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Subjective sleep dysfunction and insomnia symptoms in Parkinson's disease: Insights from a cross-sectional evaluation of the French CoPark cohort

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ABSTRACT

Introduction: Twenty-seven to 80% of patients with Parkinson's Disease (PD) complain of subjective sleep dysfunction and insomnia symptoms. Our aim is to describe the prevalence and features of subjective sleep dysfunction and insomnia symptoms in patients with PD compared to other patients.
Methods: Cross-sectional analysis of 636 adult PD patients compared to 143 age and sex-matched non-PD control patients consulting their general practitioners. Insomnia symptoms and other sleep features were assessed by the Pittsburgh Sleep Quality Index (PSQI), a global score > 5 defining impaired sleep. The Chi-square test or the Student's t-test were used to assess the potential clinical and demographic differences between groups and between PD patients with vs. without sleep dysfunction. Logistic regression analysis was employed to test multivariate effects.
Results: Sleep dysfunction and insomnia symptoms were more frequent in PD patients compared to control patients (63 vs. 45%, $p = 0.001$). Female gender, PD duration, presence of depression and anxiety were associated with the presence of insomnia in PD. Subjective sleep efficiency, habitual sleep quality, sleep disturbance and daytime dysfunction, but not sleep latency, were reduced in PD patients compared to controls.
Conclusions: The prevalence of sleep dysfunction is higher in PD than in other general medical conditions. Insomnia in PD seems to affect sleep maintenance and consolidation, but not sleep onset.

1. Introduction

Parkinson's Disease (PD) patients frequently report unsatisfactory sleep [1]. Although several studies in the literature have evaluated sleep quality in PD [2–10], only few of them specifically focused on the prevalence of sleep dysfunction and insomnia symptoms [2–5,8,9,11–13], and even less included a control group [2–5,8,9,11,12]. The definitions and assessment methods of insomnia symptoms in PD in the different studies result in prevalence estimates ranging from 27% to 80%. According to the International Classification of Sleep Disorders, 3rd edition (ICSD-3), "insomnia disorder" defines the persistence of difficulty with sleep initiation, consolidation, or quality in an individual who has adequate circumstances and opportunity for sleep, resulting in general sleep dissatisfaction [14]. There is only one previous study to our knowledge addressing subjective sleep dysfunction and insomnia symptoms in PD compared to other unhealthy patients

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[2]. Moreover, evidence in the literature is limited on whether parkinsonian patients experience poor sleep as a consequence of PD itself or rather from being ill in general.

The aim of this study was to evaluate the prevalence of sleep dysfunction and insomnia symptoms in patients with PD compared to a population of patients affected with other medical conditions, by mean of the Pittsburgh Sleep Quality Index (PSQI). As secondary outcomes, we looked for potential relationships between insomnia symptoms and demographic and PD-related features.

2. Patients and methods

2.1. Study characteristics and sample

We performed a cross-sectional analysis of the baseline assessment of 683 adult PD patients recruited in the prospective COPARK cohort [15] between 2004 and 2010, compared to 177 sex- and age-matched control patients enrolled during the same period. This cohort was set up to improve knowledge on the natural history of PD and in particular on non-motor symptoms and pharmacological treatment of this disease, based on the methodology set up in the previous DoPaMiP study [16].

PD subjects were recruited from consecutive referrals to neurologists working in four different French regions (Midi-Pyrénées, Aquitaine, Pays de Loire and Nord-Pas de Calais), and regardless from their specific expertise in movement disorders. They were either neurologists working in public, academic hospitals or in private clinics or independent practitioners consulting in private settings. PD diagnosis was confirmed according to the UK PD Society Brain Bank criteria [15,16]. Exclusion criteria were secondary or atypical parkinsonism, Mini-Mental State Examination (MMSE) score below 24, the presence of deep brain stimulation or treatment with apomorphine pump or intrajejunal levodopa infusion, or comorbidity with potentially life-threatening medical conditions. Control subjects were recruited among consecutive patients consulting general practitioners of the same regions for non-neurological conditions or neurological conditions other than PD and who had a MMSE score $\geq$24 and were able to fulfil the questionnaires. They were group-matched for age and sex to PD patients. Every patient meeting the eligibility criteria was offered to participate in the study in an unselected, consecutive manner.

