Published in final edited form as:

J Neuropsychiatry Clin Neurosci. 2013 ; 25(4): 319–326. doi:10.1176/appi.neuropsych.12070175.

Associations of Sleep Disturbance Symptoms with Health-Related Quality of Life in Parkinson's Disease

Alon Avidan, MD, MPH¹, Ron D. Hays, PhD², Natalie Diaz, MD³, Yvette Bordelon, MD, PhD¹, Alexander W. Thompson, MD, MPH⁴, Stefanie D. Vassar, MS^{1,5}, and Barbara G. Vickrey, MD, MPH^{1,5}

¹Department of Neurology, UCLA, Los Angeles CA

²Departments of Medicine and Department of Health Policy and Management, UCLA, Los Angeles CA

³Department of Neurology, Harbor-UCLA, Los Angeles CA

⁴Group Health Cooperative, Behavioral Health Service, Seattle, WA

⁵Parkinson's Disease Research, Education, and Clinical Center; VA Greater Los Angeles Healthcare System; Los Angeles, CA

Abstract

We examined associations of different sleep disturbance symptoms with health-related quality of life (HRQOL) in 153 adults with Parkinson's disease (PD). PD patients reported more snoring, sleep inadequacy, daytime somnolence, and sleep maintenance problems than the general population ($p < 0.001$). Symptoms having the broadest and strongest unique associations with generic HRQOL (8 scales; 2 composites of SF-36) were daytime somnolence (5 scales; 1 composite), sleep initiation (8 scales; 2 composites), and awakening short of breath or with headache (6 scales; 2 composites) (p 's < 0.05). Associations of selected sleep disturbance symptoms – some unanticipated – suggest that assessing specific symptoms is worthwhile in clinical care.

Keywords

sleep disturbance; Parkinson's disease; health-related quality of life

INTRODUCTION

Parkinson's disease (PD), the most common neurodegenerative movement disorder, has an annual incidence of 13.4 per 100,000 in the United States.^{1} Inability to fall asleep and stay asleep, disturbed motor activity during sleep, and excessive daytime somnolence are common in PD patients.^{2} In a community-based sample of 239 PD patients in Norway in

Corresponding Author, to receive reprint requests: Alon Avidan, MD, MPH, Address: UCLA, Department of Neurology, David Geffen School of Medicine at UCLA, 710 Westwood Blvd., Room 1-169/ RNRC, Los Angeles, CA 90095-1769, Phone: (310) 825-0703, Fax: (310) 825-6956, avidan@mednet.ucla.edu.

Previous Presentation:

Previously presented at the 25th Anniversary Meeting of the Associated Professional Sleep Societies, LLC, held from June 11–15, 2011, at the Minneapolis Convention Center in Minneapolis, Minnesota. "Health-Related Quality of Life Associations Vary by Type of Sleep Disturbances in Parkinson's Disease" was presented on Monday, June 13, 2011.

Location of work:

Department of Neurology, University of California, Los Angeles; Los Angeles, California

the mid-1990s, 60% reported having any sleep problem; 27% of the 239 patients rated their overall nighttime problem as moderate to severe, and the most commonly reported sleep symptoms included frequent awakening (sleep fragmentation) and early awakening.{3} Sleep problems in PD have been attributed to many diverse causes, for example, prescribed therapy for PD such as dopaminergic treatment, or excessive nocturia due to dysautonomia in PD, among many others. {4} Although the impact of sleep disturbances - one of the many different non-motor manifestations of PD - have received recognition relatively recently, James Parkinson in 1817 wrote that persons with PD were often “constantly sleepy” and “exhausted.”{5}

Health-related quality of life (HRQOL) includes physical, social, and mental health. Previous research suggests that insomnia is associated with poor HRQOL, especially depressive symptoms, in PD. A study of an Australian PD cohort found that nocturnal sleep disruption was associated with depressive symptoms early in the disease course.{6} In another study, insomnia was related to longer PD duration and worse HRQOL including depression.{7} Yet another study showed that insomnia was associated with greater pain and depressive symptoms.{8} In addition, short sleep duration (< or = 6 hours) and early morning awakening are strongly correlated with fatigue in PD.{9}

