

REM SLEEP BEHAVIOR DISORDER: DIAGNOSIS AND TREATMENT

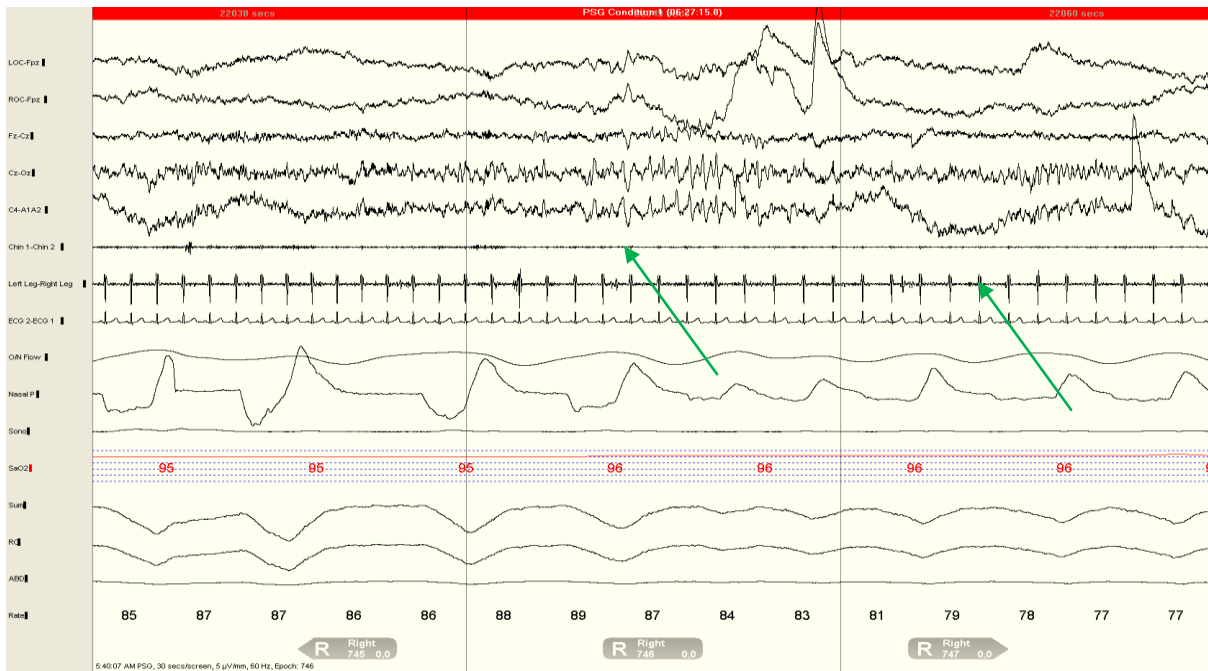
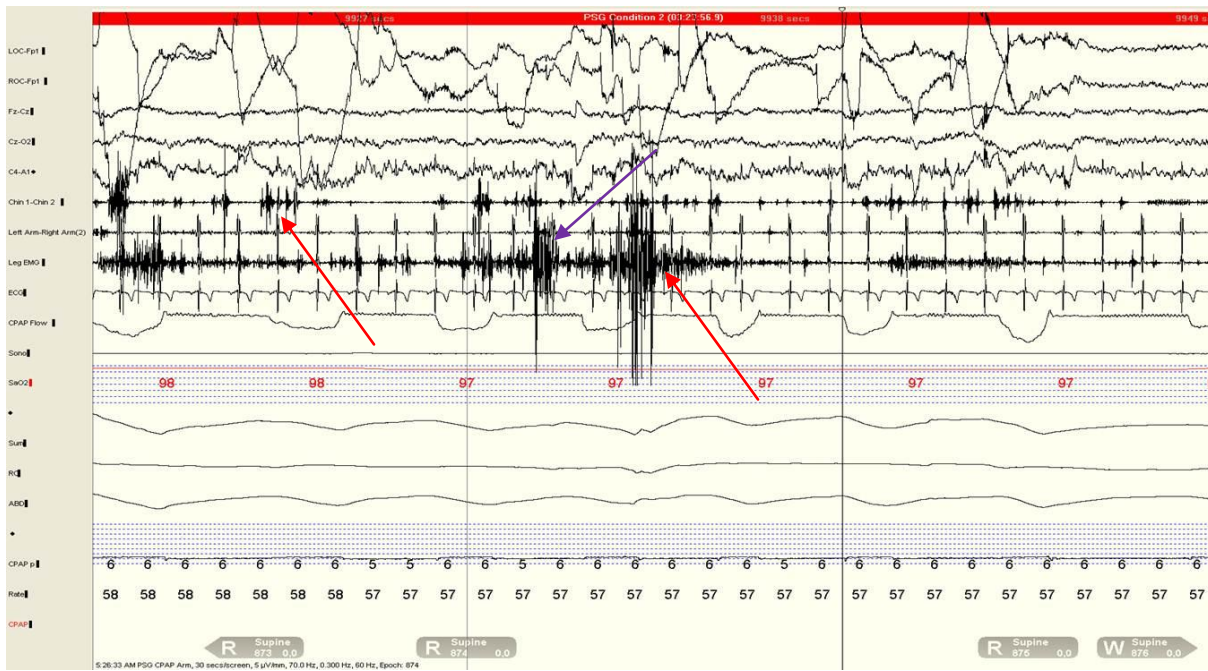
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REM sleep behavior disorder (RBD) is a common parasomnia affecting between 0.5% – 9.0% of the general population that may lead to serious injury to patients or their bedpartners.¹⁻³ RBD is characterized by dream enactment behavior and REM sleep without atonia (RSWA), an abnormal elevation of muscle tone during REM sleep (**Figure**).^{1,4} Dream mentation in RBD patients characteristically involves defending oneself against attackers or being chased, with witnessed dream enactment manifested often by violent thrashing movements and screaming or shouting vocalizations during REM sleep.¹ Polysomnography is necessary for determination of RSWA in making a RBD diagnosis, and video during polysomnography also aids in the diagnosis through viewing of corresponding excessive phasic limb jerking during REM and may infrequently actually capture diagnostic episodes of complex motor behavior indicative of dream enactment. Comorbid obstructive sleep apnea (OSA) affects approximately two-thirds of RBD patients.¹⁴ can sometimes mimic its symptoms, and treatment of comorbid OSA in RBD patients may aid its control by reducing the frequency and severity of dream enactment episodes.

