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Original Article

Validation study of REM Sleep Behavior Disorder Questionnaire – Hong Kong (RBDQ-HK) in East China

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ABSTRACT

Objective: To validate the REM Sleep Behavior Disorder (RBD) Questionnaire – Hong Kong (RBDQ-HK) in polysomnography (PSG)-confirmed RBD and non-RBD subjects, and to evaluate its usefulness in different clinical populations.
Methods: In total, 325 subjects (115 RBD and 210 controls) from East China were enrolled. After patients had finished the structured interview, and completed the RBDQ-HK and video-PSG test, we evaluated the reliability of RBDQ-HK (areas under the curves (AUC), the best cut-off values, factor 2 of RBDQ-HK, and overall scale) and validated the usefulness of RBDQ-HK between the Parkinson disease (PD) and obstructive sleep apnea (OSA) groups.
Results: The best cut-off values for factor 2 of RBDQ-HK were located at 7/8 with a sensitivity of 90% and specificity of 82% (AUC = 0.911), and for RBDQ-HK overall scale were located at 17 with a sensitivity of 85% and specificity of 81% (AUC = 0.892) in all subjects. Both factor 2 and overall scale of RBDQ-HK are valid in all subjects (PD and OSA patients), with a higher accuracy given by factor 2 of RBDQ-HK.
Conclusions: RBDQ-HK and its factor 2 are useful and validated RBD screening instruments, and could be used as a tool for screening RBD in patients with PD and OSA.

1. Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is characterized by intermittent loss of REM sleep electromyographic (EMG) atonia and appearance of elaborate motor activity associated with dream mentation [1]. RBD has been increasingly recognized as a specific predictor for neurodegenerative disorder. Many prospective and cross-sectional studies reveal that quite a number of idiopathic RBD (iRBD) patients will develop into neurodegenerative diseases such as Parkinson disease (PD) after several years or decades [2–4], and iRBD patients share similar changes with neurodegenerative diseases in pathological, clinical, and ancillary test findings [3,5–8]. RBD should be screened as early as possible and followed up.

According to the second edition of the International Classification of Sleep Disorders (ICSD-II), polysomnography (PSG) is essential to establish the criterion for the diagnosis of RBD; however, it is costly, labor intensive, and impractical to perform in large numbers of subjects. Some available subjective and objective clinical tools have been used for RBD assessment [9]. A few RBD screening questionnaires have been designed to facilitate population-based studies and future neuroprotective studies. These screening questionnaires contain: Mayo Sleep Questionnaire (MSQ) whose validation study yielded a sensitivity of 98% and specificity of 74% [10]; the REM sleep behavior disorder screening questionnaire (RBDSQ) of which the sensitivity and specificity are moderate (sensitivity: 84–96%; specificity: 56–96%) at the cut-off value of 5 points in general population and 6 points in PD patients [11–13]; the RBD Single-Question Screen (RBD1Q) whose validity had been examined in an international multicentre case–control study with good sensitivity (93.8%) and specificity (87.2%) [14]; and the Innsbruck RBD inventory (RBD-I) with a cut-off score of 0.25, showing excellent sensitivity and specificity (91.4% and 85.7%, respectively) [15].

The above-mentioned scales may not keep in mind the variation of severity of RBD nocturnal behaviors, and so may overlook the

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frequency and severity of RBD symptoms. For these reasons the REM Sleep Behavior Disorder (RBD) Questionnaire – Hong Kong (RBDQ-HK) was developed and certified originally by Li et al. [16], with moderate sensitivity (82.2%, 87.9% respectively) and specificity (86.9%, 81.3% respectively) using a cut-off value of 17/18 points on overall scale and 7/8 points on subscale (factor 2 of RBDQ-HK). In 2012, Sasai et al. found that the best cut-off point for the Japanese version of the RBDQ-JP total score was 19/20, with a sensitivity of 97.2% and specificity of 97.5%, but the control subjects did not undergo PSG [17]. Their work demonstrated that RBDQ (RBDQ-HK and RBDQ-JP) had satisfactory reliability and validity as a tool for screening and modifying severity of RBD.

However, there are still some limitations on the validity studies of RBDQ. First, there are only two validation studies until now, and they have not been fully validated. Second, some subjects were not PSG-confirmed, which might decrease the accuracy of diagnosis. Third, as a screening tool, it was expected that RBDQ would identify RBD patients in different clinical populations, such as those with comorbid neurodegenerative and psychiatric disorders, but this has not yet been achieved. Based on these reasons, we assessed the reliability and validity of RBDQ in all PSG-confirmed RBD subjects and non-RBD subjects in East China, and further validated the questionnaire in different clinical populations.

