Sleep Quality in Parkinson Disease: An Examination of Clinical Variables

Karina Stavitsky, MA and Alice Cronin-Golomb, PhD

Abstract: The etiology of sleep problems in Parkinson disease (PD) is not well understood, as they may arise from the pathology of the disease or from other disease-related factors such as motor dysfunction, dopaminergic medication, and mood disturbances. The aim of this study was to investigate factors associated with sleep, including disease-related variables such as motor symptom severity, dose of medication, and mood and disease subtypes. Thirty-five nondemented patients with PD were included. Sleep was measured using 24-hour wrist actigraphy over a 7-day period, during which time participants kept a sleep diary. Subjective sleep and arousal questionnaires included the PD Sleep Scale and Epworth Sleepiness Scale. Motor symptom severity and dopaminergic medication were significantly related to measures of sleep quality. Sex differences in sleep quality were found, with men having worse sleep quality and more excessive daytime sleepiness than women. We also found that actigraphy may serve as a useful tool for identifying individuals with possible rapid eye movement behavior disorder, a sleep disorder that has important implications in early detection of PD.

Key Words: Parkinson, sleep, actigraphy, sex

(*Cogn Behav Neurol* 2011;24:43–49)

S leep problems in Parkinson disease (PD) are among the most prominent nonmotor symptoms of the disease, impacting the quality of life of patients and caregivers.[1] Patients with PD experience a variety of sleep-related problems, including rapid eye movement (REM) Behavior Disorder (RBD), sleep fragmentation and reduced sleep efficiency, and excessive daytime sleepiness.[1]

Some aspects of sleep disruption arise from the underlying pathology of the disease.[2] The pathogenesis of PD, which begins in the brainstem and results in neuronal loss in the cholinergic, dopaminergic, and serotonergic systems, is likely to affect the reticular formation that is implicated in sleep and wake regulation.[2] Sleep disturbances may also be secondary to motor discomfort[3] or to nonmotor features of the disease.[4] Dopaminergic medication may increase sleep fragmentation and reduce sleep efficiency,[5] or may cause daytime sleepiness.[3,6] Anxiety and depression, common in PD, can also cause problems with sleep onset and maintenance and daytime alertness.[7,8]

PD is heterogeneous in its presentation. Studies have focused on disease subtypes including PD into left (LPD) and right (RPD) side of motor symptom onset, type of initial motor symptom, and sex. Differences in cognitive performance, disease progression, and nonmotor features have been reported in subtypes of the disease. In regard to side of onset, LPD and RPD show distinct profiles of cognitive functioning,[9,10] sleep disturbances,[11] and visual hallucinations.[11,12] Findings of sleep differences in LPD and RPD, however, have been limited to use of sleep questionnaires. In regard to type of initial motor symptom, individuals who present with tremor dominant (TD) versus nontremor dominant (NTD) symptoms express distinct clinical and cognitive profiles. Patients who present with primarily gait and balance disturbance tend to have more rapid progression of disease, including more severe cognitive deficits and a faster onset of dementia than patients with TD.[13] No studies have examined sleep quality with respect to TD and NTD.

Sex differences have been found in both motor and nonmotor aspects of PD.[14] In the general population, women report more frequent insomnia and restless legs syndrome, whereas REM behavior sleep disorder, characterized by loss of normal muscle atonia and acting-out of dreams, is more common in men.[15] The examination of sleep quality with respect to sex has not been investigated in patients with PD.

The aim of this study was to examine the association of sleep and varying clinical presentations and symptoms in patients with PD, using an objective measure [actigraphy (ACT)] and subjective assessments (sleep questionnaires). This study focuses on the correlates of sleep disturbance in those with PD rather than the question of whether such disturbance exists, as this has already been demonstrated in numerous previous studies.[1]

METHODS

Participants

Thirty-five patients with PD (22 men, 13 women) were recruited from the outpatient Movement Disorders

Clinic at the Boston Medical Center (Table 1). The study was approved by the Boston University Institutional Review Board and all participants provided informed consent. On the modified Mini-Mental State Examination (mMMSE),[16] a cut-off score of 25 was used, as this form of the MMSE is particularly sensitive to specific cognitive deficits found in PD without dementia (scores converted from the 57-point scale). Individuals with a history of substance abuse, head injury, or neurologic disorders besides PD were excluded. None of the patients met criteria for dementia with Lewy bodies as per McKeith et al.[17]

