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Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases

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Summary

We describe demographic, clinical, laboratory and aetiological findings in 93 consecutive patients with rapid eye movement (REM) sleep behaviour disorder (RBD), which consists of excessive motor activity during dreaming in association with loss of skeletal muscle atonia of REM sleep. The patients were seen at the Mayo Sleep Disorders Center between January 1, 1991 and July 31, 1995. Eighty-one patients (87%) were male. The mean age of RBD onset was 60.9 years (range 36–84 years) and the mean age at presentation was 64.4 years (37–85 years). Thirty-two per cent of patients had injured themselves and 64% had assaulted their spouses. Subdural haematomas occurred in two patients. Dream content was altered and involved defence of the sleeper against attack in 87%. The frequency of nocturnal events decreased with time in seven untreated patients with neurodegenerative disease. MRI or CT head scans were performed in 56% of patients. Although four scans showed brainstem pathology, all of these patients had apparently unrelated neurodegenerative diseases known to be associated with RBD. Neurological disorders were present in 57% of patients; Parkinson's disease, dementia without parkinsonism and multiple system atrophy accounted for all but 14% of these. RBD developed before parkinsonism in 52% of the patients with Parkinson's disease. Five of the 14 patients with multiple system atrophy were female, and thus the strong male predominance in RBD is less evident in this condition. Psychiatric disorders, drug use or drug withdrawal were rarely causally related to RBD. Clonazepam treatment of RBD was completely or partially successful in 87% of the patients who used the drug. We conclude that RBD is a well-defined condition and that descriptions from different centres are fairly consistent. It is commonest in elderly males and may result in serious morbidity to patients and bed partners. There is a strong relationship to neurodegenerative disease, especially Parkinson's disease, multiple system atrophy and dementia, and neurologists should explore the possibility of RBD in patients with these conditions. RBD symptoms may be the first manifestations of these disorders and careful follow-up is needed. Neuroimaging is unlikely to reveal underlying disorders not suspected clinically. We confirm the effectiveness of clonazepam, but note that attention to the safety of the bed environment may be sufficient for patients with contraindications to the drug.

Keywords: REM sleep behaviour disorder; Parkinson's disease; dementia; dreams

Abbreviations: RBD = REM sleep behaviour disorder; MSLT = Multiple Sleep Latency Test; PSG = polysomnography; REM = rapid eye movement

Introduction

Rapid eye movement (REM) sleep behaviour disorder (RBD) is characterized by loss of the normal voluntary muscle atonia during REM sleep, associated with excessive motor activity while dreaming (Mahowald and Schenck, 1994). Behaviours result frequently in injuries to the patient or sleeping partner (Schenck and Mahowald, 1990). Japanese investigators first described the condition in patients with alcohol withdrawal, using the term 'stage I-REM with tonic EMG' (Tachibana *et al*., 1975). Similar findings were reported in patients with olivopontocerebellar atrophy (Shimizu *et al*., 1981; Quera Salva and Guilleminault, 1986), and later work has confirmed the association with neurodegenerative disorders (Schenck and Mahowald, 1996*a*). A model of RBD in cats (Hendricks *et al*., 1982) indicates that bilateral pontine tegmental lesions

of varying sizes and locations can produce paradoxical (REM) sleep behaviours, ranging from minimal movements to violent attack behaviour.

Much of our knowledge of the human disorder comes from the case series of Schenck and colleagues (Schenck and Mahowald, 1990, 1996*a*; Schenck *et al*., 1993), who first named the condition (Schenck *et al*., 1986, 1987). Apart from a brief description in a review article of a series of 52 patients (Sforza *et al*., 1997), no other large general series of cases of RBD has been published. We thus felt that a report of our centre's experience would be of interest and describe here the demographic, clinical and laboratory findings in 93 patients with RBD. Our aims were to confirm or refute the features of RBD described by Schenck and colleagues, and in particular, to examine the relationship between RBD and neurological disease.

Patients and methods

All patients with a diagnosis of RBD seen at the Mayo Sleep Disorders Center between January 1, 1991 and July 31, 1995 were identified from the Mayo Clinic computerized record system. RBD was defined according to standard criteria (Mahowald and Schenck, 1994) (excessive phasic or tonic EMG activity during recorded REM sleep, a history of injurious or disruptive sleep behaviour or documentation of abnormal behaviour during REM sleep in the laboratory, and an absence of EEG epileptiform activity during REM sleep). The study was approved by the Mayo Institutional Review Board.

