ORIGINAL COMMUNICATION

The impact of sleep and mood disorders on quality of life in Parkinson's disease patients

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Abstract Sleep disturbances are common and often severe in patients with Parkinson's disease (PD) and their symptoms can be present at any time of day. The purpose of our study was to examine how excessive daytime sleepiness or poor nocturnal sleep quality and mood disorders influence the quality of life (QoL) in PD patients. Ninety-three PD patients from eastern Slovakia were recruited (49.5% males, mean age 68.0 ± 9.5 years, mean disease duration 6.1 ± 5.9 years). Sleep disturbances were measured using the Epworth Sleepiness Scale (ESS) and the Pittsburgh Sleep Quality Index (PSQI); QoL with the Parkinson's Disease Quality of Life Questionnaire (PDQ-

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39); depression and anxiety with the Hospital Anxiety and Depression Scale (HADS) and disease severity with the Unified Parkinson's Disease Rating Scale (UPDRS). γ^2 test, bivariate correlations and multiple linear regressions were performed. PSQI and ESS had significant correlations with worse QoL (p < 0.01, p < 0.05, respectively). HADS-D (p < 0.01), HADS-A (p < 0.01), UPDRS (p < 0.01) and disease duration (p < 0.05) were also significantly related to worse QoL. In the linear regression analysis, however, only PSQI (p < 0.01), anxiety (p < 0.001) and UPDRS (p < 0.001) remained significant. The model with PSOI explained 74% of the variance, and the model with ESS explained 63% of the variance in PDQ-39 when analyses were performed separately. In an overall model, however, only PSQI remained significant, accounting for 82% of the variance in PDQ-39. Nighttime poor sleep and anxiety are important contributors leading to a worse QoL. As these are treatable conditions, they should be recognized by clinicians and managed properly.

Keywords Parkinson's disease · Quality of sleep · Anxiety · Depression · Disease severity · Quality of life

Introduction

Sleep disorders are common and often severe in patients with Parkinson's disease (PD). Their symptoms can occur at any time of day or night. As many as 98% of PD patients suffer from nocturnal symptoms that can disturb their sleep [1]. Nighttime problems, such as reduced total sleep time and sleep efficiency, and an increased number of sleep arousals and fragmentations of sleep have all been reported in PD patients [1]. Sleep disturbance correlates with disease severity, cognitive decline and pain. Depression and anxiety are other factors strongly related to sleep problems [2, 3].

Excessive daytime sleepiness (EDS) can result in poor attention and memory and even in accidents. A study by Borek et al. [4] found that EDS correlated with depression, anxiety, disease duration, male gender and use of dopamine agonists. In the linear regression model they found only anxiety, male gender and disease duration to be significant predictors of EDS. The same study also evaluated nocturnal sleep disruption and found that the use of medication for depression and sleep disturbances significantly worsened poor nighttime sleep.

Patients with PD have lower quality of life (QoL) scores compared to the general population. Schrag et al. [5] and Karlsen et al. [6], using the Nottingham Health Profile, reported worse scores in the emotional reactions, energy, pain, sleep, social isolation and physical mobility domains, social functioning, physical role limitations and general health perceptions. Various clinical and psychosocial variables have been evaluated with regard to QoL. Disease severity [7], motor complications [8, 9], sleep problems [10], pain [11], cognitive decline [12, 13], depression [7] and anxiety [14], have all been found to significantly worsen QoL. Karlsen et al. [15] found a significant relationship between older age and the physical mobility domain, while other studies did not report such a relationship [6]. Longer disease duration was a significant predictor of the worse QoL domains [8]. Female gender was also associated with worse QoL [16].

The aim of our study was to evaluate how sleep problems—poor quality of sleep or daytime somnolence, mood disorders and disease severity—affect quality of life, controlled for age, gender and disease duration.

Methods

Patients

This cross-sectional study evaluated quality of life and sleep disturbances in a study population of 93 patients with Parkinson's disease. The patients were recruited from one hospital (10 patients) and 18 outpatient departments (83 patients) in the east Slovakian region between February 2004 and November 2005. All patients were diagnosed in accordance with the UK PD Society Brain Bank Clinical Criteria [17] and their mental abilities were assessed with the Mini-Mental State Examination (MMSE) [18]. Exclusion criteria were as follows: (1) MMSE lower than 24, as well as a negative response to an acute levodopa challenge, (2) secondary parkinsonism, (3) sign of brain ischemia revealed by computer tomography (CT), (4) patients with thyroid pathological hormone levels, (5) severe comorbidity associated with the study variables—severe diseases, where we expected patients not to survive for at least 4 years, or which could confound the main variables in our study, such as quality of life and fatigue (e.g., rheumatoid diseases, end stage renal diseases and others).

The study was approved by the local Ethics Committee. Informed consent was obtained from each patient prior to the study.

Data collection

All the PD patients found in the database records from outpatient neurologists and hospitals were asked for participation by means of a mailed questionnaire comprised of questions on sociodemographic background, medical history and current medication, and self-report questionnaires: the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Hospital Anxiety and Depression Scale (HADS) and Parkinson's Disease Quality of Life Questionnaire (PDQ-39). After 3 weeks, all patients were invited for an interview on relevant issues that were not part of the questionnaires and were checked for inclusion and exclusion criteria. After this structured interview, a neurologist assessed the disease severity of each patient using the Unified Parkinson's Disease Rating Scale (UP-DRS) Version 3.0 [19], including Hoehn and Yahr staging [20] and the Schwab and England disability scale [21]. All of the examined patients were in the ON stage during the interview and neurological examination. Patients who were not able to fill in the questionnaires due to impairment of their vision or motor impairment of their hands answered the questions during an oral interview. Caregivers were not allowed to provide questionnaires inputs.

