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Original Article

Investigation on sleep and mental health of patients with Parkinson's disease during the Coronavirus disease 2019 pandemic

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic is adversely affecting sleep quality and mental health, especially in individuals with chronic disease such as Parkinson's disease (PD).
Methods: We conducted a quantitative study, which included 119 Chinese PD patients who had been treated in an outpatient neurology clinic in Wuhan and 169 age- and sex-matched healthy controls. The questionnaire survey focused on the impact of the COVID-19 pandemic on sleep, mental status, symptoms, and daily life and medical treatment of PD patients.
Results: Compared to healthy controls, PD patients had significantly higher scores in both the Pittsburgh Sleep Quality Index (PSQI) (8.13 vs 5.36, p < 0.001) and the Hospital Anxiety and Depression Scale (HADS) –Depression (4.89 vs 3.82, p = 0.022), as well as a higher prevalence of sleep disturbances with PSQI > 5 points (68.9% vs 44.4%, p < 0.001). Sleep disturbance was identified in 68.9% of PD patients. A logistic regression analysis showed that sleep disturbance of PD patients was independently associated with exacerbation of PD symptoms (OR = 3.616, 95%CI= (1.479, 8.844), p = 0.005) and anxiety (OR = 1.379, 95%CI= (1.157, 1.642), p < 0.001). Compared to male PD patients, female ones had higher PSQI scores (9.28 ± 4.41 vs 7.03 ± 4.01, p = 0.009) and anxiety (32.8% vs 0.1%, p = 0.002) and depression prevalence (34.5% vs 11.5%, p = 0.003).
Conclusion: The findings of the present study emphasize the importance of mental and sleep health interventions in PD patients during the COVID-19 pandemic. Additional attention should be paid to the difficulty encountered by PD patients in seeking medical treatment.

1. Introduction

Since 31 December 2019, outbreaks of coronavirus disease 2019 (COVID-19) have been reported in cities including Wuhan, Milan, and New York City [1]. On 11 March 2020, the World Health Organization declared COVID-19 a global pandemic [2]. With the spread of COVID-19, daily hospital activities were suspended and many hospitals in Wuhan began to focus solely on treating COVID-19 patients. Individuals with chronic disease could be influenced substantially by the psychological pressure and the inconvenience caused by inadequate medical consultation due to the COVID-19 pandemic, resulting in worsening of sleep quality and mental health.

It is well known that deficiency of dopamine in the nigrostriatal system is the core pathological feature of Parkinson's disease (PD) [3]. The lack of dopamine can lead to a loss of emotional control and increased mental stress [4]. This may explain the frequent stress-related symptoms such as anxiety and depression in PD patients even in the absence of particular life events that may cause these symptoms [5]. During the COVID-19 pandemic, the uncontrollable risk of infection and the difficulty in seeking medical care might increase the psychological pressure and worsen the mental and sleep states of PD patients. Notably, the mental and sleep states of PD patients are closely related to the subjective symptoms of PD [6]. Therefore, the present study aimed to investigate the incidence of

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anxiety, depression, and sleep disturbances in PD patients and compare it to that of the healthy population, to determine the impact of PD on the mental and sleep states. Moreover, studying the causes of sleep problems in PD patients during the COVID-19 pandemic was an important objective of this research.

2. Methods

2.1. Participants

The present study was a cross-sectional and questionnaire-based interview investigation. The questionnaire was issued from April 20, 2020 to April 30, 2020 and was used to retrospectively assess the mental health status and sleep quality of PD patients from February 2020 to April 2020. It was sent to PD patients who had been treated at an outpatient neurology clinic in Wuhan. All patients were Chinese and satisfied the United Kingdom Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria. Sex- and age-matched control subjects that were able to fulfill the questionnaires were recruited from the general population of the same regions. The exclusion criteria of controls were listed as follow: (1) medical workers; (2) unstable/serious physical illness; (3) history of PD and dementia; and (4) use of medications for insomnia, anxiety or depression for one year before the outbreak. None of the enrolled subjects or relatives living with them suffered from COVID-19. Data were collected through an online questionnaire, which provided functions equivalent to Amazon Mechanical Turk. Individuals who agreed to participate were asked to complete the questionnaire through a link in text messages or social media such as WeChat. All subjects included in the study were anonymous and volunteered to participate.

