Acute REM Sleep Behavior Disorder

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12.1 Introduction

The concept of RBD has changed since its first description in 1986 [1]. Although RBD is usually considered to be a chronic parasomnia affecting primarily older men and with a close relationship with degenerative neurological conditions, there is an increasing body of literature reporting cases of acute or subacute RBD, occurring irrespective of age and sex. RBD, or isolated REM sleep without atonia (RSWA), has been associated with various medications or substances, in particular antidepressants, and with the abrupt withdrawal from barbiturates, tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), and alcohol. Less frequently, structural brain lesions (vascular, demyelinating disease, tumors), especially in the pontine region, may cause RBD. RBD can appear acutely after a stressful life event and in post-traumatic stress disorder (PTSD). This chapter focuses on these incidental forms of secondary RBD, in which RBD does not appear as a classic clinical feature of the underlying conditions, but rather as an unexpected epiphenomenon. Apart from the importance of RBD recognition and management in these clinical conditions, acute RBD manifestations could also have crucial importance in understanding the full spectrum of the pathophysiology of RBD [2].

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12.2 RBD and Drugs

12.2.1 Antidepressants

An association with most classes of antidepressants has been implicated in RBD and RSWA, but never bupropion, a dopaminergic-noradrenergic agent [3–7].

Tricyclic antidepressants and fluoxetine cause changes in sleep architecture and polysomnographic (PSG) findings, causing abnormal, prominent eye movements during non-REM sleep and suppressing REM sleep [8, 9]. In 11 young adult subjects who underwent 3 nights of PSG recordings after administration of 25 or 50 mg of clomipramine, or non-active placebo, clomipramine induced tonic mentalis EMG activity during REM sleep [10]. Winkelman and James [3] demonstrated that tonic, but not phasic, submental EMG activity during REM sleep was significantly more common in the 15 subjects taking serotonergic antidepressants than in the 15 age-matched individuals not on such medication. Sertraline (50–200 mg/day) may induce or exacerbate tonic and phasic RSWA as shown in an 8-week open-label trial in 31 depressed patients. In contrast to idiopathic RBD, sertraline-related RSWA had the specific characteristics of being correlated with the degree of the prolonging of REM latency without any predominance of male sex and elder age, suggesting possible different pathophysiological mechanisms [11]. Sertraline-induced RBD was reported in an 87-year-old male veteran treated for PTSD, who was also taking bupropion and lorazepam. RBD completely disappeared upon sertraline discontinuation and returned within 1 month of restarting sertraline [12].

Although most reported data are case reports or case series, there are no controlled studies showing that antidepressants cause frank RBD, nor are there studies comparing PSG findings before and after the initiation of antidepressants in the same subjects. In contrast, multiple groups have reported individual patients who developed RBD after initiating treatment with antidepressants [13–16].

In some cases of narcolepsy, clomipramine hydrochloride improved the cataplexy and partially alleviated the daytime sleep attacks, but resulted in episodes of severe motor hyperactivity during sleep, which were most intense during REM sleep [13, 17]. Olson et al. in reviewing 93 cases of RBD found that in only one patient (who also had Parkinson's disease) RBD developed at about the same time when medication (amitriptyline) was commenced [18].

Fluoxetine has been found to be similar to the tricyclic antidepressants in its capacity to induce clinical or subclinical RBD, as first reported in 1992 by Schenck et al. [9]. In a retrospective review of adults undergoing PSG while taking antidepressants, 93 consecutive adults were treated with fluoxetine or tricyclic antidepressants. Among them the authors reported the case of a 31-year-old man with obsessive-compulsive disorder (OCD) who developed RBD shortly after starting fluoxetine therapy, which persisted at PSG study 19 months after fluoxetine discontinuation. In this fluoxetine-induced RBD, the history provided by the patient's wife virtually excluded any preexisting parasomnia, and the dream disturbance was very typical for RBD and did not incorporate any of the patient's OCD activity. After that initial case, some other case reports documented RBD that was clearly associated

with the use of fluoxetine and then paroxetine [16] and venlafaxine [19]. Fluoxetine also probably aggravated a mild form of RBD in a case of voltage-gated potassium channel antibody-associated limbic encephalitis (VGKC-LE) [20].

Mirtazapine was associated with RBD in four patients with parkinsonism, which was then resolved after the drug was discontinued [21]. Two large retrospective studies seem to suggest that a unique clinical profile exists with a strong association among antidepressant use, early-onset RBD, female sex, and younger age, while usually RBD is typically seen in older men [22, 23]. Although there are associations between antidepressants and RBD, and also between psychiatric disease and RBD, the interrelationships and causalities remain to be more fully elucidated, as discussed in Chap. 10. The current literature suggests that antidepressants are not likely to be the sole causative agent, both for older adult and especially for younger adult onset RBD. Probably a complex mechanism with both predisposing individual vulnerabilities and precipitating effects from the use of antidepressants is involved.

Most patients prescribed with an SSRI, SNRI, TCA, or MAOI antidepressant do not develop RBD. Literature data in psychiatric patients (pRBD) seem to document that RBD may be related to a constellation of factors, including individual predisposition, and the presence of a depressive illness, instead of RBD being merely secondary to antidepressants [24–27]. A clinical epidemiological study conducted in a psychiatric outpatient setting found that the risk of developing RBD among those taking SSRI antidepressants was only about 1 out of 20 [24]. A follow-up study of the psychiatric patients with RBD features was subsequently conducted by ceasing or switching SSRI to other classes of antidepressant [25]. Clinical and PSG reassessment after 6 months of intervention reported a partial improvement of the RBD symptoms, but the PSG feature of REM atonia was not fully restored [25]. It is also possible that antidepressants unmask latent RBD rather than cause it. On the other hand, in some cases RBD dramatically improved with SSRIs and deteriorated with a 5-HT_{1A} partial agonist, tandospirone, and acute RBD appeared during withdrawal from imipramine [28, 29].

The intriguing relationship between depression and RBD was further investigated by evaluating if RBD with antidepressant use can be an early signal of an underlying neurodegenerative disease. To address this possibility, Postuma et al. [6] analyzed a cohort of 100 idiopathic RBD (iRBD) patients in order to understand whether RBD occurring with prescription of antidepressants is a relatively benign side effect or is a marker of prodromal neurodegenerative disease that requires further evaluation and follow-up. In their interesting prospective cohort, 27 patients were taking antidepressants. Compared to matched controls, RBD patients taking antidepressants demonstrated abnormalities indistinguishable in severity from RBD patients not taking antidepressants, and, in a prospective follow-up, RBD patients taking antidepressants had a lower risk of developing neurodegenerative disease during the follow-up period than those without antidepressant use. However, although patients with antidepressant-associated RBD had a lower risk of conversion to neurodegeneration during the follow-up period than patients with "purely idiopathic" RBD, markers of prodromal neurodegeneration (such as olfaction impairment, systolic blood pressure drop, constipation, depression, etc.) were

clearly present. The conclusion from this study was that the antidepressants accelerated the emergence of RBD in patients already in the early stages of alpha-synucleinopathy neurodegeneration, without accelerating the emergence of the neurodegeneration.