Records were reviewed and the data recorded and tabulated. As this was a retrospective study, complete information was not always available for each patient; where information was incomplete the patient denominator is noted in the results. Historical data was compiled from a standard sleep questionnaire completed by all patients and a history elicited by a physician at the initial consultation. Polysomnography (PSG) was performed according to a standard clinical protocol with recording of EEG (a minimum of the following three derivations: Fz–Cz, Cz–Oz, C3–A2, but often with additional derivations to assess for epileptiform activity), EOG, ECG, oronasal airflow, thoracoabdominal movement by impedance plethysmography, upper airway sound and oxyhaemoglobin saturation. All patients had surface EMG recorded from submental and anterior tibial muscles, and the majority also from the extensor digitorum communis muscles. Data were recorded either on analogue polygraphs or on digital equipment. Split-screen or time synchronized video recordings were performed. When sleep disordered breathing was noted, a split-night protocol was followed, with nasal continuous positive airway pressure applied in the second half of the study. Scoring of sleep stages followed standard methods (Rechtschaffen and Kales, 1968).

Eighty-three patients (89%) underwent neurological examinations. Associated neurological disorders were diagnosed clinically by consultant neurologists at the clinic; the authors reassessed the diagnoses during the record review. In general, a diagnosis of Parkinson's disease required two or more extrapyramidal signs (rest tremor, bradykinesia, rigidity, postural instability) with a therapeutic response to levodopa. Multiple system atrophy was diagnosed according to standard criteria (Consensus Committee of the American Autonomic Society and the American Academy of Neurology, 1996). Dementia was diagnosed following neuropsychometric testing. A diagnosis of narcolepsy required the Multiple Sleep Latency Test (MSLT) to confirm excessive daytime sleepiness in association with either a history of cataplexy, or two or more sleep-onset REM sleep periods on the MSLT. Twenty-seven patients were assessed by psychiatrists or psychologists at the Clinic because of suspicion of psychiatric illness, and active diagnoses were based on their opinions. Past psychiatric diagnoses were based on the patients' history. It was not possible to apply formal psychiatric criteria retrospectively.

Results

Demographic features (Table 1)

Gender and age distributions are summarized in Table 1. Seventy-one patients (76%) resided outside Minnesota. A past history of parasomnias (all sleep walking) was obtained in five of 74 patients (7%).

Clinical features (Table 1)

In 92 patients, abnormal nocturnal behaviour was reported by observers to occur at home. In one patient, however, such behaviour was observed only during PSG. Nocturnal events were reported to occur between once every 3 months and several times a night. Information about changes in the frequency of events was available in 49 patients; the frequency remained stable in 26, increased in 16 and decreased in seven patients prior to the administration of therapy. All seven with decreasing frequency had a neurodegenerative disease (three multiple system atrophy, three Parkinson's disease and one dementia; 26% of patients with neurodegenerative disease).

In all but 10 patients the abnormal behaviours occurred in bed or resulted in falling out of bed. The most common behaviours consisted of flailing and punching the arms, kicking and vocalization. The remaining 10 patients (11%) at times exhibited sleep walking or nocturnal wandering in addition to the more typical activities in bed. Thirty patients (32%) reported injuries to themselves during sleep (17 while falling out of bed, 15 by striking or bumping into furniture or walls). Injuries included lacerations or ecchymoses to the head or face in at least 10 patients, while other injuries involved the limbs or trunk. One patient lacerated his hands grabbing venetian blinds, one patient kicked a hole in the bedroom wall and one attempted to leap through a window. Also, one patient fired an unloaded gun, while another attempted to set fire to his bed. Subdural haematomas occurred

Table 1 *Demographic details and numbers or percentages of patients showing various clinical features of RBD*

