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Depression and associated factors in nondemented Chinese patients with Parkinson's disease

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ABSTRACT

Objectives: Depression is more common in Parkinson's disease (PD) than other chronic and disabling disorders. This study aimed to estimate the prevalence and identify potential risk factors influencing depression in 519 consecutive nondemented Chinese PD patients.

Patients and methods: Depression was assessed using the Hamilton Rating Scale for Depression (HAMD), PD severity was assessed using Hoehn and Yahr (H & Y) staging, motor symptoms were measured with the Unified PD Rating Scale (UPDRS) part III, and the Non-Motor Symptoms Questionnaire (NMS-Quest) was used to evaluate the global non-motor symptoms (NMS). The PD Sleep Scale (PDSS), and Mini-Mental State Examination (MMSE) were also administered.

Results: The mean total HAMD score was 12.60 ± 9.29, and the most prevalent depressive domain was retardation (84.4%). There were significant correlations between the total HAMD score and sex, PD-duration, UPDRS-III, H & Y stage, PD-NMS, PDSS, and MMSE. Non-motor symptoms, poor sleep quality, younger age, and cognitive dysfunction are independent predictors of depression. Among these, non-motor symptoms or sleep disturbances are the most powerful predictors of each depressive domain. We observed a significantly higher total HAMD score and domains of anxiety/somatization, mental disorder, and hopelessness in female patients. However, there was no difference in HAMD total scores and HAMD sub-items between young-onset PD and late-onset PD patients when adjusted by potential confounding factors.

Conclusions: The prevalence rate of depression among nondemented Chinese PD patients is high and similar to those reported in previous studies. The presence of depression in PD patients should be routinely assessed in clinical practice.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease, affecting approximately 1.7% of people > 65 years in China [1]. PD is a complex debilitating disease characterized by motor symptoms of tremor, rigidity, bradykinesia, and postural instability, and can be accompanied by various non-motor symptoms ranging from neuropsychiatric symptoms, autonomic and sensory dysfunctions, and sleep disturbances [2,3].

Up to 90% of PD patients experience psychiatric complications [4]. Depression is the most prevalent and is more frequent in PD patients compared to the general population [5,6]. Rather than a secondary reaction to psychosocial stress and motor deficits, depression may be an intrinsic part of PD. Several lines of evidence support this hypothesis. Firstly, depressive symptoms often precede typical motor symptoms, and there is no linear correlation with PD duration or severity [5]. Secondly, the prevalence of depression in PD is greater than in patients suffering from other diseases with the same degree of disability [7–9]. Thirdly, levodopa and other antiparkinsonian drugs can relieve motor symptoms, but do not alleviate and can even induce or aggravate depressive symptoms. The precise pathophysiological mechanism of depression in PD remains to be fully elucidated. Postmortem studies of depressed PD patients have confirmed decreased densities of serotonin and dopamine neurons in the dorsal raphe and ventral tegmental area, respectively [10,11].

Most patients with depression go undiagnosed, and only 25% with

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depressive symptoms are adequately treated [12,13]. Depression is difficult to diagnose in this population partly because symptoms such as sleep disturbances, psychomotor retardation, easily fatigued state, and loss of energy overlap with those of PD [14]. Several potential risk factors associated with depression in PD have been identified, including cognitive dysfunction, early disease onset, and longer disease duration; however, reports in this area remain inconsistent.

Despite earlier studies, the prevalence rate of and clinical features associated with depression in nondemented Chinese PD populations remain largely unknown. We carried out a large cross-sectional study to estimate the prevalence of depressive symptoms and investigate the risk factors of depression in Chinese PD patients.

2. Patients and methods

2.1. Patients

A consecutive series of 519 patients with clinically confirmed idiopathic PD were enrolled from the neurology outpatient clinics at the authors' affiliated institutions from May 2012 to April 2015. PD was diagnosed according to the PD United Kingdom Brain Bank criteria [15]. Individuals were excluded if their Mini-Mental State Exam (MMSE) score was < 24 or had a history of cerebrovascular accidents, encephalitis, brain tumor, trauma, or epilepsy. All patients were free of atypical parkinsonism. The local ethics committee approved the study. All subjects signed written informed consent.

2.2. Methods

A standard questionnaire was utilized to obtain demographic information including age, sex, age of onset, illness duration, and education level.

The Unified PD Rating Scale (UPDRS) part III was used to assess motor disability [16]. The Hoehn and Yahr (H & Y) scale was used to evaluate disease severity [17] as 1–2 (mild), 2.5–3 (moderate), or 4–5 (severe). All patients completed the Non-Motor Symptoms Questionnaire (NMS-Quest), a validated tool for screening global non-motor symptoms in PD [18]. Cognitive evaluation was performed using the MMSE [19], and the PD Sleep Scale (PDSS) was used to assess sleep quality [20]. We used the Hamilton scale with 24 items (HAMD) to quantify depression severity[21]; a total score between 8 and 20, 21 and 35, and > 35 indicated mild, moderate, and severe depression, respectively. The 24 items were grouped into 7 domains: 1) anxiety/somatization (contains 6 items: psychic anxiety, somatic anxiety, gastro-intestinal symptoms, hypochondriasis, insight, general somatic symptoms), 2) weight loss, 3) mental disorders (6 items: feeling of guilt, suicide, agitation, depersonalization and derealization, paranoid symptoms, obsessional symptoms), 4) diurnal variation, 5) retardation symptoms (4 items: depressed mood, work and interests, retardation, sexual symptoms), 6) sleep disturbances (3 items: early, middle, and late insomnia), and 7) hopelessness symptoms (3 items: helplessness, hopelessness, worthlessness).

