Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD

A. Iranzo, MD; J. Santamaría, MD; D.B. Rye, MD, PhD; F. Valldeoriola, MD; M.J. Martí, MD; E. Muñoz, MD; I. Vilaseca, MD; and E. Tolosa, MD

Abstract—Objective: To compare the clinical and video-polysomnographic (VPSG) characteristics of idiopathic REM sleep behavior disorder (RBD) vs the RBD seen in multiple system atrophy (MSA) and Parkinson disease (PD). Methods: Clinical features and VPSG measures were evaluated in 110 consecutive nondemented subjects (26 MSA, 45 PD, and 39 idiopathic RBD) free of psychoactive medications referred for suspected RBD to our sleep unit over a 5-year period, with extended follow-up (mean 26.9 ± 21.3 months). Results: Across the three groups studied, logistic regression analysis demonstrated that there were no differences in the quality of RBD symptoms (e.g., nature of unpleasant dream recall or behaviors witnessed by bed partners), most PSG variables, abnormal behaviors captured by VPSG, and clinical response to clonazepam. When compared to subjects with PD, however, patients with MSA had a significantly shorter duration of disease, a higher REM sleep without atonia percentage, a greater periodic leg movement index, and less total sleep time. Subjects with idiopathic RBD, as compared to those with either MSA or PD, were more often male, had greater self-reported clinical RBD severity, and were more often aware of their abnormal sleep behaviors. Conclusions: REM sleep behavior disorder (RBD)-related symptoms and neurophysiologic features are qualitatively similar in RBD subjects with the idiopathic form, multiple system atrophy (MSA), and Parkinson disease (PD). Polysomnographic abnormalities associated with RBD in the setting of MSA are greater than in PD, suggesting a more severe dysfunction in the structures that modulate REM sleep.

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REM sleep behavior disorder (RBD) is a parasomnia characterized by vigorous movements and increased muscle activity during REM sleep, which may be idiopathic or associated with neurodegenerative diseases, including most of the subjects with multiple system atrophy (MSA) and at least one third with Parkinson disease (PD). The pathophysiology of RBD is thought to reflect dysfunction of brainstem structures that modulate REM sleep and their connections with the striatum, substantia nigra, and limbic system. Although these brain regions can be involved by the primary pathology of MSA and PD, these two conditions exhibit different degrees of cell loss and regional patterns of α-synuclein deposition. The burden of pathology in MSA, for example, is greater in the striatum and lateral part of the substantia nigra pars compacta, and more universally involves the pons and medulla. Moreover, some abnormalities shared by MSA and PD such as parkinsonism and dysautonomia have different clinical features, course, and response to treatment. While RBD is common in MSA and PD, no study has systematically characterized and compared the RBD features of these two different diseases. We sought to study the RBD clinical and video-polysomnographic (VPSG) features that might characterize and differentiate MSA and PD. We also evaluated the clinical and VPSG characteristics of the idiopathic form of RBD and compared them with those accompanying MSA and PD because idiopathic RBD often precedes the waking symptoms of MSA and PD by many years.

Methods. Patient selection. A total of 151 consecutive subjects with RBD fulfilling the criteria for probable MSA (n = 41), PD (n = 65), and idiopathic RBD (n = 45) were diagnosed and followed prospectively at the Hospital Clinic de Barcelona over a 5-year period between April 1, 1998, and March 31, 2003. Subjects with idiopathic RBD were referred to our sleep unit by their primary care physician, and patients with MSA and PD from neurologists in our movement disorders unit.

Diagnosis of RBD required 1) history of dream-enactment behaviors and 2) VPSG evidence of increased tonic or phasic electromyographic (EMG) activity during REM sleep associated with abnormal behaviors. At the time of RBD diagnosis, neurologic examination, Mini-Mental State Examination, and brain MRI or CT were normal in all subjects with idiopathic RBD.

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From the Neurology Service (Drs. Iranzo, Santamaría, Valldeoriola, Martí, Muñoz, and Tolosa), Hospital Clinic and Institut d’Investigació Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona; Department of Neurology (Dr. Rye), Emory University School of Medicine, Atlanta, GA; and Otorhinolaryngology Service (Dr. Vilaseca), Hospital Clinic, Barcelona, Spain.

