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Original Article

Polysomnographic data in Dementia with Lewy Bodies: correlation with clinical symptoms and comparison with other α-synucleinopathies

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ABSTRACT

Introduction: Sleep dysfunction is frequent in Dementia with Lewy Bodies (DLB), but polysomnographic (PSG) data is scarce. Our objectives were to: (1) compare PSG data between DLB patients and age normative values (NV), Parkinson's Disease (PD) and idiopathic REM sleep behavior disorder (iRBD) patients; (2) evaluate the relation between of OSA, Fluctuations and Hypersomnolence and PSG data.
Methods: We selected all consecutive patients with DLB, PD and iRBD that underwent video-PSG during a two year period. Clinical data was collected by file review. Video-PSG data included sleep structure, Apnea-Hypopnea Index (AHI), REM sleep atonia indexes and video file inspection of motor events (ME) during REM sleep.
Results: Subjects: In this study, 19 DLB, 51 PD and 20 iRBD patients participated. Of those, nine DLB (DLB-RBD) and 23 PD (PD-RBD) patients had RBD. Compared to NV, DLB patients had significantly lower sleep efficiency, total sleep time, and REM sleep duration and higher sleep latency, wake after sleep onset and N2 duration. There were no significant relations between PSG data and OSA, hypersomnolence or fluctuations. Sleep latency and AHI were significantly higher and lower, respectively, in DLB compared to PD patients. ME frequency was higher in iRBD.
Conclusion: DLB patients present significant sleep fragmentation and shortened total and REM sleep time. These changes were not related with OSA, fluctuations or hypersomnolence, suggesting a different pathophysiology. PSG data was similar in the three RBD groups, in accordance with a common neuropathological origin, except for an increase in RBD severity in patients with iRBD.

1. Introduction

Dementia with Lewy Bodies (DLB), the second most prevalent degenerative dementia in patients older than 65 years [1], is caused by an accumulation of alfa-synuclein aggregates (Lewy bodies) in the posterior cortical regions, brain stem and basal ganglia [2]. Parkinson's Disease (PD) and Multiple System Atrophy, which share some of the typical symptoms of DLB, are also related to Lewy bodies accumulation, the three disorders constituting a pathophysiological continuum defined as Lewy Body Diseases (LBD). Sleep disorders are exceedingly common in DLB, particularly REM sleep behavior disorder (RBD) [3]. RBD is a parasomnia characterized by loss of normal muscular atonia during REM sleep, with patients retaining the capacity to move and enact the content of their dreams [4]. RBD can occur in the absence of overt signs of neurodegenerative disorder (idiopathic RBD – iRBD), but it is known that most patients will, in the long run, develop a LBD [5]. RBD has been recognized as a core clinical feature in the last report of the DLB Consortium [3], due to its high sensitivity and specificity as a diagnostic marker [6].

Despite the high prevalence and diagnostic utility of sleep disorders in DLB, there have been only few studies providing polysomnographic data [7,8]. In particular, we have little knowledge of which sleep features are altered when compared to normative values, and in what way they relate with daytime sleep symptoms,

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like hypersomnolence and fluctuations. The clinical consequences of Obstructive Sleep Apnea syndrome (OSA), which is frequent in these patients, have also been a matter of debate [9]. Several studies [10–12] have evaluated RBD motor events in PD and iRBD patients, but there are few studies with video files examination in DLB patients [7,13]. Comparison between DLB, PD and idiopathic RBD cases could be valuable to evaluate the progression of sleep changes in alfa-synucleinopathies, as the three disorders represent different stages of LBD progression. Our objectives were as follows: (1) compare PSG parameters of DLB patients with normative values for the same age group; (2) assess the relation between PSG parameters in DLB and the presence of fluctuations, hypersomnolence and OSA; and (3) compare RBD features between DLB with RBD (DLB-RBD), PD with RBD (PD-RBD) and iRBD patients.

