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Poor nighttime sleep is positively associated with dyskinesia in Parkinson's disease patients

Cheng-jie Mao^{a,1}, Ya-ping Yang^{a,1}, Ju-ping Chen^b, Fen Wang^c, Jing Chen^a, Jin-ru Zhang^a, Hui-jun Zhang^a, Sheng Zhuang^a, Yi-tong Xiong^a, Chen-chen Gu^a, Wen Yuan^a, Juan-ying Huang^a, Alexander Fay^d, Chong-ke Zhong^e, and Chun-feng Liu^{a,c,*}

^aDepartment of Neurology and Suzhou Clinical Research Center of Neurological Disease, the Second Affiliated Hospital of Soochow University, Suzhou 215004, China

^bDepartment of Neurology, Changshu Traditional Chinese Medicine Hospital, East Huanghe Road, Changshu 215000, China

^cInstitute of Neuroscience, Soochow University, Suzhou 215123 China

^dDepartment of Neurology, UCSF School of Medicine, Medical Center, San Francisco, California CA94143, United States

^eDepartment of Epidemiology, School of Public Health, Medical College of Soochow University, Suzhou 215123, China

Abstract

Background—Dyskinesia is a troublesome complication of long-term dopaminergic medications in Parkinson's disease (PD) patients. Many factors are reported to be associated with dyskinesia in PD.

Objective—To investigate the association between sleep quality and dyskinesia in patients with PD.

Methods—Four hundred twenty-five patients with PD were enrolled in this study. Demographic information was collected. Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn and

*Corresponding author. Department of Neurology, Second Affiliated Hospital of Soochow University, No. 1055, Sanxiang Road, Suzhou, Jiangsu 215004, China. liuchunfeng@suda.edu.cn (C.-f. Liu).

¹These authors contributed equally to this work.

Author contributions

Cheng-jie Mao, Ya-ping Yang and Chun-feng Liu designed the study. Ju-ping Chen, Fen Wang, Jing Chen, Jin-ru Zhang, Hui-jun Zhang, Sheng Zhuang, Yi-tong Xiong, Chen-chen Gu, Wen Yuan, and Juan-ying Huang collected the data. Cheng-jie Mao and Ya-ping Yang analyzed the data and drafted the manuscript, Chong-ke Zhong participated to design the study and do the statistical analysis, Alexander Fay participated to draft and revise the manuscript, and all authors wrote and revised the article.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Yahr (H-Y) stage scale were also performed. Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI) were applied to evaluate daytime sleepiness and overall nighttime sleep quality, respectively, in PD patients.

Results—Patients with dyskinesia tended to have a longer duration of disease, higher daily levodopa-equivalent dose (LED), H-Y stage, UPDRS II and PSQI score, and a higher percentage of levodopa treatment than those without dyskinesia. After adjusting for age, sex, age at onset of PD, disease duration, UPDRS I, UPDRS II, UPDRS III, cigarette smoking, use of different antiparkinsonian drugs, phenotype, daily LED, and restless leg syndrome (RLS), PSQI score was still associated with dyskinesia, with corresponding ORs 1.111 (95% CI, 1.004–1.229) as a continuous variable, and 2.469 (95% CI, 1.051–5.800) as a categorical variable, respectively. Further analysis of PSQI components showed that subjective sleep quality and sleep latency were associated with dyskinesia in PD patients.

Conclusions—Our data showed that poor nighttime sleep is positively associated with dyskinesia in PD patients. Attention to the management of nighttime sleep quality may be beneficial to dyskinesia in patients with PD.