The protocol was approved by the local Institutional Review Board (authorization n° 1-06-28) and French regulatory authorities, including local ethics committees. The study was undertaken in accordance with Guidelines for Good Epidemiology Practice, the French Association of Epidemiologist (ADELF) recommendations and the Declaration of Helsinki. All patients provided written informed consent.

2.2. Patients' assessment

The baseline COPARK evaluation was conducted on the model of a previous cross-sectional study on PD patients living in Midi-Pyrénées, known as the DoPaMiP study [15,16]. Each PD patient was evaluated with a structured interview encompassing socio-demographic characteristics, medical history and drug treatment. Levodopa daily equivalent dose (LDED) was calculated as previously described [16]. Medications were classified according to the Anatomical Therapeutic Chemical classification. A complete clinical examination by a neurologist co-investigator of the COPARK study was then performed, including an evaluation of parkinsonian symptoms and signs at “on” state by mean of the Unified Parkinson's Disease Rating Scale (UPDRS) and the Hoehn and Yahr scale. Clinical features of PD were assessed by the UPDRS scale in PD patients [15,16]. Global motor dysfunction was defined as the sum of UPDRS part II and III (activity of daily living + motor examination, i.e. items 5–31, the maximal score of 160 indicating the most severe dysfunction). The following additional single items were also considered from UPRDS-IV and I, respectively: dyskinesias (item 32), wearing-off (item 39), intellectual dysfunction (item 1), thought disorders (item 2), depression (item 3), motivation/initiative (item 4). The patients were considered as suffering from each of these symptoms when scoring $\geq$1 at the corresponding item and not suffering otherwise. These single items were dichotomised to create binary variables for analyses. Global cognitive functioning was assessed by the Mini-Mental State Examination (MMSE) [15,16]. Anxiety and depressive symptoms were assessed by the Hospital Anxiety and Depression Scale (HADS) [16]. The presence of such symptoms was confirmed by a sub-score greater than 7 at either HADS-anxiety (HADS-A) or at the HADS-depression (HADS-D) scales, respectively. Chronic pain was assessed according to the International Association for the Study of Pain definition (unpleasant sensory and emotional experiences with actual or potential tissue damage or described in terms of such damage and lasting for more than 3 months), as previously reported [16]. Control patients were assessed by general practitioners with the same principles, except for PD-specific features. Random independent monitoring of data quality was performed in 10% of the sample. A PD specialist reviewed for consistency all clinical datasets at the end of data collection. Inconsistencies on specific PD descriptive symptoms were discussed case-by-case with the investigator who had collected the data. Once an agreement between the investigator and the expert was reached, the dataset was rectified consequently. Only subjects with complete datasets (considering only the above-mentioned variables) were included in this study.

2.3. Assessment of sleep dysfunction and insomnia symptoms

Sleep dysfunction, insomnia symptoms and other sleep features were assessed in PD and control patients by the PSQI [17], a self-administered sleep questionnaire evaluating sleep dysfunction and insomnia symptoms in the previous 30 days. From the scores at each question, 7 component scores are obtained, each of which ranging from 0 (best, i.e. “no difficulty”) to 3 (worst, i.e. “severe difficulty”). The 7 components provide a description of different sleep features: (1) subjective sleep quality, (2) sleep latency, (3) sleep duration, (4) habitual sleep efficiency, (5) sleep disturbance, (6) use of sleeping medication and (7) daytime dysfunction.

A global score results from the sum of the 7 sub-scores (range: 0–21, higher values indicating worse sleep). A PSQI global score >5 discriminates sleep disturbances in insomnia patients versus controls with a sensitivity of 99% and a specificity of 84% [18]. In addition to the global score, the 7 component scores provide information about specific sleep features, with a cutoff value of $\geq$2 (i.e. presence of the symptom at least once a week) [6,17,19].

As secondary objective, the distribution of demographic, general medical, disease-specific and pharmacologic characteristics in PD patients with insomnia (PSQI global score >5) were evaluated compared to PD patients without insomnia among the population of all PD patients.

We also described sleep habits and specific sleep disturbances based on patients' subjective report or on caregivers'/spouses observation in the two groups (PSQI questions number 5 and number 10, respectively).

