Intraindividual Variability of REM Sleep Behavior Disorder in Parkinson's Disease: A Comparative Assessment Using a New REM Sleep Behavior Disorder Severity Scale (RBDSS) for Clinical Routine

Friederike Sixel-Döring, M.D.; Marcus Schweitzer, M.Sc.; Brit Mollenhauer, M.D.; Claudia Trenkwalder, M.D.

Paracelsus-Elena-Klinik, Center of Parkinsonism and Movement Disorders, Kassel, Germany

SCIENTIFIC INVESTIGATIONS

Objectives: To develop a polysomnographic video-based scale for rating the severity of REM sleep behavior disorder (RBD), to classify the severity of RBD and to determine the intraindividual variability of RBD in patients with Parkinson disease (PD).

Methods: Twenty PD patients identified with RBD were investigated with video-supported polysomnography (PSG). Seventy-three motor behavior events during REM sleep were graded visually and polysomnographically on an event-to-event basis according to categorical location of movements: "0" = no visible movement; "1" = slight movements or jerks "2" = movements involving proximal extremities, including violent behavior; "3" = axial involvement including bed falls. Vocalizations were rated as "1" for present or "0" for absent. Ratings were performed by 2 blinded raters. Reliability was calculated with Cohen's κ. Final RBD severity was determined by the highest score given. This rating scale was then used to compare RBD severity and density, calculated as RBD episodes per REM sleep minute over 2 consecutive nights in 10 additional PD patients with RBD. Statistical significance was determined by effect size (Hedges' g) and calculation of the confidence interval.

Results: Interrater reliability of the scale was 0.8 for movement data and 0.89 for vocalization data. Intraindividual RBD density varied significantly (effect size 0.5 ± 0.22; confidence interval 0.2 to 0.79) by factor 2.5 between the 2 PSG nights. Final RBD severity score differed in 60% of patients between nights 1 and 2. Forty percent of patients showed violent behavior, but only on one night. All patients had severely disturbed sleep with reduced sleep efficiency, loss of slow wave sleep, sleep fragmentation, and an increased periodic limb movement (PLM) index.

Conclusion: The RBD severity scale (RBDSS) is a reliable, easy-to-use tool for assessing motor events during REM sleep with PSG. Severity and phenomenology of RBD shows a significant variability in the individual PD patient.

Keywords: Parkinson's disease, REM sleep behavior disorder, rating scale, severity, polysomnography

Citation: Sixel-Döring F; Schweitzer M; Mollenhauer B; Trenkwalder C. Intraindividual variability of REM sleep behavior disorder in parkinson's disease: a comparative assessment using a new REM sleep behavior disorder severity scale (RBDSS) for clinical routine. *J Clin Sleep Med* 2011;7(1):75-80.

The International Classification of Sleep Disorders (ICSD-2) defines REM sleep behavior disorder (RBD) as REM sleep without atonia (RWA) plus either sleep related injuries, potentially injurious or disruptive behaviors documented by medical history or polysomnography.[1] RBD was first described as a REM parasomnia with dream-enacting behaviors and loss of physiological REM sleep muscle atonia,[2] including vocalizations, scenic behavior, or violent movements.[3] In clinical practice, diagnosis and adequate treatment of abnormal nocturnal behaviors is of great importance for the well-being of the patient as well as for care-givers and the family. Moreover, the correct diagnosis of RBD may enable us in the future to identify PD patients in the early pre-motor stage of the disease for treating them with new neuroprotective agents.[4] We therefore have to know the clinical variability of RBD in PD and need a classification of its severity.

RBD in firmly diagnosed moderate to advanced Parkinson's disease (PD) patients is frequent and needs to be differentiated from psychotic phenomena and other distressing sleep-disruptive symptoms such as nighttime akinesia or periodic limb

---

BRIEF SUMMARY

Current Knowledge/Study Rationale: The study aims at investigating the phenomenology of REM sleep behaviour disorder (RBD) in Parkinson's disease (PD) patients. For this a polysomnographic severity scale was developed, rating REM sleep behaviour disorder clinically on an event-to-event basis.

Study Impact: The newly developed REM sleep disorder severity scale (RBDSS) is a suitable and valid instrument for assessing RBD in PD. There is a significant intraindividual night-to-night variability in the expression of RBD in PD patients, to be considered when evaluating their nighttime sleep disturbances.