Keywords

Parkinson's disease; Dyskinesia; Sleep disorder

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease, and is characterized by motor and non-motor dysfunction [1]. Although Levodopa is the most effective agent for the symptomatic treatment of PD, the emergence of side effects, particularly motor fluctuations and dyskinesia, can limit its use in some patients [2]. Though its incidence rate differs between western countries and eastern countries, dyskinesia seriously affects patients' quality of life [2–4]. The pathogenesis of dyskinesia is unknown. Multiple lines of evidence show that Levodopa-induced dyskinesia (LID) is associated with neurodegeneration in cortical and subcortical areas, including prefrontal cortex, primary motor cortex (via the pallidothalamocortical motor pathway), striatum, subthalamic nucleus, and cerebellum. Dysregulation of neurotransmitters other than dopamine, such as serotonin, γ -aminobutyric acid (GABA), glutamate, adenosine, and acetylcholine is also implicated in dyskinesia [5]. Changes in cellular signaling pathways and enhanced dopamine D1 receptor stimulation resulting in widespread molecular adaptations in striatal medium spiny neurons, play important roles in LID [6]. Uncontrolled long-term potentiation (LTP) of corticostriatal synapses is also associated with the development of LID [7]. Other risk factors that have been identified related to dyskinesia in PD patients include a younger age of onset, longer duration of levodopa therapy, female sex, disease duration, and the total daily levodopa dose [4,5,8].

Disordered sleep is one of the most frequent non-motor symptoms in PD patients, and has a significant negative impact on quality of life [9]. In PD patients, sleep disorders include insomnia, vivid dreams, restless legs syndrome (RLS), rapid eye movement sleep behavior disorder (RBD), periodic limb movements (PLM), circadian rhythm disruption and

excessive daytime sleepiness (EDS) [10]. The etiology of sleep disorders in PD are likely to be multifactorial. Potential contributing factors include degeneration of central sleep regulatory areas, adverse effects of anti-parkinsonian medications, age-related sleep changes, and the impact of motor symptoms (nighttime akinesia, dyskinesia, tremor, and rigidity) [9]. Degeneration of multiple areas of the central nervous system involving various neurotransmitters is associated with sleep disorders in PD, including the dopaminergic ventral tegmental area, serotonergic dorsal raphe nuclei, noradrenergic locus coeruleus and dorsal nucleus of the vagal nerve, and cholinergic laterodorsal tegmental nucleus and pedunculopontine nucleus [11].

Recently, some studies have shown that slow homeostatic adjustment of intrinsic excitability occurring during sleep was very important for network stabilization [12]. Spike-timing-dependent plasticity such as LTP has a crucial role in network stability. Slow-wave activity (SWA) is considered to be the basis for overnight homeostatic processes, and is associated with spike-timing-dependent plasticity. Impaired synaptic homeostasis during sleep correlated with dyskinesia in an animal model of PD [7]. Furthermore, “sleep benefit” on motor symptoms was observed in the morning in PD patients [13]. Common impaired brain regions and altered neurotransmitters, as well as the “sleep benefit” phenomenon, suggest a correlation between sleep and dyskinesia among PD patients.

So far, the association of sleep and LID in PD patients has not been investigated. Therefore, in this study, we aim to investigate the relationship between sleep disorders and dyskinesia in PD patients.

2. Methods

2.1. Subjects

A total of 425 PD patients were enrolled in this study at the Second Affiliated Hospital of Soochow University from Jan 2014 to Dec 2016. The clinical diagnosis of idiopathic PD was determined based on UK Parkinson’s disease Brain Bank criteria [14]. Demographic information, including age, sex, disease duration, concurrent diseases, medication information for PD and other diseases such as hypertension and diabetes mellitus, and detailed medical history, was collected. All the subjects were carefully evaluated by a movement disorder specialist. Unified Parkinson’s disease rating scale (UPDRS) and Hoehn & Yahr stage (H-Y stage) scale were applied to all PD subjects during the medication “on” state [15,16]. PD subjects were classified as tremor-dominant (TD) subtype, akinetic-rigid (AR) subtype, or mixed subtype using the numerical ratio, which was derived from a patient’s mean tremor score and mean akinetic-rigidity score. The tremor score was derived from the sum of a 7-item scale that included action or postural tremor of the hands (two items) and rest tremor of the face/lips/chin and each limb (five items). The non-tremor score was also derived from the sum of a 12-item scale that included passive range of motion, rigidity of the neck and each extremity (5 items), facial expression and speech (2 items), rising from a chair (1 item), posture and postural instability (2 items), gait (1 item), and body bradykinesia (1 item). Each item was rated 0–4 with 0 representing the absence of symptoms. The mean of each scale was calculated and then the ratio (mean TD/mean AR

score) determined. Based on this method, AR subjects had a ratio <0.8 , whereas TD subjects had a ratio >1.0 , and mixed subjects had a ratio range from 0.8 to 1 [17].