2.2. Questionnaire

The questionnaire consisted of five parts: socio-demographic characteristics, sleep quality, psychological distress, COVID-19 epidemic-related questions and clinical characteristics of PD.

Data regarding sex, age, education, and geographic location were collected. Clinical characteristics of PD patients were evaluated according to Hoehn and Yahr scale, clinical symptoms, disease duration, and medications. Additionally, patients were inquired about changes in their parkinsonian symptoms in the previous three months, as well as some questions whether they developed any new symptoms including tremors, stiffness, sluggish movement, fatigue, pain, salivation, disturbed gait, and difficulty in turning over in bed and whether the symptoms worsened during the outbreak. Assessments of the degree of PD progression were mainly dependent on chief complaints of the patients.

Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). PSQI includes seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction. The score for each component ranged from 0 to 3, with 3 points indicating extreme negative. The global PSQI score is the sum of all component scores (ranging from 0 to 21). Higher scores indicate poorer sleep patterns as compared to those with lower scores, and subjects with PSQI score >5 were considered as "poor sleepers" [6,7]. Psychological distress of PD patients was assessed using the Hospital Anxiety and Depression Scale (HADS). HADS has been suggested for use in PD patients, as somatic symptoms that may potentially overlap with parkinsonian manifestations, that are not assessed in this scale [8,9], which can avoid false high scores caused by overlapping symptoms to some extent. The clinical diagnostic threshold for anxiety and depression in PD patients is 8 points [10].

Questions related to the COVID-19 pandemic were emphasized in the questionnaire. This questionnaire was designed by referring to several published literatures and combining the specific conditions of PD patients [11,12], and was modified by two neurologists. The self-design questionnaire included a comprehensive assessment of participants' understanding and concerns regarding COVID-19, its negative impact on their daily lives, exercise during the outbreak of COVID-19, difficulties in purchasing medicines, COVID-19-related symptoms, such as fever, headaches, myalgia, sore throat, diarrhea and dry cough, and access to medical care.

2.3. Statistical analysis

Statistical analysis of the data was performed using the IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as frequency (percentage). The Pearson's chi-squared test was used to compare the categorical variables and the Mann–Whitney U test was used to compare the continuous variables between the groups. Logistic regression analyses were conducted to determine the risk factors for sleep disturbance or for exacerbation of symptoms. A p-values <0.05 was considered statistically significant in all the tests.

3. Results

A total of 347 questionnaires (149 PD patients and 198 controls) were collected, of which 288 were included in this study. The socio-demographic features, sleep quality, psychological distress, epidemic-related factors of the included 119 PD patients and 169 healthy controls were presented in Table 1. No statistically significant differences were observed in the demographic characteristics between the control group and the PD group. The scores of PSQI, HADS-anxiety and HADS-depression in PD patients were 8.13 ± 4.34, 4.34 ± 3.87, and 4.89 ± 4.19, respectively, and in healthy controls, they were 5.36 ± 3.22, 4.07 ± 3.71, and 3.82 ± 3.78, respectively. Compared to healthy controls, PD patients had significantly higher scores of PSQI (8.13 vs 5.36, $p < 0.001$) and HADS-depression (4.89 vs 3.82, $p = 0.022$). Notably, PSQI >5 points was observed in 68.9% PD patients and 44.4% healthy controls, which indicated that over 60% of the PD patients had sleep disturbances. Furthermore, compared to healthy controls, PD patients had reduced sleep quality (1.41 vs 0.84, $p < 0.001$), shortened sleep duration (1.61 vs 0.99, $p < 0.001$), severe sleep disturbance (1.39 vs 0.96, $p < 0.001$) and worse daytime dysfunction (1.50 vs 0.63, $p < 0.001$). However, sleep latency (1.12 vs 1.03, $p = 0.609$), sleep efficiency (1.01 vs 0.84, $p = 0.183$) and use of sleeping medication (0.08 vs 0.07, $p = 0.970$) did not differ between the two groups.

