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ORIGINAL ARTICLE

Prevalence and determinants of rapid eye movement sleep behavior disorder in the general population

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Abstract

Study Objectives: Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia associated with neurodegenerative synucleinopathies. Its prevalence is largely unknown. This study determined the prevalence and characteristics of RBD in the general population using gold-standard polysomnography.

Methods: Full polysomnographic data from 1,997 participants (age = 59 ± 11.1 years, 53.6% women) participating in a population-based study (HypnoLaus, Lausanne, Switzerland) were collected. Sleep-related complaints and habits were investigated using various sleep measures including the Munich Parasomnia Screening (MUPS) questionnaire, which includes two questions evaluating complex motor behaviors suggestive of RBD. Full polysomnography was performed at home. For participants screening positive for RBD, muscle activity during REM sleep was quantified to diagnose RBD.

Results: Three hundred sixty-eight participants endorsed dream-enactment behavior on either of the two MUPS questions, and 21 fulfilled polysomnographic criteria for RBD, resulting in an estimated prevalence of 1.06% (95% CI = 0.61–1.50), with no difference between men and women. Compared with RBD– participants, RBD+ took more frequently antidepressants and antipsychotics (23.8% vs. 5.4%, $p = .005$; 14.3% vs. 1.5%, $p = .004$, respectively) and were more frequently smokers or ex-smokers (85% vs. 56.6%, $p = .011$). On polysomnography, RBD+ had more stage N2 sleep (52 ± 11.5% vs. 46.3 ± 10.2%, $p = .024$) and less REM sleep (18 ± 6.4% vs. 21.9 ± 6.2%, $p = .007$), lower apnea–hypopnea index in REM sleep (3.8 ± 5.2 vs. 8.9 ± 13/hour, $p = .035$), and lower autonomic arousal index (31 ± 14.9 vs. 42.6 ± 19.5/hour, $p = .002$).

Conclusions: In our middle-to-older age population-based sample, the prevalence of RBD was 1.06%, with no difference between men and women. RBD was associated with antidepressant and antipsychotic use and with minor differences in sleep structure.

Statement of Significance

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia frequently associated or preceding neurodegenerative diseases such as synucleinopathies. Its occurrence in the general population is largely unknown. Analyzing data from 1,997 participants to the population-based HypnoLaus study who completed the Munich Parasomnia Screening questionnaire and had a complete polysomnography at home, we estimate the prevalence of RBD at 1.06%, with no significant difference between men and women. RBD was associated with antidepressant and antipsychotic use, and with minor differences in sleep structure. Knowing the prevalence and characteristics of RBD has important implications, as people with RBD can be ideal candidates for neuroprotective approaches, and can help us to better understand the progression of neurodegenerative disorders.

Key words: polysomnography; synucleinopathies; parasomnia; sleep; REM sleep without atonia

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Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is characterized by complex motor behaviors during sleep related to the loss of the normal atonia of REM sleep [1, 2]. Affected patients appear to act out their dreams; for example, talking, yelling, thrashing, or punching while asleep. RBD is the strongest known risk factor for neurodegenerative synucleinopathies, including Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy. Long-term studies have shown that the majority of persons with onset of idiopathic RBD in mid-life are actually in prodromal stages of neurodegeneration [3–5].

Accurate diagnosis of RBD requires polysomnography (PSG), which documents the abnormal increase in tone during REM sleep. The use of questionnaires alone is prone to false positive identification of RBD [6] because many other conditions such as severe periodic limb movements during sleep (PLMS), NREM parasomnia, obstructive sleep apnea, and nocturnal epilepsy can mimic RBD [7, 8]. The prevalence of RBD in the general population is difficult to evaluate as it requires large-scale PSG population-based studies. However, knowing the prevalence of RBD in the general population can have important implications in terms of the development of strategies for diagnosis and management of affected patients. RBD patients can be ideal candidates for testing new neuroprotective approaches, and to better understand the pathophysiology and progression of synucleinopathies from their presymptomatic stages.

The aim of our study was to examine the prevalence of PSG-confirmed RBD and to assess demographics, environmental risk factors, and comorbidities of RBD in the general population. For this purpose, we analyzed data gathered through the HypnoLaus cohort, a large population-based study that assessed overnight PSG as well as validated sleep questionnaires and environmental risk factors in over 2,000 participants.

Methods

Participants

The HypnoLaus Sleep Cohort study included participants of the population-based CoLaus/PsyCoLaus Cohort study described previously [9, 10]. Briefly, the CoLaus/PsychoLaus study included a random sample of 6,734 participants (age range: 35–75 years) selected from the residents of Lausanne city (Switzerland) between 2003 and 2006. The distribution of age groups, gender, and zip codes of participants was similar to the source population [9]. During the first follow-up of the cohort, 5 years after the initial phase, all participants were invited to undergo new physical (n = 5064) and psychiatric (n = 4005) examination. During this first follow-up, a random subsample also took part in HypnoLaus, an evaluation of self-reported and objective sleep characteristics [11, 12]. CoLaus/PsyCoLaus and HypnoLaus were approved by the Ethics Committee of the University of Lausanne and a written informed consent was obtained from all participants.

