JCSM
Journal of Clinical Sleep Medicine

CASE REPORTS

REM Sleep Behavior Disorder—Psychiatric Presentations: A Case Series from the United Kingdom

Irshaad Osman Ebrahim M.B., Ch.B, MRCPsych; Kevin Wayne Peacock

The London Sleep Centre, London, United Kingdom

Rapid eye movement sleep behavior disorder (RBD) has rarely been associated with a psychiatric condition. We report a series of cases of RBD presenting as psychiatric disorders. These patients were assessed at a specialist sleep disorders center and investigated using polysomnography and, where appropriate, magnetic resonance imaging of the brain and neuropsychological tests. These cases of RBD highlight the varying presentations and causes of RBD that may involve psychiatrists, sleep specialists, and primary care physicians. These include idiopathic RBD presenting as depression, antidepressant-induced RBD, and a patient with undiagnosed Parkinson disease presenting with RBD. There is an increasing body of knowledge about RBD. At least 10% of patients with RBD are likely to present with psychiatric symptoms. It is essential that the condition is recognised and distinguished from other causes of sleep interruption. After recognizing the disorder, it is essential that the clinician undertake a thorough assessment, including a sleep history and formal investigation of sleep patterns at a specialized unit.

Key Words: REM Sleep Behavior Disorder, psychiatry, Parkinson's disease, depression, anti-depressants

Citation: Ebrahim IO; Peacock KW. REM sleep behavior disorder—psychiatric presentations: a case from the United Kingdom. *J Clin Sleep Med* 2005;1(1):43-47

Rapid eye movement (REM) sleep behavior disorder (RBD) is a REM-stage parasomnia characterized by a history of excessive nocturnal motor activity, which usually involves the violent enactment of dreams, associated with the absence of muscle atonia during REM sleep. In the 17 years since the initial description, there have been more than 300 cases reported in the literature, the majority from 3 large case series.[1-5]

The exact prevalence of RBD is unclear, but almost 90% of patients are men aged 52 to 61 years at the time of presentation, and, in about a quarter of these patients, there is a history of sleeptalking, shouting, and limbs twitching or jerking without complex behaviors that may have preceded the development of RBD by many years, with a mean of 22 years (range: 2 to 48 years) While transient (acute) RBD can be seen after taking certain drugs or during drug withdrawal, the chronic type is usually idiopathic or associated with an underlying degenerative neurologic condition. RBD may manifest as a subclinical (asymptomatic) entity and be a chance finding on polysomnography (PSG). Characteristic PSG findings include the loss of normal REM atonia, or increased phasic electromyographic (EMG) activity during REM sleep, or both. The literature suggests that RBD is effectively treated with clonazepam in most cases.[3]

The classification and causes of RBD are shown in Table 1. Psychiatric disorders or their treatment have been causally associated with RBD onset in approximately 10% of patients.[3] The most common psychiatric associations are with alcohol withdrawal, stimulant abuse, and treatment with psychotropic medication (fluoxetine, venlafaxine, and tricyclic antidepressants) and an association with major stressful events.[6-8]

In the United Kingdom, there has been a single case report of RBD associated with depression and cognitive decline.[9] We report here a series of 4 cases of RBD presenting as psychiatric disorders and discuss the potential role of the psychiatrist, sleep medicine specialists, and primary care physicians in patients with RBD.

CASE HISTORIES

Case History 1: Patient PS

A 45-year-old company director was referred by her general practitioner to the London Sleep Centre for assessment and treatment of a depressive episode that had recently recurred. She was treated for depression with fluoxetine 6 years previously and had a 10-year history of sporadic nocturnal enuresis. Recent screening blood tests and urologic investigations were all normal. At the initial assessment, she presented with a history of worsening symptoms of depression over the previous 6 months associated with gastrointestinal symptoms, particularly constipation. She complained of increasing frequency of her nocturnal enuresis, and this was associated with vivid dreams of urinating in the toilet. A detailed sleep history uncovered the following symptoms: unrefreshing sleep, daytime tiredness and sleepiness on most days, a history of snoring since childhood, excessive movement while asleep, and on occasion sitting up with a start. The timing of these movements varied throughout the night. She had a clear recollection of her dreams. The history from her husband confirmed that the patient occasionally kicked and lashed out with her hands while asleep and, particularly, during the second half

Disclosure Statement
This was not an industry supported study. Dr. Ebrahim and Mr. Peacock have indicated no financial conflicts of interest.

