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Parasomnias, sleep-related movement disorders and physiological sleep variants in focal epilepsy: A polysomnographic study

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ABSTRACT

Purpose: The link existing between epilepsy and sleep is widely recognized. However, little is known about the prevalence and the clinical consequences of the comorbidity between focal epilepsy and sleep disorders, especially those sleep phenomena classified as isolated symptoms or normal variants. Objective of the study was to evaluate the frequency of sleep disorders and physiological sleep variants in a group of adult patients with focal epilepsy as compared to healthy controls by means of nocturnal polysomnography.

Methods: We performed a retrospective observational study in the Neurological Clinic of the University of Catania in adult patients with a diagnosis of focal epilepsy and in a group of control subjects. All subjects underwent an overnight polysomnography. The following sleep disorders were considered: NREM-related parasomnias; REM-related parasomnias; sleep-related movement disorders; isolated symptoms or normal variants.

Results: 100 patients [mean age 30.3 ± 14.7 years, 40 men] and 62 controls [mean age 36.4 ± 15.9, 20 men] were studied. A significant higher percentage of sleep disorders was recorded in patients as compared to controls (73 % vs 48.4 %; p = 0.002). In particular, we found a higher frequency of periodic limb movements (PLM) (20 % vs 4.8 %; p = 0.007), bruxism (20 % vs 4.8 %; p = 0.007) and neck myoclonus (22 % vs 4.8 %; p = 0.003). Moreover, alternating limb muscle activation was associated with sleep-related hypermotor epilepsy (OR = 7.9; p = 0.01).

Conclusion: Sleep disorders and physiological sleep variants are common in adult patients with focal epilepsy.

1. Introduction

Sleep and epilepsy are two bidirectionally interconnected phenomena [1]. The close link existing between epilepsy and sleep is well known since the times of Hippocrates [2]; and the activating function of sleep on epilepsy has been widely recognized, as well as the effect of epilepsy on sleep [3].

The influence of sleep on epilepsy is supported by the observations that, in many epileptic syndromes, seizures and interictal discharges are more frequent during NREM sleep [4,5]. On the other hand, the influence of epilepsy on sleep is demonstrated by some studies showing that sleep disorders are two to three times more common in adults and children with epilepsy compared with age-matched controls [6].

In this regard, the research has mostly focused on the sleep alterations of Idiopathic Generalized Epilepsies (IGE), and in particular in Juvenile Myoclonic Epilepsy (JME), for which a close link to the sleep–wake cycle has been demonstrated [7–9]. Regarding focal epilepsies, focal seizures have been shown to disrupt normal sleep, particularly stage REM sleep, the following night after a seizure [10]. Among focal epilepsies, temporal lobe epilepsy has been found to be more related with sleep changes showing an alteration of sleep architecture with reduced sleep efficiency and greater sleep fragmentation [11]. Moreover, patients with frontal lobe epilepsy seem to show a higher tendency to have seizures during sleep [11].

Another convincing evidence of the comorbidity between epilepsy and sleep disorders is about obstructive sleep apnoea (OSA) which

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seems to coexist with epilepsy in about 10 % of adult patients with epilepsy and up to 30 % of drug resistant subjects [12,13]. Moreover, while there is some literature about the coexistence of sleep disorders, and in particular NREM parasomnia and epilepsy in children [13,14], data regarding sleep disorders, and especially normal sleep variants, and epilepsy are scarce in adult patients [13,15].

The majority of studies exploring the comorbidity between epilepsy and sleep disorders were mainly based on the clinical history through structured interviews and validated questionnaires [13,16,17]. The studies exploring through video-polysomnography (VPSG) the frequency of sleep disorders in patients with epilepsy mainly focused on sleep apnoea and on sleep correlates of restless legs syndrome (RLS) [13]. Less is known about the nosological entities classified as isolated symptoms and normal variants, according to the last International classification of Sleep Disorders (ICSD third edition) [18].

Objective of the present study was to evaluate the frequency of sleep disorders and physiological sleep variants in a group of adult patients with focal epilepsy as compared to controls without epilepsy, by means of nocturnal polysomnography.