12.2.2 Other Drugs and Substances

Some reports suggested that other agents may play a role in inducing acute RBD. In 1995 Louden et al. reported three non-demented PD patients who manifested RBD while on recommended doses of selegiline. None of them had problems severe enough to suggest RBD while they were being treated with varying doses of other dopaminergic agents (carbidopa/L-dopa, pergolide) unaccompanied by selegiline [30]. Phenelzine, another MAOI, can induce RBD in healthy young subjects [31], but at the same time parnate, another MAOI, suppressed behavioral manifestations in a patient with iRBD [32]. Carlander et al. documented RBD in a 62-year-old man with Alzheimer's disease (AD) induced by the acetylcholinesterase inhibitor rivastigmine (SDZ-ENA 713) during a phase III clinical trial, at a dose of 8 mg daily. RBD subsided on discontinuation of the treatment [33]. Another 88-year-old man with probable AD (without pathological confirmation) developed RBD after increasing the nightly dose of rivastigmine, from 1.5 to 3 mg (total daily dose, 4.5 mg), as therapy for his dementia [34]. The underlying brain substrate appears to play a crucial role in whether cholinergic therapy will induce RBD, although the mechanism of action remains unclear. On the other hand, in a few cases, cholinergic therapy of iRBD with the acetylcholinesterase inhibitors (AIs) donepezil or rivastigmine was reported to be effective [35]. Twenty-five milligrams of quetiapine (an atypical antipsychotic drug) per night added to chronic fluoxetine therapy (40 mg per day) was reported to cause RBD in a 55-year-old woman [36].

Finally, beta-adrenergic blockers such as bisoprolol [37] and propranolol [38] and heavy caffeine abuse may possibly induce RBD [39]. Another report linked heavy caffeine use and RBD in a patient with prolific coffee intake [40]. Chocolate ingestion even of modest amounts seemed to exacerbate RBD in a single patient [41].

12.2.3 Drug or Substance Withdrawal: PSG Studies in Pre-RBD Days

RSWA and an acute, transient, form of RBD induced by abrupt withdrawal from barbiturates [42], meprobamate [43], pentazocine [44], nitrazepam [45], MAOI (phenelzine) [46], and ethanol have been well documented [47–49].

Barbiturates, phenelzine, and ethanol rapid withdrawal can induce a rebound of REM sleep during which motor paralysis is breached, muscle tone is regained, and dreams are acted out. Hence, this is the so-called REM intrusion or "spillover" theory of drug withdrawal psychosis or acute delirium first proposed and elaborated by Dement and Fisher [46] and Gross [47].

Delirium tremens (DTs) represent the most severe complication of alcohol withdrawal syndrome, appearing after a significant reduction or complete discontinuation of alcohol consumption in patients suffering from chronic alcohol dependence. DTs are characterized by features of alcohol withdrawal itself (tremor, motor violent agitation, diaphoresis, hypertension, tachycardia, etc.) together with acute-onset severe insomnia, visual hallucinations, and dream enactment. Even though the pathogenetic mechanism of DTs is not fully understood, we can assume that sudden alcohol withdrawal results in a transient homeostatic imbalance within the limbic system, due to the sudden dramatic changes in GABAergic synapses, downregulated by chronic alcohol abuse.

In 1980 Kotorii and colleagues described the sleep pattern of 13 alcoholics who were recorded for 5 consecutive nights after the cessation of alcohol intake. In six of them, DTs occurred. PSG recordings showed a dramatic reduction or absence of synchronized sleep (spindle or delta sleep) even when the disorder did not evolve into DTs. The predominant EEG pattern of alcohol withdrawal consisted in a mixture of stage 1 and REM sleep associated with tonic EMG [48]. This is the same polygraphic pattern described in 1975 by Tachibana et al. who reported that the peculiar sleep pattern of alcoholics who developed DTs was characterized by a concomitant appearance of low-voltage EEG activity, REM burst, and tonic mental EMG. Tachibana et al. called it "stage 1-REM with tonic EMG" reporting that this sleep stage was found also in a meprobamate addict with delirium [43].

12.2.4 Drug or Substance Withdrawal: RBD-Like Phenotype with Different Pathophysiology

Later we observed similar findings in a case of DTs who we followed up for 7 months with serial PSG registrations [50]. During the acute phase of the disease, PSG recordings disclosed a complete sleep-wake disruption with a drastic reduction of spindle and delta sleep and with the presence of an atypical transitional state between REM sleep without atonia and wake, associated with hallucinations and enactment of dream behaviors. We named this condition "oneiric stupor" (OS), with peculiar motor behaviors shown by the patient and characterized by simple stereotyped and repetitive gestures which, on some occasions, could be organized in more complex and quasi-purposeful behaviors mimicking daily-life activities such as dressing, combing the hair, washing, eating, and drinking. Movements performed by the patient during OS mimic the contents conveyed by his dreams, which he was able to recall upon awakening. OS appears not only in DTs but also in fatal familial insomnia (FFI), an autosomal dominant disease caused by a point mutation at codon 178 of the prion protein gene (PRPN), and in Morvan's syndrome, an autoimmune limbic encephalopathy [51, 52]. OS bears some resemblance to RBD, but the two entities are clearly different, as shown in Table 12.1. RBD arises from a normal sleep-wake cycle in which the only abnormality is the lack of muscular atonia during REM sleep. OS, in contrast, arises in a context of severe alteration of the sleep structure with a profound loss of slow-wave sleep and a predominance of a mixed

Table 12.1 Differences between oneiric stupor episodes (OS) and REM sleep behavior disorder (RBD)

Feature	RBD	OS
Timing	At least 60–90′ after sleep onset; usually in the latter part of the night	Throughout the 24 h
Stage	From REM sleep only	Generally from a mixed EEG state with features of both N1and REM sleep
Sleep structure	Normal; REM without atonia	Completely disorganized
Duration	Short	Long
Episode frequency	Usually once per night	Continuous or subcontinuous state
Episode motor pattern	Violent behaviors mimicking the content of a dream	Quiet, stereotyped, and repetitive gestures usually mimicking daily-life activities
Episode dream content	Patients usually report a complex "dream tale" including defense against attack by unfamiliar people or animals	Patients tend to describe a single "oneiric scene," generally neutral

Modified from Guaraldi et al. 2011 [53]

state with features of both stage 1 NREM and REM sleep, as depicted in Fig. 12.1. OS is not restricted to the last part of the night, as with RBD, but occurs throughout the night due to the loss of a physiological sleep structure. OS tends to present in clusters or subcontinuously if the patient is left alone and not stimulated, whereas a complex RBD episode usually occurs once a night [53].

