# Rapid Eye Movement Behavior Disorder and Other Parasomnias

Maksim Korotun, DO*, Luis Quintero, DO, MPH, Stella S. Hahn, MD

**KEYWORDS**

- Parasomnias • Elderly • Alpha-synuclein • Neurodegeneration
- Rapid eye movement sleep behavior disorder • Dream enactment behavior
- Rapid eye movement without atonia

**KEY POINTS**

- Rapid eye movement (REM) behavior disorder (RBD) is a REM parasomnia that occurs primarily in the elderly.
- RBD can be the initial symptom of a neurodegenerative disorder that may only be evident decades later.
- The pathophysiology of the disorder is loss of skeletal muscle atonia in REM sleep and subsequent dream enactment.
- Definitive diagnosis is achieved with a history of dream enactment and an in-laboratory polysomnography showing REM sleep without atonia.
- Treatment of the disorder includes providing a safe sleeping environment and pharmacotherapy (eg, melatonin or clonazepam).

## INTRODUCTION

Parasomnias are undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousal from sleep and can occur during non-rapid eye movement sleep (NREM), rapid eye movement sleep (REM), or during transition to and from sleep.[1]

NREM parasomnias typically occur during N3 sleep, also known as slow wave sleep (SWS). SWS occurs with greater frequency during the first third of the night. Therefore, NREM parasomnias tend to occur earlier in the night. As SWS is the deepest stage of sleep with the greatest arousal threshold, NREM parasomnias are not usually recalled by the patient, who may be difficult to awaken. SWS is maximal in children in whom it can be up to 40% of the night, but a reduction in the amount of this deeper stage of

Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, Donald and Barbara Zucker School of Medicine-Northwell, 410 Lakeville Road, Suite 107, New Hyde Park, NY 11042, USA
* Corresponding author.
*E-mail address:* mkorotun@northwell.edu

Clin Geriatr Med 37 (2021) 483–490
https://doi.org/10.1016/j.cger.2021.04.008
geriatric.theclinics.com

sleep is seen during adolescence, with a marked decrease seen starting middle age.[2,3] There are reports of complete absence of SWS after 90 years of age.[4] Consequently, NREM parasomnias occur less frequently in older adults.

NREM sleep and REM sleep alternate cyclically throughout the night. The first REM sleep period is short, typically under 10 minutes, but periods become longer as the night progresses, and are longest in the last third of the night. Accordingly, REM parasomnias tend to occur later in the night,[3] in contrast to NREM parasomnias, which are more likely to occur early in the sleep period. Normal REM sleep is characterized by suppression of muscle tone, known as atonia, which is evident on the electromyogram during polysomnography. Most vivid dreaming occurs during REM sleep. The percentage of REM sleep, unlike SWS, is preserved into adulthood.

## RAPID EYE MOVEMENT SLEEP BEHAVIOR DISORDER

REM sleep behavior disorder (RBD) is a REM-related parasomnia seen typically in the older population and is characterized by abnormal behaviors emerging during REM sleep because of loss of muscle atonia that is seen during normal REM sleep. This loss of muscle atonia allows for enactment of dreams, which are usually violent and action-filled, and can lead to sleep-related injury of patients or bed partners.[1,5]

### *Clinical Symptoms*

RBD consists of episodes related to dream enactment behavior during REM sleep. These dream enactments may range from vocalization to possible complex motor behaviors.[6,7] RBD occurs in greater frequency in the last half of the night given the increased duration of REM sleep during this time.[3] Enactments may be short in duration but can progress to several minutes. Unlike non-REM parasomnias, patients with RBD are usually able to describe the dream content and recall their enactment behaviors. The dreams are often categorized as fight or flight in origin which may prompt aggressive and repetitive movements (ie, thrashing, punching, kicking, and yelling). Patients may inadvertently harm their bed partners or themselves during this behavior, and may fall out of bed. Individuals diagnosed with REM behavior disorder associated with a degenerative neurologic disorder will exhibit an increase in dream-enactment as the neurologic condition progresses.[6,7]

### *Epidemiology*

The prevalence of RBD varies in the literature. Most population-based studies of REM behavior disorder in the general population show a prevalence of 0.5% to 1.0%.[8] However, in a recent community-based Korean study looking at subjects over the age of 60 years, the prevalence was 2.0%.[9] These numbers may not be reflective of the overall disease burden in the population, as many of the cases are undiagnosed.