Sleep questionnaires

Sleep-related complaints and habits were investigated using questionnaires, including the Pittsburgh Sleep Quality Index (PSQI) [13], the Epworth Sleepiness Scale (ESS) [14], and the French version of the Munich Parasomnia Screening (MUPS) questionnaire, a validated self-rating instrument with 21 items assessing the lifetime prevalence and current frequency of parasomnias and nocturnal behaviors in adult persons, experienced by themselves or reported to them by others [15]. Two specific questions evaluate the presence of nocturnal activity suggestive of RBD: "Have you ever lashed about, hitting or kicking?" and "Have you ever actually done what you dreamt, e.g., gesticulating or lashing about?" We considered those participants who answered yes to either of the two questions as screen positives for possible RBD.

Polysomnography

All participants had a complete PSG at home (Titanium, Embla® Flaga, Reykjavik, Iceland), as described previously [11], including a total of 18 channels, in accordance with 2007 American Academy of Sleep Medicine (AASM) recommended setup specifications [16]. Two trained sleep technicians, who were unaware of the results of screening questionnaires, manually scored the PSG recordings using Somnologica software (Version 5.1.1, Embla® Flaga, Reykjavik, Iceland). Sleep stages were scored in 30-second epochs according to the 2007 AASM criteria, as well as the arousals [16]. Apneas, hypopneas, and respiratory effort-related arousals were scored according to the 2012 AASM criteria [17]. The average number of apneas/hypopneas per hour of sleep (apnea–hypopnea index [AHI]) was calculated. PLMS were scored according to the official World Association of Sleep Medicine standards (WASM) [18], and the PLMS index (PLMSI) was calculated. As autonomic arousals were considered, the pulse-wave amplitude (PWA) drops (of at least 30% of baseline PWA) obtained from finger photoplethysmography, reflecting peripheral vasoconstriction [19, 20]. The number and index per hour of sleep of autonomic arousals were calculated.

Muscle activity during REM

This analysis was performed using the software Brain RT (OSG Ltd., Bussestraat 17, 2840 Rumst, Belgium. Contact person: Sabine Wuytens; website: http://www.osg.be). This software has previously been validated for RBD [21] and allows classification of REM-related EMG activity according to the Sleep Innsbruck Barcelona (SINBAR) criteria for "any," phasic, and tonic EMG activity in the mentalis muscle [22].

For all participants scoring positive in at least one of the RBD-related questions of the MUPS, quantitative analysis of muscle activity during the full REM sleep was performed. Recordings exceeding the SINBAR cutoff values of 18.2% for "any," 16.3% for phasic, and 9.6% for tonic EMG activity during REM sleep in the Mentalis muscle [23] were reviewed by a board-certified sleep expert with experience in RBD (BF) for verification of the results, and exclusion of false positive detections due to snoring, EKG or electrode artifacts, or increased EMG activity related to arousals or respiratory events. Only patients who scored positive in at least one of the two questions of the MUPS and whose recordings exceeding the SINBAR cutoff values for RBD after manual artifact correction were classified as having PSG-confirmed RBD.

Clinical and laboratory measurements

The body-mass index (BMI) was calculated and participants were classified as overweight if their BMI was between 25 and 30 kg/m^2 and obese if BMI ≥30 kg/m^2. Blood pressure (BP) was measured in triplicate on the left arm and values averaged between the last

two readings. Arterial hypertension was defined as a systolic BP (SBP) ≥140 mm Hg and/or a diastolic BP (DBP) ≥90 mm Hg and/or current use of antihypertensive medication. Diabetes was defined as a fasting blood glucose level of ≥7 mmol/L (126 mg/dL) and/or current use of antidiabetic medication. Smoking habits were self-reported and dichotomized as current smoker/ex-smoker or never-smoker. Alcohol drinking was dichotomized as currently drinking or no alcohol consumption. Caffeine intake was estimated based on the number of cups recorded per day. Medication use at the time of sleep studies was recorded and coded according to the ATC classification of the World Health Organization (http://www.whocc.no/atcddd).

Statistical analyses

Statistical analyses were performed using R (R Core Team, 2014) [24] and Matlab (The MathWorks Inc. version 8.3.0.532 [R2014a]). For descriptive statistics, continuous variables were summarized as mean and standard deviation (*SD*), whereas categorical variables were summarized as number of participants and percentages. Chi-square test and Fisher's exact test for the categorical variables and *t*-test or Wilcoxon rank-sum test for the continuous variables were used for comparisons between groups. Finally, we also performed a sensitivity analysis to assess prevalence estimates using different case definitions. Statistical significance was considered for a two-sided test *p*-value of <.05.

