Insomnia in Parkinson's disease: frequency and progression over time

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Objectives: To examine the development of nocturnal sleeping problems in patients with Parkinson's disease (PD) over an 8-year period and to study the clinical and demographic correlates of insomnia.

Methods: 231 patients were included in a population-based prevalence study in 1993, and re-examined in 1997 and 2001. At all study visits, we applied semi-structured interviews to obtain information on clinical and demographic data, as well as on nocturnal sleeping problems. Standardised rating scales of parkinsonism, depression and cognitive impairment were used. The relationship between insomnia and demographic and clinical variables was analysed using population-averaged logistic regression models for correlated data. 231 patients were included at baseline, 142 were available for re-evaluation in 1997 and 89 patients in 2001.

Results: Most nocturnal sleeping problems varied little in prevalence over time, whereas problems related to turning in bed and vivid dreaming or nightmares increased. Insomnia was present in 54–60% of the patients at each of the three study visits and varied considerably in individual patients over time. The presence of insomnia was closely related to disease duration, higher Montgomery-Åsberg Depression Rating Scale scores and female sex.

Conclusion: Insomnia is a highly frequent complaint in patients with PD. It fluctuates over time in individual patients, and its origin seems to be multifactorial. Physicians should be aware of the high prevalence of insomnia in patients with PD and should examine their patients for a possible coexisting depression.

Diurnal and nocturnal sleeping problems are frequent in patients with Parkinson's disease (PD).^{1,2} In a community-based cross-sectional study, nearly two-thirds of the patients with PD reported night time sleeping problems compared with 46% of patients with diabetes mellitus and 33% of healthy elderly people.³ It has also been reported that insomnia has a major impact on health-related quality of life in these patients.⁴ However, there are few data on the development of nocturnal sleeping problems in patients with PD.^{5,6}

Insomnia is the most common sleep disturbance and is classified as sleep initiation problem, sleep fragmentation or early awakening. It is common in the general population aged >65 years, with an incidence of approximately 5% per year and a spontaneous remission of 50% over 3 years. Remission is mostly related to the resolution of acute or chronic illness,⁷ and is less likely among older subjects than among younger individuals.⁸

Nocturnal symptoms in PD can be categorised into insomnia, motor and urinary symptoms, neuropsychiatric symptoms, parasomnias and sleep-related movement disorders.⁹ Patients with PD have problems with sleep fragmentation and early awakening compared with controls, whereas sleep initiation problems are equally frequent among patients and healthy elderly people.³ The causes of sleep disruption in patients with PD may be related to ageing, the cerebral pathology of the disease process itself, dopaminergic and other sleep-altering drugs, motor dysfunction, neuropsychiatric symptoms, breathing disorders while sleeping, excessive daytime sleepiness, sleep hygiene, sleep-related movement disorders and urinary difficulties. There is, however, a need for more knowledge, as the progression of insomnia and its causes in patients with PD are poorly investigated over time.

The aim of this study was therefore to evaluate the development and changes of insomnia in patients with PD

over an 8-year period and to study the correlation between the presence of insomnia and risk factors during the study period.

MATERIALS AND METHODS

Study population

In all, 245 patients were diagnosed with PD on 1 January 1993 in a prevalence study in the county of Rogaland, Norway.¹⁰ The prevalence rate was 110.9 per 100 000 inhabitants. The patients were diagnosed according to published criteria¹¹ and patient recruitment has previously been described in detail.¹⁰ So far, a subgroup of 22 patients has been examined by autopsy and the clinical diagnosis of PD was confirmed in all cases.¹²

In 1993, 231 of the 245 patients were evaluated for insomnia and possible causes for their nocturnal sleeping problems.^{3,13} Seven patients were re-diagnosed as not having PD during follow-up, three patients died before the scheduled day for examination, two patients refused to participate and two patients could not be evaluated owing to incomplete data. During the 8-year study period, 126 patients died and 16 either refused to participate or data were incomplete owing to severe illness or dementia. Data were available from 142 patients after 4 years (in 1997) and from 89 patients after 8 years (in 2001).

Study design

This study is a prospective longitudinal cohort study of nocturnal sleeping problems in patients with PD over 8 years. The original study population of 231 patients at baseline was derived from a community-based prevalence study. Patients were examined with the same standardised examination programme in 1993, 1997 and 2001.

