



Subtypes of Sleep Disturbance in Parkinson's Disease Based on the Cross-Culturally Validated Korean Version of Parkinson's Disease Sleep Scale-2

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Background and Purpose This study aimed to determine the clinimetric properties of the Korean version of Parkinson's Disease Sleep Scale-2 (K-PDSS-2) and whether distinct subtypes of sleep disturbance can be empirically identified in patients with Parkinson's disease (PD) using the cross-culturally validated K-PDSS-2.

Methods The internal consistency, test–retest reliability, scale precision, and convergent validity of K-PDSS-2 were assessed in a nationwide, multicenter study of 122 patients with PD. Latent class analysis (LCA) was used to derive subgroups of patients who experienced similar patterns of sleep-related problems and nocturnal disabilities.

Results The total K-PDSS-2 score was 11.67 ± 9.87 (mean \pm standard deviation) at baseline and 12.61 ± 11.17 at the retest. Cronbach's α coefficients of the total K-PDSS-2 scores at baseline and follow-up were 0.851 and 0.880, respectively. The intraclass correlation coefficients over the 2-week study period ranged from 0.672 to 0.848. The total K-PDSS-2 score was strongly correlated with health-related quality of life measures and other corresponding nonmotor scales. LCA revealed three distinct subtypes of sleep disturbance in the study patients: "less-troubled sleepers," "PD-related nocturnal difficulties," and "disturbed sleepers."

Conclusions K-PDSS-2 showed good clinimetric attributes in accordance with previous studies that employed the original version of the PDSS-2, therefore confirming the cross-cultural usefulness of the scale. This study has further documented the first application of an LCA approach for identifying subtypes of sleep disturbance in patients with PD.

Key Words Parkinson disease, sleep, Parkinson's Disease Sleep Scale-2, Korean version, validity, latent class analysis.

INTRODUCTION

Sleep-related problems in Parkinson's disease (PD) have received increasing attention in past years due to their occurrence in early stages of the disease, as well as their clinical influence on morbidity, disability, and the health-related quality of life (HRQoL) of patients with advanced disease.^{1–4} Parkinson's Disease Sleep Scale (PDSS) is a patient-reported instrument recommended by the Movement Disorder Society task force, and is designed to rate overall sleep problems in the PD population.^{5,6} A revision of PDSS (PDSS-2) was recently published that places particular emphasis on improving scale properties and encompassing nocturnal symptoms that were not previously included (e.g., restless leg syndrome, sleep apnea, akinesia, and nocturnal pain).⁷ PDSS-2 has been successfully applied in several clinical trials as a reliable patient-reported outcome measure.^{7–11} This prompted us to translate and adapt PDSS-2 to Korean individuals and evaluate its clinimetric properties in the assessment of sleep disturbances among Korean-speaking patients with PD.

This study also sought to determine the discriminatory capacity of the new Korean version of PDSS-2 (K-PDSS-2) by conducting latent class analysis (LCA) to characterize subtypes of sleep disturbance in PD. Several studies have applied LCA in PD populations to address depression-anxiety subtypes^{12,13} and neurocognitive subtypes.¹⁴ The potential causes of sleep disturbances vary widely, and have been suggested

to include primary insomnia, depression, rapid-eye-movement sleep-behavior disorder (RBD), restless leg syndrome, nocturnal motor symptoms, antiparkinsonian drug side effects, nocturia, and sleep-related breathing disorders, all of which frequently co-occur.^{1,3,4} However, few studies have attempted to empirically outline the clinical heterogeneity of sleep-related problems in patients with PD. LCA has previously been used to identify subtypes of sleep disturbance in patients with Alzheimer's disease.¹⁵ An empirical search for latent homogeneous subgroups of patients who experience similar patterns in sleep-related problems and nocturnal disabilities could help to elucidate the pathophysiology of these conditions and lead to the development of more-targeted management strategies. To our knowledge, the present study is the first to document the application of an LCA approach for identifying subtypes of sleep disturbance in patients with PD.