Demographic analysis shows a 2-fold increase in frequency in men compared with women over the age of 50. The mean age of diagnosis was 53.7 years old. In addition, men were more likely to exhibit aggressive and violent behavior that would awaken them from sleep [10]

### *Diagnosis*

To achieve a definitive diagnosis of RBD, the patient should clinically present with symptoms of dream enactment with overnight in-laboratory polysomnography showing evidence of REM sleep without atonia (RSWA). These findings need to be present in the absence of epileptiform activity and with no alternative explanation for the parasomnia (**Box 1**).

**Box 1**
**Diagnostic criteria for rapid eye movement sleep behavior disorder**

All of the following must be met:
- Repeated episodes of sleep-related vocalization and/or complex behaviors
- These behaviors are documented by polysomnography to occur during REM sleep, or, based on clinical history of dream enactment, are presumed to occur during REM sleep
- Polysomnographic recording demonstrates REM sleep without atonia[a]
- The disturbance is not better explained by another sleep disorder, mental health disorder, medication, or substance use

[a]On occasion, there may be patients with a typical clinical history of RBD with dream-enacting behaviors, who also exhibit typical RBD behaviors observed on video polysomnography (vPSG), but do not demonstrate sufficient RSWA to satisfy PSG criteria for diagnosing RBD. RBD may be provisionally diagnosed on these patients, based on clinical judgment. The same rule applies when vPSG is not readily available.

*Data from* Medicine AAoS. International Classification of Sleep Disorders. 3rd edition, 2014.

The gold standard for diagnosis of RBD is to perform an in-laboratory PSG. In addition to the standard monitoring of the chin and anterior tibialis muscle activity, monitoring of the flexor digitorum brevis and biceps brachii can improve the diagnostic accuracy of RSWA in patients who may predominantly exhibit upper extremity behavior during REM sleep. Video recording may obviously correlate motor activity with REM. To diagnose RSWA during REM sleep, more than half of the epoch should exhibit an increase in muscle tone.[11]

In cases where an in-laboratory polysomnography evaluation is not feasible, a concept that is becoming more accepted in clinical practice is probable RBD, which can be diagnosed by using a validated screening tool. The Mayo Sleep Questionnaire includes questions about dream enactment behavior (DEB) for both patient and bed partner and is highly specific for RBD.[12] It is available free to the public and can be downloaded from the Web site: http://www.mayoclinic.org/pdfs/MSQ-copyrightfinal.pdf.[13] In addition, the RBD questionnaire (RBDQ-HK) is a 13-item self-reported screening tool with a moderate sensitivity (82.2%) and specificity (86.9%) for RBD.[14] These questionnaires, although not the gold standard, can be useful in identifying and monitoring patients with reported sleep disturbances and suspicion for RBD. The violent nature of DEB can cause significant injury to patient and bed partner; if a classic history is obtained, empiric treatment may be indicated prior to definitive diagnosis by polysomnography, particularly if this is likely to be delayed.

### *Normal Rapid Eye Movement Sleep and Pathophysiology*

RBD is characterized by loss of skeletal muscle atonia during REM sleep with subsequent dream enactment. During normal REM sleep, there are 2 motor systems involved in stabilizing REM sleep; one is generating REM with atonia or REM-on region and the other being the locomotor generator region responsible for locomotor activity suppression. The REM-on region is comprised of the precoeruleus and sublateraldorsal nuclei (SLD) that work through direct and indirect mechanisms. The direct mechanism has neurons projecting to the spinal interneuron (inhibitory) that acts on the spinal motor neuron to inhibit skeletal muscle activity. The indirect pathway has projections to the magnocellular reticular formation (MCRF), which acts directly on the skeletal muscle to induce inhibition. The locomotor pathway is poorly understood but is thought to project to the spinal motor neuron in an inhibitory fashion.[15]

The proposed pathophysiology of RBD disorder is thought to be neurodegeneration or the deposition of alpha-synuclein at the SLD nucleus, which compromises the direct and indirect pathway pathways of the REM-on region responsible for skeletal muscle inhibition.

