characteristics and overall cognitive performance of the 2 groups did not differ from baseline. During the follow-up assessment, patients with PD-SCD exhibited a more significant annual decline in Chinese-Beijing version of Montreal Cognitive Assessment-Test (BJ-MoCA) and semantic fluency than patients without PD-SCD. Stepwise logistic regression analysis showed that the MMSE Scores ($P=0.000$), HAMD Scores ($P=0.008$), male ($P=0.026$), and the presence of SCD ($P=0.022$) were risk factors for language and related functions domain. There are significant improvements detected in 2 groups after rehabilitation training in terms of BJ-MoCA. Pairwise comparisons showed that language at post-intervention in the PD-SCD⁺ groups were significantly higher than at pre-intervention in the PD-SCD⁻.

Conclusion: With the progression of the disease, the cognitive performance of patients with PD-SCD⁺ was worse than PD-SCD⁻. Meanwhile, the present data indicate that semantic fluency might be a key component to evaluate the cognitive subset of PD. Rehabilitation training is a viable intervention for PD that can improve several non-motor domains, produced larger improvements in cognition.

Background

Parkinson's disease (PD) is the second prevalent neurodegenerative disorder, next only to Alzheimer's disease. It is defined primarily as a movement disorder, also has non-motor symptoms. Cognitive impairment is one of the common and important non-motor symptoms in PD. It has been the subject of increasing research in recent decades, and occurs in around 25%-80% of PD patients[1–3]. Subjective cognitive decline (SCD)[4] refers to individual's perceived decline in memory and/or other cognitive abilities relative to their previous level of performance, in the absence of objective neuropsychological deficits, which is a common manifestation of the elderly[5]. Since it was considered a research topic related to Alzheimer's disease, there has been controversy, several studies report[6–8] that SCD is associated with depression or personality traits rather than cognitive decline. Whereas Han and colleagues[9] investigated that extensive white matter(WM) damage were observed in SCD patients, it might indicate that the SCD subjects had suffered from the pathological changes while the pathological changes were unable detected by conventional objective neuropsychological tests. Basic research[10–12]

also reports that SCD is associated with the neurodegenerative process of Alzheimer's disease(AD). Hong et al.[13] demonstrate that the SCD in cognitively normal patients with PD is an independent risk factor for incident MCI and acts as a predictor of future cognitive decline.

Compared to early conceptions, the awareness and understanding of cognitive decline in Parkinson's disease has made a lot of progress. Several researches[13–14] demonstrated that the SCD in cognitively normal patients with PD is an independent risk factor for incident MCI and acts as a predictor of future cognitive decline. The Movement Disorders Society's (MDS) diagnostic criteria from 2012 for PD-MCI confirmed that view, from which it shows that in order to identify PD-MCI, PD patients must both have objective cognitive impairment and subjective cognitive impairment, reflects the significance of SCD progress on to mild cognitive impairment or dementia.

One of the most worried PD complications for patients and their caregivers is the development of dementia[15]. Given the relative importance of cognitive impairment, there was considerable interest to find specific and appropriate therapeutic interventions. Many studies[16–17] have agreed that aerobic exercise can improve memory and executive dysfunction. Other Studies[18] have shown that learning can improve brain memory decline since the local cerebral blood flow in the occipital lobe is significantly increased when people are reading.

There are few studies[13, 19, 20] having focused on SCD in PD patients by a long-term follow-up study. Therefore, the aims of this study were (1) to investigate the neuropsychological profile of PD-SCD,(2) a longitudinal analysis of changes in cognitive performance,(3) and to investigate the feasibility of the rehabilitation training for patients with PD-SCD.

Materials And Methods

Participants

The study selected cognitively normal patients with PD from the First Hospital of Harbin Medical University. All the patients met the newly clinical diagnostic criteria for PD published by the Movement Disorders Society in 2015[21]. Cognitive performance was evaluated using the Chinese Mini-Mental State Examination (C-MMSE) and neuropsychological tests at the diagnosis of cognitively normal patients with PD. Exclusion criteria were as follows:(a) focal brain lesions or multiple lacunar infarctions in the basal ganglia based on magnetic resonance imaging (MRI),(b) cognitive deterioration defined by the C-MMSE score ≤ 25 or dementia associated with PD[22],(c) major psychiatric disorder,(d) possible comorbidities affecting cognition were excluded by laboratory testing, including thyroid function tests, human immunodeficiency syndrome(HIV),and syphilis,(e) secondary Parkinson's syndrome, Parkinsonism-Plus syndrome(PPS), and (f) Hamilton Depression Scale(HAMD) ≥ 7 .

Among 54 patients who were eligible for this study, excluding 12 patients (11 patients were lost to follow-up, and 1 patients underwent the deep-brain stimulation).The study included 42 PD patients finally. All participants received cognitive training for six months, out 6 of 42patients received no feedback scores.