Results

Description of the sample

Among 3,043 consecutive participants from the first follow-up of the population-based CoLaus/PsyCoLaus cohort study, 2,168 (71.1%) agreed to have a PSG at home. Technical problems resulting in insufficient data for complete PSG scoring were encountered in 60 cases (2.8%); fifty-four participants accepted to repeat the PSG and six participants declined, resulting in 2,162 participants. Of these participants, 165 did not answer RBD-screening questions of the MUPS, resulting in 1,997 participants (mean age: 59 ± 11.1 years, 53.6% women) included in the final analysis. Compared with the whole CoLaus/PsyCoLaus cohort, they were similar in terms of age, sex, BMI, and ethnic origin, and they were representative of Lausanne's general population [9].

Prevalence of RBD

A positive answer to current occurrence of sleep-related behaviors described on either of the two questions of the MUPS was provided by 368 (18.4%) participants. These participants were then evaluated for excessive muscle activity during REM sleep. Due to artifacts in the mentalis channel, in 16 participants it was not possible to assess REM atonia; these participants were excluded from analysis and from the total number of participants for the calculation of the prevalence of RBD. Of the remaining 352 participants, 21 had REM sleep without atonia exceeding the quantitative cutoff values for REM-related EMG activity. This resulted in a RBD population prevalence of 1.06% (95% CI = 0.61–1.50) (Figure 1).

Clinical characteristics of RBD positive participants

Compared with participants with no clinical suspicion of RBD (RBD–), participants with RBD (RBD+) were similar in terms of age, sex, and BMI. Compared with RBD– participants, RBD+ participants were more frequently taking antidepressants [23.8% vs. 5.4%, p = .005; unadjusted OR and (95% CI): 5.41 (1.94–15.11), p = .001] and antipsychotics [14.3% vs. 1.5%, p = .004; OR: 10.98 (3.03–39.8), p < .001]. There was also a nonsignificant trend toward a more frequent intake of hypnotics (19% vs. 8.2%, p = .091). No significant differences were found for the prevalence of hypertension and diabetes, nor in alcohol or coffee consumption, but RBD+ participants reported higher tobacco consumption [85.0% vs. 56.6%, p = .011; OR: 4.34 (1.26–14.89), p = .019] (Table 1). In a multivariate analysis, antidepressants, antipsychotics, and smoking remained independently and significantly associated with RBD (Table 2).

Regarding PSG variables, RBD+ participants spent more time in stage N2 (52 ± 11.5% vs. 46.3 ± 10.2%, p = .024) and less in REM sleep (18 ± 6.4% vs.21.9 ± 6.2%, p = .007), and exhibited longer REM sleep latency from sleep onset (157.5 ± 108.7 vs. 94.6 ± 62.3 minutes, p = .003) than RBD– participants. The total AHI was similar in both groups, but the AHI in REM sleep was lower in the RBD+ group (3.8 ± 5.2 vs. 8.9 ± 13/hour, p = .035). A trend towards higher PLMSI and arousal index was also noted. There was a significantly lower autonomic arousal index (31 ± 14.9 vs. 42.6 ± 19.5/hour, p = .002). Finally, RBD+ participants had a higher ESS score but still in the nonsleepy range (8.2 ± 5 vs. 5.9 ± 3.8, p = .016), and similar self-reported sleep quality, as measured by the PSQI score (Table 3).

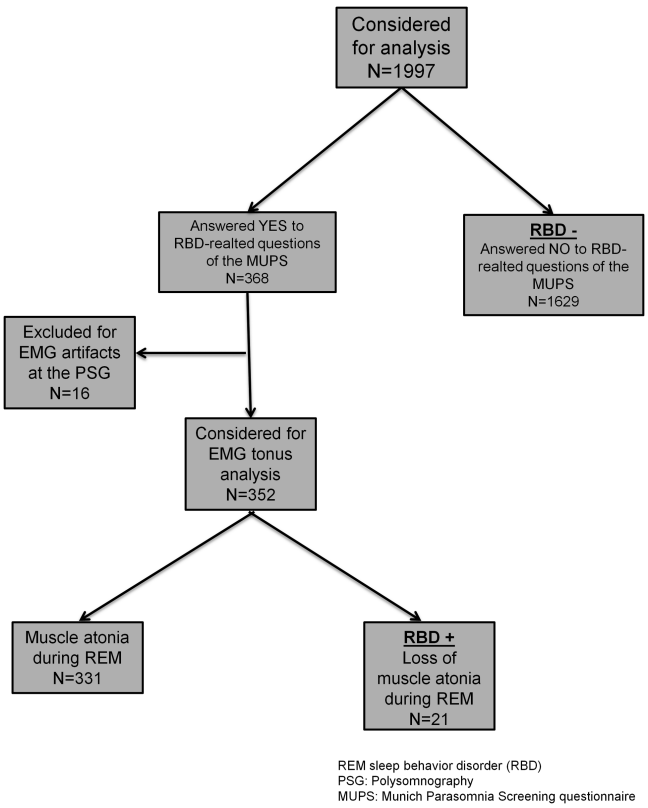

Figure 1. Study population and diagnostic procedure of rapid eye movement sleep behavior disorder cases.

