REM Sleep Behavior Disorder and REM Sleep Without Atonia in Probable Alzheimer Disease

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Study Objective: To determine the frequency of rapid eye movement (REM) sleep behavior disorder (RBD) and REM sleep without atonia among patients with Alzheimer disease and control subjects.
Design: Overnight polysomnography.
Settings: Sleep laboratory.
Patients: Fifteen patients with probable Alzheimer disease (mean age ± SD, 70.2 ± 5.6) and 15 age-matched healthy control subjects (mean age ± SD, 67.9 ± 5.4).
Intervention: N/A.
Results: Four patients with Alzheimer disease presented REM sleep without atonia. One of these patients had all the polysomnographic features of RBD, including behavioral manifestations during REM sleep.
Conclusion: RBD is rare, but REM sleep without atonia is relatively frequent in patients with probable Alzheimer disease, a tauopathy.
Keywords: REM sleep behavior disorder; Alzheimer disease; REM sleep without atonia; polysomnography, tauopathy, synucleinopathy.
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INTRODUCTION

Rapid eye movement (REM) sleep behavior disorder (RBD) is a clinical condition characterized by the presence of REM sleep without atonia (RSWA) and involves complex motor activity occurring specifically during REM sleep. The diagnostic criteria for RBD include the presence of RSWA (excessive amounts of sustained or intermittent elevation of submental electromyographic tone) and at least 1 of the following: (1) sleep-related injurious, potentially injurious, or disruptive behaviors by history or (2) abnormal REM sleep behaviors documented during polysomnographic (PSG) monitoring.[1]

RBD and RSWA are strongly associated with Parkinson disease (PD),[2,3] multiple system atrophy (MSA),[3,4] and dementia with Lewy bodies (DLB).[5] At autopsy, these neurodegenerative disorders are characterized by deposits of α-synuclein protein in neurons and are labeled as synucleinopathies. Sporadic cases of RBD or RSWA have also been reported in corticobasal degeneration (CBD), a tauopathy.[6-8] There is no published report of RBD or RSWA in primary progressive aphasia (PPA), Pick disease, or frontotemporal dementia (FTD), all tauopathies. Because RBD or RSWA are rare and were only sporadically reported in non-synucleinopathy disorders, it has been suggested that RBD could be a marker of synucleinopathies.[9]

However, RBD and RSWA have been reported more frequently in progressive supranuclear palsy (PSP), a tauopathy.[10-15] Recently, RBD and RSWA have been systematically evaluated by PSG in 15 patients with probable PSP; 4 of the patients had RSWA and 2 of the latter had PSG-confirmed RBD.[16] In Alzheimer disease (AD), another tauopathy, only 1 patient has been reported to have PSG characteristics of RBD,[17] but subsequent postmortem analysis demonstrated that this patient had a Lewy body variant of AD (i.e., DLB).[18] To our knowledge, RBD and RSWA have never been systematically studied using PSG in a group of patients with AD. We assessed the presence of RBD and RSWA using PSG recordings in consecutive patients with probable AD.

METHODS

Subjects

We studied 15 patients with AD (7 men) and 15 healthy control

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subjects (11 men) without clinical evidence of sleep disturbance in a sleep laboratory for 1 night. The patients were recruited by neurologists at the McGill Center for Studies in Aging (M.P. and S.G.) and the Neurology Department of the Maisonneuve-Rosemont Hospital (A.R.). They were consecutive patients seen at their annual evaluation and were referred for this study regardless of the patient's sleep complaints. The control subjects were recruited either through a newspaper advertisement or in a word-of-mouth fashion.

Patients with AD met the criteria of the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association work group for probable AD.[19] They were at mild to moderate stages of AD, as assessed using the Global Deterioration Scale (stages 3 and 4)[20] and the Mini-Mental State Examination (scores ranged from 12 to 26).[21] Other causes of dementia were ruled out by a Hachinski ischemic score less than 4, computed tomographic scan and blood analyses, which included a complete blood cell count, and thyroid, B_{12}/folic acid, and VDRL, and urine analyses. All patients underwent a clinical neurologic investigation, which was reported to be normal. None of the patients showed evidence of having parkinsonism, fluctuating cognition, or visual hallucinations, which are considered the defining characteristics of DLB.[22] Depression was excluded by the Hamilton scale.

One patient with AD was taking donepezil 10 mg. None of the patients with AD or control subjects was taking benzodiazepines or tricyclic or serotonin reuptake inhibitor antidepressants. In addition, none of the control subjects was taking any other medication known to influence sleep or motor activity. The hospital ethics committee approved the study, and an informed written consent was obtained from both patients and spouses.