---

movement disorder (PLMD). Despite careful evaluation of a patient's history, including their sleep habits and questioning of bed partners, clinical diagnosis of the nocturnal disturbance is often not correct, and calls for video-supported polysomnography (PSG), as required for the diagnosis of RBD according to the ICSD-2.[1] Various studies have attempted to characterize and quantify RBD, including electromyographic measurements of tonic and phasic muscle activity during REM sleep[5]; differ-

entiation between simple and complex movements[6,7]; grading of RBD intensity as mild, moderate or severe[8]; and qualitative descriptions of RBD manifestations in video-supported polysomnography.[9] A detailed analysis of the number and types of motor events occurring during REM sleep uses a complex and thorough, but time-consuming video classification system.[10] Many of these methods may yield interesting scientific information about the complex phenomenology of RBD; however, they do not appear feasible for use in clinical practice or for comparative studies.

To look into night-to-night variability of RBD and for use in further comparative studies, we developed a simple video-polysomnographic rating scale for RBD to be used in PD patients.

METHODS

Study design

We performed a 2-night PSG in 20 patients who were scored according to the newly developed RBD severity scale (RBDSS). All video-based ratings of the RBDSS were performed by 2 independent raters (F S-D, CT) on 2 nights and evaluated independently. An interrater-analysis was performed.

The night-to-night variability of 2 consecutive nights was then analyzed by one rater (F S-D) in a further independent sample of 10 PD patients with RBD using the same scale.

Patients

For the development of the RBDSS, we selected 20 consecutive PD patients who had been diagnosed with clinical RBD by video-supported PSG from our sleep laboratory. These patients were part of our inpatient population of PD patients who had nocturnal sleep problems. Patient pre-selection was performed by the technician who included only those patients who showed polysomnographic signs of RBD. Fifteen men and 5 women, mean age 69 ± 5 years (range 57–76), with an average disease duration of 8 ± 6 years (range 1–28) were included. Mean Hoehn and Yahr stage was 3 ± 1 (range 2–4); 5 patients had cognitive impairment, with Mini Mental Status Exam (MMSE) score < 26. Patients on nocturnal ventilation therapy, those treated with benzodiazepines, neuroleptics, barbiturates, or tricyclic antidepressant medication, as well as patients with severe dementia (MMSE < 10) were excluded. Diagnosis of PD was established according to clinical criteria (UK Brain Bank Criteria), including a > 30% response to levodopa on the Unified Parkinson's Disease Rating Scale (UPDRS) – Part III.[11]

For investigation of the intraindividual variability of RBD in PD patients, we selected 10 consecutive PD patients diagnosed with RBD.[1] Seven men and 3 women, mean age 68 ± 9 years (range 44–78) with an average disease duration of 12 ± 8 years (range 3-30) were included. Mean Hoehn and Yahr stage was 4 ± 1. Three patients had cognitive impairment with MMSE < 26. Criteria for exclusion and for establishing diagnosis were identical to the first patient population of the study.

All patients in this investigation received their stable PD medication on their PSG nights and gave written informed consent to participate in this study including the use of video-taping (approved by the ethical committee of the Ärztekammer Hessen).

Polysomnography

All nighttime sleep recordings started immediately after connecting the patient and calibration with lights off at 22:00 and ended at 6:00 the next morning. Cardiorespiratory PSG (Xeltec: Excel Tech Ltd; Oakville, Ontario; Canada) was applied including bilateral monopolar central EEG with 2 channels, electrooculogram (EOG), chin and bilateral tibialis anterior surface electromyography (EMG), air flow registration, tracheal sound registration by microphone, thoracic and abdominal belts to measure respiratory movements, electrocardiogram, and oximetry. All patients were documented with an infrared video recording synchronized to the PSG. A sleep lab technician monitored each recording. For the comparative study in the 10 PD patients, 2 consecutive nights were registered and evaluated. Sleep stages, awakenings, leg movements, and respiratory events were scored visually according to standard criteria.[1,12-15] Sleep efficiency was defined as total sleep time (TST) / time in bed (TIB). Quantitative analysis of sleep stages was calculated as a percentage of TST. The presence of RBD was evaluated by time-synchronized video analysis in accordance with EEG and EOG, in line with criteria established by Schenck et al. and the ICSD-2.[1,2] RWA was determined by the presence of tonic or phasic muscle activity on the chin EMG with an amplitude at least equal to the amplitude observed during quiet wakefulness.