Gender (n = 93)	81 (87%) male; 12 (13%) female
Mean age of onset (years) (n = 56)	60.9 (range 36–84)
Mean age at diagnosis (years) (n = 93)	64.4 (range 37–85)
Past history of parasomnias (n = 74)	5 (7%)
Family history of parasomnias (n = 64)	5 (5%)
Injuries to self (n = 93)	30 (32%)
Assaults on sleeping partner (n = 83)	53 (64%)
Injuries to sleeping partner (n = 83)	13 (16%)
Dreams associated with RBD activity (n = 67)	62 (93%)
Dream content described (n = 67)	37 (55%)
Defence against attack by people	57%
Defence against attack by animals	30%
Adventure dreams	9%
Sports dreams	2%
Aggression by the dreamer	2%
Reported sleep disruption (n = 70)	49 (70%)
Reported daytime sleepiness (n = 82)	57 (63%)
Identified causes (n = 57)	39 (68%)
OSA (RDI >10/h)	21
PLMD (PLMI >20/h)	26
Narcolepsy	4
CSA (RDI >10/h)	2
Possible causes (n = 57)	11 (19%)
Neurodegenerative disorder	9
Polysubstance abuse	2

OSA = obstructive sleep apnoea syndrome; RDI = respiratory disturbance index; PLMD = periodic limb movement disorder; PLMI = periodic limb movement index; CSA = central sleep apnoea syndrome.

in two patients, one related to motor activity in sleep and one of uncertain cause in a patient with Parkinson's disease. Fifty-three spouses (64% of 83 patients with sleeping partners) reported being assaulted; 13 reported injuries caused by punching, slapping, kicking, pulling of hair and attempted strangulation (two spouses). One spouse required dental work, one was injured by a falling vase and one by a falling picture. Twelve spouses (15%) chose to sleep in separate rooms and one patient constructed a plywood barrier to separate himself from his wife. Sixty-two of 67 patients reported dreams associated with motor activity and 37 patients reported dream content (see Table 1). Fifty-seven of 82 patients (63%) reported excessive daytime sleepiness.

Laboratory findings

Brain imaging was obtained in 52 patients (CT scan in 24 patients, MRI scan in 39 patients). Reasons for imaging in all patients were known or suspected neurological disease other than RBD (see Table 2).

All patients underwent PSG (see Table 3), 68 with full night diagnostic PSGs and 25 with split-night protocols in which the second half of the night was devoted to a trial of nasal positive airway pressure. Ninety of 93 PSGs showed increased phasic or tonic EMG activity in REM sleep. In the remaining three PSGs, ambiguous sleep with REMs intruding into non-REM sleep without atonia was seen, but no sustained periods of REM sleep. Two of these patients had parkinsonism and dementia, and one dementia alone. Abnormal gross motor behaviour was recorded on videotape in 42 patients (45%). Unilateral temporal epileptiform spike or sharp wave discharges in non-REM sleep were seen in two patients. One had a past history of encephalitis with clinical seizures different from the RBD activity and one had dementia without clinical epilepsy. Of the 10 patients with histories of sleep walking in addition to abnormal motor activity in bed, gross motor activity was recorded only during REM sleep in five. Two patients showed both confusional arousals from slow wave sleep and increased muscle tone in REM sleep, and three others showed only increased muscle tone in REM sleep without recording of abnormal behaviour. Five of the 10 patients had underlying neurodegenerative diseases.

MSLTs were performed in eight patients. A mean initial sleep latency <8 min was found in three patients, two with narcolepsy and one with Parkinson's disease. Sleep onset REM sleep was seen in three patients, two with narcolepsy and one believed due to withdrawal of imipramine prior to the MSLT.

Associated illnesses (Table 4)

CNS disease occurred in 53 patients (57% of the total number; 64% of the 83 who underwent neurological examination). Thirteen of the patients with dementia have been reported as part of another study (Boeve *et al*., 1998). Of the 25 patients with Parkinson's disease, RBD symptoms preceded those of

Table 2 *Imaging features of the patients imaged (*n = *52)*

Imaging feature	No. of patients
Normal imaging	15
Non-specific areas of increased T_2-signal in periventricular region	20
Generalized cerebral atrophy	24
Cerebellar atrophy*	2
Brainstem pathology†	4
Increased T_2-signal in the pons	2
Increased T_2-signal in the medulla	1
Cavernous hemangioma in the middle cerebellar peduncle	1
Corpus callosum lipoma	1
Frontal venous angioma	1

*Both patients had multiple system atrophy; †all four patients also had neurodegenerative diseases (dementia, Parkinson's disease, Parkinson's disease and dementia, multiple system atrophy).

