Validation of a Polysomnographic Score for REM Sleep Behavior Disorder

Flavia B. Consens, MD; Ronald D. Chervin, MD, MS; Robert A. Koeppe, PhD; Roderick Little, PhD; Suyu Liu; Larry Junck, MD; Karen Angell, RPT; Mary Heumann, BA; Sid Gilman, MD,FRCP

University of Michigan, Ann Arbor, MI

Study Objectives: Rapid eye movement (REM) sleep behavior disorder (RBD) was described more than 2 decades ago, but only 1 report on 5 patients and 5 normal subjects has tested the effectiveness of a method by which relevant polysomnographic findings can be quantified. We sought to validate this method in a larger sample of patients and control subjects.

Design: Cross-sectional.

Setting: Academic hospital.

Interventions: A clinician interviewed 17 patients at risk for RBD secondary to neurodegenerative disorders and 6 controls to assess whether RBD was present by history. Bed partners completed a questionnaire that quantified RBD symptom severity. From 2 consecutive nocturnal studies in each patient, 2 different polysomnographic RBD scores were generated: the percentage of 30-second REM epochs with at least 15 seconds of tonically maintained electromyographic activity, and the percentage of 3-second REM mini-epochs that contained phasic electromyographic bursts.

Measurements and Results: The tonic and phasic measures, combined together, were higher in patients with clinical determinations of probable or possible RBD (n = 9) than in patients judged unlikely to have RBD (n = 14, *P* = .023). The overall polysomnographic measure correlated with the symptom scores (*rho* = 0.42, *P* = . 048). Specific polysomnographic RBD measures on night 1 correlated highly with those on night 2 (*rho* > 0.70, *P* < .0001).

Conclusions: This quantitative method to assess the severity of RBD polysomnographic features appears to be both valid and reliable in patients at risk for RBD because of neurodegenerative disorders.

Keywords: REM sleep behavior disorder, polysomnography, reliability of results, diagnosis, synucleinopathies, parasomnia

Citation: Consens FB; Chervin RD; Koeppe RA et al. Validation of a polysomnographic score for REM sleep behavior disorder. *SLEEP* 2005;28(8):993-997.

INTRODUCTION

RAPID EYE MOVEMENT (REM) SLEEP BEHAVIOR DISORDER (RBD) WAS FIRST DESCRIBED MORE THAN 2 DECADES AGO.[1] THE CHRONIC FORM HAS been associated with some neurodegenerative disorders and may be a harbinger for α-synucleinopathies.[2,3] The RBD can precede the onset of the clinical manifestations of a neurologic disorder by many years, as shown in a study involving 38% of subjects diagnosed as having idiopathic RBD 10 years earlier.[4] The underlying cause of RBD remains unknown, but it has been associated with central dopaminergic deficits.[5] The disorder is characterized by intermittent loss of REM sleep electromyographic (EMG) atonia and by the appearance of elaborate motor activity associated with dream mentation.[6] Clinical manifestations include violent or injurious behavior, potentially harmful sleep behavior, dreams that appear to be "acted out," or sleep behavior that disrupts sleep continuity. Polysomnographic manifestations include excessive tonic or phasic EMG activity during REM sleep.

Iranzo recently suggested that the diagnosis of RBD can be missed when clinical evaluation consists only of history without sleep medicine consultation and polysomnography.[7] The availability of a validated method to quantify REM sleep without atonia could benefit both clinical practice and sleep research. A single report by Lapierre and Montplaisir on 5 patients and 5 normal subjects provides a method by which relevant polysomnographic findings might be quantified.[8] This RBD polysomnographic scoring method (RPSM) involves scoring of EMG phasic bursts and tonic EMG elevation during REM sleep. The RPSM differentiates RBD patients from controls, though validity data are limited to this initial small sample. Another approach has been proposed to capture shorter tonic increases in muscle activity and activation of limb muscles, in addition to those of the chin, but even here timeframes have been chosen arbitrarily according to the authors, and the validity of the approach has not been specifically tested.[9] Thus, we and other authors have used the original RPSM approach in RBD research,[5,10,11] but still none have provided additional data to validate the method. We now provide new data on the validity of the RPSM in a sample of RBD patients and control subjects. The patients had neurodegenerative diseases that placed them at risk for RBD.