Study Design

Lights-out time was based on the patient's habitual bedtime. The recording montage includes left and right electrooculograms, chin electromyogram, and central (C3-A2) and occipital (O2-A1) electroencephalogram leads. Sleep stages 1 to 4 were scored according to a modified version of the method of Rechtschaffen and Kales,[23] using 20-second epochs. REM sleep was scored according to a method developed for RBD, using electroencephalogram and electrooculogram only.[24] In all subjects, the occurrence of the first REM was used to determine the onset of a REM sleep period. The occurrence of a specific EEG feature indicative of another stage (K complex, sleep spindle, or EEG sign of arousal) or the absence of REM during 3 consecutive minutes ended the REM period. The percentage of REM sleep muscle activity corresponds to the total duration of time spent with electromyographic activity during REM sleep with an amplitude at least twice that of the background or greater than 10μV, divided by the total REM sleep duration. The amplitude of the chin electromyogram signal in REM sleep was determined for each subject; it was found to be between 3 and 7 μV. RSWA was defined as the percentage of a REM submental muscle activity of at least 2 SD above the mean of controls. Sleep-stage scoring and calculation of RSWA were performed by a trained technician who was not aware of the patient's diagnosis (S.R.) and who had extensive expertise in scoring PSG recordings of patients with RBD and neurodegenerative disorders. All subjects were also monitored with infrared video in order to observe movements during REM sleep. The presence of RSWA (see definition above) associated with motor behaviors (i.e., talking, laughing, yelling, jerking, gesturing, reaching, punching, sitting, kicking) seen on a PSG-synchronized videotape was essential for the diagnosis of RBD.

Table 1—Polysomnographic Variables in Control Subjects and Patients With Alzheimer Disease

	Controls	AD	p Value
Age, y	67.9 ± 5.4	70.2 ± 5.6	NS
Total sleep time, min	402.4 ± 47.7	353.0 ± 83.0	.05
Sleep latency, min	14.4 ± 12.1	35.2 ± 44.8	NS
Sleep efficiency, %	84.6 ± 9.0	76.7 ± 13.9	.08
Sleep stage, %			
1	13.3 ± 7.5	22.3 ± 15.5	.05
2	65.4 ± 8.1	58.5 ± 14.0	NS
SWS	3.1 ± 6.2	1.9 ± 3.5	NS
REM	18.3 ± 5.5	17.3 ± 8.7	NS
REM sleep latency, min	84.2 ± 31.6	118.4 ± 64.7	.09
REM sleep efficiency, %	87.8 ± 7.0	90.2 ± 10.3	NS
REM sleep periods, no.	4.4 ± 1.1	3.4 ± 1.1	.01
Percentage of REM submental muscle activity	13.2 ± 10.7	23.3 ± 28.0	NS

Data are presented as mean ± SD. AD refers to Alzheimer disease; SWS, slow-wave sleep; REM, rapid eye movement.

Data were presented as means ± SD. Log transformations were performed for variables not normally distributed. Student t tests were performed to evaluate between-group differences on the PSG variables listed in Table 1, and significance level was set at .05. The PSG recording had to be interrupted for 1 patient with AD because of a confusional arousal and agitated motor activity during the postepisode awakening not allowing his return to bed. For this reason, the patient's data were not included in the sleep-architecture analysis. However, this patient presented 1 REM-sleep period that allowed the calculation of the REM-sleep muscle activity.

RESULTS

Frequency of RBD and RSWA in AD

None of the patients had a clinical history of RBD. One patient with probable AD (woman) showed RSWA (35% of REM submental muscle activity) with concomitant complex movements during REM sleep, supporting the diagnosis of RBD. Her computed tomography scan showed a mild cerebral atrophy with no evidence of vascular infarct. The neurologic examination was normal. Cognitive assessments showed a Mini Mental State Examination score of 22 out or 30 and problems with memory, spatial orientation, and picture comprehension. Four (including the patient with RBD) of 15 patients with probable AD (3 women) had RSWA (Figure 1). The patient with AD receiving donepezil did not have RBD or RSWA. None of the control subjects met the PSG criteria for RBD.

