

Neuropsychiatric Symptoms and Cognitive Impairment in Chinese Patients with Parkinson's Disease in Han and Hui Ethnicity

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Summary: Neuropsychiatric symptoms are common in patients with Parkinson's disease (PD) and they are likely to outweigh the motor symptoms and become a major factor affecting the quality of life of PD patients. However, the studies focusing on the non-motor symptoms in Chinese PD patients from different ethnicity are scarce. The aim of this retrospective study was to investigate neuropsychiatric symptoms and cognitive impairment in Chinese PD patients from Han and Hui populations from central China. Seventy-two Han Chinese PD patients (Han PD group) and 71 age- and sex-matched Hui Chinese PD patients (Hui PD group) were enrolled from Zhongnan Hospital of Wuhan University between Sept. 2011 and Aug. 2014 in the study. The neuropsychiatric symptoms and cognitive impairment were assessed using Neuropsychiatric Inventory (NPI) and Mini Mental State Examination (MMSE). We found that the proportion of depression, anxiety, apathy, irritability, euphoria and night time behavior disturbances were higher in the Han PD group than in the Hui PD group ($P < 0.05$ or $P < 0.01$). But the proportion of delusion, hallucination, agitation, disinhibition, aberrant motor behavior and change in appetite were not significantly different between the Han PD group and the Hui PD group ($P > 0.05$). The total mean scores of the MMSE from patients in the Han PD group were similar to those in the Hui PD group ($P > 0.05$). However, the subscale scores of recall domain and language domain in the Han PD group were significantly different from those in the Hui PD group ($P < 0.05$). No significant difference was noted in the orientation, memory and calculation domains between the two PD groups ($P > 0.05$). This study first showed the recall domain and language domain were different between the Han PD patients and the Hui PD patients. Depression, anxiety, apathy, irritability, euphoria and night time behavior disturbances were less presented in the Hui PD patients. All these differences may be related to the different ethnicity, which would be helpful for clinical physicians to recognize the different non-motor symptoms in Chinese PD patients with different ethnicity.

Key words: Parkinson's disease; neuropsychiatric symptoms; cognitive impairment; Han Chinese; Hui Chinese

Parkinson's disease (PD) is a common neurodegenerative disease after Alzheimer's disease^[1]. Clinically, the common performance of PD is tremor, rigidity, slow movement and posture instability. In addition, non-motor symptoms such as anxiety, depression, sleep disorders, cognitive impairment and other disturbances are also common in PD patients. It is estimated that non-motor symptoms affect at least one-third of patients with PD. These symptoms can occur throughout the stages of PD, and some even predate the development of motor symptoms. They

can exacerbate the general condition of PD patients, especially if left untreated. They are easily missed and may go unreported during consultations, unless patients or caregivers are specifically asked by the physician about these symptoms. In addition, this is confounded by the fact that both physicians and patients may be unaware of what exactly constitutes non-motor symptoms. Although medical drug, neurosurgery and rehabilitation can alleviate motor symptoms^[2-7], there are no therapies available to effectively stop non-motor symptoms^[8]. Meanwhile, there is a scarce of studies examining non-motor symptoms in Chinese PD patients from different ethnicity.

