



## Clinical Study

## Sex differences in cognition among Chinese people with Parkinson's disease



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## ARTICLE INFO

## Article history:

Received 23 May 2014

Accepted 14 August 2014

## Keywords:

Cognitive impairment

MMSE

MoCA

Parkinson's disease

Sex differences

WAIS-RC

WMS-RC

## ABSTRACT

To investigate sex differences in cognitive function in Parkinson's disease patients, a cohort of 172 male patients and 139 female patients were recruited for this study. Their demographic and clinical features, including age, disease duration, education level, Unified Parkinson's Disease Rating Scale-III, Hoehn-Yahr Scale, activities of daily living, Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale score were recorded. The Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Wechsler Adult Intelligence Scale-Chinese Revision (WAIS-RC) and Wechsler Memory Scale-Chinese Revision (WMS-RC) scores were compared to distinguish the cognitive properties between the two groups. The MMSE values did not show a significant difference between the groups. However, the MoCA scores of male patients were significantly higher than those of female patients (adjusted  $p < 0.05$ ). The male group demonstrated better performances with respect to visuospatial function, naming and abstraction (adjusted  $p < 0.05$ ). The WAIS-RC data showed that female patients had lower scores in information, vocabulary, picture completion, block design and picture arrangement (adjusted  $p < 0.05$ ), and the WMS-RC data showed that 100-1 and cumulative addition abilities were significantly weaker in females than males (adjusted  $p < 0.05$ ). Cognitive disturbances were more prevalent and severe in women among Chinese Parkinson's disease patients.

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## 1. Introduction

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder characterized by symptoms of resting tremor, rigidity, bradykinesia, and postural instability. There are limited data on sex differences in this disorder although there is evidence that there are sex discrepancies in its incidence, symptoms, and treatment response.

PD is more common in men (age-adjusted male to female ratio 1.87:1) [1] and females have a delayed onset of symptoms [2]. Women are more likely than men to present with tremor as the initial symptom and have a worse initial Unified Parkinson's Disease Rating Scale (UPDRS) instability score [3]. More men than women exhibit rigidity and symptom symmetry in the face, neck and arms, whereas more women exhibit dyskinesias and postural problems [4,5].

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The Non-Motor Symptoms Scale score in females was shown to be significantly higher than that in males [3]. Depression, anxiety, mood/apathy, fatigue, feelings of nervousness, feelings of sadness, constipation, restless legs, cardiovascular issues and miscellaneous problems (pain, loss of taste or smell, weight change and excessive sweating) have been reported to be more common and severe in women. In contrast, daytime sleepiness, excessive drooling, urinary symptoms, orthostatic hypotension, impulse control disorders, increased interest in sex and sexual dysfunction have been reported to be more prevalent and severe in men [3,5–8]. During sleep, men had a greater rate of rapid eye movement behavior disorder [5]. Female PD patients are reported to have significantly less aggressive behavior during dreams but more disturbed sleep [9].

Cognitive impairment is a major non-motor feature of PD, and recent research has shown that dementia will occur in over 80% of PD patients after 20 years of disease [10]. Cognitive differences between men and women have not been extensively examined. In the present study, we utilized a set of cognitive assessment methods including the Mini-Mental State Examination (MMSE),

Montreal Cognitive Assessment (MoCA), Wechsler Memory Scale-Chinese Revision (WMS-RC) and Wechsler Adult Intelligence Scale-Chinese Revision (WAIS-RC) to distinguish the cognitive profiles of male and female patients.

## 2. Methods

### 2.1. Participants

Our cross-sectional and observational study included 311 PD patients who attended the Department of Neurology, Guangdong General Hospital, between January 2009 and November 2013. All subjects from both the outpatients department and the ward, urban dwelling and rural, were examined by experienced neurologists and met the UK Parkinson's Disease Society Brain Bank Diagnostic Criteria [11] (bradykinesia associated with tremor or rigidity or postural instability). Individuals with atypical or secondary parkinsonism, dementia with known causes or a history of neurosurgery were excluded. Moreover, those with parkinsonian syndromes including progressive supranuclear palsy, multiple system atrophy and corticobasal degeneration, as well as those with a psychological illness, such as anxiety, depression or schizophrenia, were also excluded. All subjects were southern Han Chinese. Written informed consent was obtained from all subjects before participation in the study. The study was approved by the Ethics Committee of Guangdong General Hospital.