Table 1. Demographic and Clinical Characteristics of the Study Population Stratified by RBD Status

	RBD negative N = 1,629	RBD positive N = 21	*p*
Age*	59 (11)	56 (11)	.342
Women (%)	874 (53.7)	10 (47.6)	.580
BMI (kg/m²)*	26.05 (4.4)	25.65 (3.1)	.880
Hypertension (%)	676 (41.6)	6 (28.6)	.270
Diabetes (%)	155 (9.4)	1 (4.8)	.714
Alcohol consumption (%)	1.389 (85.4)	17 (81.0)	.535
Tobacco consumption (%)	902 (56.6)	17 (85.0)	.011
Coffee consumption (%)			.304
No	106 (6.5)	1 (5.0)	
1–3 cups/day	1.077 (66.6)	14 (70.0)	
4–6 cups/day	380 (23.5)	3 (15.0)	
>6 cups/day	55 (3.4)	2 (10.0)	
Treatment (%)			
Antipsychotics	24 (1.5)	3 (14.3)	.004
Hypnotics	132 (8.2)	4(19.1)	.091
Antidepressants	87 (5.5)	5 (23.8)	.005

RBD = rapid eye movement sleep (REM) behavior disorder; BMI = body mass index.
Results are expressed as number (%) or as * mean (*SD*).
p-**Value: RBD– vs.** RBD+.

Sensitivity analysis

The addition of a minimum current dream enactment behavior frequency of at >1 per year (termed as "rarely" in the questionnaire) resulted an estimate of 0.86%, and requiring >1 episode/month (termed as "sometimes") resulted in an estimate of 0.71%. We used the mentalis muscle to assess REM atonia; addition of other muscles, particularly flexor digitorum superficialis, can increase sensitivity. When adjusting for the estimated sensitivity of the mentalis compared with a complete EMG montage (i.e., 93.5% [23]), the prevalence estimate increases slightly to 1.14%.

Discussion

Capitalizing upon a large 2,000-participant PSG-studied cohort, we were able to reliably estimate the prevalence of RBD in the general population. Our central finding is that the prevalence of PSG-confirmed RBD is 1.06% in those aged 40–80. This estimate is higher than previous studies which screened for sleep injury [25], considerably lower than questionnaire-based studies without PSG confirmation [26, 27], and notably consistent with a smaller PSG-based study [28]. On analysis of risk factors, people with RBD use more antidepressants and antipsychotics and are more likely to have smoked. Regarding sleep variables, RBD patients endorse higher sleepiness scores but still in the non-sleepy range and have more stage N2 sleep, a slight reduction of REM sleep duration, increased latency of the appearance of REM sleep, lower autonomic arousal index, and lower AHI during REM sleep on PSG. There were no differences in other sleep stages, or in the total AHI.

Table 2. Multivariate Analysis of Clinical Characteristics Associated With RBD

RBD	Odds ratio	95% Conf. interval	*p*
Age	0.96	0.92 – 1.01	.138
Male gender	1.30	0.52 – 3.23	.573
Antidepressants	4.56	1.40 – 14.83	.011
Antipsychotics	5.61	1.26 – 25.00	.024
Tobacco consumption	3.71	1.06 – 12.96	.039

RBD = rapid eye movement sleep (REM) behavior disorder.
Results are expressed as odds ratio and 95% confidence interval.
Statistical analysis performed using logistic regression.

Prevalence estimates

The prevalence of PSG-confirmed RBD in the general population aged 40–80 was approximately 1%. For this analysis, our case definition of RBD was the description of at least one symptom of dream enactment (regardless of frequency) combined with quantitatively confirmed loss of REM atonia on PSG. We preferred a relatively inclusive definition of dream enactment because true RBD has a wide range in frequency and severity and can occasionally remit for periods of time. However, we also performed sensitivity analysis to assess different case definitions, with broadly similar results (range = 0.71–1.14%).

