

L. Ferini-Strambi • M.L. Fantini • M. Zucconi • V. Castronovo • S. Marelli • A. Oldani • S. Cappa

REM sleep behaviour disorder

Abstract REM sleep behaviour disorder (RBD) is a parasomnia characterised by nocturnal complex motor activity associated with dream mentation. RBD, which affects mainly older men, may be idiopathic or associated with other neurological disorders. A strong association between RBD and alpha-synucleinopathies has been recently observed, with the parasomnia often heralding the clinical onset of the neurodegenerative disease. The idiopathic form accounts for up to 60% of the cases reported in the three largest series of RBD patients. Follow-up studies in small samples revealed that a proportion of RBD patients will eventually develop Parkinson's disease and/or a dementia of Lewy bodies type in the years following the RBD diagnosis. Recently, neurophysiological and neuropsychological studies in idiopathic RBD have found evidence of central nervous system dysfunction. An impairment of cortical activity, specific neuropsychological deficits, signs of autonomic dysfunction and olfactory impairment have been observed in these patients, challenging the concept of idiopathic RBD. The detection of early markers of neurodegenerative disorders in idiopathic RBD, and the evaluation of their value by the combined application in prospective studies may be crucial for developing early intervention strategies.

Key words REM sleep • Parasomnia • RBD

L. Ferini-Strambi (✉) • M.L. Fantini • M. Zucconi • V. Castronovo
S. Marelli • A. Oldani • S. Cappa
Sleep Disorders Center
Department of Neurology
Università Vita-Salute San Raffaele
Via Stamira d'Ancona 20, I-20127 Milan, Italy
e-mail: ferinistrambi.luigi@hsr.it

Introduction

REM sleep behaviour disorder (RBD) is a parasomnia characterised by complex motor activity during REM sleep, usually associated with dream mentation [1]. Patients have elaborate nocturnal motor behaviours, such as screaming, punching and grasping, which are potentially harmful for themselves or their bed partner [1, 2]. In RBD patients polysomnographic (PSG) recording reveals intermittent or complete loss of REM sleep muscle atonia and excessive phasic electromyographic (EMG) activity during REM sleep [1].

RBD affects mainly men over the age of 50 years and the prevalence remains largely unknown. A study performed among 1034 individuals aged 70 years and more in the Hong Kong area found self-injury during sleep in 8 patients, 4 of whom received a PSG diagnosis of RBD yielding an estimated prevalence of 0.04% [3].

RBD is frequently encountered in a category of neurodegenerative diseases called synucleinopathies, including Parkinson's disease (PD) [4, 5], dementia with Lewy bodies (DLB) [6, 7] and multiple system atrophy (MSA) [8, 9]. Moreover, a number of neurological conditions with the involvement of the brainstem may result in RBD. If no neurological signs or central nervous system (CNS) lesions are found, RBD is defined as "idiopathic". This form accounts for up to 60% of the observed cases in the largest published series of RBD patients [2, 10, 11].

Pathogenesis of RBD

The pathogenesis of RBD is still unclear. Multiple neural substrates, mainly located in the brainstem, contribute in REM sleep atonia and may be potentially involved in the pathogenesis of RBD. These include the ventral mesopontine junction, the laterodorsal and pedunculopontine tegmental nuclei (LTD-PPN), the locus coeruleus (LC) and the peri-LC area in the pons and the magnocellularis (NMC), gigantocellularis (NGC)

and paramedianus (NPM) nuclei in the medial medulla [12]. An experimental animal model of RBD has been obtained in cats after dorsal pontine lesion, and a variety of behavioural manifestations have been found to be dependent on specific sites of pontine lesions [13, 14]. Mesostriatal dopaminergic neurons might be also implicated and brain imaging studies, performed in idiopathic RBD patients using PET or SPECT, showed a decreased striatal dopaminergic innervation [15] and a reduced pre-synaptic striatal DA transporter binding [16], similarly to what was observed in patients with early PD.

The notion of an impairment of the striatal dopaminergic system is also supported by data from a prospective study performed on idiopathic RBD showing that 11 out of 29 (38%) male patients developed a parkinsonian syndrome within 3.7 years from RBD onset [5]. The study has been recently updated, showing that 17 out of 26 (65.4%) idiopathic RBD patients originally enrolled eventually developed a parkinsonian disorder (n=16) and/or a dementia without parkinsonism (n=1) after an average interval of 13.3 years from RBD onset, although in nine patients RBD was still idiopathic after a mean of 20.3 years [17]. Another study found the eventual emergence of a parkinsonian syndrome in 21% of 19 idiopathic RBD patients, after a mean interval of 11 years from the RBD onset and a mean follow-up of 4.6 years [18], while others reported the occurrence of neurological signs in 36% of 20 idiopathic RBD patients longitudinally followed for a period ranging from 6 months to 10 years [19].

