

Validation of the Beijing Version of the REM Sleep Behavior Disorder Questionnaire (RBDQ-Beijing) in a Mainland Chinese Cohort

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REM sleep behavior disorder (RBD) is one type of parasomnia characterized by nocturnal complex motor activity associated with dream mentation. Growing evidence has indicated that RBD is a preclinical stage of neurodegenerative diseases. Therefore screening RBD patient is becoming important. The RBD Questionnaire-Hong Kong (RBDQ-HK) is an effective questionnaire to screen RBD patients. However, it is hard to distinguish RBD with the questionnaire from severe OSAS patients, who could mimic some symptoms of RBD patients. Therefore, we made RBDQ-Beijing by adding two screening questions for OSAS into original RBDQ-HK, including habitual loud snoring and witnessed apnea during sleep. To validate and compare these two questionnaires, 224 subjects were enrolled and screened with these questionnaires, and consequently analyzed with video-polysomnography. Receiver-operator characteristics curve analysis was conducted to attain the best cut-off values of the RBDQ-HK and RBDQ-Beijing. For the RBDQ-HK, the sensitivity was 97.1% and the specificity was 83.2%. More than half of misclassified RBD patients were proved to be severe OSAS patients. For the RBDQ-Beijing, the sensitivity was 95.8% and specificity was 94.3%, indicating that our questionnaire is able to distinguish RBD from severe OSAS patients. In conclusion, RBDQ-Beijing is of help to improve the specificity in RBD screening without excluding the patients with RBD combined OSAS. Therefore the RBDQ-Beijing may be a better screening and preliminary diagnostic tool for RBD than the RBDQ-HK. Moreover, the RBDQ-Beijing would be important for early diagnosis of neurodegenerative diseases and for prevention of injuries to the patient or the patient's bed partner.

Keywords: neurodegenerative disease; obstructive sleep apnea syndrome; questionnaire; REM sleep behavior disorder; validity

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Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is one type of parasomnia characterized by excessive motor activity during REM sleep, often in the form of dream enactment behavior, such as sleep talking, shouting, and vigorous or elaborate body movements including

punching, kicking, sitting up, and even falling out of bed. Such prominent motor activities could result in significant injury to either the patient or the patient's bed partner. Moreover, RBD has been associated with neurodegenerative diseases, with 81% conversion in a longitudinal study with a 16-year follow-up (Schenck et al. 2013). Therefore, early diagnosis of RBD can aid in the early diagnosis of

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neurodegenerative diseases. It is still debated whether idiopathic RBD (iRBD) is the preclinical stage of neurodegenerative disease and which factors would trigger the development of neurodegenerative disease (Lam et al. 2013). If iRBD is the preclinical stage of neurodegenerative disease, early RBD screening would be essential.

The clinical diagnosis of RBD requires video-polysomnographic (vPSG) evidence of the absence of atonia during REM sleep, according to the second edition of the International Classification of Sleep Disorders (ICSD-II) (American academy of sleep medicine 2005; Neikrug and Ancoli-Israel 2012). However, it is not practical to screen for RBD in the population using vPSG. Therefore, a convenient and suitable screening tool is needed for epidemiological research and clinical screening (Lam et al. 2013). A limited number of questionnaires developed for screening RBD have been applied in Chinese populations (Stiasny-Kolster et al. 2007; Miyamoto et al. 2009; Li et al. 2010; Boeve et al. 2011, 2013; Neikrug and Ancoli-Israel 2012; Postuma et al. 2012; Sasai et al. 2012; Lam et al. 2013).

The REM Sleep Behavior Disorder Questionnaire-Hong Kong (RBDQ-HK) (Li et al. 2010) is one of the effective questionnaires in Chinese, having been validated in Cantonese speaking populations with traditional Chinese characters. The questionnaire places emphasis on obtaining information on the currency, frequency, and severity of RBD symptoms and has been demonstrated to have moderate sensitivity and specificity (Li et al. 2010). The RBDQ-HK has also been translated into Japanese and was proven to be quite sensitive and specific with different cut-off scores (Sasai et al. 2012). However, it has not been verified in Mandarin-speaking Chinese populations with simplified Chinese characters.