Dyskinesia was assessed using UPDRS Part IV based on item 32. Item 32: “What proportion of the waking day is dyskinesia present? (historical information)”, where a score of 0 = none, 1 = 1–25%, 2 = 26–50%, 3 = 51–75%, and 4 = 76–100%. Dyskinesia was defined as present if the response to UPDRS IV item 32 was ≥ 1 .

Calculation of a daily levodopa equivalent dose (LED) for each patient was based on theoretical equivalence to levodopa as follows: levodopa dose + levodopa dose $\times 1/3$ if on entacapone + pramipexole (mg) + pramipexole (mg) $\times 100$ + selegiline (mg) $\times 10$ + amantadine (mg) + controlled release levodopa (mg) $\times 0.75$.

Epworth Sleepiness Scale (ESS)(a measure of daytime sleepiness) and Pittsburgh Sleep Quality Index (PSQI) (a measure of the quality of nighttime sleep over the previous month) were completed by each PD patient [18,19]. The 8-item ESS is a useful and widely used questionnaire for assessing general level of daytime sleepiness. The scale comprises eight items that address typical day-to-day situations. Each item can range from 0 to 3 points (0 = would never doze, 3 = high chance of dozing). The total ESS score is from 0 to 24 (lowest to highest sleep propensity). The proposed range for normal sleep propensity is 0–10. The Chinese version of Epworth sleepiness scale also appears to have good internal consistency and reliability among Mandarin-speaking subjects as a standardized screening test of sleepiness in daily life, with the same cut-off value [20]. The PSQI is a self-report questionnaire that assesses sleep quality over a 1-month time period. Nineteen individual items generate seven ‘component’ scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The scores for these components range from 0 (no difficulty) to 3 (severe difficulty) and are summed to produce a global measure of sleep disturbance, with a score ranging from 0 to 21. Higher scores represent poorer subjective sleep quality. The Chinese version of PSQI showed good validity and reliability for assessment of sleep quality in the Chinese population. The highest sensitivity and specificity of PSQI for evaluating sleep disorders in the Chinese population were obtained when using a cut-off value of 7.5, with a sensitivity of 88% and a specificity of 84% [21]. So in this study, subjects with PSQI >7 were considered as poor sleepers. Diagnosis of RLS was made according to the RLS diagnostic criteria proposed by the International Restless Legs Syndrome Study Group (IRLSSG) in 2014 [22].

All patients received dopaminergic medications.

Subjects were excluded if they had a secondary parkinsonism syndrome, atypical parkinsonian syndrome, malignant neoplasm, epilepsy, or severe cardiopulmonary disease.

This study was approved by the ethics committee of the Second Affiliated Hospital of Soochow University and informed consent was obtained from all participants.

2.2. Statistics

The study participants were divided into two groups, those with and those without dyskinesia. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range [IQR]) and were compared using Student's t-test or Wilcoxon rank-sum test. Categorical variables were expressed as frequency (%) and were compared using chi-square or Fisher exact test. Spearman correlation analyses were used to assess the correlations between ESS or PSQI with other variables, such as age, sex, age at onset of PD, duration of disease, daily LED, H-Y stage, first part of UPDRS (UPDRS I) score, second part of UPDRS (UPDRS II) score, third part of UPDRS (UPDRS III) score, cigarette smoking, PD family history, RLS, and different motor phenotypes. In addition, multivariate non-conditional logistic regression models were used to assess the association of sleep with dyskinesia in PD patients. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were used to evaluate the risk of dyskinesia after adjusting for important confounders. We ultimately included age, sex, age at onset of PD, disease duration, UPDRS I, UPDRS II, and UPDRS III scores, cigarette smoking, use of levodopa, dopamine agonists, monoamine oxidase-B inhibitor (MAOBI), Catechol-O-methyltransferase inhibitor (COMTI), amantadine, phenotype, daily LED, and RLS in adjusted models.

All P values were 2-tailed, and a significance level of 0.05 was used. Statistical analysis was conducted using SAS statistical software (version 9.2, Cary, North Carolina, USA).