Abbreviations: EDS, excessive daytime sleepiness; MADRS, Montgomery and Åsberg Depression Rating Scale; MMSE, Mini-Mental State Examination; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale

Clinical assessment

All patients were interviewed and evaluated by a neurologist and a psychiatrist or a psychiatric nurse from the study group. A close family member or daily caregiver was asked to attend the session for support and additional information if necessary.

The standardised evaluation programme applied in 1993, 1997 and 2001 included a semistructured questionnaire on disease history and demographic data and the Unified Parkinson's Disease Rating Scale (UPDRS),¹⁴ the Hoehn and Yahr staging,¹⁵ the Montgomery and Aasberg Depression Rating Scale (MADRS)¹⁶ and the Mini-Mental State Examination (MMSE).¹⁷ The thought disorder question of the UPDRS subscale I was used for the assessment of hallucinations. If the patient scored ≥ 2 (benign hallucinations with insight retained), he was defined as a hallucinator. The duration, use and type of dopaminergic treatment were recorded at each study visit.

Assessment of sleep disorders

A self-constructed sleepiness questionnaire, the Stavanger sleepiness questionnaire, was used for the evaluation of night-time sleeping problems. The same questionnaire was used by the authors in previous studies, covering both daytime and night-time sleeping problems.^{3 13 18} The questionnaire used was easy to understand and use. Mainly "yes" or "no" answers were given. The accompanying family member or daily caregiver was, if necessary, actively involved in obtaining answers as accurate as possible. Patients were asked whether they had night-time sleeping problems in general, problems falling asleep, early morning or frequent awakenings during the night, whether they used sleeping pills and whether they had discussed the problem with their physician. They were, furthermore, asked for how long they had experienced sleeping problems and how many hours they slept every night. Patients who reported sleeping problems during the night or used sleeping pills due to sleeping problems and had experienced these symptoms for at least 1 month were classified as having insomnia. The patients were also asked to rate the existing pain or cramps, dystonic and myoclonic movements during the night, the intensity of motor and vocal activity during sleep, and problems turning in bed, on a scale from 0 to 3. These symptoms were accounted for if the patient scored 2 (rather frequent symptom—moderate in intensity) or 3 (very distressing symptom—often experienced). Rapid eye movement sleep behaviour disorder was suspected when a patient reported a score of 2 (very active during sleep, tend to wake up spouse) or 3 (very active physically and verbally, have been hitting or hurting myself or caregiver while sleeping). Patients were also asked to report bothersome vivid dreams or nightmares. For the evaluation of daytime sleepiness, the time spent asleep during daytime was registered, as well as the mean number of naps per day. Excessive daytime sleepiness (EDS) was assumed if a patient fell asleep ≥ 3 times or slept for >2 h during daytime.¹⁸

Statistical analysis

SPSS V.11.0 and Stata were used for statistical analyses. We used the Mann-Whitney U test to compare continuous variables and the χ^2 test for categorical variables of patients with and without insomnia. We used McNemar's test to compare changes in prevalence of 1993 data versus 1997, and 1993 data versus 2001.

The relationship between insomnia and demographic and clinical variables was analysed by population-averaged logistic regression models for correlated data (Stata procedure xtlogit) using all observations available. Since there were three consecutive examinations, unstructured correlations were used. At baseline there were 117 people without and 108 people with

insomnia, and a model with 11 degrees of freedom was used. Covariates considered for the multivariate model were age, sex, disease duration, UPDRS motor score, MMSE score, MADRS score, levodopa dose, use of agonists at baseline (yes or no) and hallucination (present or absent). Significant covariates from the final population-averaged logistic regression model were used to identify patients with low levels of these risk factors, and the proportion of insomnia in these patients at each occasion was investigated to judge whether insomnia occurred independently of the identified risk factors. A two-sided p value <0.05 was considered significant.

RESULTS

Frequency of sleep disorders and other nocturnal features

Table 1 presents the prevalence of sleep disorders and other nocturnal features in patients with PD in 1993, 1997 and 2001. More than 50% of the patients reported insomnia at each study visit. The frequency of problems with sleep initiation and frequent awakenings varied from 23% to 30% and from 23% to 44%, respectively. In all, 19–24% of the patients reported early morning awakening during the study period. Problems turning in bed, vivid dreaming or nightmares, and EDS were also common complaints, and their frequency increased significantly over time, whereas rapid eye movement sleep behaviour disorder suspect features varied in prevalence. The proportion of patients who had discussed the sleeping problem with their general practitioner increased over the years. The use of sleeping pills varied little. Other problems like pain or cramps, dystonia and myoclonic jerks during the night occurred in $<20\%$ of patients, and their frequencies were rather stable during the study period. Among patients with insomnia, it was only in 1993 that the occurrence of problems turning in bed was more common than that related to insomnia (data not shown).

