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A Single-Question Screen for REM Sleep Behavior Disorder: A Multicenter Validation Study

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Abstract

Background—Idiopathic REM sleep behavior disorder (RBD) is a parasomnia that is an important risk factor for PD and Lewy body dementia. Its prevalence is unknown. One barrier to determining prevalence is that current screening tools are too long for large-scale epidemiologic surveys. Therefore, we designed the REM Sleep Behavior Disorder Single-Question Screen (RBD1Q), a screening question for dream enactment with a simple yes/no response.

Methods—Four hundred and eighty-four sleep-clinic– based participants (242 idiopathic RBD patients and 242 controls) completed the screen during a multicenter case-control study. All participants underwent a polysomnogram to define gold-standard diagnosis according to standard criteria.

Results—We found a sensitivity of 93.8% and a specificity of 87.2%. Sensitivity and specificity were similar in healthy volunteers, compared to controls or patients, with other sleep diagnoses.

Conclusions—A single-question screen for RBD may reliably detect disease, with psychometric properties favorably comparable to those reported for longer questionnaires.

Keywords

REM sleep behavior disorder; screening; diagnosis

REM sleep behavior disorder (RBD) is a parasomnia characterized by dream-enactment behavior, diagnosed by clinical history in combination with video-polysomnography to document REM atonia loss. Idiopathic RBD (iRBD) is receiving increased attention as an important risk factor for neurodegenerative diseases, especially alpha-synucleinopathies.[2–4]

Despite increasing recognition of its importance, knowledge of RBD epidemiology is limited. Except for two studies, which primarily screened for sleep injury (a subtype of RBD)[5,6] no large-scale epidemiologic surveys have estimated RBD prevalence. A major barrier to conducting prevalence studies is that RBD is probably uncommon, thus requiring very large epidemiologic surveys. Such large surveys are generally broad, assessing many nonsleep outcomes, with strict limitations upon the time demands upon respondents. This precludes the use of polysomnographic diagnosis and lengthy screening questionnaires. Therefore, simple (i.e., one- or two-question) screens are needed to assess RBD in large-scale epidemiologic surveys. To meet this need, we designed the RBD Single-Question Screen (RBD1Q) a single “yes-no” question that queries the classic dream-enactment behavior of RBD. We present here the validation results of this question, in relation to gold-standard polysomnographic diagnosis, in a 12-center case-control study.

Patients and Methods

Participants

Participants were selected from 12 centers of the International REM Sleep Behavior Disorder Study Group and were recruited from 2008 to 2011. All RBD patients had RBD diagnosis confirmed by polysomnography according to the International Classification of Sleep Disorders-2[7]; namely, loss of REM atonia on polysomnographic trace in association with history of dream-enactment or witnessed dream enactment during REM sleep on video polysomnogram. Patients were not blinded to RBD diagnosis when they completed the questionnaire. Convenience sampling was used (i.e., maximal recruitment each center). All cases had neurological examination confirming the absence of dementia (defined as Mini-Mental State Examination [MMSE] <24 with functional impairment resulting from cognitive decline[8]— note that MMSE was required only if symptoms of dementia were present) and parkinsonism (by UK Brain Bank criteria[9]). Each center also recruited controls (both healthy subjects and patients with other sleep disorders), frequency-matched 1:1 on age (within 5 years) and sex (10% tolerance outside perfect matching allowed). All controls underwent a polysomnogram confirming the absence of RBD. Participants with asymptomatic REM atonia loss were not included. Ethics approval was obtained from the research ethics board of each participating center. All patients gave informed consent according to the Declaration of Helsinki.

Screening Question

The RBD1Q consists of a single question, answered “yes” or “no,” as follows: “Have you ever been told, or suspected yourself, that you seem to ‘act out your dreams’ while asleep (for example, punching, flailing your arms in the air, making running movements, etc.)?”

This question was translated into French, German, Japanese, Italian, Spanish, Czech, and Danish by native-speaking medical translators or by RBD expert investigators fluent in English and the local language. Translations of the question are provided in the Supporting Materials. The question was administered as part of a multicenter questionnaire study of environmental risk factors for RBD (Postuma et al, in press). The screen was designed to be self-administered, with participation by spouses/caregivers encouraged. If literacy was poor, centers were allowed to administer the screen in person. The screen is freely available for use in patient care or research (no fee may be charged for its use).

Analysis

Analysis was carried out by R.B.P. using IBM *SPSS Statistics Version 20* (IBM Corporation, Armonk, NY). Sensitivity and specificity, along with 95% confidence intervals (CIs), were estimated. Separate subgroup analysis was performed to assess sensitivity/specificity in healthy volunteers versus controls with other diagnosis, in sleep apnea patients (who can have symptoms that mimic RBD[10]), and after excluding patients who live alone and who take medications that could affect symptomatology.

Results

Participants

A total of 484 participants were enrolled, including 242 patients with RBD and 242 controls. Forty-eight (19.8%) controls were healthy volunteers, and 194 had other sleep diagnosis (sleep apnea = 37%, restless legs syndrome = 16.9%, insomnia = 13.6%, and other = 12.3%). Mean RBD patient age was 66.4 ± 9.5 (controls = 64.2 ± 10.1). Seventy-eight percent of RBD patients were male, compared to 74% of controls. Eighty-six percent of RBD patients and 82% of controls lived alone. A total of 483 of 484 participants answered the RBD1Q screen.