Montagna and Lugaresi of the Bologna group focused on the striking clinical and polygraphic similarities of DT, FFI, and Morvan's syndrome and put forward the concept of Agrypnia excitata (AE) [54]. The prime clinical features of AE are composed of severe insomnia (Agrypnia) coupled with excessive motor and autonomic hyperactivity (excitata). Polygraphically, AE is characterized by the inability to generate the EEG activity typical of deep sleep, viz., delta activity. Remarkably, however, in AE stage 1 NREM sleep is still present, and there is a pathologically increased REM sleep, often with a lack of muscle atonia. The concept of AE thus implies that divergent and actually opposite outcomes pertain to the SWS stages (which disappear) and to light sleep stage 1 (which is conserved and actually augmented). Neuropathologically, the thalamo-limbic circuitry is involved in all of the clinical conditions that exemplify AE [54], and this intralimbic disconnection triggers the generalized activation associated with the inability to sleep [55].

12.3 Acute Lesions

Acute RBD has been observed in humans in association with focal brain lesions damaging the key structures that modulate REM sleep, especially the pontine tegmentum and medial medulla, as shown in Table 12.2. These reports have important

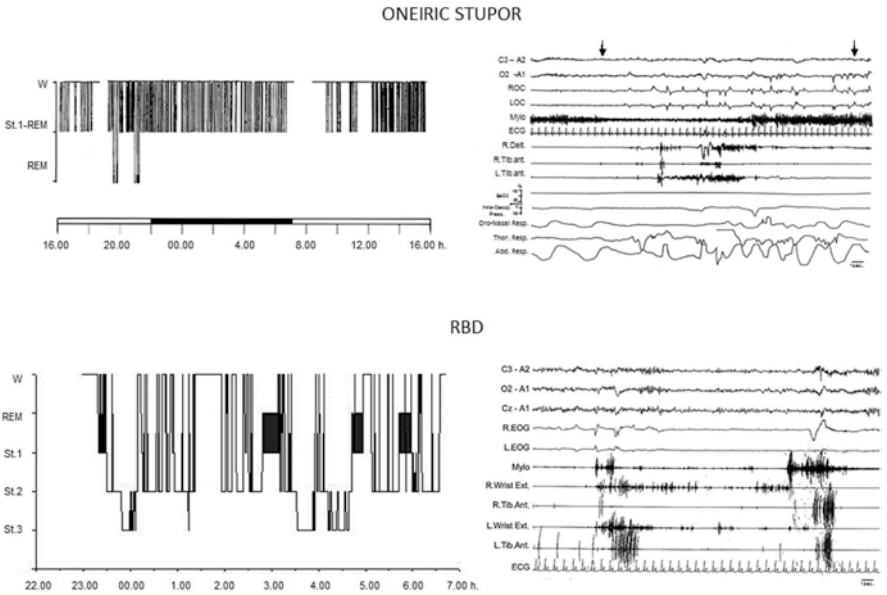

Fig. 12.1 Wake-sleep histograms in an FFI patient with oneiric stupor (top) and in a RBD patient (bottom). Whereas RBD emerges from a normal sleep structure, oneiric stupor arises in the context of a completely disorganized sleep structure with a predominance of a mixed state with features of both stage 1 NREM and REM sleep (N1-REM)

implications for more fully understanding the underlying mechanisms of RBD. Although the preexistence of subclinical RBD cannot be ruled out with full-blown RBD occurring within the context of subacute or acute cerebral dysfunction, in most of the cases, incidental RBD seems to be a de novo event and not an exacerbation of a previously unrecognized RBD. In some cases, it is crucial to establish whether a lesion found in a neuroimaging study is the direct cause of RBD or if it is simply an incidental finding when the imaging was obtained years after the onset of RBD [2]. Iranzo et al. propose five criteria to determine whether a focal structural brain lesion is the direct cause of RBD: (1) RBD onset should be temporally associated with the appearance of the brain lesion; (2) RBD onset should be coincident with the onset of other symptoms caused by the lesion if they do appear (e.g., oculomotor abnormalities, hypersomnia, limbic syndrome, etc.); (3) the lesion should be located in a brain area known to regulate REM sleep (e.g., mesopontine tegmentum, ventromedial medulla, amygdala, hypothalamus, etc.); (4) disappearance of the lesion whenever possible (e.g., by surgery in tumors or by immunotherapy in multiple sclerosis and autoimmune mediated limbic encephalitis) is associated with remission or improvement of the RBD-related nocturnal symptoms and PSG abnormalities; and (5) RBD is not better explained by another current disorder (e.g., Parkinson's disease), medication use, or withdrawal [2].

Small ischemic lesions [18, 56–61], hemorrhages from vascular malformations [2, 62], tumors [63–65], demyelinating plaques [66–68], and inflammatory diseases

Table 12.2 Reported cases of acute RBD: etiological origins

Etiology	Authors (year)	Age (sex)	Lesion type/diagnosis	Lesion location	RBD disappearance/ improvement after etiological therapy (if possible)
Vascular—ischemic	Kimura et al. (2000) [58]	75 (F)	Ischemic infarct	Left paramedian upper pons	
	Peter et al. (2008) [59]	79 (M)	Ischemic infarcts	Bilateral cerebellar and pontine white matter	
	Xi and Luning (2009) [60]	68 (M)	Lacunar ischemic infarct	Right paramedian pons	
	Reynolds and Roy (2011) [61]	67 (M)	Ischemic infarct	Rostral medial pons left of midline	
Vascular—malformation	Iranzo and Aparicio (2009) [2]	81 (M)	Acute hemorrhage from a cavernous hemangioma	Left medulla	
	Felix et al. (2016) [62]	75 (M)	Repeated microbleeds from pontine cavernoma	Midline lower pons	
Tumoral—lesional	Zambelis et al. (2002) [63]	59 (M)	Neurinoma	Left pontocerebellar angle	Complete remission of RBD after surgery
	Jianhua et al. (2013) [65]	30 (M)	B cell lymphoma	Pontomesencephalic junction and upper/mid pons	Improvement of RBD after chemotherapy
Tumoral—paraneoplastic	Adams et al. (2011) [81]	55 (M)	Ma1 and Ma2 antibody-positive neurological disorder (squamous cell tonsillar carcinoma)		Not available
	Vale et al. (2016) [78]	66 (F)	Cerebellar degeneration (breast cancer)		Improvement of RBD after IVIG
		43 (F)	Cerebellar degeneration (breast cancer)		Remission of RBD after IVIG

