

REM sleep behaviour disorder

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Summary

REM sleep behaviour disorder (RBD) is an important parasomnia characterized by the intermittent loss of physiologic REM sleep muscle atonia and the appearance of abnormal, frequently violent, complex movements during sleep. This motor activity is associated with dream mentation and may lead to the injuries of the patient and/or of the persons in the bedroom. The exact etiological factors of RBD remain unknown. RBD can be misdiagnosed as a psychiatric disorder. It usually affects middle-aged or older men and may present itself as an acute illness after overdosed or suddenly withheld medications (e.g. antidepressants), and – more frequently – as a chronic disease. In its chronic form it is usually followed by the development of neurodegenerative diseases, especially by Parkinson's disease. The association of RBD with narcolepsy or cerebrovascular diseases is also common. Very rare coincidence with obstructive sleep apnea syndrome may indicate its protective action against upper airway collapse during sleep. A polysomnographic study is necessary to assess the diagnosis of RBD showing the absence of REM sleep atonia and related abnormal behaviour. Clonazepam, pramipexol, and melatonin have been tried in the treatment of RBD.

Key words: REM sleep behaviour disorder, parasomnia, Parkinson's disease, sleep apnea

About 2% of adults experience abnormal behaviour during sleep, activity which is sometimes aggressive or leading to injuries [1]. Violent behaviour during sleep may occur in the course of REM (rapid eye movement) sleep behaviour disorder (RBD) or may be associated with the other disorders, such as sleep terrors, sleepwalking, nocturnal seizures, hypnogenic paroxysmal dystonia, obstructive sleep apnea (with agitated arousals), rhythmic movement disorders of sleep, and psychogenic dissociative disorder [2, 3].

REM sleep, also known as the stage of sleep with dreams, is associated with generalized atonia of somatic muscles, except the diaphragm and extra ocular muscles; it is an active process that originates in the pons: the stimulus from the peri-locus ceruleus excites neurons of the nuclei reticularis magnocellularis in the medulla, which then transmit descending excitatory projections to the spinal alpha motoneurons resulting in the muscle atonia [4]. The loss of physiologic muscle tone protects against the physical enactment of dreams [5].

RBD, formally recognized and named in 1986, is defined as loss of muscle atonia during REM sleep in association with complex, vigorous, or violent movements that

correspond to acting out of dreams [6]. In 1990 RBD was incorporated within the international classification of sleep disorders [7].

Many years before discovery of human RBD, a similar behaviour was evoked in cats by bilateral perilocus coeruleus lesions. In this classical experiment, performed in 1965, bilateral, symmetrical, dorsolateral tegmental pontine lesions in cats caused prominent motor behaviour during REM sleep due to the absence of the expected atonia during REM sleep [8]. Later animal studies have shown that the atonia of REM sleep is also influenced by other brainstem regions [9, 10].

RBD usually affects middle-aged or older men, but can affect either gender in any age group [3, 5, 11, 12, 13]. About one fourth of the patients have a prodrome: sleeptalking, yelling, limb twitching, and jerking. These often appear many years before RBD onset [3]. The clinical features of RBD include aggressive or exploratory, complex movements like gesturing, arm flailing, grabbing, kicking, crawling, punching or kicking the person in the room, falling out of bed, sitting, jumping out of bed, staggering about the room, crashing into objects and running, but also talking, laughing, yelling and swearing; these symptoms usually appear at least 90 minutes after sleep onset [3, 14, 15]. When awakened, the patients recall vivid, action-filled, and violent dreams, usually involving confrontation and aggression with unfamiliar people and animals [3, 15]. Frequently dream-enacting behaviours lead to complications, including ecchymoses (76%), lacerations (32%) and fractures (7%) [3]. A case of subdural haematoma as a result of RBD has been described [16]. Violent episodes typically occur about once per week and occasionally appear as frequently as four times per night over several consecutive nights [3].

Rarely, RBD presents itself as an acute disorder induced by medications (tricyclic antidepressants, monoamine oxidase inhibitors, mirtazapine, fluoxetine, or selegiline), caffeine abuse or is associated with withdrawal of drugs (tricyclic antidepressants, anticholinergics, sedatives-hypnotics) or alcohol [17, 18].

RBD usually has the form of a chronic disorder. It may be idiopathic (without any demonstrable neuroanatomic brainstem abnormalities), but more often is related with different central nervous system disorders, such as neurodegenerative diseases, narcolepsy or cerebrovascular diseases [3, 14]. Especially, there is a strong association between RBD and Parkinson's disease [19]. RBD can precede the onset of Parkinson's disease by several years [20, 21, 22]. In one study 38% of male patients with Parkinson's disease developed symptoms of RBD with a mean of 3.7 years before the onset of Parkinson's disease and the maximal interval between RBD onset and Parkinson's disease diagnosis was 12.7 years [6]. In the other study the symptoms suggesting RBD or sleep-related injurious behaviours were reported in 25% of the patients with Parkinson's disease: 15% of the patients responded to strict RBD criteria (with dream recall) and nocturnal violence without dream recall was reported in another 10% [23]. Another study, based on a questionnaire, reported that 43% of the patients with Parkinson's disease experienced "acting out of dreams" [24].

There is also a strong association between RBD and multiple system atrophy: in one large study dream-acting behaviours were reported in 69% and RBD was diagnosed by sleep studies in 90% of patients [25].

The other neurological and psychiatric diseases occurring in patients with RBD include Alzheimer's disease, olivopontocerebellar degeneration, corticobasal degeneration, Shy-Drager syndrome, diffuse Lewy body disease, progressive supranuclear palsy, multiple sclerosis, brain stem astrocytoma, dementia, or depression [3, 5, 19, 26, 27, 28, 29, 30, 31, 32, 33]. Sleep disordered breathing is uncommon in RBD and, when present, is usually mild; it is possible that RBD may protect against obstructive sleep apnea (OSA) syndrome [34]. However, some cases of coexisting RBD and OSA syndrome have been reported [35].

The diagnosis of RBD is based upon a detailed history and examination, followed by a polysomnographic (PSG) study. The minimum diagnostic criteria of RBD include: 1) PSG abnormality during REM sleep: elevated muscle tone or excessive phasic submental or limb twitching seen in electromyography, 2) prominent limb or truncal jerking, or complex, vigorous, or violent behaviours (or a history of injurious or disruptive sleep behaviours), and 3) the absence of epileptiform activity during REM sleep noted in the electroencephalography [17]. PSG studies usually reveal an elevated percentage of deep, slow-wave sleep and there may be an elevated index of periodic leg movements in RBD patients [5].

Clonazepam, taken nightly, is usually efficacious in the treatment of RBD patients [5, 36]. The therapeutic action of clonazepam depends on its ability to suppress phasic electromyographic activity during REM sleep [37]. About 90% of patients with chronic RBD respond well to clonazepam; the usual dose at the beginning of treatment is 0.5 mg [5, 38]. In some patients melatonin, as mono-therapy or added to clonazepam, may be efficacious in the treatment of patients with RBD [38]. Recently, a sustained reduction in the frequency or intensity of sleep motor behaviours in patients with idiopathic REM sleep behaviour disorder treated with pramipexol has been reported [39].

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