In addition, there is evidence that severe obstructive sleep apnea syndrome (OSAS) could mimic the symptoms of RBD, particularly in cases of severe OSAS, which are quite common among the elderly. Consequently, OSAS is a major disease to be differentiated from RBD (Iranzo and Santamaría 2005; Schredl 2008; BaHamman et al. 2013). Therefore, it is important and preferable to include questions in the RBD screening questionnaire to exclude OSAS and enhance the specificity for RBD detection. Although the RBDQ-HK has been shown to be able to exclude OSAS, the original research did not report details about the characteristics of OSAS patients enrolled in the study or information about their dream enactment behaviors. Therefore, it is difficult to conclude that the RBDQ-HK can differentiate RBD from severe OSAS, which might mimic the symptoms of RBD (Li et al. 2010).

The present study aims to (1) verify the simplified Mandarin version of the RBDQ-HK at a cut-off level of 18/19 in Mandarin speaking Chinese population, and (2) modify the simplified Mandarin version of the RBDQ-HK with screening questions added on severe OSAS (RBDQ-Beijing) to increase the specificity of the RBDQ-HK for diagnosing RBD and then validate the RBDQ-Beijing in

our study population.

Methods

Subjects

Subjects visited our sleep clinic and received vPSG examinations from January 1, 2012 to October 31, 2013. These subjects were enrolled through the Sleep Disorders Center of Xuanwu Hospital. Only subjects older than 18 who had a vPSG were included. iRBD was diagnosed according to the ICSD-II and the American Academy of Sleep Medicine Manual (AASM) (American academy of sleep medicine 2005; Berry et al. 2012). Patients with neurological conditions (e.g., epilepsy or neurodegenerative diseases), psychiatric disorders (e.g., post-traumatic stress disorder), or patients taking any psychotropic medications (e.g., antidepressants including fluoxetine and venlafaxine) were excluded owing to potential influences on vPSG results. The study was approved by our Institutional Review Board (IRB) and written informed consent was obtained from each subject.

RBD screening

All subjects were screened using the RBDQ-Beijing at most one week prior to the one-night vPSG examination. Both the subjects and the technicians were blind to the result of the questionnaires. The original version of the RBDQ-HK is a self-administered (by the patient and/or bed partner) questionnaire comprising 13 items (Li et al. 2010). Each item is designed to assess the lifetime occurrence and recent (one-year) frequency. The total score can range from 0 to 100 and consists of the lifetime occurrence score (0-20) and the score on recent frequency in the past year (0-80). The RBDQ-HK was translated into simplified Mandarin. To screen for severe OSAS symptoms, the following two questions were added: "Do you have habitual loud snoring while asleep?" and "Has anyone witnessed you having an apnea during sleep?" (Chung et al. 2008; Abrishami et al. 2010). The two questions were reverse weighted as "no" = 5 and "yes" = 0. The range of the RBDQ-Beijing total score is 0-110.

Polysomnography interpretation

vPSG was performed using a standard system (E-Series, Compumedics Limited, Abbotsford, Australia) with video monitoring of patient behavior, diagnostic PSG recordings, and measurements, including four channels of the scalp EEG (C3/A2, C4/A1, O1/A2, and O2/A1), two electrooculograms (EOG), submental electromyography (EMG), electrocardiogram (ECG), nasal/oral airflow, peripheral capillary oxygen saturation (SpO₂) recording taken by oximetry sensor, amplification of snoring sounds using a microphone, chest/abdominal respiratory effort, and anterior tibialis EMGs for leg movements. All patients were simultaneously videotaped and closely observed by a technician for any movement or vocalization. REM sleep without atonia (RWA) was scored according to the 2012 AASM scoring manual (Berry et al. 2012). Tonic RWA was defined as an epoch of REM sleep with at least 50% of the duration of the epoch having a chin EMG amplitude greater than the minimum amplitude demonstrated in non-rapid eye movement (NREM) sleep. In a 30-second epoch of REM sleep divided into 10 sequential, three-second mini-epochs, at least 5 (50%) of the mini-epochs contain bursts of phasic muscle activity. Excessive phasic muscle activity bursts are 0.1-5.0 seconds in duration and at least four times as high in amplitude as the background EMG activity in RBD patients. The polysomnographic characteristics of RBD are characterized by either or both of the following features: 1) sustained muscle activity (tonic activity)

in REM sleep in the chin EMG and 2) excessive transient muscle activity (phasic activity) during REM in the chin or limb EMG. The total EMG activity was presented as the percentage of REM related EMG activity (REMREEA) with the percentage of tonic EMG activity plus the percentage of phasic EMG activity. In this study, we used the 10% REMREEA as a cut-off point for indicating probable diagnosis of RBD (Zhang et al. 2008).