Tumoral—Other	Shinno et al. (2010) [79]	76 (M)	Metastatic renal carcinoma	Not available	
		70 (M)	Stage IV gastric carcinoma with carcinomatous peritonitis	Not available	
		75 (W)	Gastric carcinoma	Not available	
Autoimmune	Iranzo et al. (2006) [20]	65 (M)	VGKC autoantibodies associated encephalitis	Bilateral mesial temporal lobe	Remission of RBD after IVIG and steroids
	Compta et al. (2006) [80]	69 (M)	Ma2 antibody-positive encephalitis	Bilateral amygdala and dorsolateral midbrain	No response after IVIG and steroids
Inflammatory—Demyelinating	Plazzi and Montagna (2002) [66]	25 (F)	Multiple sclerosis	Multiple cerebral periventricular, Pons	Improvement of RBD symptoms after ACTH treatment
	Tippmann-Peikert et al. (2006) [67]	51 (F)	Multiple sclerosis	Dorsal pons	Not available
	Gomez-Choco et al. (2007) [68]	49 (M)	Multiple sclerosis	Pons	Not available
Inflammatory—Others	Mathis et al. (2007) [69]	30 (M)	Acute parainfectious brain stem encephalitis	Medial and bilateral pontine tegmentum, ventral to the fourth ventricle	No response after steroid treatment
	Lin et al. (2009) [70]	46 (M)	Aseptic limbic encephalitis	Bilateral unci and medial temporal lobes	Not available
	St. Louis et al. (2014) [71]	47 (M)	Vasculitis	Dorsomedial pons	Not available
Postsurgical	Piette et al. (2007) [77]	56 (M)	DBS implantation surgery	Left subthalamic nucleus, substantia nigra	
Parasomnia overlap disorder					

(continued)

Table 12.2 (continued)

Etiology	Authors (year)	Age (sex)	Lesion type/diagnosis	Lesion location	RBD disappearance/ improvement after etiological therapy (if possible)
	Schenck et al. (1997) [75]	24 (M)	Post astrocytoma resection	Pons	Not available
		34 (M)	Multiple sclerosis	Not available	Not available
		50 (M)	Cerebral contusion	Not available	Not available
	Limousin et al. (2009) [76]	40 (F)	Acute inflammatory rhombencephalitis, myelitis, intracranial thrombophlebitis	Right pontine tegmentum and right dorsal medulla	Improvement of RBD after steroids
Status dissociatus					
	Provini et al. (2004) [73]	36 (M)	Post cavernoma resection	Ponto mesencephalic tegmentum	
	Condurso et al. (2006) [74]	62 (M)	Multilacunar state	Left basal ganglia and capsula, bilateral paratrigonal white matter, and median pons	Not available

Abbreviations: *IVIG* Intravenous immunoglobulin, *VGKC* Voltage-gated potassium channel, *DBS* Deep brain stimulation

[69–71] have been found in a few patients with RBD, as shown in Table 12.2. Moreover, lack of muscle atonia and disturbances of tonic-phasic REM sleep relationships were described in a case of an infiltrating tumor of the pons, before the formal identification of RBD in 1986 [72]. This topic is covered in detail in Chap. 9.

An acute status dissociatus (characterized by the complete NREM/REM sleep state boundary breakdown) has been described after surgical resection of a cavernoma [73] and in a multilacunar state [74].

In other cases RBD is part of parasomnia overlap disorder (POD), as described in different conditions including tumors [75] and inflammatory diseases [75, 76].

A nightly-recurring POD, secondary to a recurrent inflammatory disease of the brain stem and spinal cord of unknown origin, has been described in a 40-year-old woman with no prior parasomnia who developed an acute inflammatory rhombencephalitis with multiple cranial nerve palsies and cerebellar ataxia, followed by myelitis (6 months later), and by an intracranial thrombophlebitis (1 month after). Between and after these episodes, she presented severe RBD. During the episodes she talked, sang, and moved nightly while asleep and injured her son (co-sleeping with her) while asleep. In addition, she walked while asleep on a nightly basis. MRI revealed small hypointensities in the right pontine tegmentum and in the right dorsal medulla, documenting that a unilateral lesion is sufficient to enhance/release the axial and bilateral limb muscle tone and complex behaviors during REM sleep and also to trigger sleepwalking [76].

Finally, Piette et al. described a case of a 56-year-old parkinsonian patient who presented a unique episode of RBD beginning after the implantation of the exactly placed electrode for subthalamic stimulation. Immediately after the implantation of the left electrode (but not after a similar operation on the right side), the patient fell asleep and presented episodes of behavioral agitation or aggression during REM sleep. The authors suggested that a microlesion made by the electrode was responsible for triggering this parasomnia. Possible causes could be a lesion of the descending input from orexin neurons to the mesopontine region or the interruption of some descending inputs to the pontine REM sleep regulatory regions or, alternatively, a lesion in the substantia nigra might itself have been directly responsible for the emergence of the RBD [77].

12.4 Autoimmune Diseases

As discussed in greater detail in Chap. 8, RBD has been described in several rare paraneoplastic and autoimmune encephalopathies. Two patients with paraneoplastic cerebellar degeneration related to breast cancer presented with video-PSG confirmed RBD. RBD substantially improved after immunotherapy, raising the hypothesis that secondary RBD, at least in some cases, may be an immune-mediated sleep disorder [78]. In a few other cases, the relationship between the presence of advanced cancer and RBD was less evident and did not allow the possibility to discriminate whether the acute onset was of paraneoplastic or lesional origin or secondary to the effect of antitumor/palliative treatments [79].

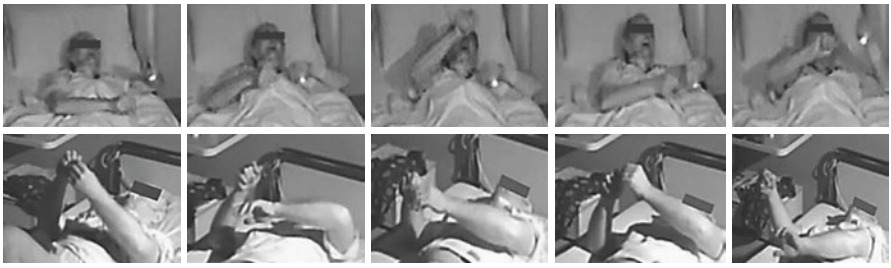

Fig. 12.2 Video recordings (selected frames) of oneiric stupor in two patients with Morvan's syndrome. Both patients perform the same gestures mimicking daily-life activities such as searching for objects

RBD is frequent in the setting of limbic encephalitis secondary to voltage-gated potassium channel (VGKC) antibody or anti-Ma1 and Ma2 antibodies [20, 80, 81]. In a series of six patients with non-paraneoplastic limbic encephalitis associated with antibodies to VGKC and RBD, immunosuppression resulted in the resolution of RBD in three patients, in parallel with remission of the limbic syndrome [20]. VGKC complex antibodies are associated also with Morvan's syndrome (MS), a disorder characterized by profound insomnia, dysautonomia, and peripheral neuromuscular irritability, sometimes associated with tumors such as malignant thymoma. In a case of paraneoplastic MS associated with antiVGK antibodies, 24-h PSG recordings documented a striking reduction in sleep spindles and in delta activity and the presence of autonomic and motor hyperactivity persisting throughout the 24-h [82]. As in DTs and FFI cases, this Morvan's patient presented with OS, and dream enactments mimicking daily-life activities (dressing, combing the hair, manipulating objects, etc.) coinciding with clusters of short REM sleep episodes, as shown in Fig. 12.2. The involvement of the thalamus and corticolimbic regions was shown in this case by serum immunoglobulin-G binding to neurons in these brain regions of the rat brain and by direct immunochemistry of frozen sections of the patient's brain tissues showing antibody leakage in the thalamus [82].