While these and other studies have described associations of insomnia with HRQOL in PD{10}, none have analyzed the relative associations of different types of sleep disturbance symptoms with HRQOL in PD. We hypothesize, based on prior research, that insomnia and daytime sleepiness will each be associated with worse HRQOL including depressive symptoms in PD. As an exploratory analysis, we analyze the relative contributions of additional sleep symptoms with HRQOL in PD, including snoring and other indicators of sleep-disordered breathing.{11–12}

METHODS

Sample

Three hundred seventy-one adults with idiopathic Parkinson’s disease from three counties in central California counties were enrolled between 1998 and 2006 in a population-based study of predictors of onset of PD {13}. Eligibility for that study included being diagnosed with PD within the prior three years, English- or Spanish-speaking, and over 18 years old. Participants received routine care for their PD from general neurologists in this region. Of the 371 participants in that study of PD incidence, 254 were eligible for and subsequently enrolled in a follow-up study of determinants of progression in PD {14}. The diagnosis of PD was confirmed for all study participants by movement disorder specialists at enrollment in the prior study and was re-assessed in this follow-up study. The study was approved by the UCLA IRB (#G06-07-055), and all subjects provided informed consent following full explanation of study procedures.

Measures

The MOS Sleep measure (Appendix) is a 12-item, self-administered measure assessing six specific sleep problem symptoms: sleep disturbance-initiation (2 items), sleep disturbance-maintenance (2 items), awakening short of breath or with headache (1 item), daytime somnolence (3 items), sleep inadequacy (2 items), and snoring (1 item). {15} Items were developed based on literature review and piloted with adults who were outpatients in an academic clinic and in a rural health clinic setting. Support for the reliability and validity of the MOS Sleep Measure in the general US population and among patients with chronic medical conditions has been reported.{16} Internal consistency reliability for multi-item scales exceeded 0.70 for all but daytime somnolence (Cronbach’s alpha=0.63). Impairment

on the MOS Sleep measure was associated with worse mental health, and with lower work productivity and quality. {17} The frequency with which each problem has been experienced during the previous 4 weeks is rated on a 6-point scale ranging from “none of the time” to “all of the time”, except for one of the sleep disturbance-initiation items on usual length of time to fall asleep, which has 5 categories of duration. All scores are transformed linearly to range from 0 to 100; higher scores indicate more of the attribute implied by the scale name (e.g. more snoring or more inadequate sleep). {15, 18}

The SF-36 (version 2.0) is a generic health-related quality of life survey administered in the RAND Medical Outcomes Study with 36 items defining eight scales: Physical Functioning, Role Limitations due to Physical Health, Role Limitations due to Emotional Problems, Pain, Emotional Well-Being, Energy, General Health, and Social Functioning. A Physical Health Composite score (PCS) and Mental Health Composite score (MCS) are derived from the 8 scales. All scales and composite scores are calculated as T-scores with a mean of 50 and a standard deviation of 10. Age- and gender-adjusted general population norms are calculated. Evidence for its reliability and validity in PD patients has been reported. {19}

Depressive symptoms were assessed by the Patient Health Questionnaire (PHQ)-9 and the Geriatric Depression Scale (GDS)-15. The PHQ-9 is a brief, self-administered depression assessment measure found to be accurate in medical settings. {20} PHQ-9 items map onto nine depression symptoms from the DSM-IV-TR, including one item: “trouble falling or staying asleep, or sleeping too much.” Subjects answer how many days over the past two weeks they had the symptom: 0=“none,” 1=“several days,” 2=“more than half the days,” and 3=“nearly every day.” A symptom severity measure (range: 0 – 27) is the sum of the numerical responses for all questions. The PHQ-9 was self-administered, although a research assistant could assist any study participant who had difficulty writing responses. The GDS-15 is a self-administered, 15-item yes/no questionnaire (range: 0-to-15), which does not contain any items about sleep. The GDS-15 performs well as a screening tool in distinguishing depressed from non-depressed PD patients. {21}

Movement disorder specialists evaluated and rated stage of PD using the Modified Hoehn and Yahr score; {22–23} these assessments were conducted with patients who were off Parkinson’s disease medication since the previous evening (“off” state). Stage 0 is no sign of disease, and Stage 5 is wheelchair bound or bedridden.