METHODS

Subject Selection

We studied patients with diagnoses of multiple system atrophy (MSA),[12] Parkinson disease (PD),[13] dementia with Lewy bodies (DLB),[14] progressive supranuclear palsy (PSP),[15] and sporadic olivopontocerebellar atrophy (OPCA).[16] Diagnoses were made by board-certified neurologists who specialize in neurodegenerative disorders. The patients were volunteer participants in a National Institutes of Health-funded study of RBD in the α-synucleinopathies, including MSA, PD, and DLB. They were recruited from the ataxia, movement disorders, and cognitive disorders clinics at the Department of Neurology, University of Michigan. Subjects were recruited sequentially from these clinics if they met criteria

Disclosure Statement

This was not an industry supported study. Drs. Consens, Chervin, Koeppe, Little, Liu, Junck, Angell, Heumann, and Gilman have indicated no financial conflicts of interest.

Submitted for publication November 2004
Accepted for publication May 2005

Address correspondence to: Flavia B. Consens, MD, Michael S. Aldrich Sleep Laboratory, 8D-8702 University Hospital, Box 0117, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0117; Tel: 734 647 9064; Fax 734 647 9065; E-mail: fconsens@umich.edu

for diagnosis; indicated interest in the research study; and signed a consent form or, if demented, had a consent form cosigned by the next of kin or legal guardian. The patients had not previously been referred to a sleep disorders center, and the consultation with sleep experts was included as part of their study. Patients with PSP were included to have a group of patients with a neurodegenerative disorder causing parkinsonian symptoms unassociated with RBD, for comparison with the MSA, DLB, and PD patients. For comparison to patients with neurodegenerative disorders, we studied normal control subjects with a similar age and sex distribution. The controls were individuals not genetically related to the patients but still interested in participating in the study. Control subjects had no neurodegenerative disease. They were recruited from the community and not specifically selected for any sleep complaints. For the most part they shared the same environment as the subjects (significant other, friend, church member, etc.). The Institutional Review Board of the University of Michigan approved this investigation, and all participants provided signed informed consent.

Clinical Interview

Subjects were admitted to the General Clinical Research Center Sleep Disorders Laboratory, where they underwent a complete history and physical examination. A comprehensive evaluation of their sleep history was performed by either of 2 neurologists who are each diplomates of the American Board of Sleep Medicine and the American Board of Psychiatry and Neurology. Based on the *International Classification of Sleep Disorders* (ICSD) entry for RBD,[6] the physicians generated an overall clinical impression of whether the likelihood of RBD was probable, possible, or unlikely. Because evidence-based definitions of these states do not exist, this rating represents a Likert scale only. In general, patients with a history of frequent, clear dream enactment were rated as "probable," those with no history of such episodes as "unlikely," and those with behavioral episodes that were not clearly repeated dream enactment were rated as "possible." At the time of the interview, the clinicians were masked to questionnaire and polysomnographic results but not to any medical history.

Questionnaire Information

All subjects received a questionnaire to be completed by the bed partner. Symptom items reflected each criterion listed in the ICSD (Table 1). When no partner was available, the subjects themselves were asked to complete the questionnaire. Responses for symptom items, which had different numbers of response levels in some cases, were expressed as a proportion of the maximal item value: each response therefore varied from 0 (denied) to 1 (fully endorsed). For example, a response of 2 on item E was converted to a value of 0.50, whereas a response of 2 on item B was converted to a value of 0.25. The average score on all question items then was used as the overall RBD symptom score.

