

The REM Sleep Behavior Disorder Screening Questionnaire— A New Diagnostic Instrument

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Abstract: Many patients with assumed idiopathic REM sleep behavior disorder (RBD) may actually represent an early clinical manifestation of an evolving neurodegenerative disorder, such as the α -synucleinopathies, Parkinson's disease or multiple system atrophy. Early detection of these patients is clinically relevant for long-term prospective as well as future neuroprotective studies. For this purpose, we validated a 10-item patient self-rating questionnaire (maximum total score 13 points) covering the clinical features of RBD. The RBD screening questionnaire (RBDSQ) was applied to 54 patients with polysomnographically confirmed RBD (29 men; mean age 53.7 ± 15.8 years), 160 control subjects (81 men; mean age 50.8 ± 15.5 years) in whom RBD was excluded by history and polysomnography (PSG, control group 1) and 133 unselected healthy subjects (58 men; mean age 46.9 ± 12.3 years; no PSG,

control group 2). In most subjects ($n = 153$) of control group 1, other sleep-wake disturbances were present. The mean RBDSQ score in the RBD group was 9.5 ± 2.8 points compared with 4.6 ± 3.0 points in control group 1 ($P < 0.0001$). Considering an RBDSQ score of five points as a positive test result, we found a sensitivity of 0.96 and a specificity of 0.56. The RBDSQ poorly discriminated patients with the most challenging differential diagnoses such as sleepwalking or epilepsy. In control group 2, the mean RBDSQ score (2.02 ± 1.78) was significantly lower than in the RBD group ($P < 0.0005$), revealing a specificity of 0.92. Due to its high sensitivity, the RBDSQ appears to be particularly useful as a screening tool. © 2007 Movement Disorder Society

Key words: REM sleep behavior disorder; Parkinson's disease; screening questionnaire; sensitivity; specificity.

REM sleep behavior disorder (RBD) is clinically characterized by the intermittent loss of normal skeletal muscle atonia during rapid eye movement (REM) sleep with the appearance of elaborate motor activity associated with dream mentation. Disruptive nocturnal behaviors, usually accompanied by vivid, action-filled, unpleasant, and violent dreams, in which the individual is being confronted, attacked, or chased by unfamiliar people or animals dreams, are the most common complaints presented by RBD patients. Typically, at the end of an episode, the individual can be awakened quickly, rapidly

being alert, and most often reporting dreams containing a coherent story that correspond to the observed behaviors. The character of clinical manifestation, its severity, and frequency vary over time. Medical attention is usually sought after sleep-related injury has occurred to either the person or the bed partner.^{1,2} For establishing the diagnosis, polysomnography (PSG) is required and represents the diagnostic gold standard revealing loss of REM-related muscle atonia with excessive amounts of sustained or intermittent elevation of submental EMG tone or excessive phasic submental or limb EMG twitching. In addition, an abnormal behavioral episode during REM sleep must be documented during PSG studies or history of injurious or disruptive sleep behaviors such as talking, laughing, shouting, gesturing, punching, kicking, sitting up, leaping from bed, and running.^{1,3} Although there have been different approaches to quantify REM sleep without atonia,^{4–7} there are no valid and reliable methods established in the current diagnostic system.

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Received 22 December 2006; Revised 15 August 2007; Accepted 20 August 2007

Published online 25 September 2007 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21740

There is no solid data on the prevalence of RBD. Data predominantly derived from surveys report the prevalence of RBD to be as high as 0.8% in the general population.^{8,9} The idiopathic form of RBD has a male preponderance and usually emerges after the age of 50, although any age group can be affected.¹ Besides other forms, symptomatic RBD can be associated with narcolepsy,^{10–12} which is characterized by the degeneration of hypothalamic hypocretin-containing neurons.^{13,14} In this subgroup, patients are frequently younger and more often female. In addition, RBD is frequently associated with other neurodegenerative disorders, in particular the α -synucleinopathies: Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA).¹⁵ Even more important, evidence is growing that RBD precedes the first motor symptoms of neurodegenerative disorders characterized by parkinsonism by years or even decades, and that RBD might present an early stage in the development of neurodegenerative disorders. Thus, to identify clinical RBD as early as possible appears to be useful for early diagnosis, clinical trials with

a potentially neuroprotective substance, and also for epidemiological studies. To meet the need for an easily applicable diagnostic screening tool, we developed a short RBD screening questionnaire (RBDSQ). Data on the validation of the RBDSQ are presented as compared to polysomnographically confirmed diagnosis of RBD.