RBD Assessment

For the development of the RBDSS, motor events in REM sleep were rated on a digital scale from 0–3 according to the localization and severity of movements. No visible movement but registration of RWA scored as 0, slight movements including facial movements, jerks or movements restricted to the distal extremities scored as 1, movements involving the proximal extremities, complex and/or violent behaviors scored as 2, and any axial involvement with a possibility of falling or observed falls scored as 3; vocalizations were rated as absent, indicated by "0", or present, indicated by "1", for any sound generated during REM sleep other than respiratory noises. Motor and vocalization scores were separated by a full stop. **Table 1** compiles the complete RBDSS. (See supplementary online videos) The highest scoring given for each individual patient had to be present in at least one REM episode to define the final RBD severity score.

For investigation of the intraindividual variability of RBD, all RBD episodes during each night were counted and classified using the RBDSS. RBD density was calculated as the number of episodes per REM sleep minute. Results of nights 1 and 2 for all RBD parameters were compared.

Statistical Analysis

Statistical analysis was carried out by an experienced statistician, using SPSS. For testing the reliability of the RBDSS, all types of motor behaviors observed during REM sleep in the 20 patients were rated independently according to the aforementioned criteria. Each rater was blinded to the ratings of the other. Interrater agreement was evaluated using Cohen's κ,[16] which compares the observed agreement to that expected if the ratings were independent; κ equals 0 when the agreement equals that expected under independence and equals 1.0 when perfect agreement occurs. Kappa was calculated separately for movement

evaluation and vocalization. Weighted κ was used for movement evaluation, and unweighted κ was used for the vocalization data.

Computation of effect sizes for intraindividual RBD variability was accomplished using Hedges' g. The calculation of Hedges' g was based on mean and standard deviations.[17] The confidence interval was also calculated.[18]

RESULTS

RBDSS

Altogether 73 events were scored according to the RBDSS criteria. Comparative results of these ratings by the 2 blinded raters are shown in **Figure 1**. Cohen's κ was calculated at 0.80 for movement data and 0.89 for vocalization data, showing good interrater reliability in both categories.[19] In cases where results differed between raters, the events in question were re-scored together and consensus established for final evaluation. Final RBD severity score comprised 7 patients with a severity score of 3.1, 3 patients with a severity score of 3.0, 3 patients with a severity score of 2.1, 5 patients with a severity score of 2.0, 1 patient with a severity score of 1.0, and 1 patient with a score of 0.1, showing only RWA and vocalizations.

Intraindividual RBD Variability in 10 PD Patients

RBD density ranged between 0 (only RWA) and 0.72 episodes per REM minute. Intraindividual RBD density between night 1 and 2 varied by a factor of 2.5 (range 1.4–3.9). Mean effect size was calculated at 0.5 (± 0.22), showing a medium effect size. The confidence interval was calculated at 0.2 to 0.79, which is defined as statistically significant. Overall RBD severity ranged from 0.0 (RWA) to 3.1 with violent behavior and risk of bed falls. Final RBD severity score on nights 1 and 2 differed in 6/10 patients (60%) concerning motor events and/or vocalization criteria. Four of 10 patients (40%) showed violent

behavior; however, this was observed only on one night. The number of REM periods per night ranged from 1 to 6, showing an intraindividual difference between the 2 consecutive nights in 6 of 10 patients (60%) by a factor of 1.9. (See **Table 2**)

Sleep Analysis

The 20 PD patients in the RBDSS validation study showed severely disturbed sleep with sleep efficiency of 66% ± 17%

Table 1—REM sleep behavior disorder severity scale (RBDSS) (See supplementary online videos)

Motor Events

0. = no visible motor activity, RWA present
Only definition criteria of RWA according to ICSD are fulfilled, no other phasic muscle activity in the limbs or face is visible or obvious on recording.

1. = small movements or jerks
Isolated, single hand or foot movements or facial jerks visible, restricted to the distal extremities and/or face.

2. = proximal movements including violent behavior
Single movements or series of movements including proximal extremities, no change of position.