Population-based epidemiological studies on RBD using PSG are scarce. One of these studies is based on 348 individuals from South Korea aged 60 years and over [28]. This study had a methodology different from ours, as there was no initial question for RBD. Rather, REM tone was quantified on PSG and participants with abnormal tone were contacted by phone asking for dream enactment behavior. This produced a prevalence estimate of 1.15%, very close to our estimate. A recent study evaluated the prevalence of RBD in a sample from the elderly Spanish community [29]. The authors applied a two-phase design, using a validated single question for the screening of RBD followed, in those who screened positive, by clinical assessment and video-PSG. From an initial group of 539 individuals aged 60 years or older who underwent routine visits in primary care centers, four (three men and one woman) were diagnosed as having RBD, yielding an estimated prevalence of 0.74% (95% CI = 0.29–1.89), which is within the range of what we found in our study. Two other studies estimated the prevalence of RBD related to sleep injury (i.e., severe RBD only) [25, 30]. One asked for history of sleep injury in 1,034 patients aged over 70 years and found a positive history in eight. Of these, four had RBD confirmed on PSG, translating to a 0.4% prevalence of severe injury-causing RBD [25]. The second used a telephone-based interview to screen for sleep injury, followed by a more in-depth telephone interview to delineate the possible cause; it found that approximately 0.5% of interviewees had a history consistent with injury due to RBD (but there was no confirmation of diagnosis on PSG [30]). Other studies assessed the prevalence of dream enactment behavior without further PSG diagnostic confirmation. Boot et al. assessed 651 patients aged over 70 years with the Mayo Sleep Questionnaire and found possible RBD in 6.7% [26]. Mahlknecht et al. assessed 456 participants aged over 60 years form the Bruneck cohort with the RBD Screening Questionnaire and the Innsbruck RBD-Inventory, and found a prevalence of RBD of 4.6% and 7.7%, respectively [27]. Wong et al. found that 5.9% of men and 4.1% of women in a large Chinese general population aged over 24 years screened positive on the RBD single question screen [31]. Importantly, there might be many reasons other than RBD for endorsing possible dream enactment

or violent behavior during sleep on a screening questionnaire, including NREM parasomnia, obstructive sleep apnea, sleep-related hypermotor epilepsy, complex partial seizures, restless legs/PLMS, nonspecific sleep behaviors, etc. Indeed, we found that only 5.9% of those who endorsed possible dream enactment using the MUPS questionnaire had confirmed RBD at the PSG. Therefore, it seems to be essential to confirm RBD diagnosis by PSG in order to reliably estimate the prevalence in studies conducted in the community.

Characteristics of RBD positive participants

We assessed numerous determinants for RBD in our cohort. A notable finding of this study was the absence of a sex difference in RBD: in our population-based cohort, 52% of RBD+ were men vs. 48% of those RBD–. This is clearly different from what has been seen in clinical cohorts, which have a striking male predominance. The primary reasons for the sex difference in sleep-center cohorts are not clear. This presentation bias could be due to several factors. For example, men were reported to have higher proportion of violent behaviors, in general [32] and sleep-related [33] (during arousal disorders [34], RBD episodes [35], or during epileptic seizures [36]), which may stimulate them to seek medical advice more frequently. Contrary to sleep clinics, in this study, all participants were screened for dream enactment regardless of severity, removing much of this bias. Our finding is consistent with studies in PD which also actively screen for RBD and show smaller differences in prevalence in men vs. women [37, 38]. It appears thus that the strong sex differences seen in sleep centers are at least partially artifactual and illustrate the advantages of population-based studies for studying risk factors for disease. It also implies that efforts should be made to actively screen for RBD in women.

The connection between RBD and increased smoking is notable, because it is well-established that smoking is actually associated with a lower risk of PD and is also not associated with higher risk of DLB [39]. This has also been reported in other studies: the RBD study group in PSG-confirmed RBD cases found an OR of 1.41 for ever-smokers [40]. This surprising finding suggests that RBD has a unique epidemiology, which is different from that of PD. There have been many studies suggesting that RBD marks a specific subtype of PD, with high risk of dementia, motor worsening, and autonomic dysfunction, termed the "diffuse-malignant" subtype [41]. If so, its environmental risk factors may also differ.

We found a clear connection between antidepressants and RBD. This association has been frequently reported in other studies [42–45] and may reflect a complex relationship. Antidepressants can trigger RBD, perhaps via a direct modulation of serotonergic innervation of spinal interneurons [46]. In many cases, the antidepressants trigger a subclinical RBD that is already present, as demonstrated by studies in which people with antidepressant-associated RBD clearly had other markers of prodromal synucleinopathy [47]. Also, antidepressants are a marker of depression, which is a prodromal marker of PD [48]. By contrast, antipsychotics have not been previously linked to RBD, but this is line with studies suggesting that dopaminergic modulation can influence RBD [49].

There were only modest differences in sleep parameters. On PSG, RBD+ participants had an increased proportion of time spent in stage N2 sleep, a decrease in REM sleep, and longer latency to REM sleep. It should be noted that in scoring sleep, one of the hallmarks of REM sleep is loss of REM atonia; this may be more difficult to identify in RBD and could result in a false-positive difference. The robust difference in REM latency could also be explained by antidepressant medication effect. The lower AHI in REM could be explained by the increase in muscle tone during REM sleep, preventing upper airway collapse. We found that autonomic arousals, measured by the PWA drops, were less frequent among people with RBD than controls, without differences in other arousals. Autonomic dysfunction has been well described in idiopathic RBD, as assessed with clinical symptoms and signs [50, 51], Valsalva testing, cardiac sympathetic