Table 3 *PSG findings of all patients (*n = *93)*

Increased phasic or tonic EMG in REM Sleep	90 (97%)
Ambiguous sleep	3 (3%)
Abnormal gross motor behaviour in REM sleep	42 (45%)
Short initial REM sleep latency (2, 6, 18 min)	3 (3%)
Probable narcolepsy	1
Major depression	1
Progressive supranuclear palsy and OSA	1
Obstructive sleep apnoea syndrome (AHI >10/h)	32 (34%)
Central sleep apnoea syndrome (AHI >10/h)	2 (2%)
Periodic limb movements >20/h	44 (47%)
Mean % REM sleep	17%
Mean % slow wave sleep	12.5%
Patients older than 58 years with >15% slow wave sleep (n = 45)	30 (33%)

OSA = obstructive sleep apnoea syndrome; AHI = apnoea–hypopnoea index.

Table 4 *Associated neurological disorders of patients (*n = *53)*

Type of neurological disorder	No. of patients
Parkinson's disease (idiopathic, levodopa responsive)	25 (47%)
With dementia	10
Without dementia	15
Dementia without parkinsonism	7 (13%)
Multiple system atrophy	14 (26%)*
Narcolepsy	4 (8%)*
Prior encephalitis	2 (4%)
Progressive supranuclear palsy	1 (2%)
Brainstem infarction	1 (2%)

Neurological disorders were found to occur in 53 of the 93 patients (57%). *One patient with narcolepsy subsequently developed multiple system atrophy.

Parkinson's disease in 13 (52%) by a median of 3 years (range 1–30 years), occurred simultaneously in two and followed onset of Parkinson's disease symptoms in 10 by a median of 3 years (range 0.5–15 years). One patient with an initial diagnosis of idiopathic RBD subsequently developed Parkinson's disease 18 months later. RBD preceded the onset of dementia in five of seven patients with dementia alone by a median of 3 years (range 1–12 years). Thirty of the 32 patients with Parkinson's disease, dementia or both were male. Of the 14 patients with multiple system atrophy, RBD preceded onset of multiple system atrophy symptoms in five by a median of 4 years (range 1–11 years). Five of the 14 patients with multiple system atrophy were female (43%; χ^2 test comparing gender in multiple system atrophy versus Parkinson's disease and/or dementia, $P = 0.007$). One of the four patients with narcolepsy was female, and thus eight of 12 female patients with RBD had underlying neurological disease (67%), compared with 44 of 81 male patients (54%) ($P = 0.38$).

Twenty-four patients (25.8%) had lifetime histories of psychiatric disorders, including affective disorders (10), substance abuse (9), anxiety disorder (4) and personality disorders (3). In one of two patients with post-traumatic stress disorder, RBD commenced 20 years after the post-

traumatic stress disorder had resolved; the relationship was uncertain in the other patient. Of eight patients with alcohol abuse, RBD symptomatology commenced while alcohol use was continuing in six and during abstinence in one (20 years after cessation); the relationship was uncertain in one patient. Three of the eight patients had degenerative CNS disease. One patient developed two episodes of RBD after sudden withdrawal from high dose barbiturate use. Fourteen patients used tricyclic or selective serotonin reuptake inhibitor antidepressants. Of the 11 patients with adequate information, RBD commenced before use of these drugs in nine patients, while using the medication in one (who also had Parkinson's disease) and at about the same time that medication (amitriptyline) commenced in one patient.

Management

Clonazepam was prescribed in 57 out of 93 patients (61%) in doses of 0.25–1.5 mg before sleep. Of 38 patients on clonazepam therapy for whom information was available (mean follow-up 23.7 months), the medication was completely successful in 21 (55%), partially successful in 12 (32%) and unsuccessful in five (13%). Nine patients reported early morning sedation, which was usually dose related. Two patients developed early morning motor incoordination, which resolved either spontaneously or with dose adjustment. One patient developed impotence, necessitating discontinuation of the drug. Triazolam was used by two patients, with complete success in one and uncertain results in the other. Clozapine was used by two patients with dementia in whom clonazepam had failed; RBD resolved completely in one patient and partially in the other. No medication was used in 34 patients (37%), because the symptoms were judged to be mild in 20, concomitant obstructive sleep apnoea syndrome or nocturnal stridor was present in six, the symptoms had diminished as underlying neurological disease had progressed or resolved in four and because of patient refusal in four.