Other retrospective data have been obtained from patients with RBD and neurodegenerative disorders. One study showed that, in 13 out of 25 (48%) patients with RBD and PD, the RBD had preceded the onset of PD by a mean of 3 years [2]. Another study found that 44% of 35 patients affected by RBD and MSA developed RBD from 1 to 19 years before the appearance of MSA [8]. In 77% of 31 patients with RBD associated to DLB, the latter had heralded the onset of the dementia by an average period of 9 years [7].

Based on these data, idiopathic RBD may represent, in a certain number of cases, an early manifestation of an impending neurodegenerative disease. Recent studies have examined various neurophysiological and neuropsychological functions in idiopathic RBD, in order to detect early signs of CNS dysfunction associated to the REM sleep motor dyscontrol and several abnormalities have been observed in such patients, challenging the concept of "idiopathic" RBD. The recent converging evidence on CNS dysfunction during both wakefulness and sleep in idiopathic RBD are reviewed.

Neurovegetative and olfactory functions in idiopathic RBD

Braak and colleagues have recently identified a stereotyped pattern of evolution in Lewy body disease (PD and

DLB) [20]. Lewy body pathology begins in the anterior olfactory nucleus and in the lower brainstem nuclei, affecting olfactory and autonomic functions initially, and progressing rostrally to ultimately affect the cerebral cortex. It is known that synucleinopathies are frequently associated with autonomic impairment, often preceding motor symptoms. In PD, manifestations of autonomic dysregulation are frequent, including orthostatic hypotension, reduced heart-rate variability and impairment in the sudomotor, gastrointestinal and urinary functions [21, 22]. In DLB, recurrent syncopes represent a supportive feature for the diagnosis and they may precede the manifestations of cognitive decline [23]. In MSA, autonomic failure may be the dominant finding in the clinical picture [22].

A lack of autonomic activation during the nocturnal dream-enacting motor behaviours has been occasionally observed in RBD patients. However, Ferini-Strambi et al. first reported that idiopathic RBD patients not only have a reduced tonic and phasic heart-rate variability during sleep, but the majority of these patients also have an impairment in one or more tests assessing sympathetic or parasympathetic functions during wakefulness, compared to age- and sex-matched healthy controls [24]. In agreement with these results, Fantini et al. found a reduced cardiac activation related to periodic limb movements (PLMS) during stage 2 sleep in patients with idiopathic RBD compared to age- and sex-matched patients affected by restless legs syndrome (RLS) [25].

Olfactory dysfunction, which involves odour identification, detection and differentiation, is a frequent feature of PD and DLB, often preceding by several years the motor and/or cognitive symptoms [26]. We recently performed a preliminary study on the olfactory functions in idiopathic RBD. Thirty-three PSG-confirmed idiopathic RBD patients (28M, 5F; mean age: 70.9±7.2 years; mean duration of symptoms: 6.0±2.9 years) and 8 patients with RBD+PD (6M, 2F; mean age=70.7±7.8 years; mean Hoen-Yahr score=1.7) and 16 controls (12M, 4F; mean age: 70.7±6.3 years) underwent the Brief Smell Identification Test (B-SIT), a smaller and cross-cultural 12-item version of the University of Pennsylvania Smell Identification Test (UPSIT). This test has been developed to assess the individual ability to perceive and name an odorant. Participants were free of psychotropic medication that may influence dopamine transporter binding and/or olfactory function and none had a history of nasal surgery (except septoplasty), significant head trauma, hepatitis, endocrine disorders, allergies or abuse of drugs or alcohol. A significantly lower score ($p<0.0001$) was found in both patients with the idiopathic RBD (6.6±2.4) and patients with RBD+PD (5.0±2.0) compared to control subjects (9.1±1.6) (Fig. 1).