An epidemiological study^[9] from China showed

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that an incidence of PD was 1.07% in Chinese more than 55 years old, 1.7% in Chinese more than 65 year old, and 2.5% in Chinese more than over 75 year old. The age dependence is the same to that reported in the United States and Europe^[10]. A previous study from Germany showed that the prevalence of PD varies in people of the same race, but living in different environments^[11]. It has also been shown that aging, genetic, and environmental factors may be related to the onset of PD^[11]. China is a large country with 56 ethnic groups, among which, more than 92% was Han Chinese. The rest Chinese in the 55 ethnic groups are called together as minorities, including Uygur ethnic minority, Hui and so on. There are many differences among different Chinese ethnic groups, such as names, religion, genetics, literature, language, education, clothing and so on. Recently, genetic studies on the mechanisms of PD from the Han and Uygur Chinese populations showed that Thr12Met and Ala1144Thr mutations of the ATP13A2 gene were rare in the Uygur PD patients as compared to the Han PD patients in Xinjiang region^[12]. Significant differences were observed in the T313M allele and genotype frequencies between the Uygur and the Han populations^[13]. Clinical study also showed that the patients with resting tremor, increased muscle tone and bradykinesia as the presenting symptoms in the Uygur PD group were more than those in the Han PD group^[14]. In this study, we aimed to examine whether there are some differences in neuropsychiatric symptoms and cognitive impairment between Chinese Han PD patients and Hui PD patients from central China in order to provide valuable information for clinicians to effectively treat the Han and Hui PD patients.

1 MATERIALS AND METHODS

1.1 Participants

This retrospective study was conducted at the Department of Neurology in Zhongnan Hospital of Wuhan University. The diagnosis of PD patients was based on the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria^[15]. One hundred and forty-three patients with PD and their care givers were selected from the inpatient or outpatient clinic from Sept. 2011 to Aug. 2014. Among them, 72 PD patients and their care givers were Han Chinese (Han PD group) and the rest of 71 PD patients and their care givers were Hui Chinese (Hui PD group). In the Han PD group, there were 40 males and 32 females aged from 45–79 years (average age 61.4±6.4 years), while in the Hui PD group, there were 39 males and 32 females aged from 46–78 years (average age 62.3±6.2 years). The neurological examinations and evaluations for PD patients were performed by experienced neurologists. All patients completed the following measurements including demography forms, unified

Parkinson's disease rating scale part III (UPDRS III-motor) and modified Hoehn and Yahr staging scale (H & Y)^[16, 17]. The motor dysfunctions and disease severity were assessed by the UPDRS III-motor and H & Y scales. Cognitive impairment was evaluated by Mini-Mental State Examination (MMSE) scores^[18, 19]. The exclusion criteria included PD patients with motor dysfunctions due to other neurological diseases, such as cerebrovascular disease; PD patients with a potential malignancy, pain syndromes, severe anemia, diabetes mellitus, heart diseases, hepatic or renal failure, or any other debilitating or life threatening diseases^[20]; PD patients with moderate or severe cognitive impairment^[16, 18, 19]; and those who refused to attend this study. Detailed information sheets were given to all PD patients or family members and the signed informed consents were obtained. This study was conducted in accordance with the Declaration of Helsinki and approved by the local bioethics committee of Zhongnan Hospital of Wuhan University.

1.2 Assessments and Measurements

The neuropsychiatric symptoms were measured in PD patients, and their caregivers were consulted using Neuropsychiatric Inventory (NPI)^[19, 21, 22]. NPI was used to screen following question including delusions, hallucinations, depression, anxiety, apathy, irritability, euphoria, agitation, disinhibition, aberrant motor behavior, night time behavior disturbances and change in appetite. The NPI has been used and shown to be valid in PD populations^[23]. The Chinese version of NPI was also shown to be a reliable and valid tool to assess neuropsychiatric syndromes in PD patients^[24, 25]. Based on the NPI, all domains are rated in terms of presence and magnitude of symptoms (frequency × severity). The maximum score is 12 scores per domain, for a given domain with significant symptoms occurring at scores (frequency × severity) ≥ 4. The total NPI score ranged from 0 to 144, with higher scores indicating greater behavioral problems. The cognitive impairment was measured in PD patients using MMSE^[18, 19]. MMSE has been administered to a lot of patients to assess an overall level of cognitive impairment, and provides a total score ranging from 0 to 30, with lower scores indicative of greater cognitive impairment.

1.3 Statistical Analysis

All data were expressed as mean±standard deviation (SD) or *n* (%). The differences between the two groups were analyzed by unpaired *t* test or chi-squared test. The statistical analyses were carried out with SPSS 11 for Windows. The significant level was set at *P*<0.05.