2. Methods

2.1. Subject selection and diagnosis

We included all DLB, PD and iRBD patients that underwent video-polysomnography in the Neurology Department Sleep Lab of Egas Moniz Hospital, a tertiary center covering part of Lisbon's metropolitan area. We revised the clinical files of all patients registered in the sleep lab data base during the period between January 2015 and March 2018 and selected patients who had a diagnosis of DLB, PD or iRBD at the time of PSG recording. DLB was diagnosed according to the Fourth consensus report of the DLB Consortium [3]. As determined in this last version of the consensus report, the presence of REM sleep behavioral disorder was used as diagnostic criteria. All diagnosis were discussed with a dementia specialist and dubious cases were excluded from analysis. To differentiate DLB patients from PD patients with dementia, the one year rule was used. DLB patients attended the Dementia Outpatient Clinic and were proposed PSG during routine clinical follow-up, for investigation of possible RBD (either because of spontaneous complaints of sleep disturbance or as part of diagnostic workup) or to exclude OSA in individuals who presented with suggestive clinical symptoms. All PD and iRBD patients were followed in the Movement Disorders and Sleep Disorders outpatient clinics, respectively. PD patients were diagnosed according to the U.K. brain bank criteria [14], staged according to Hoehn and Yahr scale [15] and assessed with the Unified Parkinson's Disease Rating Scale III (UPDRS III) [16]. PD with dementia (PDD) was defined according to established recommendations [17]. iRBD cases were diagnosed according to the third version of the International Classification of Sleep Disorders (ICSD III) [18] (see below). PD patients were referred for PSG evaluation if they presented with sleep symptoms demanding objective evaluation of sleep parameters (eg, hypersomnolence not explained by medication, RBD symptoms). iRBD group was formed mostly by patients who recurred to the Outpatient Clinic for complaints related to dream enactment behavior.

Patients were not excluded if they were medicated, and, for ethical reasons, their habitual medication was not interrupted during PSG.

2.2. DLB symptom assessment

Age at time of PSG, gender, disease duration (defined as time from first cognitive symptom to PSG), medications with CNS action, Mini-mental state examination (MMSE) scores, Global deterioration scale (GDS) scores and Body Mass Index (BMI) were collected from patients' files. We created a structured check-list containing all the clinical features (core and supportive) and clinical biomarkers (indicative and supportive) proposed by the Fourth consensus report of the DLB Consortium [3]. All DLB clinical files were reviewed by a trained neurologist, who used the check-list to register the presence or absence of the core and supportive clinical features, according to the descriptions given in the Consortium documents and related references. The presence of hypersomnolence and fluctuations were assessed through clinical file review, based on clinician, patients and caregiver reports, and classified as either “present” or “absent”. The neurologist responsible for collecting these data did not participate in the diagnosis of DLB patients and was blinded to PSG evaluation.

2.3. Video-polysomnography

All subjects underwent one-night, in lab, video-PSG. PSG was performed with a digital polygraph (XLTEK-TREX, Natus Medical Inc., Middleton, USA) and included electrooculography, electroencephalography (six channels F1-A1, F2-A2, C4-A1, C3-A2, O1-A2, O2-A1) electrocardiography, electromyography of the mentalis, right and left tibial muscles, recording of nasal air flow, thoracic and abdominal respiratory effort, oxygen saturation, microphone, and digital EEG-synchronized videography with infrared camera. Sleep staging and REM sleep muscular tone were scored according to the American Academy of Sleep Medicine (AASM) recommendations [19]. The ICSD III [18] criteria were used for RBD diagnosis:

(1) repeated episodes of behavior or vocalization that are either documented by PSG to arise from REM or are presumed to arise from REM based on reports of dream enactment;
(2) evidence of REM sleep without atonia (RSWA) on PSG.