Sleep Studies

All subjects were studied on 2 consecutive nights with laboratory-based polysomnography (PSG). Digital recordings included electroencephalogram (C3-A2, C4-A1, O1-A2, O2-A1 by International 10-20 system), chin EMG, electrooculogram, electrocardiogram, snoring, respiratory effort using piezoelectric belts over the chest and abdomen, and airflow at the nose and mouth using thermocouples. We also recorded bilateral surface EMGs from the arms (with electrodes placed over the forearm extensor compartment) and legs (with electrodes placed over the anterior tibialis muscles). We monitored oxyhemoglobin saturation by pulse oximetry and behavior by continuous video observation. Experienced polysomnographic technologists masked to patients' diagnoses applied the electrodes and continuously monitored the studies.

Table 1—Questionnaire That Bed Partners Used To Rate The Severity of RBD

ICSD Criterion	Scale	Question item
A	1-5	My bed partner has a problem with violent or injurious behavior during sleep
B or C-1	1-5	My bed partner moves his/her arms, legs, body during dreams
C-1	1-5	My bed partner's behavior during sleep is harmful or potentially harmful
C-2	1-5	My bed partner appears to act out dreams
C-3	1-5	My bed partner's behaviors during sleep disrupt his/her sleep
D	1-4	How much discomfort does your bed partner's behavior cause you?
E	1-3	What is the duration of your bed partner's symptoms?

RBD refers to REM (rapid eye movement) sleep behavior disorder; ICSD, *International Classification of Sleep Disorders*. Scales for items A-C3 ranged from (1) never to (5) nightly; for item D, from no discomfort (1) to severe discomfort (4); for item E, from less than 1 month (1) to more than 6 months (3).

Scoring

Polysomnographic technologists used 21-inch-high resolution (1600 x 1200 pixel) computer monitors and standard techniques[17] to score manually all recordings for sleep stages, limb movements and respiratory events. One senior registered polysomnographic technologist masked to patients' clinical data scored PSG measures of RBD according to the method described by Lapierre and Montplaisir (RPSM) and used in several recent investigations.[11] Lapierre and Montplaisir have suggested that patients with RBD could be distinguished from normal control subjects with 2 measurements: the proportion of 20-second REM sleep epochs that contain a predominance of abnormally elevated background chin muscle tone (tonic component), and the proportion of 2-second mini-epochs (within 20-second REM sleep epochs) that show bursts of EMG activity (phasic component). The present study employed identical measures except that the epochs to assess tonic activity were 30 seconds in duration (a more widely used standard), and the mini-epochs to assess phasic activity were 3 seconds in duration. Following the RPSM, each REM sleep epoch was scored as tonic or atonic depending upon whether tonic chin EMG activity was present for more or less than 50% of the epoch. Following published methods, no particular exclusions were made when physiologic evidence for REM sleep may not have occupied the entire epoch, or when an arousal (for example, after an apnea) occurred during an epoch scored as REM sleep. After disruption of REM sleep by movement arousals or by arti-

Table 2—Summary of Demographic, Diagnostic, and RBD Data

Subject	Sex	Age, y	Diagnosis	RBD polysomnographic score	RBD symptom score	ICSD-based clinical impression*	Medications at time of study
1	M	81	PD	11.85	0.59	0	L/C, venlafaxine
2	M	74	PD	59.33	0.62	2	L/C
3	M	68	PD	57.45	0.64	2	L/C, buspirone
4	M	65	PD	14.25	0.59	2	L/C, pramipexole
5	F	52	PD	43.14	0.67	2	L/C, pramipexole
6	F	74	PD	68.19	0.31	0	
7	M	60	MSA	50.92	0.52	1	SSRI
8	M	64	MSA	37.36	0.29	0	
9	F	48	MSA	5.88	0.41	0	
10	M	53	MSA	64.98	0.65	2	SSRI
11	M	65	MSA	59.16	0.21	0	
12	F	61	PSP	0.72	0.35	0	
13	F	69	PSP	9.14	0.53	1	
14	F	76	PSP	9.96	0.35	0	SSRI
15	M	66	DLB	46.29	0.79	2	
16	M	78	DLB	12.75	0.59	2	SSRI; L/C
17	F	52	OPCA	1.98	0.28	0	
18	F	58	NC	14.78	0.21	0	
19	F	49	NC	10.24	0.24	0	
20	M	54	NC	2.03	0.21	0	bupropion
21	F	53	NC	5.19	0.28	0	
22	F	57	NC	3.64	0.58	0	SSRI
23	F	74	NC	6.23	0.21	0	