Course of insomnia

Eighty-nine patients with PD were examined at each of the three study visits. Of these, 83% of the patients experienced insomnia at one or more study visits during the 8-year study period. A total of 29 (33%) patients reported insomnia at all three visits, while 27 (30%) patients with PD experienced insomnia only at baseline (1993) or at baseline and at one more visit. In all, 18 (20%) patients did not have insomnia at baseline, but developed insomnia during the study period.

Clinical associations to insomnia

Table 2 shows the clinical and demographic data of patients with PD with and without insomnia at all the study visits. In the univariate analysis, we found that patients with insomnia had higher MADRS scores and were more often female compared with those without insomnia in 1993 and 1997. In 1993, disease duration was longer and levodopa dosage higher than among those without insomnia.

In the population-averaged logistic regression model (generalised estimating equation), age at baseline, sex, disease duration, UPDRS motor and activity of daily living scores, MADRS score, MMSE score, use of levodopa, use of dopamine agonists, presence of hallucination and time were included in the estimation. The Wald χ^2 value was 30.59 (11 degrees of freedom, $p=0.001$). Insomnia was found to be significantly related only to female sex ($p=0.001$, OR 2.21, 95% CI 1.36 to 3.59), disease duration ($p=0.009$, OR 1.07, 95% CI 1.02 to 1.13) and MADRS score ($p=0.03$, OR 1.06, 95% CI 1.01 to 1.11).

DISCUSSION

In this longitudinal cohort study, we have confirmed the high frequency of insomnia among patients with PD. The complaint

Table 1 Prevalence of diurnal and nocturnal symptoms in patients with Parkinson's disease over an 8-year study period

Patients with PD	1993	1997	2001
Total number of patients	231	142	89
Insomnia, n (%)	136 (58.9)	76 (53.5)	50 (56.2)
Sleep initiation problems, n (%)	69 (30.0)	39 (27.5)	21 (23.3)
Frequent awakening during the night, n (%)	90 (39.1)	33 (23.2)**	40 (44.4)
Early morning awakening, n (%)	55 (23.9)	27 (19.0)	18 (20.0)
Use of sleeping drugs due to insomnia, n (%)	90 (39.0)	47 (32.9)	37 (41.1)
Discussed sleeping problems with physician, n (%)	50 (21.6)	54 (38.0)*	43 (48.3)*
Problems turning in bed, n (%)	103 (44.8)	82 (57.7)**	60 (67.4)*
Pain or cramps during the night, n (%)	39 (16.9)	24 (16.9)	12 (13.3)
Dystonia during the night, n (%)	17 (7.4)	9 (6.3)	10 (11.1)
Myoclonic jerks during the night, n (%)	11 (4.8)	8 (5.6)	6 (6.7)
Vivid dreaming and/or nightmares, n (%)	57 (24.7)	57 (40.7)**	38 (42.2)*
RBD suspect features, n (%)	34 (14.7)	39 (27.3)**	13 (14.6)
Excessive daytime sleepiness, n (%)	35 (15.1)	41 (28.7)**	40 (44.9)**

PD, Parkinson's disease; RBD, rapid eye movement sleep behaviour disorder.

McNemar's test for comparison of change in prevalence from 1993 to 1997 and from 1993 to 2001. All p values are two tailed. All available observations are included in the results.

*p ≤ 0.05.

**p ≤ 0.005.

did not become more common during the study period, but varied over time. The factors associated with insomnia were depressive symptoms, disease duration and female sex. Vivid dreaming or nightmares, EDS and problems turning in bed increased in frequency in all patients as the disease developed. The results from this study show that insomnia is highly frequent, and indicate that insomnia in PD is associated with several possible causes as in the general population.

To achieve more knowledge on sleep wake regulation and the different sleep disorders is important, although complicated. Insomnia is to some extent a subjective symptom, and its severity is differently experienced in each individual.¹⁹ There is a multitude of possible causes, a large variability in duration, and it is difficult to stage its intensity objectively by questionnaires. Few previous studies have examined the development of insomnia in PD over time,^{5, 6} and this study is the first to examine a large variety of possible factors that may influence insomnia over a long period of time in an unselected patient cohort.