The assessment of SCD is defined based on the SCD research standards proposed by the SCD Advocacy Group in 2014. The presence of SCD was assessed by the questionnaire: (a) "Do you feel that you have a declining memory?", (b) "Do you feel any persistent distractions recently?", (c) "Can you complete the previous job or operation?", (d) "Do you feel that your spoken language have gotten worse?", (e) "Do you feel that you have a declining in the recognition of graphics and shapes?". We classified the subjects into the PD-SCD⁻ (n = 20) and PD-SCD⁺ (n = 22) groups based on the responses (at least one question answered "yes"). The assessment of baseline firstly was performed, then cognitive performance was evaluated again to a mean follow-up of 3.0 (1395.88 ± 108.11d, 1006 days to 1555 days) years from the baseline assessment.

We received approval from the First Hospital of Harbin Medical University ethical standards committee. Written informed consent was obtained from all subjects participating in this study.

Clinical assessment

Motor symptom severity was measured with the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III), and disease severity was measured using the Hoehn and Yahr Scale. The general white matter hyperintensities (WMHs) score was used to grade the degree of white matter signal intensity increase in the periventricular and subcortical white matter. Depression was assessed using the Hamilton Depression Scale (HAMD).

Neuropsychological assessment

Cognitive assessments of patients were evaluated with the C-MMSE and BJ-MoCA. Attention tasks was examined using the forward and backward digit span, one hundred consecutive minus seven. Executive function were assessed by modified trail making test (follow the 1-A-2-B-3-C-4-D-5-E connection). Language and related functions were consisted of semantic fluency (asking the participants to quickly generate only animals in one minute) and naming and repeat. Memory was examined with immediate and delayed recall 1 (three words), immediate and delayed recall 2 (five words). Orientation (Orientation to time and place). Finally, visuospatial function was assessed by clock drawing test (asked the patient to draw a clock and mark 11:10), copy of cross pentagon. All assessments were performed in the PD medication "on" state.

In addition to, we calculated annual cognitive decline rate by dividing the performance score change between the baseline and follow-up assessments by the interval between the 2 assessments.

Rehabilitation training

Because no single task can adequately improve a particular cognitive construct, this study used comprehensive rehabilitation training on patients. Rehabilitation tasks covered three aspects: intellectual training (Reading, communication, moving wrist fingers), physical exercise (usually aerobic training performed 3 times a week for about 30 minutes for a period of 6 months), healthy diet (Quitting smoking and limiting alcohol. Daily intake of pure alcohol ≤ 20 grams). Most of the participants had high

adherence, rehabilitation training duration was 6 months. All assessments were performed in the "on" state.

Statistical analysis

To compare demographic and clinical characteristics between 2 groups, a 2-sample t test was used to examine the mean differences for continuous variables and a chi-square test for categorical variables. All data were tested for normality, a nonparametric statistic was used to evaluate differences between groups deviated from the standard normal distribution. The Mann–Whitney was used to compare the means in pairs of groups, respectively. We analyzed the assessment of SCD using the Multiple Response Test to make a description. Stepwise logistic regression analysis was used to examine the contribution of SCD at the baseline to cognitive performance. All the analysis were performed with SPSS-PC software version 25.0 for Windows and a $P < 0.05$ was considered significant.

Results

Baseline demographic and neuropsychological characteristics

There were a total of 42 patients with PD with normal cognition at baseline, including 22 (52.38%) who reported subjective cognitive decline. Mean disease duration of PD and UPDRS motor scores of study subjects were 7.10 years (range 3.0–34.0 years) and 18.45 points (range), respectively. No significant difference was observed between the PD-SCD⁺ and PD-SCD⁻ in terms of age, sex, duration of motor symptom, years of education, HAMD score, UPDRS motor, baseline C-MMSE and BJ-MoCA score (Table 1). Comprehensive neuropsychological tests showed that the PD-SCD⁺ and PD-SCD⁻ groups did not differ significantly regarding the baseline cognitive performance on each cognitive subsets except immediate and delayed recall 2 (Table 1). The frequency distribution of SCD assessment procedure in this study are shown in (Fig. 1). These data implied that the cognitive decline of memory were the most in the PD-SCD⁺ group.

Table 1 Baseline demographic data and clinical characteristics of PD patients according to the presence (PD-SCD⁺) or absence (PD-SCD⁻) of subjective cognitive decline