*Clinical impression: likelihood of REM (rapid eye movement) sleep behavior disorder (RBD) was probable 2, possible 1, or unlikely 0.
PD refers to Parkinson disease; MSA, multiple system atrophy; PSP, progressive supranuclear palsy; DLB, dementia with Lewy bodies; OPCA, sporadic olivopontocerebellar atrophy; NC, normal control; L/C, levodopa/carbidopa; SSRI, selective serotonin reuptake inhibitor.

Table 3—Polysomnographic RBD Scores, Along With Component Scores: Percentage Phasic And Tonic Measures

	All subjects subjects* (n = 9)	RBD subjects* (n = 14)	Non-RBD P value	T test
Polysomnographic RBD Score	25.89 ±24.22	39.81 ± 21.88	16.94 ± 21.85	0.02
Phasic, %	22.10 ± 17.87	29.33 ±19.10	17.46 ± 16.02	0.12
Tonic, %	29.67± 37.53	50.29 ± 41.35	16.42 ± 29.13	0.03

Data are presented as mean ± SD.
*REM (rapid eye movement) sleep behavior disorder (RBD) defined by clinical impression of possible or probable diagnosis, based on definition in *International Classification of Sleep Disorders*.

fact, the continuation of rapid eye movements, increased motor activity with erratic behavior, or incongruous vocalizations were used to identify reemergence of REM sleep if the electroencephalogram signal was consistent with REM sleep and alpha frequencies were absent.

Analysis

Data from both nights of observation were used to calculate a single weighted mean for each of the 2 RBD measures. For example, if 60 epochs of REM sleep were recorded on the first night and 30 epochs on the second night, the first night was weighted by a factor of 2 relative to the second night. If 20% of the 60 epochs recorded on the first night and 50% of the 30 epochs on the second night were abnormal, the weighted average was (0.2 x 60 + 0.5 x 30)/(60 + 30) = 0.3 or 30%, and not simply the average of 20% and 50%, which would have been 35%. This approach is identical to analyzing the data of the 2 nights as if they were obtained from 1 long night.

The RBD measure for the proportion of epochs containing elevated muscle tone and the measure for the proportion of mini-epochs containing burst activity were then averaged to obtain an overall RBD polysomnographic score. This score was used in the main analyses: nonparametric Spearman correlations that tested for associations with the RBD symptom score, and *t* tests that assessed for associations with the ICSD-based clinical impression. The level of significance was set at $P < .05$.

RESULTS

We studied 23 patients (12 women) aged 48 to 81 years (mean 63 ± 10 [SD]). Seventeen subjects had neurodegenerative diseases, including 1 with OPCA, 2 with DLB, 3 with PSP, 5 with MSA, and 6 with PD. Six normal control subjects (5 women) were aged 49 to 74 years (mean 53 ± 4). Only 1 control subject had no partner and therefore completed her own questionnaire.

Table 2 lists subject ages, sexes, diagnoses, and scores for each RBD measure: polysomnographic, symptom-based, and overall clinical impression. Only 2 subjects were thought by clinicians to have "possible RBD," and these subjects therefore were combined with the "probable" group for analyses. The mean RBD polysomnographic score and component measures are listed in Table 3.