In total, 119 patients with PD were included in the study, including 61 (51.3%) male and 58 (48.7%) female patients, with an average age of 61.18 ± 8.77 years. The mean disease duration was 6.84 ± 4.60 years, and the mean Hoehn and Yahr scale was 2.54 ± 1.40. Table 2 shows the differences in the demographic, psychological distress, epidemic-related factors and clinical characteristic between the PD patients with and without sleep disturbance. The results suggest that sleep disturbance showed a statistically significant association with postural instability and gait disorder (PIGD) (75.6% vs 51.4%, $p = 0.009$), exacerbation of PD symptoms (65.9% vs 32.4%, $p = 0.001$), anxiety (5.30 vs 2.19, $p < 0.001$), depression (5.61 vs 3.30, $p = 0.002$) and inadequate medical consultation (79.3% vs 56.8%, $p = 0.011$).

Factors related to sleep disturbance contain exacerbation of PD symptoms, anxiety, depression, inadequate medical consultation, PIGD, epidemic-related symptom, Hoehn-Yahr stage and geographic location. These factors were included in the multiple

Table 1
Characteristics of the participants.

Variables	Patients	Control	P value
	n = 119	n = 169	
Socio-demographic characteristics			
Age, years (mean ± SD)	61.18 ± 8.77	59.84 ± 8.15	0.057
Sex, Female, n (%)	58 (48.7%)	93 (55.0%)	0.293
Education level, Junior college or below, n (%)	79 (66.4%)	122 (72.2%)	0.291
Geographic location, Wuhan, n (%)	69 (58.0%)	80 (47.3%)	0.075
Geographic location, Urban, n (%)	91 (76.5%)	123 (72.8%)	0.480
Sleep quality			
Global PSQI score (mean ± SD)	8.13 ± 4.34	5.36 ± 3.22	**<0.001**
Global PSQI score > 5, n (%)	82 (68.9%)	75 (44.4%)	**<0.001**
Sleep quality	1.41 ± 0.87	0.84 ± 0.68	**<0.001**
Sleep latency	1.12 ± 0.98	1.03 ± 0.89	0.609
Sleep duration	1.61 ± 1.13	0.99 ± 0.86	**<0.001**
Sleep efficiency	1.01 ± 1.06	0.84 ± 0.98	0.183
Sleep disturbance	1.39 ± 0.71	0.96 ± 0.53	**<0.001**
Use of sleeping medication	0.08 ± 0.44	0.07 ± 0.39	0.970
Daytime dysfunction	1.50 ± 1.03	0.63 ± 0.74	**<0.001**
Psychological distress			
HADS-anxiety (mean ± SD)	4.34 ± 3.87	4.07 ± 3.71	0.579
HADS-depression (mean ± SD)	4.89 ± 4.19	3.82 ± 3.78	**0.022**
HADS-anxiety ≥ 8, n (%)	25 (21.0%)	29 (17.2%)	0.410
HADS-depression ≥ 8, n (%)	27 (22.7%)	27 (16.0%)	0.151
Epidemic-related factors			
Following news about COVID-19, n (%)	109 (91.6%)	151 (89.3%)	0.526
Worry about getting COVID-19, n (%)	17 (14.3%)	24 (14.2%)	0.984
Negative effects on daily life, n (%)	68 (57.1%)	113 (66.9%)	0.093
Exercise, n (%)	87 (73.1%)	132 (78.1%)	0.328
COVID-19-related symptoms, n (%)	9 (7.6%)	18 (10.7%)	0.376

Continuous variables are expressed as mean ± standard deviation. Categorical variables are expressed as frequency (percent).
The bold in the table indicates P < 0.05.

