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Is there a common motor dysregulation in sleepwalking and REM sleep behaviour disorder?

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SUMMARY

This study sought to determine if there is any overlap between the two major NREM and REM parasomnias, i.e., sleepwalking/sleep terrors (SW/ST) and REM sleep behaviour disorder (RBD). We assessed adult patients with SW/ST using RBD screening questionnaires and determined if they had enhanced muscle tone during REM sleep. Conversely, we assessed RBD patients using the Paris Arousal Disorders Severity Scale (PADSS) and determined if they had more N3 awakenings. The 251 participants included 64 RBD patients (29 with idiopathic RBD and 35 with RBD associated with Parkinson's disease), 62 patients with SW/ST, 66 old healthy controls (age-matched with the RBD group), and 59 young healthy controls (age-matched with the SW/ST group). They completed the RBD screening questionnaire, RBD single question, and PADSS. In addition, all the participants underwent a video-polysomnography. The SW/ST patients scored positive on RBD scales and had a higher percentage of 'any' phasic REM sleep without atonia when compared with controls; however, these patients did not have higher tonic REM sleep without atonia or complex behaviours during REM sleep. RBD patients had moderately elevated scores on the PADSS but did not exhibit more N3 arousals (suggestive of NREM parasomnia) than the control group. These results indicate that dream-enacting behaviours (assessed by RBD screening questionnaires) are commonly reported by SW/ST patients, thus decreasing the questionnaire's specificity. Furthermore, SW/ST patients have excessive twitching during REM sleep, which may result either from a higher dreaming activity in REM sleep or from a more generalised NREM/REM motor dyscontrol during sleep.

INTRODUCTION

Sleepwalking and sleep terrors (SW/ST) are NREM parasomnias characterised by abnormal behaviours arising during partial and local arousals from N3 sleep (American Academy of Sleep Medicine, 2014). Patients can open their eyes, look around, sit, walk around or run, manipulate furniture, shout or speak, answer (although inappropriately) questions, and show reduced judgement and no or partial recall of the behaviour, except for some brief catastrophic visual scenes (Oudiette *et al.*, 2009). Patients with SW/ST are mostly children and young adults with a strong familial predisposition. In contrast, REM sleep behaviour disorder (RBD) usually affects patients older than 50 years of age and is strongly associated with neurodegenerative disorders. The behaviours occur during REM sleep due to imperfect muscle atonia (Schenck *et al.*, 1986). They include brief limb or trunk jerks, complex gesticulations, kicks, slaps, mumbles, speeches, shouts, swears, laughs or punches and are mostly performed with the eyes closed while lying in the bed (Arnulf, 2012). In contrast to SW/ST, ambulation does not occur. These behaviours are described by the dreamer as an attempted enactment of dreams or nightmares in which the individual is confronted, attacked, or chased by individuals or animals (American Academy of Sleep Medicine, 2014). Because these two parasomnias occur during different sleep stages (NREM vs. REM sleep), in young vs. aged patients, with familial vs. neurodegenerative predisposition, and with unclear vs. clearly associated dream mentation, they should have no common features. However, a rare overlap (named parasomnia overlap disorder, POD) has been described in aged individuals who had both RBD and evidence of confusional arousals, sleep terrors or ambulation during sleep (Schenck *et al.*, 1997; Poryazova *et al.*, 2007; Limousin *et al.*, 2009). The presence of this rare disorder raises the possibility that motor control could be affected in both NREM and REM sleep in RBD and SW/ST

patients, at least in some individuals. Furthermore, the classical opposition between a clear dream recall after dream enactment in RBD vs. amnesia of behaviour and concomitant mentation in SW/ST may not always be accurate (Ugucioni *et al.*, 2013), which creates potential pitfalls when using screening questionnaires in the general population. Thus, we examined SW/ST patients for evidence of RBD symptoms (such as scoring positively on the RBD screening questionnaire (Stiasny-Kolster *et al.*, 2007) or exhibiting increased REM sleep without atonia) and RBD patients for evidence of SW/ST symptoms (ambulation, scoring positively on the SW/ST questionnaire (Arnulf *et al.*, 2013), and frequency of N3 arousals), in a controlled prospective study.

