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Original Article

# Characteristics of early- and late-onset rapid eye movement sleep behavior disorder in China: a case–control study

Junying Zhou [a,d], Jihui Zhang [b], Lina Du [a], Zhe Li [a], Yun Li [a], Fei Lei [a], Yun-Kwok Wing [b], Clete A. Kushida [c], Dong Zhou [d], Xiangdong Tang [a,*]

[a] Sleep Medicine Center, West China Hospital, Sichuan University, Chengdu, China
[b] Department of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong Special Administrative Region
[c] Sleep Medicine Center, Stanford University, CA, USA
[d] Department of Neurology, West China Hospital, Sichuan University, Chengdu, China

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ABSTRACT

*Objective:* To investigate demography and clinic and polysomnographic characteristics in Chinese rapid eye movement (REM) sleep behavior disorder (RBD) patients across onset ages.
*Methods:* Ninety consecutive patients fulfilling the criteria for RBD were recruited for study in our sleep center. Patients were separated into early- and late-onset groups according to age when symptoms began (⩽50 and >50 years, respectively). Ninety age- and gender-matched healthy subjects served as controls. All subjects were interviewed for their clinical history, completed an RBD questionnaire, and underwent an overnight video polysomnography assessment. Demographics, comorbidities, scores on the RBD questionnaire, sleep architecture, and EMG activity were compared between the patients and controls and between the early- and late-onset groups.
*Results:* Of all RBD patients, 63 were male, and mean age of RBD onset was 54.3 ± 15.7 years. In 25 patients (28%), RBD was secondary and associated with neurodegenerative disease, narcolepsy or antidepressant use. Twenty-three patients (26%) had early-onset RBD and 67 (74%) were in the late-onset group. RBD patients had significantly more comorbidities, dreams and dream-enacting behaviors, and poorer sleep quality than did controls. The early-onset group had a high proportion of females (48%) and an increased proportion of cases associated with narcolepsy. The early-onset group also had fewer movements, lower EMG activity during REM sleep, and better sleep quality when compared to the late-onset group. EMG activity was positively correlated with age of onset. The mean follow-up time was 1.57 ± 0.82 years, and four patients in the late-onset group were subsequently diagnosed with neurodegenerative diseases.
*Conclusions:* Stratifying patients into early and late-onset RBD revealed different characteristics from those previously described as typical for RBD. EMG activity during REM sleep was positively correlated with age of onset. We suggest that it will be valuable to explore the relationship between age of onset conversion and neurodegenerative diseases.



## 1. Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by a loss of normal muscle atonia during REM sleep. It is associated with dream-enacting behaviors such as talking, yelling, punching, kicking or jumping out of bed that disrupt sleep and may result in severe injuries for the patient or the bed partner [1,2]. RBD was first described as a medical disorder in humans in 1986 [3], and it was observed predominantly in elderly men [4]. A new study reported that the prevalence of idiopathic RBD was about 1.15% in the Korean elderly population [5]. RBD is categorized as idiopathic or secondary according to associations with other functional or structural disorders of the nervous system. A strong relationship between RBD and neurodegenerative diseases including Parkinson disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA) has been described. It also has been linked with narcolepsy, cerebrovascular disease and medication (particularly antidepressants).

* Corresponding author. Address: Sleep Medicine Center, West China Hospital, Sichuan University, 28 Dian Xin Nan Jie, Chengdu, Sichuan 610040, China. Tel.: +86 28 8542 2733; fax: +86 28 8542 2632.
*E-mail address:* xiangdong.tang@gmail.com (X. Tang).

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Current evidence indicates that a high proportion of patients (48–75%) has secondary RBD [2,6,7]. Furthermore, idiopathic RBD cases frequently develop a neurodegenerative disease within 5–20 years [8]. Recently, the term 'idiopathic' RBD has been questioned, with the suggestion that it should be replaced by 'cryptogenic' RBD [9].

Since RBD patients have the potential injuries to themselves or their bed partners and have the possibility of developing neurodegenerative disease, it is an important clinical disease. Several case series have described the demographic and clinical features of RBD. However, there are few studies of RBD in Chinese patients [10–12] and it has not received adequate attention in the Chinese community. Moreover, recent studies report different demographic and clinical features of RBD according to onset age [8,13,14]. Studies distinguishing age of onset have reported a higher proportion of females, higher rates of psychopathology, a potential role for autoimmune dysfunction, and a lower rate of neurodegenerative disease in early-onset patients [8,13,14]. These studies suggest that early-onset RBD may have a significantly different clinical profile than late-onset RBD, which is linked more closely to elderly men and a high probability for neurodegenerative diseases [8,13]. Therefore our aim in this study was to compare the clinical characteristics of Chinese RBD patients with healthy controls to determine potential differences between 'early-onset' and 'late-onset' RBD.