PSG-confirmed RBD patients need to meet the diagnostic criteria of RBD: (1) history of problematic sleep behaviors that were harmful, potentially harmful, or disruptive of sleep continuity or disturbing to self and/or sleep partner; (2) PSG abnormality of excessive augmentation of chin EMG tone or excessive chin or limb EMG twitching during REM sleep; and (3) identifiable motor activities related to dream enactment during REM sleep by video records (not related to periodic limb movement disorder or respiratory events).

Apnea was defined as the cessation of airflow for at least 10 seconds. Hypopnea was defined as an airflow amplitude decrease greater than 50% for at least 10 seconds with either an arousal or an oxygen desaturation greater than 3%. The apnea-hypopnea index (AHI) was calculated as the total number of apnea/hypopnea episodes per hour of sleep and was used to classify the severity of OSAS, typically categorized as “mild” for 5-15/hour, “moderate” for 15-30/hour, and “severe” for ≥ 30 /hour (American academy of sleep medicine 2005; Berry et al. 2012).

Statistical analysis

Statistical Package for Social Science (SPSS) 19.0 was used for database management and analysis. Descriptive data are presented as means \pm standard deviations for continuous variables and as frequencies for categorical variables. Pearson's Chi-square tests and *t*-tests were used to compare the differences between groups. The cut-off value of 18/19 for the RBDQ-HK and 28/29 for the RBDQ-Beijing were applied to separate the subjects into two groups: predicted RBD

and predicted non-RBD (Figs. 1 and 2). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the simplified Mandarin version of the RBDQ-HK were calculated in our population for primary validation. Exploratory factor analysis (EFA) was performed to determine the structural validity of the RBDQ-Beijing. Internal consistency was assessed using Cronbach's alpha coefficient. Receiver-operator characteristics (ROC) curve analysis was performed, and values of sensitivity and specificity for the screening of RBD at different cut-off points were calculated for the RBDQ-Beijing. The diagnostic value was calculated using the area under the curve (AUC), which was independent of an arbitrary choice of a best cut-off value. Analysis of variance (ANOVA) was used to compare the scores in different disease groups, and least significant difference (LSD) was used to analyze the differences between groups.

Results

Characteristics of participants

A total of 224 eligible subjects met the inclusion criteria and were enrolled in this study (Figs. 1 and 2). There were 118 PSG-confirmed RBD subjects. Males were more commonly represented among the PSG-confirmed RBD patients (77.1%) than among the PSG-confirmed non-RBD patients (53.8%, $p < 0.01$). RBD patients (66.5 ± 8.4) were older than non-RBD patients (61.6 ± 8.4 , $p < 0.01$), with 39% of RBD patients older than 70 years. Average AHI was significantly lower in the RBD group than in the non-RBD group (9.2 ± 12.4 vs. 21.9 ± 22.9 , $p = 0.0001$) (Table 1). A self-report was completed by 73.7% of the PSG-confirmed RBD subjects and 66% of the PSG-confirmed non-RBD subjects. Assistance from relatives to complete the report was received by 20.4% of the PSG-confirmed