Table 3. Sleep Characteristics of the Study Population Stratified by RBD Status

	RBD negative*N* = 1629	RBD positive*N* = 21	*p*
PSQI score	5.09 (3.34)	4.61 (2.45)	.798
Epworth sleepiness score	5.91 (3.77)	8.25 (5.03)	.016
Total sleep time, min	400.94 (71.93)	421.35 (57.70)	.165
Sleep onset latency, min	17.33 (22.86)	22.02 (24.89)	.270
Sleep efficiency, %	84.49 (10.91)	85.98 (11.46)	.322
WASO, min	75.37 (56.8)	73.58 (67.58)	.478
Stage N1, %	11.88 (7.21)	12.76 (6.97)	.316
Stage N2, %	46.31 (10.23)	51.99 (11.56)	.024
Stage N3, %	19.89 (8.44)	17.16 (7.71)	.118
REM, %	21.90 (6.20)	18.05 (6.39)	.007
REM latency, min	94.61 (62.32)	157.54 (108.67)	.003
AHI, *n*/h	15.29 (16.39)	10.21 (10.14)	.136
AHI in REM, *n*/h	8.9 (13)	3.8 (5.2)	.035
ODI, *n*/h	14.45 (15.13)	10.16 (8.68)	.293
PLMSI, *n*/h	13.78 (23.54)	23.81 (27.97)	.075
Arousal index, *n*/h	21.25 (11.03)	23.23 (7.14)	.082
Autonomic arousal index, *n*/h	42.61 (19.48)	31.02 (14.88)	.002

RBD = rapid eye movement sleep (REM) behavior disorder; PSQI = Pittsburgh Sleep Quality Index; WASO = wake after sleep onset; AHI = apnea/hypopnea index; ODI = oxygen desaturation index (≥3%); PLMSI = periodic limb movements during sleep index.
Results are expressed as mean (*SD*).
p-Value: RBD– vs. RBD+.

denervation on MIBG scintigraphy [52], and loss of the normal beat-to-beat variability on electrocardiogram [53]. These differences in sleep parameters do not seem to have an impact on the overall self-reported quality of sleep, as measured by the PSQI (scores were similar in the two groups). Finally, RBD participants had higher ESS sleepiness scores than controls, even if the values remained in the nonsleepy ranges. Two other studies from sleep centers have documented increased somnolence in RBD [54, 55]. There is therefore the possibility that the RBD+ group may have an evolving neurodegenerative disorder that in the future would be manifested by excessive daytime sleepiness and an ESS in the sleepy range (score >10). However, the question if excessive daytime sleepiness predicts neurodegeneration in RBD is still a matter of debate [56, 57]. It should be kept in mind that RBD+ participants were also taking antidepressant and antipsychotic drugs more frequently, and so the higher ESS score could be explained by sedating side effects from these medications.

Strengths and limitations

Some limitations of the study should be pointed out. Symptoms of dream enactment were screened using questions, without a sleep physician interview. The sensitivity of the questions is unknown, and therefore, some patients would presumably have been missed. Nor do we have precise information about whether the participants were sleeping alone or with a bed partner. We can also assess only symptomatic RBD; if patients were unaware of any dream enactment, they would not be detected in our study. Encouraging the input of bed partners in future studies would lower the rate of false negative findings. Therefore, we are unable to estimate the prevalence of asymptomatic RBD. There is also some night-to-night variability of REM atonia measurement; presumably, a few screen positives that were near cutoffs for REM atonia might have been indeed positive, if PSG was performed and results averaged over multiple nights. As this is the first-ever large population-based polysomnographic study, we assessed markers without a priori hypotheses, with no adjustment for multiple comparisons. Therefore, the findings regarding correlates of RBD should be considered exploratory in nature [58]. With a total of 21 people with RBD, the power is limited to assess risk factors and correlates; larger studies might be able to detect more significant correlations. Conversely, our study had some strengths; the first, it relied on a large sample size, which provided higher statistical power than the previous studies; second, all participants were assessed using PSG, allowing the most precise estimate of RBD prevalence yet performed.

Conclusions

In this large population-based PSG study, we estimated the prevalence of RBD to be 1.06%, with no difference between men and women. RBD is associated with the use of antidepressants and antipsychotics, symptoms of somnolence, and differences in polysomnographic measures.