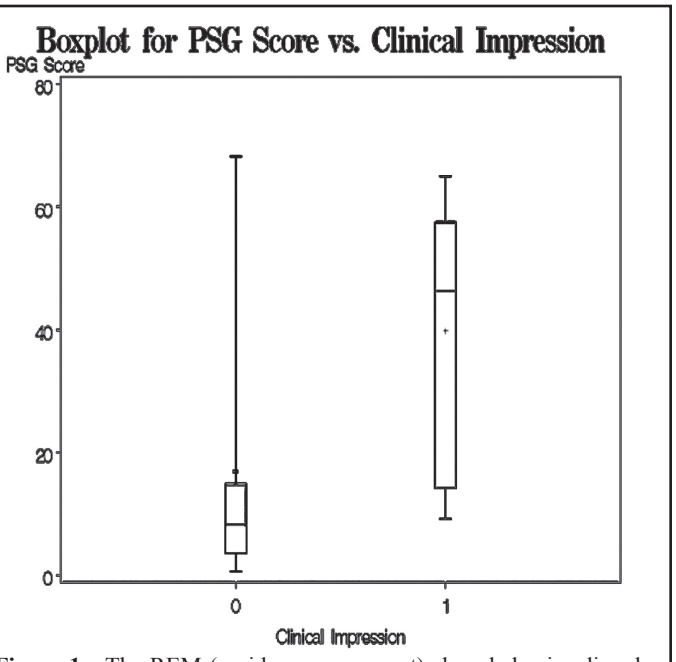

Figure 1—The REM (rapid eye movement) sleep behavior disorder (RBD) polysomnographic score (PSG Score) is plotted against the International Classification of Sleep Disorders-based clinical impression of RBD presence (1) or absence (0). Plots show median scores (midline), mean (cross), and 10th, 25th, 75th, and 90th percentiles.

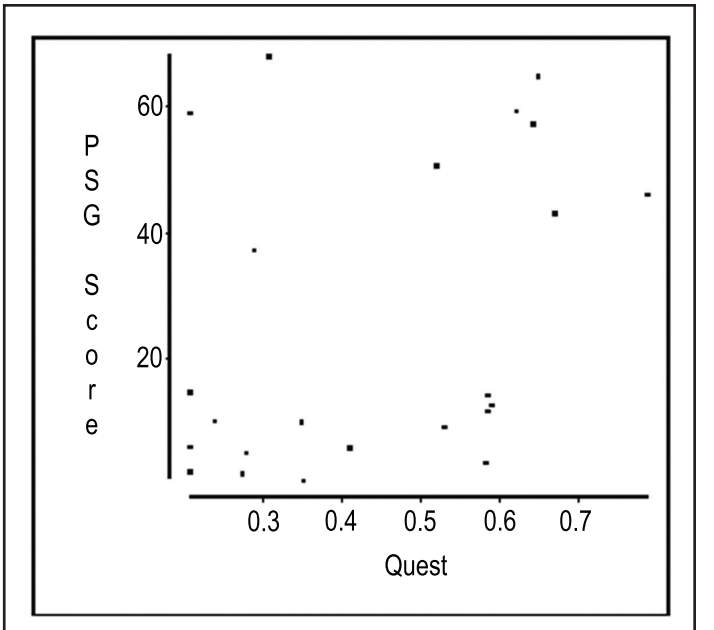

Figure 2—The REM (rapid eye movement) sleep behavior disorder (RBD) polysomnographic score (PSG score) is plotted against the RBD symptom score derived from bed partner questionnaires (Quest).

The polysomnographic RBD score showed an association with the ICSD-based clinical impression of RBD (*t* test, $P = .023$; Figure 1). The tonic component of the overall score also showed an association with clinical impression of ICSD ($P = .031$). The phasic component was in the expected direction but was not statistically significant ($P = .122$).