Age, gender, education level, marital status, employment status, medical comorbidities, and duration of diagnosis of Parkinson’s disease were obtained through survey and interview questions at the baseline assessment for the PD incidence study and updated at the follow-up assessment.

Data Collection

Data collection for the follow-up study took place over a 25-month period beginning in June 2007. Sleep, depression, the SF-36, and disease stage measures were collected through self-administered and interviewer-administered questionnaires or in-person examination by a movement disorders specialist. The sleep measures were added to the study partway through the data collection period.

Data Analysis

Demographic and clinical characteristics of 153 included and 101 excluded participants were compared using bivariate statistics (t-tests, Wilcoxon rank-sum, chi-square). Reasons for exclusion were: either the MOS Sleep measure or SF-36 was not completed or were completed more than 23 days apart from each other (n=70), disease stage was not assessed using the Hoehn and Yahr scale (n=30), or the diagnosis of PD was not confirmed at the

follow-up examination (n=1). MOS Sleep measure and SF-36 responses were compared with age- and gender-adjusted general population norms {18, 24} using t-tests. Zero order correlations between the MOS Sleep measure and SF-36 HRQOL scales were used to see if there were any suppression effects in the subsequent multivariate analyses.

To determine relative associations of each MOS Sleep scale with the SF-36 health-related quality of life scales and depressive symptoms, we used linear regression models adjusting for age, gender, and Parkinson's disease stage (Hoehn and Yahr). For each of the 12 models (8 SF-36 scales, 2 SF-36 composite scores, and 2 depression measures), backwards stepwise regression was used to determine a reduced model that included only variables whose associations with the dependent variable (SF-36 scales or depression measures) were a p-value of less than 0.05 (two-tailed). Analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Characteristics of the 153 subjects included in this analysis are presented in Table 1. Of 254 subjects enrolled in the PD progression study, characteristics of the 153 included and 101 excluded subjects were not different with the exception that the 153 included subjects had PD duration of 4.6 years (SD=2.2), compared to 6.4 years (SD=2.1) years ($p < 0.0001$) for those excluded.

Compared with age- and gender-adjusted US general population norms, study participants reported worse sleep maintenance disturbance, snoring, sleep inadequacy, and daytime somnolence (all $p < 0.001$). Participants also reported significantly worse HRQOL than the general population on 7 of 8 SF-36 scales (no difference in pain scores) and on both SF-36 composite scores (Table 2).

Awakening short of breath or with headache and disturbances in sleep initiation were broadly associated with worse HRQOL, with significant associations of these sleep symptoms and 7 of the 8 SF-36 scales (role limitations – physical was the exception), and both SF-36 composite scores (Table 3). Daytime somnolence was significantly and uniquely associated with five SF-36 scales and the physical health composite score. In contrast, snoring was not associated with any SF-36 scale or composite, and sleep inadequacy was only associated with pain. (The Sleep disturbance – maintenance scale was excluded from multivariable regression models because of suppression effects.)

In the multivariable models, awakening short of breath or with headache was most strongly associated with worse depression on both depression measures ($p \leq 0.0006$; Table 3). Sleep inadequacy was also associated with more severe depressive symptoms on the PHQ-9 ($p \leq 0.0002$), and sleep initiation disturbance was associated with worse depression as assessed by the GDS-15 ($p < 0.0001$). Snoring and daytime somnolence were not associated with depressive symptoms.

DISCUSSION

Our findings confirm that PD patients experience a disproportionate number of sleep complaints and worse health-related quality of life compared to the general population. {25–27} While it is known that the majority of PD patients have sleep disturbances affecting their ability to fall asleep, their ability to maintain sleep, or daytime somnolence, {28} we are unaware of studies that have evaluated the relative contributions of different types of sleep disturbances and symptoms in PD to HRQOL. As hypothesized, insomnia and daytime somnolence had strong negative associations with HRQOL, but we also uncovered significant unique associations of awakening with shortness of breath or with headache with

worse HRQOL in PD. Our results are different than those by {29}Martinez-Martin, 2006, which demonstrate a weak association between sleep disturbances and HRQOL, but are in line with a later study by the same author showing that sleep and fatigue are associated with poorer HRQOL {30}, and another study demonstrating a similar correlation utilizing the Parkinson's disease Sleep Scale (PDSS) by Scaravilli et al. {31} It is presumed that different sleep assessment inventories may have contributed to these differences.