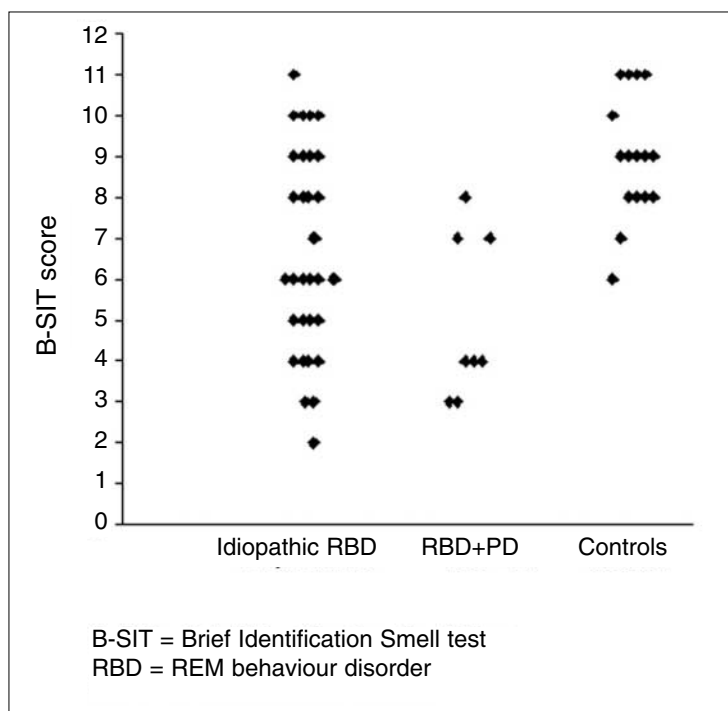


Fig. 1 Individual B-SIT scores in idiopathic RBD (n=33), RBD+PD (n=8) and controls (n=16)

EEG activity in idiopathic RBD

Fantini et al. [27] recently found higher theta power in the frontal, temporal and occipital regions with a lower beta power in the occipital region during wakefulness in idiopathic RBD patients, compared to age- and sex-matched healthy controls (Fig. 2). Also, a lower dominant occipital frequency (DOF) during wakefulness was found in idiopathic RBD patients. Indeed, the whole mean EEG power spectrum recorded in the occipital region appeared to be shifted toward slower frequencies, compared to controls, although significant differences were noted for the increase in theta and the decrease in beta2 bands only. Four out of the fifteen idiopathic RBD patients presented a DOF value in the theta range (below 8 Hz), a value considered as pathological. During REM sleep, beta power in the occipital region was lower in RBD patients compared to controls, whereas no difference in any region was observed in the amount of theta power. As only theta and beta2 bands showed significant differences, the ratio of the power in theta over beta2 (TH/BE2) was calculated as an index of cortical slowing that could differentiate RBD patients from controls.

Therefore, the authors postulated that the slowing of the EEG found in idiopathic RBD patients may be associated with subtle cognitive deficits and those patients showing the highest values of TH/BE2 ratio may represent a subgroup of subjects who are more likely to eventually develop a degenerative disorder associated with dementia. Alternatively, the distribution of the TH/BE2 ratio values

might reflect the severity of the neurodegenerative process associated with RBD. However, no correlation was observed between the values of the TH/BE2 ratio and either the duration of the disease or its clinical severity. Objective measures such as percentages of muscle atonia or of phasic EMG activity during REM sleep also failed to correlate with the EEG slowing. These results support the notion of a heterogeneity of RBD, with some patients but not all presenting a slowing of the EEG and being possibly at higher risk for developing cognitive impairment and eventually dementia.

This hypothesis is supported by electrophysiological studies conducted in patients with cognitive impairment. For example, a slowing of the EEG is commonly observed in the early stages of dementia, such in Alzheimer's disease and in patients with mild cognitive impairment. Indeed, an increase of theta activity is believed to represent a sensitive index of early cognitive deterioration [28]. A slowing of the DOF is also frequently observed in neurodegenerative conditions such as AD, PD and DLB [29–31]. On the other hand, isolated decrease of beta activity has also been found to be associated with early signs of intellectual decline [32].

Moreover, similarities may be observed between the topographical distribution of the EEG slowing in idiopathic RBD patients (predominant involvement of the occipital region) and the pattern of the perfusional and metabolic impairment observed in DLB and in PD [33–35]. These observations are in agreement with the notion of a common pathophysiological mechanism between these conditions.