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References

1. Schenck CH, *et al*. Rapid eye movement sleep behavior disorder: devising controlled active treatment studies for symptomatic and neuroprotective therapy–a consensus statement from the International Rapid Eye Movement Sleep Behavior Disorder Study Group. *Sleep Med*. 2013;**14**(8):795–806.
2. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*, 3rd ed. Darien, IL: American Academy of Sleep Medicine, 2014.
3. Schenck CH, *et al*. Delayed emergence of a parkinsonian disorder or dementia in 81% of older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder: a 16-year update on a previously reported series. *Sleep Med*. 2013;**14**(8):744–748.
4. Iranzo A, *et al*. Neurodegenerative disorder risk in idiopathic REM sleep behavior disorder: study in 174 patients. *PLoS One*. 2014;**9**(2):e89741.
5. Postuma RB, *et al*. Parkinson risk in idiopathic REM sleep behavior disorder: preparing for neuroprotective trials. *Neurology*. 2015;**84**(11):1104–1113.
6. Stiasny-Kolster K, *et al*. Diagnostic value of the REM sleep behavior disorder screening questionnaire in Parkinson's disease. *Sleep Med*. 2015;**16**(1):186–189.
7. Gaig C, *et al*. Periodic limb movements during sleep mimicking REM sleep behavior disorder: a new form of periodic limb movement disorder. *Sleep*. 1 March 2017;**40**(3). doi:10.1093/sleep/zsw063

8. Iranzo A, *et al*. Severe obstructive sleep apnea/hypopnea mimicking REM sleep behavior disorder. *Sleep*. 2005;**28**(2):203–206.
9. Firmann M, *et al*. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. *BMC Cardiovasc Disord*. 2008;**8**:6.
10. Preisig M, *et al*. The PsyCoLaus study: methodology and characteristics of the sample of a population-based survey on psychiatric disorders and their association with genetic and cardiovascular risk factors. *BMC Psychiatry*. 2009;**9**:9.
11. Haba-Rubio J, *et al*. Prevalence and determinants of periodic limb movements in the general population. *Ann Neurol*. 2016;**79**(3):464–474.
12. Heinzer R, *et al*. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med*. 2015;**3**(4):310–318.
13. Buysse DJ, *et al*. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;**28**(2):193–213.
14. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;**14**(6):540–545.
15. Fulda S, *et al*. Development and validation of the Munich Parasomnia Screening (MUPS): a questionnaire for parasomnias and nocturnal behaviors. *Somnologie*. 2008;**12**(1):56–65.
16. Iber C A-IS, *et al*. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*. 1st ed: Westchester, Illinois: American Academy of Sleep Medicine; 2007.
17. Berry RB, *et al*.; American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the american academy of sleep medicine. *J Clin Sleep Med*. 2012;**8**(5):597–619.
18. Zucconi M, *et al*.; International Restless Legs Syndrome Study Group (IRLSSG). The official World Association of Sleep Medicine (WASM) standards for recording and scoring periodic leg movements in sleep (PLMS) and wakefulness (PLMW) developed in collaboration with a task force from the International Restless Legs Syndrome Study Group (IRLSSG). *Sleep Med*. 2006;**7**(2):175–183.
19. Delessert A, *et al*. Pulse wave amplitude drops during sleep are reliable surrogate markers of changes in cortical activity. *Sleep*. 2010;**33**(12):1687–1692.
20. Haba-Rubio J, *et al*. Obstructive sleep apnea syndrome: effect of respiratory events and arousal on pulse wave amplitude measured by photoplethysmography in NREM sleep. *Sleep Breath*. 2005;**9**(2):73–81.
21. Frauscher B, *et al*. Validation of an integrated software for the detection of rapid eye movement sleep behavior disorder. *Sleep*. 2014;**37**(10):1663–1671.
22. Frauscher B, *et al*.; SINBAR (Sleep Innsbruck Barcelona) Group. Normative EMG values during REM sleep for the diagnosis of REM sleep behavior disorder. *Sleep*. 2012;**35**(6):835–847.
23. Frauscher B, *et al*.; SINBAR (Sleep Innsbruck Barcelona) Group. Normative EMG values during REM sleep for the diagnosis of REM sleep behavior disorder. *Sleep*. 2012;**35**(6):835–847.
24. Team RDC. *R: A Language and Environment for Statistical Computing*: Vienna, Austria: the R Foundation for Statistical Computing; 2011.
25. Chiu HF, *et al*. Sleep-related injury in the elderly–an epidemiological study in Hong Kong. *Sleep*. 2000;**23**(4):513–517.
26. Boot BP, *et al*. Probable rapid eye movement sleep behavior disorder increases risk for mild cognitive impairment and Parkinson disease: a population-based study. *Ann Neurol*. 2012;**71**(1):49–56.
27. Mahlknecht P, *et al*. Probable RBD and association with neurodegenerative disease markers: A population-based study. *Mov Disord*. 2015;**30**(10):1417–1421.
28. Kang SH, *et al*. REM sleep behavior disorder in the Korean elderly population: prevalence and clinical characteristics. *Sleep*. 2013;**36**(8):1147–1152.
29. Pujol M, *et al*. Idiopathic REM sleep behavior disorder in the elderly Spanish community: a primary care center study with a two-stage design using video-polysomnography. *Sleep Med*. 2017;**40**:116–121.
30. Ohayon MM, *et al*. Violent behavior during sleep. *J Clin Psychiatry*. 1997;**58**(8):369–76.
31. Wong JC, *et al*. Risk factors for probable REM sleep behavior disorder: A community-based study. *Neurology*. 2016;**86**(14):1306–1312.
32. Stanton B, *et al*. A quarter century of violence in the United States. An epidemiologic assessment. *Psychiatr Clin North Am*. 1997;**20**(2):269–282.
33. Siclari F, *et al*. Violence in sleep. *Brain*. 2010;**133**(Pt 12):3494–3509.
34. Schenck CH, *et al*. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. *Am J Psychiatry*. 1989;**146**(9):1166–1173.
35. Schenck CH *et al*. Potentially lethal behaviors associated with rapid eye movement sleep behavior disorder: review of the literature and forensic implications. *J Forensic Sci*. 2009;**54**(6):1475–1484.
36. Delgado-Escueta AV, *et al*. Special report. The nature of aggression during epileptic seizures. *N Engl J Med*. 1981;**305**(12):711–716.
37. Sixel-Doring F *et al*. Associated factors for REM sleep behavior disorder in Parkinson disease. *Neurology*. 2011;**77**(11):1048–1054
38. Rolinski M, *et al*. REM sleep behaviour disorder is associated with worse quality of life and other non-motor features in early Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2014;**85**(5):560–566.
39. Boot BP, *et al*. Risk factors for dementia with Lewy bodies: a case-control study. *Neurology*. 2013;**81**(9):833–840.
40. Postuma RB, *et al*. Environmental risk factors for REM sleep behavior disorder: a multicenter case-control study. *Neurology*. 2012;**79**(5):428–434.
41. Fereshtehnejad SM, *et al*. New clinical subtypes of Parkinson disease and their longitudinal progression: a Prospective cohort comparison with other phenotypes. *JAMA Neurol*. 2015;**72**(8):863–873.
42. Frauscher B, *et al*. Comorbidity and medication in REM sleep behavior disorder: a multicenter case-control study. *Neurology*. 2014;**82**(12):1076–1079.
43. Teman PT, *et al*. Idiopathic rapid-eye-movement sleep disorder: associations with antidepressants, psychiatric diagnoses, and other factors, in relation to age of onset. *Sleep Med*. 2009;**10**(1):60–65.
44. Ju YE, *et al*. Changing demographics in REM sleep behavior disorder: possible effect of autoimmunity and antidepressants. *Sleep Med*. 2011;**12**(3):278–283.