Medication information was obtained for all participants. Levodopa equivalent dosages (LED) were calculated based on previous reports with LED: (regular levodopa dose × 1) + (levodopa controlled-release dose × 0.75) + (pramipexole dose × 67.0) + (ropinirole dose × 16.67) + (rotigotine × 16.67) + (pergolide dose and cabergoline dose × 67.0) + (bromocriptine dose × 10) + [(regular levodopa dose + levodopa controlled-release dose × 0.75) × 0.25] (if taking tolcapone or entacapone)].[18]

Motor symptom severity was quantified using the Unified Parkinson Disease Rating Scale (UPDRS) and Hoehn and Yahr stage. Information on the side and type of motor symptom at onset was obtained through patient report, confirmed when possible by neurologist review. Mood was assessed using the Beck Depression Inventory (BDI-2) and Beck Anxiety Inventory (BAI). All patients received the PD Quality of Life questionnaire-39).[19]

Sleep Measures
Objective Measure

To measure activity during the sleep/wake cycle, the participants wore wrist actigraphs (Actiwatch AW-64; Mini Mitter, Sunriver, OR) continuously over a 1-week period on each wrist. Data from the nondominant wrist only was used for this study, as per convention. The actigraphs were set to a medium sensitivity with 40 counts assessed as "wake" and an epoch length of 30 seconds. The Actiwatch data were downloaded to the Actiware

sleep software version 5.3 (Mini Mitter). Results were averaged across the 7 days of monitoring. The measures were sleep latency (first 10-min period with < 2 epochs of activity), sleep time [sum of time (in minutes) of epochs not exceeding the sensitivity threshold], sleep efficiency (sleep time divided by the time in bed multiplied by 100), wake after sleep onset (total time awake after the first sleep onset period), and movement and fragmentation index (number of 1-min periods of immobility relative to the total number of immobility phases).

Subjective Measures

Sleep complaints were assessed using the Parkinson Disease Sleep Scale (PDSS),[20] which has been used to identify disturbances such as sleep maintenance, insomnia, and excessive daytime sleepiness. The scale consists of 15 common symptoms. A score of 10 indicates worse symptoms and 0 indicates no symptoms. We examined the 15 items as 9 factors comprising composite scores of the individual items, as described elsewhere.[20] The factors were overall quality of sleep, sleep onset and maintenance, insomnia, nocturnal restlessness, nocturnal hallucinations, distressing/vivid dreams, nocturia, nocturnal motor symptoms (sensory complaints, early morning dystonia, and cramps during the night), sleep refreshment, and daytime dozing. We also used the PD Sleep Questionnaire from our laboratory, which captures some symptoms not assessed by the PDSS, including questions assessing for RBD.

Owing to the relationship between sleep disorders and subjective daytime sleepiness, we administered the Epworth Sleepiness Scale (ESS).[21] The score range is 0 to 24, with a score of 10 or more indicating excessive daytime sleepiness. The questionnaire is commonly used in PD[22,23] to assess the likelihood of dozing off in a variety of daily situations.

Statistical Analyses

Patients were recruited without regard to sex or motor symptom subtype. Independent sample t tests were used to compare demographic and clinical characteristics of the sex and motor symptom subgroups. Pearson correlations reflected associations between sleep and clinical variables such as mood and disease severity (ie, UPDRS total, disease stage and duration, and LED). Alpha of 0.01 was used for all correlations and analyses by subgroups. As there were significant correlations among all 5 ACT variables, Bonferroni adjustment was used to set α to 0.01 (0.05/5). Of the 9 PDSS variables, only some of them were correlated (number depending on variable), and accordingly an α of 0.01 was used here as well.