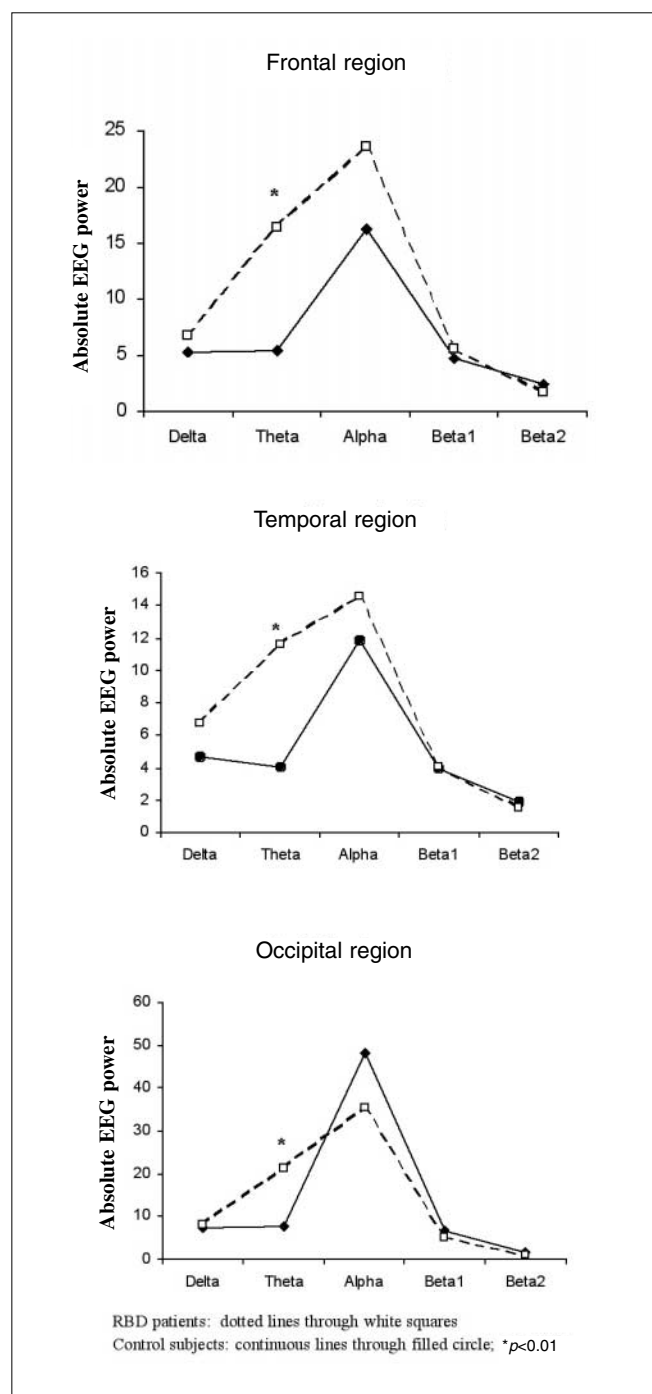


Fig. 2 Absolute EEG power in the frontal, temporal and occipital regions in patient with RBD and control subjects

Neuropsychological assessment in idiopathic RBD

Cognitive functions are apparently preserved in idiopathic RBD, as assessed by the standard clinical evaluation. Neither patients nor their relatives usually report symptoms of cognitive decline, and Mini Mental State Examination (MMSE) score has been reported as normal

[27]. However, a recent study evaluated patients with idiopathic RBD (average duration of symptoms 5.7 ± 5.3 years) by an extensive neuropsychological assessment for a broad range of cognitive functions [36]. The results of this study showed, for the first time, that idiopathic RBD patients have an impairment in both visuo-spatial constructional performances and visuo-spatial learning compared to age- and sex-matched controls, as assessed by Rey-Osterreith's Complex Figure Test and the Corsi Supraspan Learning Test, respectively. Other authors reported an impairment in visuo-spatial planning and a deficit in the recall of both a visuo-constructive task and verbal material in two idiopathic RBD patients with slowing of the EEG [27].