3. = axial movements including bed falls
Movements with axial involvement and/or change of body position, falls.

Vocalizations

0. = no vocalization
Snoring with some sound may be present and should be differentiated from REM-associated vocalization.

1. = all sleep associated sounds other than respiratory noises
Talking, shouting, murmuring, laughing or screaming, either tonic or phasic, are present during at least one REM episode.

ICSD, International Classification of Sleep Disorders; RWA, REM sleep without atonia

---

Figure 1—REM sleep behavior disorder (RBD) severity scale (RBDSS) ratings for 73 RBD episodes in 20 Parkinson's disease patients by 2 blinded raters
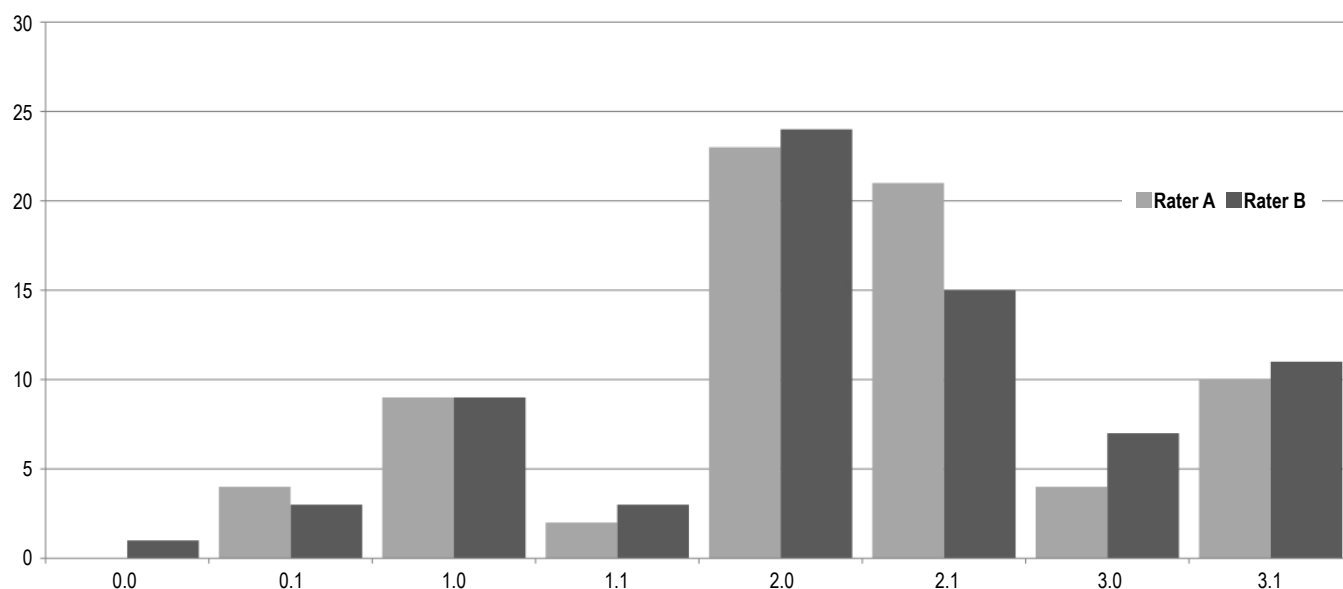
Table 2—REM sleep characteristics in 10 Parkinson disease patients with REM sleep behavior disorder on 2 consecutive nights

Patient	Age	Disease duration	Sleep efficiency %		REM % TST		No. REM episodes		RBDSS diagnosis		RBD density	
	yrs.	yrs	night 1	night 2	night 1	night 2	night 1	night 2	night 1	night 2	night 1	night 2
1	72	13	81.1	72.8	16.8	19.4	6	3	2.1	2.0	0.197	0.281
2	65	9	76.6	75.0	19.5	9.7	3	6	3.0	1.0	0.249	0.125
3	73	10	75.1	50.8	8	5.3	1	1	3.1	1.0	0.072	0.272
4	68	22	65.2	72.8	27.7	10.2	3	2	3.1	3.1	0.196	0.386
5	73	7	40.6	49.1	20.6	22.3	2	2	1.0	1.0	0.254	0.082
6	44	11	87.1	70.7	9.0	24.1	3	2	2.1	3.1	0.366	0.197
7	68	14	63.7	56.9	35.7	4.2	2	2	3.1	0.0	0.214	—
8	66	30	50.5	68.8	2.5	7.3	1	1	3.0	2.0	0.722	0.212
9	78	3	40.3	66.3	9.7	10.8	1	2	2.1	2.1	0.258	0.066
10	72	5	52.0	77.9	13.7	13.4	2	5	2.1	2.1	0.186	0.129