Transient RBD, improving as the disease resolves, has also been associated with Guillain–Barré syndrome, particularly in patients experiencing autonomic dysfunction and hallucinations [83].

12.5 Post-traumatic Stress Disorder (PTSD)

RBD can appear acutely after a stressful life event. In a cohort of 203 consecutive patients with iRBD, six patients (3%) were able to determine the date of onset of RBD because they associated it with a highly stressful situation (a robbery, a fraud, a cancer diagnosis) or a few days after a surgical procedure (a pacemaker implantation and cardiac bypass surgery in two patients) [84, 85]. At least four other cases of RBD triggered by major life stress have been published, involving a divorce, a frightening automobile accident without physical injury, a sea disaster, and public

humiliation, as reviewed [64]. The unresolved question in these ten cases was whether there was preexisting REM without atonia that predisposed these patients to develop rapid-onset RBD, since most people subjected to these stressful circumstances and medical procedures do not develop RBD [85].

RBD has been reported also in patients with prolonged PTSD, a disabling, chronic anxiety disorder resulting from exposure to life-threatening events, such as a serious accident, assault, abuse, or combat (DSM V) [86]. In one study of sleep muscle activity in a group of Vietnam combat veterans with current PTSD, an elevated percentage of REM sleep epochs with increased phasic twitching activity, as a presumed initial RBD-like sign in PTSD, was found [87]. Hefez et al. described two patients who were sea disaster survivors, and who had subsequently increased motor activity during REM sleep [88]. Schenck et al. reported an automobile accident survivor (without physical injury), who had nightmares reliving the accident and who presented with violent movements during sleep. His PSG showed increased phasic and tonic EMG during REM sleep [29].

Similarly increased EMG activity during REM sleep has been found in a unique series of 27 US veterans, 15 of whom also presented with PTSD [89]. More recently, Wallace et al. reported vPSG-confirmed RBD in four recent veterans of Operations Iraqi Freedom and Enduring Freedom, all of whom were taking SSRIs at the time of their PSG, although the time relation between SSRI initiation and RBD onset was not well clarified [90].

Furthermore, a novel parasomnia encompassing features of RBD (REM without atonia of variable degree) with nightmares and disruptive sleep behaviors has been proposed: "Trauma Associated Sleep Disorder (TSD)" [91, 92]. The authors described four young male soldiers, all with traumatic experiences (three involving combat and one involving divorce) heralding the onset of disruptive nocturnal behaviors and nightmares. All patients had RSWA and developed TSD from their traumatic experiences. According to the authors' suggestions, the term "Trauma Associated Sleep Disorder" (TSD) could describe a unique sleep disorder encompassing distinct clinical features, PSG findings, and treatment response to prazosin in patients with disruptive sleep behaviors, nightmares, and REM without atonia presenting after trauma.

12.6 Conclusions and Future Directions

Although our knowledge of acute RBD is based on a limited number of anecdotal, cross-sectional reports, literature data have documented that acute RBD is anything but rare [93, 94]. Acute RBD could have important implications for more fully understanding the underlying mechanisms of RBD, and, on the other hand, acute RBD can be of clinical value as a telltale sign. Sleep clinicians should be aware of the heterogeneous profile of RBD that can facilitate correctly diagnosing this parasomnia and enhance patient management and counseling. Physicians lacking special expertise in sleep medicine who are biased by the prevailing diagnostic perspective that links RBD with neurodegenerative diseases may fail to recognize cases

of incidental RBD. There are no published data on emergency department registry-based acute RBD incidence. Thus more awareness of the existence of these other forms of RBD and greater familiarity with the various potential clinical pictures may help to avoid misdiagnosis and inappropriate treatments. All patients who present with complaints of sleep-related behaviors and movements together with sleep talking and excessive dreaming should be screened for RBD, along with patients with neurologic or psychiatric disorders. Due to the possibility of iatrogenic RBD, a detailed medication history (including psychoactive medication and recently discontinued drugs) and stress-related social history should also be obtained [95]. Currently, studies that address treatment and long-term prognosis in antidepressant-associated or depression-associated RBD are lacking.

Among psychiatric patients, the association with RBD, although it can be mediated by antidepressant use, seems to involve a particular subgroup of patients, because it is present in more females, in younger patients, and with weaker association with neurodegenerative disease than previously described for RBD. If prospective studies confirm the existence of separate RBD subgroups (e.g., older men with neurodegenerative disease, younger patients with narcolepsy, and middle-aged women with autoimmune disease), further prospective studies will be necessary to determine whether these groups represent distinct pathophysiological mechanisms, how they manifest the same RBD phenotype, what the optimal treatments for these possible subgroups are, and what the prognostic differences across these subgroups are. This topic is covered in more detail in Chaps. 15 and 16.

Further research is necessary to clarify whether POD (RBD-NREM sleep overlap parasomnias) has a natural history different from that of typical RBD.

Finally, RBD should be clearly differentiated from OS or AE and more specifically DTs, FFI, and Morvan's syndrome. Despite the widely different etiologies and clinical courses, OS or AE is most likely to have a common pathogenetic mechanism different from disinhibition of the brain stem structures that control motor behavior during REM sleep found in RBD.

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References

1. Schenck CH, Bundlie SR, Ettinger MG, Mahowald MW. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep. 1986;9(2):293–308.
2. Iranzo A, Aparicio J. A lesson from anatomy: focal brain lesions causing REM sleep behavior disorder. Sleep Med. 2009;10(1):9–12. https://doi.org/10.1016/j.sleep.2008.03.005.
3. Winkelman JW, James L. Serotonergic antidepressants are associated with REM sleep without atonia. Sleep. 2004;27(2):317–21.
4. Hoque R, Chesson AL Jr. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. J Clin Sleep Med. 2010;6(1):79–83.
5. Mahowald MW, Schenck CH. REM sleep parasomnias. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. Philadelphia: Elsevier Saunders; 2010. p. 1083–97.