Discussion

Clinical, demographic and laboratory features

Many of our findings confirm descriptions of RBD by Schenck and colleagues (Schenck and Mahowald, 1990, 1996*a*; Schenck *et al*., 1993). Although our centre is also in Minnesota, 76% of our patients lived outside the state and, to the best of our knowledge, only one of our patients had been seen at the Minnesota Regional Sleep Disorders Center. The mean age of onset was 60.9 years, slightly older than the 52.4 years reported by Schenck and colleagues (Schenck *et al*., 1993). Eighty-seven per cent of our patients were male, strikingly similar to the 87.5% found by Schenck and colleagues (Schenck *et al*., 1993). The reason for the male preponderance is unknown, but androgenic hormonal influences have been suggested (Goldstein, 1974; Mahowald and Schenck, 1994). Our data show that this gender effect is preserved in RBD associated with Parkinson's disease and dementia, but not in RBD associated with multiple system atrophy. These results are in keeping with the lack of gender effect reported in a study of 27 patients with multiple system atrophy and RBD (Plazzi *et al*., 1997). A careful assessment for multiple system atrophy should be made in female patients presenting with RBD.

Forty-five per cent of our patients demonstrated gross abnormal motor behaviour in REM sleep during their night in the laboratory. Despite demonstration of definite increases in muscle tone during REM sleep or ambiguous sleep in the remainder, the question arises whether the nocturnal motor behaviour described at home was due to RBD or to a non-REM arousal parasomnia. In a series of 54 patients with histories of violent sleepwalking (49 associated with abnormal arousals from slow wave sleep on PSG), 10.2% were also found to have abnormal muscle twitching during REM sleep (Schenck *et al*., 1989). A patient with Machado–Joseph disease was shown to have episodes of nocturnal wandering from non-REM sleep as well as violent outbursts of kicking, thrashing and yelling arising from REM sleep (Kushida *et al*., 1995). These and other descriptions (Bokey, 1993; Guilleminault *et al*., 1995) have led to the concept of an 'overlap syndrome' with features of both REM and non-REM parasomnias (Schenck *et al*., 1997*a*). Sleepwalking or nocturnal wandering behaviour was described in only 10 of our patients. Of these, two clearly had an overlap syndrome with both confusional arousals recorded from slow wave sleep and increased muscle tone in REM sleep. The other eight patients may well also fall into this category, although abnormal motor behaviour in bed was recorded only during REM sleep in five. The remaining 83 patients were all either observed in the home or laboratory to exhibit behaviour typical of RBD—thrashing, kicking, vocalization in bed or falling on to the floor. However, we cannot be certain that some of those in whom only increased muscle tone was recorded in the laboratory may also have had confusional arousals from non-REM sleep at home.

RBD patients have a high propensity for serious injury to themselves or others; 32% of our patients injured themselves, while 64% of sleeping partners reported being assaulted. Others have also reported subdural haematomas (Gross, 1992; Dyken *et al*., 1995) and attempted strangulation of a sleeping partner (Schenck *et al*., 1989). Seven per cent of patients in the case series of Schenck and colleagues suffered fractures (Schenck *et al*., 1993). In contrast to sleep walking, homicide associated with RBD has not been reported (Mahowald *et al*., 1990). In 26% of our patients with RBD associated with neurodegenerative disease, the frequency of clinical nocturnal events decreased with time; in four of seven such patients treatment was not deemed necessary at all. However, increased muscle tone during REM sleep persisted on PSG. Activation of brainstem locomotor centres, in addition to loss of atonia, appears to be necessary for the vigorous motor activity of RBD (Hendricks *et al*., 1982; Lai and Siegal,

1990) and we thus hypothesize that this decrease in frequency may reflect progressive degeneration of these centres by the primary disease. This finding contrasts with the experience of Schenck and Mahowald who reported that no case of spontaneous remission was identified in their case series (Schenck and Mahowald, 1990).