The similarity between the type of cognitive deficits found in idiopathic RBD and those observed in patients with DLB [37] and PD, with or without dementia [38, 39], is remarkable, and argues in favour of a common pathophysiological mechanism between these conditions. In early stages of PD, subtle abnormalities in verbal fluency, executive functions and visuospatial abilities have been variously reported [40, 41], although some authors have argued that the poor performance of PD patients in spatial tasks may result from attentive deficit rather than visuospatial impairment [42]. Cognitive deficits associated with DLB seem to be more homogeneous than those found in PD, affecting particularly perceptual functions, namely visual constructional and visuo-spatial abilities [37, 43]. A comparative study of neuropsychological performance in Lewy body disease (LBD) and AD found greater memory impairment in the AD group, but greater visuo-constructive skills deficits in the LBD group without AD [44]. A recent study showed that dementia with RBD is neuropsychologically indistinguishable from early probable DLB. Both groups showed significantly worse visuo-perceptual organisation, sequencing and letter fluency but significantly better confrontation naming and verbal memory when compared with definite AD patients of a similar early stage [45].

As RBD often heralds a LBD, either PD or DLB, by several years, it may be hypothesised that the neuropsychological deficits observed in idiopathic RBD represent an early manifestation of one of these neurodegenerative diseases.

Dreams and daytime temperament in RBD

Patients with RBD typically report vivid, unpleasant and action-filled dreams that are generally congruent with the observed behaviours, although no study has systematically assessed dream characteristics in RBD. Regardless of the aetiology, it is commonly assumed that the lack of motor inhibition during REM sleep in these patients allows the enactment of the oneiric imagery. Patients with RBD usually report dreams in which they are attacked by animals or

unfamiliar people and they would either fight back in self-defence or attempt to flee [46, 47]. It has also been observed that the violence and aggressiveness displayed during nocturnal behaviours is in contrast with the often placid and mild-mannered daytime temperament [46, 48].

Recently, we systematically assessed dream characteristics and daytime aggressiveness in RBD and controls. Thirty-nine RBD patients (18 idiopathic, 11 symptomatic: 7 PD, 3 MSA, 1 LBD) and 63 sex/age-matched controls were asked to recall their most recent dreams and to fill in the Aggression Questionnaire (AQ). Only 32 (82%) RBD patients (mean age=68.5±7.6 years) and 30 (47.6%) controls (mean age=69.1±5.9 years) were able to remember their dreams and a total of 83 and 60 dreams were collected in the two groups, respectively.

Subjects were asked to recall one or more recent dreams. First, a trained interviewer collected a verbatim description of these dreams. Then a semi-structured interview was performed in order to more precisely assess specific elements of the dream such as characters, social interactions, activities, success and failures, misfortune and good fortune, emotions, settings, objects and descriptive elements, as described in the Hall and Van De Castle method [49]. The Hall and Van De Castle is the most comprehensive and widely used empirical system for dream content analysis [50]. Dreams are coded according to several nominal categories and percentage and ratios related to 28 indicators are obtained.

RBD patients showed a higher percentage of “dream with at least one aggression” than controls (63 vs. 16%,

$p<0.00001$), a higher aggression/friendliness interactions ratio (90 vs. 55%; $p<0.01$) and a greater frequency of animals characters (18 vs. 4%; $p=0.001$). In contrast to controls, none of RBD patients had “dreams with at least one element of sexuality” (0 vs. 11%, $p<0.0001$) (Table 1). No correlation was observed between any indicator of dream aggressiveness and either age, duration or frequency of RBD symptoms.

The AQ is a validated test developed to assess aggression, which consists of 29 items [51] and a validated Italian version is available [52]. The subjects rate each item on a five-point scale to indicate the degree to which the item is characteristic of themselves. The two groups did not differ in total AQ scores (Table 2), except for a lower score on “Physical Aggressiveness” in RBD compared to control subjects (16.8±6.7 vs. 20.8±8.8; $p=0.03$).

A lower prevalence of Male characters characterised dreams of symptomatic RBD compared to idiopathic RBD, despite a similar gender distribution of dreamers in the two groups. The increased percentage of male characters in dreams is usually associated to more threatening and aggressive dream content [53]. If this is true, the observed male under-representation may reflect a milder aggressive content in symptomatic RBD, and this would be concordant with the observation that intensity of RBD manifestation often decreases as the neurodegenerative disease progresses [46].