Insomnia is common and has an important influence on health-related quality of life in patients with PD.^{1, 4, 20} The problems with sleep initiation are, however, not more common

in patients than among healthy elderly people.³ In this longitudinal cohort study of a rather large group of patients with PD from an unselected cross-sectional prevalence study, we have prospectively examined the development of insomnia and other nocturnal problems over an 8-year period. We found that the frequency of insomnia remained high over time. The complaint did, however, vary considerably in individual patients. This is a known feature of insomnia in the general population and also among older people,^{5, 6} and is most likely due to specific treatments and resolved causes. These causes therefore seem to be important and relevant among patients with PD as well, and in some patients it should be possible to modify their nocturnal sleeping problem.

Several possible causes for insomnia in patients with PD have been proposed previously.^{21, 22} With age, the prevalence of sleep disorders and the variability in sleep quality increase. Pathological lesions of the PD process in the upper brainstem and lower midbrain may cause sleep disorders in patients.^{23, 24} Other factors that can influence sleep in patients with PD are motor symptoms, depression and other psychiatric symptoms, parasomnias and nocturia. In addition, the drugs used by patients may cause sleep problems. Levodopa and other

Table 2 Clinical data of patients with PD with and without insomnia at each study visit during the 8-year study period

	Patients with PD in 1993		Patients with PD in 1997		Patients with PD in 2001	
	With insomnia	Without insomnia	With insomnia	Without insomnia	With insomnia	Without insomnia
Number of patients	136	95	76	66	50	39
Female, n (%)	78 (57.4)*	39 (41.1)	49 (64.5)*	29 (43.9)	32 (64.0)	19 (48.7)
Age (years), mean (SD)	73.1 (8.9)	73.8 (7.7)	74.3 (8.2)	74.3 (7.8)	77.4 (6.6)	74.4 (10.0)
Disease duration (years), mean (SD)	9.8 (5.7)**	7.8 (5.4)	13.4 (5.3)	11.7 (4.5)	16.7 (5.0)	16.8 (4.7)
Levodopa dose (mg), mean (SD)	518 (255)*	451 (231)	693 (416)	554 (319)	649 (444)	628 (391)
Use of dopamine agonist, n (%)	31 (22.8)	21 (22.1)	13 (17.1)	11 (16.7)	13 (26.0)	14 (35.9)
UPDRS II score, mean (SD)	15.1 (9.3)	13.5 (8.2)	17.6 (9.7)	19.5 (10.4)	25.0 (10.8)	25.5 (11.3)
UPDRS motor score, mean (SD)	28.7 (16.0)	28.1 (15.6)	29.7 (18.0)	37.5 (24.7)	48.0 (18.9)	46.1 (22.9)
Dementia, n (%)	35 (25.7)	25 (26.3)	30 (39.5)	26 (39.4)	28 (56.0)	25 (64.1)
Hallucination, n (%)	25 (18.4)	14 (14.7)	31 (40.8)	17 (25.8)	19 (38.0)	20 (51.3)
Hoehn and Yahr stage, mean (SD)	2.9 (1.1)	2.7 (1.1)	3.2 (1.0)	3.3 (1.1)	3.4 (1.0)	3.5 (1.2)
MMSE score, mean (SD)	24.4 (6.1)	24.4 (7.8)	23.8 (7.6)	23.1 (9.0)	20.1 (9.4)	16.7 (10.6)
MADRS score, mean (SD)	9.1 (6.5)**	6.5 (5.7)	5.6 (6.5)*	3.9 (5.7)	8.7 (8.0)	7.1 (6.4)

MADRS, Montgomery and Aasberg Depression Rating Scale; MMSE, Mini-Mental State Examination; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale.

χ^2 test for categorical, and Mann-Whitney U test for continuous variables.

All p values are two tailed. All available observations are included in the results.

*p ≤ 0.05.

**p ≤ 0.005.

dopaminergic agents can disrupt nocturnal sleep either by direct effect on the sleep/wake regulation or because of end of dose symptoms.^{25, 26}

In this study, we found in the multivariate model that insomnia was associated with depressive symptoms, female sex and disease duration. However, none of these variables were associated with insomnia in the univariate analysis at each study visit (table 2). The large variety of influencing factors and the inconsistency of many of the symptoms may explain these findings and demand a sophisticated statistical analysis, such as the generalised estimating equation model, in order to find reliable associations.