6. Postuma RB, Gagnon JF, Tuineaig M, Bertrand JA, Latreille V, Desjardins C, et al. Antidepressants and REM sleep behavior disorder: isolated side effect or neurodegenerative signal? Sleep. 2013;36(11):1579–85. https://doi.org/10.5665/sleep.3102.
7. Lee K, Baron K, Soca R, Attarian H. The prevalence and characteristics of REM sleep without atonia (RSWA) in patients taking antidepressants. J Clin Sleep Med. 2016;12(3):351–5. https://doi.org/10.5664/jcsm.5582.
8. Reynolds CF 3rd, Kupfer DJ. Sleep research in affective illness: state of the art circa 1987. Sleep. 1987;10(3):199–215.
9. Schenck CH, Mahowald MW, Kim SW, O'Connor KA, Hurwitz TD. Prominent eye movements during NREM sleep and REM sleep behavior disorder associated with fluoxetine treatment of depression and obsessive-compulsive disorder. Sleep. 1992;15(3):226–35.
10. Niiyama Y, Shimizu T, Abe M, Hishikawa Y. Cortical reactivity in REM sleep with tonic mentalis EMG activity induced by clomipramine: an evaluation by slow vertex response. Electroencephalogr Clin Neurophysiol. 1993;86(4):247–51.
11. Zhang B, Hao Y, Jia F, Tang Y, Li X, Liu W, et al. Sertraline and rapid eye movement sleep without atonia: an 8-week, open-label study of depressed patients. Prog Neuropsychopharmacol Biol Psychiatry. 2013;47:85–92. https://doi.org/10.1016/j.pnpbp.2013.08.010.
12. Sheyner I, Khan S, Stewart JT. A case of selective serotonin reuptake inhibitor-induced rapid eye movement behavior disorder. J Am Geriatr Soc. 2010;58(7):1421–2.
13. Bental E, Lavie P, Sharf B. Severe hypermotility during sleep in treatment of cataplexy with clomipramine. Isr J Med Sci. 1979;15(7):607–9.
14. Matsumoto M, Mutoh F, Naoe H, Kamata S, Chiba S, Miyagishi T. The effects of imipramine on REM sleep behavior disorder in 3 cases. Sleep Res. 1991;20A:351.
15. Attarian HP, Schenck CH, Mahowald MW. Presumed REM sleep behavior disorder arising from cataplexy and wakeful dreaming. Sleep Med. 2000;1(2):131–3.
16. Parish JM. Violent dreaming and antidepressant drugs: or how paroxetine made me dream that I was fighting Saddam Hussein. J Clin Sleep Med. 2007;3(5):529–31.
17. Guilleminault C, Raynal D, Takahashi S, Carskadon M, Dement W. Evaluation of short-term and long-term treatment of the narcolepsy syndrome with clomipramine hydrochloride. Acta Neurol Scand. 1976;54(1):71–87.
18. 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.
19. Schutte S, Doghramji K. REM behavior disorder seen with venlafaxine (Effexor). Sleep Res. 1996;25:364.
20. Iranzo A, Graus F, Clover L, Morera J, Bruna J, Vilar C, et al. Rapid eye movement sleep behavior disorder and potassium channel antibody-associated limbic encephalitis. Ann Neurol. 2006;59(1):178–81. https://doi.org/10.1002/ana.20693.
21. Onofrj M, Luciano AL, Thomas A, Iacono D, D'Andreamatteo G. Mirtazapine induces REM sleep behavior disorder (RBD) in parkinsonism. Neurology. 2003;60(1):113–5.
22. Teman PT, Tippmann-Peikert M, Silber MH, Slocumb NL, Auger RR. Idiopathic rapid-eye-movement sleep disorder: associations with antidepressants, psychiatric diagnoses, and other factors, in relation to age of onset. Sleep Med. 2009;10(1):60–5. https://doi.org/10.1016/j.sleep.2007.11.019.
23. Ju YE. Rapid eye movement sleep behavior disorder in adults younger than 50 years of age. Sleep Med. 2013;14(8):768–74. https://doi.org/10.1016/j.sleep.2012.09.026.
24. Lam SP, Fong SY, Ho CK, Yu MW, Wing YK. Parasomnia among psychiatric outpatients: a clinical, epidemiologic, cross-sectional study. J Clin Psychiatry. 2008;69(9):1374–82.
25. Lam SP, Zhang J, Tsoh J, Li SX, Ho CK, Mok V, et al. REM sleep behavior disorder in psychiatric populations. J Clin Psychiatry. 2010;71(8):1101–3. https://doi.org/10.4088/JCP.l05877gry.
26. Lam SP, Li SX, Mok V, Wing YK. Young-onset REM sleep behavior disorder: beyond the antidepressant effect. Sleep Med. 2012;13(2):211. https://doi.org/10.1016/j.sleep.2011.04.018.
27. Lam SP, Li SX, Chan JW, Mok V, Tsoh J, Chan A, et al. Does rapid eye movement sleep behavior disorder exist in psychiatric populations? A clinical and polysomnographic case-control study. Sleep Med. 2013;14(8):788–94. https://doi.org/10.1016/j.sleep.2012.05.016.

28. Takahashi T, Mitsuya H, Murata T, Murayama J, Wada Y. Opposite effects of SSRIs and tandospirone in the treatment of REM sleep behavior disorder. Sleep Med. 2008;9(3):317–9. https://doi.org/10.1016/j.sleep.2007.05.003.
29. Schenck CH, Hurwitz TD, Mahowald MW. REM sleep behavior disorder. Am J Psychiatry. 1988;145(5):652.
30. Louden MB, Morehead MA, Schmidt HS. Activation by selegiline (Eldepryle) of REM sleep behavior disorder in parkinsonism. W V Med J. 1995;91(3):101.
31. Akindele MO, Evans JI, Oswald I. Mono-amine oxidase inhibitors, sleep and mood. Electroencephalogr Clin Neurophysiol. 1970;29(1):47–56.
32. Mike ME, Kranz AJ. MAOI suppression of RBD refractory to clonazepam and other agents. Sleep Res. 1996;25:63.
33. Carlander B, Touchon J, Ondze B, Billiard M. REM sleep behavior disorder induced by cholinergic treatment in Alzheimer's disease. J Sleep Res. 1996;5(Suppl 1):28.
34. Yeh SB, Yeh PY, Schenck CH. Rivastigmine-induced REM sleep behavior disorder (RBD) in a 88-year-old man with Alzheimer's disease. J Clin Sleep Med. 2010;6(2):192–5.
35. Ringman JM, Simmons JH. Treatment of REM sleep behavior disorder with donepezil: a report of three cases. Neurology. 2000;55(6):870–1.
36. Tan L, Zhou J, Liang B, Li Y, Lei F, Du L, et al. A case of quetiapine-induced rapid eye movement sleep behavior disorder. Biol Psychiatry. 2016;79(5):e11–2. https://doi.org/10.1016/j.biopsych.2014.08.002.
37. Iranzo A, Santamaria J. Bisoprolol-induced rapid eye movement sleep behavior disorder. Am J Med. 1999;107(4):390–2.
38. Morrison I, Frangulyan R, Riha RL. Beta-blockers as a cause of violent rapid eye movement sleep behavior disorder: a poorly recognized but common cause of violent parasomnias. Am J Med. 2011;124(1):e11. https://doi.org/10.1016/j.amjmed.2010.04.023.
39. Ohayon MM, Caulet M, Priest RG. Violent behavior during sleep. J Clin Psychiatry. 1997;58(8):369–76; quiz 77.
40. Stolz S, Aldrich M. REM sleep behavior disorder associated with caffeine abuse. Sleep Res. 1991;20:341.
41. Vorona RD, Ware JC. Exacerbation of REM sleep behavior disorder by chocolate ingestion: a case report. Sleep Med. 2002;3(4):365–7.
42. Silber MH. REM sleep behavior disorder associated with barbiturate withdrawal. Sleep Res. 1996;25:371.
43. Tachibana M, Tanaka K, Hishikawa Y, Kaneko Z. A sleep study of acute psychotic states due to alcohol and meprobamate addiction. Adv Sleep Res. 1975;2:177–205.
44. Tanaka K, Kameda H, Sugita Y, Hishikawa Y. [A case with pentazocine dependence developing delirium on withdrawal (author's transl)]. Seishin Shinkeigaku Zasshi. 1979;81(4):289–99.
45. Sugano T, Suenaga K, Endo S. [Withdrawal delirium in a patient with nitrazepam addiction (in Japanese)]. Jpn J EEG EMG. 1980;8:34–5.
46. Fisher C. Physiological concomitants of unconscious mental processes: some clinical and therapeutic application of recent research on sleep and dreaming. In: Prangshvili AS, Sherozia AE, Bassin FV, editors. The unconscious: nature, functions, methods of study. Tblisi, USSR: Metsniereba Publishing House; 1978. p. 81–5.
47. Gross MM, Goodenough D, Tobin M, Halpert E, Lepore D, Perlstein A, et al. Sleep disturbances and hallucinations in the acute alcoholic psychoses. J Nerv Ment Dis. 1966;142(6):493–514.
48. Kotorii T, Nakazawa Y, Yokoyama T, Kurauchi H, Sakurada H, Ohkawa T, et al. The sleep pattern of chronic alcoholics during the alcohol withdrawal period. Folia Psychiatr Neurol Jpn. 1980;34(2):89–95.
49. Hishikawa Y, Sugita Y, Teshima Y, Iijima S, Tanaka K, Tachibana M. Sleep disorders in alcoholic patients with delirium tremens and transient withdrawal hallucinations, reevaluation of the REM rebound and intrusion theory. In: Karacan I, editor. Psychophysiological aspects of sleep: proceedings of the third International Congress of Sleep Research. Park Ridge: Noyes Medical Publishers; 1981. p. 109–22.