The overall polysomnographic RBD score showed a significant association with the RBD symptom score (Spearman rho = 0.42, $P = .048$; Figure 2), as did the separate tonic and phasic components of the polysomnographic score (*rho* = 0.49, $P = .018$, and *rho* = 0.43, $P = .042$, respectively).

The ICSD-based clinical impression of RBD showed a close association with RBD symptom scores ($P < .0001$). If a cutoff of 10 or more percentage points on the polysomnographic RBD score was used to indicate RBD (as suggested by receiver-operator curves), the RPSM in comparison with the clinical impression gold standard showed a sensitivity of 89% and a specificity of 57%.

Each of the 23 subjects had some scored REM sleep on each of the 2 nights, though the amount ranged from 1.5 minutes to 174.5 minutes. Nonetheless, the tonic, phasic, and combined (averaged) measures on night 1 correlated closely with the same measures on night 2 (*rho* = 0.73, $P < .0001$; *rho* = 0.83, $P < .0001$; and *rho* = 0.92, $P < .0001$, respectively).

DISCUSSION

This study of patients with neurodegenerative disorders and control subjects recruited form the community confirms that previously proposed, quantitative measures of RBD polysomnographic features are valid markers for the target sleep disorder. Whether RBD was defined by ICSD-based clinical impressions or bed-partner symptom ratings, the overall polysomnographic RBD measure showed an association with the presence of the disorder and with its severity. Decomposition of the polysomnographic RBD measure into its component parts—tonic and phasic scores—generated similar results. In addition, the high correlation between polysomnographic RBD measures on nights 1 and 2 reveals little test-retest variability. Together, these results suggest that the Lapierre and Montplaisir approach to quantification of RBD polysomnographic severity will be a valid, reliable, and therefore useful tool in clinical practice and research.

The current ICSD does not require polysomnographic evidence to meet minimal criteria for the diagnosis of RBD.[6] This supports our use of sleep-specialist clinical impressions and symptom-rating scales as "gold-standards" against which polysomnographic measures were compared. The ICSD is under revision, and the new entry will require polysomnographic features to confirm the diagnosis. Nevertheless, these polysomnographic features will remain, as in the 1992 edition, subjectively determined. A more quantitative method, such as the RPSM, would help to standardize RBD determinations between clinical laboratories, research sites, and polysomnographers at any specific site. Using this method, the cutpoint of 10% (average of tonic REM percentage and phasic REM percentage) appeared to be optimal, in our data, to define findings suggestive of RBD. Further studies with a larger sample size potentially could more precisely define a cutpoint. Investigation of many more healthy individuals will be needed to characterize the normal range of values generated by the RPSM. However, in clinical practice, the distribution of polysomnographic RBD scores is more likely to be unimodal than bimodal, and clinical judgment based on clinical findings along with laboratory results, without a strict cutpoint, may be most useful. In research studies, a well-defined objective cutpoint could help to identify a homogenous study sample and improve generalizability of results.

One limitation of the current study is that it did not test interscorer or intrascorer reliability. We noted that an important challenge in patients with α-synucleinopathies is to initially identify REM sleep, the first step in the RPSM. In practice, exceptions to Rechtschaffen and Kales scoring rules[17] must be made to score REM periods with elevated electromyographic tone despite clear

evidence of rapid eye movements and EEG activity consistent with REM sleep. We have not determined whether such exceptions can be made on a reliable basis by different scorers or upon rescoring by the same individual. The potential for inadequate reliability, and the length of time (up to several hours) required to score nocturnal PSGs with the current technique, suggest that an automated computer algorithm might provide the best, most consistent, least expensive, and most generalizable data. No such algorithm has yet been developed or tested. Another potential limitation arises from combining the percentage of phasic and percentage of tonic measures into 1 overall polysomnographic RBD score. This approach seems logical at this point, when the numbers of studied patients remains somewhat limited, but 1 measure could potentially obscure physiologically informative information in the other. Another potential limitation, as in any initial cross-sectional study, is that results could have been sensitive to potential confounds, difficult to assess within the current sample size, such as age, sex, duration of illness, severity of parkinsonian symptoms, or medication status. Finally, this study sought to confirm the validity of a previously proposed methodology, not to improve it or develop a new approach. This methodology appears to be effective, but we did not test possible advantages of other approaches, such as inclusion of limb electromyographic activity[9] or videotaped movement analysis[7] in the scoring system.