METHODS

Participants

The participants were selected from the patient and control populations of the sleep disorder centre at the Pitié-Salpêtrière hospital between January 2011 and April 2016. All participating patients were diagnosed with either RBD or SW/ST by one of the department's physicians. Patients with parasomnia met the international criteria (American Academy of Sleep Medicine, 2014). Accordingly, RBD was defined using four criteria: i) repeated episodes of vocalisation or complex motor behaviour during sleep; ii) documentation of these behaviours during REM sleep by either video-polysomnography or evidence from the clinical history of the patient; iii) increased REM sleep without atonia; and iv) the symptomatology cannot be explained by other sleep disorders, mental disorders, medications or drug use. The patients were further classified into idiopathic or symptomatic RBD depending on the concomitant presence of parkinsonism or dementia. However, we did not include patients with concomitant

dementia in this study because it required patients to appropriately answer questionnaires. Sleepwalking was defined using three criteria (American Academy of Sleep Medicine, 2014): (i) a history of ambulation during sleep; (ii) the persistence of sleep or impaired judgement during ambulation; and (iii) the disturbance could not be better explained by another sleep, medical, mental, or neurological disorder or medication/drug use. Sleep terror was defined using three criteria (American Academy of Sleep Medicine, 2014): (i) a history of a sudden episode of terror occurring during sleep, usually initiated by a cry or loud scream with sympathetic and behavioural manifestations of intense fear; (ii) difficulty in arousing the person, mental confusion when awakened from an episode, complete or partial amnesia from the episode, or dangerous or potentially dangerous behaviours; and (iii) the disturbance could not be better explained by another sleep, medical, mental, or neurological disorder or medication/drug use. In addition to these clinical criteria, all SW/ST patients showed at least one of the following features on video-polysomnography (although these features were not completely sensitive nor specific, they were applicable in the context of a systematic study): (i) at least one arousal during N3 sleep was associated with an abnormal motor behaviour suggestive of surprise, confusion, or fear (e.g., startling, sitting in the bed, or looking around surprised); or (ii) at least 2 sudden arousals during N3 sleep. For simplicity, we indifferently refer to patients with sleepwalking and sleep terrors as “sleepwalkers.” RBD and SW/ST patients with apnoea-hypopnea index greater than 15 were not included in this study.

Healthy controls were recruited through press announcements, word of mouth, and recruitment of the family members of patients or clinical team. The controls were asked to take part in various research programmes of the unit (NUCLEIPARK, ALICE, and ICEBERG programmes for aged controls and AEP, PAAP, and HYPERSOMNIA

programmes for young controls) and received an indemnity for their participation. Participants who did not complete one of the parasomnia questionnaires at the time of video-polysomnography were contacted by phone and then received, completed and returned the missing questionnaire. A physician examined all participants to verify the absence of sleep disorders (following ICSD-3 criteria), Parkinson's disease or dementia, other neuronal or psychiatric diseases, and psychotropic drug use. This study also used data from earlier studies approved by the local ethical committee (CPP-IDF6 Pitié-Salpêtrière). Additionally, some of the patients volunteered to participate in the context of their regular treatment routine after having read the information available in the hospital waiting room. A signed written consent was obtained from all healthy controls and the majority of RBD and SW/ST patients (because they were included in other various research programmes related to their disease). However, the ethics committee waived written consent for the reuse of routine clinical measures, provided that no participant opposed to it after being informed by the research assistant, in accordance with French ethical regulations.

Questionnaires

All participants had a medical interview with a sleep physician of the unit and completed the Epworth sleepiness scale (Johns, 1991), the RBD1Q (Postuma *et al.*, 2012), the RBD screening questionnaire (Stiasny-Kolster *et al.*, 2007), and the Paris Arousal Disorder Severity Scale (Arnulf *et al.*, 2014). The Epworth sleepiness scale evaluates the subjective chance to nod or fall asleep in 8 daily life routines, which include mostly passive conditions (Johns, 1991). Scores can range from 0 to 24 and are usually considered abnormal when greater than 10 (Johns, 2000). The RBD1Q consists of a