2. Material and methods

2.1. Study population

We performed a retrospective observational study at the Neurological Clinic of the University of Catania. All patients with a diagnosis of focal epilepsy [19] who underwent a nocturnal VPSG in the 2015–2019 period were considered for the study. Nocturnal VPSG was routinely performed as part of the standard diagnostic procedures. Patients underwent neurological examination, a standard EEG recording and conventional structural magnetic resonance imaging (MRI). Exclusion criteria were the presence of an epileptic encephalopathy and the diagnosis of obstructive sleep apnoea syndrome.

Controls without epilepsy were selected among subjects who underwent a polysomnographic recording in the same study period for episodes of loss of consciousness and for whom a diagnosis of epilepsy or any other neurological disease, following accurate diagnostic procedures, has been excluded. Subjects with diagnosis of obstructive sleep apnoea syndrome have been excluded as well.

Subjects who had undergone PSG for any sleep complaint were excluded. All subjects signed a written informed consent. The study conforms with World Medical Association Declaration of Helsinki. It was approved by the local Ethical Committee.

The study was developed in accordance with the STROBE [20] guidelines for observational studies (Table A.1).

2.2. Clinical variables

All the clinical data of patients were retrospectively extracted by their medical records. The following clinical variables were taken into account for patients: sex, age, lobe of origin, etiology according to the most recent classification [1], age of onset of epilepsy, clinical reports of seizures during sleep, comorbidities, use of antiseizure medications (ASMs), antidepressants or benzodiazepines and drug resistance [21]. Regarding the lobe of origin, it was ascertained through the evaluation of the anamnestic report of seizures semiology and the study of ictal and interictal EEG abnormalities recorded during a standard video-EEG and a long-term EEG monitoring performed by all our patients with epilepsy in our center. For the patients with a structural etiology, also the neuroimaging data were taken into account for the definition of the lobe of origin. For control subjects the following variables were analysed: sex, age, comorbidities, use of drugs such as antidepressants or benzodiazepines.

2.3. Polysomnographic recordings

All patients and the majority of controls underwent an overnight VPSG, performed according to the American Association of Sleep Medicine guidelines [22]. The study of night sleep through PSG is routinely performed in our center in all subjects with episodes of loss of consciousness and in all patients with epilepsy.

All the subjects spent a previous night in the ward in order to reduce the first night effect. The PSG recording was carried out using a minimum of eight-channel EEG, placed according to the International $10-20$ system, two electrocardiographic derivations, chin and right and left anterior tibialis electromyography (EMG) electrodes, electrooculogram. Nasal thermistor, snore monitor, chest and abdominal movements, pulse rate and oximetry have been used. The following polysomnographic macrostructural parameters were assessed: total sleep time; sleep efficiency; sleep latency; time spent in nocturnal wakefulness; percentage of NREM (N1, N2, N3) and REM sleep stages. The following sleep disorders were taken into account: NREM-related parasomnias such as disorders of arousal (DoA) from NREM; REM-related parasomnias such as REM sleep behaviour disorder (RBD); sleep-related movement disorders such as periodic limb movements in sleep (PLMs) and bruxism; isolated symptoms or normal variants such as alternating leg muscle activation (ALMA), excessive fragmentary myoclonus (EFM), and neck myoclonus (NM). All the sleep entities examined, except neck myoclonus, are present in the ICSD3 [18]. However, in the ICSD3, for all categories of sleep disorders, a subcategory exists named “isolated symptoms and normal variants”. This group consists of nosological entities that are borderline abnormal but not otherwise specific disorders. The evaluation of sleep disorders and normal variants was based on polysomnographic criteria according to the AASM guidelines, due to the absence of a clinical report of a sleep complaint [22].