PATIENTS AND METHODS

A questionnaire was developed assessing the most prominent clinical features of RBD (see Table 1) according to the International Classification on Sleep Disorders.¹ It was applied to patients with RBD and control subjects, in whom RBD was excluded by history and polysomnography (PSG; control group 1). Subjects assigned to the control group were patients referred to our sleep center because of sleep-wake complaints, i.e., insomnia or hypersomnia, frequently with the suspicion of RLS, narcolepsy, or sleep related breathing disorders. Patients with subclinical RBD, who only present with PSG findings typical of RBD but without a clinical history of RBD, were excluded from the study. Since the sleep center has a particular expertise in narco-

TABLE 1. RBD Screening Questionnaire

	Question	Answer
English		
1.	I sometimes have very vivid dreams.	yes/no
2.	My dreams frequently have an aggressive or action-packed content.	yes/no
3.	The dream contents mostly match my nocturnal behaviour.	yes/no
4.	I know that my arms or legs move when I sleep.	yes/no
5.	It thereby happened that I (almost) hurt my bed partner or myself.	yes/no
6.	I have or had the following phenomena during my dreams:	
6.1.	speaking, shouting, swearing, laughing loudly	yes/no
6.2.	sudden limb movements, "fights"	yes/no
6.3.	gestures, complex movements, that are useless during sleep, e.g., to wave, to salute, to frighten mosquitoes, falls off the bed	yes/no
6.4.	things that fell down around the bed, e.g., bedside lamp, book, glasses	yes/no
7.	It happens that my movements awake me.	yes/no
8.	After awakening I mostly remember the content of my dreams well.	yes/no
9.	My sleep is frequently disturbed.	yes/no
10.	I have/had a disease of the nervous system (e.g., stroke, head trauma, parkinsonism, RLS, narcolepsy, depression, epilepsy, inflammatory disease of the brain), which?	yes/no
German		
1.	Ich habe teilweise sehr lebhafte Träume.	ja/nein
2.	Meine Träume haben des öfteren aggressiven oder aktionsgeladenen Inhalt.	ja/nein
3.	Die Traum inhalte stimmen meist mit meinem nächtlichen Verhalten überein.	ja/nein
4.	Mir ist bekannt, dass ich meine Arme oder Beine im Schlaf bewege.	ja/nein
5.	Es ist dabei vorgekommen, dass ich meinen Partner oder mich selbst (beinahe) verletzt habe.	ja/nein
6.	Bei mir treten oder traten während des Träumens folgende Erscheinungen auf:	
6.1.	laut Sprechen, Schreien, Schimpfen, Lachen	ja/nein
6.2.	plötzliche Bewegungen der Gliedmaßen, „Kämpfen“	ja/nein
6.3.	Gesten, Bewegungsabläufe, die im Schlaf sinnlos sind wie z.B. winken, salutieren, Mücken verscheuchen, Stürze aus dem Bett	ja/nein
6.4.	um das Bett herum umgefallene Gegenstände wie z.B. Nachttischlampe, Buch, Brille	ja/nein
7.	Es kommt vor, dass ich durch meine eigenen Bewegungen wach werde.	ja/nein
8.	Nach dem Erwachen kann ich mich an den Inhalt meiner Träume meist gut erinnern.	ja/nein
9.	Mein Schlaf ist häufiger gestört.	ja/nein
10.	Bei mir liegt/lag eine Erkrankung des Nervensystems vor (z.B. Schlaganfall, Gehirnerschütterung, Parkinson, RLS, Narkolepsie, Depression, Epilepsie, entzündliche Erkrankung des Gehirns), welche?	ja/nein