	PD-SCD ⁻ (n=20)	PD-SCD ⁺ (n=22)	p value
Age	64.10±7.20	66.45±8.71	0.348 ^a
Number of male, n (%)	10(50.0)	9(40.9)	0.550 ^c
Duration of motor symptom, (y)	6.06±2.27	8.05±6.29	0.197 ^b
Years of education	9.75±4.83	10.86±4.54	0.377 ^b
HAMD score	3.45±1.91	4.23±1.45	0.179 ^b
White matter hyperintensity score	0.70±0.47	0.95±0.49	0.121 ^b
UPDRS motor score	18.05±10.22	18.82±12.21	0.827 ^a
Baseline C-MMSE score	28.30±2.11	27.83±2.67	0.549 ^b
Baseline BJ-MoCA score	24.85±4.49	24.68±3.40	0.891 ^a
Attention tasks			
forward and backward digit span	1.80±0.41	1.86±0.35	0.691 ^b
one hundred consecutive minus seven	4.20±1.40	3.96±1.56	0.655 ^b
Executive function			
attachment experiment	0.70±0.47	0.64±0.49	0.750 ^b
Language and related functions			
semantic fluency	1.00±0.00	0.95±0.21	>0.9999 ^b
naming and repeat	2.90±0.31	2.68±0.57	0.213 ^b
Memory			
immediate and delayed recall 1	4.90±0.45	4.86±0.47	>0.9999 ^b
immediate and delayed recall 2	3.35±1.60	2.32±1.64	0.033 ^b
Orientation	9.65±0.49	9.77±0.61	0.214 ^b
Visuospatial function			
clock drawing test	8.45±1.88	7.64±2.82	0.354 ^b
copy of cross pentagon	0.85±0.37	0.86±0.35	>0.9999 ^b

Data are expressed as mean± SD.

Key: BJ-MoCA, Chinese-Beijing version of Montreal Cognitive Assessment-Test; HAMD, Hamilton Depression Scale; C-MMSE: Chinese version of Mini-mental state examination; PD, Parkinson's disease; SCD, subjective cognitive decline; UPDRS, Unified Parkinson's disease rating scale.

^a Independent t test.

^b Mann-Whitney U test.

^c χ^2 test

Longitudinal assessment

As showed in (Table 2), compared the annual changes in the cognitive performance of patients with PD-SCD⁺ and PD-SCD⁻ during the follow-up period, patients with PD-SCD⁺ exhibited a more significant annual decline in BJ-MoCA (-0.48 vs. 0.07 point/ year, $P= 0.038$) and semantic fluency (-0.14 vs. -0.03 point/year, $P= 0.035$) than patients with PD-SCD⁻. The groups in performance on the other cognitive subsets did not reach statistical significance. During follow-up, out 12 of 20 patients with PD-SCD⁻ were newly diagnosed with PD-SCD⁺ based on the above SCD assessment procedure in this study, whereas no PD-SCD⁺ patients revert back to PD-SCD⁻. There is no patient who converted to MCI in this study.

Table 2 Annual changes of neuropsychological performance in patients with Parkinson's disease according to the presence or absence of subjective cognitive decline

Assessment	PD-SCD- (n=20)	PD-SCD+ (n=22)	<i>p</i> value
BJ-MoCA	0.07±1.00	-0.48±1.08	0.038
C-MMSE	-0.31±0.58	-0.14±0.83	0.985
Attention tasks	-0.14±0.42	-0.15±0.37	0.723
Executive function			
Attachment experiment	0.07±0.18	-0.06±0.13	0.853
language and related functions			
Semantic fluency	-0.03±0.10	-0.14±0.17	0.035
Naming and repeat	-0.02±0.17	-0.09±0.15	0.207
Memory			
immediate and delayed recall 1	0.01±0.05	0.00±0.18	0.630
immediate and delayed recall 2	-0.20±0.40	-0.08±0.59	0.653
Orientation	0.05±0.20	-0.05±0.37	0.273
Visuospatial function	-0.17±0.37	-0.23±0.44	0.555

Stepwise logistic regression analysis was conducted to determine which clinical variables had the greatest ability to differentiate between each cognitive subsets(Fig. 2). Age, sex, UPDRS score, years of education, duration of motor symptom, HAMD score, degree of WMHS, the presence or absence of SCD, baseline C-MMSE, or BJ-MoCA score at onset of the disease were included in the regression analysis as

independent variables, and each cognitive subsets was the dependent variable. Multicollinearity index VIF \leq 5, showed that there was no multicollinearity problem. R Square = 0.583, Adjusted R Square = 0.538, suggesting a goodness-of-fit for the model. The analysis showed that the C-MMSE Scores(OR = 1.14, $P=$ 0.000), HAMD Scores(OR = 1.10, $P=$ 0.008), Sex = male(OR = 1.30, $P=$ 0.026), and the presence of SCD(OR = 0.76, $P=$ 0.022) significantly contributed to the prediction of language and related functions domain.

Rehabilitation training

A total of 42 patients completed 2 follow-up, then all participants implement appropriate therapeutic interventions, and finally retrieved 36 cognitive report forms. Seven patients were lost to follow-up(Among the PD-SCD $^-$ 2 patients, PD-SCD $^+$ 5 patients). Due to COVID-19, the assessment of motor symptom severity and disease severity were administered by investigator by face-to-face interviews cannot be implemented. Then in this study exclude UPDRS scores and Hoehn and Yahr Scale. Pre and post rehabilitation training cognitive test scores were showed in (Table 3). The significant improvement was observed in both groups after rehabilitation training in terms of BJ-MoCA scores (SCD $^+$ vs. SCD $^-$: 23 vs. 12patients). C-MMSE and Memory scores was found a significant improve in PD-SCD $^-$ groups. Meanwhile, patients with PD-SCD $^+$ exhibited a significant improve in Language. Pairwise comparisons between pre-intervention and post-intervention showed that language at post-intervention in the PD-SCD $^+$ groups were significantly higher than at pre-intervention in the PD-SCD $^-$. The results in the present study support the feasibility of the rehabilitation training for people with PD.