In particular, a DoA was defined as the presence of a dissociation EEG pattern characterized by an α rhythm in posterior channels, and an anterior and midline theta-delta activity, associated with muscular artifact or a video event of complex motor behavior [22–24]. RBD was represented by episodes of behavior or vocalization documented by PSG to arise from REM sleep with evidence of REM sleep without atonia on PSG [18,22]. PLMs was diagnosed when the frequency of typical periodic limb movements was ≥ 15/h [18,22]. Sleep-related bruxism was considered as brief or sustained elevations of chin EMG activity that are at least twice the amplitude of background EMG, of at least 0.25 s in duration, occurring in sequences [18,22]. ALMA was defined as at least 4 brief activations of the anterior tibialis in one leg alternated with similar activation contralaterally, with a movement duration of 0.1–0.5 s and a frequency of 0.5–3 Hz, with sequences lasting between several and 20 s [18,22]. Neck myoclonus was considered as a “short stripe-shaped movement-induced artifact” visible vertically over the polysomnographic traces with a duration up to 2 s [25]. EFM was scored if at least 20 min of NREM sleep with EMG bursts on both legs of about 150 msec duration was recorded [18,22].

2.4. Statistics

Statistical analysis was performed using STATA 12 software packages (version 12.0, College Station, TX). Qualitative variables were described as percentages while quantitative variables as mean ± standard deviation (SD). Prior to statistical testing, the data were examined for normality using Shapiro-Wilk test. Pearson chi squared test (χ^2) or Fisher’s exact test were employed to study categorical variables; comparison between means were performed using unpaired *t*-test for parametric data and Mann-Whitney test for non-parametric data. The Bonferroni correction for multiple comparison was applied when appropriate. A multivariate logistic regression was manually constructed to identify predictive factors for all and each one of the sleep disorders in patients and controls, using variables with $p < 0.25$ in univariate

Table 1
Clinical characteristics of patients and controls.

	Patients (n = 100)	Controls (n = 62)	p
Age (mean ± SD)	30.3 ± 14.7	36.4 ± 15.9	**0.01**
Sex (men)	40 (40)	20 (32.2)	0.40
Age at onset (mean ± SD)	20.2 ± 14.1	/	
Epilepsy type		/	
Structural (%)	34 (34)		
Unknown etiology (%)	64 (64)		
Undetermined (%)	2 (2)		
Lobe of origin		/	
Frontal (%)	40 (40)		
Temporal (%)	53 (53)		
Occipital (%)	5 (5)		
Parietal (%)	2 (2)		
History of focal to bilateral tonic-clonic seizures	62 (62)	/	
Treatment during the recording			
ASMs (%)	65 (65)	/	/
Benzodiazepines (%)	15 (15)	11 (17.4)	0.64
Antidepressants (%)	6 (6)	9 (14.5)	0.07
ASMs taken by the patients			
Carbamazepine (%)	19 (27.8)		
Clobazam (%)	5 (7)		
Felbamate (%)	1 (1.4)		
Lacosamide (%)	3 (4.2)		
Levetiracetam (%)	21 (29.5)		
Lamotrigine (%)	5 (7)		
Phenytoin (%)	3 (4.2)		
Phenobarbital (%)	9 (12.7)		
Primidone (%)	1 (1.4)		
Oxcarbazepine (%)	14 (19.7)		
Topiramate (%)	18 (25.3)		
Valproate (%)	11 (15.5)		
Zonisamide (%)	1 (1.4)		

N, number; SD, standard deviation; ASMs, antiseizure medications.

calculations and retaining gender and age. The model was manually constructed using the likelihood ratio test (LRT) to compare the log-likelihood of the model with and without a specific variable. A $p \leq 0.05$ was set as level of significance.

3. Results

3.1. Clinical features of patients and controls

A total of 100 patients were studied (Table 1). Among patients with structural epilepsy, 12 (35.3 %) had malformations of cortical development and neuronal migration defects such as periventricular nodular heterotopia, polymicrogyria, and focal cortical dysplasia, whereas six patients (17.6 %) had hippocampal sclerosis. Twelve subjects (30 %) among patients with frontal lobe epilepsy had a diagnosis of sleep related hypermotor epilepsy (SHE). 33 % of patients was drug resistant. 55 % of patients had a clinical report of seizures during sleep. Regarding comorbidities, 7 patients had dysthyroidism, 5 hypertension and 2 diabetes. Among subjects who were taking ASMs, 33 (50.8 %) were on monotherapy, while of the remaining 32 (49.2 %) on polytherapy, six (18.7 %) were taking more than two ASMs.