To define RSWA we used the criteria from the AASM scoring manual [19]. Tonic excessive muscular activity was assessed in 30 s epochs and considered when sub-mental EMG activity exceeded twice that of background activity for more than 50% of the epoch. Phasic excessive muscular activity was measured in 3 s mini-epochs and defined as sub-mental EMG activity bursts lasting 0.1–5 s and exceeding four times that of the background. Phasic and tonic activities indexes were calculated by dividing the number of epochs with excessive activity by the total number of REM epochs. According to the work by Frauscher et al. [20], the cut-off for excessive muscular activity was 16% for phasic activity and 10% for tonic excessive EMG activity in the mentalis muscle.

Apneas and hypopneas were defined according to AASM recommendations [19]. An apnea-hypopnea index (AHI) > 4 was considered as indicative of OSA.

2.4. REM sleep motor events (ME) assessment

We defined REM sleep ME as any movement visible in video recordings during this sleep stage, regardless of type, duration or severity. We determined total number of events and duration, in seconds, of each event. ME were individually classified according to the system developed by Frauscher et al. [11], which rates movement events according to type (myoclonic vs. simple vs. stereotypies vs. scenic vs. vocalizations vs. violent); emotional tone (negative vs. positive); complexity (elementary vs. complex); body region (trunk, neck/head vs. upper extremity vs. lower extremity); spatial distribution (focal vs. segmental vs. multifocal vs. global); and proximal vs. distal. A global measurement of ME severity was also used, according to the method proposed by Sixel-Döring et al. [21], which grades each ME according to categorical location of movements (“0" = no visible movement; "1" = slight movements or jerks "2" = movements involving proximal extremities, including violent behavior; "3" = axial involvement including bed falls). Global RBD severity corresponds to the highest score given.

2.5. Data analysis

For comparison with normative values, each DLB patient was matched with the correspondent normative value for the same age range, using published data [22]. To evaluate the magnitude of change in relation to norms, DLB patients' values for Total Sleep Time (TST), Sleep Efficiency, wake after sleep onset (WASO), Sleep Latency, REM sleep latency, and percentage of N1, N2, N3 and REM sleep were converted to modified Z-scores. Mann–Whitney tests were used to test the significance of differences.

To evaluate the relation between medication, sleep symptoms (hypersomnolence, fluctuations, OSA, RBD) and objective sleep data, patients were divided in two groups (with and without the respective medication/sleep feature) and compared by means of T-test, Mann–Whitney tests (for continuous variables and depending on the normality of distributions) or Chi-square tests (for categorical variables, and using Fisher test whenever indicated). The relation between MMSE scores and PSG data was tested with Pearson or Spearman tests (depending on the normality of distributions).

To evaluate the differences between DLB (all patients) and PD patients and between DLB-RBD, PD-RBD and iRBD patients, and because there were significant differences regarding age, comparisons of PSG variables were made with General Linear Model proceedings, with age as covariate, disease group as factor and PSG data as dependent variables.

2.6. Ethics

Patients signed informed consent forms. The ethics committee of the institution approved the investigation protocol.

3. Results

We selected a total of 19 DLB patients. Supplementary Table 1 presents demographic and clinical symptoms data for the DLB group. In average, the sample was constituted by aged patients, with short disease duration, relatively high MMSE and low GDS scores, probably reflecting the fact that most PSGs were proposed as one of the initial ancillary tests in this population. Fluctuations and hypersomnolence were present in six and nine patients, respectively. All patients were medicated with at least one drug with CNS action.

Nine patients fulfilled current criteria for RBD (REM sleep without atonia + history of dream enactment during sleep), but only five actually presented motor events during REM sleep in the video-PSG recording. In seven patients, the presence of RBD was not determinable, due to a total absence of REM sleep. Two of these patients had been referred to PSG for symptoms suggestive of RBD. Of the remaining three patients, in whom RBD diagnosis was excluded by PSG, two had been referred to PSG because of sleep complaints compatible with RBD.