Table 3 Changes in Cognitive test scores of patients at pre and post intervention

Assessment	PD-SCD $^-$ (n=18)			PD-SCD $^+$ (n=17)			<i>p</i> value*
	pre	post	<i>P</i> Value	pre	post	<i>P</i> Value	
BJ-MoCA	24.67 \pm 4.35	26.94 \pm 2.41	0.001	23.59 \pm 3.16	25.41 \pm 2.98	0.009	0.598
C-MMSE	27.22 \pm 2.34	28.17 \pm 1.89	0.004	27.29 \pm 1.96	27.94 \pm 1.95	0.274	0.638
Attention tasks	5.44 \pm 2.18	6.06 \pm 1.35	0.094	5.47 \pm 2.07	6.00 \pm 1.28	0.281	0.872
Executive	0.50 \pm 0.51	0.56 \pm 0.51	>0.999	0.47 \pm 0.51	0.71 \pm 0.47	0.125	0.137
Language	3.72 \pm 0.46	3.83 \pm 0.38	0.625	2.94 \pm 0.75	3.71 \pm 0.47	0.002	0.004
Memory	7.83 \pm 1.76	8.50 \pm 1.34	0.005	6.94 \pm 1.48	7.47 \pm 1.01	0.127	0.693
Orientation	9.78 \pm 0.43	9.78 \pm 0.55	>0.999	9.77 \pm 0.56	9.59 \pm 0.80	0.531	0.436
visuospatial	9.11 \pm 1.75	9.50 \pm 1.54	0.374	8.53 \pm 2.48	8.53 \pm 2.35	0.864	0.594

* repeated measures analysis of variance between PD-SCD $^+$ and PD-SCD $^-$ at pre and post intervention

Discussion

This is a long follow-up cohort of study examining the clinical value of SCD in PD patients and progression characteristics, evaluating rehabilitation training feasibility for SCD in PD patients. We performed a 3-year follow-up investigation with the diagnosis of cognitively normal patients with PD (n = 42). Twenty-two patients were diagnosed with PD-SCD⁺ (52.4%) at the baseline. Conversion to PD-SCD⁺ during the follow-up was 54.5% in PD-SCD⁻, whereas no PD-SCD⁺ patients revert back to PD-SCD⁻. There was no patient who is converted to MCI in this study.

There was no current consensus on how to assess SCD. Most studies[23–24] were to use a brief questionnaire, or a simple yes/no question. Only capture subjective cognitive decline for one or two of the five cognitive domains. Given that these patients have been shown to have impairments in other cognitive domains, not just memory. The assessment of SCD in our study is defined based on the SCD research standards proposed by the SCD Advocacy Group in 2014, assessed by five cognitive domains. Interestingly, SCD questions presented limited overlap, we analyzed the assessment of SCD using the Multiple Response Test to make a description. These data (Fig. 1) showed that patients complain with cognitive decline of memory are the most. Baseline comprehensive neuropsychological tests in present study showed that the PD-SCD⁺ and PD-SCD⁻ groups did not differ significantly, except memory (immediate and delayed recall 2), which was not in agreement with previous report[25]. To date, the assessment of SCD is based largely on overall neuropsychological tests, there are rarely to assess cognitive subsets of SCD. For maximize understanding of SCD, further research need to standardized research, diagnostic criteria and enlarge samples. The concept of subjective “memory” complaint is derived from amnesic MCI as this subtype has been regarded as pre-dementia status[26]. Moreover, deficits in memory, which count among the most sensitive cognitive markers for early recognition of AD[27]. However, there were notable differences between AD-MCI vs PD-MCI[28]. A common cognitive profile has been established for AD-MCI, in which the first and most severe deficits are seen in memory[29], but it has not yet been possible to define such a common cognitive profile for PD-MCI[26]. This means cognitive impairment of PD might be different from AD, patients or their caregivers are often the first or the most worried in the patient's cognitive function may be still memory decline, whereas Iván Galtier[20] showed difficulties in language (60.5%) and memory (51.5%) were the most frequent cognitive complaints. This conclusion was different with our study as may be ascribed to a different assessment of SCD.