### *Clinical Vignette*

62-year-old woman with a past medical history (PMH) of Parkinson disease being treated with carbidopa-levodopa presented for evaluation of excessive daytime somnolence and dream enactment behavior. She noted snoring and had an ESS (Epworth sleepiness scale) score of 15 out of 24 on the initial visit. About 1 year ago, she was noted to be acting out her dreams with her arms flailing and talking in her sleep. On several occasions, she punched and kicked her bed partner while dreaming she was being attacked. She woke up remembering her dream and felt mortified about hurting her husband. These features would occur several times a month and were disturbing to both the patient and her bed partner. Dreams enacted were action-related dreams and she did not fall out of bed or hurt herself during these episodes.

Given the clinical presentation, the patient was referred to the sleep laboratory for an in-laboratory PSG to screen for obstructive sleep apnea (OSA) and evaluate for REM behavior disorder. No clinically significant OSA was evident on the PSG. However, there was evidence of REM sleep without atonia (**Fig. 1**). **Fig. 1**B shows a normal epoch of REM sleep with expected atonia seen.

She was counseled on ensuring a safe bedroom environment and started on melatonin at 6 mg nightly, with good response.

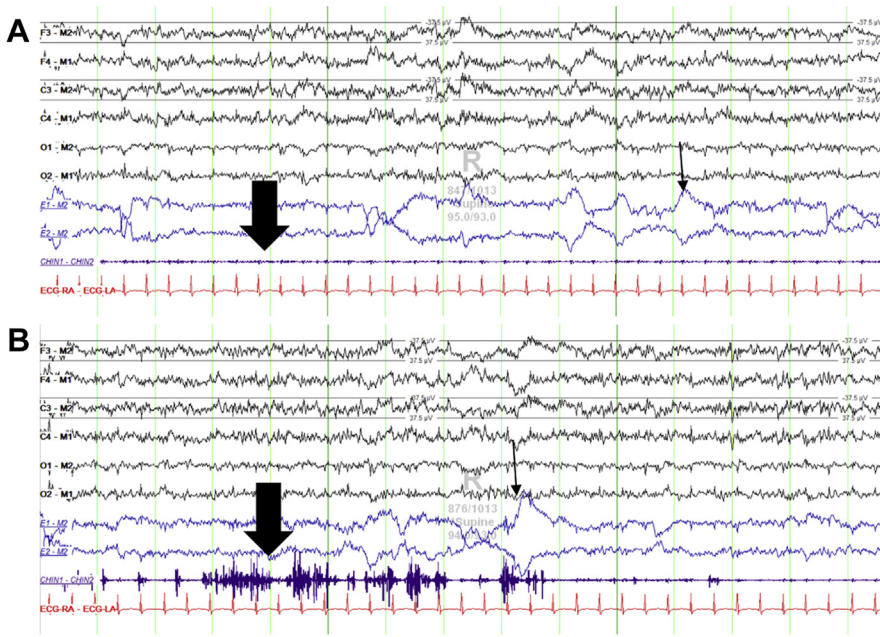


**Fig. 1.** Standard electroencephalogram (EEG) recording on an in-laboratory polysomnography. (*A*) REM sleep with atonia; black thin arrow: conjugate eye movement; thick back arrow: lack of muscle tone on the chin EMG. (*B*) REM sleep without atonia; black thin arrow: conjugate eye movement; thick back arrow: evidence of muscle tone on the chin EMG.