RESULTS
Sleep and Clinical Variable Correlations

Total sleep time as measured by ACT was associated with the UPDRS motor symptom total scores ($r = -0.43$, $P < 0.01$) and LED ($r = -0.44$, $P < 0.009$),

TABLE 1. Demographic and Clinical Characteristics of PD Sample

	(n = 35)
Age (y)	66.2 (7.9)
Education (y)	16.8 (2.4)
Men:women	22:13
BDI total	8.31 (4.7)
BAI total	8.26 (4.9)
UPDRS total	25.1 (9.4)
Disease stage*	2 (2)
Disease duration (y)	8.84 (5.1)
LED	604.3 (283.5)
Dopamine agonist (%)	77.1
Sleep medication (%)	14.7

Means (SD) are reported unless otherwise indicated.
*Median (range).
BAI indicates Beck Anxiety Inventory; BDI, Beck Depression Inventory-II; LED, levodopa equivalent dose; UPDRS, Unified Parkinson Disease Rating Scale.

in which a higher score on the UPDRS and higher dose of dopaminergic medication corresponded to fewer hours of sleep. Duration of disease, age, education, MMSE score, BDI, and BAI scores were not significantly related to ACT measures of sleep quality.

Examining associations between self-report and clinical measures revealed that subjective sleep is related to mood and quality of life and some disease-related measures. The PD Quality of Life questionnaire-39 score was significantly related to PDSS nocturnal restlessness ($r = 0.41$, $P = 0.01$), nocturnal psychosis ($r = 0.48$, $P < 0.004$), nocturnal motor symptoms ($r = 0.58$, $P < 0.0001$), sleep refreshment ($r = 0.48$, $P < 0.004$), and the PDSS total score ($r = 0.58$, $P < 0.0001$). PDSS nocturnal restlessness was also associated with the BAI total ($r = 0.44$, $P < 0.009$) and LED ($r = 0.42$, $P < 0.01$). LED was also significantly associated with the PDSS total score ($r = 0.42$, $P < 0.01$). Hoehn and Yahr stage of disease was correlated with nocturnal motor symptoms ($r = 0.47$, $P < 0.01$). The ESS score was correlated with BAI score ($r = 0.499$, $P < 0.004$).

Analysis by Sex, Side of Onset, and Type of Motor Symptom

Sex

ACT and self-report sleep scores are shown in Table 2. There were no sex-based differences in age, disease duration, UPDRS total, or Hoehn and Yahr stage. Men were taking a higher dosage or medication than women ($P < 0.01$). On the ACT measures of sleep, although not significant presumably because of high within-group variability, men had > 10% lower sleep efficiency than women, took twice as long to fall asleep, had a total sleep time that was 70 minutes shorter, and had a sleep fragmentation index that was approximately 8 points higher.

TABLE 2. Comparison of Actigraphic and Self-report Sleep Measures Between Men and Women

	Men (n = 22)	Women (n = 13)
ACT sleep onset latency	36.2 (48.7)	18.3 (18.3)
ACT WASO	72.7 (35.7)	56.8 (31.4)
ACT sleep efficiency	63.7 (21.7)	77.0 (14.0)*
ACT total sleep time	290.3 (128.8)	363.1 (93.4)
ACT sleep fragmentation	31.9 (13.0)	23.9 (11.1)
Epworth sleepiness scale	12.0 (4.8)	9.26 (3.3)
PDSS sleep quality	5.48 (2.6)	3.15 (1.8)**
PDSS sleep onset and maintenance	8.78 (5.8)	5.40 (4.0)
PDSS nocturnal restlessness	7.10 (5.6)	4.00 (2.6)*
PDSS nocturnal psychosis	2.70 (3.0)	2.92 (4.3)
PDSS nocturia	7.70 (3.3)	6.79 (4.8)
PDSS nocturnal motor symptoms	9.80 (6.9)	9.00 (7.1)
PDSS sleep refreshment	3.37 (2.7)	2.91 (2.7)
PDSS daytime dozing	4.2 (2.8)	2.91 (2.6)
PDSS total	50.1 (20.6)	38.3 (18.5)

*$P < 0.05$.
**$P < 0.01$.
ACT indicates actigraphic measure; PDSS, Parkinson Disease Sleep Scale; WASO, wake after sleep onset.

On the PDSS, men reported significantly worse quality of sleep. On the ESS, significantly more men than women scored in the clinically significant range defined by the cut-off score of 10 ($\chi^2 = 5.3$, $P < 0.02$). No other sex group differences were seen. When these analyses were repeated controlling for LED, men still reported overall worse quality of sleep on the PDSS.