lepsy, we had the opportunity to include a high number of narcolepsy patients with comorbid RBD. The study was performed in accordance with the Declaration of Helsinki and approved by the local ethical committee. All subjects provided written informed consent. To assure or exclude RBD, a one-night polysomnography was performed in each subject using a standard clinical protocol with recording of EEG (a minimum of the following derivations: C4-A1, C3-A2, C4-O1, but often with additional derivations to rule out epilepsy), EOG, ECG, oronasal airflow, thoracoabdominal movements by impedance plethysmography, upper airway sound, and oxyhaemoglobin saturation. All patients had surface EMG recorded from both mentalis, anterior tibialis and in most patients of both biceps muscles. Data were digitally recorded and visually scored. Split-screen or time-synchronized video recordings were performed to identify abnormal behavioral episodes during REM sleep or other types of abnormal nocturnal behavior. Scoring of sleep stages followed standard methods¹⁶ but allowed to identify the persistence of EMG tone during epochs of otherwise unequivocal REM sleep. Scoring of periodic leg movements (PLM) and arousals was based on the recommendation of the American Sleep Disorders Association.^{17,18} The following PSG variables were routinely analyzed: time in bed (TIB in minutes), total sleep time (TST in minutes), sleep efficiency ($TST/TIB \times 100$ in %), number of PLMs, PLM index (PLM per hour TIB), number of PLM during sleep (PLMS), PLMS index (PLMS per hour TST), number of PLMS arousals, PLMS arousal index (PLMS arousal per hour TST), number of PLM during wakefulness (PLMW), and PLMW index (PLMW per hour wake time).

In addition to the control group described earlier, the RBDSQ was applied to subjects from the general population, in whom RBD was as far as possible excluded by medical history without performing polysomnography (= control group 2).

REM Sleep Behavior Disorder Screening Questionnaire

The RBDSQ is a 10-item, patient self-rating instrument assessing the subject's sleep behavior with short questions that have to be answered by either "yes" or "no" (see Table 1). Since patients do not always have a long-time companion, the bed partner's input was encouraged but not required. Items 1 to 4 address the frequency and content of dreams and their relationship to nocturnal movements and behavior. Item 5 asks about self-injuries and injuries of the bed partner. Item 6 consists of four subitems assessing nocturnal motor behavior more specifically, e.g., questions about nocturnal vocalization, sudden limb movements, complex movements, or bedding items that fell down. Items

7 and 8 deal with nocturnal awakenings. Item 9 focuses on disturbed sleep in general and item 10 on the presence of any neurological disorder. The maximum total score of the RBDSQ is 13 points.

Outcome Measure

The primary outcome measure was the difference in the RBDSQ total score between the patients with RBD and the control groups.

Statistical Analysis

Sample means of the RBDSQ total score in RBD patients and the control groups were compared by *t*-test. Differences between RBD patients and subpopulations of control group 1 were analyzed by post hoc comparisons according to Scheffé.¹⁹ Sensitivity and specificity for different cut-off points were calculated and presented by means of an ROC function. The diagnostic value of the RBDSQ was calculated by the area under the curve (AUC), which is independent of an arbitrary choice of a cut-off point and tested for statistical significance using the Mann-Whitney *U* test. The response patterns are presented descriptively. As a measure of reliability of the questionnaire, the α -coefficient of Cronbach was calculated. As a measure of the relation between the dichotomous response to the specific test questions and the RBDSQ total score, item-test correlations were calculated.

RESULTS

Patients

Fifty-four patients (29 men and 25 women; mean age 53.7 ± 15.8 years, range 19–79 years) with RBD for 12.1 ± 10.7 years (range 2–45 years) and 160 patients without RBD (81 men and 79 women; mean age 50.8 ± 15.5 years, range 20–83 years, control group 1) participated. Nineteen patients suffered from idiopathic RBD, while in the remaining patients RBD was associated with either narcolepsy ($n = 33$) or early Parkinson's disease ($n = 2$). RBD patients with narcolepsy were younger (44.9 ± 14.8 years) than those without narcolepsy (60.1 ± 11.5 years) and more often female (54.5% vs. 33.3%). In most subjects of control group 1 ($n = 153$), other sleep-wake disturbances were present and categorized to the following diagnoses: restless legs syndrome (RLS; $n = 73$), narcolepsy ($n = 27$), obstructive sleep apnea (OSA; $n = 21$), hypersomnia ($n = 10$), periodic limb movement disorder (PLMD; $n = 8$), insomnia ($n = 4$), sleepwalking ($n = 4$), epilepsy ($n = 3$), nightmares ($n = 1$), sleep bruxism ($n = 1$), and depression ($n = 1$); (Table 2).