2. Methods

2.1. Subjects

Patients with neurological diseases, psychiatric diseases, sleep-related disorders, and undergoing health check-up were recruited from the Sleep Center of the Second Affiliated Hospital, Soochow University from August 2011 to March 2013. The local ethics committee of the hospital approved the study, and the patients signed informed consent forms for the investigation. Patients whose handwriting in the questionnaire was illegible and who failed to attain REM sleep on their video-PSG were excluded from the study.

2.2. REM Sleep Behavior Disorder Questionnaire – Hong Kong (RBDQ-HK)

The RBDQ-HK questionnaire is a 13-item patient self-administered questionnaire pertaining to various clinical features of RBD. Each item is assessed on two scales: lifetime occurrence (don't know, yes, or no) and recent one-year frequency (occurred in the last year, once or few times per year, once or few times per month, one or two times per week, and three times or more per week). It comprises factor 1 (Q1–Q5, and Q13, dream-related factor) and factor 2 (Q6–Q12, behavioral factor). Different factors have different weighted scores according to the clinical importance of manifestations of RBD. The total RBDQ-HK score was calculated by the sum of the scores of the two factors, ranging from 0 to 100 [16].

2.3. Polysomnographic recordings

All PSG recordings were collected and stored digitally using the Sandman Elite sleep diagnostic system (Embla Systems, Denver, CO, USA) or Compumedics E-Series PSG Recording System (Compumedics Limited, Australia), containing following montages: bilateral electro-oculogram (EOG) derivations, standard electroencephalographic (EEG) derivations (C3–A2, C4–A1, O1–A2, O2–A1), electrocardiogram, chin and two upper and lower limb surface EMG derivations (right and left anterior tibial, and right and left extensor digitorum communis), oronasal airflow by thermocouple and nasal pressure measurements, sonogram, oxyhemoglobin saturation, and chest and abdomen inductance plethysmography. All PSG data were recorded in synchrony with continuous video monitoring.

2.4. Procedure

Experienced neurologists performed the evaluations and completed neurological examinations of the inpatients and outpatients. After finishing the structured interview and having given informed consent, patients were arranged to undergo video-PSG test and asked not to take any drugs on the night they underwent PSG. The RBDQ-HK questionnaire was administrated to patients 30 min before PSG test. Because RBDQ-HK was composed by dream-related items which the patient self-knew better, and behavioral items which the patient's bed partner knew better, the patient and her/his bed partner were encouraged to complete the questionnaires together. Fifty random patients were asked to complete a second set of the questionnaire spaced four weeks apart from the first assessment to measure the test–retest reliability. All PSGs were reviewed by one sleep specialist who was blinded to the results of the interview and questionnaire in our sleep center. The Montplaisir group's slightly modified RBD PSG scoring method (RPSM) was used to define REM sleep without atonia (RSWA) [18,19]. Details are listed as follows: sleep stages 1–4 were scored according to the method of Rechtschaffen and Kales, using 20 s epochs. REM sleep was scored on the basis of EEG and EOG only. The occurrence of the first REM epoch was used to determine the onset of a REM sleep period. The termination of REM sleep periods was identified by the occurrence of an EEG feature indicative of another stage (*K* complex, sleep spindle, or EEG sign of arousal) or by the absence of rapid eye movements during three consecutive minutes. According to the published method, patients whose chin EMG tonic density was $\geqslant$30% or phasic chin EMG density was $\geqslant$15% were considered to meet the PSG criteria of RBD. All REM tone quantification carefully eliminates apnea-associated arousals. Moderate to severe obstructive sleep apnea (OSA) patients (AHI $\geqslant$ 15/h) who fulfilled the PSG criteria of RBD at their first PSG test were booked to have a second PSG test while using continuous positive airway pressure (CPAP) to eliminate 'pseudo-RBD' [20].

According to diagnostic criteria of RBD in ICSD-II, patients were divided into RBD group and control group. First, RBDQ-HK was validated in all subjects, and then in different clinical populations. RBD patients were subclassified into iRBD group that occurs in the absence of any other obvious associated neurological disorders, symptomatic RBD (sRBD) group that occurs with neurodegenerative diseases such as PD or narcolepsy, and RBD-like disorder group that occurs with psychotropic medications or psychiatric illness. The internal consistency (estimated by Cronbach's α coefficient) and test–retest reliability [estimated by intra-class correlation (ICC)] were employed to assess the reliability, and area under the receiver operating characteristics (ROC) curve (AUC), optimal cut-off values, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were employed to assess the validity. The features of behavioral aspects and dream aspect of RBD in three RBD subgroups were assessed by comparing questionnaire factor scores.

2.5. Statistical analyses

All analyses were performed using SPSS version 19.0 for Windows. Patients' demographic and clinical data were presented with descriptive statistics. Measurement data were reported as means ± SD (standard deviations). Non-parametric tests were used for two independent samples. Mann–Whitney *U*-test was employed to assess the differences among groups. $P < 0.05$ was considered statistically significant. Both Cronbach's α coefficient