METHODS

Subjects

This study, which had a test–retest design, recruited patients who met the United Kingdom Parkinson's Disease Society Brain Bank criteria for PD between August 2014 and September 2015 from 31 different movement-disorder centers in Korea. All of the patients included in the study were required to be on a known and stable antiparkinsonian medication for the 4 weeks prior to study commencement. Patients with

secondary parkinsonism, atypical parkinsonian syndrome, concomitant treatment with hypnotics and/or antipsychotics, a score of <20 on the Korean version of the Mini-Mental State Examination (K-MMSE), or those aged 40 years or younger at disease onset were excluded. Written informed consent was obtained from all of the study participants, and the study protocol was approved by the Institutional Review Boards at the participating centers (IRB No. 2014-08-029). This investigation formed part of a larger nationwide program studying the cultural adaptation and clinimetric validation of different scales for nonmotor manifestations of PD in Korea.^{2,16}

Translation and cross-cultural adaptation of K-PDSS-2

The original questionnaire was translated from English into Korean by two independent bilingual translators. A translation committee consisting of movement disorder experts reviewed both translated versions to reconcile a single forward-translated version, which was then backward translated from Korean to English by another independent bilingual translator who was blinded to the previous steps. The back-translated version was compared to the original English questionnaire, and forward-backward amendments were made by the translation committee based on consensus. The amended translated version was pretested on four patients with PD who were not a part of this study in order to assess its interpretation of items, ease of comprehension, and cross-cultural relevance. These processes produced the final harmonized version of the K-PDSS-2 instrument.^{5,9,11}

Study procedure

Both demographics and clinical data were collected for all study patients. The overall severity of disease was evaluated using Hoehn and Yahr (H-Y) staging and parts I–III of the Unified Parkinson's Disease Rating Scale (UPDRS). The motor phenotype was classified based on the ratio of UPDRS items proposed by Jankovic et al.¹⁷ We administered the Korean version of the Non-Motor Symptoms Scale (K-NMSS) consisting of the following nine domains to quantify the range of nonmotor manifestations of the disease: cardiovascular, sleep/fatigue, mood, perceptual problems, attention/memory, gastrointestinal, urinary, sexual function, and miscellaneous.¹⁸ The disease-specific HRQoL was investigated using the Korean version of the 39-item Parkinson's Disease Questionnaire (K-PDQ-39).¹⁹ The Korean version of the Montgomery-Åsberg Depression Rating Scale (K-MADRS) was used to assess depressive symptoms, while K-MMSE and the Korean version of the Montreal Cognitive Assessment (MoCA-K) were administered to evaluate cognitive function.^{20,21} Sleep-related problems and nocturnal disabilities among the

study patients were globally addressed using the K-PDSS-2 instrument obtained from the above-described cross-cultural adaptation process. The test-retest reliability was measured by applying the K-PDSS-2 questionnaire twice over an interval from 10 to 14 days.

Statistical analysis

Clinimetric properties were statistically evaluated using IBM SPSS (version 19, IBM Corporation, Armonk, NY, USA) for internal consistency, test-retest reliability, convergent validity, and scale precision for measurement errors. Cronbach's α coefficients for total scores and item-total correlations for individual items were calculated to assess internal consistency.⁵ Cronbach's α coefficients >0.70 and item-total correlation coefficients >0.30 were used to tentatively define an acceptable level of consistency.^{9,11,16} Test-retest reliability was measured with the intraclass correlation coefficient (ICC) using a two-way random model and a criterion of >0.60.^{7,22} The scale precision for measurement errors was tested through the standard error of the mean (SEM) using the ICC as the reliability coefficient. The measurement errors of K-PDSS-2 were considered sufficiently low if the SEM was less than half of the standard deviation (SD).^{7,9} Convergent validity with the K-NMSS sleep/fatigue domain score and other nonmotor measures of PD were evaluated using the Spearman rank-order correlation coefficient (r_s), with a value of r_s >0.40 considered to indicate a moderate or stronger correlation.^{11,16} The Jonckheere-Terpstra test for trend detection was used to evaluate the relationship between K-PDSS-2 total scores and the H-Y stages of the study patients, and p values <0.05 were considered to reflect statistical significance.