This is the first study quantitatively assessing the dream characteristics in RBD. An increased occurrence of

Table 1 Dream characteristics in patients with RBD (n=32) and in control subjects (n=30) according to the Hall and Van De Castle method

Dreams with at least one	RBD, %	Controls, %	<i>h</i>	<i>p</i>	RBD, n	Controls, n
Aggression	63	16	1.01	0.00000*	86	60
Friendliness	8	16	-0.25	0.14	86	60
Sexuality	0	11	-0.68	0.00005*	86	60
Misfortune	16	16	0.02	0.91	86	60
Good fortune	0	1	-0.21	0.21	86	60
Success	4	11	-0.29	0.08	86	60
Failure	2	11	-0.36	0.03	86	60
Striving	6	22	-0.48	0.004*	86	60

RBD, n, total number of elements occurring in the category for the RBD group; *Controls, n*, total number of elements occurring in the category for the control group

Table 2 Aggression Questionnaire (AQ) scores in patients with RBD and control subjects

	RBD patients (n=26)	Control subjects (n=29)	<i>p</i>
Physical aggression	16.8±6.7	20.8±8.8	0.03*
Verbal aggression	15.8±4.2	14.7±4.3	0.17
Anger	17.8±6.6	17.5±5.9	0.44
Hostility	20.5±4.8	22.0±6.3	0.16
AQ total score	70.9±16.0	75.0±21.0	0.14

both aggression themes and animals is reported also in children's dreams, and their frequency decreases with age. Thus, one may hypothesise that a neurodegenerative process often underlying chronic RBD would lead to a release of archaic dream patterns. Alternatively, the elevated aggressiveness of dream content and the excessive EMG activity during REM sleep in RBD might be related to the hyperactivity of a common neuronal generator. The increased ability to recall dreams in RBD may be related to the peculiar dream content or it may reflect differences in memory processes.

Conclusions

Some studies indicate that idiopathic RBD, a condition previously considered as a pure parasomnia, may be associated with a number of neurological abnormalities. These observations support the notion of RBD as an early manifestation of a more pervasive neurodegenerative process and challenge the concept of idiopathic RBD.

However, it should be noted that the neurophysiological and neuropsychological abnormalities reported in RBD affect a variable proportion of idiopathic RBD patients, but not the totality. Long-term follow-up studies revealed that a proportion of idiopathic RBD patients never develop other neurological illnesses, even several decades after the diagnosis of RBD. Idiopathic RBD seems to be characterised by heterogeneous clinical phenotypes, but data are still insufficient to identify specific subgroups of patients with possible implication in prognosis and/or treatment.

Further studies assessing reciprocal relationship between neurophysiologic parameters (EEG, autonomic, olfactory) and/or neuropsychological functions in these patients would help to identify specific phenotypes. With the improved life expectancy and the subsequent growth of the elderly population, the prevalence of neurodegenerative diseases has significantly increased, with high social costs. Therefore, it would be crucial to detect early markers of neurodegeneration and to identify those subjects presenting with a higher risk of developing a neurodegenerative illness, in order to develop early intervention strategies. This may be critical to stop or slow down the impending neurodegenerative process and functional deterioration.

