

Relationship between Sleep Quality and Cognitive Function in Patients with Mild-to-Moderate Parkinson's Disease

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To the Editor: Parkinson's disease (PD) is a common degenerative disease of the central nervous system (CNS) in middle-aged and elderly people. PD is characterized by resting tremor, myotonia, bradykinesia, abnormal posture, and gait. The incident of PD increases with age. In addition to motor symptoms, nonmotor symptoms have raised additional concerns in recent years. Cognitive impairment is very common in PD patients. It is estimated that the incidence of PD mild cognitive impairment (PD-MCI) is 20–50%,^[1] which is present at the initial visit in some patients and a great number of patients with PD-MCI eventually develop PD with dementia (PDD). PD patients are much more likely to develop dementia than the normal population. It has been found that 2/3 of PD patients suffer from different forms of sleep disorders, which are indicated to be one of the common nonmotor symptoms in PD patients. The symptoms of various sleep disorders in PD patients include night insomnia, increased sleepiness, sleep fragmentation, reduced sleep efficiency, and rapid eye movement (REM) sleep behavior disorder, thus having a serious impact on the patient's sleep quality and increasing the risk of dementia.^[2] Therefore, cognitive dysfunction and sleep disorders are two important nonmotor symptoms of PD, exerting greater impacts on the quality of life (QOL). Here, we evaluated the relationship between sleep quality and cognitive function of PD patients.

From May 2016 to May 2017, we enrolled a total of 111 native Chinese patients with primary PD and without audiovisual dysfunction who were admitted to the Department of Neurology, the First Hospital of Hebei Medical University. The diagnosis of PD was based on the criteria of the United Kingdom PD Society Brain Bank. Moreover, the diagnosis of PDD conformed to the diagnostic criteria of dementia proposed by the Movement Disorder Society Task Force: (1) diagnosis of primary PD, (2) PD-related cognitive decline by the Mini-Mental State Examination (MMSE), (3) cognitive impairment that affected the patient's daily life ability, and (4) development of extrapyramidal system of PD before dementia, with regular time interval.

Patient information was collected by two trained neurologists, including name, sex, age, duration of illness, and educational

level. Of these, duration of disease was calculated from the time the patient initially complained of discomfort. The assessment was performed since medications were initiated. The Unified PD Rating Scale (UPDRS) was used to assess the severity of the disease, and Hoehn-Yahr (H-Y) staging was utilized for disease rating. According to the severity, the patients were divided into stage 1.0–5.0, including mild (1.0–2.0), moderate (2.5–3.0), and severe (4.0–5.0). According to complaints of patients and their family concerning declined cognitive function and interference with daily life activities in our study, PD patients were divided into three groups as follows: normal group, MCI group, and dementia group, according to MMSE and MoCA (Beijing version) normal cognitive function. MoCA ≥ 26 points and denying cognitive decline was categorized as a normal cognitive function, MoCA < 26 points and MMSE ≥ 26 as well as a complaint of decreased cognitive function but denying interference with daily life activities as MCI, and MMSE < 26 and complaint of decreased cognitive function and affected daily lives as dementia. The Pittsburgh Sleep Quality Index (PSQI) was used to evaluate the quality of sleep in PD patients over the past month. Patients with PSQI score ≥ 6 points were classified as suffering sleep disorders, and patients with long-term use of sleeping pills were excluded. SPSS version 19.0 software (SPSS, USA) was used for statistical analysis. Student's *t*-test was used for the comparisons. The significance level was set at a value of $P < 0.05$.

There were a total of 111 (61 males and 50 females) PD patients, with a mean age of 66.5 ± 8.7 years, a mean educational level of 11.2 ± 3.5 years and a mean duration of 6.1 ± 4.1 years. The mean H-Y staging was 2.20 ± 0.80 , which was classified as mild-to-moderate PD, including mild in 59 (53.15%) patients, and moderate in 52 (46.85%) patients. Patients with PSQI ≥ 6 were

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diagnosed with having sleep disorders. There were 67 (60.36%) patients with cognitive impairment, including 30 (27.03%) with MCI and 37 (33.33%) with dementia. The MMSE score in dementia group was 23.04 ± 1.73 , which was categorized as mild dementia.

The results of the comparison of sleep quality in PD patients with different cognitive levels showed different sleep quality in mild PD patients with different cognitive levels, with the poorest sleep quality in the dementia group. Pairwise comparison showed that the PSQI score was significantly higher in the dementia group than in the normal group, and the difference was statistically significant ($P < 0.05$) [Supplementary Table 1]. Different cognitive levels in moderate PD patients were associated with different sleep quality, with the poorest quality in the dementia group. The pairwise comparison indicated significantly higher PSQI scores in dementia group than in the normal group ($P < 0.01$) [Supplementary Table 2]. Regarding sleep quality, no significant differences were noted in mild and moderate PD patients ($P = 0.935$).

With respect to general information in PD patients with different sleep quality, there was no significant difference between the two PD groups regarding age, educational level, duration of disease, and H-Y staging ($P > 0.05$). However, UPDRS score was significantly higher in the sleep disturbance group than in the normal group, whereas MoCA score and MMSE score were remarkably lower than those in the normal group (both $P < 0.05$) [Table 1]. The correlation analysis showed a positive correlation between cognitive level and sleep quality in PD patients after controlling H-Y variables ($r = 0.461$, $P < 0.01$).