Measures

Sleep disorders

The Pittsburgh Sleep Quality Index (PSQI) [22] was used to assess nighttime sleep problems. PSQI assesses global sleep quality and disturbances in sleep patterns during the previous month in seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. Scoring of the answers ranges from 0 (no difficulty) to 3 (severe difficulty). Each component has possible scores of 0–3, where 3 indicates the negative extreme. The global PSQI score is the sum of all the component scores (range 0–21), with a score of 5 or more indicating a poor sleeper. This instrument was found to have good internal consistency, with a Cronbach's alpha coefficient of 0.81 in our sample. For evaluation of daytime somnolence the Epworth Sleepiness Scale (ESS) [23] was used. ESS relies on measuring dozing behavior in eight different situations. The questionnaire asks the respondent to rate the likelihood of falling asleep on a scale were 0 indicates no chance and 3 represents the greatest chance of dozing. The total ESS score is the sum of all the responses and ranges from 0 to 24. A score of 10 was used as the cutoff point for normal, while scores above this imply pathological sleepiness. This instrument has been found to have good psychometric properties in PD patients [24] with a Cronbach's alpha coefficient of 0.84 in our sample.

Mood disorders

Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS). This selfadministered scale simultaneously evaluates anxiety (HADS-A) and depression (HADS-D). It consists of 14 items (7 for the assessment of anxiety and 7 for the assessment of depression) scoring from 0 (no problem) to 3 (extreme problem). The cutoff values proposed by the HADS developers [25] were applied in order to determine the proportion of patients considered as unimpaired (not depressed, scoring \leq 7 on each subscale), possibly impaired (8–10 on each subscale), or probably impaired (\geq 11 on each subscale). In the present study Cronbach's alpha was 0.69 for anxiety and 0.79 for the depression subscale.

Disease severity

The Unified Parkinson's Disease Rating Scale is a foursubscale combined instrument for assessing mental state, activities of daily living, motor examination and complications. Two further instruments are used together with the UPDRS, namely: (1) a modified Hoehn and Yahr Staging, and (2) the Schwab and England Scale. It is currently used as a standard reference scale in clinical practice and research [19–21]. For our research we used the UPDRS-III section.

Quality of life

Quality of life was assessed using the Parkinson's Disease Quality of Life Questionnaire (PDQ-39) as the primary outcome measure [26]. It is comprised of 39 questions, each of them using a five-point ordinal scoring system ranging from 0 (never had this problem) to 4 (always have this problem), from which a single summary index can be calculated. For the summary index the scores were standardized from 0 to 100, so that higher scores indicate poorer life quality. PDQ-39 has been shown to be feasible, reliable, valid, and responsive to change in patients with PD and to have good internal consistency [27]; in our sample Cronbach's alpha was 0.94.

Basic sociodemographic data (age, gender) and disease duration were obtained from a structured interview.

Statistical analysis

Discrete variables were compared using the χ^2 test. Continuous variables were normally distributed in the current study (Shapiro–Wilk, p > 0.05), and therefore, for comparisons between the samples, the Student's t test was used and in the table means \pm standard deviations (SD) are presented. Initial correlations between the study variables were made, and then hierarchical regression analyses were performed in order to determine the relative strength of the effects of age, gender and disease duration, UPDRS, HADS-A and HADS-D and PSQI on Quality of Life; the variables were entered in this order into the analysis using the enter method. The same method was then used with the ESS in place of the PSQI. As a final step, multiple linear regression analysis was performed with the PSOI and the ESS together, using the enter method. These analyses were performed using the statistical software program SPSS 14.0 for windows.

Results

Descriptive data

Of the 218 PD patients who met the inclusion criteria, 14 did not wish to participate in the study and 91 did not respond to the invitation. The total response rate was 43.0%. Out of those who agreed to participate, 7 patients were eliminated because of the exclusion criteria, 13 patients were not included because of missing data (these patients agreed to participate in the study, filled in the questionnaire, but refused to come for the oral interview including the MMSE testing), and 93 remained for analysis. Non-responders did not differ significantly from the analyzed group in age, as measured by the Student's *t* test (mean age of responders: 68.0 ± 9.5 years, of non-responders 71.8 ± 8.1 years, *t* test sig 0.280, CI -0.91 to 0.069), or gender using the χ^2 test (difference between proportions 0.095, SE = 0.066, 95% CI -0.0343 to 0.224) [28].

Ninety-three patients (46 men, 49.5%) completed the questionnaire. The mean age of the patients was 68.0 ± 9.5 years. Mean disease duration was 6.1 ± 5.9 years. The total UPDRS—ON stage was 35.3 ± 20.4 , Hoehn and Yahr Staging (H&Y) was 2.0 ± 1.2 , in 69.9% patients this was ≤ 2.0 , which means that most of our patients had mild parkinsonian symptoms. Patients were treated with

dopamine agonists or with L-dopa alone, or in different combinations: dopamine agonists 22.6%, L-dopa 10.7%, L-dopa + COMT inhibitors 12.9%, L-dopa + dopamine agonists 8.6%, L-dopa + COMT inhibitor + dopamine agonists 6.5%; another therapy was used in 38.7% of patients. 73.1% had sleep problems during the night and 23.7% suffered from sleepiness. Details of the clinical profile and the study variables of the patients stratified by H&Y are shown in Table 1. We found no significant differences in age, gender or disease severity between the group of patients who were able to fill out the questionnaires by themselves and those who filled them out during an interview.