In the general population, there is a higher prevalence of sleep apnea in men than in women.[24] We therefore repeated the sex analyses excluding individuals with a diagnosis of sleep apnea (8 men and 1 woman). There were no significant ACT differences between men and women, although relative to women the men still had a 10% lower sleep efficiency, slept 50 minutes less, and their fragmentation index was 7 points higher. On the self-report measures, a greater proportion of men still reported significant daytime sleepiness ($\chi = 7.5$, $P < 0.006$), and there was a trend for men to still report worse quality of sleep than women ($P < 0.05$).

Side and Type of Symptom at Disease Onset

Comparisons by side and type of symptom at onset are shown in Table 3. There were 19 RPD and 15 LPD participants (1 patient reported bilateral onset of motor symptoms) with no significant differences on any clinical or demographic characteristics, or on any objective or subjective sleep measures, or in regard to daytime sleepiness. Three patients with RPD and 3 with LPD were on sleep medications. When these patients were removed from the analyses, there was a trend for patients with LPD to report a higher score on the PDSS sleep refreshment subscale ($P < 0.05$), indicating feeling less rested in the morning.

Data from the same group of 35 patients with PD were subject to a separate set of analyses using initial symptom for categorization (16 TD and 19 NTD). They were matched on age, UPDRS total, disease duration, stage of disease, medication dose, and BDI score. There were no group differences on any of the sleep measures. Two patients with NTD and 4 with TD were on sleep medication. When the data from these patients were removed, there were still no significant group differences between these patients. As patients with NTD had significantly more years of education than patients with TD, analyses were repeated using education as a covariate, and showed a trend for patients with NTD to report more difficulty with sleep onset and maintenance on the PDSS ($P < 0.05$).

Effects of RBD and Medication

Comparisons of patients with PD, with and without RBD, and patients who were and were not taking dopamine agonists, are shown in Table 4. Nine patients with PD (7 men and 2 women) reported acting-out of their dreams at night, indicating possible RBD. There were no significant clinical or demographic differences between these patients and the rest of the group. These patients had a higher ACT sleep fragmentation index ($P < 0.002$). Those with possible RBD also reported more

TABLE 3. Comparison of ACT and PDSS Measures of Sleep Quality and Epworth Sleepiness Scale Between Subgroups of PD Participants

	RPD (n = 18)	LPD (n = 13)	NTD (n = 16)	TD (n = 16)
ACT sleep onset latency	32.8 (39.4)	15.5 (7.5)	30.6 (40.0)	19.3 (17.9)
ACT WASO	68.8 (35.9)	59.8 (37.0)	67.2 (33.3)	62.7 (38.5)
ACT sleep efficiency	66.6 (21.0)	74.2 (14.3)	70.0 (20.0)	70.1 (17.2)
ACT total sleep time	310.9 (136.3)	333.6 (95.8)	320.0 (103.9)	321.5 (133.6)
ACT sleep fragmentation	29.5 (11.5)	25.5 (15.0)	29.3 (13.8)	26.6 (12.0)
Epworth sleepiness scale	11.2 (4.5)	11.0 (4.9)	11.9 (4.1)	10.4 (5.0)
PDSS sleep quality	4.9 (2.8)	4.5 (2.5)	4.79 (3.0)	4.7 (2.3)
PDSS sleep onset and maintenance	7.4 (6.5)	8.0 (3.6)	9.16 (5.7)	5.9 (4.7)
PDSS nocturnal restlessness	5.9 (4.2)	7.6 (5.6)	7.3 (5.4)	5.6 (4.2)
PDSS nocturnal psychosis	2.7 (2.8)	3.1 (4.4)	3.0 (3.0)	2.6 (3.9)
PDSS nocturia	6.4 (3.6)	8.4 (4.0)	7.9 (3.4)	6.8 (4.3)
PDSS nocturnal motor symptoms	9.8 (7.4)	9.8 (6.1)	10.3 (7.2)	8.8 (6.6)
PDSS sleep refreshment	2.7 (2.5)	3.9 (2.4)	3.8 (2.0)	2.7 (2.7)
PDSS daytime dozing	3.9 (2.5)	3.9 (3.1)	3.7 (2.7)	3.8 (3.0)
PDSS total	44.4 (19.6)	49.2 (21.5)	50.6 (20.3)	40.8 (19.8)

Subgroups shown are RPD and LPD and patients with NTD and those with TD. Means (SD) are reported.