Insomnia is common as a symptom of depression in general and may also contribute to the development of depression. Depression is a rather common non-motor problem of PD, with a prevalence of about 50%.^{27, 28} Symptoms of depression in patients with PD may differ from the general population,²⁹ complicating its assessment, and even if recognised, it is often treated inadequately.³⁰ It is therefore important to examine patients with PD with insomnia for signs of depression, as this may represent a treatable cause to the complaint.

In this analysis, problems with sleep initiation were included in the definition of insomnia and, as expected from results from the general population, female sex was related to insomnia.^{31–33} The association with disease duration was, however, less straightforward to explain. This could be seen as a relationship between insomnia and a more advanced progression of the cerebral lesions of PD. In contrast, a high proportion of patients had insomnia as an inconsistent complaint, which may be due to different stages of severity; usually, the Hoehn and Yahr stage is seen as a better marker of disease progression than time. The patients may also over time develop comorbidities that may by themselves disturb normal sleep. Finally, according to the Braak hypothesis,²³ the areas of the brain involved in sleep/wake regulation²⁴ should be lesioned rather early in the disease development, and this may be supported by the high frequency of insomnia at baseline and no consistent increase during the study period.

Nocturia and sleep disordered breathing were not accounted for in this study. Impairment of the autonomic function and end of dose urge incontinence may lead to excessive nocturia. Conflicting results are reported for sleep disordered breathing in PD.^{34–37} In general, the prevalence of sleep apnoea increases with age and is likely to be underdiagnosed in older people.

In conclusion, in this prospective longitudinal cohort study, we found that insomnia is a highly frequent complaint in patients with PD. We have also shown that insomnia in patients with PD is an inconsistent and reversible complaint. By a new and robust statistical approach, we found that insomnia was significantly associated with female sex, duration of disease and depression. This underlines the clinical importance of evaluating and diagnosing depression in these patients.

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REFERENCES

- 1 **Lees AJ**, Blackburn NA, Campbell VL. The nighttime problems of Parkinson's disease. *Clin Neuropharmacol* 1988;**11**:512–19.