References

- Mahowald MW, Schenck CH (2000) REM sleep parasomnias. In: Kryger MH, Roth T, Dement C (eds) Principles and practice of sleep medicine, 3rd edn. W.B. Saunders Company, Philadelphia, pp 724–741
- Olson EJ, Boeve BF, Silber MH (2000) Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. *Brain* 123:331–339
- Chiu HF, Wing YK, Lam LC, Li SW, Lum CM, Leung T, Ho CK (2000) Sleep-related injury in the elderly – an epidemiological study in Hong Kong. *Sleep* 23:513–517
- Comella CL, Nardine TM, Diederich NJ, Stebbins GT (1998) Sleep-related violence, injury, and REM sleep behavior disorder in Parkinson's disease. *Neurology* 51:526–529
- Schenck CH, Bundlie SR, Mahowald MW (1996) Delayed emergence of a parkinsonian disorder in 38% of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder. *Neurology* 46:388–393
- Boeve BF, Silber MH, Ferman TJ, Kokmen E, Smith GE, Ivnik RJ, Parisi JE, Olson EJ, Petersen RC (1998) REM sleep behavior disorder and degenerative dementia: an association likely reflecting Lewy body disease. *Neurology* 51:363–370
- Ferman TJ, Boeve BF, Smith GE, Silber MH, Kokmen E, Petersen RC, Ivnik RJ (1999) REM sleep behavior disorder and dementia: cognitive difference when compared with AD. *Neurology* 52:951–957
- Plazzi G, Corsini R, Provini F, Pierangeli G, Martinelli P, Montagna P, Lugaresi E, Cortelli P (1997) REM sleep behavior disorders in multiple system atrophy. *Neurology* 48:1094–1097
- Wetter TC, Collado-Seidel V, Pollmacher T, Yassouridis A, Trenkwalder C (2000) Sleep and periodic leg movement patterns in drug-free patients with Parkinson's disease and multiple system atrophy. *Sleep* 23:361–367
- Sforza E, Krieger J, Petiau C (1997) REM sleep behavior disorder: clinical and physiopathological findings. *Sleep Med Rev* 1:57–69
- Schenck CH, Hurwitz TD, Mahowald MW (1993) REM sleep behaviour disorder: an update on a series of 96 patients and a review of the world literature. *Sleep Res* 2:224–231
- Lai YY, Siegel J (1999) Muscle atonia in REM sleep. In: Mallick BN, Inoué S (eds) Rapid eye movement sleep. Narosa Publishing House, New Delhi, pp 69–90
- Jouvet M, Delorme F (1965) Locus coeruleus et sommeil paradoxal. *C R Soc Biol* 159:895–899
- Hendricks JC, Morrison AR, Mann GL (1982) Different behaviors during paradoxical sleep without atonia depend on pontine lesion site. *Brain Res* 239:81–105
- Albin RL, Koeppe RD, Chervin RD et al (2000) Decreased striatal dopaminergic innervation in REM sleep behavior disorder. *Neurology* 55:1410–1412
- Eisensehr I, Linke R, Noachtar S, Schwarz J, Gildehaus FJ, Tatsch K (2000) Reduced striatal dopamine transporters in idiopathic rapid eye movement sleep behaviour disorder. Comparison with Parkinson's disease and controls. *Brain* 123:1155–1160
- Schenck CH, Bundlie SR, Mahowald MW (2003) REM behavior disorder (RBD): delayed emergence of parkinsonism and/or dementia in 65% of older men initially diagnosed with idiopathic RBD, and analysis of the minimum and maximum tonic and/or phasic electromyographic abnormalities found during REM sleep. *Sleep* 26:A316
- Fantini L, Filipini D, Montplaisir J (2001) Idiopathic REM behavior disorder: a longitudinal study. *Mov Disord* 16[Suppl 1]:S58