ACT indicates actigraphic measure; LPD, left side of onset PD; NTD, nontremor dominant; PDSS, Parkinson Disease Sleep Scale; RPD, right side of onset PD; TD, tremor dominant; WASO, wake after sleep onset.

nocturnal psychosis on the PDSS ($P < 0.0001$), and had a higher Epworth score, indicating more daytime sleepiness ($P < 0.01$) than the others.

As dopaminergic medication has been reported to increase the severity of sleep problems, we compared patients who were on dopamine agonists to those who were not. Eight patients were not taking any dopamine agonist medication. These individuals were significantly older than the rest. They had significantly longer ACT total sleep time ($P < 0.01$). There were no other ACT or self-report sleep differences between these groups.

DISCUSSION

This study examined multiple clinical and demographic variables that are known to impact objective and subjective sleep. We found that self-reported quality of life and mood are associated with subjective, but not objective, measures of sleep quality. These findings also confirm previous reports that the severity of disease and the dose of dopaminergic medication are associated with sleep problems in PD, as UPDRS total and LED were significantly related to ACT sleep time. One possible explanation for a relationship between sleep and motor function is that ACT may be unable to distinguish between sleep and motor problems in PD. Arguing against this notion is the observation that only total sleep time, and not sleep efficiency or fragmentation, was significantly related to these variables. This suggests that ACT is in fact sensitive to sleep symptoms apart from general disease severity. The association between the disease-related variables and total sleep time may be a marker of worsening disease,[25] which is related to an increase in severity of motor symptoms, a higher dose of dopaminergic medication, and worse sleep problems.

We did not find a relationship of mood with ACT measures of sleep quality. Sleep problems experienced by individuals with anxiety and depression as a primary diagnosis (without PD) may be more related to difficulties with sleep initiation and total sleep time than with sleep maintenance.[26] This is the converse of what is experienced by patients with PD, for whom difficulties with sleep initiation are less frequent than sleep fragmentation.[27] Anxiety was associated with self-reported nocturnal restlessness, which may reflect the self-perception of bad sleep in individuals with high levels of anxiety and other mood

TABLE 4. Comparison of Actigraphic Measures of Sleep Quality Between Patients Who Reported Having Symptoms of REM Behavior Disorder (RBD) and Those Who Did Not (N-RBD) and Between Those on a Dopamine Agonist (DA) and Those Who Were Not Taking a Dopamine Agonist (N-DA)

	N-RBD (n = 24)	RBD (n = 8)	N-DA (n = 7)	DA (n = 25)
ACT sleep onset latency	20.9 (36.9)	36.9 (40.8)	15.9 (9.8)	27.4 (34.4)
ACT WASO	62.4 (37.4)	72.5 (29.9)	70.5 (51.9)	63.4 (30.7)
ACT sleep efficiency	72.8 (17.6)*	61.8 (14.6)	77.7 (10.4)	67.9 (19.7)*
ACT total sleep time	337.2 (115.0)*	271.5 (119.3)	412.0 (82.9)	295.2 (114.4)**
ACT sleep fragmentation	25.0 (13.0)**	36.9 (7.2)	23.7 (13.3)	29.1 (12.7)

Means (SD) are reported.

*$P < 0.05$.

**$P < 0.01$.

ACT indicates actigraphic measure; WASO, wake after sleep onset.

problems.[28] Anxiety was also significantly related to increased daytime sleepiness, a finding we have previously reported that has also been confirmed by other researchers.[7,8]

Men with PD reported worse quality of sleep and more excessive daytime sleepiness than women. The dose of dopaminergic medication did not account for the differences in sleep quality between men and women, as after controlling for LED, men still reported worse overall quality of sleep and had more daytime sleepiness. We also examined whether there was an impact of sleep apnea on the sex differences in sleep and daytime somnolence, and found that taking out those with a diagnosis of sleep apnea eliminated the sex difference in self-reported quality of sleep. In contrast, excluding those with sleep apnea actually strengthened the finding of significant sex differences in excessive daytime sleepiness. In light of this information, it is important to further investigate sex differences in sleep quality of patients with PD, as these may be relevant to differential disease management for men and women.