## 2. Methods

### 2.1. Subjects

The present study was conducted with a prospective design. Ninety consecutive patients fulfilling the criteria for RBD were recruited between November 2009 and July 2012 at the Sleep Medicine Center of West China Hospital. RBD was diagnosed according to the International classification of sleep disorders (2nd edition) (ICSD-2) criteria [1]. Control subjects were recruited through newspaper advertisement. They were 90 age- and gender-matched healthy volunteers without history of abnormal behaviors during sleep, without any neurological disorder (e.g. stroke, brain trauma, neurodegenerative disease and narcolepsy), and who were not receiving any central nervous system active medication. The study was approved by the hospital ethics committee and all subjects gave written informed consent before their participation.

All subjects were required to complete an RBD questionnaire (RBDQ-HK) and underwent overnight video-polysomnography (PSG) assessment. Patients were interviewed to obtain age and gender, and clinical details including duration of disease, comorbidity, and the use of medications or substances. Associated neurological disorders were diagnosed by consulting neurologists. RBD was classified as secondary in cases of comorbid neurological disorder (e.g. narcolepsy, neurodegenerative disease), or when it was associated with medication use (e.g. antidepressant). All other cases were categorized as idiopathic. Patients were defined as early- or late-onset according to the onset age. Patients aged $\leqslant$50 years were classified as early-onset RBD and those aged >50 years were classified as late-onset RBD.

### 2.2. RBDQ-HK questionnaire

All participants and their bed partners were asked to complete a 13-question RBD questionnaire (RBDQ-HK) with items related to the subjects' dream content and dream-enacting behaviors [15]. This questionnaire has established validity and reliability for assessing the clinical symptoms and severity of RBD [15]. Each questionnaire item was scored according to the frequency of occurrence of relevant dream- and behavior-related factors during sleep. Factor 1 (dream-related) characterized the dreams and nightmares that led to nocturnal behaviors and disrupted sleep; factor 2 (behavioral) assessed the sleep-related behavior including vocalization, abnormal motor activities, and injuries to self and/or bed partners. Questionnaire scoring followed previous work and used a cut-off for total score (range, 0–100) at 18/19 and a cut-off for factor 2 (range, 0–70) at 7/8 [15].

### 2.3. Polysomnography

All subjects underwent one full-night of PSG assessment synchronized with video recording. Overnight PSG consisted of continuous recordings from electroencephalography (EEG) (F4–M1, C4–M1, O2–M1, F3–M2, C3–M2, O1–M2), electro-oculography (EOG) (ROC–M1, LOC–M2), submental electromyography (EMG), right and left anterior tibialis surface EMG, electrocardiography (ECG), nasal and oral airflow, thoracic and abdominal respiratory movements, oxygen saturation, and body position. Audiovisual recordings were simultaneously performed. Sleep stages and REM sleep without atonia were scored according to the criteria described in the American Academy of Sleep Medicine (AASM) manual [16].

The following sleep variables were obtained and analyzed: sleep latency (SL), REM sleep latency, sleep efficiency (SE), total sleep time (TST), percentage spent in stage N1, N2, N3 and REM sleep, number of REM sleep periods, wake after sleep onset (WASO), apnea–hypopnea index (AHI), and periodic leg movement index (PLMI).

### 2.4. Analysis of EMG activity

Quantification of tonic and phasic EMG activity during REM sleep was performed manually in each participant. Increases in EMG tone due to arousals from respiratory events and artifacts (e.g. snoring) were excluded from analysis. Tonic and phasic EMG activity were scored manually according to the criteria of the 2007 AASM manual [16]. Tonic EMG activity was scored from the EMG recording in 30 s epochs. An epoch was scored as 'tonic' when the sustained EMG activity was present in more than 50% of the duration of the epoch with amplitude greater than the minimum amplitude in non-REM. Phasic EMG activity was scored from a 30 s epoch of REM sleep recording which was divided into 3 s mini-epochs requiring that at least five (50%) of the mini-epochs contain bursts of EMG activity lasting between 0.1 and 5.0 s with amplitude four times the background EMG activity. We calculated separately the percentage of 30 s epochs with tonic and phasic EMG activity. Total EMG activity was calculated as the percentage of phasic EMG activity plus the percentage of tonic EMG activity [17].

### 2.5. Follow-up visit

All of the patients included in this study were assessed in a follow-up visit through October 8, 2012. The main purpose of the follow-up was to determine potential conversion from idiopathic RBD to neurodegenerative disease.

### 2.6. Statistical analysis

SPSS 17.0 was used for all statistical analyses. Data are presented as mean ± standard deviations or frequencies (percentages). The qualitative data were analyzed using chi-square or Fisher's exact test as appropriate. Comparison between two groups on continuous variables was conducted using Student's *t*-test. If the data had an abnormal distribution, non-parametric tests (Mann–Whitney test) were performed. Associations between variables were