Submitted for publication October 2004
Accepted for publication November 2004
Address correspondence to: Dr. Irshaad Ebrahim, Consultant Neuropsychiatrist, The London Sleep Centre, 137 Harley Street, London, W1G 6BF; E-mail: info@londonsleepcentre.com; Web: www.londonsleepcentre.com

Downloaded from jcsm.aasm.org by 217.138.206.86 on March 25, 2022. For personal use only. No other uses without permission.
Copyright 2022 American Academy of Sleep Medicine. All rights reserved.

of the night. He also confirmed the history of nocturnal enuresis during some of these episodes, as well as the history of snoring and of possible witnessed apneic episodes. Apart from a brief period, during her late teens, of recreational use of cocaine and ecstasy, there was no significant history of harmful use of illicit drugs or alcohol. PS was treated as an outpatient for a depressive episode in 1996 over a 2-year period. She was initially prescribed paroxetine, to which she was intolerant, and was subsequently successfully treated with fluoxetine 20 mg daily. She was not on any regular medication in the 6 months prior to her referral. On self-report measures, she scored 26 on the Beck Depression Inventory, indicating moderately severe depressive symptoms, and 11 on the Epworth Sleepiness Scale, indicating clinically significant excessive daytime sleepiness.[10,11]

Table 1—Causes of REM Sleep Behavior Disorder

REM sleep behavior disorder	Etiology
Acute	
Withdrawal	Alcohol Meprobamate Pentazocine Nitrazepam Rapid withdrawal of tricyclic antidepressants
Intoxication	Biperiden Tricyclic antidepressants Monoamine oxidase inhibitors Caffeine Mirtazapine
Chronic	
Idiopathic	
Traumatic	
Toxic-metabolic	Tricyclic antidepressants Fluoxetine Venlafaxine Selegeline Anticholinergics
Vascular	Subarachnoid hemorrhage Vasculitis Ischemia
Tumors	Acoustic neuroma Pontine neoplasms
Infectious or postinfectious	Guillain-Barré syndrome
Degenerative	Parkinson disease Multiple system atrophy Dementia with Lewy bodies Progressive supranuclear palsy Shy-Dräger syndrome Olivopontocerebellar degeneration Amyotrophic lateral sclerosis Anterior/dorsomedial thalamic syndrome (fatal familial insomnia) Dementia, including Alzheimer disease and corticobasal degeneration Normal pressure hydrocephalus Multiple sclerosis and other demyelinating disorders
Developmental, congenital, familial	Familial or congenital REM sleep behavior disorder Narcolepsy Tourette syndrome Group A xeroderma pigmentosum Mitochondrial encephalomyopathy

REM refers to rapid eye movement.

In addition to the clear presentation of a depressive episode, we considered the following in our differential diagnosis—nocturnal seizures; a parasomnia, possibly RBD; and obstructive sleep apnea (Table 2). An extended-montage nocturnal PSG, performed according to Lapierre's criteria,[12] revealed a normal sleep onset of 10 minutes, a shortened REM latency of 34 minutes (in keeping with depression), total sleep time of 490 minutes (stage 1, 12.5%; stage 2, 38.1%; stage 3, 5.2%; stage 4, 8.7%, REM, 28.6%; REM without atonia, 9.4%;), alpha intrusion in all stages of sleep, excessive spindling in stage 2 sleep, increased REM density, and absence of REM atonia in submental and limb EMG leads during phasic REM periods. There was no evidence of obstructive sleep apnea, cardiac abnormality, or epileptiform activity. The final diagnosis of idiopathic RBD comorbid with a depressive episode was reached based on the above findings.