We had previously found significant differences by side of motor symptom onset on several subjective sleep measures, including daytime sleepiness and nocturnal hallucinations.[11] These findings were not replicated in this study. Several differences between the 2 studies may be relevant. First, the previous study included a men-only sample from a Veterans Affairs population, in comparison to a community sample with both men and women included. Second, men with RPD in that sample were significantly more depressed than those with LPD; depression was related to the sleep factors, and controlling for depression strengthened the findings. In this study, RPD and LPD participants were not different on any mood measure. Excluding patients who were on medications did not reveal any significant LPD/RPD differences in sleep quality. The incongruity between these findings and those of the previous study merits further investigation of the interaction between sex and side of onset, and the impact of mood on sleep in patients with PD.

No significant differences in quality of sleep were found between patients with TD and those with NTD. Despite the different progression and profile of disease in patients with TD and those with NTD, it may be that both of these subgroups experience significant sleep problems. Neuropathologically, it has been found that individuals with NTD PD have a more widespread distribution of Lewy bodies in their neocortex,[29] which explains increased incidence of cognitive impairment and dementia, but not necessarily a greater impact on areas that would affect sleep quality. Alternatively, these results do show evidence of trend-level differences in self-reported sleep quality between patients with TD and those with NTD after controlling for education. To clarify this and further our understanding of meaningful subtypes of PD, a more thorough study of the quality and type of sleep problems in motor symptom subtypes is needed.

RBD is one of the more commonly studied sleep disorders in PD, reflecting its potential as a harbinger of the disease.[30] RBD is characterized by vigorous motor activity and vivid dreams that seem to be acted out.[31] The gold standard for diagnosis of RBD is patient/caregiver report of dream enactment and a sleep study confirming loss of muscle atonia. We found that patients who reported acting-out of their dreams at night had a significantly worse ACT sleep fragmentation index, indicating that this ACT variable may be a sensitive marker of the presence of RBD in conjunction with patient report of dream enactment. This was recently corroborated in another report that also found ACT to be sensitive to distinguishing between those with and without RBD.[32] This is an important finding as many patients may present with RBD but are not diagnosed due to the high cost and burden of a full-scale overnight sleep study. ACT can serve as a convenient and cost-effective diagnostic and research tool for RBD in patients with PD and in those with idiopathic RBD that may be a precursor to PD.

Dopaminergic medication has been reported to be one of the key causes of impaired sleep in individuals with PD. Although the literature reveals some dissent on this topic, these findings show that dopaminergic medication plays at least some role in the sleep problems of PD. LED was significantly related to ACT and self-reported measures of sleep. There were also significant sleep quality differences between those who were taking dopamine agonists and those who were not, again confirming that dopaminergic medication may be a factor in impaired sleep in treated PD. It is still not clear that dopaminergic medication can contribute to the severity of the sleep problems of PD alone. There is sufficient evidence in the literature that the pathology of PD itself affects brainstem and midbrain areas that are important for control of sleep and wake mechanisms.[2] In this study, the dose of the dopaminergic medication was related to ACT total sleep time and self-reported measures of sleep quality but not to ACT sleep fragmentation and reduced sleep efficiency, which are the most frequent night time complaints in PD.[3]

A limitation of this study was that we used ACT rather than polysomnography (PSG), which is the gold standard for studying sleep. ACT cannot differentiate between nocturnal activity due to wakefulness and other common sleep disturbances of PD such as RBD, periodic limb movements, or sleep apnea. All of these nocturnal sleep problems disrupt sleep and, therefore, decrease sleep quality, which is the main area of interest of this study. To evaluate the presence of the common sleep disturbances in PD, we used a self-report measure in addition to ACT. Unlike PSG, ACT is relatively inexpensive and is not as burdensome to the patient. The ecological validity of ACT is enhanced in comparison to PSG because it permits multiple-night recording in the patient's home environment. Reliability and validity studies in healthy adults have demonstrated that ACT is highly correlated with PSG for differentiating sleep from wake states,[33,34] and it has been frequently used to assess sleep and wake behavior in healthy individuals and those with insomnia.[35] Although ACT is yet to be validated with PSG in

patients with PD, it has been shown to be correlated with self-report measures of sleep[36] and has been used to study efficacy of medication[37] and transcranial magnetic stimulation[38] related to sleep in PD.