single question that is answered with “yes” or “no”: “Have you ever been told, or suspected yourself, that you seem to ‘act out your dreams’ while asleep (for example, punching, flailing your arms in the air, making running movements, etc.)?” In the questionnaire development study, a positive response yielded a 93.8% sensitivity and an 87.2% specificity for distinguishing RBD patients from healthy controls and patients with other sleep disorders, mainly including patients with obstructive sleep apnoea (Postuma *et al.*, 2012). The RBD screening questionnaire (RBDSQ) contains 13 yes-no questions about vivid, action-filled dreams, matching with nocturnal behaviour, arms and legs movements asleep, injuries, speaking, shouting, sudden limb movements or fights, gestures, things falling down around the bed, awakenings caused by movements, dream recall upon awakening, disturbed sleep and concomitant neurological disorders. In this questionnaire development study, which included patients with various sleep disorders (but none with NREM parasomnia), an RBDSQ score of five points or more yielded a 96% sensitivity and a 56% specificity for an RBD diagnosis (Stiasny-Kolster *et al.*, 2007). The Paris Arousal Disorder Severity Scale (PADSS) contains three parts (Arnulf *et al.*, 2014). The PADSS-A is an inventory of 17 amnestic behaviours performed asleep (e.g., screaming, raising to an upright position in bed, making a violent gesture, falling out of bed, leaving the room, climbing or descending, leaving the house, opening or vaulting a window, manipulating light, heavy or inflammable objects, eating or preparing a meal or a drink, and engaging in involuntary sexual behaviours). These questions are scored with the following rubric: “never” = 0, “sometimes” = 1, and “often” = 2), which yields a sub-score between 0 and 34. The frequency (PADSS-B) of these episodes is scored with the following rubric: twice nightly =6, nightly or almost nightly =5, weekly =4, monthly= 3, and yearly = 2, less than yearly =1, never =0. The PADSS-C includes the five most common consequences of the episodes (i.e., disturbing someone

asleep, injuring oneself or other, being tired the next day, and disturbing oneself psychologically) and is scored with the following scale: “never” = 0, “sometimes” = 1, and “often” = 2), which yields a sub-score between 0 and 10 (Arnulf *et al.*, 2013). In the development study for this questionnaire, the best cut-off for the total PADSS score (0-50) was 13/14 when comparing SW/ST patients with healthy controls and RBD patients and resulted in an 83.6% sensitivity and 87.8% specificity.

Sleep monitoring

All participants completed a video-polysomnography at the sleep unit. Lights were switched off by patients at 11 PM at the latest and remained off until switched on by staff the next morning. The subjects slept in a special room with at least one camera and one microphone facing the bed and synchronised with the polysomnography. The system consisted of a minimum of 3 channels for EEG (Fp1/C3, C3/A2 and C3/O1), 2 channels for EOG (inferior left epicanthi/A2 and superior right epicanthi/A2) and 3 channels for surface EMG (chin [*mentalis*] muscle and right and left *tibialis anterior* muscles) as well as an electrocardiogram (EKG), thoracic and abdominal belts to measure the respiratory efforts via an inductive plethysmography, a measure of naso-oral airflow through nasal pressure and oral thermistors, and a measure of trans-cutaneous oxygen saturation. The sleep stages, arousals, apnoea and hypopnea periods, and periodic leg movements (PLM) were scored by experienced sleep neurologists (IA and SLS) in 30 s epochs according to international rules (Iber *et al.*, 2007).

Two additional specific analyses were performed either retrospectively or prospectively. The number of direct awakenings from N3 (as an indicator of NREM sleep dysfunction) and the presence of REM sleep without atonia (RWA) were

measured in all sleep studies. Tonic RWA was defined as the percentage of REM sleep epochs containing more than 15 s of enhanced chin (*mentalis*) muscle tone characterised by an amplitude at least twice higher than the lowest background amplitude (Iber *et al.*, 2007). For phasic RWA, we used the SINBAR criteria of “any” chin muscle activity during REM sleep (Frauscher *et al.*, 2012). “Any” chin EMG activity was defined as the presence of any EMG activity with an amplitude greater than twice the background EMG and a duration ≥ 0.1 sec irrespective of its total duration. A 30 s epoch containing “any” muscle activity, whether on the *mentalis* or on the left or right *tibialis anterior* muscles, was counted as phasic. The percentage of “any” phasic activity was obtained by dividing the phasic epochs by the total number of REM sleep epochs.

Statistical analyses

Descriptive statistics included the means \pm standard deviation (SD), and percentages for qualitative measures. A multiple ANOVA was performed among the four groups; when P was lower than 0.05, two-groups differences were evaluated using Bonferoni tests with a significance level of $p < 0.0125$.

RESULTS

Subject characteristics

A total of 251 participants were analysed, including 66 old healthy controls, 59 young healthy controls, 64 patients with RBD (29 with idiopathic RBD and 35 with RBD associated with Parkinson’s disease), and 62 patients with SW/ST. Their demographic and clinical characteristics are listed in Table 1. Patients with SW/ST were younger than those with RBD.