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Address correspondence and reprint requests to Dr. Alex Iranzo, Neurology Service, Hospital Clinic de Barcelona, C/Villarreal 170, Barcelona 08036, Spain; e-mail: airanzo@clinic.ub.es

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Exclusion criteria included temporal assecciation of RBD onset with the administration or withdrawal of a medication, an acute onset of RBD, chronic alcoholism, use of clonazepam before RBD diagnosis, treatment with antipsychotics or anticholinergics, and Mini-Mental State Examination score <28.

Patients fulfilling Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) dementia criteria and those with chronic hallucinations that were not thought to be exclusively drug-related were excluded since many of these patients have dementia with Lewy body pathology, and because our clinical characterization of RBD required self-reported history (e.g., age at onset of RBD, self-awareness of sleep behaviors, and dream recall). We excluded 38 subjects taking antidepressants or benzodiazepines (14 with MSA, 20 with PD, and 4 with idiopathic RBD) since these medications are known or suspected to modify dream recall and several sleep stages, measured as part of sleep staging (e.g., light, REM sleep). EMG activity during REM sleep, total sleep time, and periodic leg movements in sleep. We also excluded three unmedicated subjects with status dissociatus (one with MSA and two with idiopathic RBD) because PSG could not distinguish the conventional sleep stages. Thus, the clinical and VPSG analysis and comparisons were based upon 110 subjects (26 MSA, 45 PD, and 39 idiopathic). Informed consent was obtained from each subject.

Clinical evaluation. All 110 subjects were systematically interviewed regarding their medical histories, sleep habits and complaints, and the types and frequency of unpleasant dreams, vocalizations, and abnormal motor behaviors occurring during sleep. The subject's bed partner was also interviewed to substantiate the history and provide additional information. According to the International Classification of Sleep Disorders, clinical severity of RBD was classified as mild (RBD occurs less than once per month but less than once per week and is usually recognized by the patient and the bed partner), moderate (RBD occurs more than once per month but less than once per week and is associated with physical discomfort), or severe (RBD occurs more than once per week and is associated with physical injury). In patients with MSA and PD treated with dopaminergic agents, total clinical improvement was calculated. VPSG evaluation. All 110 patients underwent a nocturnal VPSG which included EEG (C3, C4, O1, O2 referred to the contralateral ear), electro-oculograms, submental EMG, right and left anterior tibialis surface EMG, right and left biceps surface EMG, electrocardiogram, nasal and oral air flow, thoracic and abdominal movements, and oxyhemoglobin saturation. Sleep stages were scored according to standard criteria with the allowance for REM sleep without atonia. In each subject, we quantified the percentage of 20-second REM-sleep epochs with tonic activity in the submental channel (REM sleep without atonia percentage). During REM sleep, we also assessed the submental phasic EMG activity and the four limb (right and left anterior tibialis plus right and left biceps muscles) phasic EMG activity, as the percentage of 2-second epochs containing phasic EMG activity (burst/suppression, bursts lasting > 0.1 seconds with an amplitude exceeding four times the background EMG activity). In the limbs, a 2-second mini-epoch was considered phasic when 10% of the four limb channels. Tonic or phasic EMG increases concurrent with respiratory arousals and snoring signal artifacts were excluded from analysis.

Periodic leg movements in sleep (PLMS) were scored following the Atlas and Scoring Rules by the Atlas Task Force of the American Sleep Disorders Association, and the PLMS index (number of periodic leg movements per hour of sleep) was calculated. During REM sleep, PLMS were carefully distinguished from phasic muscle activity in the legs based upon their regular periodicity and characteristic flexor withdrawal appearance by videography. The apnea-hypopnea index (AHI) was defined as the mean number of respiratory apneas and hypopneas per hour of sleep. Video-endoscopies temporally synchronized with the PSG were used to detect and classify the intensity of the abnormal behaviors displayed during REM sleep as previously reported: A: mild: excessive proximal or distal limb jerking with minimal separation from the body, head or body jerking, mumuring, whispering, groaning, smiling, repetitive mouth opening; B: moderate: gesturing, rolling over the arm or leg, the hand or head abruptly > 90 degrees, talking, laughing, crying, singing; C: severe: waving the arms vigorously, kicking, punching, sitting up in bed, jumping out of bed, loud talking, shouting.

When the audiovisual recordings showed behaviors belonging to more than one category, the default classification was the most severe category.