2.4. Statistical analysis

Demographic and clinical characteristics are presented as frequencies, proportions or means ± standard deviation. Bivariate analyses were carried out with chi-square statistic or Student's t-

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test with a level of significance set at 0.05. Multivariated models with PSQI domains scores as dependent variables were constructed by forward logistic regression. Covariates that were statistically significant ($P < 0.05$) were included in the model as explanatory variables (gender, age, PD duration, MMSE, UPDRS I scores, UPDRS II + III sub-score, presence of dyskinesias and/or motor fluctuations, presence of depressive or anxiety symptoms, intake of amantadine, MAO-B inhibitors, anticholinergics or levodopa, levodopa equivalent daily dose, intake of opioids, antidepressants, antiepileptics or anxiolytics) until no further covariates were significant. Goodness of fit was explored by the Hosmer & Lemeshow score. Age, age at the end of academic studies, PD duration, UPDRS scores and LDED were dichotomized to median values to facilitate the interpretation of the logistic regression models, as has been done in the past [15,16]. Adjustments for depression (HADS > 7) were made by Mantel–Haenszel test for categorical variables or with ANCOVA for numerical variables. Potential interactions and multicollinearity were tested for these models. None was found. All other regression analyses assumptions were also met.

All statistical analysis was performed using SAS statistical software release 9.1 (SAS institute Inc., Cary, NC, USA).

3. Results

The COPARK database included 860 subjects (683 PD patients and 177 controls). The present analyses included 636 (93%) PD and 143 (81%) control patients who completed and returned the PSQI questionnaire. Caregivers/spouses' questionnaires were available for 405 PD patients and 89 control patients. The demographic and clinical features of PD and control patients are shown in Table 1. Control patients had the same main demographic characteristics than PD ones, except that they were more frequently active workers, had lower anxiety and depressive scores and less frequently consumed antidepressants. They suffered from various co-morbid diseases, including cardiovascular (55%), endocrine (51%), musculo-skeletal (27%), gastroenterological (20%), nervous (18%), mental (17%), genito-urinary (16%) or respiratory disorders (10%).

Prevalence of sleep dysfunction was higher in PD than in control patients. Four hundred (63%) PD patients and 64 (45%) controls had a PSQI global score >5 ($p = 0.001$). PSQI global score was also greater in PD than in control patients (7.3 ± 3.9 vs. 5.8 ± 3.2 $p = 0.001$). Among nocturnal symptoms, PD patients reported reduced sleep efficiency (34 vs. 22%, $p = 0.004$) and severer sleep disturbance (41 vs. 17%, $p = 0.001$), and these differences were still significant after adjustment for depression. PD patients reported more frequently impaired sleep quality than control patients (23 vs. 14%, $p = 0.02$), but this difference was not significant after adjustment for depression. Sleep latency and habitual sleep duration did not differ between the two groups. Daytime dysfunction was also more frequent in PD than in control patients (25 vs. 3%, $p = 0.001$, depression-adjusted p value = 0.001). Table 2 displays the prevalence of sleep dysfunction and insomnia symptoms in both populations.

As regards sleep habits, we found no significant differences between PD and control patients about habitual bedtime (10:18 p.m. vs. 10:36 p.m., p = n.s), getting up time (7:00 a.m. vs. 7:12 p.m., p = n.s.) or total sleep duration (6.8 vs. 7.0 h, p = n.s.).

PD patients reported more frequently cough or snoring (35 vs. 12%, $p = 0.001$), cold sensations (16 vs. 5%, $p = 0.001$), heat sensations (38 vs. 26%, $p = 0.005$), bad dreams (33 vs. 14%, $p = 0.001$) and pain (44 vs. 24%, $p = 0.001$). Conversely, they did not complain more than control patients of middle-night or early morning awakenings (81 vs. 76%, p = n.s), need to use the bathroom (77 vs. 72%, p = n.s) nor of difficulties to breath comfortably (11 vs. 7%, p = n.s). Based on information from caregivers'/spouses questionnaires, PD patients had more frequently witnessed snoring or apneas (51 vs. 35%, $p = 0.007$ and 17 vs. 5%, $p = 0.003$, respectively), leg jerks (49 vs. 15%, $p = 0.001$) or confusion (16 vs. 1%, $p = 0.001$) than control patients.

The factors associated with a pathological score at PSQI in the PD group at logistic regression are shown in Table 3. Female gender, longer PD duration and greater score of HADS depression and anxiety scores correlated with a pathological (>5) PSQI score.