RBD density was calculated as the number of RBD episodes per REM sleep minute. PD, Parkinson's disease; RBD, REM sleep behavior disorder; TST, Total sleep time; RBDSS, RBD severity scale.

(mean ± SD). Disruption of physiological sleep cycles was evident with a loss of slow wave sleep and a consecutive increase in sleep stages 1 and 2. Sleep stage distribution calculated as a % of TST was 32% ± 1% in stage 1, 41% ± 16% in stage 2, 5% ± 10% in slow wave sleep, and 22% ± 12% in REM sleep. Patients had an average of 3 ± 1 (range 1–5) REM episodes per night, with an average REM latency of 95 ± 92 minutes. Increased sleep fragmentation became manifest in an average of 39 ± 25 awakenings per night, and a PLM index average of 34 ± 33 per hour. Previously unknown sleep disordered breathing (SDB) with a respiratory distress index (RDI) > 5 was detected in 11 patients (55%).

Results from the 10 PD patients for the comparative RBD study showed a similar pattern of impaired sleep architecture: Mean sleep efficiency was 65% ± 14%. Sleep stage distribution calculated as a % of TST was 27% ± 10% in stage 1, 52% ± 11% in stage 2, 7% ± 7% in slow wave sleep, and 15% ± 9% in REM sleep. Patients had an average of 3 ± 2 (range 1–6) REM episodes per night, with an average REM latency of 140 ± 90 minutes. All patients had increased sleep fragmentation, with an average of 33 ± 14 awakenings per night. PLM index averaged 23 ± 33 per hour. Previously unknown SDB with a RDI > 5 was found in 4 patients (40%).

DISCUSSION

In this study of RBD in PD patients, we first developed and evaluated a polysomnographic severity scale for rating RBD in PD patients to better describe the different phenomena of RBD. We then used this scale to investigate the night-to-night variability of RBD in the individual patient.

For the RBDSS, a good to excellent interrater reliability could be established. For practical reasons, we defined the final RBD severity score according to the most severe episode seen during the sleep recording. Accordingly, 50% of the PD patients showed RBD with the highest severity score of 3.- involving axial movements, bed falls being prevented by the use of bed railings at the patients' request in two cases. Proximal limb movements defined a RBD severity score of 2.- in 40%

of the patients. Only 10% of patients showed slight movements or only jerks during two nights of recording. In this study we were not able to confirm the frequent occurrence of purposeful behaviors as described by de Cock et al.[20]

A scale using simple phenomenological categories such as localization of movements—distal, proximal, or axial—and the presence or absence of vocalizations, is easy to perform on an event-to-event basis while evaluating standard PSG. Also, the scale allows estimation of the risk for potentially harmful behaviors. Falling out of bed when axial movements are present and injuring the bed partner in case of proximal limb movements are major risks for PD patients.

One potential limitation to the scale tested here is that movements may be missed or not scored accurately because they are hidden by the blanket or not recorded on the video. Also, differentiation between vocalizations, i.e., grunting and respiratory noises can be difficult, especially if the patient snores. Actually, these difficulties accounted for the interrater variability in this study and cannot be solved, because patients will not tolerate sleeping without a blanket or in a fixed position where the face is constantly in the focus of the camera. However, standard PSG will pick up muscle activity in the chin and tibialis anterior muscles, thus permitting the calculation of RWA as a prerequisite for the presence of RBD. For treatment decisions, minor movements or quiet REM related noises appear negligible, as they do not endanger the patient or bed partner. Also, for optimal evaluation of each patient, the bed partner's history of nocturnal disturbances should possibly be added to the scale. Unfortunately, this was not feasible in this study, as many PD patients of this age group do not live with a spouse, or the spouse is already sleeping in a separate room because of the nocturnal disturbances. Future studies and increased awareness of RBD may help to improve this situation.