### *Treatment*

Treatment for RBD is approached in 3 ways: ensuring safety in the bedroom, assessing for reversible causes, and pharmacologic treatment to suppress dream enactment. A survey of patients who had RBD found that 55% of those surveyed reported injury to self or to their bed partners. Providers should suggest making the bedroom a safe environment, which includes but is not limited to: bedrails, lowering the bed, removing night stands, or even having a bed partner sleep in another bed.[6]

Several medication classes are known to elicit iatrogenic RBD and should be reviewed. The classes of medications that are known to cause REM without atonia are selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOIs). Discontinuation of these medications may lead to the resolution of iatrogenic RBD.

Severe OSA has been shown to destabilize sleep, which can cause dysregulation of the muscle suppression pathways during REM. This can mimic dream enactment and present like RBD (pseudo-RBD). The use of continuous positive airway pressure (CPAP) in patients with OSA can eliminate dream enactment by stabilizing REM sleep.[16] All patients being evaluated for RBD should be treated for OSA, if present, prior to making the diagnosis.

Pharmacologic treatment for RBD is limited. The goal of treatment should be to reduce or eliminate the number of dream enactments that occur.[6] Clonazepam was the first medication used that had significant efficacy in the treatment of RBD with a reduction in RBD symptoms in 87% of patients.[17] The use of clonazepam may act by reducing the number of violent dreams, which can lead to a reduction in dream enactment in bed. A dosage range between 0.25 mg and 4 mg has been shown by to be efficacious. Because of the potential adverse effects of clonazepam in the elderly, the lowest efficacious dose should be chosen.[18]

Melatonin is the only medication that has been shown to restore muscle atonia during REM sleep. Melatonin has been shown to be effective in reducing the RBD frequency also. Doses between 3 mg and 15 mg (with an average dose of 6 mg) have been used with good efficacy and tolerability.[3,8,19] Because of the safety profile, melatonin may be used as the first agent in elderly patients.

Other classes of medications have been studied in RBD, but none have shown as much efficacy as clonazepam and melatonin. These include melatonergic agents, cannabidiol, and dopamine agents.[7,20] Acetylcholinesterase inhibitors such as donepezil and rivastigmine show promise, but more research is needed to validate these small studies.[21] Finally, there is some evidence to suggest that other benzodiazepines, such as temazepam, triazolam, and alprazolam, can be as effective as clonazepam.[20] Medications used to treat alpha-synucleinopathies (ie, Parkinson disease, multisystem atrophy disorder) do not diminish the frequency of RBD, as they focus on different pathways and mechanisms in the brain that do not interact with the areas affected with RBD.

As neurodegeneration progresses, the frequency and intensity of RBD can worsen. Therefore, treatment of RBD should focus on frequency of events and safety of the patient and bed partner. The goal of treatment is not to necessarily eliminate all abnormal movements during REM. There may continue to be evidence of REM without atonia (ie, mumbling, talking while asleep, and slight movements of extremities). The focus of treatment is to diminish the number of events that the patient has while also decreasing the severity of those behaviors. This will help ensure a safer environment for the patient and bed partner.[22]

### *Prognosis*

Delayed emergence of a neurodegenerative disorder is common in men 50 years of age and older. It is now well established that RBD has been linked to the alpha synucleinopathies.[23] Up to 90.9% of patients with idiopathic RBD may ultimately develop a neurodegenerative disorder over a longitudinal follow-up.[24] It has been reported that RBD can precede the neurodegenerative process by up to 25 years. The risk for developing neurologic disease over the first 2 to 5 years is approximately 15% to 35%. This risk increases to 41% to 90.5% on follow-up between 12 and 25 years.[24] In patients with known established neurodegenerative disease, the prevalence of RBD was: 58% to 65% in Parkinson disease, 50% in Lewy-body dementia, and 68% to 90% in multisystem atrophy.[15,22,25] Patients with these conditions should be specifically asked about DEB and treated, given the risk of violent behavior.