3. Results

A total of 425 patients was included in this study. The baseline characteristics are presented in Table 1. Patients with dyskinesia tended to have a longer duration of disease, higher daily levodopa-equivalent dose, higher H-Y stage, greater UPDRS II and PSQI score and a higher percentage of levodopa treatment than those without dyskinesia. There were no significant differences in score of ESS or other variables between the two groups.

The Spearman correlation analyses showed that ESS score positively correlated with sex ($r = 0.177$, $p < .001$), duration of disease ($r = 0.180$, $p < .001$), H-Y stage ($r = 0.155$, $p = .001$), UPDRS I ($r = 0.323$, $p < .001$), UPDRS II ($r = 0.215$, $p < .001$), and UPDRS III ($r = 0.186$, $p < .001$) scores, cigarette smoking ($r = 0.118$, $p = .015$), use of COMTI ($r = 0.118$, $p = .015$) and PSQI score ($r = 0.180$, $p = .027$) (Table 2). For dopamine agonists, the Spearman correlation analysis with ESS score showed a coefficient of 0.095, and P value of 0.05. In addition, PSQI score was positively correlated with duration of disease ($r = 0.168$, $p = .001$), daily LED ($r = 0.163$, $p = .001$), H-Y stage ($r = 0.265$, $p < .001$), UPDRS I ($r = 0.254$, $p < .001$), UPDRS II ($r = 0.256$, $p < .001$), and UPDRS III ($r = 0.236$, $p < .001$) scores, and RLS ($r = 0.147$, $p = .002$). After adjusting for age, sex, age at onset of PD, PD family history, and other important covariates, PSQI score was still associated with dyskinesia, with ORs 1.111 (95% CI, 1.004–1.229) as a continuous variable and 2.469 (95% CI, 1.051–5.800) as a categorical variable (Table 3). Further analysis of PSQI components showed that subjective sleep quality and sleep latency were associated with dyskinesia in PD patients (Table 4).

4. Discussions

Our study demonstrates that the PSQI score, rather than ESS score is associated with dyskinesia in patients with PD. The PSQI score remained significant even after adjusting for several potential confounders. Subjective sleep quality and sleep latency were the factors most associated with dyskinesia in PD patients.

Although more attention has been given recently to non-motor symptoms of PD, such as psychiatric manifestations, sleep disorders, fatigue, pain, autonomic dysfunction and cognitive impairment, motor symptoms remain the primary treatment target [23,24]. Long-term use of dopaminergic agents may lead to drug-induced dyskinesia. The median dyskinesia frequency is slightly less than 40% after 4–6 years of levodopa therapy among modern era patients [25]. In a recent survey including 28 movement disorders clinics in China, 1558 PD patients completed the 9-item wearing off questionnaire (WOQ-9), and 160 patients were finally diagnosed with dyskinesia [3]. In our study, the prevalence of dyskinesia was 7.3% (31/425), which was lower than in studies from the western countries, but similar to the survey in China. This may be partly because the subjects in the study had, on average, a lower dosage of daily LED and shorter disease duration of PD.

Dyskinesia may have a deleterious impact on both patients' and their caregivers' quality of life. Once dyskinesia occurs, even movement disorder specialists find treatment to be a challenge. In spite of clinical trials of many medications, only a few studies have shown promising results. Currently, only amantadine and clozapine have demonstrated efficacy in treating dyskinesia. The novel monoamine oxidase B- and glutamate-release inhibitor safinamide had no obvious effect on existing LID. An antagonist of the metabotropic Glutamate-receptor (AFQ056) showed promising results in some studies, but these findings still need to be confirmed [26]. Nonpharmacological interventions for dyskinesia include surgical treatment and transcranial magnetic stimulation. The surgical treatments, including pallidotomy and globus pallidus internus (GPi) deep brain stimulation (DBS), reduce dyskinesia and motor fluctuation markedly. However, long-term clinical evolution of these surgical patients currently seems to be associated with a new PD phenotype, mainly characterized by axial motor problems and cognitive impairment [27].