Waking up with "shortness of breath or headaches" does not appear to be more common in PD than the general population, but when it is present, it is associated with worse HRQOL. While patients with PD are not more likely to have worse symptoms of OSA than the general population, some PD patients have noteworthy OSA symptoms. Possible mechanisms may be related to wearing off overnight of PD medication, resulting in anxiety or re-emergence of PD symptoms such as increased muscular rigidity. Levodopa therapy may also be associated with the emergence of irregular and rapid breathing, alternating with brief periods of apnea, in a pattern consistent with a central origin. This temporal relationship of the respiratory disturbance to the administration of levodopa may suggest a peak-dose drug effect. {32} One additional theory focuses on an underlying autonomic dysregulation of breathing associated during REM sleep, {33} which is more likely to wake up patients during the latter part of the night, hence waking up short of breath, or with a headache. The underlying pathophysiology of sleep disordered breathing in PD may be less dependent on weight (i.e. obesity) as a predisposing factor to the anatomical restriction at the level of the hypopharynx, because body mass index (BMI) does not change before the onset of PD {34} and PD patients tend to have lower BMI than controls. {35} However, as noted above, other mechanisms could include respiratory dyskinesia, rigidity of the rib cage musculature, and the possible negative impact of dopaminergic therapy on respiratory tone. {36}

Other findings that emerge from these data are that daytime sleepiness and difficulties initiating sleep are associated with virtually every domain of HRQOL. In PD, sleep initiation difficulties are often related to depression, wearing off effects of dopaminergic drugs, and movement disorders of sleep such as restless legs syndrome. {7} Hypersomnia in PD is most likely centrally mediated, but could well be related to prescribed dopaminergic agents that are used to treat the disease, and comorbid psychiatric disorders. While underlying sleep disturbances due to inadequately controlled nighttime PD symptoms - such as periodic leg movements or nocturia seen in the latter stages of PD - may cause sleep maintenance difficulties, they may also contribute to sleepiness during the day due to their contribution to poor and insufficient sleep.

Depressive symptoms are common in patients with PD. In this sample, there were significant associations of worse scores on one or both depression measures with waking up feeling short of breath or with a headache, and with initiation of sleep disturbance. These types of sleep disturbance were commonly associated with problems in most domains of HRQOL and were significantly associated with both SF-36 composite scores. This underscores the complex relationships of sleep with depression and HRQOL. Given the high frequency of depression in people with PD, sleep disturbance must be assessed as both a primary symptom of PD in addition to a marker of an underlying depressive disorder. Depression measures such as the GDS-15 that do not screen using items about sleep and movement disturbance may be better tools for depression assessment in those with PD, {14} minimizing confounding due to the occurrence of these sleep disturbances as a primary symptom in PD independent of depression.

This is a cross-sectional study of associations, limiting any interpretation regarding causality. In addition, there may be residual confounding or inadequate adjustment due to

unmeasured covariates. While one group of investigators concluded that the generic SF-36 may not be sufficient for assessing HRQOL in PD, others found it performed the same or better than two disease-targeted measures.{19} The PHQ-9 contains a question specifically addressing sleep, which may confound the relationship between sleep disturbance and score on the PHQ-9. While we did not conduct polysomnography in this study, at least one study of treatment of sleep problems in epilepsy found greater improvement in patients' self-reports of sleep on the MOS Sleep Measure than from polysomnogram assessments. The authors of that study posited the explanation that even "relatively small improvements in sleep continuity might be perceived as a relief to the patient," but that additional research was needed to understand the implications of differences in these two assessment methods.{37} The MOS Sleep Scale was not included in the recent Movement Disorders Society taskforce review of sleep measures{38}, however it has been shown to have good psychometric properties in patients with restless leg syndrome{39} and in a patient population with pure sleep-related seizure.{40}

In conclusion, our community-dwelling sample of PD patients report more significant sleep disturbances, particularly sleep maintenance insomnia, daytime sleepiness and inadequate sleep, than a general population sample. Virtually every HRQOL domain is also impacted in PD. Further, while we confirmed our hypothesized associations of insomnia and of daytime somnolence with HRQOL in PD, we also identified strong associations of awakening short of breath or with headache and HRQOL in PD. The selective association of certain sleep disturbance symptoms – some of which were unanticipated – suggests that assessing specific symptoms may be worthwhile in the clinical setting. While we speculate about possible mechanisms for symptoms such as awakening short of breath or morning headaches, their etiology in PD patients is not known and warrants further investigation given the strong associations with HRQOL.