The discriminatory capacity of the K-PDSS-2 instrument was statistically assessed using LCA, which identifies classes of patients with similar patterns of sleep disturbances. A polytomous-variable LCA was conducted with the open-source statistical software R (version 3.4.1, R Foundation for Statistical Computing, Vienna, Austria) using the R package *depmixS4* (version 1.3-3).²³ The discrete model fit was assessed based on the interpretability, parsimony of latent classes, Akaike information criterion, and Bayesian information criterion statistics.^{12,14} Demographics and clinical differences were compared among identified latent classes using the chi-square test or the Kruskal-Wallis test followed by post-hoc comparisons with Bonferroni-corrected Mann-Whitney U tests, as appropriate.

RESULTS

Table 1 presents demographics and clinical data of the 122 patients enrolled in this study. At the baseline evaluation, the

Table 1. Demographics and clinical characteristics of the study patients with Parkinson's disease

Characteristic	Value (n=122)
Age, years	66.55±8.64 [60-73]
Sex	
Male	62 (50.8)
Female	60 (49.2)
Disease duration, months	45.82±46.51 [30-72]
Motor subtype	
Tremor-dominant	32 (26.2)
Intermediate	13 (10.7)
PIGD	77 (63.1)
Present medication use	
LEDD, mg/day	371.92±401.95 [0-600]
Levodopa	99 (81.2)
Dopamine agonists	61 (50.0)
COMT inhibitors	3 (2.5)
MAO inhibitors	23 (18.9)
Amantadine	31 (25.4)
Anticholinergics	14 (11.5)
Acetylcholinesterase inhibitors	5 (4.1)
Antidepressants	16 (13.1)
Hoehn and Yahr stage	2.16±0.67 [2-2.5]
Stage 1	16 (13.1)
Stage 2	57 (46.7)
Stage 3	47 (38.5)
Stage 4 or 5	2 (1.6)

Data are mean±standard deviation [interquartile range] or n (%) values. COMT: catechol-O-methyltransferase, LEDD: levodopa equivalent daily dosage, MAO: monoamine oxidase, PIGD: postural instability and gait difficulty.

K-PDSS-2 score was 11.67±9.87 (mean±SD), with a median of 9 and an interquartile range (IQR) of 4–16. Most (97.5%, n=119) of the 122 study patients who completed the baseline evaluation also participated in the retest K-PDSS-2 evaluation, in which the score was 12.61±11.67, with a median of 10 and an IQR of 4–17. In terms of internal consistency, the item-total correlation coefficient ranged from 0.169 to 0.739 at baseline and from 0.138 to 0.746 at the retest. All items except for item 8 (nocturia) satisfied the criterion of the item-total correlation coefficient (>0.30; Table 2). Cronbach's α coefficients for the K-PDSS-2 total scores at baseline and the retest were 0.851 and 0.880, respectively, thereby meeting the standard established for internal consistency (Cronbach's α >0.70; Table 3). With regards to the test-retest reliability over the interval from 10 to 14 days, the ICCs ranged from 0.672 (item 4) to 0.848 (item 7), with ICC >0.60 for all items (Table 2). The ICC of the K-PDSS-2 total score was 0.867, and hence exceeded the threshold of 0.60. The scale precision as determined by the SEM was 3.60, therefore also meeting the criterion (<½SD=4.94).

Table 3 lists the coefficients for the correlations between K-PDSS-2 and the range of clinical rating scales of PD used to assess convergent validity. The total K-PDSS-2 score showed significant correlations with the K-PDQ-39 summary index ($r_s=0.496$) and K-MADRS score ($r_s=0.523$), and was strongly correlated with the total K-NMSS score ($r_s=0.552$) and the scores in some of the corresponding K-NMSS domains. As expected, the strongest correlation among K-NMSS domains was observed for the K-NMSS sleep/fatigue domain ($r_s=$