- 2 **Askenasy JJ**. Sleep in Parkinson's disease. *Acta Neurol Scand* 1993;**87**:167–70.
- 3 **Tandberg E**, Larsen JP, Karlsen K. A community-based study of sleep disorders in patients with Parkinson's disease. *Mov Disord* 1998;**13**:895–9.
- 4 **Karlsen KH**, Tandberg E, Arslan D, et al. Health related quality of life in Parkinson's disease: a prospective longitudinal study. *J Neurol Neurosurg Psychiatry* 2000;**69**:584–9.
- 5 **Goetz CG**, Wu J, Curgian LM, et al. Hallucinations and sleep disorders in PD: six-year prospective longitudinal study. *Neurology* 2005;**64**:81–6.
- 6 **Happe S**, Berger K. The association of dopamine agonists with daytime sleepiness, sleep problems and quality of life in patients with Parkinson's disease—a prospective study. *J Neurol* 2001;**248**:1062–7.
- 7 **Foley DJ**, Monjan A, Simonsick EM, et al. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep* 1999;**22**(Suppl 2):S366–72.
- 8 **Dodge R**, Cline MG, Quan SF. The natural history of insomnia and its relationship to respiratory symptoms. *Arch Intern Med* 1995;**155**:1797–800.
- 9 **Chaudhuri KR**. Nocturnal symptom complex in PD and its management. *Neurology* 2003;**61**(Suppl 3):S17–23.
- 10 **Tandberg E**, Larsen JP, Nessler EG, et al. The epidemiology of Parkinson's disease in the county of Rogaland, Norway. *Mov Disord* 1995;**10**:541–9.
- 11 **Larsen JP**, Dupont E, Tandberg E. Clinical diagnosis of Parkinson's disease. Proposal of diagnostic subgroups classified at different levels of confidence. *Acta Neurol Scand* 1994;**89**:242–51.
- 12 **Aarsland D**, Perry R, Brown A, et al. Neuropathology of dementia in Parkinson's disease: a prospective, community-based study. *Ann Neurol* 2005;**58**:773–6.
- 13 **Tandberg E**, Larsen JP, Karlsen K. Excessive daytime sleepiness and sleep benefit in Parkinson's disease: a community-based study. *Mov Disord* 1999;**14**:922–7.
- 14 **Fahn S**, Mordon CD, Calne DB, et al, eds. Members of the UPDRS Development Committee. Unified Parkinson's Disease Rating Scale. *Recent developments in Parkinson's disease*. Florham Park, NY: Macmillan Health Care Information, 1987:153–63.
- 15 **Hoehn MM**, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology* 1967;**17**:427–42.
- 16 **Montgomery SA**, Asberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry* 1979;**134**:382–9.
- 17 **Folstein MF**, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;**12**:189–98.
- 18 **Gjerstad MD**, Aarsland D, Larsen JP. Development of daytime somnolence over time in Parkinson's disease. *Neurology* 2002;**58**:1544–6.
- 19 **Vitiello MV**, Larsen LH, Moe KE. Age-related sleep change: gender and estrogen effects on the subjective-objective sleep quality relationships of healthy, noncomplaining older men and women. *J Psychosom Res* 2004;**56**:503–10.
- 20 **Nausieda PA**, Weiner WJ, Kaplan LR, et al. Sleep disruption in the course of chronic levodopa therapy: an early feature of the levodopa psychosis. *Clin Neuropharmacol* 1982;**5**:183–94.
- 21 **Kamel NS**, Gammack JK. Insomnia in the elderly: cause, approach, and treatment. *Am J Med* 2006;**119**:463–9.
- 22 **Thorpy MJ**, Adler CH. Parkinson's disease and sleep. *Neural Clin* 2005;**23**:1187–208.
- 23 **Braak H**, Ghebremedhin E, Rub U, et al. Stages in the development of Parkinson's disease-related pathology. *Cell Tissue Res* 2004;**318**:121–34.
- 24 **Saper CB**, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. *Nature* 2005;**437**:1257–63.
- 25 **Rye DB**. The two faces of Eve: dopamine's modulation of wakefulness and sleep. *Neurology* 2004;**63**(Suppl 3):S2–7.
- 26 **van Hilten B**, Hoff JI, Middelkoop HA, et al. Sleep disruption in Parkinson's disease. Assessment by continuous activity monitoring. *Arch Neurol* 1994;**51**:922–8.
- 27 **Tandberg E**, Larsen JP, Aarsland D, et al. The occurrence of depression in Parkinson's disease. A community-based study. *Arch Neurol* 1996;**53**:175–9.
- 28 **Cummings JL**, Masterman DL. Depression in patients with Parkinson's disease. *Int J Geriatr Psychiatry* 1999;**14**:711–18.
- 29 **Ehrt U**, Bronnick K, Leentjens AF, et al. Depressive symptom profile in Parkinson's disease: a comparison with depression in elderly patients without Parkinson's disease. *Int J Geriatr Psychiatry* 2006;**21**:252–8.
- 30 **Weintraub D**, Moberg PJ, Duda JE, et al. Recognition and treatment of depression in Parkinson's disease. *J Geriatr Psychiatry Neurol* 2003;**16**:178–83.
- 31 **Johnson EO**, Roth T, Schultz L, et al. Epidemiology of DSM-IV insomnia in adolescence: lifetime prevalence, chronicity, and an emergent gender difference. *Pediatrics* 2006;**117**:e247–56.
- 32 **Dorsey CM**, Bootzin RR. Subjective and psychophysiological insomnia: an examination of sleep tendency and personality. *Biol Psychiatry* 1997;**41**:209–16.
- 33 **Perlis ML**, Giles DE, Buysse DJ, et al. Self-reported sleep disturbance as a prodromal symptom in recurrent depression. *J Affect Disord* 1997;**42**:209–12.
- 34 **Happe S**, Schrodl B, Falit M, et al. Sleep disorders and depression in patients with Parkinson's disease. *Acta Neurol Scand* 2001;**104**:275–80.
- 35 **Ferini-Strambi L**, Franceschi M, Pinto P, et al. Respiration and heart rate variability during sleep in untreated Parkinson patients. *Gerontology* 1992;**38**:92–8.
- 36 **Wetter TC**, Collado-Seidel V, Pollmacher T, et al. Sleep and periodic leg movement patterns in drug-free patients with Parkinson's disease and multiple system atrophy. *Sleep* 2000;**23**:361–7.
- 37 **Arnulf I**, Konofal E, Merino-Andreu M, et al. Parkinson's disease and sleepiness: an integral part of PD. *Neurology* 2002;**58**:1019–24.