### 2.2. Clinical assessment protocol

The demographic features and clinical data including age, age of onset, sex, disease duration, education level, and use of anti-Parkinson medication were collected by movement disorder specialists using a standard questionnaire during face-to-face interviews. The UPDRS part III [12] was used to assess motor disability, and the Hoehn–Yahr stage [13] was used to establish disease severity. We calculated a “tremor score” and a “non-tremor score” for each patient in a manner similar to Lewis et al. [14]: the tremor score was derived from the sum of UPDRS items 20 (tremor at rest) and 21 (action or postural tremor of hands) divided by 7 (the number of single sub-items [for each body region if separated] included). The non-tremor score was derived from the sum of UPDRS items 18 (speech), 19 (facial expression), 22 (rigidity), 27 (rising from a chair), 28 (posture), 29 (gait), 30 (postural stability) and 31 (body bradykinesia and hypokinesia) divided by 12 (the number of single sub-items [for each body region if separated] included).

The cognitive tests were administered during a quiet and suitable rest period. The MMSE and MoCA were used to evaluate global cognitive function [15]. The WAIS-RC and WMS-RC were employed to test intellect and memory, respectively [16–19]. Attention was assessed using the digit span of the WAIS-RC. Executive function was evaluated using the WAIS-RC for the similarity and graphic arrangement subsets, while a block design was used for visuospatial functional assessment. The WMS-RC, which includes visual recognition, visual reproduction and understanding, was chosen for memory assessment [19]. In addition, affective disturbances were assessed with the Hamilton Depression Rating Scale (HAMD) and Hamilton Anxiety Rating Scale (HAMA); these questionnaires include somatic items that may be related to the physical disability of PD patients [20].

### 2.3. Statistical analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences version 13.0 (SPSS, Chicago, IL, USA). All data are presented as the mean  $\pm$  standard deviation. The homogeneity

of variance of the variables was assessed by Levene's test. Differences in demographic and clinical characteristics between the male and female groups were analyzed using independent two-tailed *t*-tests. Clinical characteristics requiring covariate adjustment were analyzed using multivariate linear regression. Cognitive comparisons between the male and female groups were adjusted for age and years of education as covariates by univariate analysis of covariance. *p* values of  $<0.05$  were considered statistically significant.

## 3. Results

### 3.1. Clinical characteristics

A total of 311 patients were recruited for this study. Of these patients, 172 patients were male and 139 were female. The demographic characteristics of the PD patients are shown in Table 1, and there were no significant differences regarding age, age at onset or disease duration between the groups. Males had more years of education than females ( $p < 0.05$ ). Motor disorders were evaluated using the UPDRS-III and Hoehn–Yahr rating scale, and the motor scores did not differ significantly between the two groups. However, the symptom improvement rate as measured by the acute Madopar (Roche, Basel, Switzerland) reaction test was higher in females ( $p < 0.05$ ). In addition, tremor scores were higher in females ( $p < 0.05$ ) and the Activities of Daily Living (ADL) scores of the female group were also higher than those in the male group ( $p = 0.05$ ). Depression and anxiety may exacerbate cognitive dysfunction in PD patients [20], therefore HAMA and HAMD were also assessed. The results showed that the HAMA and HAMD scores of the female group were higher than those of the male group ( $p < 0.05$ ).

### 3.2. Cognitive performance

Global cognitive function of the PD patients was assessed using the MMSE and MoCA. As shown in Table 2, the MMSE values did not show a significant difference between males and females, but the mean MoCA scores of male patients were significantly higher than those of the female patients (adjusted for years of education and age at onset  $p < 0.05$ ). To examine the detailed differences in cognitive dysfunction we further compared the multiple domains of the MoCA between the two groups. Males demonstrated better performances with respect to visuospatial function, naming and abstraction (adjusted  $p < 0.05$ ). Intelligence was assessed with the WAIS-RC, with information, vocabulary, picture completion, block design and picture arrangement scores significantly lower among females versus males (adjusted  $p < 0.05$ ) (Table 3). The WMS-RC was applied to assess memory function. The patients' 1-100, figural memory, delayed recall, visual reproduction, verbal paired associates, tactile memory and reciting figures skills were at similar levels, and there were no significant differences between the groups (Table 4). However, the 100-1 and cumulative addition scores were significantly lower among females versus males (adjusted  $p < 0.05$ ).

### 3.3. Association between clinical features and cognition scores in PD patients

Pearson's correlation was used to analyze the correlation of clinical features and cognition scores in PD patients. As shown in Table 5, age at examination, age at onset, years of education, UPDRS-III and Hoehn–Yahr score correlated with MMSE and MoCA scores ( $p < 0.05$ ). Years of education, UPDRS-III and Hoehn–Yahr score correlated with WAIS-RC and WMS-RC scores ( $p < 0.05$ ).

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