2.3. Statistical analysis

All continuous data are presented as the mean ± standard deviation, and categorical variables are shown as percentages. The Student's *t*-test was applied for continuous data comparisons, and chi-square tests were performed to examine associations between categorical variables. The differences in continuous variables were assessed by analysis of variance (ANOVA) with post hoc analysis using the Dunnett's T3 and Scheffe's tests. Correlations between clinical features and HAMD were analyzed by Spearman rank correlation analysis. Multiple stepwise linear regression analysis was carried out to assess the predictive power of variables. All analyses were performed with the SPSS 19.0 (IBM Corp., Armonk, NY). $P < 0.05$ was considered statistically significant.

Table 1
Subject demographic and clinical features.

	n = 519	Range
Male, n (%)	326 (62.8%)	–
Female, n (%)	193 (37.2%)	–
Age (years)	65.35 ± 10.19	32–90
Age of onset	59.70 ± 10.22	26–84
PD duration (years)	5.62 ± 4.19	0.5–26
Education level	–	–
Illiterate	27 (5.2%)	–
Primary school	78 (15.0%)	–
Middle school	130 (25.0%)	–
High school	129 (24.9%)	–
College	79 (15.2%)	–
Graduate school	14 (2.7%)	–
Master's or Doctorate	62 (11.9%)	–
UPDRS-III	24.18 ± 13.55	1–80
H & Y stage	2.16 ± 0.88	1–5
1	97 (18.7%)	–
1.5	77 (14.8%)	–
2	136 (26.2%)	–
2.5	69 (13.3%)	–
3	98 (18.9%)	–
4	38 (7.3%)	–
5	4 (0.8%)	–
Mean number of NMS	10.50 ± 5.09	0–24
HAMD[a]	12.60 ± 9.29	0–55
Not depressed (< 8)	187 (36.0%)	
Mild (8–20)	240 (46.2%)	
Moderate (20–35)	80 (15.4%)	
Severe (> 35)	12 (2.3%)	
PDSS	117.88 ± 20.53	51–150
MMSE	27.83 ± 1.95	24–30

PD: Parkinson's disease. UPDRS, Unified PD Rating Scale. H & Y, Hoehn and Yahr. NMS: Non-Motor Symptoms. HAMD: Hamilton Rating Scale for Depression. PDSS, PD Sleep Scale. MMSE, Mini-Mental State Examination

3. Results

The demographic characteristics for 519 PD patients (326 males and 193 females) are presented in Table 1. The mean age was 65.35 ± 10.19 (32–90). The mean disease duration was 5.62 ± 4.19 years (0.5–26 years), and the mean age of onset was 59.70 ± 10.22 (26–84). The mean UPDRS-III score was 24.18 ± 13.55, and the distribution of patients in H & Y stages 1, 1.5, 2, 2.5, 3, 4, and 5 were as follows: 18.7%, 14.8%, 26.2%, 13.3%, 18.9%, 7.3%, and 0.8%. The range in total NMS was from 0 to 24 with a mean of 10.50 ± 5.09. The mean scores of PDSS and MMSE were 117.88 ± 20.53 and 27.83 ± 1.95. The HAMD score was 12.60 ± 9.29 (0–55), and 64.0% of patients satisfied the criteria for depression: 240 (46.2%), 80 (15.4%), and 12 (2.3%) had mild, moderate, and severe depression, respectively. The prevalence, mean score, and range of each HAMD domain are listed in Table 2. Retardation was the most prevalent in depressed subjects with PD; 84.4% of patients had at least one symptom of this domain, followed by anxiety/somatization (81.9%) and hopelessness (81.1%).

The Spearman correlation coefficients between global depression and clinical features were also calculated. Statistically positive

Table 2
Prevalence, mean, standard deviation, and range of each HAMD domain.

	Prevalence	Mean ± SD	Range
Anxiety/somatization	425 (81.9%)	2.93 ± 2.57	0–14
Weight loss	174 (33.5%)	0.45 ± 0.69	0–3
Mental disorders	314 (60.5%)	1.59 ± 2.16	0–16
Diurnal variation	118 (22.7%)	0.25 ± 0.50	0–3
Retardation symptoms	438 (84.4%)	2.88 ± 2.33	0–11
Sleep disturbances	339 (65.3%)	1.85 ± 1.94	0–11
Hopelessness symptoms	452 (81.1%)	2.65 ± 2.15	0–10