Does dream content change in patients who develop RBD? Patients certainly report that it does, with our data indicating that aggressive themes comprise 89% of the recalled dreams. In contrast, a study of 1320 dreams of educated adults (Hall, 1951) revealed that subjects reported hostile acts by or against the dreamer in 34%, of which only about one-third involved physical acts of aggression. In the same study, only 34% of 2668 actions in 1000 dreams involved movements, such as walking and running. Despite their violent character, the most common theme of dreams in patients with RBD was defence of the sleeper against attack and only 2% of dreams involved the patient as the aggressor.

Sixty-three per cent of our patients reported excessive daytime sleepiness, but other possible causes or associated conditions could explain sleepiness in the majority. The mean initial MSLT latency in 40 non-narcoleptic patients with RBD has been reported as 12.5 min, with only 10% having mean latencies of <5 min (Schenck and Mahowald, 1990). Obstructive sleep apnoea syndrome was more common among our patients than those of Schenck and Mahowald, who found 14.6% of their group of 96 patients had more than five obstructive sleep apnoeas or hypopnoeas per hour (Schenck and Mahowald, 1992*b*). These differences may be explained by the slightly older age of our patients and the possibility that suspected obstructive sleep apnoea triggered referral in some, but we think the suggestion that RBD may protect against obstructive sleep apnoea (Schenck and Mahowald, 1992*b*) unlikely to be correct. Periodic limb movements are common, occurring in 47% of our patients (periodic limb movement index >20/h), and in 59% of the series of Schenck and colleagues (Schenk *et al*., 1993). A periodic limb movement index >20/h has been reported in 20% of normal subjects older than 65 years (Ancoli-Israel *et al*., 1991).

Imaging of the brain in 52 of our patients showed changes compatible with age or underlying disease. Only four patients had brainstem pathology and all four of these patients also had an unrelated neurodegenerative disorder known to be associated with RBD. MRI scans of 42 patients with RBD were reported to show clinically significant abnormalities in 14.6% (brainstem astrocytoma, multiple infarcts and severe cerebral atrophy) and non-specific areas of increased T_2-signal in deep white matter in 46% (Schenck and Mahowald, 1990). Areas of increased signal intensity on the MRI scans of six patients with RBD, aged 64–74 years, were reported in the periventricular white matter in five patients and in the pontine tegmentum in three (Culebras and Moore, 1989). However, without control cases in an elderly population, the clinical significance of areas of increased T_2-signal on MRI scans is uncertain.

Our PSG findings were similar to those reported by others (Lapierre and Montplaisir, 1992; Schenck *et al*., 1992*a*). The ambiguous sleep noted in three patients with neurodegenerative diseases is similar to the sleep state dissociation reported in patients with olivopontocerebellar degeneration, narcolepsy and other conditions (Mahowald and Schenck, 1992). Schenck and colleagues have reported that 80% of their RBD patients older than 58 years have an elevated percentage of stages 3 and 4 of non-REM sleep, defined as >15% of total sleep time (Schenck *et al*., 1993). We found similar findings in 33% of our patients older than 58 years. Although this is certainly higher than found in studies of normal older subjects (Reynolds *et al*., 1985), it should be noted that our laboratory uses a modification of standard criteria (Rechtschaffen and Kales, 1968) in the scoring of slow wave sleep (amplitude criterion of >50 μV), which may artificially increase the slow wave percentage.

Associated disorders

As experience with RBD has increased, a high percentage of patients with associated neurological disease has been noted. In 1990, Schenck and Mahowald reported that 37.5% of 64 cases had neurological disease (Schenck and Mahowald, 1990); in a 1996 report of their extended series of 148 cases this had increased to 52% (Schenck and Mahowald, 1996). Fifty-seven per cent of our patients had associated neurological disorders, a figure similar to the 53% of all cases reported in the world literature up to 1996 (Schenck and Mahowald, 1996*a*). Selection bias may have resulted in inflation of these percentages, as all case series have been reported from academic institutions with a greater likelihood of seeing patients with serious neurological disease. No community-based studies of RBD have been reported. All but seven of our neurological patients had neurodegenerative disorders, the majority being idiopathic Parkinson's disease, multiple system atrophy or dementia. We have elsewhere described our experience with RBD and dementia (Boeve, 1998; Ferman *et al*., 1999) and have hypothesized that the majority of these patients are likely to have dementia with Lewy bodies. Autopsies have confirmed Lewy body disease or the Lewy body variant of Alzheimer's disease in three cases (Schenck *et al*., 1997*b*; Boeve *et al*., 1998). Clearly, further pathological data are required to delineate more exactly the significance of a lack of REM sleep muscle atonia in dementia. Motor dyscontrol in REM sleep has been described in 90% of patients with multiple system atrophy (Plazzi *et al*., 1997; Tachibana *et al*., 1997) and clinical RBD in 69% (Plazzi *et al*., 1997). Of 61 patients with Parkinson's disease, 15% were reported to fulfil clinical criteria for RBD (Comella *et al*., 1998). Other associations reported in case reports include brainstem tumours (Schenck *et al*., 1993), cerebrovascular disease (Culebras and Moore, 1989; Schenck and Mahowald, 1996*a*) and cortical basal ganglionic degeneration (Kimura *et al*., 1997). Two of our patients had prior encephalitis and one progressive supranuclear palsy.