We conclude that the RPSM for quantitative analysis of polysomnographic RBD features has both demonstrable validity and test-retest reliability. Although total numbers of subjects are not large, the current sample more than triples published validity data for the technique. Results suggest that the method may be useful in both clinical and research settings. Optimal cutpoints for research purposes deserve confirmation, but 10% or more of REM sleep spent with elevated background EMG tone or phasic burst activity seems to suggest a diagnosis of RBD. Future work should assess intrascorer and interscorer reliability, explore the possibility that automated scoring could simplify the assessment and further improve reliability, and study a larger number of healthy subjects to examine more precisely what constitutes a normal range of RPSM results.

ACKNOWLEDGMENTS

The authors thank the participants and Cory Martin, RPSGT, for their assistance. This work was supported by NIH grants P01 NS15655 and M01 RR000042

REFERENCES

1. Schenck C, Bundie S, Ettinger M, Mahowald M. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep 1986;9:293-308.
2. Turner RS. Idiopathic rapid eye movement sleep behavior disorder is a harbinger of dementia with Lewy bodies. J Geriatr Psychiatry Neurol 2002;15:195-9.
3. Olson E, Boeve B, Silber M. Rapid eye movement sleep behavior disorder: demographic, clinical and laboratory findings in 93 cases. Brain 2000;123:331-9.
4. Schenck C, Hurwitz T, Mahowald M. REM sleep behavior disorder: an update on a series of 96 patients and a review of the world literature. J Sleep Res 1993;2:224-31.
5. Gilman S, Koeppe R, Chervin R, et al. REM sleep behavior disorder is related to striatal monoaminergic deficit in MSA. Neurology 2003;61:29-34.
6. International Classification of sleep disorders: Diagnostic and Coding Manual, revised. Rochester, MN: American Sleep Disorders Association; 1997.
7. Iranzo A. The importance of sleep medicine consultation for diagnosis of REM sleep behavior disorder in patients with Parkinson's disease. Sleep Med 2002;3:537-8.
8. Lapierre O, Montplaisir J. Polysomnographic features of REM sleep behavior disorder: development of a scoring method. Neurology 1992;43:1371-4.
9. Eisensehr I, Linke R, Tatsch K, et al. Increased muscle activity during rapid eye movement sleep correlates with decrease of striatal presynaptic dopamine transporters. IPT and IBZM SPECT imaging in subclinical and clinically manifest idiopathic REM sleep behavior disorder, Parkinson's disease, and controls. Sleep 2003;26:507-12.
10. Fantini M. Sleep laboratory diagnosis of REM sleep behavior disorder. Sleep 2004:A290.
11. Gagnon J, Bedard M, Fantini M, et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. Neurology 2002;59:585-9.
12. Gilman S, Low PA, Quinn N, et al. Consensus statement on the diagnosis of multiple system atrophy. J Neurol Sci 1999;163:94-8.
13. Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson's disease. Arch Neurol 1999;56:33-9.
14. McKeith IG, Galaski D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 1996;47:1113-24.
15. Litvan I, Agid Y, Calne D, et al. Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): report of the NINDS-SPSP international workshop. Neurology 1996;47:1-9.
16. Gilman S, Little R, Johanns J, et al. Evolution of sporadic olivopontocerebellar atrophy into multiple system atrophy. Neurology 2000;55:527-32.
17. Rechtschaffen A, Kales A. A Manual for Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Washington DC: US Govenment Printing Office; 1968.