Considering the challenge of treating dyskinesia in PD patients and the negative effects of dyskinesia on patients' quality of life, strategies to prevent dyskinesia are needed, as is identification of risk factors for dyskinesia. The exact mechanism of dyskinesia in PD patients is unclear. Several risk factors were found to be associated with the development of dyskinesia, including age of onset of PD, female sex, disease duration, and the level of exposure to L-DOPA [4,5,8]. Our study showed that disease duration of PD patients with dyskinesia is longer than in patients without dyskinesia, which is consistent with previous studies. The critical factor in the occurrence of dyskinesia appears to be chronic and progressive dopaminergic denervation and the subsequent long-term exposure to dopamine replacement therapy, which promotes changes in the receptor environment eventually leads to an altered clinical response to dopamine [28]. Pulsatile stimulation of the basal ganglia dopamine receptor results in altered neural activity, which is associated with dyskinesia in PD patients. Among these factors, the amount of synaptic dopamine, which is gradually

reduced, may be more important for the pathogenesis of dyskinesia. This could also explain why disease duration is an important factor in the occurrence of dyskinesia. Besides the dopaminergic system, the serotonergic and noradrenergic systems may homeostatically counteract the dysregulation in dopamine levels associated with dyskinesia [5]. Slow homeostatic adjustment of intrinsic excitability occurring during sleep has been considered fundamental for network stabilization, by gradually modifying plasticity thresholds [12]. Impairment of synaptic homeostasis during the disease course reaches a critical point that exceeds the compensatory mechanisms of the corticocortical and corticostriatal synapses, leading to the “runaway” LTP associated with dyskinesia. These effects alter the function of the corticobasal ganglia-thalamic loop. Galati S et al. measured synaptic downscaling across sleep episodes in a parkinsonian animal model showing dyskinetic movements similar to LID. Their results demonstrated an impaired synaptic homeostasis and non-rem (NREM) sleep-induced reduction of SWA in animals with dyskinesia, suggesting that sleep deprivation caused an anticipation and worsening of LID, supporting a link between sleep and the development of LID [7]. There was a progressive reduction of the amount of NREM sleep during the disease course in PD patients [29]. “Sleep benefit” on motor symptoms can also be observed in PD patients. Dyskinesia is usually more pronounced during the afternoon or in the evening than in the morning [13]. Clinically, we have also noticed patients complaining about exacerbated dyskinesia in the morning after poor sleep the previous night. All these may be indicators of the interactions between the increasingly altered sleep architecture and dyskinesia in PD patients. So far, how sleep affects LID in PD patients has yet to be investigated. Our study results showed PSQI score was significantly associated with dyskinesia in PD patients, even after adjusting for several potential confounders. Subjective sleep quality and sleep latency were the main factors associated with dyskinesia in PD patients. Our findings suggest that poor nighttime sleep quality may promote the occurrence of dyskinesia in PD patients. This finding is a better indicator of the association between sleep and dyskinesia confirmed in PD patients, which provides a basis for further longitudinal studies on the possible role of sleep disorders in dyskinesia with more objective methods, and the effect of treating sleep disorders on dyskinesia in PD patients.

In summary, we have demonstrated that poor sleep quality is positively associated with dyskinesia in PD patients. Subjective sleep quality and sleep latency were the main factors associated with dyskinesia in PD patients. Considering the impact of sleep and dyskinesia on patients’ quality of life, physicians caring for PD patients should pay attention to night-time sleep quality, especially in patients with a relatively large amount of daily LED and longer disease duration who are at high risk for dyskinesia.

Limitations

Our study has several limitations. First, subjects of our study were only from the Second Affiliated Hospital of Soochow University, so the study findings may not be generalizable to the entire PD population. Secondly, this is a retrospective study. Patients were enrolled in this study because they were being evaluated for sleep quality by ESS and PSQI, which may contribute to selection bias. Thirdly, PSQI is a self-report questionnaire with relatively low sensitivity and specificity. Studies with large samples in multiple centers and using more

objective methods, such as actigraphy or polysomnography, are needed to investigate the relationship between sleep dysfunction and dyskinesia with disease progression in PD patients. Fourthly, using just part IV of the UPDRS for defining dyskinesia rather than the Unified Dyskinesia Rating Scale is another limitation. Moreover, most of PD patients in the study were in the mild to moderate stage, and the number of patients with dyskinesia is relatively small. Further study with more advanced PD patients from different centers is needed.

