Sleep disturbance subtypes in Parkinson's disease based on the cross-culturally validated Korean version of the Parkinson's Disease Sleep Scale-2

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Research Article

Keywords: Parkinson's disease; sleep; PDSS-2; validity; reliability; Korean version; latent class analysis

Posted Date: February 5th, 2019

DOI: <https://doi.org/10.21203/rs.2.299/v1>

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Version of Record: A version of this preprint was published at Journal of Clinical Neurology on January 1st, 2020. See the published version at <https://doi.org/10.3988/jcn.2020.16.1.66>.

Abstract

Background: Sleep-related problems in Parkinson's disease (PD) have received greater attention in recent years due to their clinical influence on morbidity, disability, and the health-related quality of life (HRQoL) of patients. This study aimed to evaluate the clinimetric properties of the Korean version of the Parkinson's Disease Sleep Scale-2 (K-PDSS-2), and to analyze whether distinct sleep disturbance subtypes could be empirically identified in patients with PD based on the cross-culturally validated K-PDSS-2.

Methods: The internal consistency, test-retest reliability, scale precision, and convergent validity of the 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 mean total K-PDSS-2 scores were 11.67 ± 9.87 (mean $\pm$ standard deviation) at baseline, and 12.61 ± 11.17 upon follow up testing. The Cronbach's α coefficients of the total K-PDSS-2 score at baseline and at follow up testing were 0.851 and 0.880 respectively. Intraclass correlation coefficient over the 2-week period ranged from 0.672 to 0.848. The total K-PDSS-2 score was strongly correlated to HRQoL measures and other corresponding nonmotor scales. LCA indicated three distinct sleep disturbance classes in the study patients, namely "less troubled sleepers", "PD-related nocturnal difficulties", and "disturbed sleepers".

Conclusions: The K-PDSS-2 showed good clinimetric attributes in accordance with prior studies that were using the original version of the PDSS-2, therefore confirming the cross-cultural usefulness of the scale. Further, this study documents the first application of an LCA approach for identifying sleep disturbance subtypes in patients with PD.

Keywords: Parkinson's disease; sleep; PDSS-2; validity; reliability; Korean version; latent class analysis.

Background

Sleep-related problems in Parkinson's disease (PD) have received greater attention in recent years due to their occurrence in early stages of 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]. The Parkinson's Disease Sleep Scale (PDSS), a patient-reported instrument recommended by the Movement Disorder Society task force, is designed to rate overall sleep problems in the PD population [5, 6]. A revision of the 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]. The PDSS-2 has been successfully applied in several clinical trials as a reliable patient-reported outcome measure [7-11]. Thus, we planned to translate and adapt the PDSS-2 to Korean individuals and evaluate its clinimetric properties for the assessment of sleep disturbances among Korean-speaking patients with PD.

This study also sought to investigate the discriminatory capacity of the new Korean version of the PDSS-2 (K-PDSS-2) by conducting latent class analysis (LCA) to characterize sleep disturbance subtypes in PD. Several studies have applied LCA in PD populations to address depression-anxiety subtypes [12, 13] or neurocognitive subtypes [14]. The potential causes of sleep disturbances are highly variable in nature, and have been suggested to range from primary insomnia, depression, restless leg syndrome, nocturnal motor symptoms, parkinsonian drug side effects, nocturia and sleep-related breathing disorders, which all frequently co-occur [1, 3, 4]. However, few studies have tried to empirically outline the clinical heterogeneity of sleep-related problems in patients with PD. LCA has been previously used to identify sleep disturbance subtypes in patients with Alzheimer's disease [15]. The empirical search to detect latent homogenous subgroups of patients who experience similar patterns in sleep-related problems and nocturnal disabilities can help elucidate the pathophysiology and lead to the development of more targeted management strategies. To our knowledge, this study documents the first application of an LCA approach for identifying sleep disturbance subtypes in patients with PD.

Methods

Study patients

In this test-retest design study, patients who met the United Kingdom Parkinson's Disease Society Brain Bank criteria for PD were recruited between August 2014 and September 2015 from 31 different movement disorder centers in Korea. All study patients were required to be on a known and stable anti-parkinsonian medication for the 4 weeks prior to the study. Patients with secondary parkinsonism, atypical parkinsonian syndrome, concomitant treatment with hypnotics and/or antipsychotics, a score of < 20 on the Korean version of Mini-Mental State Examination (K-MMSE) or aged 40 years or younger at the onset of disease were excluded. Written informed consent was obtained from all patients participating in the present study, and the study protocol was approved by the institutional review boards at the participating centers. This investigation was performed as part of a larger nationwide program studying the cultural adaptation and clinimetric validation of the different scales for non-motor manifestations of PD in Korea [2, 16].