NREM and REM parasomnia scales

As expected, SW/ST patients had a higher score on the total PADSS than all other groups (Table 1). However, the RBD group had a mean PADSS score higher than the old control group. Three patients with RBD (7%) reported having left the bed and even the room during the night, without any recall. As expected, the detection scores for RBD differed between the RBD and control groups (Table 2). However, the RBD detection scores were equally elevated between the SW/ST and RBD groups. Almost all SW/ST and RBD patients scored equal to or higher than 5, which is the cut-off with the best specificity/sensitivity for RBD. When compared with controls, more SW/ST patients (69%) had a positive score on the RBD1Q; however, this proportion was slightly lower than that of RBD patients. When examining each item of the RBDSQ, more patients with RBD than patients with SW/ST scored on Item 6d: “I have sudden limb movements, “fights”” and on Item 10 “I have/had a disease of the nervous system (e.g., stroke, head trauma, parkinsonism, RLS, narcolepsy, depression, epilepsy, inflammatory disease of the brain)” were more frequently answered positively. No other item was different between patients groups.

General sleep characteristics

As indicated in Table 3, the alpha EEG frequency, total sleep time, latency to sleep onset, N3 and REM percentages, index of sleep stage changes, of awakenings and of arousals, minimal transcutaneous oxygen saturation and time spent below an SaO₂ lower than 90% were different between the four groups. The patient with RBD had on average a slower alpha EEG frequency, a longer wake after sleep onset than the other

groups. The sleepwalkers slept longer than the other groups, and had lower sleep changes and awakening indices than the RBD group more frequent sleep stage changes than the young controls.

Markers of NREM and REM parasomnias

The number of awakenings from N3, a marker of NREM parasomnia, was higher in the SW/ST group when compared with all other groups and lower in the RBD group when compared with the old control group. The percentage of REM sleep without atonia (tonic) was higher in RBD patients than in all other groups. The percentage of REM sleep without atonia (phasic, defined as “any” chin muscle activity lasting more than 0.1 s) was higher in RBD patients than in all other groups. Surprisingly, this parameter was higher in SW/ST patients when compared with the young controls. A visual assessment of the corresponding video-clip showed no complex behaviours during REM sleep in SW/ST patients, but it did reveal frequent and brief non-purposeful jerks.

DISCUSSION

Main results

In this large controlled study of 252 subjects, SW/ST patients scored positive on RBD scales and had higher phasic ‘any’ (but not tonic) REM sleep without atonia when compared with controls; however, the SW/ST patients showed no complex behaviours during REM sleep. Conversely, RBD patients had moderately elevated scores on the NREM parasomnia scale, but did not exhibit more N3 arousals (suggestive of NREM parasomnia) than the control groups.

Dream-enacting behaviours in sleepwalkers

Most, if not all, SW/ST patients had high, positive scores on the two RBD scales, suggesting that they considered themselves to have dream-enacted behaviours. The absence of complex behaviours during REM sleep in these patients strongly suggests that they refer to dream-enacted behaviours during NREM sleep. Indeed, we previously reported that the sleep mentations associated with abnormal behaviours from N3 were congruent with the behaviours in sleepwalkers and ST patients (Oudiette *et al.*, 2009) to the point that most ST patients were referred for agitated nightmares. This clinical concept of “dream walking” was further substantiated by several home and laboratory videos showing enacted dreams, later recalled as such, in sleepwalkers. A patient dreamt that her baby was falling off the bed and consequently got out of bed with her arms forwards to catch her (Mwenge *et al.*, 2013). Another patient dreamt that the boom of a sailboat was about to hit her head and rapidly protected herself during a partial N3 awakening (Arnulf, 2014). An ST patient dreamt she was buried alive and shouted (Arnulf, 2014), while another patient dreamt that the roof was collapsing and tried holding it up by raising his arms (Bhat *et al.*, 2012). Although a theoretical debate remains as to whether these sleep mentation are dreams or hypnopompic hallucinations (Zadra *et al.*, 2013), the patients clearly report them as dreams on the RBDSQ and RBD1Q. However, fights and sudden movements were more frequently reported in the RBD than in the SW/ST group, in accordance with the more frequent dream contents of fights in RBD than in SW/ST groups previously found (Ugucioni *et al.*, 2013). Differences are however insufficient to highlight this item as discriminant between RBD and SW/ST on questionnaires.