Bivariate correlations between QoL and study variables

Table 2 presents the correlations between sociodemographic variables, disease severity, mood disorders,

Table 1 Demographic and clinical characteristics, psychological distress and self-reported health-related functioning stratified by $H\&Y \le 2.0$ versus > 2.0

Age in years (mean \pm SD)67.8 \pm 8.270.3 \pm 10.8NS ^a Male n (%)33 (50.7)12 (42.9)NS ^b Female n (%)52 (49.3)16 (57.1)Disease Duration (mean \pm SD)5.43 \pm 4.38.06 \pm 5.2NS ^a UPDRSUPDRS11.0 \pm 6.127.2 \pm 9.60.001 ^a UPDRS-III11.0 \pm 6.127.2 \pm 9.60.001 ^a -36.9 to -21.9UPDRS-IV2.2 \pm 2.14.7 \pm 3.70.001 ^a -36.0 to -1.1S&E80.1 \pm 13.246.7 \pm 19.30.01 ^a -3.8 to -1.1S&E50.7 n (%)14 (21.5)26 (92.8)0.001 ^b S&E \leq 70% n (%)51 (78.5)2 (7.2)HADS-DHADS-D \geq 11 n (%)58 (89.2)23 (82.1)NSHADS-D \geq 11 n (%)7 (10.8)5 (17.9)HADS-AHADS-A \geq 1118 (27.7)8 (28.6)PSQIPSQI \geq 519 (29.2)4 (14.3)NSPSQI \leq 519 (29.2)4 (14.3)NSPSQI \leq 519 (29.2)14 (50)NSESS \leq 1019 (29.2)14 (50)NSESS \leq 1019 (29.2)14 (50)NSESS \leq 1010 (10.7)Dopamine agonists21 (22.6) ι -dopa + dopamine agonists21 (22.6) ι -dopa + dopamine agonists6 (6.5)UPOR10 (10.7)Dopamine agonists6 (6.5)UCMT inhibitor + dopamine agonists6 (6.5)UPOR10 (10.7)Dopamine agonists6 (6.5)UCMT inhibitor + dopamine agonists <td< th=""><th>Patient characteristics (total)</th><th>Hoehn and Yahr ≤ 2.0 N = 65</th><th>Hoehn and Yahr >2.0 $N = 28$</th><th>Р</th><th>95% CI differences between H&Y ≤2.0 versus >2.0</th></td<>	Patient characteristics (total)	Hoehn and Yahr ≤ 2.0 N = 65	Hoehn and Yahr >2.0 $N = 28$	Р	95% CI differences between H&Y ≤2.0 versus >2.0
Male n (%)33 (50.7)12 (42.9)NS ^b Female n (%)32 (49.3)16 (57.1)Disease Duration (mean \pm SD)5.43 \pm 4.38.06 \pm 5.2NS ^a UPDRS5.43 \pm 4.38.06 \pm 5.2NS ^a UPDRS total-ON stage26.2 \pm 12.25.7 \pm 19.90.001 ^a -36.9 to -21.9UPDRS-III11.0 \pm 6.127.2 \pm 9.60.001 ^a -36.9 to -12.5UPDRS-IV2.2 \pm 2.14.7 \pm 3.70.001 ^a -3.8 to -1.1S&ES&E80.1 \pm 13.246.7 \pm 19.30.01 ^a 2.6 0 to 41.1S&E570% n (%)14 (21.5)26 (92.8)0.001 ^b -2.1 (1.1 (1.1 (1.1 (1.1 (1.1 (1.1 (1.1 (Age in years (mean \pm SD)	67.8 ± 8.2	70.3 ± 10.8	NS ^a	
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UPDRS total-ON stage 262 ± 12.2 55.7 ± 19.9 0.001^a -36.9 to -21.9 UPDRS-III 11.0 ± 6.1 27.2 ± 9.6 0.001^a -19.9 to -12.5 UPDRS-IV 2.2 ± 2.1 4.7 ± 3.7 0.001^a -3.8 to -1.1 S&E 80.1 ± 13.2 46.7 ± 19.3 0.01^a 26.0 to 41.1 S&E > 70% n (%) $51 (78.5)$ $26 (92.8)$ 0.001^b S&E > 70% n (%) $51 (78.5)$ 27.2 NSHADS-D 6.15 ± 3.6 7.7 ± 4.2 NSHADS-D $\geq 11 n (\%)$ $58 (89.2)$ $23 (82.1)$ NSHADS-A $\geq 11 n (\%)$ $7 (10.8)$ $5 (17.9)$ -12.5 HADS-A $\geq 11 n (\%)$ 8.2 ± 3.9 8.4 ± 3.9 NSHADS-A $\geq 11 n (\%)$ $8(27.7)$ $8 (28.6)$ -12.5 PSQI 86 ± 4.8 10.2 ± 4.7 NSPSQI ≥ 5 $19 (29.2)$ $4 (14.3)$ NSPSQI ≤ 5 $46 (70.8)$ $24 (85.7)$ $-12.5 (10.9)^2$ ESS > 10 $10 (10.7)$ 11 ± 17.8 $0.001 - 32.5$ to -9.7 Antiparkinsonian drugs ⁶ $11 (22.6)$ -11 ± 17.8 $0.001 - 32.5$ to -9.7 Antiparkinsonian drugs ⁶ $12 (12.9)$ $-14 (50.5)$ -11 ± 17.8 -11 ± 17.8 $-40pa + COMT inhibitors21 (22.6)-11 \pm 17.8-12 \pm 1.5 \pm 1$	UPDRS				
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UPDRS-IV 2.2 ± 2.1 4.7 ± 3.7 0.01^a -3.8 to -1.1 S&E80.1 ± 13.2 46.7 ± 19.3 0.01^a 26.0 to 41.1 S&E $\leq 70\%$ n (%)14 (21.5) 26 (92.8) 0.001^b S&E > 70\% n (%)51 (78.5) 2 (7.2)HADS-D 6.15 ± 3.6 7.7 ± 4.2 NSHADS-D ≥ 11 n (%)58 (89.2) 23 (82.1)NSHADS-D < 11 n (%)	UPDRS-III	11.0 ± 6.1	27.2 ± 9.6	0.001^{a}	-19.9 to -12.5