3.1. Comparison between DLB and normative values

DLB patients presented significant differences from age normative values, as depicted in Fig. 1. Total sleep time and sleep efficiency were significantly lower in DLB patients, whereas sleep latency, WASO and N2 stage duration were significantly higher. Conversely, REM sleep duration was significantly below the norm. To test if this reduction in REM sleep was determined by the seven patients in whom REM sleep was completely absent, we run a second comparative analysis, excluding patients with no REM

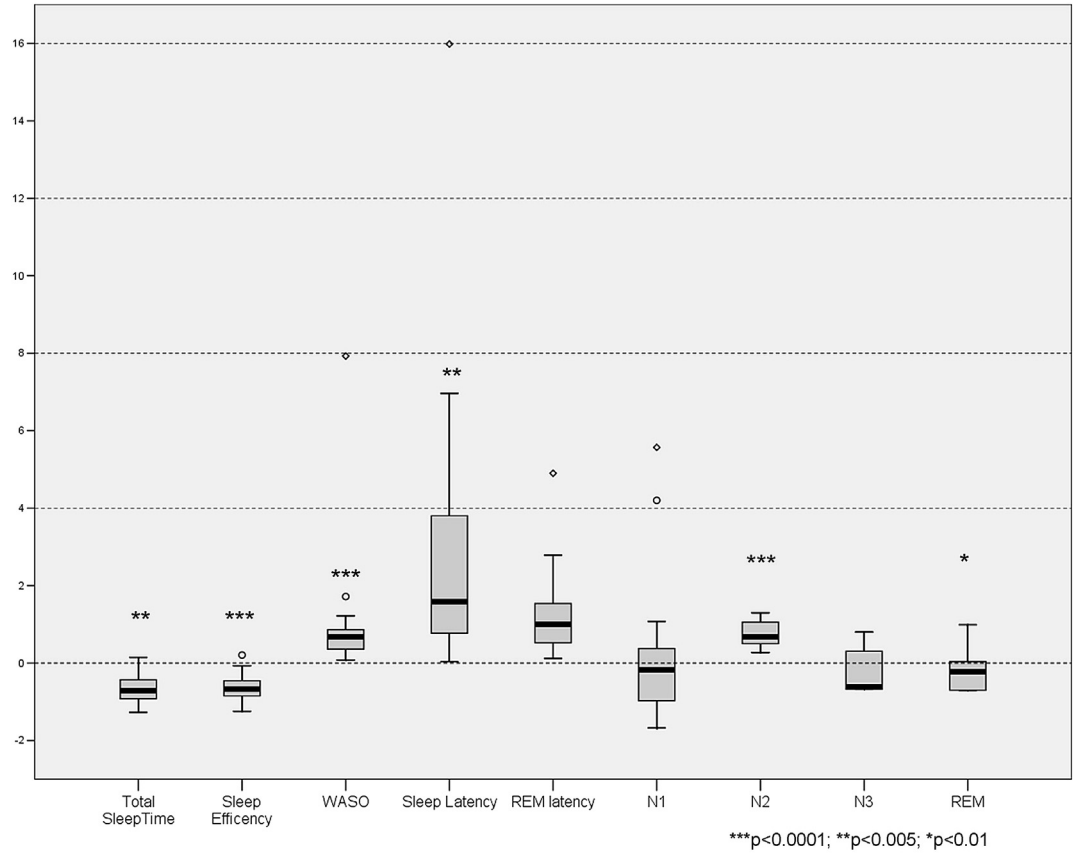

Fig. 1. PSG data in DLB: differences from normative values. Values are modified z-scores.

sleep, and found that there were no significant differences in percentage of REM duration between DLB patients with REM sleep and normative values (mean percentage of REM duration of 12.3 ± 7.3, mean modified z-score of 0.560 ± 0.50).