A longitudinal analysis of cognitive performance changes showed that patients with PD-SCD⁺ exhibited a more rapid decline in BJ-MoCA and semantic fluency compared with those without SCD. While the C-MMSE scores were no changes between two groups. To date, there were only three studies[13, 19, 20] conducted a follow-up study to investigate the association between SCD and cognitive impairment in PD patients. No studies have found evidence of overall cognitive function (BJ-MoCA) exhibited a more decline in PD-SCD⁺ than PD-SCD⁻, which may due to differential use of comprehensive neuropsychological assessment as cognitive performance was evaluated using the Korean version of Mini-Mental State Examination (K-MMSE) in Hong's study. This result somewhat reiterates that BJ-MoCA is a more sensitive instrument than C-MMSE in detecting cognitive impairment, specifically the cognitive

changes associated with the SCD stage. The above result was similar to Hong's study[30], which have found that PD patients with SCD performed significantly worse on semantic fluency($r=0.40$), compared with healthy controls. Language output in PD was often more sparse and less informative than healthy peers[31–33]. Williams and Mason[34] demonstrated in their study that semantic fluency deficits in PD has been identified as a potent risk factor of the development of PD related dementia, with these impairments might reflect the spread of PD pathology to posterior temporal networks. In a word, the present data demonstrated that BJ-MoCA is more sensitive than C-MMSE in detecting cognitive impairment, semantic fluency impairments may represent important cognitive markers to help tracking disease progression and should be key component of the cognitive subsets in assessing PD-SCD.

Language, as a tools of communication, is a higher cortical function and closely related to other cognitive functions. Much of the research capture different sub-domains of language and its progression characteristic over time in PD, this is an ever increasing number of topic. The findings of the present study focused on determining which clinical variables had the greatest ability to differentiate between each cognitive subsets. We evaluated whether the SCD reported by patients with PD at baseline was closely related to each cognitive subsets. The stepwise regression analyses revealed that MMSE scores, HAMD scores, male and the presence of SCD as significant predictors in language domain of PD. Our data showed that cognitive performance in patients with PD may differ based on the presence of SCD, particularly in language function(semantic fluency), suggesting that SCD in patients with PD reflects cognitive-related semantic fluency more closely than PD without SCD. SCD in patients with PD is one of risk factors for cognitive domain of language function[13], which was in agreement with the results of the present study. Ignacio Obeso[35] found that the non-motor features as well as depression(HAMD) and global cognitive ability(MMSE) influence semantic fluency of PD patients, which was in agreement with the results of the present study. While gender did not affect semantic fluency scores in Obeso's study, this conclusion was different from our study which may be ascribed to a difference in age, educational level, duration of motor symptom, stage of disease. Yet, relatively little information is available about how key clinical features of PD patients with SCD influence performance on semantic fluency tests. Therefore, the role of sex and the presence of SCD in the predictive value of language function should be clarified more concretely in future studies.

Rehabilitation training has shown benefits in Parkinson's disease in the past decades[36]. There has been relatively few trials of rehabilitation training strategies for SCD in patients with PD. The present study focused on the effects of interventions at the stage of SCD in patients with PD. All participants maintained high levels of effort and most of them had high homework adherence (36 of the 42 participants' complete homework). The results of the present study supported the feasibility of rehabilitation training that could improve cognitive function in terms of BJ-MoCA scores for PD -SCD⁺ and PD-SCD⁻. Similar results were reported that the tango dancing for PD patients promoted significant improvement in global cognitive function (MoCA) when compared to the control group who attended lectures only[37], the group of patients is diagnosed with idiopathic PD, compared to our study patients is diagnosed with SCD in patients with PD. C-MMSE and memory scores was found a significant

improvement in our PD-SCD⁻ groups. Pairwise comparisons showed that language at post-intervention in the PD-SCD⁺ groups were significantly higher than at pre-intervention in the PD-SCD⁻. It is established that different exercises have been found to selectively affect different regions of the brain as physical exercises affect brain plasticity[38]. A meta-analysis of randomized controlled trials(RCTs)[39] showed that aerobic exercise produced improvements in attention, speed, executive function and memory among adults without dementia. Altmann[40] demonstrated that aerobic exercise can positively impact mood and executive function performance in PD. Generally, dementia is still not remediable, early interventions might slow down the degenerative process[41–43]. Thus, our results suggest that SCD in patients with PD should engage in the intervention of rehabilitation training, it is of great value for the maintenance of overall cognitive function and avoid the continuous decline of language function. Future studies with greater sample sizes are recommended to explore more applications of rehabilitation training.

Several limitations of the present study need to be acknowledged: the limitations may be limited due to small sample size and comprehensive assessment of each cognitive subsets during the follow-up was not included which may not be reflective of other samples. Therefore, further studies with larger samples, a long-term follow-up period, and a more comprehensive neuropsychological assessment would be able to confirm these findings.

In summary, the clinical utility of language and related functions as an early marker for cognitive decline in Parkinson's disease deserves further exploration in longitudinal studies. PD patients with SCD should be carefully screened for the potential cognitive impairment. Early diagnosis and treatment of SCD are of great value in maintaining overall cognitive function and preventing continuous decline in language function.