A second limitation of this study is the small sample sizes for our subgroup analyses. With larger samples it is possible that more subgroup differences would emerge. We did, however, find significant differences with moderate effect sizes for the subgroup analyses looking at sex and dopamine agonists and possible RBD, indicating that at least for those variables the sample sizes were sufficient to detect meaningful subgroup differences. Though significant differences were found with small subgroup sizes, these results should be confirmed by future studies with larger samples.

In summary, these findings underscore that sleep problems in PD are multifactorial in nature. There are disease-related and individual factors (ie, sex) that contribute to the degree, severity, and type of sleep problems. Motor symptom severity and medication are among the primary correlates of sleep disruption, but additional factors differentiate sleep in PD, including subtypes of the disease, with patients with NTD reporting worse sleep quality, and sex, with men having worse sleep quality and more excessive daytime sleepiness. We also found that ACT may serve as a useful tool for identifying individuals with possible RBD, a sleep disorder that may presage PD. Understanding the cause and nature of sleep disturbances in PD and identifying them early in the disease process may lead to the development of new therapies for symptom management and enhancement of quality of life.

ACKNOWLEDGMENTS

REFERENCES

1. Comella CL. Sleep disturbances and excessive daytime sleepiness in Parkinson disease: an overview. *J Neural Transm Suppl.* 2006; 70:349–355.
2. Grinberg LT, Rueb U, Alho AT, et al. Brainstem pathology and non-motor symptoms in PD. *J Neurol Sci.* 2010;289:81–88.
3. Comella CL. Sleep disturbances in Parkinson's disease. *Curr Neurol Neurosci Rep.* 2003;3:173–180.
4. Larsen JP, Tandberg E. Sleep disorders in patients with Parkinson's disease: epidemiology and management. *CNS Drugs.* 2001;15: 267–275.
5. Mehta SH, Morgan JC, Sethi KD. Sleep disorders associated with Parkinson's disease: role of dopamine, epidemiology, and clinical scales of assessment. *CNS Spectr.* 2008;13(3 suppl 4):6–11.
6. Rye DB, Bliwise DL, Dihenia B, et al. FAST TRACK: daytime sleepiness in Parkinson's disease. *J Sleep Res.* 2000;9:63–69.
7. Borek LL, Kohn R, Friedman JH. Mood and sleep in Parkinson's disease. *J Clin Psychiatry.* 2006;67:958–963.
8. Stavitsky K, Saurman J, Griffith E, et al. Excessive daytime sleepiness and mood disturbances in Parkinson's disease. Abstracts, Society for Neuroscience Program 2009 Abstract Viewer and Itinerary Planner. Chicago IL: Society for Neuroscience. Online.
9. Amick MM, Grace J, Chou KL. Body side of motor symptom onset in Parkinson's disease is associated with memory performance. *J Int Neuropsychol Soc.* 2006;12:736–740.
10. Cronin-Golomb A, Amick MM. Spatial abilities in aging, Alzheimer's disease, and Parkinson's disease. In: Boller F, Cappa S, eds. *Handbook of Neuropsychology.* Vol 6. 2nd ed. Amsterdam: Elsevier; 2001:119–143.
11. Stavitsky K, McNamara P, Durso R, et al. Hallucinations, dreaming, and frequent dozing in Parkinson disease: impact of right-hemisphere neural networks. *Cogn Behav Neurol.* 2008;21:143–149.
12. Cubo E, Martinez Martin P, Martin-Gonzalez JA, et al. Motor laterality asymmetry and nonmotor symptoms in Parkinson's disease. *Mov Disord.* 2010;25:70–75.
13. Alves G, Larsen JP, Emre M, et al. Changes in motor subtype and risk for incident dementia in Parkinson's disease. *Mov Disord.* 2006; 21:1123–1130.
14. Haaxma CA, Bloem BR, Borm GF, et al. Gender differences in Parkinson's disease. *J Neurol Neurosurg Psychiatry.* 2007;78:819–824.
15. Bordelon YM, Fahn S. Gender differences in movement disorders. In: Kaplan PW, ed. *Neurologic Disease in Women.* New York: Demos; 2006.
16. Stern Y, Sano M, Paulson J, et al. Modified Mini-Mental State Examination: validity and reliability [abstract]. *Neurology.* 1987; 37(suppl 1):179.
17. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. *Neurology.* 2005;65:1863–1872.
18. Gjerstad MD, Boeve B, Wentzel-Larsen T, et al. Occurrence and clinical correlates of REM sleep behaviour disorder in patients with Parkinson's disease over time. *J Neurol Neurosurg Psychiatry.* 2008; 79:387–391.
19. Peto V, Jenkinson C, Fitzpatrick R, et al. The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Qual Life Res.* 1995;4:241–248.
20. Chaudhuri KR, Pal S, DiMarco A, et al. The Parkinson's disease sleep scale: a new instrument for assessing sleep and nocturnal disability in Parkinson's disease. *J Neurol Neurosurg Psychiatry.* 2002;73: 629–635.
21. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 1991;14:540–545.
22. Kumar S, Bhatia M, Behari M. Excessive daytime sleepiness in Parkinson's disease as assessed by Epworth Sleepiness Scale (ESS). *Sleep Med.* 2003;4:339–342.
23. Ghorayeb I, Loundou A, Auquier P, et al. A nationwide survey of excessive daytime sleepiness in Parkinson's disease in France. *Mov Disord.* 2007;22:1567–1572.
24. Lin CM, Davidson TM, Ancoli-Israel S. Gender differences in obstructive sleep apnea and treatment implications. *Sleep Med Rev.* 2008;12:481–496.
25. Maetzler W, Liepelt I, Berg D. Progression of Parkinson's disease in the clinical phase: potential markers. *Lancet Neurol.* 2009;8:1158–1171.
26. Papadimitriou GN, Linkowski P. Sleep disturbance in anxiety disorders. *Int Rev Psychiatry.* 2005;17:229–236.
27. Askenasy JJ. Sleep disturbances in parkinsonism. *J Neural Transm.* 2003;110:125–150.
28. Spira AP, Stone K, Beaudreau SA, et al. Anxiety symptoms and objectively measured sleep quality in older women. *Am J Geriatr Psychiatry.* 2009;17:136–143.
29. Selikhova M, Williams DR, Kempster PA, et al. A clinico-pathological study of subtypes in Parkinson's disease. *Brain.* 2009; 132(Pt 11):2947–2957.
30. Schenck CH, Bundlie SR, Mahowald MW. REM behavior disorder (RBD): delayed emergence of parkinsonism and/or dementia in 65%