Table 2
Demographic and clinical characteristics of PD patients.

Variables	Total	PSQI >5	PSQI ≤5	P value
	n = 119 (100%)	n = 82 (68.9%)	n = 37 (31.1%)	
Socio-demographic characteristics				
Age, years (mean ± SD)	61.18 ± 8.77	61.41 ± 8.84	60.68 ± 8.71	0.441
Sex, Female, n (%)	58 (48.7%)	43 (52.4%)	15 (40.5%)	0.229
Education level, Junior college or below, n (%)	79 (66.4%)	55 (67.1%)	24 (64.9%)	0.813
Geographic location, Wuhan, n (%)	69 (58.0%)	47 (57.3%)	22 (59.5%)	0.827
Geographic location, Urban, n (%)	91 (76.5%)	59 (72.0%)	32 (86.5%)	0.084
Clinical characteristics of PD				
Hoehn and Yahr scale, (mean ± SD)	2.54 ± 1.40	2.67 ± 1.34	2.24 ± 1.50	0.074
PIGD, n (%)	81 (68.1%)	62 (75.6%)	19 (51.4%)	**0.009**
Tremor, n (%)	71 (59.7%)	50 (61.0%)	21 (56.8%)	0.664
Disease duration (mean ± SD)	6.84 ± 4.60	6.99 ± 4.45	6.51 ± 4.97	0.262
Use of levodopa, n (%)	112 (94.1%)	79 (96.3%)	33 (89.2%)	0.265
Use of dopamine agonists, n (%)	90 (75.6%)	62 (75.6%)	28 (75.7%)	0.994
Use of MAOBI, n (%)	37 (31.1%)	26 (31.7%)	11 (29.7%)	0.829
Use of amantadine, n (%)	23 (19.3%)	19 (23.2%)	4 (10.8%)	0.184
Exacerbation of PD symptoms, n (%)	66 (55.5%)	54 (65.9%)	12 (32.4%)	**0.001**
Psychological distress				
HADS-anxiety (mean ± SD)	4.34 ± 3.87	5.30 ± 3.89	2.19 ± 2.88	**<0.001**
HADS-depression (mean ± SD)	4.89 ± 4.19	5.61 ± 4.26	3.30 ± 3.60	**0.002**
HADS-anxiety ≥ 8, n (%)	25 (21.0%)	22 (26.8%)	3 (8.1%)	**0.038**
HADS-depression ≥ 8, n (%)	27 (22.7%)	23 (28.0%)	4 (10.8%)	0.066
Epidemic-related factors				
Following news about COVID-19, n (%)	109 (91.6%)	75 (91.5%)	34 (91.9%)	1.000
Worry about getting COVID-19, n (%)	17 (14.3%)	13 (15.9%)	4 (10.8%)	0.657
Negative effects on daily life, n (%)	68 (57.1%)	48 (58.5%)	20 (54.1%)	0.647
Exercise, n (%)	87 (73.1%)	60 (73.2%)	27 (73.0%)	0.982
COVID-19-related symptoms, n (%)	9 (7.6%)	9 (11.0%)	0 (0%)	0.085
Inadequate medical consultation, n (%)	86 (72.3%)	65 (79.3%)	21 (56.8%)	**0.011**
Difficulties in buying medicines, n (%)	8 (6.7%)	6 (7.3%)	2 (5.4%)	1.000

Continuous variables are expressed as mean ± standard deviation. Categorical variables are expressed as frequency (percent).
Abbreviations: mean ± SD, mean and standard deviation; PD, Parkinson's disease; PIGD, Postural instability and gait disorder; MAOBI.
Monoamine Oxidase B Inhibitor; PSQI, Pittsburgh Sleep Quality Index; HADS, Hospital Anxiety and Depression Scale.
The bold in the table indicates P < 0.05.

Table 3
Logistic regression analysis of multiple factors influencing sleep disturbance.