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Table 1

Baseline characteristics of patients with Parkinson's disease.

Characteristic*	Patients Without Dyskinesias (n = 394)	Patients With Dyskinesias (n = 31)	P-value
Age, years	65.9 ± 9.1	67.0 ± 8.6	.513
Male sex	231 (58.9)	14 (45.2)	.269
Age at onset of PD, years	61.6 ± 9.5	58.3 ± 7.8	.128
Education, years	9.0 (6.0–12.0)	9.0 (6.0–15.0)	.266
Duration of disease, month	37.5 (24.0–72.0)	90.0 (69.5–132.0)	<.001
Daily levodopa-equivalent dose, mg/d	300.0 (200.0–450.0)	512.5 (387.5–700.0)	<.001
Hoehn-Yahr stage	2.0 (1.5–2.5)	2.5 (2.0–3.0)	.037
UPDRS I	3.0 (2.0–5.0)	4.0 (2.0–5.0)	.144
UPDRS II	11.0 (8.0–15.0)	13.0 (8.75–17.0)	.038
UPDRS III	26.0 (16.0–35.0)	23.0 (15.0–27.5)	.471
Cigarette smoking	77 (19.5)	6 (19.3)	.974
PD family history	28 (7.1)	5 (16.1)	.076
Restless legs syndrome	91 (23.1)	12 (38.7)	.051
Phenotype			.472
Tremor	78 (19.8)	4 (12.9)	
Akinetic	263 (66.8)	24 (77.4)	
Mixed	53 (13.5)	3 (9.7)	
Use of levodopa	349 (88.6)	31 (100)	.047
Use of dopamine agonists	146 (37.1)	16 (51.6)	.108
Use of MAOBI	43 (10.9)	4 (12.9)	.734
Use of amantadine	78 (19.8)	7 (22.6)	.709
Use of COMTI	15 (3.8)	0 (0)	.269
ESS	5.5 (2.0–9.0)	5.0 (3.0–10.0)	.529
ESS >10	86 (21.8)	5 (16.1)	.457
PSQI	6.0 (3.0–9.0)	8.5 (6.0–11.0)	.005
PSQI >7	132 (53.1)	24 (77.4)	.009

* Continuous variables are expressed as mean ± standard deviation or as median (interquartile range). Categorical variables are expressed as frequency (percent).

Abbreviations: PD, Parkinson's disease; UPDRS I, first part of Unified Parkinson Disease Rating Scale score; UPDRS II, second part of Unified Parkinson Disease Rating Scale score; UPDRS III, third part of Unified Parkinson Disease Rating Scale score; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; MAOBI, Monoamine oxidase-B inhibitor; COMTI, catechol-O-methyltransferase inhibitor.

Table 2

Spearman correlation coefficients of ESS and PSQI with other factors among Parkinson's disease patients.

Variables	ESS		PSQI	
	Coefficient	P-value	Coefficient	P-value
Age	0.138	0.004	0.077	0.114
Sex	0.177	<0.001	0.016	0.750
Age at onset of PD	0.092	0.058	0.006	0.900
Duration of disease	0.180	<0.001	0.168	0.001
Daily levodopa-equivalent dose	0.084	0.082	0.163	0.001
Hoehn-Yahr stage	0.155	0.001	0.265	<0.001
UPDRS I	0.323	<0.001	0.254	<0.001
UPDRS II	0.215	<0.001	0.256	<0.001
UPDRS III	0.186	<0.001	0.236	<0.001
Cigarette smoking	0.118	0.015	0.031	0.525
Restless legs syndrome	0.033	0.501	0.147	0.002
Phenotype	0.017	0.727	0.027	0.575
Use of levodopa	0.043	0.378	0.049	0.314
Use of dopamine agonists	0.095	0.050	−0.067	0.170
Use of MAOBI	−0.018	0.706	0.030	0.541
Use of amantadine	−0.017	0.721	0.054	0.267
Use of COMTI	0.118	0.015	−0.029	0.545
ESS	–		0.108	0.027
PSQI	0.108	0.027	–	

Abbreviations: PD, Parkinson's disease; UPDRS I, first part of Unified Parkinson Disease Rating Scale score; UPDRS II, second part of Unified Parkinson Disease Rating Scale score; UPDRS III, third part of Unified Parkinson Disease Rating Scale score; MAOBI, Monoamine oxidase-B inhibitor; COMTI, catechol-O-methyltransferase inhibitor; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale.