S&E 80.1 ± 13.2 46.7 ± 19.3 0.01^a $26.0 to 41.1$ S&E < 70% n (%)	UPDRS-IV	2.2 ± 2.1	4.7 ± 3.7	0.001^{a}	-3.8 to -1.1
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$\&\&E > 70\% n (\%)$ $51 (78.5)$ $2 (7.2)$ $HADS-D$ 6.15 ± 3.6 7.7 ± 4.2 NS $HADS-D \ge 11 n (\%)$ $58 (89.2)$ $23 (82.1)$ NS $HADS-D < 11 n (\%)$ $7 (10.8)$ $5 (17.9)$ $HADS-A$ 8.2 ± 3.9 8.4 ± 3.9 NS $HADS-A \le 11$ $47 (72.3)$ $20 (71.4)$ NS $HADS-A < 11$ $18 (27.7)$ $8 (28.6)$ $PSQI$ 8.6 ± 4.8 10.2 ± 4.7 NS $PSQI \ge 5$ $19 (29.2)$ $4 (14.3)$ NS $PSQI < 5$ $46 (70.8)$ $24 (85.7)$ $ESS > 10$ $19 (29.2)$ $14 (50)$ NS $ESS > 10$ $9 (29.2)$ $14 (50)$ NS $PSQI < 5$ $10 (10.7)$ $10 (10.7)$ $Dc.39$ summary index $29 + 17.9$ 51.1 ± 17.8 $0.001 - 32.5$ to -9.7 $Artiparkinsonian drugs^c$ $10 (10.7)$ $12 (12.9)$ $14 (50)$ $L-dopa + COMT inhibitors$ $12 (12.9)$ $14 (50)$ $14 (50)$ $L-dopa + COMT inhibitor + dopamine agonists8 (8.6)14 (50)14 (50)L-dopa + COMT inhibitor + dopamine agonists6 (6.5)10 (10.7)L-dopa + COMT inhibitor + dopamine agonists6 (6.5)10 (10.7)$	$S\&E \le 70\% \ n \ (\%)$	14 (21.5)	26 (92.8)	0.001 ^b	
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HADS-D \geq 11 n (%)58 (89.2)23 (82.1)NSHADS-A 11 n (%)7 (10.8)5 (17.9)HADS-A8.2 \pm 3.98.4 \pm 3.9NSHADS-A \geq 1147 (72.3)20 (71.4)NSHADS-A < 11	HADS-D	6.15 ± 3.6	7.7 ± 4.2	NS	
HADS-D < 11 n (%)7 (10.8)5 (17.9)HADS-A8.2 \pm 3.98.4 \pm 3.9NSHADS-A \geq 1147 (72.3)20 (71.4)NSHADS-A < 11	HADS-D \geq 11 n (%)	58 (89.2)	23 (82.1)	NS	
HADS-A 8.2 ± 3.9 8.4 ± 3.9 NSHADS-A ≥ 11 47 (72.3)20 (71.4)NSHADS-A < 11 18 (27.7) $8 (28.6)$ PSQI 8.6 ± 4.8 10.2 ± 4.7 NSPSQI ≥ 5 19 (29.2)4 (14.3)NSPSQI < 5 46 (70.8)24 (85.7)ESS7.1 ± 4.4 9.1 ± 5.6 NSESS ≤ 10 19 (29.2)14 (50)NSPDQ-39 summary index29.9 ± 17.9 51.1 ± 17.8 $0.001 - 32.5$ to -9.7 Antiparkinsonian drugs ^c 1(22.6)1L-dopa21 (22.6)111L-dopa + COMT inhibitors21 (22.9)11L-dopa + COMT inhibitor + dopamine agonists6 (6.5)11Other36 (38.7)111	HADS-D < 11 n (%)	7 (10.8)	5 (17.9)		
HADS-A \geq 1147 (72.3)20 (71.4)NSHADS-A < 11	HADS-A	8.2 ± 3.9	8.4 ± 3.9	NS	
HADS-A < 1118 (27.7)8 (28.6)PSQI 8.6 ± 4.8 10.2 ± 4.7 NSPSQI > 519 (29.2)4 (14.3)NSPSQI < 5	HADS-A ≥ 11	47 (72.3)	20 (71.4)	NS	
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PSQI \geq 519 (29.2)4 (14.3)NSPSQI $<$ 546 (70.8)24 (85.7)ESS7.1 \pm 4.49.1 \pm 5.6NSESS $>$ 1046 (70.8)14 (50)NSESS \leq 1019 (29.2)14 (50)NSPDQ-39 summary index29.9 \pm 17.951.1 \pm 17.80.001 $-$ 32.5 to $-$ 9.7Antiparkinsonian drugs ^c 10 (10.7)12 (22.6)12 (22.6)L-dopa + COMT inhibitors12 (12.9)12 (12.9)L-dopa + dopamine agonists6 (6.5)6 (6.5)Other36 (38.7)36 (38.7)	PSQI	8.6 ± 4.8	10.2 ± 4.7	NS	
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ESS ≤ 10 19 (29.2)14 (50)PDQ-39 summary index29.9 \pm 17.951.1 \pm 17.80.001 - 32.5 to - 9.7Antiparkinsonian drugs°10 (10.7)L-dopa10 (10.7)Dopamine agonists21 (22.6)L-dopa + COMT inhibitors12 (12.9)L-dopa + dopamine agonists8 (8.6)L-dopa + COMT inhibitor + dopamine agonists6 (6.5)Other36 (38.7)	ESS > 10	46 (70.8)	14 (50)	NS	
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L-dopa + dopamine agonists8 (8.6)L-dopa + COMT inhibitor + dopamine agonists6 (6.5)Other36 (38.7)	L-dopa + COMT inhibitors	12 (12.9)			
L-dopa + COMT inhibitor + dopamine agonists 6 (6.5) Other 36 (38.7)	L-dopa + dopamine agonists	8 (8.6)			
Other 36 (38.7)	L-dopa + COMT inhibitor + dopamine agonists	6 (6.5)			
	Other	36 (38.7)			