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

The original questionnaire was translated from English to Korean by two independent bilingual translators. A translation committee consisting of movement disorder experts reviewed both translated versions and reconciled a single forward translation. The reconciled translated version was backward translated from Korean to English by another independent bilingual translator who was blinded to the previous steps. The back-translation was compared to the original English questionnaire, and forward-backward amendments were made by the consensus of the translation committee. The amended translation was pre-tested on four patients with PD who were not a part of this study to assess the interpretation of items, ease of comprehension, and cross-cultural relevance. The final harmonized version of the K-PDSS-2 instrument was developed after these processes [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 part I-III of the Unified Parkinson's Disease Rating Scale (UPDRS). 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 nine domains (cardiovascular, sleep/fatigue, mood, perceptual problems, attention/memory, gastrointestinal, urinary, sexual function, and miscellaneous) to quantify a range of non-motor manifestations of disease [18]. 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 the K-MMSE and Montreal Cognitive Assessment-Korean version (MoCA-K) was administered to evaluate cognitive function [20, 21]. Sleep-related problems and nocturnal disabilities among study patients were globally addressed using the K-PDSS-2 instrument obtained from the cross-cultural adaptation described above. To measure the test-retest reliability, the K-PDSS-2 questionnaire was applied twice over a 10 to 14-day interval.

Statistical analysis

Clinimetric properties were statistically evaluated using IBM SPSS version 19 (IBM corporation, Somers, NY, USA) for internal consistency, test-retest reliability, convergent validity, and scale precision for measurement error. Cronbach's α coefficients for total score and item-total correlations for individual items were calculated to assess internal consistency [5]. Cronbach's α coefficients > 0.70 and item-total correlations > 0.30 for items were used to tentatively define an acceptable level of consistency [9, 11, 16]. Test-retest reliability was measured by intraclass correlation coefficient (ICC) using a two-way random model and a threshold value > 0.60 [7, 22]. The scale precision for measurement error was tested through standard error of measurement (SEM) using the ICC as the reliability coefficient. Measurement error of the K-PDSS-2 was 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 non-motor measures of PD was evaluated by Spearman correlation coefficient (r_s). Rank-order correlation coefficient of $r_s > 0.40$ was considered to support a moderate or greater 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 reflective of statistical significance.

The discriminatory capacity of the K-PDSS-2 instrument was statistically assessed by 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 interpretability, parsimony of latent classes, Akaike information criterion (AIC), and Bayesian information criterion (BIC) statistics [12, 14]. For comparisons of the demographic and clinical differences among identified latent sleep disturbance subtypes, we used the chi-square test or the

Kruskal-Wallis test followed by post-hoc comparisons with Bonferroni-corrected Mann-Whitney *U* tests as appropriate.

Results

Demographic and clinical data of the 122 patients enrolled in this study are described in Table 1. At the baseline evaluation, the mean K-PDSS-2 score was 11.67 ± 9.87 (mean $\pm$ SD). The median score of the baseline K-PDSS-2 was 9, and the lower and upper quartile range (Q1–Q3) was 4–16. Among the 122 study patients that completed the baseline evaluation, 119 patients (97.5%) carried out the retest evaluation of the K-PDSS-2. The mean score of the retest evaluation was 12.61 ± 11.67 and the median was 10 (Q1–Q3: 4–17). In terms of internal consistency, the item-total correlation ranged from 0.169 to 0.739 at baseline and 0.138 to 0.746 upon retesting. All items except for item 8 (nocturia) satisfied the threshold value of the item-total correlation (> 0.30 ; Table 2). The Cronbach's α coefficients which corresponded to the K-PDSS-2 total score at baseline and upon retesting were 0.851 and 0.880, meeting the standards established for internal consistency (Cronbach's $\alpha > 0.70$; Table 3). With regards to the test-retest reliability over the 10 to 14-day interval, ICCs ranged from 0.672 (item 4) to 0.848 (item 7), with ICCs > 0.60 for all items (Table 2). The ICC of the K-PDSS-2 total score was 0.867, exceeding the 0.60 threshold value. The scale precision determined by the SEM was 3.60, therefore meeting the criterion value ($< \frac{1}{2}$ SD = 4.94).