45. Lam SP, *et al*. Does REM sleep behavior disorder exist in psychiatric populations? A clinical and polysomnographic case-control study. *Sleep Med*. 2012;**14**(8):788–794
46. Arnulf I. REM sleep behavior disorder: motor manifestations and pathophysiology. *Mov Disord*. 2012;**27**(6): 677–689.
47. Postuma RB, *et al*. Antidepressants and REM sleep behavior disorder: isolated side effect or neurodegenerative signal? *Sleep*. 2013;**36**(11):1579–1585.
48. Berg D, *et al*. MDS research criteria for prodromal Parkinson's disease. *Mov Disord*. 2015;**30**(12):1600–1611.
49. Fantini ML, *et al*. The effects of pramipexole in REM sleep behavior disorder. *Neurology*. 2003;**61**(10):1418–1420.
50. Postuma RB, *et al*. Prodromal autonomic symptoms and signs in Parkinson's disease and dementia with Lewy bodies. *Mov Disord*. 2013;**28**(5):597–604.
51. Ferini-Strambi L, *et al*. Autonomic symptoms in idiopathic REM behavior disorder: a multicentre case-control study. *J Neurol*. 2014;**261**(6):1112–1118.
52. Miyamoto T, *et al*. Reduced cardiac 123I-MIBG scintigraphy in idiopathic REM sleep behavior disorder. *Neurology*. 2006;**67**(12):2236–2238.
53. Frauscher B, *et al*. Investigation of autonomic function in idiopathic REM sleep behavior disorder. *J Neurol*. 2012;**259**(6):1056–1061.
54. Arnulf I, *et al*. Sleepiness in idiopathic REM sleep behavior disorder and parkinson disease. *Sleep*. 2015;**38**(10):1529–1535.
55. Zhou J *et al*. Excessive daytime sleepiness predicts neurodegeneration in idiopathic REM sleep behavior disorder. *Sleep*. 2017;**40**(5). doi: 10.1093/sleep/zsx041.
56. Iranzo A, *et al*. Excessive daytime sleepiness does not predict neurodegeneration in idiopathic REM sleep behaviour disorder. *Sleep*. 2017;**40**(12):zsx161.
57. Zhou J, *et al*. Any prediction of neurodegeneration by excessive daytime sleepiness in idiopathic RBD? *Sleep*. 1 December 2017;**40**(12):zsx185
58. Bender R *et al*. Adjusting for multiple testing–when and how? *J Clin Epidemiol*. 2001;**54**(4):343–349.