2 RESULTS

2.1 Baseline Characteristics of the Two PD Groups

The differences in age, sex, disease duration,

educational level, past medical history and the scores of H&Y were not significant between the two Chinese PD groups ($P>0.05$). All patients took usual antiparkinsonian medicine, and the therapeutic effect was not significantly different between the two Chinese PD groups (data not shown).

2.2 Comparison of the Proportion of Neuropsychiatric Symptoms between the Two PD Groups

As shown in table 1. The proportions of neuropsychiatric symptoms, including depression, anxiety, apathy, irritability, euphoria and night time behavior disturbances were higher in the Han PD group than those in the Hui PD group ($P<0.05$ or $P<0.01$). But, the proportions of delusions, hallucinations, agitation, disinhibition, aberrant motor behavior and change in appetite showed no significant difference between the Han PD group and the Hui PD group ($P>0.05$).

2.3 Comparison of the MMSE Scores between the Two PD Groups

As shown in table 2, the total mean score of the MMSE was 22.23 ± 7.78 in the Han PD group, which was not significantly different from that in the Hui PD group (21.18 ± 6.48) ($P>0.05$). However, the subscale scores of recall domain and language domain in the Han PD group were significantly different from those in the Hui PD group ($P<0.05$). The recall domain in Han PD patients was weaker than that in the Hui PD patients, while their language domain was stronger than that in the Hui PD patients ($P<0.05$). No significant difference was found in the orientation domain, memory domain and calculation domain between the two PD groups

($P>0.05$).

3 DISCUSSION

In general, non-motor symptoms such as cognitive impairments, psychiatric symptoms, autonomic dysfunction and sleep problems can be frequently observed in PD^[1]. In this study, we compared the non-motor symptoms between the Han and the Hui Chinese PD patients. The results showed that neuropsychiatric symptoms such as depression, anxiety, apathy, irritability, euphoria and night time behavior disturbances were less presented in the Hui PD patients than in the Han PD patients. Meanwhile, the proportion of delusions, hallucinations, agitation, disinhibition, aberrant motor behaviors and change in appetite were similar in both groups. It is well known that neuropsychiatric disturbances could occur at any stage of PD progression, and some of them may happen before the onset of motor symptoms^[1,26]. Research data from European countries showed the neuropsychiatric syndromes may lower the quality of life of patients, cause family caregiver distress, and increase risk for patients to be admitted to hospital^[27-30]. Aarsland *et al*^[31] reported that 61% of PD patients had at least one psychiatric symptom. Among them, 38% patients showed depression, 27% patients had hallucinations. Their investigation also showed that euphoria and disinhibition were not common in PD patients, but depression, apathy and hallucination were found with the highest mean scores. One epidemiological study^[32]

Table 1 The proportion of NPS between Han PD group and Hui PD group [n (%)]

Items	Han PD group (n=72)	Hui PD group (n=71)	P value
Delusions	6 (8.33)	4 (5.56)	>0.05
Hallucinations	13 (18.05)	11 (15.28)	>0.05
Depression	44 (61.11)	17 (23.94)	<0.01
Anxiety	39 (54.17)	18 (25.35)	<0.01
Apathy	16 (22.22)	9 (12.68)	<0.05
Irritability	23 (31.94)	13 (18.31)	<0.05
Euphoria	7 (9.72)	2 (2.82)	<0.01
Agitation	6 (8.33)	4 (5.63)	>0.05
Disinhibition	10 (13.89)	10 (14.08)	>0.05
Aberrant motor behavior	6 (8.33)	6 (8.45)	>0.05
Night time behavior disturbances	30 (41.67)	15 (21.13)	<0.01
Change in appetite	15 (20.83)	14 (19.72)	>0.05

NPS: neuropsychiatric symptoms; PD: Parkinson's disease

Table 2 MMSE scores between Han PD group and Hui PD group (mean±SD)