UPDRS Unified Parkinson's Disease Rating Scale, *S&E* Schwab and England Scale, *H&Y* Hoehn and Yahr Staging, *HADS* Hospital Anxiety and Depression Scale, *HADS-A* anxiety, *HADS-D* depression, (\geq 11 represents probable impairment), *PSQI* Pittsburgh Sleep Quality Index (\geq 5 indicates poor sleeper), *ESS* Epworth Sleepiness Scale(>10 is considered as pathological sleepiness), *PDQ-39* Parkinson's Disease Quality of Life Questionnaire

^a t Test, ^bFisher exact test, ^cwe did not stratify antiparkinsonian drugs according to H&Y because of analysing cells with observations less than n = 5 is not possible

Table 2 Bivariate correlations between quality of life and sociodemographic and clinical variables

	Age	Gender	Disease duration	UPDRS	HADS-D	HADS-A	PSQI	ESS
Gender	-0.04							
Disease duration	0.10	-0.03						
UPDRS-III	0.13	-0.10	0.24*					
HADS-D	0.09	0.14	0.19	0.38**				
HADS-A	-0.19	0.14	0.07	0.35**	0.48**			
PSQI	-0.03	0.09	0.15	0.30*	0.28*	0.38**		
ESS	0.12	-0.01	0.16	0.23	0.28*	0.36*	0.08	
PDQ-39 SI	0.10	0.01	0.29*	0.76**	0.57**	0.60**	0.46**	0.27*

Displayed are Pearson's coefficients

UPDRS Unified Parkinson's Disease Rating Scale, total score, HADS Hospital Anxiety and Depression Scale (HADS-D for depression, HADS-A for anxiety), PSQI Pittsburgh Sleep Quality Index, ESS Epworth Sleepiness Scale, PDQ-39 SI Parkinson's Disease Quality of life Questionnaire Summary Index

* p < 0.05, ** p < 0.01, *** p < 0.001

daytime and nighttime sleep disturbances, and the quality of life summary index. The PDQ-39 summary index correlated significantly with higher UPDRS-III (p < 0.01), increased levels of HADS-A and HADS-D (both p < 0.01), a higher PSQI score (p < 0.01) and higher ESS scores (p < 0.01). Sleep problems correlated positively with both HADS-D (p < 0.05) and HADS-A (p < 0.01), but only PSQI showed a significant correlation with higher UPDRS scores (p < 0.05). No significant correlations were found between ESS and UPDRS-III.

Multiple regression analysis: Associations of QoL and study variables

A series of linear regression analyses was performed in order to evaluate the influence of difficulties of sleep and mood disorders on quality of life; they are summarized in Tables 3 and 4. The variables were entered in hierarchical order into a linear regression model using the enter method in order to evaluate the changes in explained variance in PDQ-39. Table 3 shows the analysis for PSQI and ESS separately, and Table 4 shows the analysis for PSQI and ESS together.

PSQI explained 7% of the variance, with a significant ΔR^2 change (β 0.30, p = 0.000), while ESS did not contribute to PDQ-39 (β 0.01, p = 0.582, ΔR^2 0.01 was not significant). UPDRS was significant in all the models (β 0.50, respectively, 0.49, p = 0.000). Anxiety was another variable that significantly explained 29%, respectively, 28% of the variance (β 0.38–0.48, p = 0.000). Depression was not a significant predictor of QoL in our sample (β 0.13–0.18) in any of the models in our sample