Table 2. Clinimetric validation-related statistics

K-PDSS-2 item	Baseline		Item-total correlation (baseline)	Retest		Item-total correlation (retest)	ICC
	Mean	Median [IQR]		Mean	Median [IQR]		
Bad sleep quality (item 1)	1.15	1 [0-2]	0.374	1.08	1 [0-2]	0.340	0.800
Difficulties falling asleep (item 2)	0.88	0 [0-2]	0.343	0.94	0 [0-2]	0.454	0.806
Difficulties staying asleep (item 3)	1.34	1 [0-3]	0.429	1.40	1 [0-2]	0.468	0.839
Restlessness of legs or arms at night (item 4)	0.49	0 [0-1]	0.578	0.70	0 [0-1]	0.609	0.672
Urge to move legs or arms (item 5)	0.44	0 [0-0]	0.623	0.68	0 [0-0]	0.687	0.750
Distressing dreams at night (item 6)	0.61	0 [0-1]	0.502	0.62	0 [0-1]	0.478	0.694
Distressing hallucinations at night (item 7)	0.34	0 [0-0]	0.564	0.37	0 [0-0]	0.518	0.848
Nocturia (item 8)	1.99	2 [1-3]	0.169	2.07	2 [1-3]	0.138	0.804
Uncomfortable and immobility at night (item 9)	0.51	0 [0-0]	0.662	0.55	0 [0-0]	0.728	0.685
Pain in arms or legs (item 10)	0.70	0 [0-1]	0.739	0.76	0 [0-1]	0.746	0.746
Muscle cramps in arms or legs (item 11)	0.75	0 [0-1]	0.578	0.82	0 [0-1]	0.669	0.753
Painful posturing in the morning (item 12)	0.32	0 [0-0]	0.600	0.35	0 [0-0]	0.640	0.755
Tremor on waking (item 13)	0.61	0 [0-1]	0.451	0.58	0 [0-0]	0.565	0.696
Tired and sleepy after waking in the morning (item 14)	1.17	0 [0-2]	0.448	1.20	1 [0-2]	0.609	0.765
Snoring or difficulties in breathing (item 15)	0.39	0 [0-0]	0.460	0.48	0 [0-0]	0.548	0.717
Total score	11.67	9 [4-16]	Cronbach's $\alpha=0.851$	12.61	10 [4-17]	Cronbach's $\alpha=0.880$	0.867

ICC: intraclass correlation coefficient, IQR: interquartile range, K-PDSS-2: Korean version of Parkinson's Disease Sleep Scale-2.

0.544; Table 3). There was also a significant relationship between the total K-PDSS-2 score and H-Y stage (standardized Jonckheere-Terpstra statistic=2.091, $p=0.037$).

LCAs were conducted with K-PDSS-2 items to identify subtypes of sleep problems, trialing solutions involving from one to seven latent classes. A three-class solution was found to be the most-parsimonious model based on interpretability and fit indices (Table 4). Symptom profiles of the 3 subtypes of sleep disturbance are presented graphically in Fig. 1 as the

Table 3. Convergent validity of K-PDSS-2 with other motor and non-motor measurements and patient-perceived quality of life

Nonmotor measurement	Value	r_s	p
UPDRS part I score	2.00±1.99	0.377	<0.001*
UPDRS part II score	7.77±6.00	0.405	<0.001*
UPDRS part III score	20.34±10.94	0.211	0.020*
K-MMSE score	27.43±2.26	-0.145	0.111
MoCA-K score	23.03±4.26	-0.123	0.182
K-MADRS score	9.46±8.26	0.523	<0.001*
K-NMSS total score	34.17±25.12	0.552	<0.001*
Cardiovascular (including falls)	1.00±1.58	0.204	0.024*
Sleep/fatigue	5.84±6.13	0.544	<0.001*
Mood	7.43±8.28	0.416	<0.001*
Perceptual problems	0.59±2.00	0.175	0.054
Attention/memory	3.67±4.36	0.405	<0.001*
Gastrointestinal	2.68±4.47	0.094	0.303
Urinary	8.05±8.25	0.422	<0.001*
Sexual function	2.41±5.02	0.169	0.062
Miscellaneous	2.58±3.41	0.113	0.216
K-PDQ-39 summary index	31.17±26.23	0.496	<0.001*

Data are mean±standard deviation values.

* $p<0.05$. p values are from the Spearman correlation test.