Items	Han PD group (n=72)	Hui PD group (n=71)	P value
Orientation	8.69±2.56	8.74±2.63	>0.05
Memory	2.50±0.88	2.48±0.86	>0.05
Calculation	2.76±1.86	2.33±1.87	>0.05
Recall	1.84±1.28	2.98±0.76	<0.05
Language	7.86±2.84	6.08±1.58	<0.05
Total scores	22.23±7.78	21.18±6.48	>0.05

MMSE: Mini Mental State Examination; PD: Parkinson's disease

from France reported that 25%–30% PD patients had visual hallucinations. Up to now, the mechanisms and pathophysiology of non-motor symptoms in PD patients have not been clearly illustrated. Most Hui Chinese are adherents of the Muslim faith. As Muslims, they reject the consumption of pork, dog, and mule meat or any of those animals' blood. They do not eat fowl killed by non-Muslims. It is impolite to smoke and drink in the presence of Muslims. The main meats for Hui people are beef, mutton, and different kinds of fish. As for drinks, the Hui enjoy drinking tea, among which the famous ones are covered bowl tea and ba bao tea.

In this study, the results showed that there was no significant difference in the MMSE mean scores between the Han and the Hui PD patients. Also, there was no significant difference in the orientation, memory and calculation domains between the two groups of PD patients. However, the recall domain and language domain in the Han PD group were significantly different from those in the Hui PD group. A previous study showed that the cognitive impairment in PD patients was related to brain atrophy in the frontal, parietal, temporal and occipital lobe^[33]. A multicenter pooled analysis^[34] reported that 25.8% PD patients had cognitive impairment. Among them, 13.3% PD patients showed memory impairment, 11.0% PD patients presented visuospatial problem and 10.1% PD patients had attention or executive ability problem. Research data from American showed that the cognitive impairment in PD patients was associated with older age and male gender, disease onset and disease stage, and the severity of motor performance^[35]. A community-based study^[28] from Norway demonstrated that 25% PD patients had dementia. This situation was more common to be found in patients with older age at onset of syndromes, which may increase patients' depression and hospitalization. In this study, although the total score of the MMSE of the Han PD patients was similar to that of the Hui PD patients from central China, the subscale scores of recall domain and language domain were significantly different between the two groups. Our results were inconsistent with those from the other studies^[27, 28, 34, 35], which may help understand different clinical manifestations in PD patients from different regions and with different ethnicity. The corresponding clinical treatment and prevention may be different, too. In addition, it is necessary to conduct genetic and/or imaging studies in the Chinese Han and Hui PD patients to reveal the anatomical, pathological and physiological mechanisms underlying the different neuropsychiatric symptoms and cognitive impairment between the patients in the two groups.

Taken together, this retrospective study firstly demonstrated the differences of neuropsychiatric symptoms and cognitive impairment between Chinese Han PD patients and Chinese Hui PD patients. Since

the results of this study are from a single center and the sample size is small, the results of the study should be cautiously interpreted. The recalling ability in the Han patients with PD was weaker than that in the Hui PD patients, but their language ability was stronger than that in the Hui PD patients.

There are some limitations in this study. Firstly, the uses of self-reported survey in this study may give rise to bias. Secondly, PD patients and their caregivers who agreed to participate in the study may not represent the entire Chinese PD patients and family members, resulting in self-selection bias. Thirdly, although the instruments used in this study have very good reliability, cultural disparity is not taken into account in this study, which may affect the final results. Researches are still warranted to further examine the difference in neuropsychiatric symptoms and cognitive impairment between Chinese PD patients with different ethnicity in order to give them effective tailored treatments.

Acknowledgments

We would like to thank all the patients and their caregivers who attended in this study.

Conflict of Interest Statement

The authors report no conflicts of interest in this study.

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(received Jan. 12, 2018; revised Oct. 9, 2018)