4. Discussion

Although sleep disturbances have been previously investigated in other cohorts of PD patients [2–6,8–10], to our knowledge only another previous study [2] comparatively assessed insomnia symptoms and sleep dysfunction [14] in a large population of PD patients and in patients affected with other general comorbidities. Strength of our study is that patients were unselected and not only included in tertiary centres of university hospitals specialized in movement disorders, and results are therefore more likely to be generalizable than of previous reports. The choice of patients affected by medical conditions other than PD and unselected for sleep complaints as control group is another advantage allowing identifying PD-specific aspects of insomnia. The fact that PD patients have been recruited from neurologists' practices and control patients from general practitioners' offices might introduce a potential selection bias on the study population, which we acknowledge. Another potential bias is represented by the different non-participation rate between PD and control patients (7 vs. 19%). We interpret this difference as due to possible higher motivation of PD patients in partaking a study focusing on a disease they were actually suffering compared to control patients; however, we do not think this difference to substantially impact the prevalence estimate of sleep dysfunction and insomnia symptoms.

The PSQI questionnaire has a high sensitivity (84%) in identifying poor sleepers among parkinsonian patients [19] and it is considered a standard mean to evaluate insomnia in the general population and in several patients' populations[17], thus allowing comparisons with a control group. Conversely, it lacks precise characterization of the wakefulness correlates of insomnia according to the ICSD-3 definition and it does not permit discriminating between acute and chronic insomnia, as it refers to the previous month only.

We observed a higher prevalence of subjective sleep dysfunction and insomnia symptoms in PD patients compared to non-PD patients (400/636 PD patients and 64/143 control patients, $p = 0.001$). The PSQI-estimated prevalence of sleep dysfunction (63%) is close to the figures of a previous study using the same definition in a smaller sample [6].

The mean PSQI global score was also higher in PD compared to control patients (7.3 ± 3.9 vs. 5.8 ± 3.2) and this result is in accordance with published reports [6,19]. The mean PSQI global score of our control group (5.8 ± 3.2) was higher than previously reported in control populations [6,19], and in particular than in healthy elderly subjects [17]. This finding reinforces the notion of an unusually high prevalence of sleep dysfunction and insomnia symptoms in PD as opposed to other general medical conditions.

In our study, PD patients with subjective sleep dysfunction (PSQI global score >5) were more frequently females and had higher scores of depressive and anxious symptoms than PD patients without sleep dysfunction. These results are consistent with previous reports in smaller surveys [8,11,12]. Female gender, anxiety and depression have been correlated with insomnia in the general population [20]. In our population, sleep dysfunction was correlated with longer disease duration (>5 years), but not with older

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Table 1
Demographic and clinical characteristics of PD and control patients.

	PD (n = 636)	Controls (n = 143)
Females	269 (42%)	64 (45%)
Age	67.9 ± 9.9 (27–92)	68.8 ± 10.1 (40–92)
Age at the end of academic studies	18.0 ± 4.5	18.1 ± 5.5
Active worker	64 (10%)	28 (20%)**
PD duration	6.3 ± 4.9 (1–30)	–
Age at PD onset	61.5 ± 10.6 (19–90)	–
MMSE	28.1{Pfeiffer, 2009#679}2.0	28.9 ± 2.2
Hoehn & Yahr		
0.0	5 (1%)	–
1.0	74 (12%)	–
1.5	49 (8%)	–
2.0	257 (41%)	–
2.5	131 (21%)	–
3.0	85 (14%)	–
4.0	22 (4%)	–
5.0	1 (0%)	–
UPDRS I score	2.5 ± 0.1	–
UPDRS II + III score	28.7 ± 0.6	–
Dyskinesias	175 (28%)	–
Fluctuations	221 (35%)	–
HADS depression score	7.9 ± 3.8	6.1 ± 2.9**
HADS anxiety score	5.9 ± 3.8	3.1 ± 3.2**
Levodopa daily equivalent dose	581.9 ± 17.7	–
Antiparkinsonian medications		
Amantadine	62 (10%)	–
MAO-B inhibitors	88 (14%)	–
Antimuscarinic agents	34 (5%)	–
Levodopa	512 (81%)	–
Dopamine agonists	399 (63%)	–
COMT inhibitors	122 (19%)	–
Other medications		
Opioids	39 (6%)	7 (5%)
Antipsychotics[a]	10 (2%)	3 (2%)
Anxiolytic agents	82 (13%)	18 (13%)
Hypnotics	40 (6%)	14 (10%)
Melatonin	0	0
Z-drugs	35 (6%)	12 (9%)
Benzodiazepines	0	2 (1%)
Antidepressants	110 (18%)	13 (9%)*
Imipraminic antidepressants	11 (2%)	3 (2%)
SSRI antidepressant	54 (8%)	9 (6%)
Other antidepressants	45 (7%)	1 (1%)**
Stimulants	3 (0%)	0 (0%)
Antihistaminergics	8 (1%)	7 (5%)**