Abbreviations

PD: Parkinson's disease; SCD: subjective cognitive decline; WM: white matter; AD: Alzheimer's disease; MCI: Mild cognitive impairment; BJ-MoCA: Chinese-Beijing version of Montreal Cognitive Assessment-Test; MDS: The Movement Disorders Society's; RCTs: randomized controlled trials; C-MMSE: Chinese Mini-Mental State Examination; PPS: Parkinsonism-Plus syndrome; UPDRS-III: Unified Parkinson's Disease Rating Scale Part III; WMHs: white matter hyperintensities; HAMD: Hamilton Depression Scale.

Declarations

Acknowledgements

Not applicable.

Funding

This study was supported by a National Key Laboratory of Cognitive Neuroscience and Learning from BEIJING NORMAL UNIVERSITY in China (CNLZD1701).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

S-RW and YL contributed to the study concept, GY and S-JX acquired the data, GY designed the study, analyzed the data and drafted the manuscript. Y-JP and S-RW performed critical editing. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All the subjects signed an informed consent form at the start of the study, and ethical approval was obtained from the First Hospital of Harbin Medical University ethical standards committee.

Consent for publication

All authors consent for publication.

Competing interests

The authors report no conflicts of interest.

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Figures

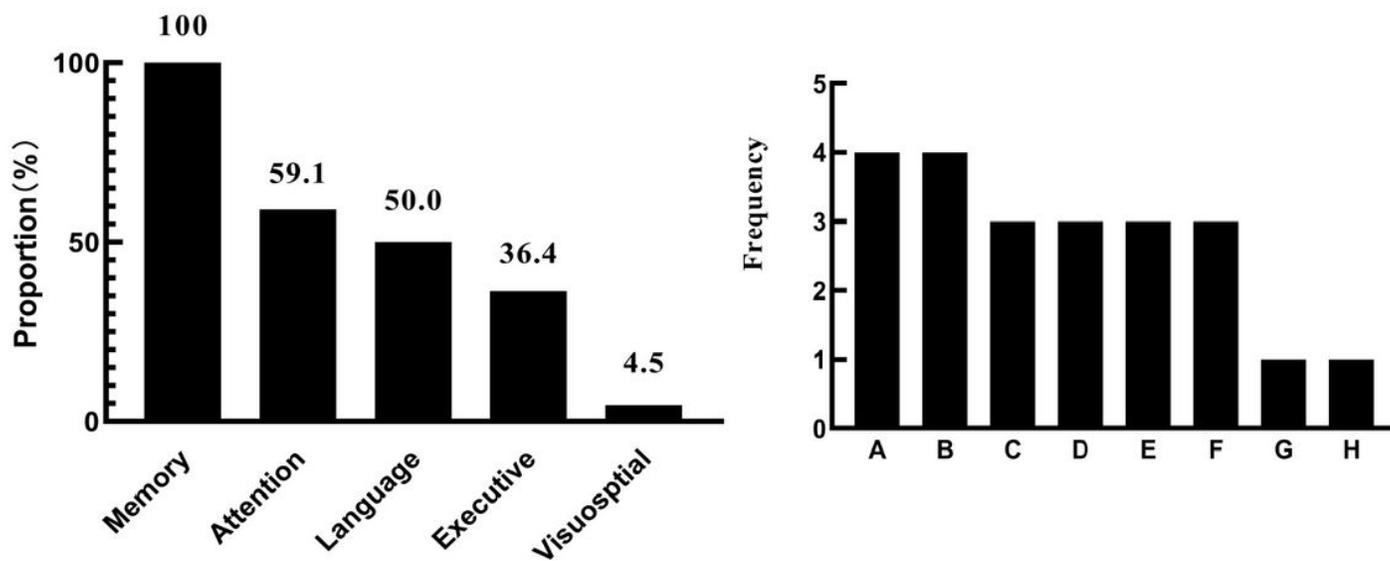


Figure 1

Baseline procedures of SCD assessment B. The frequency distribution of SCD assessment procedure. Key: A Memory B Memory+Attention+Executive+Language C Memory+Attention D Memory+Language E Memory+Attention+Language F Memory+Attention+Executive G Memory+Language+Visuospatial H Memory+Executive