3.2. Relation between medication, day-time symptoms, and sleep variables in DLB patients

There were no significant differences in PSG data between patients taking and not taking clonazepam. Patients under AChE inhibitors (rivastigmine in all cases) were significantly older. Adjusting for age, we found no significant differences in PSG variables related to the use of AChE inhibitors. Use of dopaminergic drugs, antidepressants or antipsychotics did not translate to significant differences in PSG data or clinical symptoms. Because the use of antidepressants could have caused an artificial increase in REM muscular tone, possibly creating false positive cases, particularly regarding those DLB-RBD patients that did not had motor events during REM sleep, we evaluate the relation between use of antidepressants and the prevalence of DLB-RBD without motor events in PSG, but found no significant association (two out of four DLB-RBD patients without motor events were medicated with anti-depressants, vs. four out of five in the DLB-RBD patients with motor events on PSG, $p = 0.524$). Nine patients had AHI compatible with OSA. The presence of OSA was not related to fluctuations, hypersomnolence or any clinical symptom or to differences in PSG data. MMSE and GDS scores were not significantly different between patients with and without OSA. There were no significant differences between patients with or without fluctuations. Hypersomnolence was also not related to differences either in PSG or clinical variables. Comparison between patients with and without RBD was not performed, given the small number of DLB patients without RBD.

3.3. Comparison between DLB and PD patients

Overall, 51 PD patients were included. PD patients had a mean age of 69.3 ± 9.2 years; disease duration 7.06 ± 4.9 years, levodopa equivalent dose 608.2 ± 410.3 mg/day; UPDRS-III score 21.36 ± 11.9 and Hoehn and Yahr stage of 2.40 ± 0.82. Four patients presented PPD criteria. DLB patients were significantly older than PD patients. When corrected for age, there were no significant differences in PSG data between these two groups, except for Sleep Latency, which was significantly higher in DLB patients, and AHI, which was significantly higher in PD patients (Table 1.). Excluding PDD patients from analysis did not alter these results. Although PLMS mean value was high in DLB patients, there were no spontaneous complaints compatible with Restless Legs Syndrome (RLS) in this group.

3.4. Comparison of RBD features between DLB-RBD, PD-RBD and iRBD

iRBD patients were significantly younger than PD-RBD and DLB-RBD patients (Table 2). Adjusting for age differences, there were no significant differences between DLB-RBD, PD-RBD and iRBD patients regarding sleep measures, except for sleep efficiency, better in iRBD patients. When comparing RBD features, we found a significant higher number of motor events in iRBD compared with the other groups, and a higher score on the RBD global severity score. The frequencies of each type of movement, when corrected for the total number of events, were similar in the three groups, favoring simple, elemental, distal, lower limb type of movements, with the typical complex, violent events being rarer (Table 3).

4. Discussion

4.1. Comparison between DLB and normative values

In comparison with age normative values, DLB patients presented a significant reduction in sleep efficiency and total sleep time and an increase in sleep fragmentation. These objective data are in accordance with subjective complaints found in clinical practice and with questionnaire-based studies [23]. They are also in accordance with two previous studies that presented PSG data from DLB patients [7,8]. Relative duration of sleep stages also differed from norms, with DLB patients presenting with a specific reduction in REM sleep and concomitant increase in superficial N2 sleep.

When comparing the normative data with the sub-group of DLB patients that had REM sleep in PSG, we found no significant differences in REM sleep duration (the mean modified z-score was positive, signifying increased REM duration in the DLB group). This suggests an all or nothing phenomenon, with DLB patients presenting either no REM sleep or, if REM sleep is present, a duration similar to normative values, which could signify a difficulty in initiating REM sleep, rather than in maintaining it once started. REM sleep onset depends on the coordinated actions of REM-on

Table 1
PSG data: comparison between DLB and PD patients.