Lack of specificity of RBD screening scales

The major overlap between RBD and SW/ST patients on two scales developed to screen for RBD in large populations raises a problem with the specificity of an RBD diagnosis. When developing the RBDSQ, the authors noticed that patients with SW/ST or epilepsy scored too high; however, the study only had 4 SW/ST patients (Stiasny-Kolster *et al.*, 2007). Similarly, the consortium that developed the RBD1Q did not include patients with SW/ST in the control group; however, the authors discussed the possibility that NREM parasomnia could be mistaken for RBD (Postuma *et al.*, 2012). The clarification that “probable RBD” may include SW/ST patients is important in the context of RBD epidemiology because the frequency of this disorder may be over-evaluated by asking about dream-enacted behaviours (Ohayon *et al.*, 1997). This clarification is also important in the screening for idiopathic RBD in the general population (Mahlknecht *et al.*, 2015) and aged population (Boot *et al.*, 2012). As SW/ST may persist in older age, we suggest adding a distinguishing question on wandering/ambulation behaviours to these RBD screening questionnaires.

Increased REM sleep twitching in sleepwalkers

A puzzling and new finding was the high percentage of enhanced phasic motor activity during REM sleep in SW/ST patients. Indeed, if the SW/ST group had smaller percentages than patients with genuine RBD, then their mean percentage (30%) was significantly above the young and old controls. The measure of phasic activity was restricted to “any” phasic activity of the chin and was performed identically across all groups. In a recent study of 100 healthy volunteers, the authors reported 90th percentile cut-offs for normality between 14.5% and 20.8% (depending on age), which is concordant with the controls groups in our study but lower than the 30% found in our

SW/ST patients (Frauscher *et al.*, 2014). This increased muscle activity was due to an excessive twitching restricted to “any” phasic activity and was not corroborated by increased tonic muscle activity, suggesting its mechanism is different from that of RBD. Phasic activity during REM sleep has the highest night-to-night variability in RBD patients when compared with tonic activity, suggesting that phasic activity is driven by the mental content (more active, more emotional) rather than by a permissive system like tonic activity (Cygan *et al.*, 2010). Notably, children with SW/ST have more frequent nightmares (supposedly in REM sleep) than other children (Fisher *et al.*, 2014). One may wonder whether adults with SW/ST, as observed in our study, have a more intense dreaming activity in REM sleep that could lead them to display more phasic motor activity. Alternatively, a more generalised dysregulation of motor control during NREM/REM sleep in SW/ST patients would activate (or unblock) motor activity in both N3 and REM sleep.

The PLM activity during sleep in these two groups provides also interesting negative results. This repetitive, stereotyped motor activity could be viewed as an indicator of abnormally released central pattern generator in the nervous system. First, we did not find higher PLM index in the RBD group than in age-matched control group, in contrast with some (Ferini-Strambi *et al.*, 2004; Montplaisir *et al.*, 2010), but not all (Frauscher *et al.*, 2012) studies. In the SW/ST group, the PLM index was similar to the index in the age-matched controls. This normal PLM activity (not frequently evaluated before, except in our previous works (Oudiette *et al.*, 2012)) suggests that the motor dyscontrol observed in these patients with arousal disorders in NREM and REM sleep is different from the motor dyscontrol causing PLMs.

Parasomnia overlap disorder

Parasomnia overlap disorder (POD) is a condition in which patients have both RBD and either a disorder of arousal, sleep related eating disorder, sexsomnia, or rhythmic movement disorder (American Academy of Sleep Medicine, 2014). The concomitance of RBD and SW/ST in the same patient has been previously recognised as an example of a wider NREM/REM sleep motor dyscontrol during sleep in some individuals with rare neurological disorders (including narcolepsy, Moebius syndrome, multiple sclerosis, rhombencephalitis, agrypnia excitata, and Machado-Joseph disease) as well as patients with various psychiatric disorders, including substance abuse disorders and withdrawal states (Kushida *et al.*, 1995; Schenck *et al.*, 1997; Limousin *et al.*, 2009). A history of sleepwalking was reported in 10% of 93 patients with RBD of various origins, 5 having a concomitant neurological disease (Olson *et al.*, 2000). Further videopolysomnographies identified confusional arousals from NREM sleep combined with gross motor activity during REM sleep in only two of them. In 417 patients with Parkinson's disease answering a questionnaire, 22 (5%) reported an adult-onset SW, of whom 8/10 had a concomitant RBD on videopolysomnography, suggesting POD is not uncommon in Parkinson's disease (Oberholzer *et al.*, 2011; Di Fabio *et al.*, 2013). However, getting out of bed and walking was rare (occurring "sometimes" or "often" in 3.2% of 64 patients with RBD) in Parkinson's disease (Scaglione *et al.*, 2005). Occasional ambulation at home have been reported in 24% of patients with idiopathic RBD, who later developed mild cognitive impairment or Lewy body dementia rather than Parkinson's disease, but it was not possible to determine whether these anamnestic nocturnal wanderings took place during RBD itself or during confusional awakenings in these subjects with preclinical dementia (Fernández-Arcos *et al.*, 2016). In our study, 7% of patients with RBD had sometimes left the bed and the room during the nocturnal parasomnia. Conversely, no patient in our sleepwalking group had define RBD, hence no