TABLE 2. Demographic data, medical history, and PLM indices

Variables	Patients with RBD (n = 54)	Patients with no RBD (control group 1; n = 160)
Age in years, m \pm s (range)	53.7 \pm 15.8 (19–79)	50.8 \pm 15.5 (20–83)
Male/female, n (%)	29 (53.7)/25 (46.3)	81 (50.6)/79 (49.4)
Duration of RBD, m \pm s (range)	12.1 \pm 10.7 (2–45)	n.a.
Concomitant diseases, n (%)		
RLS	0	73 (45.6)
Narcolepsy	33 (61.1)	27 (16.9)
OSA	0	21 (13.1)
Hypersomnia	0	10 (6.25)
PLMD	0	8 (5)
Insomnia	0	4 (2.5)
Sleepwalking	0	4 (2.5)
Epilepsy	0	3 (1.9)
PD	2 (3.7)	0
Nightmares	0	1 (0.6)
Sleep bruxism	0	1 (0.6)
Depression	4 (7.4)	1 (0.6)
PSG results, m \pm s (range) moderately ill		
PLM = Index	41.7 \pm 49.5 (2.8–268.8)	74.1 \pm 109.6 (2.4–887.8)
PLMS = Index	38.7 \pm 50.1 (0–283.8)	74.6 \pm 123.3 (0–962.2)
PLMS arousal = Index	17.9 \pm 16.0 (0–68.2)	31.0 \pm 42.3 (0–240)
PLMW = Index	54.6 \pm 51.0 (0–258.6)	88.1 \pm 87.7 (0–577.5)

m, arithmetic mean; s, standard deviation; n, number of patients; n.a., not applicable; PSG, polysomnography; PLM, periodic leg movements (during sleep and wakefulness); PLMS, PLM during sleep; PLMW, PLM during wakefulness.

Control group 2 consisted of 133 healthy subjects (58 men and 75 women; mean age 46.9 ± 12.3 years, range 20–72 years) in whom RBD was as far as possible excluded by medical history. Thirty-one subjects suffered from occasional sleep disturbances which were associated with depressive episodes in four subjects.

RBDSQ

The *t*-test revealed a highly significant difference between the RBD group and control group 1. The mean RBDSQ score in the RBD group was 9.5 ± 2.8 (range 2–13) points compared with 4.6 ± 3.0 (range 0–12) points in control group 1 ($P < 0.0001$).

Subanalysis within this control group revealed that the few patients with sleepwalking and epilepsy had the highest scores with 8.7 ± 3.2 (range 5–11) and 7.7 ± 3.2 (range 4–10) points, respectively. Total RBDSQ scores were lower in the other subpopulations presenting with sleep disturbances such as narcolepsy: 6.4 ± 3.2 (range 1–12) points, insomnia: 6.0 ± 4.4 (range 1–11), PLMD: 4.4 ± 2.9 (range 1–9), RLS: 4.1 ± 2.5 (range 0–11), OSAS: 3.9 ± 2.6 (range 0–11), or hypersomnia: 2.7 ± 3.2 (range 0–8), and those subjects without any subjective sleep complaints: 3.3 ± 3.7 (range 0–9). Multiple comparisons (Scheffé test) showed that the RBDSQ total score of the RBD group was significantly different from all subpopulations of this control group containing at least seven subjects ($P < 0.05$). Comparison within the

RBD group showed that the mean RBDSQ scores of RBD patients without narcolepsy ($n = 21$) and with narcolepsy ($n = 33$) were very similar (9.7 ± 2.4 vs. 9.4 ± 3.1).

An ROC plot, which is usually calculated to evaluate the discriminant threshold of different cut-off values, is shown in Figure 1. Considering an RBDSQ score of five points a positive test result, we found a sensitivity of 0.96 and a specificity of 0.56. Accordingly, 66% of the patients were correctly diagnosed. The AUC was $0.87 \pm$