Acknowledgments

Study support was provided by the Parkinson Alliance, by National Institute of Neurological Disorders and Stroke NS038367, and by the Veteran's Administration. Hays was supported in part by a National Institute of Aging (P30AG021684) and National Center on Minority Health and Health Disparities (P20MD000182) grants.

We thank Honghu Liu, Ph.D for statistical consulting assistance, Jeff Bronstein, MD, PhD for assisting in UPDRS and Hoehn and Yahr data collection, and Aaron Cook, MPH, for technical assistance in manuscript preparation.

References

1. Van Den Eeden SK, Tanner CM, Bernstein AL, et al. Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. *Am J Epidemiol.* 2003; 157:1015–1022. [PubMed: 12777365]
2. Partinen M. Sleep disorder related to Parkinson's disease. *J Neurol.* 1997; 244:S3–6. [PubMed: 9112582]
3. Tandberg E, Larsen JP, Karlsen K. A community-based study of sleep disorders in patients with Parkinson's disease. *Mov Disord.* 1998; 13:895–899. [PubMed: 9827612]
4. Stocchi F, Barbato L, Nordera G, et al. Sleep disorders in Parkinson's disease. *Journal of Neurology.* 1998; 245:S15–18. [PubMed: 9617717]
5. Parkinson, J. An essay on the shaking palsy. London: 1817.
6. Naismith SL, Hickie IB, Lewis SJ. The role of mild depression in sleep disturbance and quality of life in Parkinson's disease. *J Neuropsychiatry Clin Neurosci.* 2010; 22:384–389. [PubMed: 21037122]
7. Gjerstad MD, Wentzel-Larsen T, Aarsland D, et al. Insomnia in Parkinson's disease: frequency and progression over time. *J Neurol Neurosurg Psychiatry.* 2007; 78:476–479. [PubMed: 17098844]