	Dementia with Lewy Bodies (n = 19)	Parkinson's Disease (n = 50)	p
Age	80.21 (8.23)	70.54 (8.75)	0.0001***
Gender (male)	14 (73.7)	27 (54.0)	0.175
RBD (present/absent/undetermined)	9 (47.4)/3 (16.0)/7 (36.8)	23 (46)/18 (35.3)/9 (19.6)	0.136
BMI	25.96 (3.98)	28.91 (5.22)	0.251
Total sleep time (min)	246.42 (94.54)	345.37 (113.94)	0.053
Sleep efficiency (%)	49.16 (18.19)	53.96 (18.43)	0.876
Awakenings Index	6.92 (4.20)	6.05 (5.00)	0.521
WASO (min)	240.08 (371.21)	157.04 (72.20)	0.219
Sleep latency (min)	80.51 (100.39)	43.48 (40.43)	0.028*
REM sleep latency (mi)	196.58 (174.82)	195.90 (117.15)	0.918
Stage N1 (%)	11.00 (9.68)	9.27 (7.67)	0.638
Stage N2 (%)	70.65 (12.01)	67.56 (16.58)	0.443
Stage N3 (%)	10.55 (12.31)	12.81 (12.30)	0.340
Stage R (%)	7.81 (8.40)	9.04 (9.45)	0.836
AHI	13.34 (11.29)	16.39 (18.76)	0.217
OSA	12 (63.2)	34 (66.7)	0.045*
PLMS index	14.70 (20.96)	5.68 (10.48)	0.128

Values are number (percentage) or mean (standard deviation). RBD – REM sleep Behavior Disorder. Undetermined refers to patients without REM sleep in PSG. WASO – Wake after sleep onset. AHI – Apnea-Hypopnea Index. OSA – Obstructive Sleep Apnea Syndrome; PLMS – Periodic Limb Movements of Sleep. ***$p < 0.0005$; *$p < 0.05$. p values were adjusted for age differences.

Table 2
PSG data: comparison between DLB-RBD, PD-RBD and iRBD patients.

	DLB RBD (n = 9)	PD-RBD (n = 23)	iRBD (n = 20)	p
Age (yrs)	79.11 (8.70)	68.26 (10.21)	69.75 (8.91)	0.018*
Gender (male)	6 (46)	14 (61)	17 (85)	0.208
Total sleep time	292.56 (78.21)	372.41 (111.19)	347.25 (89.83)	0.624
Sleep efficiency	56.78 (16.92)	55.53 (20.97)	77.81 (42.95)	0.045*
Awakenings Index	6.42 (2.98)	5.01 (2.52)	4.79 (4.58)	0.940
WASO	154.28 (63.34)	134.66 (58.018)	122.71 (92.03)	0.678
Sleep latency	62.36 (54.78)	47.35 (41.60)	32.32 (31.39)	0.222
REM sleep latency	132.39 (98.97)	188.60 (103.71)	165.13 (110.66)	0.469
Stage N1%	8.30 (4.07)	7.43 (5.60)	9.44 (6.12)	0.517
Stage N 2%	67.48 (10.56)	66.80 (11.41)	62.01 (9.93)	0.087
Stage N 3%	9.74 (9.81)	13.37 (9.95)	14.03 (10.82)	0.257
Stage R %	14.49 (7.03)	12.35 (8.53)	14.54 (5.83)	0.665
AHI	16.70 (12.93)	18.83 (19.82)	12.34 (15.29)	0.269
OSA	6 (66.7)	17 (70.8)	11 (55)	0.544
PLMS index	10.48 (18.13)	8.19 (12.93)	5.63 (8.26)	0.720

DLB-RBD – Dementia with Lewy Bodies patients with REM sleep Behavior Disorder (RBD), PD-RBD – Parkinson's Disease Patients with RBD. iRBD – Idiopathic RBD patients. Values are number (percentage) or mean (standard deviation). WASO – Wake after sleep onset. AHI – Apnea-Hypopnea Index. OSA – Obstructive Sleep Apnea Syndrome; PLMS – Periodic Limb Movements of Sleep.
$p < 0.05$. p values were adjusted for age differences.

Table 3
RBD features in DLB-RBD, PD-RBD and iRBD patients.