Variables F	PDQ-39	PDQ-39 Summary Index			Variables	PDQ-39 Summary Index			
	β	р	ΔR^2	Adjusted R^2		β	р	ΔR^2	Adjusted R^2
1. Age	-0.04	0.59			1. Age	0.01	0.92		
Gender	0.10	0.18			Gender	0.04	0.60		
Disease duration	0.01	0.91	0.07	0.10	Disease duration	0.03	0.70	0.07	0.02
2.UPDRS-III	0.50	0.00	0.33***	0.35	2. UPDRS-III	0.49	0.00	0.30***	0.32
3. HADS-A	0.38	0.00	0.29 ***	0.65	3. HADS-A	0.48	0.00	0.28***	0.61
4. HADS-D	0.13	0.12	0.02	0.66	4. HADS-D	0.18	0.06	0.02	0.63
5. PSQI	0.30	0.00	0.07***	0.74	5. ESS	0.01	0.96	0.01	0.63
Adjusted R^2				0.74	Adjusted R^2				0.63

Table 3 Multiple linear regression analysis

Associations of sleep disorders, disease severity and mood disorders with quality of life, separately for quality of sleep and for excessive daytime somnolence (controlled for age, gender and disease duration). Linear regression model. Variables entered in a hierarchical way in 5 blocks—(1) age, gender and disease duration, (2) UPDRS total score, (3) anxiety, (4) depression and (5) PSQI or ESS

UPDRS-III Unified Parkinson's Disease Rating Scale, part III, HADS-A Hospital Anxiety and Depression Scale, anxiety subscale, HADS-D Hospital Anxiety and Depression Scale, depression subscale, PSQI Pittsburgh Sleep Quality Index, ESS Epworth Sleepiness Score

* p < 0.05, ** p < 0.01, *** p < 0.001, represents the significance of R^2 change. The variable p and the β represent final values, after all the steps are performed, while adjusted R^2 and ΔR^2 are the values after each step

	Table 4	Multiple	linear	regression	analysis
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Variables	PDQ-39 Summary Index						
	β	р	ΔR^2	Sig. F Change	Adjusted R^2		
1. Age	-0.06	0.443					
Gender	0.10	0.180					
Disease duration	-0.02	0.850	0.06	0.33	0.01		
2. UPDRS-III	0.48	0.000	0.33	0.00	0.35		
3. HADS-A	0.35	0.001	0.29	0.00	0.65		
4. HADS-D	0.14	0.101	0.02	0.08	0.67		
5. PSQI	0.31	0.000	0.07	0.00	0.74		
6. ESS	0.09	0.283	0.01	0.28	0.74		
Adjusted R^2					0.74		

Associations of sleep disorders, disease severity and mood disorders with quality of life (controlled for age, gender and disease duration). Linear regression model. Variables entered in a hierarchical way in 6 blocks—1. age, gender and disease duration, 2. UPDRS part III, 3. anxiety, 4. depression, 5. PSQI and 6. ESS

UPDRS-III Unified Parkinson's Disease Rating Scale, part III, HADS-A Hospital Anxiety and Depression Scale, anxiety subscale, HADS-D Hospital Anxiety and Depression Scale, depression subscale, PSQI Pittsburgh Sleep Quality Index, ESS Epworth Sleepiness Score

The variable *p* and the β represent final values, after all the steps are performed, while adjusted R^2 and ΔR^2 are the values after each step

(β 0.13–0.18). The model with PSQI explained 74%, the model with ESS 63%, and the overall model explained 74% of the variance.

Discussion

Sleep disorders

Our results show that sleep problems play an important role in the lives of the PD patients. Of our patients, 73.1% were poor sleepers during the nighttime. Adler et al. [2] reported the occurrence of nocturnal sleep disturbances in 60–98% of PD patients, whereas in a more recent study, Martinez-Martin et al. [29] reported insomnia in 45.7% of patients, using the Nonmotor Symptoms Questionnaire. Excessive daytime sleepiness was reported in 23.7% of our sample. Martinez-Martin [29] reported sleepiness in 31.1% of PD patients. In 71 idiopathic PD patients depression but also PD severity were predictors of reduced sleep quality [30].

In our study, sleep disorders correlated significantly with depression and anxiety, with the observed associations stronger for anxiety than for depression. In their longitudinal study of insomnia and depression in young adults, Buysse et al. [31] showed a strong relationship between these two symptoms. Our research in PD patients shows

significant correlations of sleep disturbances and mood disorders. These results are partly similar to the observations of Borek et al. [4], who, in a sample of 185 PD patients, found depression to have a significant association with worse PSQI scores. In their study, the use of sleep medication also appeared to be a significant predictor of worse PSQI scores, though anxiety and disease duration were not. Anxiety was also a significant predictor of worse ESS scores, together with male gender and longer disease duration, but depression and the use of dopamine agonists were not. A study by Pal et al. [3] in a sample of 40 PD patients and 23 of their caregivers showed significant correlations between nighttime sleep problems and depression and anxiety. Additionally, poor nocturnal sleep showed a relationship with worse UPDRS scores.

Sleep disorders and QoL

Quality of life showed significant correlations with poor quality of nighttime sleep as well as with excessive daytime sleepiness. Different results were obtained when analyzing separately for the model with PSQI and for the model with ESS. PSQI appeared to be a significant predictor of QoL, but ESS was not. A study by McKinlay et al. [32] with 49 patients did not report sleep disturbances influencing QoL, but only one item of UPDRS was used for measuring sleep. A study by Weintraub et al. [33] showed ESS as having no significant relationship with disability (measured by UPDRS–ADL score) in a sample of 114 PD patients. Nocturnal sleep disturbances measured with the disease specific Parkinson's Disease Sleep Scale correlated with worse QoL in a study of 77 PD patients by Scaravilli [10].