Table 3 shows 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 a significant correlation with the K-PDQ-39 summary index ($r_s = 0.496$) and K-MADRS score ($r_s = 0.523$). The total score of the K-PDSS-2 was strongly correlated with the total K-NMSS score ($r_s = 0.552$) and some of the corresponding K-NMSS domains. As expected, the highest correlation among K-NMSS domains was observed for the K-NMSS sleep/fatigue domain ($r_s = 0.544$; Table 3). There was also a significant relationship between total K-PDSS-2 score and H-Y stage (standardized Jonckheere-Terpstra statistic = 2.091, $p = 0.037$).

LCAs with K-PDSS-2 items were conducted to uncover latent sleep disturbance subtypes, trialing from one to seven latent class solutions. A three-class solution was found to be the most parsimonious model based on interpretability and fit indices (Table 4). Symptom profiles of the three sleep disturbance subtypes are presented graphically in Fig. 1 as the predicted responses of the study patients in each class on a range of 15 items of the K-PDSS-2. Across all study participants ($n = 122$), seventy-eight 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 items of the K-PDSS-2 (Fig. 1); therefore, individuals in class 1 were labeled as “less troubled sleepers”. Twenty-two patients (18.0%) were classified into class 2, with high predicted responses in restlessness of legs and arms at night (item 4), urge to move legs and arms (item 5), distressing dreams at night (item 6), distressing hallucinations at night (item 7), pain in arms and legs (item 10), muscle cramps in arms and legs (item 11), and tremors 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 sleep quality (item 1), difficulty falling asleep (item 2), difficulty staying asleep (item 3), and nocturia (item 8). Since most of these items indicate *disturbed sleep or fragmented sleep* in prior factor analysis studies [7, 9, 11], individuals in class 3 were labeled as “disturbed sleepers” (Fig. 1).

A comparison of demographic and clinical variables among the three classes is shown in Table 5. Group differences based on a Kruskal–Wallis test were found across age, total K-PDSS-2 score (both at baseline and upon retesting), K-PDQ-39 summary index, UPDRS part I, K-MADRS score, total K-NMSS score, and 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 higher total K-NMSS scores, K-NMSS sleep/fatigue domain scores, K-NMSS attention/memory domain scores, and K-PDQ-39 summary indexes than those in class 1. Class 3 patients also showed increased NMSS urinary domain scores than those in classes 1 or 2. Classes 2 and 3 showed markedly increased levels of the UPDRS part I, K-MADRS scores, and K-NMSS mood domain scores than class 1. There were no significant differences in sex, disease duration, motor phenotype, levodopa equivalent daily dosage, use of parkinsonian medication, UPDRS part II or III between the three classes.

Discussion

In conclusion, the Korean version of the PDSS-2 demonstrated clinimetric reliability and validity. As such, the scale can be a suitable tool for measuring either nocturnal disturbance or disordered sleep in Korean patients with PD. In addition, using a data-driven approach, we were able to identify latent sleep disturbance subgroups in patients with PD. The validity of our LCA-derived subtypes was supported by distinct demographic and clinical features between groups. We expect our findings to provide further information on the evaluation of sleep disturbances in PD for both research and clinical purposes.

Abbreviations

AIC: Akaike information criterion; BIC: Bayesian information criterion; HRQoL: Health-related quality of life; H-Y: Hoehn and Yahr; ICC: Intraclass correlation coefficient; K-MADRS: The Korean version of the Montgomery-Asberg Depression Rating Scale; K-MMSE: The Korean version of Mini-Mental State Examination; K-NMSS: The Korean version of the Nonmotor Symptoms Scale; K-PDQ-39: The Korean version of the 39-item Parkinson's Disease Questionnaire; K-PDSS-2: The Korean version of the Parkinson's Disease Sleep Scale-2; LCA: Latent class analysis; MoCA-K: Montreal Cognitive Assessment-Korean version; PD: Parkinson's disease; RLS: Restless leg syndrome; SEM: Standard error of measurement