sleepwalker had POD. Ambulation is exceptional during REM sleep in the videoclinal settings of RBD, except in a case with idiopathic RBD that we recently observed (Herlin *et al.*, 2015). Whether ambulation in patients with RBD corresponds to ambulation during RBD as in our unique case (Herlin *et al.*, 2015), to ambulation during NREM sleep arousals combined with non-ambulatory RBD, to confusional arousals in any sleep stage in demented and/or hallucinated patients, to a *status dissociatus* or to a NREM and REM sleep arousal disorder (Kushida *et al.*, 1995; Arnulf *et al.*, 2005; Sabater *et al.*, 2014) is an interesting but unsolved enigma. The discovery of POD has questioned the existence of a more general underlying motor dyscontrol in all these cases. In POD however, RBD is the usually the primary problem, and ambulation is secondarily found, mostly by history. We are not describing POD here, but classical sleepwalkers who are first wandering from N3 awakenings but have no major behavioral event during REM sleep, in whom we additionally found some subtle excess twitching, by systematic measure of REM sleep without atonia in all patients. This new finding is not restricted to POD, but could rather be generalizable to adult SW/ST.

Limitations

This study has some limitations. The measures of tonic and phasic muscle activity during sleep were restricted to the *mentalis* and left and right *tibialis anterior* muscles and excluded the *flexor digitorum superficialis* muscles. The *flexor digitorum superficialis* muscles were not routinely used for SW/ST patients, RBD patients, or controls until it was recently recommended in RBD (Frauscher *et al.*, 2012). The use of “any” muscle activity likely captures subtler phasic events than the classical 3 s epoch phasic measure (which is also more time-consuming). It would be interesting to measure whether the increased phasic muscle activity during REM sleep is specific of adult, primary SW/ST (as a indicator of a primary motor dyscontrol in NREM and REM

sleep), or extends to forms of SW/ST triggered by sleep-disordered breathing (which may represent a form of secondary sleepwalking).

CONCLUSIONS

This study indicates that dream-enacting behaviours, as assessed by RBD screening questionnaires, are commonly experienced not only by RBD patients but also by SW/ST patients, thus decreasing the specificity of these questionnaires. Our study also demonstrates for the first time that SW/ST patients have excessive twitching during REM sleep when compared with controls. This twitching may result from either a higher dreaming activity or a more generalised NREM/REM motor dyscontrol during sleep.

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AUTHORS' CONTRIBUTION

The patients and healthy controls were diagnosed, scored and selected by IA and SLS. MH, SWB and MC called or conducted face-to-face interviews with the patients, scored the phasic and tonic muscle activity during REM sleep, and entered the information into the database. MV obtained partial funding, referred patients and controls, and aided in project discussions. IA and SWB drafted the manuscript, which was discussed and approved by all co-authors.

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Table 1- Demographic and clinical characteristics of sleepwalkers, patients with REM sleep behaviour disorder and controls matched for age and sex

	A-Young controls	B-Sleepwalkers	C-RBD patients	D-Old controls	P for MANOVA	Between-group differences
Number of subjects	59	62	64	66		
Age (years)	31.9 ± 9.3	31.7 ± 9.5 ^{##}	68.6 ± 8.0	67.0 ± 7.8	<0.0001	A<C, A<D, B<C, B<D
Sex (% men)	49.2	46.7	68.8	65.2	0.02	A<C, B<C, B<D
Body mass index (kg/m ²)	23.9 ± 5.7	23.3 ± 3.6	24.8 ± 3.3	26.8 ± 4.0	0.13	A<D, B<C, C<D
Epworth sleepiness score (0-24)	11.2 ± 6.5	9.0 ± 5.2	8.6 ± 5.3	7.2 ± 4.7	0.45	A>C, A>D
Paris Arousal Disorders Severity Scale (PADSS)						
Completed scale, n	42	57	46	53		
Total score (0-50)	4.4 ± 5.2	15.4 ± 5.3	10.2 ± 4.7	1.9 ± 2.6	<0.0001	B>A, B>C, B>D, C>D, A>D
Total score>13 (%)	7.1	84.2	21.7	0	<0.0001	B>A, B>C, B>D, C>A, C>D
Subscore-A (behaviours), 0-34	1.5 ± 2.3	7.1 ± 3.8	4.3 ± 2.6	0.7 ± 1.5	<0.0001	B>A, B>C, B>D, C>A, C>D