Validity of RBD1Q

Of the 241 RBD patients who answered the RBD1Q, 226 screened positive, translating to a sensitivity of 93.8% (95% CI = 90.0, 96.2). A total of 211 of 242 controls screened negative, translating to a specificity of 87.2% (95% CI = 82.4, 90.8). Area under the receiver operating characteristic curve was 0.905 (95% CI = 0.875, 0.935) (Table 1).

In subgroup analysis, specificity in healthy volunteers (85.4%; 95% CI = 72.8, 92.8) was similar to sleep center controls (87.6%; 95% CI = 82.2, 91.5). Although obstructive sleep apnea can mimic RBD,[10] specificity was not lower in obstructive sleep apnea patients (92.2%; 95% CI = 84.8, 96.2). Exclusion of patients who lived alone did not improve either sensitivity (93.5%) or specificity (87.6%). Exclusion of participants taking antidepressants (n = 52; 42 with RBD) did not appreciably alter results (sensitivity = 93.8%; specificity = 90.4%). Ninety-seven patients were taking clonazepam, 30 melatonin, and 15 both medications. After patients on either symptomatic therapy were excluded, results were similar (sensitivity = 92.2%; specificity = 87.7%).

Discussion

We found that the RBD1Q could detect RBD with 94% sensitivity and 87% specificity in a well-characterized, clinic-based cohort of RBD patents and controls.

The RBD1Q compares favorably to other questionnaire-based diagnostic tools. The first questionnaire tool developed for RBD was the 13-item Stiasny-Kolster RBD-Screening Questionnaire (RBDSQ), which was evaluated in 54 patients with RBD in different conditions (19 with iRBD, 33 with narcolepsy, and 2 with PD), 133 healthy subjects, and 160 sleep-center controls. The questionnaire demonstrated 96% sensitivity, but only 56% specificity, when using sleep-center patients as controls. Specificity was 92% when healthy subjects were used as controls; however, specificity cannot be reliably assessed for these subjects, because they did not undergo polysomnography (both clinical interview and the screening questionnaire could miss RBD). A Japanese version of this questionnaire was assessed in 52 iRBD patients, 55 controls with obstructive sleep apnea on successful continuous positive airway pressure therapy, and 62 age-matched healthy subjects (again without polysomnography confirmation in healthy subjects).[12] Sensitivity was 88.5% and specificity was 90.9% in apnea patients (and 96.9% in healthy subjects). The Japanese version was also tested in 45 PD patients—at a one-point higher cut-off, sensitivity was 84%

and specificity was 96%[13]. The recently designed RBD-HK (Hong Kong) scale includes 13 questions, with two frequency assessments for each question (lifetime and 1-year frequency).[14] Using predominantly sleep-center controls, sensitivity was estimated at 82%, with 87% specificity.

Both the RBDSQ and RBD-HK involve 13 questions and therefore may not be practical in large/broad epidemiologic surveys in which sleep is one of many components assessed. Yet, the essence of RBD can be described relatively simply, suggesting that multiple questions may be unnecessary. The Mayo Sleep questionnaire contains a single question of dream enactment targeted to caregivers. Although independently designed, it is very similar to our question ("Have you ever seen the patient appear to 'act out his/her dreams' while sleeping? [punched or failed arms in the air, shouted or screamed]).[15] There are five follow-up questions in the case of a positive response. In dementia patients, the questionnaire given to their caregivers detected RBD with 98% sensitivity and 74% specificity. It has not been tested in iRBD. Therefore, there appears to be good potential for single-question RBD screens administered either to caregivers or to patients themselves, depending on circumstances.

Some limitations should be noted. Just as with validation studies for the RBDSQ and RBD-HK, our screen was tested in patients who were followed in sleep centers for RBD. Patients were therefore presumably aware of their RBD status. By virtue of having sought out medical attention, they are also likely to be more severely affected and may be knowledgeable about their condition—therefore, they may more readily recognize their symptoms on screens. Therefore, sensitivity and specificity may be different in population-based studies. Unfortunately, this limitation may be unavoidable—even assuming a poor screen sensitivity (67%), with an iRBD prevalence of 2%, 1,500 general population screen negatives would have to undergo polysomnography to detect 10 screen-negative/disease-positive individuals—therefore, reliable estimates of sensitivity in general population RBD cases may never be available. Also, in uncommon conditions, positive predictive value (PPV) can be low, even in the face of excellent specificity (e.g., with 2% prevalence, a test with 90% specificity and 100% sensitivity results in a PPV of only 16.7%). Therefore, direct estimate of PPV in a general population study would be of considerable utility. Note because of concerns about specificity, the RBD1Q does not screen for sleep talking or sleep yelling—there are a subset of patients for whom this is the only manifestation, and these may be missed by the screen. Our high sensitivity (93.8%) suggests that this is a relatively minor limitation, at least for clinic-based RBD samples. Also, this study did not include patients with non-REM parasomnias (one control with non-REM parasomnia was excluded)—clearly, these patients may respond positively to the screen, further reducing specificity. Finally, although our study size is large, sensitivity and specificity estimates in smaller subgroups have wide confidence intervals.

Conclusion

In summary, the RBD1Q demonstrated good sensitivity and specificity in diagnosing RBD. This result supports its future potential for the assessment of RBD prevalence in broad-scale epidemiologic surveys of disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Sensitivity and Specificity of the RBD1Q Screen

	RBD	Control	Total
RBD screen +	226	31	257 PPV = 87.9%
RBD screen −	15	211	226 NPV = 93.4%
	241	242	
	Sensitivity = 93.8%	Specificity = 87.2%	

Abbreviation: NPV, negative predictive value.