RBD is a core feature of synucleinopathy neurodegeneration and idiopathic RBD (without other associated neurological symptoms or signs at presentation) and may herald the future development of overt memory, motor, or autonomic disorders including mild cognitive impairment, dementia with Lewy bodies, and Parkinson's disease.^{1-2,4-8} Importantly, older adult patients newly diagnosed with idiopathic RBD have an approximate 50% – 91.9% risk of developing impaired memory or autonomic function or parkinsonism during longitudinal followup, and even those with isolated polysomnographic RSWA (without clinical dream enactment) also appear to harbor neurodegenerative biomarkers and risk for conversion to idiopathic RBD, so all patients with RBD and RSWA require serial neurological follow-up and examinations annually, or more frequently. RBD and RSWA are attractive biomarkers for synucleinopathy, signifying a potential therapeutic time window for delivery of future neuroprotective therapies that could arrest or delay the development of more devastating cognitive and motor impairments.^{1-4, 6-10,17}

However, RBD in young adults may instead be associated with mood disorder history, antidepressant medications (especially selective serotonin reuptake inhibitors (SSRIs)), narcolepsy, and lesions within or neighboring the dorsal pons.^{1,11-13,18-19} RBD was also recently reported to occur in children and adolescents as well, and RSWA may also occur in children and adolescents. When RBD or RSWA are seen in children or adolescents, a high index of suspicion should also be maintained for narcolepsy and primary CNS hypersomnia, which may cause RSWA and RBD.^{1,11-13} Removal of antidepressants or substituting an alternative mood stabilizing medication may improve or even stop dream enactment in younger adults with RBD. Longitudinal prospective cohort studies are necessary to determine whether RBD in children, adolescents, and young adults signifies covert synucleinopathy, since RBD has been noted to precede the development of overt cognitive or motor manifestations by as long as 50 years.¹³

Figure. REM sleep without atonia in a 30-second polysomnogram epoch in a 68-year-old man with RBD. Note the increased phasic muscle activity seen especially in the submental (chin) and anterior tibialis (leg) EMG channels (red arrows). The bursts of excessive activity are described as *phasic* muscle activity, while sustained lower grade elevation of muscle tone lasting for longer than half of the epoch is called *tonic* activity (seen in leg channel, purple arrow). In this example, abnormal transient/phasic muscle activity excess is predominant, and there is also underlying abnormal tonic activity confined to the leg EMG channel. An epoch of normal REM sleep muscle atonia is seen below for comparison, with normal tone in chin and leg EMG channels highlighted (green arrows).



Falls or other injurious behavior to the patient or their bed partner may complicate RBD. Injuries may occur in up to 55% of RBD patients (most mild, such as bruises), but up to 11% experience serious injuries including subdural hematoma requiring surgical intervention.^{1,14}

Treatment options include melatonin, initially at doses of 3 mg and gradually titrating toward 12 mg nightly or higher if needed, with the goal of suppressing frequent and potentially injurious dream enactment behaviors, or clonazepam 0.25 – 1.0 mg dosed to 2.0 – 3.0 mg nightly.^{1,15-16,20-22} The average effective reported doses are melatonin 6 mg and clonazepam 0.5-1.0 mg.^{15,20-23} Recent evidence also suggests that rotigotine may be helpful for the treatment of RBD in patients with Parkinson's Disease.²⁴ Great care should be taken to first exclude comorbid OSA in RBD patients prior to use of clonazepam, a potential respiratory and upper airway suppressant, and clonazepam may have more adverse effects and potential drug interactions than melatonin. Melatonin is often a reasonable initial choice in elderly patients receiving polypharmacy and those with symptomatic neurological disorders such as cognitive or autonomic impairment and parkinsonism.

Given the high risk for phenoconversion to a defined neurodegenerative disorder in the majority of RBD patients, patients should receive longitudinal follow-up so that early symptomatic treatment for impairments in cognition, motor, or autonomic dysfunction can be offered. Prognostic counseling remains controversial, although given ready availability of information about RBD on the world wide web, informing the patient of the strong association between RBD and synucleinopathies, while emphasizing that there is considerable inter-individual variability in progression and uncertain regarding the timeframe for individual risk, is the best current approach, while suggesting the patient observe a healthy lifestyle and diet with regular exercise.²⁵ There is also hope that eventual neuroprotective agents could be offered early to patients with RBD who are followed longitudinally.¹⁰

Conclusion

RBD poses injury potential and signifies the need for careful longitudinal monitoring for symptoms and signs for concurrent or future development of overt cognitive, autonomic, and motor impairments. Timely recognition, longitudinal followup, and optimization of treatment is essential for RBD management.

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