PD is a common degenerative disease of CNS in the elderly. In addition to motor symptoms, nonmotor symptoms in recent years, such as cognitive decline, sleep disorders, autonomic nerve damage, anxiety, depression, psychiatric symptoms, seriously affect the QOL of patients, thereby raising additional concerns. A considerable number of people experience decreased sleep quality at the onset of early PD or before PD symptoms. Common types of sleep disorders in PD patients include difficulty falling asleep, wakefulness/sleep fragmentation, daytime lethargy, sleep-deprivation, REM sleep behavior disorder, restless legs syndrome, and sleep episodes. In addition, altered sleep parameters have been observed, including sleep structure. Those are confronted with unapparent difficulties of falling asleep, difficulties of maintaining sleep and disordered sleep structure, higher incidence of asymptomatic periodic limb movements, and REM sleep behavior disorder, adversely impacting patients' QOL. There are studies suggesting that RBD is a risk factor for cognitive impairment in PD patients.^[3]

As we reported, mean H-Y staging of all 111 patients was 2.20 ± 0.80 , showing a mild-to-moderate PD. PQSI scale was used to assess the quality of sleep in 111 PD patients enrolled, indicating the prevalence of 54.95% in sleep disorders. PD sleep disorders have been reported to be associated with aging, the severity of illness, depression, and dopaminergic dose. There is no

consensus on the prevalence of sleep disorders in PD patients based on various studies, which is, however, generally higher than our results. Several studies have shown that PD patients suffer abnormal sleep at an early stage, which is likely to worsen as the disease progresses. Even at early stage, PD patients have a significantly decreased health-related quality of life (HR-QOL) compared with their peers, and that PD impacts HR-QOL in various manners. PD at an early stage has a limited effect on HR-QOL due to relatively mild motor symptoms. Thus, the priority should be given to nonmotor symptoms. The authors of the study recognize depression, fatigue, and sleep disorders as the leading cause of the decline in HR-QOL in early PD patients.^[4] The current findings reveal that a higher rate (54.95%) of sleep disorders is noted in mild-to-moderate PD patients, and sleep disorders negatively impact cognitive function in PD patients, thereby leading to further decline of HR-QOL.

Sleep disorders and cognitive disorders, as the two major nonmotor symptoms of PD, interact with each other. Sleep disorders can be seen as a concomitant symptom of cognitive impairment and can lead to involvement of the brainstem nerve nucleus, thus impairing cognitive function. The current results showed that sleep disorders in PD patients were associated with a high prevalence of cognitive impairment and a marked decline in cognitive function. Consistent with the above findings, PD patients with dementia had poorer sleep quality than those with normal cognitive function, suggesting an interaction between sleep quality and cognitive function. Based on studies in the Western countries,^[5] α -synuclein, A β protein, and tau protein have been found in multiple brain functional areas of PD patients with sleep disorders. Currently, A β protein and tau protein are recognized to be associated with pathological changes of Alzheimer's disease.^[6] In addition, α -synuclein abnormally aggregates to form Lewy bodies, which are characteristic pathological changes of Lewy body dementia, suggesting a common pathological basis of sleep disorders and cognitive decline.

This study has several limitations. First, patients enrolled had mild-to-moderate PD and MCI. Second, there was a small sample size. Third, the effect of medications patients took on sleep is not taken into account. Last, the types of sleep disorders patients suffered were not specified. Patients with severe PD should be included, and larger sample size is needed. In addition, research methods need to be improved to obtain more detailed and accurate data.

Conclusively, our findings suggest that sleep disorder in PD patients can be considered as a concomitant symptom of cognitive decline, and further aggravate cognitive impairment, indicating a potential interaction. Although the underlying pathophysiological processes remain incompletely understood, the association between sleep disorders and cognitive function in PD patients may suggest a decrease in dopamine levels in the limbic system.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

Table 1: Comparison of general information in Parkinson's disease patients with different sleep conditions

Characteristics	Normal sleep group (n = 50)	Sleep disturbance group (n = 61)	t	P
Age (years)	64.7 \pm 9.5	68.3 \pm 7.7	1.728	0.086
Educational level (years)	12.2 \pm 2.9	10.8 \pm 3.7	-1.592	0.115
Duration of disease (years)	6.2 \pm 4.2	6.3 \pm 4.0	0.107	0.915
H-Y staging	2.17 \pm 0.86	2.18 \pm 0.83	-0.083	0.934
MMSE	26.93 \pm 2.64	25.36 \pm 3.31	2.402	0.015
MoCA	24.44 \pm 4.25	21.77 \pm 5.39	3.004	0.003

PSQI: Pittsburgh Sleep Quality Index; H-Y: Hoehn-Yahr; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Comparison of sleep quality in mild Parkinson's disease patients with different cognitive levels

Groups	<i>n</i>	PSQI	<i>P</i>
Normal cognitive function group	19	5.47 ± 3.45	0.137*
Mild cognitive impairment group	24	7.17 ± 3.81	0.214 [†]
Dementia group	16	8.68 ± 4.56	0.030 [‡]

*Comparison between normal cognitive function group and mild cognitive impairment group; [†]Comparison between mild cognitive impairment group and dementia group; [‡]Comparison between normal cognitive function group and dementia group. PSQI: Pittsburgh Sleep Quality Index.

Supplementary Table 2: Comparison of sleep quality in moderate Parkinson's disease patients with different cognitive levels

Groups	<i>n</i>	PSQI	<i>P</i>
Normal cognitive function group	25	5.24 ± 3.45	0.051*
Mild cognitive impairment group	10	7.90 ± 3.81	0.383 [†]
Dementia group	17	9.35 ± 4.56	0.005 [‡]

*Comparison between normal cognitive function group and mild cognitive impairment group; [†]Comparison between mild cognitive impairment group and dementia group; [‡]Comparison between normal cognitive function group and dementia group. PSQI: Pittsburgh Sleep Quality Index.