19. Zucconi M, Di Gioia MR, Baietto C, Castaldi P, Castronovo VE, Oldani A, Ferini-Strambi L (2003) REM sleep behavior disorder (RBD): clinical and polysomnographic evaluation of 100 consecutive patients. *Sleep* 26:A317
20. Braak H, Del Tredici K, Rub U, de Vos RA, Jansen Steur EN, Braak E (2003) Staging of brain pathology related to sporadic Parkinson's disease. *Neurobiol Aging* 24:197–211
21. Haapaniemi TH, Pursiainen V, Korpelainen JT, Huikuri HV, Sotaniemi KA, Myllylä VV (2001) Ambulatory ECG and analysis of heart rate variability in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 70:305–310
22. Kuroiwa Y, Shimada Y, Toyokura Y (1983) Postural hypotension and low R-R interval variability in parkinsonism, spino-cerebellar degeneration, and Shy-Drager syndrome. *Neurology* 33:463–467
23. Larner AJ, Mathias CJ, Rossor MN (2000) Autonomic failure preceding dementia with Lewy bodies. *J Neurol* 247:229–231
24. Ferini-Strambi L, Oldani A, Zucconi M, Smirne S (1996) Cardiac autonomic activity during wakefulness and sleep in REM sleep behavior disorder. *Sleep* 19:367–369
25. Fantini ML, Michaud M, Gosselin N, Lavigne G, Montplaisir J (2002) Periodic leg movements in REM sleep behavior disorder and related autonomic and EEG activation. *Neurology* 59:1889–1894
26. Tissingh G, Berendse HW, Bergmans P, DeWaard R, Drukarch B, Stoof JC, Wolters EC (2001) Loss of olfaction in de novo and treated Parkinson's disease: possible implications for early diagnosis. *Mov Disord* 16:41–46
27. Fantini ML, Gagnon J-F, Petit D et al (2003) Slowing of electroencephalogram in rapid eye movement sleep behavior disorder. *Ann Neurol* 53:774–780
28. Pritchep LS, John ER, Ferris SH, Reisberg B, Almas M, Alper K, Cancro R (1994) Quantitative EEG correlates of cognitive deterioration in the elderly. *Neurobiol Aging* 15:85–90
29. Prinz PN, Vitaliano PP, Vitiello MV et al (1982) Sleep, EEG and mental function changes in senile dementia of the Alzheimer's type. *Neurobiol Aging* 3:361–370
30. Soikkeli R, Partanen J, Soininen H et al (1991) Slowing of EEG in Parkinson's disease. *Electroencephalogr Clin Neurophysiol* 79:159–165
31. Briel RCG, McKeith IG, Barker WA et al (1999) EEG findings in dementia with Lewy bodies and Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 66:401–403
32. Williamson PC, Merskey H, Morrison S et al (1990) Quantitative electroencephalographic correlates of cognitive decline in normal elderly subjects. *Arch Neurol* 47:1185–1188
33. Minoshima S, Foster NL, Sima AA et al (2001) Alzheimer's disease versus dementia with Lewy bodies: cerebral metabolic distinction with autopsy confirmation. *Ann Neurol* 50:358–365
34. Lobotesis K, Fenwick JD, Phipps A et al (2001) Occipital hypoperfusion on SPECT in dementia with Lewy bodies but not AD. *Neurology* 56:643–649
35. Bohnen NI, Minoshima S, Giordani B et al (1999) Motor correlates of occipital glucose hypometabolism in Parkinson's disease without dementia. *Neurology* 52:541–546
36. Ferini-Strambi L, Di Gioia MS, Castronovo V, Oldani A, Zucconi M, Cappa SF (2004) Neuropsychological assessment in idiopathic REM sleep behavior disorder (RBD). Does the idiopathic form of RBD really exist? *Neurology* 62:41–45
37. Mori E, Shimomura T, Fujimori M et al (2000) Visuo-perceptual impairment in dementia with Lewy bodies. *Arch Neurol* 57:489–493
38. Sahakian BJ, Morris RG, Evenden JL et al (1988) A comparative study of visuospatial memory and learning in Alzheimer-type dementia and Parkinson's disease. *Brain* 111:695–718
39. Ogden J, Growdon J, Corkin S (1990) Deficit on visuospatial tests involving forward planning in high functioning parkinsonians. *Neuropsychiatry Neuropsychol Behav Neurol* 3:125–139
40. Levin B, Llabre M, Weiner W (1989) Cognitive impairments associated with early Parkinson's disease. *Neurology* 39:557–561
41. Levin B, Llabre M, Reisman S et al (1991) Visuospatial impairment in Parkinson's disease. *Neurology* 41:365–369
42. Della Sala S, Di Lorenzo G, Giordano A, Spinnler H (1986) Is there a specific visuo-spatial impairment in Parkinsonians? *J Neurol Neurosurg Psychiatry* 49:1258–1265
43. Shimomura T, Mori E, Yamashita H et al (1998) Cognitive loss in dementia with Lewy bodies and Alzheimer disease. *Arch Neurol* 55:1547–1552
44. Salmon DP, Galasko D, Hansen LA et al (1996) Neuropsychological deficits associated with diffuse Lewy body disease. *Brain Cogn* 31:166–175
45. Ferman TJ, Boeve BF, Smith GE et al (2002) Dementia with Lewy bodies may present as dementia and REM sleep behavior disorder without parkinsonism or hallucinations. *J Int Neuropsychol Soc* 8:907–914
46. Schenck CH, Mahowald MW (2002) REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. *Sleep* 25:120–138
47. Olson EJ, Boeve BF, Silber MH (2000) Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. *Brain* 123:331–339
48. Mahowald MW, Schenck CH. REM sleep parasomnias. In: Kryger MH, Roth T, Dement WC (eds) *Principles and practice of sleep medicine*, 3rd edn. W.B. Saunders Company, Philadelphia, 2000, pp 724–741
49. Hall CS, Van De Castle R (1966) *The content analysis of dreams*. Appleton-Century-Crofts, New York
50. Domhoff GW (2000) Methods and measures for the study of dream content. In: Kryger MH, Roth T, Dement WC (eds) *Principles and practice of sleep medicine*, 3rd edn. W.B. Saunders Company, Philadelphia, pp 463–471
51. Buss AH, Perry M (1992) The Aggression Questionnaire. *J Pers Soc Psychol* 63:452–459
52. Fossati A, Maffei C, Acquarini E, Di Ceglie A (2002) Multigroup confirmatory component and factor analyses of the Italian version of the Aggression Questionnaire. *Eur J Psych Assessment* 1:54–65
53. Revonsuo A (2000) The reinterpretation of dreams: an evolutionary hypothesis of the function of dreaming. *Behav Brain Sci* 23:793–1121