Sleep Architecture

Patients with AD showed a shorter total sleep time, a higher percentage of sleep stage 1, and a lower number of REM sleep periods compared with control subjects (Table 1). Moreover, patients with AD tended to have a lower sleep efficiency and a high-

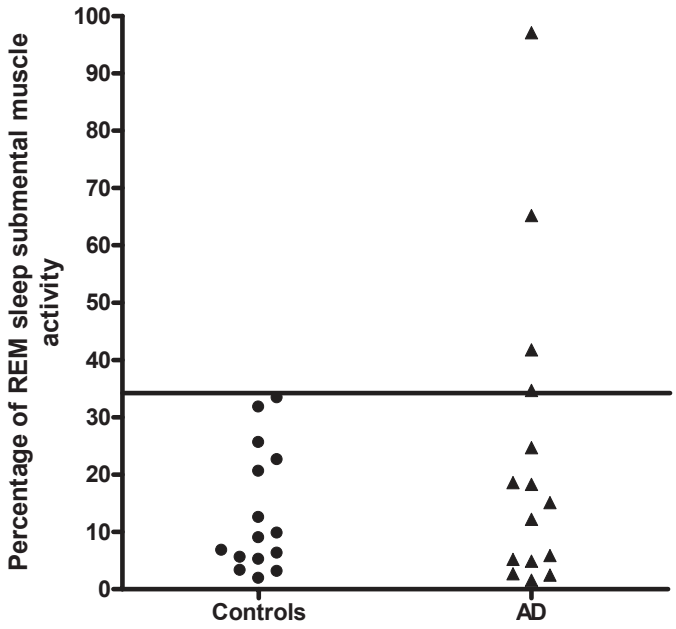

Figure 1—Percentage of rapid eye movement (REM) submental muscle activity in 15 control subjects (closed circles) and 15 patients with Alzheimer disease (AD) [closed triangles]. The horizontal line indicates the cut-off value for REM sleep without atonia (2 SD above the mean of control subjects, ie, 34.6% of REM submental muscle activity).

er REM sleep latency compared with control subjects, although this did not reach statistical significance.

DISCUSSION

The current study evaluated REM sleep muscle activity and the frequency of RBD using PSG-defined criteria in a group of patients with probable AD. This study documented 1 additional case of RBD in a patient with the probable diagnosis of AD who presented RSWA and complex motor activity during REM sleep. RSWA was found in 4 of 15 patients with AD (including the patient with RBD). This is the first study using a quantitative method to assess RSWA in patients with AD; this method has been widely used to measure RSWA in patients with idiopathic RBD[24,25] and in patients with PD[2] or PSP.[15,16] These results show that, although a small number of patients with AD have abnormal motor activity in REM sleep, a significant number of them do have RSWA. None of the patients had parkinsonism, visual hallucinations, or fluctuating cognition, considered to be the core features of DLB.[22] However, in the present study, no histopathologic data were available to confirm the diagnosis of AD. In the only case of autopsy-confirmed AD previously reported to have RBD,[17] subsequent postmortem analyses demonstrated coexisting Lewy bodies.[18] The coexistence of lesions of AD (Aβ amyloid) and Lewy bodies is frequent in the brain of patients with AD.[26,27] Thus, we cannot exclude completely that patients with AD showing RBD or RSWA in the current study may show Lewy bodies at the autopsy. One patient with AD was treated with the acetylcholinesterase inhibitor donepezil and did not show RBD or RSWA. It is possible that donepezil, which has been shown to treat RBD in a small number of patients,[28] may have masked the presence of behavioral manifestations in this case. However, none of the remaining 14 patients was treated with acetylcholinesterase inhibitor medication.

Patients with AD also showed increased percentage of sleep stage 1 and a small decrease in total sleep time and number of REM periods. All other variables were not significantly different from the values obtained in normal control subjects. This is congruent with previous reports of mild sleep disturbances in early stage of AD; more-disrupted sleep is expected in later stages of AD.[29]

RBD and RSWA affect 33% and 58% of patients, respectively, with PD.[2] RBD and RSWA are even more frequent in MSA[3,4,30] and DLB.[5] RBD is also frequent in parkinsonism associated with Parkin gene mutations,[31] in which the presence of Lewy bodies has been recently reported.[32] Recently, the neuropathologic diagnosis of 15 patients presenting with RBD with dementia or parkinsonism was Lewy body disease in 12 patients and MSA in 3 other patients.[33] Until recently, RBD or RSWA was rarely observed in nonsynucleinopathy disorders, such as AD, PSP, CBD, PPA, Pick disease, or FTD. For this reason, RBD has been considered as a hallmark of synucleinopathies.[9] Other studies have shown evidences of RBD or RSWA in patients with CBD[6-8] and PSP[10-16] and in other non–synuclein-mediated disorders, such as Machado-Joseph disease,[34,35] amyotrophic lateral sclerosis,[36,37] Guillain-Barré syndrome,[38] narcolepsy,[39] and nonparaneoplastic limbic encephalitis.[40] It appears that RBD and RSWA are frequent features of synucleinopathies, but they are also present in some cases of tauopathies and other non–synuclein-mediated neurologic disorders. Therefore, the presence of RBD or RSWA in a patient with dementia favors the diagnosis of DLB[41] (RBD is now considered as a suggestive criterion for the diagnosis of DLB)[22] but does not completely rule out the diagnosis of AD or PSP. Moreover, the presence of RBD and RSWA in neurodegenerative disorders may be related more to the localization of the degeneration than to a specific type of neuronal degeneration.