Case History 2: Patient BR

A 58-year-old retired school teacher was referred to the London Sleep Centre by his general practitioner for worsening symptoms of depression, snoring and "thrashing about in his sleep." At his initial appointment, BR complained of worsening symptoms of depression over the previous 2 years and that these had not improved even though his general practitioner had twice changed his antidepressant medication. He was more concerned about his nocturnal symptoms of 18 months duration (confirmed by a collateral history from his wife) of frightening vivid dreams, shouting out, and swearing during the night. The most distressing symptoms involved his uncharacteristic aggression during these periods in which his wife reported him kicking her, punching out, and banging his head on the wall. BR recalled these actions and the dream content with a high level of clarity. The symptoms had become an issue of safety and risk—the patient and his wife had adapted their lifestyles to prevent serious injury—she, by moving into a separate room, and he, by tying himself to the bedpost at night with a rope. There was no family history of psychiatric or neurologic disorder and no childhood history of sleep disorder. BR was initially diagnosed with depression, following a back injury 5 years earlier, and required a short inpatient admission. He felt unable to cope with his daily occupational activities and subsequently retired on grounds of ill health. He was treated with dothiepin 150 mg per day for 3 years, and, when his depression recurred, he was started on paroxetine 20 mg for day for the past 2 years. His affective symptoms continued, and his paroxetine dose was increased to 30 mg per day. He reports that his nocturnal behaviors appeared at around the time of the dosage adjustment. His depression did not improve and his general practitioner substituted venlafaxine for the paroxetine. This improved his mood slightly, but his nocturnal behaviors continued. At the time of his initial consultation, he was taking Venlafaxine 75 mg per day in 2 divided doses. He scored 24 on the Beck Depression Inventory, placing him in the moderate to severely depressed

Downloaded from jcsm.aasm.org by 217.138.206.86 on March 25, 2022. For personal use only. No other uses without permission.
Copyright 2022 American Academy of Sleep Medicine. All rights reserved.

range, and his Epworth Sleepiness Scale score of 2 was normal. On the Mental State Examination, he fulfilled the International Classification of Diseases-10 criteria for depressive episode, moderate, without somatic syndrome.[13] BR underwent video PSG with an extended montage.[12] Sleep onset was slightly delayed at 36 minutes, and the first REM period was missed due to spontaneous arousals. Total sleep time was 322 minutes, and there was a total absence of stage 3 and stage 4 sleep (stage 1, 28%; stage 2, 52%; REM, 20%) At 5:05 AM, the technician observed some facial movements and vocalizations, which were followed at 5:22 AM by violent leg jerks and kicking. When awakened by the technician, BR reported that he was dreaming of being in a fight in a pub.

Case History 3: Patient AH

This 61-year-old corporate executive was referred to the London Sleep Centre by his general practitioner for assessment of a possible depression and sleep disturbances. He had been under significant stress at home with the premature death of his daughter in a road traffic accident the year before. AH attended the first appointment with his wife and presented with a 6-month history of progressively worsening nocturnal behaviors. These started with vivid dreams and had progressed to him vocalizing during the dreams. In the 3 weeks prior to his referral, he had started acting out his dreams and, on one occasion, had hit out at his wife during one of his episodes. His wife now slept in a separate room. He reported worry and anxiety over these symptoms but denied being depressed. The patient's wife added that AH also kicked out during these periods and that the timing of the behaviors usually occurred in the second half of the night. There was also a history of snoring for the previous 7 years but no history of witnessed apneas. There was no previous history of a sleep disorder or head injury, no family history of neurologic or psychiatric disorder, and no significant alcohol and drug history. AH scored within the normal range on the Beck Depression Inventory and Epworth Sleepiness Scale. His mental state was normal, and cognitive testing was noncontributory. A magnetic resonance imaging study of the brain and a routine electroencephalogram were both normal. Apart from a slightly raised cholesterol level of 5.8 mmol/L (normal range: < 5.2 mmol/L), his blood tests were normal. Video PSG showed a normal sleep onset but with highly fragmented sleep architecture and a delayed REM onset at 127 minutes. The sleep period was 476 minutes, of which total sleep time was 336 minutes (stage 1, 17.6%; stage 2, 44.4%; stage 3, 13.3%; stage 4, 5.4%; REM, 19.4%). There were frequent spontaneous arousals and mild snoring but an absence of respiratory arousals and no evidence of obstructive sleep apnea. At 3:40 AM, AH was noted to be jerking and kicking, and half an hour later he lashed out violently with his right arm, hitting the bedpost and waking himself up. He reported a violent dream in which he was protecting himself from attackers.