Variables	Odds ratio (95% confidence interval)	P value
Exacerbation of PD symptoms	3.616 (1.479–8.844)	**0.005**
Anxiety	1.379 (1.157–1.642)	**<0.001**
Inadequate medical consultation		0.107
Depression		0.638
PIGD		0.081
COVID-19-related symptoms		0.134
Hoehn and Yahr scale		0.989
Geographic location, Urban		0.208

Exacerbation of PD symptoms, Anxiety, Geographic location: Urban, Hoehn and Yahr scale, PIGD, Depression, Lack of medical consultation and Epidemic-related symptom were included in the multiple binary logistic regression analysis. Model is logistic regression with "Forward: LR" model. In the end, Exacerbation of PD symptoms and Anxiety were included in the equation.
The bold in the table indicates P < 0.05.

binary logistic regression analysis (Table 3). Evaluation of the risk factors for sleep disturbance revealed that exacerbation of PD symptoms (OR = 3.616, 95%CI= (1.479, 8.844), p = 0.005) and anxiety (OR = 1.379, 95%CI= (1.157, 1.642), p < 0.001) were independently associated with sleep disturbance in PD patients.

It shows differences in the demographic, clinical characteristic, psychological distress, and epidemic-related factors according to different PD genders (Table 4). The results showed that females tended to present higher PSQI scores (9.28 ± 4.41 vs 7.03 ± 4.01,

p = 0.009), poorer sleep quality (1.67 ± 0.87 vs 1.16 ± 0.80, p = 0.001), shorter sleep duration (1.86 ± 1.03 vs 1.38 ± 1.17, p = 0.023) and more severe daytime sleepiness (1.75 ± 1.03 vs 1.27 ± 0.98, p = 0.011). Moreover, female patients are more susceptible to experience anxiety (32.8% vs 0.1%, p = 0.002) and depression (34.5% vs 11.5%, p = 0.003), with higher anxiety scores (5.45 ± 4.49 vs 3.28 ± 2.83, p = 0.009) during the pandemic. Furthermore, more female PD patients follow news about COVID-19 (98.3% vs 85.2%, p = 0.026). With the exception of use of

Table 4
Comparisons of demographic and clinical characteristics between female and male PD patients.

Variables	female	male	P value
	n = 58 (48.7%)	n = 61 (51.3%)	
Socio-demographic characteristics			
Age, years (mean ± SD)	60.78 ± 8.17	61.57 ± 9.35	0.540
Education level, Junior college or below, n (%)	39 (67.2%)	40 (65.6%)	0.847
Geographic location, Wuhan, n (%)	36 (62.1%)	33 (54.1%)	0.379
Geographic location, Urban, n (%)	45 (77.6%)	46 (75.4%)	0.780
Clinical characteristics of PD			
Hoehn and Yahr scale, (mean ± SD)	2.64 ± 1.45	2.44 ± 1.36	0.463
PIGD, n (%)	42 (72.4%)	39 (63.9%)	0.321
Tremor, n (%)	36 (62.1%)	35 (57.4%)	0.602
Disease duration (mean ± SD)	6.78 ± 4.89	6.90 ± 4.35	0.669
Use of levodopa, n (%)	53 (91.4%)	59 (96.7%)	0.396
Use of dopamine agonists, n (%)	44 (75.9%)	46 (75.4%)	0.954
Use of MAOBI, n (%)	23 (39.7%)	14 (23.0%)	**0.049**
Use of amantadine, n (%)	12 (20.7%)	11 (18.0%)	0.714
Exacerbation of PD symptoms, n (%)	35 (60.3%)	31 (50.8%)	0.296
Sleep quality			
Global PSQI score (mean ± SD)	9.28 ± 4.41	7.03 ± 4.01	**0.009**
Global PSQI score > 5, n (%)	43 (74.1%)	39 (63.9%)	0.229
Sleep quality	1.67 ± 0.87	1.16 ± 0.80	**0.001**
Sleep latency	1.30 ± 1.08	0.94 ± 0.84	0.098
Sleep duration	1.86 ± 1.03	1.38 ± 1.17	**0.023**
Sleep efficiency	1.07 ± 1.06	0.95 ± 1.07	0.472
Sleep disturbance	1.50 ± 0.68	1.28 ± 0.73	0.117
Use of sleeping medication	0.12 ± 0.50	0.05 ± 0.38	0.162
Daytime dysfunction	1.75 ± 1.03	1.27 ± 0.98	**0.011**
Psychological distress			
HADS-anxiety (mean ± SD)	5.45 ± 4.49	3.28 ± 2.83	**0.009**
HADS-depression (mean ± SD)	5.74 ± 4.99	4.08 ± 3.08	0.139
HADS-anxiety ≥ 8, n (%)	19 (32.8%)	6 (0.1%)	**0.002**
HADS-depression ≥ 8, n (%)	20 (34.5%)	7 (11.5%)	**0.003**
Epidemic-related factors			
Following news about COVID-19, n (%)	57 (98.3%)	52 (85.2%)	**0.026**
Worry about getting COVID-19, n (%)	8 (13.8%)	9 (14.8%)	0.881
Negative effects on daily life, n (%)	32 (55.2%)	36 (59.0%)	0.672
Exercise, n (%)	42 (72.4%)	45 (73.8%)	0.867
COVID-19-related symptoms, n (%)	6 (0.1%)	3 (0.1%)	0.440
Inadequate medical consultation, n (%)	41 (70.7%)	45 (73.8%)	0.707
Difficulties in buying medicines, n (%)	4 (0.1%)	4 (0.1%)	1.000