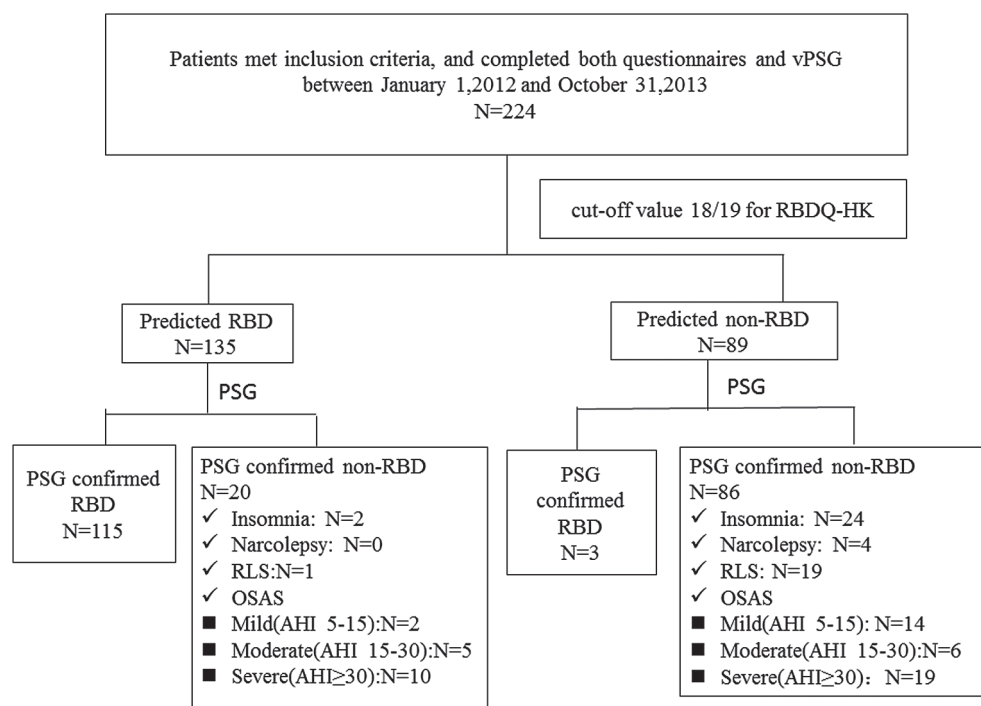


Fig. 1. Clinical characteristics of the present cohort analyzed with RBDQ-HK using a cut-off value of 18/19.

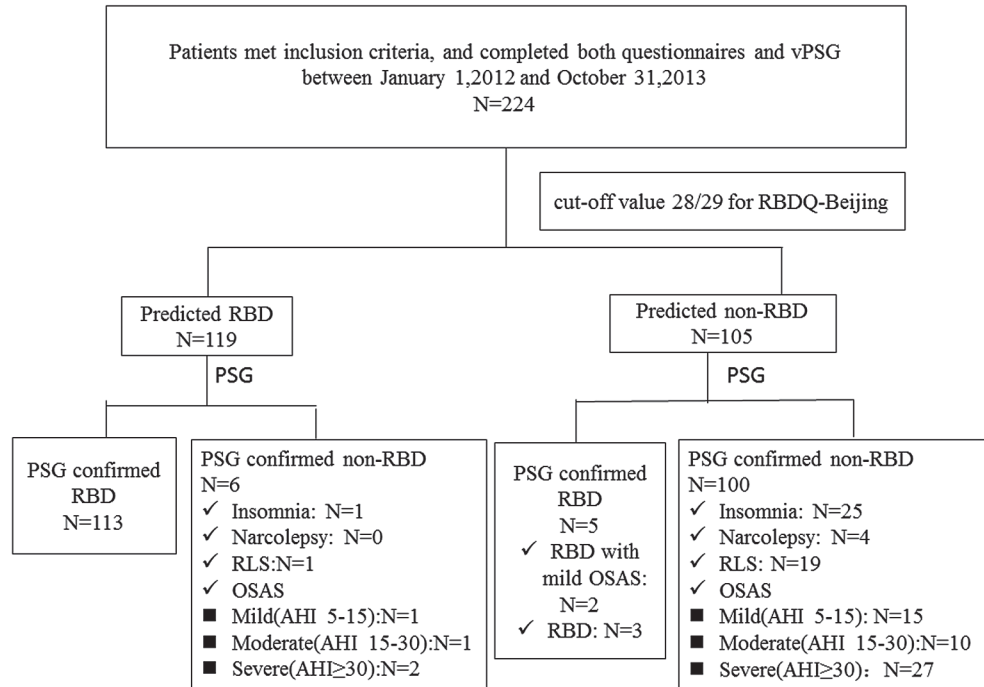


Fig. 2. Clinical characteristics of the present cohort analyzed with RBDQ-Beijing using a cut-off value of 28/29.

Table 1. Demographic and characteristics of participants.