	DLB-RBD (n = 9)	PD-RBD (n = 23)	iRBD (n = 20)	p
RSWA Tonic index	0.196 (0.182)	0.348 (0.266)	0.215 (0.217)	0.124
RSWA Phasic index	0.303 (0.287)	0.272 (0.223)	0.359 (0.210)	0.468
Motor events – global severity	0.56 (0.882)	1.13 (0.815)	1.55 (0.826)	0.015*
Motor events – mean duration (scs)	3.21 (1.35)	4.30 (2.89)	5.94 (5.230)	0.324
Number of motor events				
Total	3.00 (4.87)	10.70 (15.27)	18.65 (19.21)	0.047*
Elementary	0.37 (0.45)	0.59 (0.44)	0.79 (0.63)	0.128
Complex	0.08 (0.15)	0.14 (0.24)	0.16 (0.18)	0.645
Emotion				
positive	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.458
negative	0.00 (0.00)	0.11 (0.22)	0.04 (0.06)	0.109
Type				
myoclonic	0.02 (0.05)	0.10 (0.15)	0.14 (0.19)	0.141
simple	0.20 (0.33)	0.29 (0.32)	0.42 (0.26)	0.165
stereotypes	0.09 (0.15)	0.14 (0.29)	0.14 (0.13)	0.769
scenic	0.04 (0.13)	0.11 (0.23)	0.08 (0.10)	0.641
vocalizations	0.11 (0.33)	0.11 (0.21)	0.09 (0.16)	0.958
violent	0.00 (0.00)	0.10 (0.28)	0.04 (0.06)	0.237
Body region				
trunk	0.02 (0.07)	0.10 (0.23)	0.11 (0.12)	0.416
neck/head	0.22 (0.34)	0.35 (0.36)	0.17 (0.17)	0.162
upper limbs	0.21 (0.33)	0.36 (0.36)	0.52 (0.37)	0.095
lower limbs	0.10 (0.16)	0.26 (0.32)	0.37 (0.30)	0.218
Spatial distribution				
focal	0.17 (0.33)	0.36 (0.38)	0.34 (0.30)	0.377
segmental	0.18 (0.28)	0.20 (0.33)	0.31 (0.27)	0.390
multifocal	0.05 (0.08)	0.10 (0.15)	0.08 (0.09)	0.574
global	0.02 (0.07)	0.07 (0.21)	0.07 (0.09)	0.673
Laterality				
symmetric	0.25 (0.35)	0.43 (0.37)	0.26 (0.18)	0.139
asymmetric	0.19 (0.28)	0.29 (0.32)	0.54 (0.43)	0.006**

DLB-RBD – Dementia with Lewy Bodies patients with REM sleep Behavior Disorder (RBD), PD-RBD – Parkinson's Disease Patients with RBD. iRBD – Idiopathic RBD patients. Values are mean (standard deviation). Motor events subtype values are expressed as number of motor events subtype/total number of motor events.

and REM-off structures, responsible for a flip-flop mechanism that ensures a complete change between stages. Most of these structures are located in the mesopontine region, which is affected early in the alfa-synucleinopathies [24]. REM reduction was also described in Alzheimer's disease (AD) patients, but with a different pattern [25], patients having a difficulty in maintaining REM sleep rather then in initiating it (same number of REM periods as in normal individuals but with shorter duration). This difference is in accordance with the theory that reduction in REM sleep could stem from different causes in Alzheimer disease and DLB, due to affection of different cholinergic pathways [25].

4.2. Relation between medication, day-time symptoms, and sleep variables in DLB patients

We did not find a significant influence of rivastigmine, clonazepam, dopaminergics, antidepressants or antipsychotics in PSG or clinical variables, suggesting that the use of these medications did not bias our results. OSA was a frequent finding in DLB patients, but it was not related to either the severity of cognitive dysfunction (as measured by the MMSE), fluctuations or hypersomnolence, suggesting that daytime related symptoms are not caused by sleep disturbed breathing in DLB patients and could be mainly related

with the degenerative process that affects sleep regulation centers in the brainstem. This discrepancy between the presence of OSA and daytime function was previously reported [8,9]. Fluctuations and hypersomnolence were also not related with sleep structure differences, suggesting that these symptoms are not caused by sleep deprivation or alterations in the relative duration of sleep stages.