8. Caap-Ahlgren M, Dehlin O. Insomnia and depressive symptoms in patients with Parkinson's disease. Relationship to health-related quality of life. An interview study of patients living at home. *Arch Gerontol Geriatr.* 2001; 32:23–33. [PubMed: 11251236]
9. Goldman SE, Ancoli-Israel S, Boudreau R, et al. Sleep problems and associated daytime fatigue in community-dwelling older individuals. *J Gerontol A Biol Sci Med Sci.* 2008; 63:1069–1075. [PubMed: 18948557]
10. Gomez-Esteban JC, Tijero B, Somme J, et al. Impact of psychiatric symptoms and sleep disorders on the quality of life of patients with Parkinson's disease. *Journal of Neurology.* 2011; 258:494–499. [PubMed: 20957384]
11. Hogl B. Sleep apnea in Parkinson's disease: when is it significant? *Sleep Med.* 2010; 11:233–235. [PubMed: 20133190]
12. Mondragon-Rezola E, Arratibel-Echarren I, Ruiz-Martinez J, et al. Sleep disorders in Parkinson's disease: insomnia and sleep fragmentation, daytime hypersomnia, alterations to the circadian rhythm and sleep apnea syndrome. *Rev Neurol.* 2010; 50(Suppl 2):S21–26. [PubMed: 20205138]
13. Kang GA, Bronstein JM, Masterman DL, et al. Clinical characteristics in early Parkinson's disease in a central California population-based study. *Mov Disord.* 2005; 20:1133–1142. [PubMed: 15954133]
14. Thompson AW, Liu H, Hays RD, et al. Diagnostic accuracy and agreement across three depression assessment measures for Parkinson's disease. *Parkinsonism Relat Disord.* 2010
15. RAND. [Accessed January 9, 2011] Sleep Scale: RAND Medical Outcomes 2011. 2011. http://www.rand.org/health/surveys_tools/mos/mos_sleep.html
16. Hays, RD.; Stewart, AL. Sleep Measures. Durham: Duke University Press; 1992.
17. Manocchia M, Keller S, Ware JE. Sleep problems, health-related quality of life, work functioning and health care utilization among the chronically ill. *Qual Life Res.* 2001; 10:331–345. [PubMed: 11763246]
18. Hays RD, Martin SA, Sesti AM, et al. Psychometric properties of the Medical Outcomes Study Sleep measure. *Sleep Med.* 2005; 6:41–44. [PubMed: 15680294]
19. Brown CA, Cheng EM, Hays RD, et al. SF-36 includes less Parkinson Disease (PD)-targeted content but is more responsive to change than two PD-targeted health-related quality of life measures. *Qual Life Res.* 2009; 18:1219–1237. [PubMed: 19714487]
20. Gilbody S, Richards D, Brealey S, et al. Screening for depression in medical settings with the Patient Health Questionnaire (PHQ): a diagnostic meta-analysis. *J Gen Intern Med.* 2007; 22:1596–1602. [PubMed: 17874169]
21. Weintraub D, Oehlberg KA, Katz IR, et al. Test characteristics of the 15-item geriatric depression scale and Hamilton depression rating scale in Parkinson disease. *Am J Geriatr Psychiatry.* 2006; 14:169–175. [PubMed: 16473982]
22. Goetz CG, Poewe W, Rascol O, et al. Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: status and recommendations. *Mov Disord.* 2004; 19:1020–1028. [PubMed: 15372591]
23. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology.* 1967; 17:427–442. [PubMed: 6067254]
24. Ware, JE. SF-36 Health Survey manual and interpretation guide. Boston: Nimrod Press; 1993.
25. Hariz GM, Forsgren L. Activities of daily living and quality of life in persons with newly diagnosed Parkinson's disease according to subtype of disease, and in comparison to healthy controls. *Acta Neurol Scand.* 2010
26. Roh JH, Kim BJ, Jang JH, et al. The relationship of pain and health-related quality of life in Korean patients with Parkinson's disease. *Acta Neurol Scand.* 2009; 119:397–403. [PubMed: 18976321]
27. Ziropada L, Stefanova E, Potrebic A, et al. Quality of life in Serbian patients with Parkinson's disease. *Qual Life Res.* 2009; 18:833–839. [PubMed: 19562515]
28. Wells T, Sawatzky JA, McMillan DE. Sleep disturbance in Parkinson's disease: a human response to illness. *Can J Neurosci Nurs.* 2009; 31:24–32. [PubMed: 20085118]

29. Martinez-Martin P, Cubo-Delgado E, Aguilar-Barbera M, et al. A pilot study on a specific measure for sleep disorders in Parkinson's disease: SCOPA-Sleep. *Rev Neurol*. 2006; 43:577–583. [PubMed: 17099848]
30. Martinez-Martin P, Rodriguez-Blazquez C, Kurtis MM, et al. The impact of non-motor symptoms on health-related quality of life of patients with Parkinson's disease. *Mov Disord*. 2011; 26:399–406. [PubMed: 21264941]
31. Scaravilli T, Gasparoli E, Rinaldi F, et al. Health-related quality of life and sleep disorders in Parkinson's disease. *Neurol Sci*. 2003; 24:209–210. [PubMed: 14598091]
32. Rice JE, Antic R, Thompson PD. Disordered respiration as a levodopa-induced dyskinesia in Parkinson's disease. *Mov Disord*. 2002; 17:524–527. [PubMed: 12112201]
33. Apps MC, Sheaff PC, Ingram DA, et al. Respiration and sleep in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 1985; 48:1240–1245. [PubMed: 4086999]
34. Ragonese P, D'Amelio M, Callari G, et al. Body mass index does not change before Parkinson's disease onset. *Eur J Neurol*. 2008; 15:965–968. [PubMed: 18637822]
35. Uc EY, Struck LK, Rodnitzky RL, et al. Predictors of weight loss in Parkinson's disease. *Mov Disord*. 2006; 21:930–936. [PubMed: 16534756]
36. Maria B, Sophia S, Michalis M, et al. Sleep breathing disorders in patients with idiopathic Parkinson's disease. *Respir Med*. 2003; 97:1151–1157. [PubMed: 14561023]
37. de Haas S, Otte A, de Weerd A, et al. Exploratory polysomnographic evaluation of pregabalin on sleep disturbance in patients with epilepsy. *J Clin Sleep Med*. 2007; 3:473–478. [PubMed: 17803010]
38. Hogl B, Arnulf I, Comella C, et al. Scales to assess sleep impairment in Parkinson's disease: critique and recommendations. *Mov Disord*. 2010; 25:2704–2716. [PubMed: 20931631]
39. Allen RP, Kosinski M, Hill-Zabala CE, et al. Psychometric evaluation and tests of validity of the Medical Outcomes Study 12-item Sleep Scale (MOS sleep). *Sleep Med*. 2009; 10:531–539. [PubMed: 18805054]
40. Ekizoglu E, Baykan B, Bebek N, et al. Sleep characteristics of patients with epilepsy with pure sleep-related seizures. *Epilepsy Behav*. 2011; 21:71–75. [PubMed: 21481644]