Subscore-A>5 (%)	4.8	66.1	26.7	3.7	<0.0001	B>A, B>C, B>D, C>A, C>D
Selected amnestic behaviours (% scoring as “sometimes” or “often”) from PADSS-A						
A1. Shouting	41	81	85	13	<0.0001	B>A, B>D, C>A, C>D, A>D
A2. Sitting	34	93	62	13	<0.0001	B>A, B>C, B>D, C>A, C>D, A>D
A3. Violent gesture	22	56	87	11	<0.0001	C>A, C>B, C>D, A>D, B>A, B>D
A4. Falling from bed	2	24	60	4	<0.0001	C>A, C>B, C>D, B>A, B>D
A5. Walking	10	54	7	6	<0.0001	B>A, B>C, B>D
A6. Climbing a stair	2	15	0	0	<0.0001	B>A, B>C, B>D
A12. Breaking items	0	17	16	4	<0.0001	B>A, B>D, C>A, C>D
A16. Eating	5	20	4	6	<0.0001	B>A, B>C, B>D
A17. Having sex	5	15	2	6	<0.0001	B>A, B>C, B>D
Subscore-B (frequency of the parasomnia), 0-6	1.1 + 1.8	4.1 ± 0.7	3.3 ± 1.2	0.4 ± 0.9	<0.0001	B>A, B>C, B>D, A>D, C>A, C>D
Subscore-C	1.8 + 1.9	4.5 ± 1.5	2.8 ± 1.8	0.8 ± 1	<0.0001	B>A, B>C, B>D, A>D, C>A,

(consequences), 0-10						C>D
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RBD: REM sleep behaviour disorder; Data are shown as the means \pm SD or as a percentage.

Table 2- Detailed items of parasomnia scales in sleepwalkers, patients with REM sleep behaviour disorder and controls matched for age and sex

Group	A-Young controls	B-Sleep walkers	C-RBD patients	D- Old controls	P for MANOVA	Between-groups differences
Respondents, n	42	45	53	55		
RBD1Q (% positive)	18	69	87.8	20	0.009	B>A, B>D, C>A, C>B, C>D
RBDSQ, 0-13	4.4 ± 3.1	8 ± 2.1	8.7 ± 2.2	2.5 ± 1.9	0.001	B>A, C>D, A>D
RBDSQ>4 (% subjects)	39	98	98	12.7	<0.0001	B>A, B>D, C>A, C>D, A>D
RBD screening questionnaire, % positive items						
1. Vivid dream	75.6	88.7	80	63.6	0.049	No difference
2. Action-filled or aggressive dreams	45	64.4	69.4	12.7	<0.0001	C>D
3. Concordant dream/behaviour	14.6	64.4	69.4	0	<0.0001	B>A, B>D, C>A, C>D, A>D
4. Limbs move when asleep	46.3	75.6	82	21.8	<0.0001	B>A, B>D, C>A, C>D, A>D
5. Injuries	7	33.3	50	0	<0.0001	B>A, B>D, C>B, C>A, C>D
6a. Speaks, shouts, swears	48.8	100	92	30.9	<0.0001	B>A, B>D, C>A, C>D

6b. Sudden moves, fights	26.8	55.6	88	9	<0.0001	B>A, B>D, C>A, C>B, C>D
6c. Useless movements	12.2	75.6	68	4	<0.0001	B>A, B>D, C>A, C>D
6d. Objects fell	22	51.1	48	10.9	<0.0001	B>A, B>D, C>A, C>D
7. Movements awake me	33.3	64.4	66	14.8	<0.0001	B>A, B>D, C>A, C>D
8. Clear dream recall	48.8	40	30	42.6	0.31	No difference
9. Sleep is disturbed	39	71.1	72	32.7	<0.0001	B>A, B>D, C>A, C>D
10. Nervous system disease	14.6	15.6	56	9	<0.0001	A<C, B<C, C<D

RBD: REM sleep behaviour disorder; RBDSQ: RBD screening questionnaire; RBD1Q: RBD single question. Data are shown as the means \pm SD or as a percentage.