*p < 0.05, **p < 0.01 (Student's t-test or Chi-squared test).
Ranges are given between brackets for some variables.
COMT = Catechol-O-MethylTransferase.
HADS = Hospital Anxiety and Depression Scale.
MAO-B = Mono Amine Oxydase B.
MMSE = Mini-Mental State Examination.
PD = Parkinson's Disease.
UPDRS = Unified Parkinson's Disease Rating scale.
[a] Including levomepromazine, haloperidol and sulpiride in controls and clozapine (8 cases) and risperidone (2 cases) in PD patients.

age, nor with indicators of disease severity, not replicating the result of previous reports [11,12]. LDED was not related to sleep dysfunction after logistic regression. Our findings support the hypothesis according to which sleep dysfunction in PD might be at least partly caused by factors not directly related to motor disability. No associations were found either with other factors such as older age, chronic pain or psychotropic medications. Such negative findings may result from methodological limitations, including insufficient power or too broad pain assessment. Alternatively, they might support the concept that insomnia in PD might not be simply the consequence of dopaminergic drugs, nocturnal motor or non-motor symptoms (such as nocturnal akinesia, difficulties to in bed-turning, muscle cramps, anxiety or panic attacks during “off” phases, nycturia, nightmares, restless legs syndrome), or co-morbid sleep-disordered breathing[21], but rather an independent sleep disorder intertwined with PD itself.

Our data also suggest that insomnia seems to show peculiar characteristics in PD patients. We found reduced subjective sleep efficiency, sleep quality, and more frequent report of sleep disturbance and daytime dysfunction in PD patients compared to control patients, with no impact on sleep latency. These results agree with previous subjective and objective data [6,19,22,23].

Reduced subjective sleep efficiency and quality in PD patients could depend on depression or anxiety, as in the general population [24]. In fact, when corrected for depression, reduced sleep quality was not more frequent in PD than in control patients in our sample. As causality cannot be inferred from the present data, the opposite scenario might also be considered, insomnia being a strong predictor of the development of depression in adult general population [20]. We hypothesize that reduced subjective sleep efficiency and

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Table 2
Prevalence of sleep dysfunction and insomnia symptoms based on the analysis of the PSQI global and component scores.

	PD patients (n = 636)	Control patients (n = 143)	Unadjusted p-value	Depression-adjusted p-value
Insomnia				
PSQI global score	7.3 ± 3.9	5.8 ± 3.2	**0.001***	**0.004***
PSQI global score > 5	400 (63%)	64 (45%)	**0.001***	**0.010***
Nocturnal symptoms of insomnia				
PSQI Sleep latency ≥ 2	140 (22%)	40 (28%)	0.180**	0.074**
PSQI Habitual sleep duration ≥ 2	309 (49%)	57 (40%)	0.060**	0.083**
PSQI Sleep efficiency ≥ 2	221 (35%)	32 (22%)	**0.004****	**0.038****
PSQI Subjective sleep quality ≥ 2	146 (23%)	20 (14%)	**0.020****	0.110**
PSQI Sleep disturbance ≥ 2	259 (41%)	24 (17%)	**0.001****	**0.001****
Diurnal symptoms				
PSQI daytime dysfunction	160 (25%)	4 (3%)	**0.001****	**0.001****
Question n.8: sleepiness	157 (25%)	3 (2%)	**0.001****	**0.001****
Question n.9: lack of enthusiasm	131 (21%)	8 (6%)	**0.001****	**0.020****

PD = Parkinson's Disease.
PSQI = Pittsburgh Sleep Quality Index.
Adjustments for depression (HADS > 7) were made by Mantel–Haenszel test for categorical variables or with ANCOVA for numerical variables.
*: Unadjusted p-values are calculated with chi-square and the adjusted ones by Mantel–Haenszel tests.
**: Unadjusted p-values were obtained by Student's t-tests and the adjusted ones by ANOVA.
Significant p-values are highlighted in bold.

quality in PD patients might rather result from heightened cognitive and emotional arousal and learnt maladaptive sleep behaviors, similarly to the psychophysiological phenotype of insomnia disorder [24]. The higher prevalence of anxiety in PD patients with sleep dysfunction would be in accordance with this hypothesis. The subjective perception of reduced sleep efficiency and quality and of higher sleep disturbance in our patients could be in line with increased N1 and N2 sleep at polysomnography in previous reports [22].