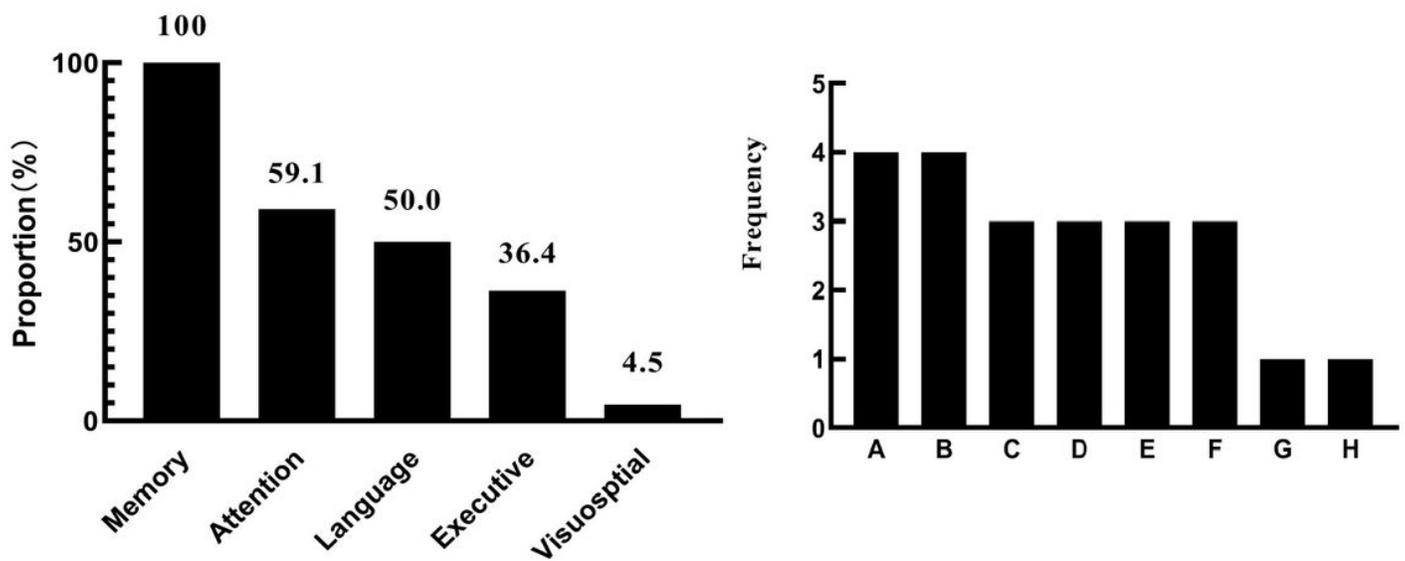


Figure 1

Baseline procedures of SCD assessment B. The frequency distribution of SCD assessment procedure. Key: A Memory B Memory+Attention+Executive+Language C Memory+Attention D Memory+Language E Memory+Attention+Language F Memory+Attention+Executive G Memory+Language+Visuospatial H Memory+Executive