When diagnosis of RBD was made by clinical history and VPSG, subjects were treated if clinically required (e.g., potential injurious sleep behaviors, restless sleep due to frightening dreams) with clonazepam at bedtime. Clonazepam was started at a dose of 0.25 to 0.50 mg and increased in 0.25 to 0.50 mg increments titrated to clinical response and tolerability. At the end of this study (May 2003), efficacy of clonazepam was assessed both by the patient and the bed partner and classified as substantial success, partial success, or no response as previously classified. During follow-up and at the end of the study we also asked the PD and MSA patients and their bed partners if the introduction and dose changes of the dopaminergic agents improved or worsened the RBD symptoms. The mean follow-up of the 110 subjects was 26.9 ± 21.3 months after RBD diagnosis.

Statistical analysis. Between-group comparisons for clinical and VPSG data were assessed by the Mann-Whitney U test, analysis of variance (ANOVA), and χ² test, as appropriate. Correlations between variables were calculated using the Pearson correlation test and ANOVA. Logistic regression analyses were performed to determine which variables distinguished MSA from PD, MSA from idiopathic RBD, and PD from idiopathic RBD. The independent contributions of variables with a p value < 0.05 on univariate analyses were assessed. Results are presented as means ± SD, adjusted OR, and corresponding 95% CI. In all tests the level of significance was set at p < 0.05.

Results. The demograhic, clinical, and VPSG characteristics and comparisons on univariate analyses among subjects with MSA, PD, and idiopathic RBD are presented in tables 1 and 2 and tables E-1 and E-2 (available on the Neurology Web site at www.neurology.org). Across the three groups studied, logistic regression analysis demonstrated that there were no differences in the quality of RBD symptoms (e.g., types of unpleasant dreams recalled and abnormal behaviors witnessed), most of the PSG measures, abnormal sleep behaviors captured by VPSG, and response to clonazepam.

Characteristics of patients with MSA. There were 16 men (61.5%) and 10 women (38.5%). The mean Schwab and England score was 50.7 ± 18. Thirteen patients (50%) were treated with dopaminergic agents. All subjects had dysautonomic symptoms, 12 predominant parkinsonism (MSA-P) (46%) and 14 predominant cerebellar syndrome (54%) (MSA-C). No clinical or VPSG differences were found between MSA-P and MSA-C groups, except that the MSA-P group was treated with a higher levodopa dose equivalent (p < 0.001).

In 14 subjects (53.8%), RBD preceded the onset of the waking motor manifestations of MSA. Seventy-seven percent of the patients were unaware of their abnormal sleep behaviors, which were only noticed by the bed partners. Recall of unpleasant dreams was present in 65.4%. Clinical RBD severity was judged by history as severe in 7.7%. Audiovisual analyses detected severe motor and vocal abnormal behaviors during REM sleep in 11.5%.

Characteristics of patients with PD. There were 34 men (75.6%) and 11 women (24.4%). The mean Hoehn and Yahr stage score was 2.3 ± 0.8 (range 1 to 4). The mean Schwab and England score was 75.5 ± 19.6. At the time of RBD diagnosis, 3 patients were untreated, 40 were treated with dopaminergic agents, 1 with unilateral pallidotomy plus levodopa/carbidopa, and 2 with bilateral deep brain stimulator nucleus stimulation plus a dopaminergic agonist.

In 8 subjects (17.8%), RBD preceded the onset of parkinsonism. Seventy-one percent of the subjects were un-
aware of their abnormal sleep behaviors. Recall of frightening dreams was present in 86.7%. Clinical severity of RBD was judged by history to be severe in 15.6% of the subjects. Nearly one-quarter (24.4%) of the subjects demonstrated abnormal behaviors in REM sleep that were categorized as severe by audiovisual analyses.