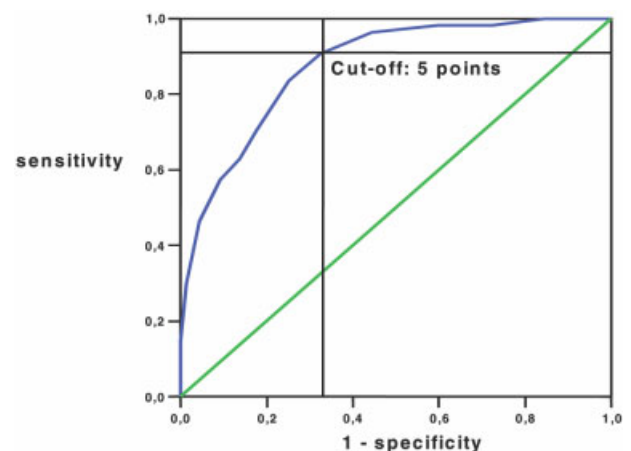


FIG. 1. Sensitivity and specificity of the RBDSQ scores as shown by an ROC curve.

0.38, and compared with the minimum possible score of 0.5, the difference was highly significant ($P < 0.0005$).

There was no correlation between the RBDSQ score and the duration of RBD (Spearman $\rho = 0.07$, $P = 0.62$). Within control group 1, there was a significant correlation for the PLMI (Spearman $\rho = 0.29$, $P = 0.001$), PLMS index (Spearman $\rho = 0.30$, $P = 0.001$) and the PLMW index (Spearman $\rho = 0.34$, $P = 0.0001$). PLM parameters did not correlate with the RBDSQ score within the RBD group.

Single item analysis revealed the highest specificity for items 6.3 (complex movements during sleep), 6.4 (things that fell down around the bed), and 5 (injury of the patient or bed partner) when compared with the entire control group 1 (Table 3). Cronbach's alpha for the entire RBDSQ was 0.885. Furthermore, the answer patterns of control subgroups with $n > 3$ patients are displayed in Figure 2.

The mean RBDSQ score in control group 2 was 2.0 ± 1.8 (range 0–9) points and markedly lower than in control group 1. Differences in the RBDSQ score between control group 2 and the RBD group were thus highly significant ($P < 0.0005$). Based on this control sample, the RBDSQ revealed a specificity of 92% when using a cut-off value of 5.

DISCUSSION

This study evaluated the diagnostic value of a newly developed screening questionnaire for RBD. Using a cut-off value of five points on the RBDSQ as a discriminatory variable, the questionnaire revealed a sensitivity of 96% and a specificity of 56%, correctly diagnosing 66% of subjects with sleep disorders. When investigating the usefulness of the RBDSQ in an unselected control group from the general population, i.e., those who did not present to a sleep center, the specificity was considerably higher with 92%, leading to the correct diagnosis

in 93%. The sensitivity of a diagnostic interview for RBD is probably high.¹ However, for a definite diagnostic decision, a polysomnography is required predominantly to definitely rule out differential diagnoses such as sleep-related epileptic seizures, non-REM parasomnias (e.g., sleepwalking), obstructive sleep apnea (OSA), or nocturnal periodic leg movements (PLM).^{1,20} In addition, it is impossible to detect patients with subclinical RBD, who present only with PSG findings typical of RBD but without a clinical history of RBD.³ Eiseensehr et al.²¹ investigated the diagnostic value of a specialized clinical interview for diagnosis of RBD according to the ICSD criteria²² and compared it to PSG-supported RBD diagnosis in a population of sleep-disordered patients similar to our control group 1, including patients with sleep apnea syndrome, RLS, PLMD, and narcolepsy and to a smaller extent patients with epilepsy and sleepwalking. The sensitivity of interviews for the clinical diagnosis of RBD compared with PSG results was 100%, and the specificity was also excellent (99.6%). The very high specificity might be due to the fact that these interviews were performed from experts not only in sleep medicine but also in movement disorders and epilepsy. Compared with expert interviews, the RBDSQ revealed a similarly high sensitivity of 96% but a lower specificity of 56%. The lower specificity might be due to the fact that most of our control patients suffered from sleep disturbances or neurologic disorders that are known to be associated with PLM, e.g., RLS, PLMD, narcolepsy, and OSA. This selection bias predisposed to positive answers in items that are related either to limb movements such as items 4, 5, 6.2, and 7 or to the presence of sleep and/or neurologic disorders such as items 9 and 10, leading to higher RBDSQ total scores and thus to a lower specificity. In contrast, the RBDSQ had an excellent specificity when RBD was assessed in a nonselected control group of the general population.