K-MADRS: Korean version of the Montgomery-Åsberg Depression Rating Scale, K-MMSE: Korean version of the Mini-Mental State Examination, K-NMSS: Korean version of the Non-Motor Symptoms Scale, K-PDQ-39: Korean version of the 39-item Parkinson's Disease Questionnaire, K-PDSS-2: Korean version of Parkinson's Disease Sleep Scale-2, MoCA-K: Korean version of the Montreal Cognitive Assessment, r_s : Spearman rank-order correlation coefficient, UPDRS: Unified Parkinson's Disease Rating Scale.

Table 4. Model-fit indices in latent class analysis with one to seven derived classes

Number of classes	AIC	BIC	Log-likelihood	Smallest class size (%)
1	3873.52	4041.77	-1876.76	122 (100.00)
2	3706.43	4045.71	-1732.21	34 (24.59)
3	3659.52	4169.86	-1647.76	22 (17.19)
4	3727.88	4409.25	-1620.94	12 (8.2)
5	3792.90	4645.33	-1592.45	11 (6.6)
6	3892.84	4916.31	-1581.42	8 (3.3)
7	3943.22	5137.73	-1545.61	9 (4.9)

AIC: Akaike information criterion, BIC: Bayesian information criterion.

predicted responses of the study patients in each class on a range of 15 items of K-PDSS-2. Across all study participants ($n=122$), 78 patients (63.9%) were assigned to class 1, the largest latent class. The symptom profiles of class 1 were characterized by overall low predicted responses on K-PDSS-2 items (Fig. 1), and so individuals in class 1 were labeled as “less-troubled sleepers.” Twenty-two patients (18.0%) were classified into class 2, with high predicted responses for the restlessness of legs or arms at night (item 4), urge to move legs or arms (item 5), distressing dreams at night (item 6), distressing hallucinations at night (item 7), pain in arms or legs (item 10), muscle cramps in arms or legs (item 11), and tremor on waking (item 13). Since most of these items have been described as PD symptoms at night and motor symptoms at night in previous factor analyses,^{7,9} class 2 was labeled “PD-related nocturnal difficulties.” Finally, 22 patients (18.0%) were assigned to class 3, which was profiled by marked predicted responses in bad sleep quality (item 1), difficulties falling asleep (item 2), difficulties staying asleep (item 3), and nocturia (item 8). Since most of these items have indicated disturbed sleep or fragmented sleep in previous factor-analysis studies,^{7,9,11} individuals in class 3 were labeled as “disturbed sleepers” (Fig. 1).

Table 5 compares demographics and clinical variables among the three classes. Group differences based on the Kruskal-Wallis test were found across age, total K-PDSS-2 score (both at baseline and the retest), K-PDQ-39 summary index, UPDRS part I score, K-MADRS score, total K-NMSS score, and scores in four K-NMSS domains (sleep/fatigue, mood, attention/memory, and urinary domains). Post-hoc analysis of between-group differences indicated that the patients in class 3 tended to be younger and have a higher total K-NMSS score, K-NMSS sleep/fatigue domain score, K-NMSS attention/memory domain score, and K-PDQ-39 summary index than those in class 1. Class 3 patients also showed a higher NMSS urinary domain score compared with those in class 1 or 2. Compared to class 1 patients, those in classes 2 and 3 showed a markedly higher UPDRS part I score, K-MADRS score, and K-NMSS mood domain score. There were no significant differences in sex, disease duration, motor phenotype, levodopa equivalent daily dosage, use of antiparkinsonian medication, or UPDRS part II or III scores between the three classes.

DISCUSSION

The purpose of the current study was twofold: to determine 1) the clinimetric properties of the K-PDSS-2 and 2) whether distinct subtypes of sleep disturbance can be distinguished among patients with PD on the basis of the validated K-PDSS-2 instrument.