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from all patients participating in the present study. The study protocol was approved by the institutional review boards at the participating centers: 1- Ulsan University Hospital, 2- Seoul National University Hospital, 3- Korea University Guro Hospital, 4- College of Medicine, The Catholic University of Korea, 5- Kyung Hee University College of Medicine, 6- Dong-A University College of Medicine, 7- Samsung Medical Center, 8- Hallym University College of Medicine, 9- Yeungnam University College of Medicine, 10- Sanggye Paik Hospital, 11- Severance Hospital, 12- Asan Medical Center, 13- Seoul National University Bundang Hospital, 14- Seoul Paik Hospital, 15- Gachon University Gil Hospital, 16- Korea University Ansan Hospital, 17- Pusan National University Yangsan Hospital, 18- Seoul Metropolitan Government-Seoul National University Boramae Medical Center, 19- Chungbuk National University Hospital, 20- Ewha Womans University Mokdong Hospital, 21- Konkuk University Medical Center, 22- Yonsei University Wonju College of Medicine, 23- Chungnam National University Hospital, 24- Kangbuk Samsung Hospital, 25- Keimyung University School of Medicine, 26- Soonchunhyang University Seoul Hospital, 27- Samsung Changwon Hospital, 28- Hanyang University College of Medicine, 29- Busan Paik Hospital

Acknowledgements

The authors wish to thank the patients and all who were involved in the present study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no commercial or other conflicts of interest.

Funding

This work was supported by a grant from Samil Pharmacy Company. The funder had no role in study design, data collection, data analysis, data interpretation or writing of the manuscript.

Authors' contributions

Designed and coordinated the study: H-JY, H-JK, S-BK, J-SK, T-BA, H-TK, and SJK. Clinical analysis: H-JY, H-JK, S-BK, J-SK, T-BA, S-MC, JWC, Y-JK, H-IM, M-YP, JSB, PHL, SJC, J-MK, I-US, J-YK, Y-HS, DYK, J-HL, J-YL, JSK(Ji Sun Kim), JYY, HJK, JYH, M-JK, JY, JSK(Ji Seon Kim), ESO, WTY, SY, K-YK, H-EP, S-YL, YK, H-TK, and SJK. Laboratory workup, acquisition and interpretation of data: H-JY, H-JK, S-BK, J-SK, T-BA, S-MC, JWC, Y-JK, H-IM, M-YP, JSB, PHL, SJC, J-MK, I-US, J-YK, Y-HS, DYK, J-HL, J-YL, JSK(Ji Sun Kim), JYY, HJK,

JYH, M-JK, JY, JSK(Ji Seon Kim), ESO, WTY, SY, K-YK, H-EP, S-YL, YK, H-TK, and SJK. Manuscript writing: H-JY, H-JK, and SJK. Critical revisions and approval of revised manuscript: S-BK, J-SK, T-BA, S-MC, JWC, Y-JK, H-IM, M-YP, JSB, PHL, SJC, J-MK, I-US, J-YK, Y-HS, DYK, J-HL, J-YL, JSK(Ji Sun Kim), JYY, HJK, JYH, M-JK, JY, JSK(Ji Seon Kim), ESO, WTY, SY, K-YK, H-EP, S-YL, YK, and H-TK. All authors reviewed and approved the final manuscript.

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Tables

Table 1. Demographic and clinical characteristics of 122 patients with Parkinson’s disease

Characteristics	Number (%)	Mean (SD)	Median (Q1–Q3)
Age, years		66.55 (8.64)	68 (60–73)
Sex			
Male, n	62 (50.8)		
Female, n	60 (49.2)		
Disease duration, months		45.82 (46.51)	30 (30–72)
Motor subtype			
Tremor-dominant, n	32 (26.2)		
Intermediate, n	13 (10.7)		
PIGD, n	77 (63.1)		
Present medication use			
LEDD, mg/day		371.92 (401.95)	300 (0–600)
Levodopa, n	99 (81.2)		
Dopamine agonists, n	61 (50.0)		
COMT inhibitors, n	3 (2.5)		
MAO inhibitors, n	23 (18.9)		
Amantadine, n	31 (25.4)		
Anticholinergics, n	14 (11.5)		
Acetylcholinesterase inhibitors, n	5 (4.1)		
Antidepressants, n	16 (13.1)		
Hoehn and Yahr stage		2.16 (0.67)	2 (2–2.5)
Stage 1, n	16 (13.1)		
Stage 2, n	57 (46.7)		
Stage 3, n	47 (38.5)		
Stage 4-5, n	2 (1.6)		