Table 2—Differential Diagnosis of REM Sleep Behavior Disorder

Disorders of Arousal	
	• Confusional arousals
	• Sleepwalking
	• Sleeptalking
	• Obstructive sleep apnea
	• Periodic limb movement disorder
	• Gastroesophageal reflux
	• Nocturnal seizures
Psychiatric Disorders	
	• Posttraumatic stress disorder
	• Nocturnal panic disorder
	• Dissociative disorder
	• Malingering
Parasomnia 'overlap' syndrome	
Rhythmic movement disorder	

REM refers to rapid eye movement.

Case History 4: Patient MM

MM, a 64-year-old retired stockbroker was referred, at his request, by his consultant psychiatrist for assessment for a possible parasomnia. His medical history included a diagnosis of Grave's disease, treated surgically 15 years previously; atrial fibrillation of a similar duration; and depression for the past 5 years. His medication at the time of referral included atenolol, 50 mg daily; citalopram, 20 mg daily; and warfarin, 6 mg daily. There had been no change in his medication for the year prior to the referral. MM complained of a 6-month history of worsening nocturnal sleep, vivid dreams, suddenly sitting up in bed, sleep talking, and excessive movements at night. In addition, he reported a 2-year history of worsening excessive sleepiness during the day and 1 episode of falling asleep while driving. Collateral history from his bedpartner of 25 years confirmed the sudden onset—6 months previously—of excessive vocalizations and swearing at about 4 AM; 2 episodes of getting out of bed and walking to the door; and, more seriously, 1 occasion, a week prior to consultation, of punching and attempting to strangle his bedpartner. Since that night, they have lived in separate houses, his bedpartner having moved back in with her mother for fear of her personal safety. On further questioning, it emerged that MM had a 20-year history of excessive movements at night, particularly of his lower limbs, and a 15-year history of bruxism, for which he used a tooth guard. Further sleep history revealed a 5-year history of snoring and a history of witnessed apneas. MM had a positive family history of depression (his mother), suicide (a maternal uncle), and problems with alcohol (his father). His parents were divorced when he 9 years old, and he was sent to boarding until he finished his schooling. MM was initially diagnosed with depression at the age of 42 years, at which time he presented to his general practitioner and was given tricyclic antidepressants for a 1-year period. Two years after this episode, he experienced a severe recurrence of depression accompanied by a serious paracetamol overdose that required a 2-month admission to his local psychiatric facility. He has been on a variety of antidepressants since that admission and was commenced on citalopram 20 mg per day 2 years prior to his referral. He scored within the moderately to severely depressed range on the Beck Depression Inventory with a score of 21. His score of 17 on the Epworth Sleepiness Scale placed him in the "severely sleepy" range. The Mental State Examination revealed an elderly male with some degree of psychomotor retardation, a lack of facial movement, and a slightly vacant stare. His speech was within the normal range though somewhat slowed, and he described all the core features of a depressive episode. He was not suicidal, and cognitive screening did not reveal any gross impairment. On physical examination,

Downloaded from jcsm.aasm.org by 217.138.206.86 on March 25, 2022. For personal use only. No other uses without permission.
Copyright 2022 American Academy of Sleep Medicine. All rights reserved.

he had a mild, asymmetrical, bilateral pill-rolling tremor present at rest in his hands and mild cogwheel rigidity in both his upper limbs. No other signs were elicited. Full blood count and thyroid function and liver function tests were all within the normal range for age. Video PSG revealed a rapid sleep onset of 3 minutes followed by central apneas that caused arousals and desaturations, giving way to periodic leg movements with a movement index of 15 per hour. Total sleep time was 287 minutes (stage 1, 11%; stage 2, 52%; stage 3, 20%; stage 4, 0%; REM, 12%), sleep efficiency was decreased at 63.6%, and REM latency was slightly short at 56.5 minutes. He had an apnea-hypopnea index of 32. There was significant loss of REM atonia, and the patient was observed to be punching and moving his arms violently on several occasions between 5:05 AM and 6:30 AM. He recalled a violent dream when awoken by the technician.