Thus, although RBD may result from a wide range of neurological problems, the majority of patients with an underlying disorder of the brain are likely to have one of a limited number of neurodegenerative disorders. The single prominent exception is narcolepsy (Schenck and Mahowald, 1992*a*), although the frequency of RBD in this condition has not been determined.

In many cases of neurodegenerative disease, RBD may precede other symptoms of the disorder, often by years (Silber and Ahlskog, 1992; Tison *et al*., 1995; Tan *et al*., 1996; Plazzi *et al*., 1997; Sforza *et al*., 1997; Turner *et al*., 1997). Parkinsonism developed in 38% of 29 older males initially diagnosed with idiopathic RBD, a mean of 12.7 years after onset of RBD symptoms and a mean of 3.7 years after RBD diagnosis (Schenck *et al*., 1996). Lewy body abnormalities have been found at autopsy in a neurologically normal patient thought to have idiopathic RBD (Uchiyama *et al*., 1995). Our retrospective data indicate that RBD symptoms were the first manifestation of Parkinson's disease, dementia or multiple system atrophy in 23 of 46 patients (50%), with RBD developing a median of 3–4 years before other symptoms. Careful neurological follow-up of patients with apparent idiopathic RBD is indicated.

Lifetime histories of psychiatric disease were obtained in 25.8% of our patients, a figure similar to the 35% noted by Schenck and Mahowald (Schenck and Mahowald, 1990) and no higher than the 29–38% found in the general population (Robins *et al*., 1984). Increased phasic twitching in REM sleep has been reported in post-traumatic stress disorder (Ross *et al*., 1994). Two of our patients had histories of post-traumatic stress disorder; in the one patient in whom the temporal relationship could be determined, RBD was clearly unrelated. Discontinuation of use of REM suppressant agents such as alcohol, amphetamines, cocaine and imipramine (Schenck *et al*., 1993), has been reported to induce RBD. No temporal relationship of cessation of alcohol use to onset of RBD was found in our eight patients with alcohol abuse. One of our patients developed episodes of RBD following barbiturate withdrawal on two occasions (Silber, 1996). RBD has occasionally been reported with the use of tricyclic antidepressants (Guilleminault *et al*., 1976; Bental *et al*.,1979) and selective serotonin reuptake inhibitors (Schenck *et al*., 1992*b*). We did not detect a temporal relationship between the use of these medications and the onset of RBD in the majority of our patients who had used them. Thus, although certain drugs and drug withdrawal may induce RBD, considerable care should be taken to establish a clear temporal association before ascribing RBD to these factors.

Management

Our 87% partial or complete success rate in treatment with clonazepam is similar to the 90% success rate reported elsewhere (Schenck *et al*., 1993). A few of our patients appeared to respond to triazolam and clozapine. Clonazepam has been shown to reduce phasic twitching in RBD, but does not re-establish REM atonia (Lapierre and Montplaisir, 1992). Although the general safety of clonazepam use has been demonstrated in a population of patients with sleep disorders (Schenck and Mahowald, 1996*b*), benzodiazepines may result in confusion or falls in elderly patients with neurodegenerative diseases (Woods and Winger, 1995), or may worsen obstructive sleep apnoea syndrome. A minority of our patients developed side-effects, which were usually dose related. We did not use medication in 39% of our patients largely because of these concerns, but did advise improvement in the safety of the sleeping environment by such measures as moving furniture away from the bed and placing a mattress on the floor alongside the bed.

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