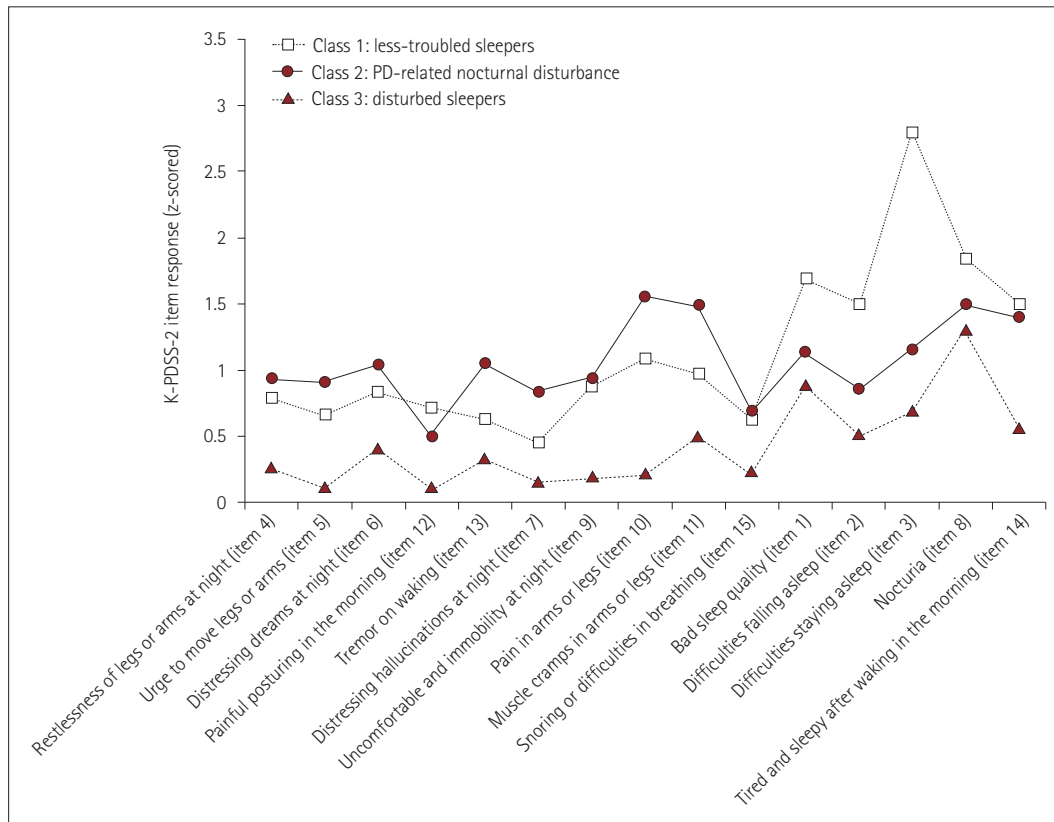


Fig. 1. Predicted symptom profiles of K-PDSS-2 item responses for the sleep-disturbance subtypes based on latent class analysis. K-PDSS-2: Korean version of Parkinson's Disease Sleep Scale-2, PD: Parkinson's disease.

Overall, the cross-cultural adaptation of the K-PDSS-2 instrument developed using a structured translation and review processes exhibited satisfactory clinimetric attributes. Similar to the original PDSS-2 validation study, we found that the new instrument had good internal consistency and good test-retest reliability.^{7,23} The scale precision of the K-PDSS-2 on measurement error was acceptable in terms of the SEM value, which was less than half the SD.^{7,9} The SEM of K-PDSS-2 of our study ($3.60 < \frac{1}{2}SD=4.94$) was comparable to that found in the original PDSS-2 validation study ($3.98 < \frac{1}{2}SD=4.45$)⁷ and the study by the Hungarian group ($2.459 < \frac{1}{2}SD=5.404$).⁹

The convergent validity of K-PDSS-2 was well supported by its statistical correlations with other clinical measures. Consistent with the findings of previously published analyses, the sleep-related problems and nocturnal disabilities as measured herein with K-PDSS-2 increased with advancing disease severity according to H-Y stages.^{9,24} Higher K-PDSS-2 scores were significantly correlated with worse K-PDQ-39 scores, indicating a relationship between HRQoL and sleep disturbance in PD patients. This finding corroborates previous reports of significant correlations between PDSS-2 scores and the HRQoL as measured via PDQ-39 or its subdomains.^{7-9,11,25} It is important to note that we found no significant correla-

tion between K-PDSS-2 and neurocognitive performance as assessed by both MoCA-K and K-MMSE, whereas depression as assessed by K-MADRS was closely related to the total K-PDSS-2 score. Our results are consistent with two other groups finding no significant correlation between the PDSS-2 total score and cognitive outcomes assessed using the original MoCA⁹ and MMSE¹¹ instruments.