Studies performed in animals have suggested that the muscle atonia and phasic motor activity observed during REM sleep are 2 different phenomena, with their own distinct physiologic mechanisms. The presence of RBD or RSWA depends of the location and the extent of the brainstem lesions. RSWA with minimal motor manifestations is observed after lesions of neurons or caudally projecting fibers of the tegmentoreticular pathway.[42] Behavioral manifestations during REM sleep are more likely to occur after additional damage to areas located more rostrally. In humans, there is some evidence of dissociation between RSWA and behavioral manifestations of RBD. For example, RSWA without behavioral manifestations has been noted after the administration of serotonergic antidepressants.[43] Moreover, the administration of clonazepam in patients with idiopathic RBD reduces the density of phasic electromyographic activity, whereas the percentage of RSWA remains elevated,[24] further supporting the hypothesis that 2 different mechanisms are involved. Several questions remain unanswered. For example, does RSWA represent an evolutional stage in the development of RBD? One observation that supports this hypothesis is a case report of a patient with CBD presenting only RSWA on the first PSG evaluation, which showed motor activities during REM sleep on the follow-up PSG 13 months later.[8] However, longitudinal PSG studies of a large group of patients with RSWA, associated or not with neurodegenerative disorders, would be mandatory to answer to this question.

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REFERENCES

1. The International Classification of Sleep Disorders: Diagnostic and Coding Manual, 2nd ed. Westchester IL: American Academy of Sleep Medicine; 2005:148-52.
2. Gagnon JF, Bedard MA, Fantini ML, et al. REM sleep behavior disorder and REM sleep without atonia in Parkinson's disease. Neurology 2002;59:585-9.
3. Iranzo A, Santamaria J, Rye DB, et al. Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. Neurology 2005;65:247-52.
4. Plazzi G, Corsini R, Provini F, et al. REM sleep behavior disorders in multiple system atrophy. Neurology 1997;48:1094-7.
5. Boeve BF, Silber MH, Ferman TJ, et al. REM sleep behavior disorder and degenerative dementia: an association likely reflecting Lewy body disease. Neurology 1998;51:363-70.
6. Gatto EM, Uribe Roca C, Martinez O. Subclinical REM sleep behavior disorder (RBD) in two patients with corticobasal degeneration (CBD). Mov Disord 2005;20 (suppl 10):S107.
7. Kimura K, Tachibana N, Aso T, Kimura J, Shibasaki H. Subclinical REM sleep behavior disorder in a patient with corticobasal degeneration. Sleep 1997;20:891-4.
8. Wetter TC, Brunner H, Collado-Seidel V, Trenkwalder C, Winkelmann J. Sleep and periodic limb movements in corticobasal degeneration. Sleep Med 2002;3:33-6.
9. 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.
10. Laffont F, Autret A, Minz M, et al. Polygraphic sleep recordings in 9 cases of Steele-Richardson's disease. Rev Neurol (Paris) 1979;135:127-42.
11. Laffont F, Leger JM, Penicaud A, et al. Sleep abnormalities and evoked potentials (VEP-BAER-SEP) in progressive supranuclear palsy. Neurophysiol Clin 1988;18:255-69.
12. 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.
13. Sforza E, Krieger J, Petiau C. REM sleep behavior disorder: clinical and physiopathological findings. Sleep Med Rev 1997;1:57-69.
14. Pareja JA, Caminero AB, Masa JF, Dobato JL. A first case of progressive supranuclear palsy and pre-clinical REM sleep behavior disorder presenting as inhibition of speech during wakefulness and somniloquy with phasic muscle twitching during REM sleep. Neurologia 1996;11:304-6.
15. Rompre S, Gagnon J, Fantini M, Petit D, Montplaisir J. REM sleep without atonia in progressive supranuclear palsy. Sleep 2004;27: A289.
16. Arnulf I, Merino-Andreu M, Bloch F, et al. REM sleep behavior disorder and REM sleep without atonia in patients with progressive supranuclear palsy. Sleep 2005;28:349-54.
17. Schenck CH, Garcia-Rill E, Skinner RD, Anderson ML, Mahowald MW. A case of REM sleep behavior disorder with autopsy-confirmed Alzheimer's disease: postmortem brain stem histochemical analyses. Biol Psychiatry 1996;40:422-5.