Differently from earlier evidence in the literature that compared subjective nocturnal sleep in PD patients vs. healthy controls [5,6,9,25], and from previous polysomnographic evidence of increased night-time awakenings or arousals in PD [22], PD patients do not report more frequent night-time or early morning awakenings than control patients in our study. In fact, we found no greater subjective report of nocturnal or early-morning awakenings in PD compared to control patients in our sample. As our control group included unhealthy, non-PD patients, we hypothesize that nocturnal awakenings in PD found by other studies [5,6,9,13,25] might not directly depend on PD, but rather on non-specific, illness-related sleep disturbance. In the study of Tandberg et al. [2], both PD and control patients (affected with diabetes mellitus) were of older age and PD patients had longer disease duration (9.1 ± 5.8 vs. 6.3 ± 4.9 years) and severer disease (Hoehn & Yahr score 2.8 ± 1.1 vs. 2.1 ± 0.7) than in our group. In spite of that, the mean levodopa daily equivalent dose in the study of Tandberg et al. was lower than in ours (400 ± 235 vs. 582 ± 18). These differences might explain inconsistency with our results, as PD patients in the study of Tandberg et al. might have been experiencing more or severer PD-related nocturnal symptoms than our patients due to lower dopaminergic drug doses. However, the differences in assessment methods and patients' demographic and clinical characteristics between our study and previous literature make it difficult to draw general conclusions.

Sleep disturbance was more prevalent in PD than in control patients (41 vs. 17%, P = 0.001), and it was independent from depression. Sleep-disturbing factors in PD patients (compared to control patients) were cough or snoring, cold sensations, heat sensations, bad dreams and pain, but not the need to use the bathroom or difficulties to breath comfortably. The higher prevalence of these non PD-specific complaints in PD patients are either non-motor symptoms of PD [26], or can be explained as consequences of motor symptoms, pharmacological treatment, dysautonomia, neurodegeneration of the sleep regulatory networks in the brain [1], reduced nociceptive threshold [27] or a combination of these factors. Of note, differently from previous evidence on healthy controls [6] and in spite of the frequent report of nycturia by PD patients [10,13], our results seem to suggest that this symptom might be generically illness-related rather than PD-specific.

PD subjects had less frequently difficulty in falling asleep (as they less frequently reported increased sleep latency) compared to control patients, in spite of reporting more frequently symptoms of anxiety than control patients. Difficulty in sleep initiation in fact usually correlates with anxiety in the general population. Our finding is in line with previous studies, which found normal subjective [2,9,13,28] or objective [22,29] sleep latency in PD. One possible explanation for this observation is that PD patients show a heightened sleep drive which can be caused by the disease itself [1], to dopaminergic drugs [1], to an alteration of nocturnal sleep [22] or from a combination of these factors. This increased propensity to sleep could overcome sleep-disturbing factors at sleep onset or during sleep.

We also found daytime sleepiness and daytime dysfunction to be more frequent in PD patients compared to control patients, in line with other previous findings [1]. Dopaminergic treatment may induce sleepiness in PD patients, although many PD patients develop sleepiness before clinical disease onset and without being treated with dopaminergic drugs [1]. Daytime dysfunction and sleepiness might also be interpreted as consequences of nocturnal sleep disruption. Nevertheless, daytime dysfunction only weakly correlated with the actual subjective habitual sleep time in our sample, further supporting the idea that daytime sleepiness might be an intrinsic feature of PD and not just a consequence of nocturnal sleep dysfunction [1].

In a similar way, it could be hypothesized that impaired sleep maintainance and consolidation (expressed by reduced sleep efficiency and quality in our sample) might depend on reduced nocturnal homeostatic sleep pressure [24] due to daytime sleepiness and to learnt “maladaptive” behaviors of PD patients, which tend to spend more time in bed than actually needed for sleeping. In fact, in routine clinical practice, PD patients frequently report to nap during the day or go to bed much earlier than their habitual sleep onset time in order to recover from fatigue. Another possible explanation is that nocturnal insomnia and diurnal sleepiness might be both consequences of the sleep disruption intrinsic to PD,

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Table 3
Factors related to sleep dysfunction (PSQI score > 5) in PD patients.