	PSG confirmed RBD (N = 118)	PSG confirmed non-RBD (N = 106)	P value
Gender, N (%)			
Male	91 (77.1)	57 (53.8)	0.0001
Female	27 (22.9)	49 (46.2)	
Age, year	66.5 ± 8.4	61.6 ± 8.4	0.0001
Age stratification, N (%)			
< 60	28 (23.7)	51 (48.1)	0.0001
60-70	44 (37.3)	35 (33.0)	
> 70	46 (39.0)	20 (18.9)	
AHI	9.2 ± 12.4	21.9 ± 22.9	0.0001

RBD subjects (8.5% for bed-partner, 11.9% for others) and 27.4% of the PSG-confirmed non-RBD subjects (8.5% for bed-partner, 18.9% for others), whereas 5.9% of the PSG-confirmed RBD subjects and 6.6% of the PSG-confirmed non-RBD subjects made the report partially by themselves and partially with the assistance of relatives. Sleeping alone was reported by 29.7% of the PSG-confirmed RBD subjects and 36.8% of the PSG-confirmed non-RBD subjects. Sleeping with bed partners was reported by 52.5% of the PSG-confirmed RBD subjects and 49.1% of the PSG-confirmed non-RBD subjects, and 17.8% of the PSG-confirmed RBD subjects and 14.2% of the PSG-confirmed non-RBD subjects slept in separate beds in the same room as someone else (Table 2).

Verification of the RBDQ-HK

When using the direct translation of the RBDQ-HK questionnaire, a cut-off point of 18/19 yielded a sensitivity of 97.1%, a specificity of 83.2%, a PPV of 86.4%, and an NPV of 96.3% for PSG-confirmed RBD patients (Table 3). Twenty patients suspected as RBD by the questionnaire were confirmed to be non-RBD by vPSG with the following diagnoses: insomnia (N = 2), restless legs syndrome (N = 1), and mild to moderate (N = 7) and severe (N = 10) OSAS (Fig. 1).

Validation of the modified RBDQ-Beijing

Face validity: The RBDQ-Beijing was composed of two parts. One part comes from the RBDQ-HK, which has been validated in RBD patients in Hong Kong, and the other part (the two OSAS questions) was discussed and

Table 2. Questionnaire responses and sleeping environment of participants.

	PSG confirmed RBD (N = 118)	PSG confirmed non-RBD (N = 106)
Informant, N (%)		
Self	87 (73.7)	70 (66)
Sleep-partner	10 (8.5)	9 (8.5)
Others (e.g., caregiver)	14 (11.9)	20 (18.9)
Self + bed-partner	6 (5.1)	7 (6.6)
Self + others (not bed-partner)	1 (0.8)	0
Sleep environment, N (%)		
Slept alone	35 (29.7)	39 (36.8)
With bed-partner	62 (52.5)	52 (49.1)
Separated bed in same room	21 (17.8)	15 (14.2)

Table 3. Sensitivity, specificity, PPV and NPV for the RBDQ-HK and RBDQ-Beijing.

Scales (score)	Cut-off score	Sensitivity	Specificity	PPV	NPV
RBDQ-HK (0-100)	18/19	97.1%	83.2%	86.4%	96.3%
RBDQ-Beijing (0-110)	28/29	95.8%	94.3%	95.0%	95.2%
	23/24	96.6%	84.0%	87.0%	95.7%
	44/45	80.5%	97.2%	96.9%	81.7%

PPV, positive predictive value; NPV, negative predictive value.

judged by a panel of experienced researchers and clinicians in terms of the association of test items to OSAS symptom representation.

Construct validity and Cronbach's alpha coefficient:

Three main factors were extracted using exploratory factor analysis (EFA) with Varimax rotation. Six items (Q1-Q5 and Q13) loaded on factor 1, which corresponded to the characterization of the individual's dreams and nightmares. Higher factor 1 scores indicated a more negative effect on sleep quality. Seven items (Q6-Q12) loaded on factor 2, which corresponded to behavioral manifestations, and higher scores of factor 2 indicated more serious RBD symptoms. Two items (Q14 and Q15) loaded on factor 3, which corresponded to OSAS symptoms. The RBDQ-Beijing had a moderate Cronbach's alpha coefficient of 0.814 (Table 4).

Receiver-operator characteristics (ROC) curve and cut-off value: ROC analysis suggested that the RBDQ-Beijing had good diagnostic accuracy [area under curve (AUC) = 0.974]. The best cut-off value for the overall scale (range 0-110) was 28/29, with a sensitivity of 95.8%, specificity of 94.3%, PPV of 95.0%, and NPV of 95.2% for diagnosis of RBD (Table 3, Fig. 3). Moreover, the cut-off score of 23/24 showed similar sensitivity and specificity to the original RBDQ-HK (sensitivity = 96.6%, specificity = 84.0%), whereas the cut-off of 44/45 had the best specificity and acceptable sensitivity for diagnosis (sensitivity 80.5%, specificity 97.2%).