4.3. Comparison between DLB and PD patients

We did not find significant differences in sleep structure between DLB and PD, except for sleep latency, which was lower in PD patients, possibly as the consequence of a significantly higher AHI. The similitude in sleep dysfunction may be interpreted as a similitude in pathophysiology, as both disorders are LBD. Our results were different from those of Terzaghi and collaborators [7], who found N1 increase and N2 decrease in DLB patients, which could be caused by differences in DLB samples (our patients were older, had less parkinsonism and were under the usual medication for this type of dementia).

4.4. Comparison of RBD features between DLB-RBD, PD-RBD and iRBD

iRBD patients had significantly better sleep efficiency, possibly in relation with a less advanced stage of neurodegeneration. We found no major differences in the pattern of REM sleep motor events, when comparing DLB-RBD patients with PD-RBD and iRBD patients. We can conclude that, similarly to what has been described for RBD associated with other disorders [10–12], ME in DLB are characterized mostly by simple, short-lived movements of the extremities and not by violent, dream enactment events reported in the first descriptions of this parasomnia. Although the pattern of movements and RSWA indexes were similar between the groups, the severity of RBD, as measured by the total number of events and global severity score, was significantly lower in DLB patients, increasing progressively in PD and idiopathic cases. According to Braaks' staging, the presence of diffuse cortical Lewy bodies represents the last stage of PD neuropathological progression [26], frequently corresponding, in the clinical ground, to PDD. This stage of cortical Lewy body deposition is also the neuropathological hallmark of DLB. In this sense, and although there isn't a complete overlap in the location of Lewy bodies between in DLB and PDD, DLB has been considered to represent a more severe stage of LBD [27]. Considering iRBD, PD-RBD and DLB-RBD as a spectrum of LBD with increasing degrees of severity, our findings could be viewed as an inverse relation between the intensity of RBD ME and the severity of LBD. PSG follow-up studies in individuals with secondary RBD [28] and longitudinal, clinical studies of PD case series [29,30] have suggested that RBD manifestations can diminish or disappear as the disease progresses. One interpretation for this finding is that increased cortical degeneration, related to a more advanced disease stage, could lower the occurrence of motor manifestations, even if RSWA persists. This hypothesis, however, should be considered with caution, as the reduction of RBD severity found in clinical investigations has not yet been confirmed in longitudinal PSG studies. Conversely, parkinsonism (absent in iRBD cases), could have diminished motor manifestations of RBD in PD and DLB cases, a notion that goes against the findings of previous studies [10,13]. Another explanation for this finding could be the difference between sample selections. Since our iRBD patients were recruited from the Sleep Outpatient Clinic, to which most resorted to because of complaints directly connected with the parassomnia, this group could contain a higher prevalence of severe cases.

4.5. Limitations of the study

The present study has some limitations, which hamper the generalization of its results. The study sample is a sample of DLB patients who presented clinical criteria for undergoing PSG, either because they had sleep complaints or because PSG data (ie, RBD) was important for a final diagnosis. Thus, the data we provided cannot be generalized to all DLB patients (sleep dysfunction would probably be less severe if non symptomatic patients were included). Furthermore, because we only investigated RBD in a sample of patients with sleep complaints, and not in the entire population of DLB patients followed in our department, we cannot provide an estimation of RBD prevalence in DLB. RBD prevalence in our sample group could be overestimated, as the presence of RBD was used as a criterion for DLB diagnosis. Finally, and though a comparison between patients taking and not taking medication did not reveal significant differences, we cannot assure that medication did not influence the differences found between patients and normative data.

5. Conclusion

In conclusion, objective data from our study indicates that DLB patients' sleep is significantly reduced and fragmented, there being a specific difficulty in REM sleep initiation. These changes appear to be unrelated with day-time sleep symptoms, suggesting a different pathophysiology. Pattern of RBD related motor events was similar between DLB-RBD, PD-RBD and iRBD patients, but the frequency of motor events was lower in DLB-RBD patients.

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Conflict of interest

None.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.12.006.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2018.12.006.

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