Mood disorders and QoL

Mood disorders are currently recognized as important nonmotor features of PD, and depression especially is thought to worsen QoL in PD patients [33]. The prevalence of depression in our sample is less common compared to previous studies [32, 33], although rates of depression in PD vary from 4 to 75%, based on selection of a study population, diagnostic criteria and the instrument use for measurement [34]. The prevalence of anxiety is consistent with other studies [29, 31].

However, our results show only anxiety as being a significant factor associated with QoL, in both the model with PSQI and the model with ESS. Depression was not significant in either model. A study by McKinlay et al. [32] in a sample of 49 PD patients, a study by Carod-Artal [14] in 115 PD patients and a study by Gómez-Esteban et al. [35] in 99 patients report depression as well as anxiety as being important factors related to QoL. A recent review of the HADS-A and HADS-D concluded that, although these instruments may be useful in Parkinson's disease for screening PD patients, they are not useful for adequately defining the severity of depression in this population [36]. For the future it might be worth considering the use of the HADS as well as a disease-specific instrument for testing depression in PD patients. In addition, in our study, the patients were recruited from outpatient departments, so the sample consisted only of patients who were able and motivated to come in for examination and interview formed the sample. Most of them were the patients with mild parkinsonian symptoms, which also could have influenced the results.

Sociodemographic and clinical variables and QoL

Female gender was found to be a factor related to QoL in the model with PSQI. This result is similar to the finding of Behari et al. [16], who also reported female gender as worsening QoL. Karlsen et al. [15] found a significant relationship of higher age with the worse physical mobility domain of QoL, while a study by Weintraiub et al. [33] did not report such a relationship. Chapuis et al. [8] found longer disease duration to be a significant predictor of worse QoL domains.

Disease severity was another factor significantly influencing QoL in both models. Previously published papers have shown conflicting results. The studies by Chapuis et al. [8] and Gomez-Esteban et al. [37] reported worse functional status as being related with worse QoL, while Karlsen [6] did not find such a relationship.

Limitations

The relatively low response rate is the main limitation of our study. Patients were recruited mostly from outpatient neurologists, not from a specialized center for PD care, and only those who agreed to participate were included. For this reason, only patients who were able to come for the examination and interview-either alone or with a family member as a companion-formed our sample, a sample with lower UPDRS motor scores. Thus, a number of patients with moderate to severe disease were not included in our research, meaning the sample is not representative for all PD patients. Despite this fact, even this sample reported a high prevalence of sleep and mood problems, worsening quality of life, so we expect these factors to be even worse in the total PD patients group. A further possible limitation of this study may be the use of a generic instrument for measuring sleep problems because we wanted to be able to compare such problems across diseases and when this study started the PDSS was not that frequently used.

Clinical implications

Sleep problems, anxiety and depression must all be assessed in every PD patient and managed properly. The treatment of disturbed nocturnal sleep should include recommendations for sleep hygiene—the maintenance of a regular sleep–wake cycle, bed-time sleep restriction, the avoidance of frequent naps during the day, moderate daytime physical exercise and exposure to bright light in the daytime, especially towards evening in order to counteract any tendency towards anticipation of the sleep phase.

Conclusions

Although sleep problems are not fully understood in their etiology (psychosocial determinants, treatment, neurodegeneration may play a role) [38], they are now regarded as important among the nonmotor symptoms of PD, closely associated, together with mood disorders, with worse QoL. Our study documents the importance of poor sleep at night and stresses not only the recognition of depression, but also the significant importance of anxiety within the factors having an impact on QoL. By influencing potentially treatable conditions, clinicians could improve the QoL of PD patients.

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Conflict of interest None.

References

- 1. Playfer J, Hindle J (2008) Parkinson's disease in the older patient, 2nd edn. Radcliffe Publishing Ltd, Abingdon
- Adler CH, Thorpy MJ (2005) Sleep issues in Parkinson's disease. Neurology 64(12 Suppl 3):S12–S20
- Pal PK, Thennarasu K, Fleming J et al (2004) Nocturnal sleep disturbances and daytime dysfunction in patients with Parkinson's disease and in their caregivers. Parkinsonism Relat Disord 10(3):157–168
- 4. Borek LL, Kohn R, Friedman JH (2006) Mood and sleep in Parkinson's disease. J Clin Psychiatry 67(6):958–963
- Schrag A, Jahanshahi M, Quinn N (2000) How does Parkinson's disease affect quality of life? A comparison with quality of life in the general population. Mov Disord 15(6):1112–1118
- Karlsen KH, Tandberg E, Arsland D, Larsen JP (2000) Health related quality of life in Parkinson's disease: a prospective longitudinal study. J Neurol Neurosurg Psychiatry 69(5):584–589
- Global Parkinson's Disease Survey Steering Committee (2002) Factors impacting on quality of life in Parkinson's disease: results from an international survey. Mov Disord 17(1):60–67