Continuous variables are expressed as mean ± standard deviation. Categorical variables are expressed as frequency (percent).
Abbreviations: mean ± SD, mean and standard deviation; PD, Parkinson's disease; PIGD, Postural instability and gait disorder; MAOBI, Monoamine Oxidase B Inhibitor; PSQI, Pittsburgh Sleep Quality Index; HADS, Hospital Anxiety and Depression Scale.
The bold in the table indicates P < 0.05.

monoamine oxidase B inhibitor, no difference was found in clinical and socio-demographic characteristics between male and female PD patients.

4. Discussion

The COVID-19 epidemic has caused a parallel epidemic of fear, anxiety, depression, and insomnia in general populations including PD patients [13–15]. The present cross-sectional survey showed that during the outbreak of COVID-19, 22.7% and 21% of the PD patients experienced depression and anxiety, respectively. Moreover, 68.9% of the PD patients suffered from sleep disturbance, a much higher incidence than that of the general population. As more than half of the patients experienced sleep disturbances, our findings raise concerns about sleep quality in PD patients during the COVID-19 pandemic.

The present survey indicated that sleep disturbance in PD patients was significantly associated with PIGD subtype, exacerbation of PD symptoms, anxiety, depression and inadequate medical consultation. Consistent with existing studies, our study confirmed that patients with the PIGD subtype had severer sleep impairment [16]. The pathological explanation for this phenomenon may be that PD patients of PIGD type has a higher degree of neuronal loss and more severe gliosis in the locus coeruleus [17], which plays an important role in maintaining arousal, sleep and wakefulness homeostasis and circadian rhythm [18]. In addition, studies have also shown that patients with PIGD subtype have more deposition of α-synuclein and Aβ in the brain [19], which may also contribute to the faster disease progression and serious sleep disturbance. The HADS scores for anxiety and depression in PD patients with sleep disturbance were significantly higher than in PD patients without sleep disturbance, indicating that anxiety and depression are important factors affecting sleep status in PD patients [20]that are affected by the sleep quality [21,22].