Table 1

Characteristics of Parkinson's disease sample (n = 153)

	Mean (SD) or N (%)
Age in years, mean (SD) (range: 43–92)	72.2 (9.2)
Female, n (%)	62 (40.5)
Currently married, n (%)	114 (75.0)
Highest level of education, n (%) *	
Less than high school diploma	29 (18.9)
High school diploma	56 (36.6)
Technical or trade school diploma	19 (12.4)
College diploma or graduate school	42 (27.5)
Ethnicity, n (%)	
White or European American	116 (75.8)
Latino or Hispanic	27 (17.7)
Other	10 (6.5)
Work Status, n (%)	
Employed	32 (21.1)
Unemployed	6 (4.0)
Retired	108 (71.1)
Other: disability (3), Emeritus (1), Housewife (1), temp work (1)	6 (4.0)
Duration of PD diagnosis in years, mean (SD)	4.6 (2.2)
UPDRS Motor Score on medication, mean (SD)	16.9 (10.6)
Hoehn and Yahr Stage off medication, n (%)	
Stage 0: No signs of disease	0
Stage 1: Unilateral disease	12 (7.8)
Stage 1.5: Unilateral plus axial involvement	7 (4.6)
Stage 2: Bilateral disease, without impairment of balance	50 (32.7)
Stage 2.5: Mild bilateral disease with recovery on pull test	45 (29.4)
Stage 3: Mild to moderate bilateral disease; some postural instability; physically independent.	29 (19.0)
Stage 4: Severe disability; still able to walk or stand unassisted	6 (3.9)
Stage 5: Wheelchair bound or bedridden unless aided	4 (2.6)
Mean # Medical Comorbidities (SD)	0.69 (1.13)
Median (IQR)	0 (0, 1)

*
n = 7 responded "Don't know" or refused

Table 2

MOS Sleep Measure and SF-36 v2.0 Scores of Study Participants and Comparison to U.S. General Population Norms (n = 153)

	Study sample N = 153 Mean (SD)	Age and gender adjusted norms *	p-value
MOS Sleep measure (range: 0–100) †			
Sleep disturbance - Initiation	21.8 (25.6)	19.2	0.20
Sleep disturbance - Maintenance	34.9 (24.5)	28.3	0.001
Awakening short of breath or with headache	9.8 (20.0)	8.1	0.29
Daytime somnolence	39.7 (20.7)	26.9	<0.0001
Sleep inadequacy	40.8 (26.8)	27.5	<0.0001
Snoring	37.3 (33.4)	26.7	<0.0001
SF-36 v2.0 (T-scores) §			
Physical function	36.8 (11.5)	42.5	<0.0001
Role limitations – physical	39.1 (11.2)	43.5	<0.0001
Role limitations – emotional	42.7 (11.9)	46.5	0.0002
Pain	46.3 (10.9)	47.0	0.37
Emotional well-being	48.0 (10.3)	51.6	<0.0001
Energy	45.9 (11.2)	49.7	<0.0001
General Health	42.0 (9.3)	46.9	<0.0001
Social function	44.3 (10.3)	48.0	<0.0001
SF-36 v2.0 Composite scores (T-scores)			
Physical health	39.2 (10.0)	43.2	<0.0001
Mental health	48.3 (11.0)	51.5	0.0005

* Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the Medical Outcomes Study Sleep measure. *Sleep Medicine* 2005; 6(1): 41–4.