50. Plazzi G, Montagna P, Meletti S, Lugaresi E. Polysomnographic study of sleeplessness and oneiricisms in the alcohol withdrawal syndrome. Sleep Med. 2002;3(3):279–82.
51. Lugaresi E, Medori R, Montagna P, Baruzzi A, Cortelli P, Lugaresi A, et al. Fatal familial insomnia and dysautonomia with selective degeneration of thalamic nuclei. N Engl J Med. 1986;315(16):997–1003. https://doi.org/10.1056/NEJM198610163151605.
52. Provini F, Cortelli P, Montagna P, Gambetti P, Lugaresi E. Fatal insomnia and agrypnia excitata: sleep and the limbic system. Rev Neurol (Paris). 2008;164(8–9):692–700. https://doi.org/10.1016/j.neurol.2007.11.003.
53. Guaraldi P, Calandra-Buonaura G, Terlizzi R, Montagna P, Lugaresi E, Tinuper P, et al. Oneiric stupor: the peculiar behaviour of agrypnia excitata. Sleep Med. 2011;12(Suppl 2):S64–7. https://doi.org/10.1016/j.sleep.2011.10.014.
54. Montagna P, Lugaresi E. Agrypnia Excitata: a generalized overactivity syndrome and a useful concept in the neurophysiopathology of sleep. Clin Neurophysiol. 2002;113(4):552–60.
55. Lugaresi E, Provini F, Montagna P. The neuroanatomy of sleep. Considerations on the role of the thalamus in sleep and a proposal for a caudorostral organization. Eur J Anat. 2004;8:85–93.
56. Culebras A, Moore JT. Magnetic resonance findings in REM sleep behavior disorder. Neurology. 1989;39(11):1519–23.
57. Schenck CH, Mahowald MW. A polysomnographic, neurologic, psychiatric, and clinical outcome report on 70 consecutive cases with REM sleep behavior disorder (RBD): sustained clonazepam efficacy in 89.5% of 57 treated patients. Clev Clin J Med. 1990;57:S9–S23.
58. Kimura K, Tachibana N, Kohyama J, Otsuka Y, Fukazawa S, Waki R. A discrete pontine ischemic lesion could cause REM sleep behavior disorder. Neurology. 2000;55(6):894–5.
59. Peter A, Hansen ML, Merkl A, Voigtlander S, Bajbouj M, Danker-Hopfe H. REM sleep behavior disorder and excessive startle reaction to visual stimuli in a patient with pontine lesions. Sleep Med. 2008;9(6):697–700. https://doi.org/10.1016/j.sleep.2007.10.009.
60. Xi Z, Luning W. REM sleep behavior disorder in a patient with pontine stroke. Sleep Med. 2009;10(1):143–6. https://doi.org/10.1016/j.sleep.2007.12.002.
61. Reynolds TQ, Roy A. Isolated cataplexy and REM sleep behavior disorder after pontine stroke. J Clin Sleep Med. 2011;7(2):211–3.
62. Felix S, Thobois S, Peter-Derex L. Rapid eye movement sleep behaviour disorder symptomatic of a brain stem cavernoma. J Sleep Res. 2016;25(2):211–5. https://doi.org/10.1111/jsr.12364.
63. Zambelis T, Paparrigopoulos T, Soldatos CR. REM sleep behaviour disorder associated with a neurinoma of the left pontocerebellar angle. J Neurol Neurosurg Psychiatry. 2002;72(6):821–2.
64. Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in *SLEEP*. Sleep. 2002;25(2):120–38.
65. Jianhua C, Xiuqin L, Quancai C, Heyang S, Yan H. Rapid eye movement sleep behavior disorder in a patient with brainstem lymphoma. Intern Med. 2013;52(5):617–21. https://doi.org/10.2169/internalmedicine.52.8786.
66. Plazzi G, Montagna P. Remitting REM sleep behavior disorder as the initial sign of multiple sclerosis. Sleep Med. 2002;3(5):437–9.
67. Tippmann-Peikert M, Boeve BF, Keegan BM. REM sleep behavior disorder initiated by acute brainstem multiple sclerosis. Neurology. 2006;66(8):1277–9. https://doi.org/10.1212/01.wnl.0000208518.72660.ff.
68. Gomez-Choco MJ, Iranzo A, Blanco Y, Graus F, Santamaria J, Saiz A. Prevalence of restless legs syndrome and REM sleep behavior disorder in multiple sclerosis. Mult Scler. 2007;13(6):805–8. https://doi.org/10.1177/1352458506074644.
69. Mathis J, Hess CW, Bassetti C. Isolated mediotegmental lesion causing narcolepsy and rapid eye movement sleep behaviour disorder: a case evidencing a common pathway in narcolepsy and rapid eye movement sleep behaviour disorder. J Neurol Neurosurg Psychiatry. 2007;78(4):427–9. https://doi.org/10.1136/jnnp.2006.099515.
70. Lin FC, Liu CK, Hsu CY. Rapid-eye-movement sleep behavior disorder secondary to acute aseptic limbic encephalitis. J Neurol. 2009;256(7):1174–6. https://doi.org/10.1007/s00415-009-5067-9.