SD, standard deviation; Q1, lower quartile; Q3, upper quartile; PIGD, postural instability and gait difficulty; LEDD, levodopa equivalent daily dosage; COMT, catechol-O-methyltransferase; MAO, monoamine oxidase

Table 2. Clinimetric validation-related statistics

K-PDSS-2 item	Baseline		Item-total correlation (baseline)	Retest		Item-total correlation (retest)	ICC
	Mean	Median (Q1-Q3)		Mean	Median (Q1-Q3)		
Bed 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 and 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 and 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 and legs (item 10)	0.70	0 (0-1)	0.739	0.76	0 (0-1)	0.746	0.746
Muscle cramps in arms and 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 α = 0.851	12.61	10 (4-17)	Cronbach's α = 0.880	0.867

K-PDSS-2, Korean version of Parkinson's Disease Sleep Scale-2; Q1, lower quartile; Q3, upper quartile; ICC, intraclass correlation coefficient.

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

Nonmotor measurements	Mean	SD	r_s	p
UPDRS part I	2.00	1.99	0.377	<0.001*
UPDRS part II	7.77	6.00	0.405	<0.001*
UPDRS part III	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*

*Significance level: $p < 0.05$. p -values are from Spearman correlation test. SD, standard deviation; r_s , Spearman rank-order correlation coefficients; UPDRS, Unified Parkinson's Disease Rating Scale; K-MMSE, Korean version of Mini-Mental Status Examination; MoCA-K, Montreal Cognitive Assessment-Korean version; K-MADRS, Korean version of Montgomery-Åsberg Depression Rating Scale; K-NMSS, Korean version of Nonmotor Symptoms Scale; K-PDQ-39, Korean version of 39-item Parkinson's Disease Questionnaire.

Table 4. Model-fit indices for latent class analysis with 1-7 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.

Table 5. Demographic and clinical characteristics of study patients assigned to 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>
Number of patients, n	78(63.9%)	22(18.0%)	22(18.0%)		
Age, years	68.06(8.07)	65.41(8.68)	62.32(9.35)	6.879	0.032 ^a
Sex, male, n	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	1.37(1.58)	2.93(2.08)	2.55(1.65)	17.210	<0.001 ^{a,b}
UPDRS part II	6.73(5.34)	8.82(6.09)	8.82(6.52)	4.591	0.101
UPDRS part III	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 ^{a,b}
K-NMSS total score	29.33(26.23)	36.77(17.39)	48.73(22.23)	16.448	<0.001 ^a
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 ^a
Mood	5.62(7.02)	10.36(7.08)	10.95(11.37)	15.647	<0.001 ^{a,b}
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 ^a
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 ^{a,c}
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 ^a
K-PDSS-2 total score (baseline)	6.03(4.44)	20.50(10.61)	22.86(6.74)	74.514	<0.001 ^{a,b}
K-PDSS-2 total score (retest)	7.78(7.41)	19.57(13.06)	22.64(10.19)	40.858	<0.001 ^{a,b}

Data are shown as means (standard deviation) unless otherwise indicated. *p*-values are from the chi-square test or the Kruskal-Wallis test followed by post-hoc comparisons with Bonferroni-corrected Mann-Whitney tests.

^aSignificant difference between class 1 and class 3. ^bSignificant difference between class 1 and class 2.

^cSignificant difference between class 2 and class 3. PD, Parkinson's disease; LEDD, levodopa equivalent daily dosage; UPDRS, Unified Parkinson's Disease Rating Scale; K-MMSE, Korean version of Mini-Mental Status Examination; MoCA-K, Montreal Cognitive Assessment-Korean version; K-MADS, Korean version of Montgomery-Åsberg Depression Rating Scale; K-NMSS, Korean version of Nonmotor Symptoms Scale; K-PDQ-39, Korean version of 39-item Parkinson's Disease Questionnaire; K-PDSS-2, Korean version of Parkinson's Disease Sleep Scale-2.

Figures

Figure 1

Predicted symptom profiles of K-PDSS-2 item responses for the latent class analysis-derived sleep disturbance subtypes.