Sixty-two subjects were studied as control group (Table 1). Comorbidities were hypertension for 8 (12.9 %), dysthyroidism for 8 (12.9 %), diabetes for three (4.8 %) and one patient (1.6 %) had chronic renal failure. Control subjects were slightly but significantly older than examined patients, whereas no differences were present in sex distribution or psychotropic drugs intake.

3.2. Sleep features of patients and controls

92 % of patients and none of controls presented EEG abnormalities during sleep. The sleep macrostructural parameters of patients and controls are described in Table 2. In particular, patients had significant lower total sleep time, longer sleep latency and lower REM sleep stage percentage than controls.

Table 2
Sleep macrostructural parameters in patients and controls.

Sleep parameters	Patients (n = 100)	Controls (n = 62)	p
Total sleep time (minutes)	340.9 ± 87	395.9 ± 78.3	< **0.001**
Sleep efficiency (%)	84 ± 16.2	86.5 ± 9.6	0.78
Sleep latency (minutes)	19.2 ± 16	12.5 ± 12.9	< **0.001**
Wake after sleep onset (minutes)	52.5 ± 49.2	58.8 ± 43.7	0.17
N1%	5.5 ± 7.1	5.2 ± 5.9	0.02
N2%	51.1 ± 10.4	49.8 ± 5.6	0.19
N3%	27.8 ± 11.5	24.7 ± 6.2	0.16
REM%	15.2 ± 6.1	20.8 ± 5.6	< **0.001**

Values in bold are those significant after Bonferroni correction (statistically significant: $p \leq 0.006$).

Seventy-three patients (73 %) had a sleep disorder while 31 % showed more than one sleep disorder (Table 2): in particular, in 24 % of patients two sleep disorders were recorded and in 7% of patients three sleep disorders were recorded. The most frequent sleep disorders recorded were sleep-related movement disorders (40 %) while normal sleep variants were present in 41 % of patients (Table 3).

Among 62 controls, 40 (64.5 %) underwent a complete VPSG while for the remaining 22 (35.5 %) video was not available. In 30 (48.4 %) of controls a sleep disorder was recorded while 7 (11.3 %) showed more than one sleep disorder: in particular, in 4 (6.4 %) of patients two sleep disorders were recorded and in 3 (4.8 %) three sleep disorders were present. The most frequent sleep disorder recorded was DoA in 17 subjects (27.4 %) while normal sleep variants were present in 14 subjects (22.6 %) and sleep-related movement disorders in 5 (8.1 %) (Table 3). Comparing the percentages of sleep disorders between patients and controls, we found a significant higher percentage of sleep disorders in patients (73 % vs 48.4 %; $p = 0.002$). More specifically we found a higher frequency of PLM, bruxism and neck myoclonus in patients compared to controls, as shown in Table 3.

At the multivariate analysis, after adjusting for age, sex and use of benzodiazepines and antidepressants, the associations between epilepsy and sleep disorders, PLM, bruxism and neck myoclonus were confirmed (Table 4).

3.3. Sleep features of patients

When performing the multivariate analysis in the group of patients in order to evaluate the influence of demographical features and specific epilepsy-related variables on sleep disorders, we found that the

Table 3
Sleep disorders recorded in patients and controls.

Sleep disorders	Patients (n = 100)	Controls (n = 62)	p*
Disorders of arousal, n (%)	26 (26)	17 (27.4)	0.84
Rem Behavior Disorder, n (%)	1 (1)*	0	0.43
Periodic Limb Movements, n (%)†	20 (20)	3 (4.8)	**0.007**
Bruxism, n (%)	20 (20)	3 (4.8)	**0.007**
Alternating leg muscle activation, n (%)	17 (17)	9 (14.5)	0.67
Excessive fragmentary myoclonus, n (%)	4 (4)	4 (6.4)	0.48
Neck myoclonus, n (%)	22 (22)	3 (4.8)	**0.003**

Values in bold are those significant after Bonferroni correction. (statistically significant: $p \leq 0.007$).