Table 3 - Sleep characteristics (on video-polysomnography) of sleepwalkers, patients with RBD and control groups matched for age and sex

	A - Young controls	B- Sleepwalkers	C-RBD patients	D-Old controls	P MANOVA	Between-groups differences
No. of subjects	59	62	64	66		
EEG α frequency (Hz)	9.8 \pm 0.8	9.8 \pm 1	8.8 \pm 1.2	9.5 \pm 1.5	0.02	C<A, C<B, C<D
Sleep efficacy (%)	86.2 \pm 12.9	86.2 \pm 8.9	75.6 \pm 10.6	82 \pm 11.9	0.74	NA
Total sleep time (min)	466 \pm 74.5	570.4 \pm 83.9	505.8 \pm 89.6	494 \pm 91.2	0.001	B>A, B>C, B>D
Wake after sleep onset (min)	66.4 \pm 66.5	79.3 \pm 56	119.5 \pm 53.8	88.5 \pm 57.1	<0.0001	A<C, B<C, C<D
Latency to (min)						
Sleep onset	19.8 \pm 15.9	26.2 \pm 22.1	30.4 \pm 38.3	30.9 \pm 36.7	0.01	A<D
N3 onset	37.9 \pm 38.3	33.2 \pm 24.5	63.1 \pm 55	49.9 \pm 36.2	0.42	NA
REM onset	123.6 \pm 78.2	121.8 \pm 66.5	113.9 \pm 73.3	99.3 \pm 69.5	0.58	NA
Sleep stages (% of total sleep time)						
N1	5.2 \pm 4.8	3.8 \pm 2.7	8.0 \pm 5.4	7.8 \pm 5.8	0.05	NA
N2	50.5 \pm 8.5	52.3 \pm 8.8	49.2 \pm 13.1	49.5 \pm 9.2	0.25	NA

N3	24.5 ± 8.7	21.7 ± 8.1	22.7 ± 11	22.7 ± 8.8	0.04	None
REM	18.7 ± 6.7	20.9 ± 6	19.7 ± 7.3	19.1 ± 5.6	0.02	None
Sleep fragmentation						
Stage changes, N/h	14 ± 5.9	14.6 ± 5	20.4 ± 8.6	16.8 ± 6.6	0.0005	A<C, B<C, D<C
Awakenings, N/h	3.4 ± 1.6	3.8 ± 1.5	5.4 ± 2.8	4.2 ± 2	<0.0001	A<C, B<C
Micro-arousals, N/h	10.6 ± 8.9	7.6 ± 4.9	8.3 ± 5.6	12.8 ± 10.7	<0.0001	B<D, C<D
Periodic leg movements, N/h	3.0 ± 5.4	3.4 ± 6.5	10.6 ± 20.9	10.5 ± 19.8	0.12	NA
PLM-related arousals, N/h	0.6 ± 1.3	0.5 ± 0.7	1.4 ± 1.7	1.5 ± 1.9	0.14	NA
N3 awakenings (N)	2.2 ± 1.4	6.0 ± 3.6	2.2 ± 3.3	2.6 ± 2	<0.0001	B>A, B>C, B>D
REM sleep without atonia (<i>levator menti</i> muscle, % of R)						
Tonic, 30 s	2.3 ± 2.1	2.5 ± 3.3	41.8 ± 30.8	4.9 ± 11.5	<0.0001	B<C, C<D, B<D
Phasic, "any", 30 s	14.3 ± 8.5	30.5 ± 17	69.7 ± 25.5	19.4 ± 16.8	<0.0001	A<B, B<C, C<D, B>D
Respiratory events						
Apnoea-hypopnea, N/h	2.3 ± 4.1	2.5 ± 4.8	9.7 ± 7.9	11.9 ± 14.6	0.06	NA
Minimal SaO ₂ , %	92.5 ± 4.5	91.1 ± 6.9	89.2 ± 4.2	86.6 ± 7.3	0.0002	A>C, A>D, B>D
Time below SaO ₂ 90%, min	3 ± 13.9	1.8 ± 5.8	8.5 ± 21.3	8.8 ± 18.8	<0.0001	B<D

Data are shown as the means \pm SD or as a percentage. MANOVA: multiple analysis of variance; NA: not appropriate; PLM: periodic leg movements.