| Table 1 Demographic and clinical findings and comparisons among the three groups |
|---------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|                                | MSA, n = 26 | PD, n = 45 | IRBD, n = 39 | MSA vs PD, p value | MSA vs IRBD, p value | PD vs IRBD, p value |
| Male, %                        | 61.5       | 75.6      | 92.3      | NS        | 0.002     | 0.040     |
| Age, y                         | 62 ± 7.1   | 64.8 ± 7.8 | 68.4 ± 5.9 | NS        | 0.001     | 0.036     |
| Age at MSA or PD onset, y      | 57.5 ± 7.3 | 56 ± 9.2  | N/A       | NS        | N/A       | N/A       |
| Duration of MSA or PD, y       | 4.5 ± 2.3  | 9 ± 5.3   | N/A       | <0.001    | N/A       | N/A       |
| Levodopa dose equivalent, mg/d | 398 ± 469  | 652 ± 451 | 0         | 0.015     | N/A       | N/A       |
| Age at RBD onset, y            | 54.8 ± 9.2 | 60.4 ± 7.7 | 61.9 ± 7.7 | 0.008     | 0.001     | NS        |
| RBD duration, y                | 7.6 ± 6.3  | 4.2 ± 4.2 | 6.5 ± 6.7 | 0.012     | NS        | 0.012     |
| RBD preceding MSA or PD, %     | 53.8       | 17.8      | N/A       | 0.002     | N/A       | N/A       |
| RBD clinical severity, %       |            |           |           | NS        | <0.001    | <0.001    |
| Severe                         | 7.7        | 15.6      | 59        |           |           |           |
| Moderate                       | 42.3       | 42.2      | 33.3      |           |           |           |
| Mild                           | 50         | 42.2      | 7.7       |           |           |           |
| Self-awareness of behaviors, % | 23.1       | 28.9      | 69.2      | NS        | <0.001    | <0.001    |
| Initial insomnia, %            | 42.3       | 20        | 15.4      | 0.044     | 0.016     | NS        |
| Frequent awakenings, %         | 61.5       | 37.8      | 17.9      | NS        | <0.001    | 0.045     |
| Early awakening, %             | 46.2       | 28.9      | 7.7       | NS        | <0.001    | 0.014     |

Values are % or mean ± SD.

MSA = multiple system atrophy; PD = Parkinson disease; IRBD = idiopathic RBD; NS = not significant; N/A = not applicable; RBD = REM sleep behavior disorder.

Table 2 Polysomnographic findings and comparisons

|                                | MSA, n = 26 | PD, n = 45 | IRBD, n = 39 | MSA vs PD, p value | MSA vs IRBD, p value | PD vs IRBD, p value |
|--------------------------------|-------------|------------|--------------|-------------------|----------------------|---------------------|
| Sleep efficiency, %            | 57.7 ± 16.9 | 65.9 ± 17.0 | 67.2 ± 12.9  | NS                | 0.022                | NS                  |
| Total sleep time, min          | 257.4 ± 76.8 | 309.3 ± 91.8 | 305.0 ± 68.3 | 0.023             | 0.024                | NS                  |
| Sleep onset latency, min       | 41.2 ± 37.2 | 21.7 ± 21.4 | 26.1 ± 19.8  | 0.028             | NS                   | NS                  |
| Awakenings, n                  | 12.6 ± 7.6  | 21.6 ± 14.3 | 18.4 ± 10.3  | 0.011             | 0.024                | NS                  |
| Arousal index, %               | 27.0 ± 13.6 | 25.4 ± 17.6 | 25.1 ± 15.6  | NS                | NS                   | NS                  |
| Stage I                        | 14.4 ± 10.2 | 19.0 ± 14.1 | 18.9 ± 13.2  | NS                | NS                   | NS                  |
| Stage II                       | 40.4 ± 11.1 | 47.2 ± 14.6 | 44.8 ± 11.4  | NS                | NS                   | NS                  |
| Stage III-IV                   | 29.0 ± 16.8 | 16.3 ± 9.8  | 18.0 ± 9.5   | 0.001             | 0.005                | NS                  |
| Stage REM                      | 16.0 ± 7.7  | 17.5 ± 8.0  | 18.0 ± 8.1   | NS                | NS                   | NS                  |
| REM sleep latency, min         | 130.6 ± 84.4 | 134.7 ± 86.2 | 124.1 ± 80.1 | NS                | NS                   | NS                  |
| REM sleep stages, n            | 2.3 ± 1.2   | 2.6 ± 1.4   | 2.7 ± 1.2    | NS                | NS                   | NS                  |
| REM sleep without atonia, %    | 68.8 ± 29.3 | 39.4 ± 31.6 | 39.0 ± 36.0  | 0.001             | 0.003                | NS                  |
| Submental phasic EMG activity, % | 30.6 ± 20   | 22.1 ± 11.2 | 27.2 ± 16.0  | NS                | NS                   | NS                  |
| Four limb phasic EMG activity, % | 28.8 ± 19.4 | 18.1 ± 13.6 | 26.7 ± 15.1  | 0.007             | NS                   | 0.005               |
| PLMS index                     | 36.0 ± 32.7 | 10.3 ± 17.1 | 11.4 ± 20.8  | 0.001             | 0.002                | NS                  |
| Apnea-hypopnea index           | 13.6 ± 13.5 | 16.5 ± 21.6 | 11.4 ± 16.5  | NS                | NS                   | NS                  |

Values are mean ± SD.