Using LCA, we were able to classify sleep disturbances in patients with PD into three latent groups: one baseline subtype (class 1), which covered approximately two-thirds of the study patients, and two subtypes (classes 2 and 3) associated with increased sleep disturbances. One remarkable LCA finding was that the three latent classes did not directly parallel all 15 K-PDSS-2 items in terms of severity (i.e., mild, moderate, and severe). Instead, the predicted item responses (Fig. 1) showed that patients in class 2 were more likely to experience more PD-related nocturnal symptoms, whereas patients in class 3 were more likely to report general sleep difficulties than patients in the other subtypes. Our LCA outcomes indicated that sleep disorders in patients with PD are more complicated than simply the degree of severity of sleep disturbances; instead, there are different subgroups of patients with sleep disturbances, including those with PD-specific or general sleep difficulties.

Table 5. Demographics and clinical characteristics of study patients in three sleep-disturbance-related latent classes

Variable	Class 1: less-troubled sleepers	Class 2: PD-related nocturnal difficulties	Class 3: disturbed sleepers	χ^2	<i>p</i>
Patients (%)	78 (63.9)	22 (18)	22 (18.0)		
Age, years	68.06±8.07	65.41±8.68	62.32±9.35	6.879	0.032*
Sex, male	40 (51.3)	10 (45.5)	12 (54.6)	0.382	0.826
Disease duration, months	41.71±40.57	49.36±42.03	56.86±66.79	0.922	0.631
Hoehn and Yahr stage	2.14±0.68	2.182±0.61	2.182±0.68	0.652	0.722
LEDD, mg/day	352.33±379.97	441.23±440.88	372.08±448.01	0.817	0.665
UPDRS part I score	1.37±1.58	2.93±2.08	2.55±1.65	17.210	<0.001**
UPDRS part II score	6.73±5.34	8.82±6.09	8.82±6.52	4.591	0.101
UPDRS part III score	18.90±9.71	22.52±13.38	20.43±12.39	0.806	0.668
K-MMSE score	27.45±2.37	26.91±2.60	27.91±1.27	1.283	0.527
MoCA-K score	23.09±4.46	22.30±4.00	23.45±3.86	0.925	0.630
K-MADRS score	7.03±8.05	13.91±7.52	13.64±6.16	27.408	<0.001**
K-NMSS total score	29.33±26.23	36.77±17.39	48.73±22.23	16.448	<0.001*
Cardiovascular (including falls)	1.01±1.61	0.86±1.42	1.09±1.69	0.115	0.944
Sleep/fatigue	4.67±6.11	6.32±5.90	9.50±5.06	19.196	<0.001*
Mood	5.62±7.02	10.36±7.08	10.95±11.37	15.647	<0.001**
Perceptual problems	0.49±1.86	1.41±3.02	0.14±0.47	4.959	0.084
Attention/memory	2.86±3.64	3.95±4.79	6.23±5.34	11.696	0.003*
Gastrointestinal	3.06±5.16	1.27±1.80	2.73±3.47	1.581	0.454
Urinary	7.10±8.49	6.64±5.39	12.82±8.34	8.986	0.011**
Sexual function	2.18±5.05	3.50±6.44	2.14±3.00	1.855	0.396
Miscellaneous	2.45±3.47	2.45±3.64	3.14±3.04	1.096	0.578
K-PDQ-39 summary index	24.92±23.03	39.10±30.44	45.73±25.98	15.216	<0.001*
K-PDSS-2 total score (baseline)	6.03±4.44	20.50±10.61	22.86±6.74	74.514	<0.001**
K-PDSS-2 total score (retest)	7.78±7.41	19.57±13.06	22.64±10.19	40.858	<0.001**

Data are *n* (%) or mean±standard deviation values. *p* values are from the chi-square test or the Kruskal-Wallis test followed by post-hoc comparisons with Bonferroni-corrected Mann-Whitney tests.