Test-retest reliability: The RBDQ-HK and RBDQ-Beijing questionnaires were retested in 15 PSG-confirmed

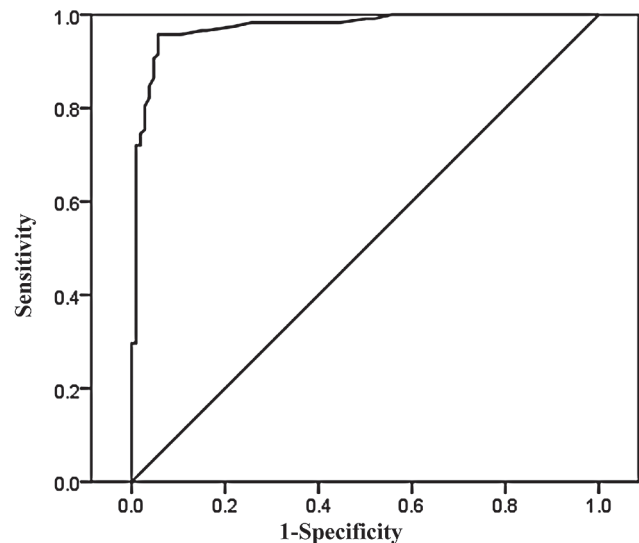


Fig. 3. The best cut-off for overall scale was located at 28/29 with a sensitivity of 95.8%, specificity of 94.3%, PPV of 95.0%, and NPV of 95.2% (AUC = 0.974).

RBD subjects and 15 PSG-confirmed non-RBD cases at an interval of 2 weeks. The test-retest coefficient was 0.89 (for factor 3), 0.99 (for RBDQ-HK), and 0.98 (for RBDQ-Beijing).

Quantitative EMG activity and the relationship between the RBDQ-Beijing score and the total EMG activity (REMREEA): In the PSG-confirmed RBD group, tonic EMG activity (%) was 18.62 ± 16.68 , phasic EMG activity

Table 4. Rotated factors loading for RBDQ-Beijing.

Scale item	Factor 1 Dreams and nightmares	Factor 2 Behavioral manifestation	Factor 3 OSAS-related
Q1* Frequent dreams	0.678		
Q2* Frequent nightmares	0.643		
Q3* Emotional dreams	0.640		
Q4* Violent or aggressive dreams	0.679		
Q5* Frightening dreams	0.531		
Q13* Disturbed sleep	0.635		
Q6* Sleep talking		0.704	
Q7* Shouting or yelling in sleep		0.781	
Q8* Dream-related movements		0.816	
Q9* Falling out of bed		0.876	
Q10* Sleep-related injuries (SRI)		0.873	
Q11* Attempts to assault/injure		0.905	
Q12* SRI-related to dream content		0.898	
Q14 Snoring or waking up due to choking			0.860
Q15 Apneas			0.809

*RBDQ-HK

Table 5. The amounts of RWA of participants.

	PSG confirmed RBD (N = 118)	PSG confirmed non-RBD (N = 106)
The amounts of RWA, (%)		
% of tonic EMG activity	18.62 ± 16.68	1.23 ± 5.46
% of phasic EMG activity	0.11 ± 0.08	0.02 ± 0.02
% of phasic + tonic EMG activity (REMREEA)	18.73 ± 16.69	1.21 ± 5.39

Table 6. RBDQ-Beijing Scores in PSG confirmed RBD and non-RBD.

	PSG confirmed RBD (N = 118)	PSG confirmed non-RBD (N = 106)		
		mild to moderate OSAS (N = 48)	severe OSAS (N = 30)	non-OSAS (N = 28)
Total score	62.6 ± 19.6	14.7 ± 4.7	15.2 ± 5.2	18.7 ± 13.4
Factor 1	16.5 ± 5.9	5.8 ± 5.8	5.8 ± 5.7	6.9 ± 5.9
Factor 2	38.9 ± 14.4	3.5 ± 6.3	6.6 ± 7.7	3.8 ± 8.7
Factor 3	7.2 ± 3.3	5.4 ± 4.2	2.8 ± 4.3	8.1 ± 3.1

(%) was 0.11 ± 0.08 , and REMREEA (the tonic + phasic EMG activity) was 18.73 ± 16.69 . In the PSG-confirmed non-RBD group, tonic EMG activity (%) was 1.23 ± 5.46 , phasic EMG activity (%) was 0.02 ± 0.02 , and REMREEA was 1.21 ± 5.39 (Table 5). REMREEA was positively associated with the RBDQ-Beijing score ($r = 0.578$, $p < 0.01$).