* The patient with RBD presented also REM sleep without atonia (RSWA).

† Mean PLM index of 36.5 ± 21.5 in patients and 23.9 ± 4.8 in controls.

Table 4
Univariate and multivariate analysis of sleep disorders in patients and controls.

	SD +	SD −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	30.2 ± 15.8	36.7 ± 13.9	0.97	0.95 − 0.99	**0.008**	0.98	0.95 − 1	0.09
Sex (men) (%)	47 (45.6)	13 (22.03)	3	1.4 − 6.1	**0.003**	2.5	1.1 − 5.4	**0.02**
Epilepsy (%)	73 (70.8)	27 (45.8)	2.9	1.5 − 5.6	**0.002**	2.6	1.3 − 5.2	**0.008**
Benzodiazepines (%)	11 (10.7)	15 (25.4)	0.3	0.1 − 0.8	**0.02**	0.4	0.2 − 1.1	0.09
Antidepressants (%)	7 (6.8)	8 (13.6)	0.5	0.1 − 1.3	0.16			
	DoA +	DoA −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	22.3 ± 6.6	36.4 ± 15.9	0.9	0.8 − 0.9	< **0.001**	0.9	0.8 − 0.9	< **0.001**
Sex (men) (%)	16 (37.2)	44 (37)	1	0.5 − 2.1	0.97	0.6	0.2 − 1.4	0.22
Epilepsy (%)	26 (60.5)	74 (62.2)	0.9	0.4 − 1.9	0.84			
Benzodiazepines (%)	2 (4.6)	24 (20.2)	0.2	0.04 − 0.8	**0.03**	0.2	0.04 − 1.1	0.07
Antidepressants (%)	1 (2.3)	14 (11.8)	0.2	0.02 − 1.4	**0.10**	1.1	0.1 − 10.5	0.95
	PLM +	PLM −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	41.9 ± 14.3	31.1 ± 15.1	1.04	1.01 − 1.07	**0.003**	1.05	1.02 − 1.08	< **0.001**
Sex (men) (%)	7 (30.4)	53 (38.1)	0.7	0.3 − 1.8	0.48	0.6	0.2 − 1.8	0.42
Epilepsy (%)	20 (87)	80 (57.5)	4.9	1.3 − 17.3	**0.01**	8.7	2.2 − 34.9	**0.002**
Benzodiazepines (%)	5 (21.7)	21 (15.1)	1.6	0.4 − 4.7	0.42			
Antidepressants (%)	4 (17.4)	11 (7.9)	2.4	0.7 − 8.5	0.16			
	Bruxism +	Bruxism −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	23.6 ± 9	34.2 ± 15.8	0.93	0.89 − 0.98	**0.004**	0.94	0.90 − 0.99	**0.02**
Sex (men) (%)	14 (60.9)	46 (33.1)	3.1	1.3 − 7.8	**0.01**	2.7	1 − 7	**0.04**
Epilepsy (%)	20 (87)	80 (57.5)	4.9	1.4 − 17.3	**0.01**	3.9	1 − 14.2	**0.04**
Benzodiazepines (%)	4 (17.4)	22 (15.8)	1.1	0.3 − 3.6	0.85			
Antidepressants (%)	1 (4.3)	14 (10.1)	0.4	0.05 − 3.2	0.39			
	ALMA +	ALMA −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	26.2 ± 9.8	33.9 ± 16	0.96	0.93 − 0.99	**0.03**	0.95	0.90 − 0.99	**0.02**
Sex (men) (%)	14 (53.8)	46 (33.8)	2.3	1 − 5.3	**0.06**	2.1	0.8 − 5.1	0.11
Epilepsy (%)	17 (65.4)	83 (61)	1.2	0.5 − 2.9	0.68			
Benzodiazepines (%)	2 (7.7)	24 (17.6)	0.4	0.1 − 1.7	0.22	0.3	0.05 − 1.7	0.18
Antidepressants (%)	4 (15.4)	11 (8.1)	2.1	0.6 − 7.1	0.25	8.4	1.7 − 41.9	**0.01**
	NM +	NM −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	25.1 ± 9.7	34 ± 15.9	0.95	0.91 − 0.98	**0.01**	0.96	0.92 − 0.99	**0.04**
Sex (men) (%)	12 (48)	48 (35)	1.7	0.7 − 4	0.22	1.4	0.6 − 3.5	0.45
Epilepsy (%)	22 (88)	78 (56.9)	5.5	1.6 − 19.4	**0.007**	4.5	1.3 − 16.2	**0.02**
Benzodiazepines (%)	3 (12)	23 (16.8)	0.7	0.2 − 2.4	0.55			
Antidepressants (%)	1 (4)	14 (10.2)	0.4	0.04 − 2.9	0.34			
	EFM +	EFM −	Univariate analysis			Multivariate analysis		
			OR	95 % CI	p	OR	95 % CI	p
Age (mean ± SD)	56.1 ± 14	31.4 ± 13.9	1.08	1.04 − 1.13	< **0.001**	1.1	1.04 − 1.15	< **0.001**
Sex (men) (%)	6 (75)	54 (35.1)	5.5	1.2 − 28.5	**0.04**	10.8	1.6 − 73.3	**0.01**
Epilepsy (%)	4 (50)	96 (62.3)	0.6	0.1 − 2.5	0.48			
Benzodiazepines (%)	1 (12.5)	25 (16.2)	0.7	0.1 − 6.2	0.78			
Antidepressants (%)	0	15 (9.7)						