71. St Louis EK, McCarter SJ, Boeve BF, Silber MH, Kantarci K, Benarroch EE, et al. Lesional REM sleep behavior disorder localizes to the dorsomedial pons. Neurology. 2014;83(20):1871–3. https://doi.org/10.1212/WNL.0000000000000978.
72. De Barros-Ferreira M, Chodkiewicz JP, Lairy GC, Salzarulo P. Disorganized relations of tonic and phasic events of REM sleep in a case of brain-stem tumour. Electroencephalogr Clin Neurophysiol. 1975;38(2):203–7.
73. Provini F, Vetrugno R, Pastorelli F, Lombardi C, Plazzi G, Marliani AF, et al. Status dissociatus after surgery for tegmental ponto-mesencephalic cavernoma: a state-dependent disorder of motor control during sleep. Mov Disord. 2004;19(6):719–23. https://doi.org/10.1002/mds.20027.
74. Condurso R, Aricò I, Romanello G, Cervasi G, Silvestri R. Status dissociatus in multilacunar encephalopathy with median pontine lesion: a video-polygraphic presentation in "Parasomnias—Other Sleep Disorders". J Sleep Res. 2006;15:211–5. https://doi.org/10.1111/j.1365-2869.2006.00540_52.x.
75. Schenck CH, Boyd JL, Mahowald MW. A parasomnia overlap disorder involving sleepwalking, sleep terrors, and REM sleep behavior disorder in 33 polysomnographically confirmed cases. Sleep. 1997;20(11):972–81.
76. Limousin N, Dehais C, Gout O, Heran F, Oudiette D, Arnulf I. A brainstem inflammatory lesion causing REM sleep behavior disorder and sleepwalking (parasomnia overlap disorder). Sleep Med. 2009;10(9):1059–62. https://doi.org/10.1016/j.sleep.2008.12.006.
77. Piette T, Mescola P, Uytdenhoef P, Henriet M, Vanderkelen B, Jacquy J, et al. A unique episode of REM sleep behavior disorder triggered during surgery for Parkinson's disease. J Neurol Sci. 2007;253(1–2):73–6. https://doi.org/10.1016/j.jns.2006.11.005.
78. Vale TC, Fernandes do Prado LB, do Prado GF, Povoas Barsottini OG, Pedroso JL. Rapid eye movement sleep behavior disorder in paraneoplastic cerebellar degeneration: improvement with immunotherapy. Sleep. 2016;39(1):117–20. https://doi.org/10.5665/sleep.5330.
79. Shinno H, Kamei M, Maegawa T, Satake A, Inami Y, Horiguchi J, et al. Three patients with cancer who developed rapid-eye-movement sleep behavior disorder. J Pain Symptom Manage. 2010;40(3):449–52. https://doi.org/10.1016/j.jpainsymman.2010.01.016.
80. Compta Y, Iranzo A, Santamaria J, Casamitjana R, Graus F. REM sleep behavior disorder and narcoleptic features in anti-Ma2-associated encephalitis. Sleep. 2007;30(6):767–9.
81. Adams C, McKeon A, Silber MH, Kumar R. Narcolepsy, REM sleep behavior disorder, and supranuclear gaze palsy associated with Ma1 and Ma2 antibodies and tonsillar carcinoma. Arch Neurol. 2011;68(4):521–4. https://doi.org/10.1001/archneurol.2011.56.
82. Liguori R, Vincent A, Clover L, Avoni P, Plazzi G, Cortelli P, et al. Morvan's syndrome: peripheral and central nervous system and cardiac involvement with antibodies to voltage-gated potassium channels. Brain. 2001;124(Pt 12):2417–26.
83. Cochen V, Arnulf I, Demeret S, Neulat ML, Gourlet V, Drouot X, et al. Vivid dreams, hallucinations, psychosis and REM sleep in Guillain-Barre syndrome. Brain. 2005;128(Pt 11):2535–45. https://doi.org/10.1093/brain/awh585.
84. Fernandez-Arcos A, Iranzo A, Serradell M, Gaig C, Santamaria J. The clinical phenotype of idiopathic rapid eye movement sleep behavior disorder at presentation: a study in 203 consecutive patients. Sleep. 2016;39(1):121–32. https://doi.org/10.5665/sleep.5332.
85. Schenck CH. Expanded insights into idiopathic REM sleep behavior disorder. Sleep. 2016;39(1):7–9. https://doi.org/10.5665/sleep.5300.
86. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington, DC; 2013.
87. Ross RJ, Ball WA, Dinges DF, Kribbs NB, Morrison AR, Silver SM, et al. Motor dysfunction during sleep in posttraumatic stress disorder. Sleep. 1994;17(8):723–32.
88. Hefez A, Metz L, Lavie P. Long-term effects of extreme situational stress on sleep and dreaming. Am J Psychiatry. 1987;144(3):344–7. https://doi.org/10.1176/ajp.144.3.344.
89. Husain AM, Miller PP, Carwile ST. REM sleep behavior disorder: potential relationship to post-traumatic stress disorder. J Clin Neurophysiol. 2001;18(2):148–57.

90. Wallace DM, Shafazand S, Ramos AR, Carvalho DZ, Gardener H, Lorenzo D, et al. Insomnia characteristics and clinical correlates in Operation Enduring Freedom/Operation Iraqi Freedom veterans with post-traumatic stress disorder and mild traumatic brain injury: an exploratory study. Sleep Med. 2011;12(9):850–9. https://doi.org/10.1016/j.sleep.2011.06.004.
91. Mysliwiec V, O'Reilly B, Polchinski J, Kwon HP, Germain A, Roth BJ. Trauma associated sleep disorder: a proposed parasomnia encompassing disruptive nocturnal behaviors, nightmares, and REM without atonia in trauma survivors. J Clin Sleep Med. 2014;10(10):1143–8. https://doi.org/10.5664/jcsm.4120.
92. Mysliwiec V, Brock MS, Creamer JL, O'Reilly BM, Germain A, Roth BJ. Trauma associated sleep disorder: a parasomnia induced by trauma. Sleep Med Rev. 2018;37:94–104. https://doi.org/10.1016/j.smrv.2017.01.004.
93. Manni R, Ratti PL, Terzaghi M. Secondary "incidental" REM sleep behavior disorder: do we ever think of it? Sleep Med. 2011;12(Suppl 2):S50–3. https://doi.org/10.1016/j.sleep.2011.10.011.
94. Jennum P, Mayer G, Ju YE, Postuma R. Morbidities in rapid eye movement sleep behavior disorder. Sleep Med. 2013;14(8):782–7. https://doi.org/10.1016/j.sleep.2012.11.002.
95. Frauscher B, Gschliesser V, Brandauer E, Marti I, Furtner MT, Ulmer H, et al. REM sleep behavior disorder in 703 sleep-disorder patients: the importance of eliciting a comprehensive sleep history. Sleep Med. 2010;11(2):167–71. https://doi.org/10.1016/j.sleep.2009.03.011.