DISCUSSION

The cases we have presented here highlight several issues of relevance to psychiatrists, sleep medicine specialists, and primary care physicians. The effects of psychiatric medication on sleep and, in particular, the potential of some psychotropic agents to precipitate RBD is of daily clinical relevance as demonstrated by case 2 (patient BR). In this instance, there was a relatively clear temporal relationship between the onset of symptoms and change in the dosage of medication. The role of serotonin in the pathophysiology of RBD is not fully understood but may relate to the actions of serotonin and possibly noradrenaline on the striatal dopamine transporter.[14] The report of an almost immediate improvement in his symptoms after removal of all his antidepressant medication and the lack of evidence for another cause clearly points to an iatrogenic cause for his RBD.

In case 1 (patient PS), we report, for the first time, comorbid depression and RBD presenting as nocturnal enuresis in a young woman. RBD is relatively easy to treat—clonazepam 0.5 mg to 2.0 mg at night relieves the symptoms in the vast majority (approximately 90%) of patients.[15] With this patient, the comorbid depressive illness posed a challenge. Specific selective serotonin reuptake inhibitors (such as fluoxetine), selective noradrenaline reuptake inhibitors, and tricyclic antidepressants have all been implicated in precipitating acute RBD.[3] Recent findings suggest that a decrease in striatal dopamine transporters may be causally linked to the symptoms of RBD.[16] Bupropion, which is licensed for the treatment of smoking cessation in the United Kingdom and for the treatment of depression in the United States, has been shown to inhibit the reuptake of dopamine by acting on the striatal dopamine transporter, thereby increasing synaptic dopamine.[14] It has been suggested that, because of its prodopaminergic actions, bupropion may be the antidepressant of choice for treating depression associated with RBD.[3] We used a combination of bupropion and clonazepam and monitored the patient over the subsequent 6 months. At 3 months, her Beck Depression Inventory score had returned to a subclinical level, and repeat video PSG at 6 months after treatment was within normal limits. There has been no recurrence of her symptom of nocturnal enuresis.

There is a close relationship between neurodegenerative disorders and RBD, particularly the synucleinopathies—Parkinson disease, multiple system atrophy, and dementia of the Lewy body type.[17] RBD may form part of the clinical picture of an established disorder, or it may herald the onset of a disorder. It is becoming established that a diagnosis of idiopathic RBD may be a risk factor for the development of a neurodegenerative disorder such as Parkinson's disease or multiple system atrophy. In cases 3 and 4 (patients AH and MM), these points are clearly demonstrated—case 3 had a diagnosis of idiopathic RBD, and in many regards he has a typical clinical presentation. His symptoms have been effectively controlled with 1 mg of clonazepam at night. A thorough neurologic examination, including magnetic resonance imaging, was found to be negative. The current understanding about the natural history of idiopathic RBD implies a 40% probability of developing a neurodegenerative disorder. After the patient underwent a session of education and counselling about the possible progression to developing a neurodegenerative disorder, it was agreed that he will return at regular intervals for monitoring of his neurologic and cognitive state. There are dilemmas regarding disclosure of risk— our view is that we will provide patients who have idiopathic RBD with access to all the current literature on the disorder and its prognosis and to assist them with appropriate support and psychological and medical assistance, where required.

Unlike case 3, case 4 presented with symptoms suggestive of significant depression and was found to have signs of parkinsonism on physical examination. He was subsequently referred to a neurologist and commenced on antiparkinsonian medication. His depression was treated with bupropion, and clonazepam was effective in reducing his nocturnal sleep behaviors. In this instance, RBD heralded the onset of Parkinson disease.