## OTHER PARASOMNIAS

The International Classification of Sleep Disorders categorizes parasomnias into 3 major categories: NREM-related parasomnias, REM-related parasomnias, and other parasomnias. However, some parasomnias overlap and may have a mixture of states.[1]

NREM-related parasomnias include disorders of arousal (eg, confusional arousals, sleepwalking, and sleep terrors), and sleep-related eating disorder (SRED). Disorders of arousal occur during partial arousals from slow wave (N3) sleep and are more commonly seen in children but can be present (up to 4%–5%) in older adults.[26,27] Treatment is often unnecessary, and reassurance to patients and families should be provided along with ensuring safety. Focus on prevention by eliminating exacerbating factors such as sleep deprivation, sedative use, or sleep disorders that may cause sleep instability may be helpful.[28] SRED consists of episodes of amnestic nocturnal sleepwalking associated with compulsive eating behavior, often of unusual food items (eg, soap, raw meat, dog food) and can have metabolic consequences including weight gain and poor glucose control. SRED is a parasomnia and should be distinguished from nocturnal eating syndrome, in which the patient is fully awake. SRED is generally most common in those with eating disorders, but a few case reports of SRED in patients with Parkinson disease have been reported.[29–31] Treatment includes management of underlying sleep disorders and ensuring safety of individuals. Medications that are associated with this condition, such as zolpidem and olanzapine, should be discontinued when possible. Dopamine agonists, SSRIs, and topiramate have been reported as pharmacologic treatment options.[32]

REM-related parasomnias include RBD, recurrent isolated sleep paralysis, and nightmare disorder. Sleep paralysis is elicited during awakening from REM sleep and is an example of state dissociation. It is common in narcolepsy but occurs often in isolation in the general population, usually in adolescence. Treatment typically involves reducing stressors and reassurance.[3] Nightmare disorder usually occurs in younger children but can be present in adults, particularly in the setting of trauma and post-traumatic stress disorder (PTSD). The best treatment for nightmare disorder is image rehearsal therapy, but lucid dreaming therapy and self-exposure therapy have also been reported. For PTSD-related nightmares, prazosin is an effective pharmacologic treatment option.[33]

## CLINICS CARE POINTS

- REM behavior disorder is a REM parasomnia that should be screened for with an overnight in-laboratory polysomnography in patients having dream enactment.

- Idiopathic REM behavior disorder is a diagnosis associated with the alpha synucleopathies which may have a prodromal period of ten or more years.
- Treatment of REM behavior disorder consists of creating a safe sleeping environment as well as the addition of medications (eg, clonazepam and melatonin) to reduce the frequency of events.
- A thorough review of the patient's history is necessary to evaluate for secondary causes of REM behavior disorder (eg, medications and sleep disordered breathing).
- NREM parasomnias occur less commonly in older adults and are not associated with development of a neurodegenerative disorder.

## DISCLOSURE

The authors have nothing to disclose.

## REFERENCES


1. Medicine AAoS. International classification of sleep disorders. American Academy of Sleep Medicine. 3rd edition 2014.
2. Cooke JR, Ancoli-Israel S. Normal and abnormal sleep in the elderly. Handb Clin Neurol 2011;98:653–65.
3. Kryger MH, Roth T, Dement WC. Principles and practice of sleep medicine. 6th edition. Philadelphia, PA: Elsevier; 2017.
4. Bliwise DL. Sleep in normal aging and dementia. Sleep 1993;16(1):40–81.
5. Feinsilver SH, Hernandez AB. Sleep in the elderly: unanswered questions. Clin Geriatr Med 2017;33(4):579–96.
6. Boeve BF. REM sleep behavior disorder: updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. Ann N Y Acad Sci 2010;1184:15–54.
7. Iranzo A. Parasomnias and sleep-related movement disorders in older adults. Sleep Med Clin 2018;13(1):51–61.
8. Rodriguez CL, Jaimchariyatam N, Budur K. Rapid eye movement sleep behavior disorder: a review of the literature and update on current concepts. Chest 2017;152(3):650–62.
9. Kang SH, Yoon IY, Lee SD, et al. REM sleep behavior disorder in the Korean elderly population: prevalence and clinical characteristics. Sleep 2013;36(8):1147–52.
10. Ju YE, Larson-Prior L, Duntley S. Changing demographics in REM sleep behavior disorder: possible effect of autoimmunity and antidepressants. Sleep Med 2011;12(3):278–83.
11. Berry RB, Brooks R, Gamaldo C, et al. AASM scoring manual updates for 2017 (Version 2.4). J Clin Sleep Med 2017;13(5):665–6.
12. Boeve BF, Molano JR, Ferman TJ, et al. Validation of the Mayo Sleep Questionnaire to screen for REM sleep behavior disorder in a community-based sample. J Clin Sleep Med 2013;9(5):475–80.
13. Available at: http://www.mayoclinic.org/pdfs/MSQ-copyrightfinal.pdf.
14. Li SX, Wing YK, Lam SP, et al. Validation of a new REM sleep behavior disorder questionnaire (RBDQ-HK). Sleep Med 2010;11(1):43–8.
15. Gagnon JF, Bedard MA, Fantini ML, et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. Neurology 2002;59(4):585–9.