There is growing evidence that RBD precedes the first motor symptoms of the neurodegenerative disorders in parkinsonism by years or even decades. Schenck and coworkers first reported that 11 of 29 (38%) patients with RBD initially considered to be idiopathic developed PD after a mean interval of 13 years (range 10–29).²³ A further follow-up seven years later showed that even 65% developed parkinsonism, dementia, or both diseases.²⁴ A recent retrospective longitudinal study confirmed that 45% of 44 patients with assumed idiopathic RBD developed a neurodegenerative disease 10.7 years after reported RBD onset.²⁵ In the meantime, the hypothesis that RBD is an early manifestation of a neurodegenerative disorder has been supported by various studies showing neurobiologic

TABLE 3. Sensitivity and specificity of single RBDSQ items

RBDSQ item	Sensitivity (%)	Specificity (%)	Item-test correlation
1	94.4	47.1	0.636 ($P < 0.0005$)
2	83.0	71.9	0.730 ($P < 0.0005$)
3	80.0	75.2	0.732 ($P < 0.0005$)
4	88.7	57.4	0.719 ($P < 0.0005$)
5	68.5	85.3	0.693 ($P < 0.0005$)
6.1	90.7	62.5	0.752 ($P < 0.0005$)
6.2	82.7	59.2	0.739 ($P < 0.0005$)
6.3	56.0	91.1	0.635 ($P < 0.0005$)
6.4	49.1	88.4	0.627 ($P < 0.0005$)
7	71.7	49.3	0.527 ($P < 0.0005$)
8	74.1	42.2	0.366 ($P < 0.0005$)
9	81.1	23.9	0.343 ($P < 0.0005$)
10	56.6	56.3	0.367 ($P < 0.0005$)