- Chapuis S, Ouchchane L, Metz O, Gerbaud L, Durif F (2005) Impact of the motor complications of Parkinson's disease on the quality of life. Mov Disord 20(2):224–230
- Pechevis M, Clarke CE, Vieregge P, Khoshnood B, Deschaseaux-Voinet C, Berdeaux G et al (2005) Effects of dyskinesias in Parkinson's disease on quality of life and health-related costs: a prospective European study. Eur J Neurol 12(12):956–963
- Scaravilli T, Gasparoli E, Rinaldi F, Polesello G, Bracco F (2003) Health-related quality of life and sleep disorders in Parkinson's disease. Neurol Sci 24(3):209–210
- Quittenbaum BH, Grahn B (2004) Quality of life and pain in Parkinson's disease: a controlled cross-sectional study. Parkinsonism Relat Disord 10(3):129–136
- Schrag A, Jahanshahi M, Quinn N (2000) What contributes to quality of life in patients with Parkinson's disease? J Neurol Neurosurg Psychiatry 69(3):308–312
- Park A, Stacy M (2009) Non-motor symptoms in Parkinson's disease. J Neurol 256(Suppl 3):S293–S298
- Carod-Artal FJ, Ziomkowski S, Mesquita HM, Martinez-Martin P (2008) Anxiety and depression: main determinants of healthrelated quality of life in Brazilian patients with Parkinson's disease. Parkinsonism Relat Disord 14(2):102–108
- Karlsen KH, Larsen JP, Tandberg E, Maeland JG (1999) Influence of clinical and demographic variables on quality of life in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 66(4):431–435
- Behari M, Srivastava AK, Pandey RM (2005) Quality of life in patients with Parkinson's disease. Parkinsonism Relat Disord 11(4):221–226
- Hughes AJ, Daniel SE, Kilford L, Lees AJ (1992) Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinicopathological study of 100 cases. J Neurol Neurosurg Psychiatry 55(3):181–184
- Folstein MF, Folstein SE, McHugh PR (1975) Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12(3):189–198
- Fahn S, Elton RL (1987) Members of the UPDRS development committee. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne DB, Lieberman A (eds) Recent developments in Parkinson's disease, vol 2. MacMillan Healthcare Information, Florham Park, pp 153–163
- Hoehn MM, Yahr MD (1967) Parkinsonism: onset, progression and mortality. Neurology 17(5):427–442
- Schwab RS, England AC (1969) Projection technique for evaluating surgery in Parkinson's disease. In: Gillingham FJ, Donaldson IMI (eds) Third symposium on surgery in Parkinson's disease. Edinburg, Livingstone, pp 152–157
- Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. Psychiatry Res 28(2):193–213
- Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14(6):540–545
- Hagell P, Broman JE (2007) Measurement properties and hierarchical item structure of the Epworth sleepiness scale in Parkinson's disease. J Sleep Res 16(1):102–109

- Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatr Scand 67(6):361–370
- 26. Peto V, Jenkinson C, Fitzpatrick R, Greenhall R (1995) The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. Qual Life Res 4(3):241–248
- Marinus J, Ramaker C, van Hilten JJ, Stiggelbout AM (2002) Health related quality of life in Parkinson's disease: a systematic review of disease specific instruments. J Neurol Neurosurg Psychiatry 72(2):241–248
- Newcombe RG, Altman DG (2005) Proportions and their differences. In: Altman DG, Machin D, Bryant TN, Gardner MJ (eds) Statistics with confidence. British Medical Journal, Bristol, pp 45–56
- Martinez-Martin P, Schapira AH, Stocchi F, Sethi K, Odin P, MacPhee G et al (2007) Prevalence of nonmotor symptoms in Parkinson's disease in an international setting; study using nonmotor symptoms questionnaire in 545 patients. Mov Disord 22(11):1623–1629
- Perez-Lloret S, Rossi M, Nouzeille MI, Trenkwalder C, Cardinali DP, Merello M (2009) Parkinson's disease sleep scale, sleep logs, and actigraphy in the evaluation of sleep in parkinsonian patients. J Neurol 256:1480–1484
- Buysse DJ, Angst J, Gamma A, Ajdacic V, Eich D, Rössler W (2008) Prevalence, course, and comorbidity of insomnia and depression in young adults. Sleep 31(4):473–480
- 32. McKinlay A, Grace RC, Dalrymple-Alford JC, Anderson T, Fink J, Roger D (2008) A profile of neuropsychiatric problems and their relationship to quality of life for Parkinson's disease patients without dementia. Parkinsonism Relat Disord 14(1):37–42
- Weintraub D, Moberg PJ, Duda JE, Katz IR, Stern MB (2004) Effect of psychiatric and other nonmotor symptoms on disability in Parkinson's disease. J Am Geriatr Soc 52(5):784–788
- McDonald WM, Richard IH, DeLong MR (2003) Prevalence, etiology, and treatment of depression in Parkinson's disease. Biol Psychiatry 54(3):363–375
- 35. Gómez-Esteban JC, Tijero B, Somme J, Ciordia R, Berganzo K, Rouco I, Bustos JL, Valle MA, Lezcano E, Zarranz JJ (2010) Impact of psychiatric symptoms and sleep disorders on the quality of life of patients with Parkinson's disease. J Neurol. doi: 10.1007/s00415-010-5786-y
- 36. Schrag A, Barone P, Brown RG, Leentjens AF, McDonald WM, Starkstein S et al (2007) Depression rating scales in Parkinson's disease: critique and recommendations. Mov Disord 22(8):1077–1092
- 37. Gómez-Esteban JC, Zarranz JJ, Lezcano E, Tijero B, Luna A, Velasco F, Rouco I, Garamendi I (2007) Influence of motor symptoms upon the quality of life of patients with Parkinson's disease. Eur Neurol 57(3):161–165
- Happe S, Baier PC, Helmschmied K, Meller J, Tatsch K, Paulus W (2007) Association of daytime sleepiness with nigrostriatal dopaminergic degeneration in early Parkinson's disease. J Neurol 254(8):1037–1043