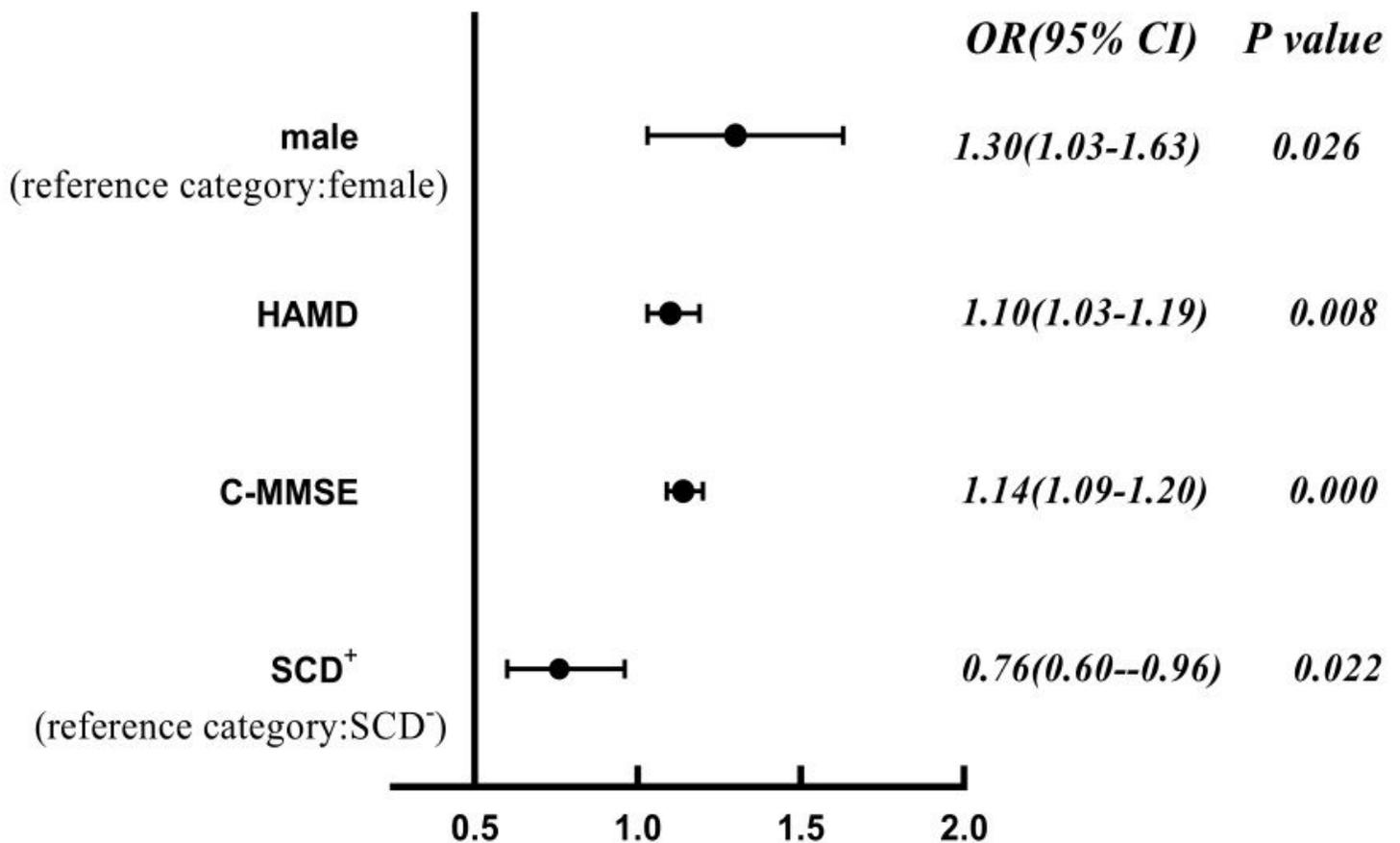


Figure 2

Stepwise logistic regression analysis of language and related function

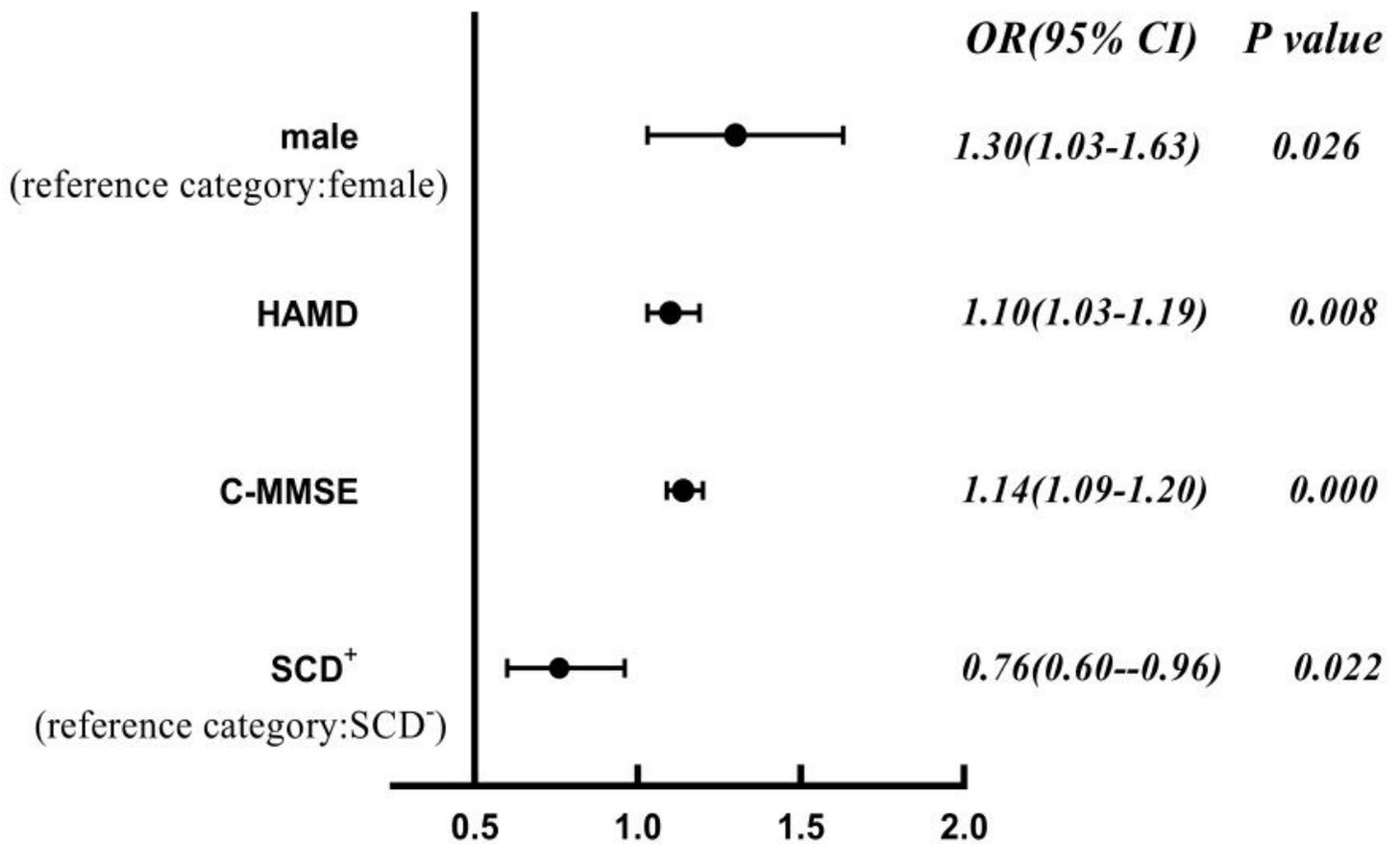


Figure 2

Stepwise logistic regression analysis of language and related function

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