Most of the patients with PD need regular outpatient visits for evaluations and prescriptions. However, due to nationwide regulations regarding commuting and the uncontrollable risk of infection, these regular visits have become more difficult and impractical. Although many general hospitals in China established online medical consultation and mail order pharmacy services by the end of February, only 27.7% of the patients received timely medical consultation according to the present survey. The lack of medical consultation affected the sleep state of PD patients. Due to the lack of network coverage in some families and the fact that a large number of elderly patients cannot use smart devices, neurologists and volunteers may need to establish active contact and perform regular follow-up for some patients through simple forms of remote services such as text messages and simple telephone communication.

The relationship between sleep disturbance and progression of PD is noteworthy [23]. Our findings suggest that subjective exacerbation of PD symptoms is an independent risk factor for sleep disturbance, including the appearance of any new symptoms or exacerbation of these symptoms, such as tremor, stiffness, sluggish movement, fatigue, pain, salivation, disturbed gait, and difficulty in turning over in bed. Since the maintenance of the sleep–wake cycle is closely related to the dopamine [24,25], PD patients with advanced motor symptoms inclined to experience aggravation of non-motor symptoms such as sleep disturbance, which may be related to the degeneration of the dopaminergic system in the nigrostriatal pathway. In addition, sleep disturbances may contribute to the progression of symptoms. Studies have shown that worsening of sleep quality and shortening of sleep duration are markers of the prodromal phase of PD and an increased number of sleep-related symptoms and poor night-time sleep are positively correlated with disease-related disability [6,26]. A recent study showed that sleep fragmentation recorded by actigraphy was associated with an increased burden of PD pathology in the brain [27]. Additionally, tyrosine hydroxylase, the rate-limiting enzyme for dopamine synthesis, is regulated by *CLOCK* and *SIRT1* genes and abnormal circadian rhythm may cause fluctuation of motor symptoms in PD patients [28,29]. Therefore, the sleep disturbance of PD patients needs to be taken seriously.

Our results show that female PD patients have worse sleep quality and pay more attention to COVID-19 related news. The proportion of female patients with anxiety and depression is much higher than that of male ones. This finding is consistent with previous studies that have shown that women were more likely to suffer from mood disorders, such as depression [30], anxiety [31], and sleep disturbance [32].

This study has also some limitations. All participants were from a single outpatient neurology clinic in Wuhan. Most of them were from the Hubei province and its surrounding areas, leading to the restrictions of the generalization of our search results. And sleep quality was evaluated using a self-report questionnaire investigation, rather than actigraphic recording or polysomnography, which makes the analysis somewhat subjective. Moreover, assessment of symptom progression had some shortcomings. Progression of symptoms was mainly estimated based on patients' chief complaint, rather than an accurate evaluation of symptoms based on standard measures such as the Unified Parkinson's Disease Rating Scale. Finally, since the study was a cross-sectional survey, it is only a hypothesis to infer the contribution of sleep disturbance to disease progression from the possible bidirectional association.

5. Conclusions

During the outbreak of COVID-19, a greater number of PD patients showed sleep disturbance compared to the healthy controls. Moreover, the HADS-depression and PSQI scores were higher in PD group. Among them, female PD patients have more severe sleep disturbance and higher rates of anxiety and depression. Sleep disturbance of PD patients was independently associated with exacerbation of PD symptoms and anxiety. These novel results give us additional insight into the sleep disturbance of PD patients and emphasize the need for sleep health interventions and timely medical consultation.

CRediT authorship contribution statement

Yun Xia: Conceptualization, Formal analysis, Writing - original draft. **Liang Kou:** Conceptualization, Formal analysis, Writing - original draft. **Guoxin Zhang:** Writing - review & editing. **Chao Han:** Writing - review & editing. **Junjie Hu:** Investigation. **Fang Wan:** Investigation. **Sijia Yin:** Investigation. **Yadi Sun:** Investigation. **Jiawei Wu:** Investigation. **Yunna Li:** Investigation. **Zhentao Zhang:** Writing - review & editing. **Jinsha Huang:** Investigation. **Nian Xiong:** Investigation. **Tao Wang:** Conceptualization, Writing - review & editing, Funding acquisition.

Conflict of interest

None.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2020.09.011.

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