MSA = multiple system atrophy; PD = Parkinson disease; IRBD = idiopathic RBD; REM sleep without atonia (%) = mean percentage of increased submental EMG tone during REM sleep; PLMS = periodic leg movements in sleep; NS = not significant.
duration (OR, 0.461; 95% CI, 0.278, 0.765, p = 0.003), higher REM sleep without atonia percentage (OR, 1.054; 95% CI, 1.007, 1.103, p = 0.023), greater PLMS index (OR, 1.126; 95% CI, 1.030, 1.250, p = 0.009), and less total sleep time (OR, 0.975; 95% CI, 0.956, 0.995, p = 0.014).

In both MSA and PD groups, levodopa daily equivalent dose was not associated with self-reported clinical severity of the RBD symptoms, intensity of the behaviors detected on VPSG, REM sleep without atonia percentage, REM sleep limb phasic EMG activity, and submental phasic EMG activity. None of the patients with MSA and PD reported that the introduction, dose changes, or withdrawal of their dopaminergic agents coincided temporally with consistent resolution, improvement, induction, or worsening of their RBD symptoms.

Characteristics of patients with idiopathic RBD. Subjects were 36 men (92.3%) and 3 women (7.7%). None of the subjects were treated with dopaminergic agents. Most of the patients and spouses reported that the RBD symptoms were the only sleep complaint. Sixty-nine percent were aware of their abnormal sleep behaviors, and 94.9% reported frequent unpleasant dreams. Clinical severity was judged as severe by history in 23 patients (59%). Audiovisual analyses detected severe abnormal behaviors in 38.5% of the subjects. During follow-up, 5 of these 39 subjects, 4 men and 1 woman, developed dementia with (n = 3) or without (n = 2) parkinsonism. None of the subjects developed cerebellar syndrome during follow-up.

MSA compared with idiopathic RBD. Logistic regression analysis demonstrated that subjects with MSA were less likely to be male (OR, 24.2; 95% CI, 2.0, 283, p = 0.011), had an onset of RBD at a younger age (OR, 1.247; 95% CI, 1.099, 1.415, p = 0.001), were less likely to be aware of their abnormal sleep behaviors (OR, 0.144; 95% CI, 0.023, 0.862, p = 0.034), had less total sleep time (OR, 1.015; 95% CI, 1.001, 1.029, p = 0.030), and higher PLMS index (OR, 0.948; 95% CI, 0.915, 0.983, p = 0.004).

PD compared with idiopathic RBD. Logistic regression analysis demonstrated that subjects with idiopathic RBD had greater self-reported clinical RBD severity (OR, 0.170; 95% CI, 0.043, 0.670, p = 0.011), were more likely to be aware of their abnormal behaviors (OR, 0.089; 95% CI, 0.023, 0.348, p = 0.001), and were older at the time of RBD diagnosis (OR, 1.118; 95% CI, 1.013, 1.233, p = 0.027).

Discussion. The present investigation represents the largest reported cohort of RBD, and is the first aimed to characterize and compare this parasomnia in consecutive subjects presenting to a neurologically based sleep unit with normal neurologic status, or affected by a neurodegenerative disease such as MSA or PD. The findings of our study indicate that idiopathic RBD or RBD occurring on the backdrop of MSA or PD share a common symptomatology and many neurophysiologic features on VPSG. Similarities found by history or VPSG documentation, for example, included 1) the nature and content of disturbing dreams recalled by the patients; 2) the type of abnormal motor and vocal behaviors witnessed by the bed partners; 3) the intensity of the abnormal behaviors detected during the audiovisual analysis; 4) several REM-sleep PSG variables such as the number of REM sleep episodes, the percentage of REM sleep, and REM sleep latency; and 5) the substantial clinical improvement with small doses of clonazepam in most of the patients with a low incidence of side-effects. Beyond these similarities, however, some clinical and PSG characteristics of RBD were found to differ in subjects with MSA, PD, and idiopathic RBD.