16. Iranzo A, Santamaria J. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. Sleep 2005;28(2):203–6.
17. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. Brain 2000;123(Pt 2): 331–9.
18. McCarter SJ, Boswell CL, St Louis EK, et al. Treatment outcomes in REM sleep behavior disorder. Sleep Med 2013;14(3):237–42.
19. Kunz D, Bes F. Melatonin as a therapy in REM sleep behavior disorder patients: an open-labeled pilot study on the possible influence of melatonin on REM-sleep regulation. Mov Disord 1999;14(3):507–11.
20. Zhang F, Niu L, Liu X, et al. Rapid eye movement sleep behavior disorder and neurodegenerative diseases: an update. Aging Dis 2020;11(2):315–26.
21. Ringman JM, Simmons JH. Treatment of REM sleep behavior disorder with donepezil: a report of three cases. Neurology 2000;55(6):870–1.
22. Boeve BF, Silber MH, Ferman TJ. REM sleep behavior disorder in Parkinson's disease and dementia with Lewy bodies. J Geriatr Psychiatry Neurol 2004;17(3): 146–57.
23. McCarter SJ, St Louis EK, Boeve BF. REM sleep behavior disorder and REM sleep without atonia as an early manifestation of degenerative neurological disease. Curr Neurol Neurosci Rep 2012;12(2):182–92.
24. St Louis EK, Boeve BF. REM sleep behavior disorder: diagnosis, clinical Implications, and future directions. Mayo Clin Proc 2017;92(11):1723–36.
25. Plazzi G, Corsini R, Provini F, et al. REM sleep behavior disorders in multiple system atrophy. Neurology 1997;48(4):1094–7.
26. Crisp AH. The sleepwalking/night terrors syndrome in adults. Postgrad Med J 1996;72(852):599–604.
27. Mahowald MW, Bornemann MC, Schenck CH. Parasomnias. Semin Neurol 2004; 24(3):283–92.
28. Fleetham JA, Fleming JA. Parasomnias. CMAJ 2014;186(8):E273–80.
29. Auger RR. Sleep-related eating disorders. Psychiatry (Edgmont) 2006;3(11): 64–70.
30. Kaur H, Jahngir MU, Siddiqui JH. Sleep-related eating disorder in a patient with Parkinson's disease. Cureus 2018;10(9):e3345.
31. Sobreira Neto MA, Pereira MA, Sobreira ES, et al. Sleep-related eating disorder in two patients with early-onset Parkinson's disease. Eur Neurol 2011;66(2):106–9.
32. Schenck CH, Hurwitz TD, Bundlie SR, et al. Sleep-related eating disorders: polysomnographic correlates of a heterogeneous syndrome distinct from daytime eating disorders. Sleep 1991;14(5):419–31.
33. Morgenthaler TI, Auerbach S, Casey KR, et al. Position paper for the treatment of nightmare disorder in adults: an American Academy of Sleep Medicine position paper. J Clin Sleep Med 2018;14(6):1041–55.