RBDQ-Beijing scores in different disease groups: We classified the vPSG-confirmed non-RBD group into mild to moderate OSAS, severe OSAS, and non-OSAS groups according to the value of AHI and then further compared

the RBDQ-Beijing scores in the three groups (Table 6). There were 78 patients with OSAS, including 56 who did not have other complications, 8 with restless leg syndrome complicated with OSAS (mild OSAS = 6, moderate OSAS = 2), 12 with insomnia complicated with OSAS (mild OSAS = 11, moderate OSAS = 1), and 2 with narcolepsy complicated with OSAS (moderate OSAS = 1, severe OSAS = 1). The RBD group had the highest total score ($p < 0.001$) compared with the other groups according to the LSD test, whereas total scores in the other three groups did not differ significantly ($p > 0.05$ from the LSD test). For

factor 1 and factor 2, the RBD group also had the highest scores ($p < 0.001$). For factor 3, the difference of average scores between the RBD group and the non-OSAS group was not significant ($p = 0.254$), whereas the score in mild to moderate OSAS group was significantly lower than the other two groups ($p = 0.006$ for difference from the RBD group, $p = 0.003$ for difference from the non-OSAS group), with the lowest score in the severe OSAS group (all $p < 0.01$).

Discussion

Our study suggested high sensitivity and modest specificity of the simplified Mandarin version of the RBDQ-HK for diagnosis of RBD in a mainland Chinese population, suggesting that the RBDQ-HK is a good screening tool for RBD in the clinical setting. However, the RBDQ-HK may not be able to distinguish OSAS, especially severe OSAS, from RBD, because more than half of those who were predicted to have RBD were in fact sufferers of severe OSAS. The RBDQ-Beijing demonstrated good sensitivity and high specificity (94.3% and 83.2%, respectively) at 28/29, and a best specificity of 97.2% at 44/45. This may serve as a preliminary diagnostic tool to help clinicians to differentiate RBD patients from “pseudo-RBD” subjects.

Dream enactment behaviors in RBD patients related to limb movements were non-specific. Marked physical movements during sleep do not always represent a pathology indicating RBD. These dream-related behaviors could also occur in other sleep disorders, a phenomenon known as “pseudo-RBD” (Iranzo and Santamaría 2005). In particular, untreated OSAS may be associated with physical movements during sleep, and it is important to differentiate patients with iRBD from those with OSAS with abnormal sleep behavior. However, the criteria for OSAS in the original RBDQ-HK was defined as AHI > 10 /hour, which included not only severe OSAS, but also mild to moderate OSAS. Without detailed characteristics of OSAS patients, the level of specificity is lower in distinguishing true RBD from severe OSAS with dream enactment behavior (Li et al. 2010). Loud snoring and witnessed apnea during sleep are the specific symptoms of OSAS, and the additional questions on these symptoms of OSAS increase the specificity of the RBDQ-HK. Our findings supported the results of a previous study reporting that clinical features similar to RBD can be observed in patients with high AHI and severe oxyhemoglobin desaturations (Iranzo and Santamaría 2005; Schredl 2008; BaHammam et al. 2013). Seventeen patients with OSAS presented with RBD-like symptoms, more than half with severe OSAS ($N = 10$), and were screened as positive for RBD using the RBDQ-HK. RBD and OSAS have different pathogenesis and treatment. RBD is thought to reflect dysfunction of the brainstem structures that modulate REM sleep, whereas OSAS is due to the repetitive obstruction of the upper airway during sleep. OSAS and RBD require different treatments, and clonazepam, one of the medications for RBD, may worsen existing OSAS (Schuld

et al. 1999). vPSG monitoring showed that the abnormal behaviors of pseudo-RBD occurred only during apneic-related arousals in REM and NREM sleep, and tonic and phasic activity was lower compared with patients with RBD. Patients with iRBD are at higher risk of developing neurodegenerative diseases, which are currently incurable, and symptom monitoring might be the only method for early detection of neurodegenerative disease. Therefore, it is important to distinguish RBD from OSAS.