	PSQI ≤ 5 (n = 236)	PSQI > 5 (n = 400)	Bivariate p-value	Multivariate OR (95% CI)	Multivariate p-value
Females	80 (34%)	189 (47%)	0.001	1.56 (1.09–2.24)	0.018
Age (Mean ± SD)	67.5 ± 10.1	68.1 ± 9.7	0.850		
Age > 70 years	118 (50%)	198 (50%)	0.869		
Age at study offset > 17 years	105 (45%)	174 (44%)	0.748		
Active worker	26 (11%)	37 (9%)	0.450		
PD duration (Mean ± SD)	5.6 ± 4.8	6.7 ± 4.9	0.002		
PD duration > 5 years	99 (42%)	217 (55%)	0.003	1.44 (1.03–2.04)	0.035
UPDRS hallucinations ≥ 1	58 (25%)	110 (28%)	0.455		
UPDRS apathy ≥ 1	120 (51%)	226 (57%)	0.180		
UPDRS II + III score > 26	107 (46%)	205 (52%)	0.180		
Levodopa-responsive sub-score > 14	113 (48%)	198 (49%)	0.723		
Axial sub-score > 7	107 (46%)	201 (50%)	0.246		
Dyskinesias	54 (23%)	120 (30%)	0.055		
Wearing-off	69 (30%)	151 (38%)	0.037	–	0.467
Levodopa daily equivalent dose > 500 mg	94 (40%)	219 (55%)	0.001	–	0.550
Antiparkinsonian medications					
Amantadine	20 (9%)	41 (10%)	0.483		
MAO-B Inhibitors	42 (18%)	46 (12%)	0.023	–	0.800
Antimuscarinic agents	10 (4%)	24 (6%)	0.750		
Levodopa	177 (76%)	334 (84%)	0.016	–	0.900
Dopamine agonists	143 (61%)	255 (64%)	0.507		
COMT Inhibitors	38 (16%)	84 (21%)	0.142		
Other medications					
Opioids	4 (2%)	7 (2%)	0.633		
Antipsychotics	4 (2%)	23 (6%)	0.264		
Anxiolytics	15 (6%)	67 (17%)	0.055		
Hypnotics	2 (1%)	38 (9%)	0.001	–	0.450
Melatonin	0	0	–		
Z-drugs	2 (1)	34 (8%)	0.001	–	0.135
Benzodiazepines	0	4 (1%)	0.125		
Antidepressants	26 (11%)	113 (22%)	0.001	–	0.280
Imipraminics	2 (1%)	38 (10%)	0.194		
SSRIs	11 (5%)	43 (11%)	0.008	–	0.452
Other ADs	13 (6%)	32 (8%)	0.247		
Chronic pain	113 (48%)	240 (60%)	0.100		
Respiratory antecedents	13 (6%)	26 (7%)	0.970		
MMSE > 29	8 (3%)	13 (3%)	0.922		
HADS-depression score > 7	84 (36%)	226 (57%)	0.001	2.51 (1.68–3.76)	0.005
HADS-anxiety score > 7	43 (18%)	157 (39%)	0.001	1.67 (1.16–2.40)	0.001

Legend.
COMT = Catechol-O-MethylTransferase.
HADS = Hospital Anxiety and Depression Scale.
MAO-B = Mono Amine Oxydase B.
MMSE = Mini-Mental State Examination.
PD = Parkinson's Disease.
UPDRS = Unified Parkinson's Disease Rating scale.
The levodopa-responsive sub-score is calculated by the sums of the UPDRS-III items defining "tremor at rest" (item 20), "akinesia" (sum of the score of the items 23, 26 and 31) and "rigidity" (item 22).
The axial sub-score is obtained by the sum of UPDRS-III items "falling" (item 13), "freezing of gait" (item 14) "speech" (item 18), "posture"(item 28) and "postural instability" (item 30).
* = $p < 0.05$.
** = $p < 0.01$.

especially including loss of circadian pacemaking, and earlier phase shift [30]. However, the analysis of sleep habits (habitual bedtime, wake up time and total sleep time) failed to highlight significant differences in these parameters compared to control patients in our study.

To conclude, subjective sleep dysfunction deserves thorough medical attention in PD, as it is more frequent than in other general medical conditions. Insomnia phenotype in PD seems to affect sleep maintainance and consolidation, yet not sleep onset.

Conflicts of interests

None.

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