Ware JE, Kosinski M, Dewey JE. How to score Version 2 of SF-36 Health Survey. Lincoln, RI: Quality Metric Incorporated, 2000.

† MOS Sleep measure scales are scored such that 0=least extent of symptom (best) and 100=worst extent of symptom (worse).

§ SF-36 v2 scales are T-scores (mean = 50, SD = 10) calculated against a U.S. general population, where higher scores mean better HRQOL.

Table 3

Unique associations of types of sleep symptoms and Parkinson's disease severity, with health-related quality of life and depression, from multivariable regression models (n = 153)^{*}

Dependent variable (SF-36 scale or depression measure)	Independent variables from backward stepwise regression models					
	Types of sleep disturbances - MOS Sleep Scales			Disease severity		
	Awaken short of breath or with headache Coef. (95% CI) p-value	Sleep initiation disturbance Coef. (95% CI) p-value	Daytime Somnolence Coef. (95% CI) p-value	Sleep Inadequacy Coef. (95% CI) p-value	Hoehn & Yahr Coef. (95% CI) p-value	
SF-36 Physical function scale	—	-0.08 (-0.15, -0.03) 0.004	-0.12 (-0.19, -0.05) 0.0009	—	-6.64 (-8.53, -4.75) <0.0001	
SF-36 Role limitations – physical scale	-0.11 (-0.19, -0.02) 0.01	-0.08 (-0.14, -0.02) 0.02	-0.14 (-0.21, -0.06) 0.0008	—	-5.25 (-7.31, -3.21) <0.0001	
SF-36 Role limitations – emotional scale	-0.12 (-0.21, -0.02) 0.02	-0.10 (-0.17, -0.03) 0.007	—	—	-2.97 (-5.38, -0.56) 0.02	
SF-36 Pain scale	-0.13 (-0.22, -0.05) 0.003	—	-0.09 (-0.15, -0.03) 0.006	—	-1.77 (-3.90, 0.36) 0.10	
SF-36 Emotional well-being scale	-0.17 (-0.25, -0.09) <0.0001	-0.12 (-0.18, -0.06) 0.0001	—	—	-1.02 (-2.98, 0.94) 0.31	
SF-36 Energy scale	-0.17 (-0.25, -0.09) <0.001	-0.08 (-0.14, -0.01) 0.02	-0.13 (-0.21, -0.05) 0.002	—	-3.08 (-5.17, -0.99) 0.004	
SF-36 General Health scale	-0.09 (-0.16, -0.02) 0.01	-0.11 (-0.16, -0.05) 0.0001	-0.08 (-0.14, -0.01) 0.03	—	-2.49 (-4.26, -0.72) 0.006	
SF-36 Social function scale	-0.10 (-0.18, -0.02) 0.01	-0.08 (-0.14, -0.02) 0.009	-0.11 (-0.18, -0.04) 0.004	—	-3.86 (-5.82, -1.89) 0.0002	
SF-36 Physical health composite score	-0.10 (-0.17, -0.03) 0.005	-0.05 (-0.11, -0.01) 0.004	-0.13 (-0.20, -0.07) 0.0001	—	-5.22 (-6.94, -3.49) <0.0001	
SF-36 Mental health composite score	-0.15 (-0.23, -0.06) 0.001	-0.11 (-0.18, -0.05) 0.001	—	—	-1.13 (-3.29, 1.03) 0.30	
Depression – PHQ-9 [†]	0.07 (0.03, 0.12) 0.0007	—	—	0.06 (0.03, 0.09) 0.0002	1.46 (0.43, 2.49) 0.006	
Depression – GDS-15	0.05 (0.02, 0.07) <0.0001	0.05 (0.02, 0.07) <0.0001	—	—	0.59 (-0.07, 1.25) 0.08	

^{*} Each of the SF-36 scales and both depression measures served as dependent variables in 12 separate regression analyses. Backwards stepwise regression (MOS- Sleep scales into the model initially followed by removal of non-significant variables sequentially) was used to determine a reduced model with only significant sleep measure associations (i.e. p 0.05). All models include age, gender and Hoehn & Yahr disease severity/stage (off medication); only Hoehn & Yahr are shown in the table.

[†] Comorbidities was significant in model for Depression – PHQ-9; Coef (95%CI) = 0.86 (0.17, 1.55), p-value = 0.02.