It is however, still an open question as to whether patients with mild RBD and only slight movements may develop violent behavior on other nights, or if this pattern remains stable over time.

Methods for characterization of RBD published so far are either verbally descriptive,[6-8]—and thus subject to interpretation

influenced by personal and/or cultural aspects—, require elaborate electromyographic measurements,[5] or call for extremely detailed video-based analysis of nocturnal motor events according to duration, complexity, and topographical distribution.[10] Although the study by Frauscher and coworkers yields interesting information on the characteristics of motor events in RBD, and may thus be relevant for scientific questions, it was not designed for the daily routine of a clinical sleep lab.

In the second comparative step of this sleep lab study, RBD shows a distinct intraindividual variability in 10 PD patients concerning overall occurrence as well as phenomenology. As sleep efficiency, the percentage of REM sleep, and total number of REM phases varied considerably in the individual patient between the two nights investigated, we calculated a somewhat arbitrary parameter of RBD density as the number of separate RBD episodes per REM sleep minute. Thus, we could demonstrate that not only does the quality of RBD described by the RBDSS score and the occurrence of violent behaviors during RBD episodes differ significantly in the individual patient from night to night, but that the quantity of RBD also differs significantly. To our knowledge, this is the first study showing that the expression of RBD varies in the individual PD patient.

These results cannot be attributed to pharmacological influences, as medication was kept constant in both PSG nights. There is, however, a need to consider the influence of treatment on the variability of RBD and longitudinal evolvement of RBD in PD. In this study, all patients showed other hallmarks of neurodegenerative disease in sleep such as sleep fragmentation, loss of slow wave sleep, and increased PLM indices.[21,22] Whether the intraindividual variability of RBD demonstrated here is also present in preclinical and early stages of PD, or if it evolves with the progressive destruction of sleep cycles over time,[23] remains open. Only one patient of the cohort of 10 PD patients was in an early stage of the disease with a disease duration ≤ 5 years. Interestingly, 15 of the 30 patients (50%) were diagnosed for the first time as having SDB, which is in agreement with the incidence mentioned in the literature.[24] Personal observations during PSG evaluation point to the possibility that apnea with oxygen desaturation may actually trigger RBD episodes. Abnormal motor behavior during apnea-induced microarousals in REM sleep following oxygen desaturation due to obstructive sleep apnea/hypopnea has been described previously in non-PD individuals and interpreted as motor behavior mimicking RBD.[25] This however requires further investigation in PD patients. Factors determining the clinical spectrum of RBD are presently not fully understood. Dream content seems to have an influence, as movements in REM are often congruent with the patient's dream recall.[2] However, this was not investigated in this study. Also, little to nothing is known on how dreams are created and which factors contribute to dream content in PD patients.

Recent studies imply that RBD is not only a preclinical manifestation of PD and other neurodegenerative diseases,[26-28] but it is also associated with cognitive impairment and an akinetic rigid subtype of PD.[29-31] If RBD is to be used as a biomarker for pre-motor diagnosis of PD, variability of RBD phenomena has to be considered–calling for several nights of PSG in order not to miss the diagnosis.