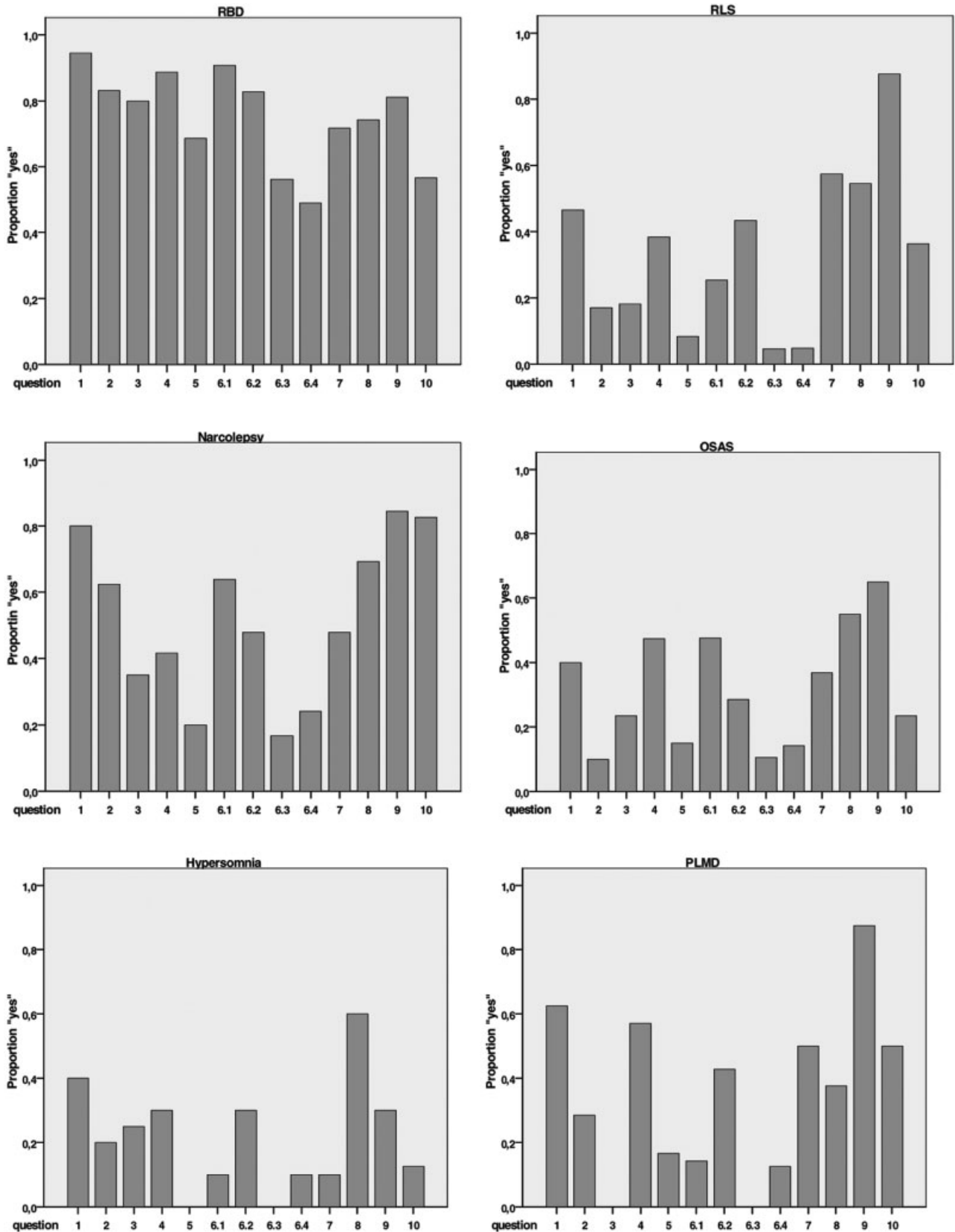


FIG. 2. Answer patterns of RBD patients and subpopulations of control group 1.

deficits in patients with RBD without concomitant medical disorders, e.g., electroencephalographic changes,²⁶ nigrostriatal dopaminergic dysfunction,^{5,27–29} cerebral blood flow impairments,³⁰ cognitive deficits,^{26,31} olfactory dysfunction,^{29,32,33} impaired color vision discrimination,^{32,33} and autonomic dysfunction^{34,35} similar to those found in MSA,^{36–39} DLB^{40–45} and, particularly, PD.^{46–57}

The fact that RBD might be a stage in the development of neurodegenerative disorders poses the challenge to identify clinical RBD as early as possible, i.e., also in neurologically unimpaired patients without any motor symptoms and who would not seek medical attention. This serves on the one hand to promptly identify and treat symptoms of neurodegenerative disorders as they appear in a neurologic follow-up and on the other hand to identify early untreated RBD patients for future trials with potential neuroprotective strategies in neurodegeneration. In addition, informing the patient about the hazardous potential of RBD is a major point of medical information and should be provided as early as possible. Not only for early diagnosis but also for epidemiologic studies, an appropriate screening tool for RBD is needed. Considering its high sensitivity, the RBDSQ represents an adequate tool to detect subjects with RBD. In subjects without additional neurologic or sleep disorders, the specificity was high and may allow a preliminary diagnosis with a high certainty. In patients with either neurologic diseases or sleep disorders, the specificity is poorer but acceptable. However, since these subjects are almost always symptomatic and consult a physician, a clinical interview and further diagnostic procedures such as polysomnography will normally take place. In clinical practice, the RBDSQ may thus be applied within a stepwise diagnostic process (questionnaire, interview, polysomnography).

Our control samples on purpose did not include patients with parkinsonism. The usefulness of the RBDSQ in these patients is therefore unknown and has to be further evaluated as the next step. Surprisingly, the sensitivity of expert interviews for the clinical diagnosis of RBD (compared with PSG results) in sleep-disordered patients with PD in the aforementioned study was very low (33%), whereas the specificity was good (90%).²¹ It is likely that PD patients in whom RBD was not detected in a clinical interview had subtle nocturnal symptoms, i.e., brief movements of extremities or talking while asleep, which were only detected in the PSG-synchronized videotape. The sensitivity of a standardized questionnaire might be higher compared to a clinical interview if symptoms are mild and possibly not reported by the patient. The fact that there was no correlation be-

tween the RBDSQ scores and the duration of RBD suggests that the RBDSQ also detects mild RBD cases. Overall, detecting RBD in PD patients without performing polysomnography may be problematic⁵⁸ and any diagnostic instrument for RBD has to be validated against polysomnography before being used in epidemiologic studies.

In summary, the RBDSQ will hopefully facilitate the diagnosis and the recruitment of RBD patients necessary for research studies as well as for therapeutic trials.

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