18. Schenck CH, Mahowald MW, Anderson ML, Silber MH, Boeve BF, Parisi JE. Lewy body variant of Alzheimer's disease (AD) identified by postmortem ubiquitin staining in a previously reported case of AD associated with REM sleep behavior disorder. Biol Psychiatry 1997;42:527-8.
19. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34:939-44.
20. Reisberg B, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psychiatry 1982;139:1136-9.
21. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
22. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies. Third report of the DLB consortium. Neurology 2005;65:1863-72.
23. Rechtschaffen A, Kales AA. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Washington, DC: US Government Printing Office, Public Health Service; 1968.
24. Lapierre O, Montplaisir J. Polysomnographic features of REM sleep behavior disorder: development of a scoring method. Neurology 1992;42:1371-4.
25. Fantini ML, Gagnon JF, Filipini D, Montplaisir J. The effects of pramipexole in REM sleep behavior disorder. Neurology 2003;61:1418-20.
26. Mikolaenko I, Pletnikova O, Kawas CH, et al. Alpha-synuclein lesions in normal aging, Parkinson disease, and Alzheimer disease: evidence from the Baltimore Longitudinal Study of Aging (BLSA). J Neuropathol Exp Neurol 2005;64:156-62.
27. Hamilton RL. Lewy bodies in Alzheimer's disease: a neuropathological review of 145 cases using alpha-synuclein immunohistochemistry. Brain Pathol 2000;10:378-84.
28. Ringman JM, Simmons JH. Treatment of REM sleep behavior disorder with donepezil: a report of three cases. Neurology 2000;55:870-1.
29. Petit D, Gagnon JF, Fantini ML, Ferini-Strambi L, Montplaisir J. Sleep and quantitative EEG in neurodegenerative disorders. J Psychosom Res 2004;56:487-96.
30. Vetrugno R, Provini F, Cortelli P, et al. Sleep disorders in multiple system atrophy: a correlative video-polysomnographic study. Sleep Med 2004;5:21-30.
31. Kumru H, Santamaria J, Tolosa E, et al. Rapid eye movement sleep behavior disorder in parkinsonism with parkin mutations. Ann Neurol 2004;56:599-603.
32. Pramstaller PP, Schlossmacher MG, Jacques TS, et al. Lewy body Parkinson's disease in a large pedigree with 77 Parkin mutation carriers. Ann Neurol 2005;58:411-22.
33. Boeve BF, Silber MH, Parisi JE, et al. Synucleinopathy pathology and REM sleep behavior disorder plus dementia or parkinsonism. Neurology 2003;61:40-5.
34. Friedman JH. Presumed rapid eye movement behavior disorder in Machado-Joseph disease (spinocerebellar ataxia type 3). Mov Disord 2002;17:1350-3.
35. Iranzo A, Munoz E, Santamaria J, Vilaseca I, Mila M, Tolosa E. REM sleep behavior disorder and vocal cord paralysis in Machado-Joseph disease. Mov Disord 2003;18:1179-83.
36. Laffont F, Autret A, Minz M, Beillevaire T, Gilbert A, Cathala HP. Polygraphic study of nocturnal sleep in three degenerative diseases: ALS, oligo-ponto-cerebellar atrophy, and progresssive supranuclear palsy. Waking Sleeping 1979;3:17-29.
37. Minz M, Autret A, Laffont F, Beillevaire T, Cathala HP, Castaigne P. A study on sleep in amyotrophic lateral sclerosis. Biomedicine 1979;30:40-6.
38. Cochen V, Arnulf I, Demeret S, et al. Vivid dreams, hallucinations, psychosis and REM sleep in Guillain-Barre syndrome. Brain 2005;128:2535-45.

39. Schenck CH, Mahowald MW. Motor dyscontrol in narcolepsy: rapid-eye-movement (REM) sleep without atonia and REM sleep behavior disorder. Ann Neurol 1992;32:3-10.
40. Iranzo A, Graus F, Clover L, et al. Rapid eye movement sleep behavior disorder and potassium channel antibody-associated limbic encephalitis. Ann Neurol 2006;59:178-81.
41. Ferman TJ, Boeve BF, Smith GE, et al. REM sleep behavior disorder and dementia: cognitive differences when compared with AD. Neurology 1999;52:951-7.
42. Hendricks JC, Morrison AR, Mann GL. Different behaviors during paradoxical sleep without atonia depend on pontine lesion site. Brain Res 1982;239:81-105.
43. Winkelman JW, James L. Serotonergic antidepressants are associated with REM sleep without atonia. Sleep 2004;27:317-21.