There is an increasing body of knowledge about RBD. At least 10% of patients with RBD are likely to present to psychiatrists. It is essential that the condition is recognized and distinguished from other causes of sleep interruption. After recognition, it is essential to undertake a thorough assessment, including a sleep history and formal investigation of sleep patterns at a specialized unit. We have presented these cases in the anticipation that it will stimulate our colleagues to ask about symptoms at night and thereby benefit patients who have diagnosable and, more importantly, easily treatable disorders of sleep associated with complex behaviors. A possible future role of the psychiatrist, sleep medicine specialists, and primary care physicians may be as gatekeepers for the early detection of patients with neurodegenerative disorders, particularly Parkinson's disease, multiple system atrophy, and dementia with Lewy bodies.

REFERENCES

1. American Sleep Disorders Association. International Classification of Sleep Disorders: Diagnostic and Coding Manual. New York: Raven Press; 1990.
2. Schenck CH. Bundlie SR. Ettinger MG. Mahowald MW. Chronic behavioral disorders of human REM sleep: A new category of parasomnia. Sleep 1986;9:293-308.
3. Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. Sleep 2002;25:120-38.
4. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. Brain 2000;123:331-9.
5. Sforza E, Krieger J, Petiau C. REM sleep behavior disorder: clinical and physiopathological findings. Sleep Med Rev 1997;1:57-69.
6. Schenck CH, Hurwitz TD, Mahowald MW. REM sleep behavior

Downloaded from jcsm.aasm.org by 217.138.206.86 on March 25, 2022. For personal use only. No other uses without permission.
Copyright 2022 American Academy of Sleep Medicine. All rights reserved.

disorder. Am J Psychiatry 1988;145:652-9.
7. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatry 1989;146:1166-73.
8. Hefez A, Metz L, Lavie P. Long-term effects of extreme situational stress on sleep and dreaming. Am J Psychiatry 1987;144:344-7.
9. Clarke NA, Williams AJ, Kopelman MD. Rapid eye movement sleep disorder, depression and cognitive impairment. Br J Psychiatry 2000;176:189-92.
10. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71,
11. Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 1991;14:540-5.
12. Lapierre O, Montplaisir J. Polysomnographic features of REM sleep behavior disorder: development of a scoring method. Neurology 1992;42:1371-4.
13. Clinical descriptions and diagnostic guidelines. In: International Classification of Diseases, 10th rev. Geneva: World Health Organization; 1992.
14. Learned-Coughlin SM, Bergstrom M, Savitcheva I, Ascher J, Schmith VD, Langstrom B. In vivo activity of bupropion at the human dopamine transporter as measured by positron emission tomography. Biol Psychiatry 2003;54:800-5.
15. Schenck CH, Bundlie SR, Patterson AL, Mahowald, MH. Rapid eye movement sleep behavior disorder. A treatable parasomnia affecting older adults. JAMA 1987;257:1786-9.
16. Eisensehr I, Linke R Tatsch K, et al. Increased muscle activity during rapid eye movement sleep correlates with decrease of striatal presynaptic dopamine transporters. IPT and IBZM SPECT imaging in subclinical and clinically manifest idiopathic REM sleep behavior disorder, Parkinson's disease, and controls. Sleep 2003;26: 507-12.
17. Boeve BF, Silber MH, Ferman TJ, Lucas JA, Parisi JE. Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord 2001;16:622-30.

Downloaded from jcsm.aasm.org by 217.138.206.86 on March 25, 2022. For personal use only. No other uses without permission.
Copyright 2022 American Academy of Sleep Medicine. All rights reserved.

Time to Take a Closer Look…

…at Actiwatch®

The Ideal Actigraphy Monitor for Your Sleep Lab

Accurate, objective knowledge of patient sleep history before, during and after therapy has never been easier, more reliable or more affordable.

- ✦ New Actigraphy CPT Code
- ✦ New Updated Software
- ✦ Special Introductory System Pricing

MINI MITTER

Mini Mitter Co., Inc.
20300 Empire Avenue, Bldg. B-3
Bend, OR 97701 • USA

Telephone: (800) 685-2999 or (541) 322-7272 Email: mm@minimitter.com
www.minimitter.com

Actiwatch® is a registered trademark of Mini-Mitter Co., Inc.

Downloaded from jcsm.aasm.org by 217.138.206.86 on March 25, 2022. For personal use only. No other uses without permission.
Copyright 2022 American Academy of Sleep Medicine. All rights reserved.