Subjects with MSA could be differentiated from those with PD as they exhibited shorter disease duration, a greater percentage of REM sleep without atonia, higher PLMS index, and less total sleep time. These findings suggest that the PSG features of RBD, and sleep in general, are more severely disturbed in MSA than in PD. These differences may have their basis in different direct or indirect effects of disease specific pathology upon brain structures that modulate sleep in these two diseases. Pathologic involvement in MSA is more severe and diffuse and clinically MSA is characterized by faster progression and poorer prognosis. Thus, a more widespread and severe dysfunction in the brainstem structures that regulate REM sleep probably accounts for higher proportions of REM sleep without atonia in MSA, and RBD occurring earlier in MSA than in PD. This is supported by the finding that RBD is much more common, nearly ubiquitous, in MSA as compared to PD.

RBD preceded parkinsonism in 17.8% of the patients with PD. In PD, the degenerative process has been proposed to start in the medulla advancing rostrally to the pons and midbrain. Thus, RBD preceding parkinsonism might reflect early involvement of nondopaminergic medullary and pontine REM sleep-related structures preceding impairment of dopaminergic neurons in the substantia nigra pars compacta. Additional findings in our study argue similarly that the midbrain dopaminergic deficiency is not the primary cause of RBD. First, levodopa dose equivalent was not associated with measures of RBD severity (self-reported severity of the RBD symptoms, percentage of REM sleep without atonia, REM sleep submental and limb phasic EMG activity, and intensity of the behaviors detected on VPSG). Second, our patients with PD and MSA did not endorse any consistent benefit of dopaminergic drug replacement on their RBD symptomatology. Third, RBD developed in many PD and MSA subjects many years after clinical improvement of their parkinsonism with dopaminergic agents. These findings are in line with observations that surgical interventions aimed at restoring balance in basal ganglia circuits denervated by dopamine do not improve RBD symptoms or diminish REM sleep-related EMG activity. Thus, although striatal dopamine transporters are reduced in idiopathic RBD, these changes may represent an epiphenomenon, rather than the primary pathogenetic determinant of RBD.

Subjects with idiopathic RBD, as compared to those with MSA or PD, had greater self-reported severity of RBD, were more aware of their abnormal sleep behaviors, and were more frequently male. The
finding that subjects with idiopathic RBD had greater self-reported clinical RBD severity can be in part explained by a referral bias. An epidemiologic study has shown that patients with mild idiopathic RBD do not seek medical attention. Patients with idiopathic RBD diagnosed in our sleep unit were self-referred, parasomnian behaviors were their sole complaint, and in most of them the severity of RBD was judged to be moderate or severe. Thus, it seems that most patients with idiopathic RBD seeking medical consultation are those with the most severe forms. In contrast, MSA and PD patients with RBD were referred from our movement disorders unit, and a high proportion of these patients and spouses considered the manifestations of RBD less bothersome than their diurnal motor symptoms that interfered with activities of daily living. We acknowledge that the inclusion of patients with differing levels of RBD severity may be a limitation of our study. However, this study was focused on comparing all RBD subjects with the idiopathic form, MSA, and PD presenting to our sleep unit over a 5-year period. Our findings should help to design future research strategies that could confirm these observations and address potentially confounding variables such as RBD severity.

In the idiopathic and PD groups, RBD was much more frequent in men than women, suggesting a possible sex-linked influence or other yet to be defined factors. It has been hypothesized that androgenic abnormalities might account for the more violent nature of RBD-associated behaviors in men. Also, it cannot be excluded that idiopathic RBD seeking medical attention may be biased toward men because a man injuring his female bed partner during sleep may be a more likely indication for referral than a woman injuring a man. The male predominance, however, was not evident in the MSA group, where 38.5% of the patients were female, in line with other observations.

RBD as a clinical entity has only recently received considerable attention, so that the field is still in the process of developing the most appropriate clinical and PSG based metrics of REM sleep dysfunction. VPSG detection of increased EMG activity and abnormal behaviors during REM sleep is necessary to diagnose RBD and exclude other conditions that may resemble this parasomnia. Obstructive sleep apnea, for example, may mimic the symptoms of RBD in subjects with PD and no underlying neurologic disease. Conversely, clinical history alone may be inadequate to identify RBD because subjects with VPSG REM sleep without atonia plus abnormal behaviors during REM sleep may not provide clinical reports of their nocturnal behaviors. Moreover, a recent study showed that clinical history may be inadequate in identifying RBD and inconsistently applied by physicians. However, present VPSG methodologies have limitations. In our study, abnormal behaviors detected during VPSG ranged from simple motor activities such as excessive limb jerk-

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