of older men initially diagnosed with idiopathic RBD, and an analysis of the minimum & maximum tonic and/or phasic electromyographic abnormalities during REM sleep. *Sleep*. 2003; 26:A316.

31. Schenck CH, Bundlie SR, Ettinger MG, et al. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. *Sleep*. 1986;9:293–308.

32. Naismith SL, Rogers NL, Mackenzie J, et al. The relationship between actigraphically defined sleep disturbance and REM sleep behaviour disorder in Parkinson's Disease. *Clin Neurol Neurosurg*. 2010;112:420–423.

33. Jean-Louis G, von Gizycki H, Zizi F, et al. Determination of sleep and wakefulness with the actigraph data analysis software (ADAS). *Sleep*. 1996;19:739–743.

34. Blood ML, Sack RL, Percy DC, et al. A comparison of sleep detection by wrist actigraphy, behavioral response, and polysomnography. *Sleep*. 1997;20:388–395.

35. Ancoli-Israel S, Cole R, Alessi C, et al. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*. 2003;26:342–392.

36. Stavitsky K, Saurman JL, McNamara P, et al. Sleep in Parkinson's disease: a comparison of actigraphy and subjective measures. *Parkinsonism Relat Disord*. 2010;16:280–283.

37. Comella CL, Morrissey M, Janko K. Nocturnal activity with nighttime pergolide in Parkinson disease: a controlled study using actigraphy. *Neurology*. 2005;64:1450–1451.

38. van Dijk KD, Most EI, Van Someren EJ, et al. Beneficial effect of transcranial magnetic stimulation on sleep in Parkinson's disease. *Mov Disord*. 2009;24:878–884.