Table 3

Multivariate logistic regression analysis of sleep quality and dyskinesia in Parkinson's disease patients.

Variables	Odds ratio (95% confidence interval)	P-value
ESS [*]		
Continuous	1.011 (0.928–1.102)	.798
Categorical (>10)	0.549 (0.161–1.876)	.339
PSQI [†]		
Continuous	1.111 (1.004–1.229)	.042
Categorical (>7)	2.469 (1.051–5.800)	.038

^{*} Adjusted for age, sex, age at onset of PD, disease duration, daily levodopa-equivalent dose, UPDRS I, UPDRS II, UPDRS III, cigarette smoking, phenotype, restless legs syndrome, PSQI score, and use of levodopa, dopamine agonists, MAOBI, amantadine, and COMTI.

[†] Adjusted for age, sex, age at onset of PD, disease duration, daily levodopa-equivalent dose, UPDRS I, UPDRS II, UPDRS III, cigarette smoking, phenotype, restless legs syndrome, ESS score, and use of levodopa, dopamine agonists, MAOBI, amantadine, and COMTI.

Abbreviations: PD, Parkinson's disease; UPDRS I, first part of Unified Parkinson Disease Rating Scale score; UPDRS II, second part of Unified Parkinson Disease Rating Scale score; UPDRS III, third part of Unified Parkinson Disease Rating Scale score; PSQI, Pittsburgh Sleep Quality Index; MAOBI, Monoamine oxidase-B inhibitor; COMTI, catechol-O-methyltransferase inhibitor; ESS, Epworth Sleepiness Scale.

Table 4

Association between component scores of Pittsburgh Sleep Quality Index with dyskinesia in Parkinson's disease patients.

	Non-Dyskinesias (n = 394)	Dyskinesias (n = 31)	P value [*]	OR (95% CI) [†]	P value
Total	6.0 (3.0–9.0)	8.5 (6.0–11.0)	.005	1.111 (1.004–1.229)	0.042
Subjective sleep quality	1.0 (1.0–1.0)	1.0 (1.0–2.0)	.006	1.830 (1.074–3.119)	0.026
Sleep latency	1.0 (0.0–1.0)	1.0 (0.0–2.0)	.132	1.547 (1.023–2.339)	0.039
Sleep duration	1.0 (0.0–1.0)	1.0 (0.0–1.0)	.426	1.039 (0.662–1.633)	0.867
Sleep efficiency	1.0 (0.0–2.0)	1.0 (0.0–2.0)	.304	1.180 (0.762–1.826)	0.459
Sleep disturbance	1.0 (1.0–2.0)	1.0 (1.0–2.0)	.366	0.982 (0.505–1.907)	0.957
Use of sleep medication	0.0 (0.0–0.0)	0.0 (0.0–1.0)	.067	1.128 (0.781–1.628)	0.522
Daytime dysfunction	1.0 (0.0–2.0)	1.0 (1.0–2.0)	.101	0.993 (0.742–1.328)	0.960

The scores are expressed as median (interquartile range).

^{*} Calculated by Wilcoxon rank-sum test.

[†] Adjusted for age, sex, age at onset of PD, disease duration, daily levodopa-equivalent dose, UPDRS I, UPDRS II, UPDRS III, cigarette smoking, phenotype, restless legs syndrome, ESS score, and use of levodopa, dopamine agonists, MAOBI, amantadine and COMTI.

Abbreviations: OR, Odds ratio; CI, confidence interval; PD, Parkinson's disease; UPDRS I, first part of Unified Parkinson Disease Rating Scale score; UPDRS II, second part of Unified Parkinson Disease Rating Scale score; UPDRS III, third part of Unified Parkinson Disease Rating Scale score; ESS, Epworth Sleepiness Scale; MAOBI, Monoamine oxidase-B inhibitor; COMTI, catechol-O-methyltransferase inhibitor.