Consistent with the original report, the Mandarin version of the RBDQ-HK showed good sensitivity for RBD screening, but the specificity was moderate. At the cut-off score of 28/29, the RBDQ-Beijing presented both excellent sensitivity and excellent specificity, with the specificity increasing from 83.2% to 94.3%. The comparison of scores for the RBDQ-Beijing among different OSAS groups indicated that only six non-RBD patients were predicted to have RBD. This suggested that the RBDQ-Beijing is capable of increasing the accuracy rate of distinguishing RBD from OSAS and other sleep disorders, and it might be a better preliminary diagnostic tool for RBD. OSAS has been reported to be highly prevalent in RBD patients (Olson et al. 2000; Wing et al. 2008). Five patients with vPSG-confirmed RBD were assigned to the predicted non-RBD group at a cut-off level of 28/29 for the RBDQ-Beijing, more than it would be the case using a cut-off value of 18/19 for the simplified Mandarin version of RBDQ-HK, but the number of patients with RBD complicated OSAS was not increased (Fig. 2). Furthermore, the analysis of factor 3 in different disease groups confirmed that the factor 3 scores could differentiate OSAS symptoms and also the severity of OSAS.

Eisensehr and colleagues (2001) reported that the performance of specialized interviews for identifying RBD clinically was good in non-Parkinson Disease (PD) patients with a perfect sensitivity (100%) and specificity (99.6%). However, an expert clinical interview may require experienced clinicians, training, time, and resources. In addition, there could be a long waiting time and limited access to clinical and vPSG confirmation in some medical regions. As a result, many underlying cases of RBD may be missed or misdiagnosed. Because of the potential different purposes for the use of the RBDQ-Beijing, our study presented different cut-off values. We suggest 28/29 as a conventional cut-off for screening and preliminary diagnosis of RBD. If the questionnaire is used in an epidemiological study aiming to screen for potential RBD patients, a cut-off value of 23/24 would be recommended because it has the highest sensitivity (96.6%) at an acceptable specificity level. For clinical differential diagnosis, a cut-off value of 44/45 is suggested because it has the highest specificity (97.2%) at an acceptable sensitivity level.

A higher proportion of men have been observed in the RBD group in comparison with the non-RBD group in our study. This is consistent with a previous report on gender differences in prevalence and clinical manifestations (Wing et al. 2008). Gender differences in dream content and

dream enactment behaviors have also been previously described. Whereas men experience fear and anger in their dreams and have violent nocturnal behaviors, women experience mainly fear and do not act aggressively in their dreams. It is possible that patients with non-aggressive nocturnal behaviors receive less medical attention, which might lead to an underestimation of RBD frequency in women. Similar to other studies, we did not find any association with age (Wing et al. 2008; Nomura et al. 2011; Poryazova et al. 2013).

We performed a prospective study in an eligible population. All subjects were blind to their sleep disorder before completing the questionnaires, minimizing the recall bias caused by the awareness of the diagnosis. The availability of the RBD screening questionnaire in Mandarin is helpful for the early diagnosis of RBD and potentially also the early diagnosis of neurodegenerative diseases and the prevention of injuries to the patient or the patient's bed partner.

However, there are some limitations to the present study. First, all participants came to our sleep clinics with sleep complaints, and our results might not be generalizable to the general population. Second, patients with common sleep disorders (insomnia, etc.) may not be transferred to Xuanwu Hospital, possibly leading to selection bias. Third, the study included no patients with NREM-parasomnia, probably because most patients with NREM-parasomnia are referred to psychiatric hospitals, and the RBDQ-Beijing, similarly to the RBDQ-HK, was not sensitive enough to differentiate RBD from NREM-parasomnia. Moreover, because the sensitivity and specificity of these scales may vary by patient population, the RBDQ-Beijing and the RBDQ-HK should be validated prospectively in a variety of subjects, ages, and populations, including individuals with comorbid neurological disease. Further studies will be needed to validate the RBDQ-Beijing in the community population.

Our findings indicated that the RBDQ-Beijing may be capable of differentiating RBD from OSAS and could be used as a screening and preliminary diagnostic tool for RBD.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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