REFERENCES

1. American Academy of Sleep Medicine. REM sleep behavior disorder. In: *International classification of sleep disorders; diagnostic and coding manual. 2nd ed.* Westchester, IL: American Academy of Sleep Medicine, 2005:148-52.
2. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. *Sleep* 1986;9:293-308.
3. Schenck CH, Hurwitz TD, Mahowald MW. Symposium: Normal and abnormal REM sleep regulation: REM sleep behaviour disorder: an update on a series of 96 patients and a review of the world literature. *J Sleep Res* 1993;2:224-31.
4. Hart RG, Pearce LA, Ravina BM, Yaltho TC, Marler JR. Neuroprotection trials in Parkinson's disease: systematic review. *Mov Disord* 2009;24:647-54.
5. Consens FB, Chervin RD, Koeppe RA, et al. Validation of a polysomnographic score for REM sleep behavior disorder. *Sleep* 2005;28:993-7.
6. Sforza E, Zucconi M, Petronelli R, Lugaresi E, Cirignotta F. REM sleep behavioral disorders. *Eur Neurol* 1988;28:295-300.
7. Fantini ML, Gagnon JF, Filipini D, Montplaisir J. The effects of pramipexole in REM sleep behavior disorder. *Neurology* 2003;61:1418-20.
8. Iranzo A, Santamaria J, Rye DB, et al. Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. *Neurology* 2005;65:247-52.
9. Gagnon JF, Bedard MA, Fantini ML, et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. *Neurology* 2002;59:585-9.
10. Frauscher B, Gschliesser V, Brandauer E, et al. Video analysis of motor events in REM sleep behavior disorder. *Mov Disord* 2007;22:1464-70.
11. Fahn S, Elton R, Members of the UPDRS Development Committee. Unified Parkinson's Disease Rating Scale. Florham Park NJ: Macmillan Healthcare Information, 1987.
12. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep* 1999;22:667-89.
13. Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. Bethesda, MD: Neurological Information Network, 1968.
14. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep* 1992;15:173-84.
15. Coleman R. Periodic movements in sleep (nocturnal myoclonus) and restless legs syndrome In: Guilleminault C, ed. *Sleeping and waking disorders: indications and techniques*. Menlo Park ; London: Addison-Wesley, 1982: 265-95.
16. Robinson BF, Bakeman R. ComKappa: a Windows '95 program for calculating kappa and related statistics. *Behav Res Methods Instrum Comput* 1998;30:731-2.
17. Hedges LV, Olkin I. *Statistical methods for meta-analysis*. Orlando: Academic Press, 1985.
18. Ray JW, Shadish WR. How interchangeable are different estimators for effect size? *J Consult Clin Psychol* 1996;64:1316-25.
19. Fleiss JL. *Statistical methods for rates and proportions*. 2nd ed. New York, Chichester: Wiley, 1981.
20. De Cock VC, Vidailhet M, Leu S, et al. Restoration of normal motor control in Parkinson's disease during REM sleep. *Brain* 2007;130:450-6.
21. Chokroverty S. Sleep and degenerative neurologic disorders. *Neurol Clin* 1996;14:807-26.
22. Comella CL. Sleep disorders in Parkinson's disease: an overview. *Mov Disord* 2007;22 Suppl 17:S367-73.
23. Diederich NJ, Vaillant M, Mancuso G, Lyen P, Tiete J. Progressive sleep 'destructuring' in Parkinson's disease. a polysomnographic study in 46 patients. *Sleep Med* 2005;6:313-8.
24. Happe S, Trenkwalder C. Sleep disorders in Parkinson's disease. In: Ebadi MS, Pfeiffer R, eds. *Parkinson's disease*. Boca Raton, Fla. ; London: CRC, 2005:212-27.
25. Iranzo A, Santamaria J. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. *Sleep* 2005;28:203-6.
26. Schenck CH, Bundlie SR, Mahowald MW. REM behavior disorder (RBD): delayed emergence of parkinsonism and/or dementia in 65% of older men initially diagnosed with idiopathic RBD, and an analysis of the minimum and maximum tonic and phasic electromyographic abnormalities found during REM sleep. *Sleep* 2003;26:A316.
27. Boeve BF, Silber MH, Saper CB, et al. Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. *Brain* 2007;130:2770-88.

28. Eisensehr I, Linke R, Noachtar S, Schwarz J, Gildehaus FJ, Tatsch K. Reduced striatal dopamine transporters in idiopathic rapid eye movement sleep behaviour disorder. Comparison with Parkinson's disease and controls. *Brain* 2000;123 (Pt 6):1155-60.

29. Vendette M, Gagnon JF, Decary A, et al. REM sleep behavior disorder predicts cognitive impairment in Parkinson disease without dementia. *Neurology* 2007;69:1843-9.

30. Postuma RB, Gagnon JF, Vendette M, Charland K, Montplaisir J. REM sleep behaviour disorder in Parkinson's disease is associated with specific motor features. *J Neurol Neurosurg Psychiatry* 2008;79:1117-21.

31. Sinforiani E, Pacchetti C, Zangaglia R, Pasotti C, Manni R, Nappi G. REM behavior disorder, hallucinations and cognitive impairment in Parkinson's disease: a two-year follow up. *Mov Disord* 2008;23:1441-5.

SUBMISSION & CORRESPONDENCE INFORMATION

DISCLOSURE STATEMENT