*Significant difference between classes 1 and 3, †Significant difference between classes 1 and 2, ‡Significant difference between classes 2 and 3.

K-MADRS: Korean version of the Montgomery-Åsberg Depression Rating Scale, K-MMSE: Korean version of the Mini-Mental State Examination, K-NMSS: Korean version of the Non-Motor Symptoms Scale, K-PDQ-39: Korean version of the 39-item Parkinson's Disease Questionnaire, K-PDSS-2: Korean version of Parkinson's Disease Sleep Scale-2, LEDD: levodopa equivalent daily dosage, MoCA-K: Korean version of the Montreal Cognitive Assessment, PD: Parkinson's disease, UPDRS: Unified Parkinson's Disease Rating Scale.

In a recent review, Diederich and McIntyre³ proposed categorizing sleep problems in PD into 1) primary causes relating to degeneration of the brainstem regulatory center and impaired thalamocortical arousal, 2) secondary causes including motor symptoms, nocturnal dyskinesia, and dysautonomia, 3) tertiary causes mainly due to medication, and 4) other causes including depression, cardiac, and pulmonary comorbidity. Louter et al.¹ also suggested three main subgroups of sleep disorders in patients with PD: 1) primary sleep symptoms caused by neurodegeneration in sleep-regulating regions, 2) nocturnal disturbances due to PD symptoms, and 3) medication-related sleep disorders. Our study empirically characterized the underlying structure of sleep disturbances in PD that have been and continue to be observed routinely by movement disorder experts and clinical neurologists in practice. The present LCA results suggested that pa-

tients in class 3 can suffer from neurodegeneration in sleep-regulating regions, whereas patients in class 2 manifest with PD-related nocturnal disturbances.^{1,3,4} Since the K-PDSS-2 instrument did not directly address the medications taken by patients, medication-related sleep problems might not have been sufficiently captured.

It is particularly interesting that the differences between groups of motor symptoms as assessed by UPDRS parts II and III remained small. In contrast, patients identified as being in either class 2 or 3 had more-severe nonmotor symptoms. Our findings of a discrepancy between motor and nonmotor symptoms in relation to sleep-disturbance subtypes are consistent with those of several data-driven subtyping studies in PD that have found patients experiencing PD motor symptoms of similar severities exhibiting considerable differences in the severities of their nonmotor symptoms.²⁶⁻²⁹

It is important to note the potential limitations of this study. First, our classification of sleep disturbances was based on the K-PDSS-2 instrument, which does not include items related to RBD-related nocturnal motor features.^{8,30} The validity of this subtyping has not been tested using polysomnography, sleep latency testing, or actigraphy.^{31,32} RBD, obstructive sleep apnea, or other sleep-related respiratory disturbances can account for some instances of sleep disturbance observed in class 3, warranting further evaluation by objective testing methods such as polysomnography. The second limitation is that our study included only patients with K-MMSE scores ≥ 20 at the time of registration, and the mild cognitive impairments in PD could go unrecognized if screening is performed using MMSE scores.³³ Third, convergent validity was only tested against the corresponding K-NMSS domain (domain 2 of K-NMSS), and not against other generic sleep scales such as the Pittsburgh Sleep Quality Index or the Wisconsin Sleep Questionnaire.^{6,34} Fourth, our study did not determine the optimal cutoff score for K-PDSS-2. No such information is provided for Korean patients with PD, and thus further studies are needed to address the cutoff value for the K-PDSS-2 instrument.^{10,24} Another drawback of our study is that measure of daytime sleep disturbances (e.g., excessive daytime sleepiness) and related assessment instruments were not utilized.

In conclusion, the K-PDSS-2 instrument demonstrated clinimetric reliability and validity, indicating that it is a suitable tool for measuring nocturnal disturbances and sleep disorders in Korean patients with PD. Moreover, using a data-driven approach, we were able to identify subtypes of sleep disturbance in patients with PD. The validity of our LCA-derived subtypes was supported by distinct differences in demographics and clinical features between the groups. We expect our findings to be useful in both research and clinical evaluations of sleep disturbances in PD.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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