CI, confidence intervals; OR, odds ratio; SD, sleep disorders; DoA, disorders of arousal; PLM, periodic limb movements; ALMA, alternating leg muscle activation; NM, neck myoclonus; EFM, excessive fragmentary myoclonus.

presence of a DoA was associated with a younger age (OR = 0.9; 95 %CI = 0.8 − 0.9; p = 0.01) as well as bruxism (OR = 0.9; 95 %CI = 0.9 − 0.99; p = 0.03). PLM was significantly associated with a higher age (OR = 1.1; 95 %CI = 1–1.2; p = 0.01) as well as EFM (OR = 1.1; 95 %CI = 1.0–1.2; p = 0.02); moreover, PLM was associated with the use of antidepressants (OR = 13.1; 95 %CI = 1–178.4; p = 0.05). ALMA was associated with male sex (OR = 3.5; 95 %CI = 1–11.8; p = 0.04) and sleep-related hypermotor epilepsy (SHE) (OR = 7.9; 95 %CI = 1.8–34.6; p = 0.01). In fact, ALMA was present in 50 % of SHE patients (Tables B.1-B.5). The

presence of EEG abnormalities during sleep was not associated with having a sleep disorder (OR = 0.4; 95 %CI = 0.5–3.7; p = 0.44).

3.4. Effect of ASMs on sleep disorders

In the subgroup of patients taking ASMs (65 %) (mean age 32.2 ± 14.3 years, 26 men), we evaluated the association between ASMs and sleep disorders, after adjusting for age and sex.

Levetiracetam was found to be negatively associated with the presence of sleep disorders (OR = 0.09; 95 %CI = 0.01 − 0.48; p = 0.004), especially PLM (OR = 0.04; 95 %CI = 0.002 − 0.5; p = 0.01) while topiramate use was positively associated with it (OR = 5.2; 95 %CI = 1–26.5; p = 0.05).

4. Discussion

Acknowledging the strict relationship between epilepsy and sleep is relevant in order to ensure an optimal seizures control, also through the management of potentially treatable comorbidities such as sleep disorders.

The main finding of our study was the significant higher frequency of sleep disorders among patients with epilepsy as compared to normal controls. This finding is not surprising since many previous studies showed that epilepsy is associated with an increase in subjective sleep-related complaints, such as excessive daytime sleepiness, insomnia and poor sleep quality as well as objective evidence of altered sleep architecture [26]. However, the evidences are scarce as regard to those nosological entities, classified as normal variants, for which the physiological nature and clinical significance are still debated, thus placed in a borderline area between normal and abnormal sleep [18].

In our study, not all the considered sleep disorders have been found to be more frequent in patients with epilepsy and each of them seems to disclose peculiar features.

Regarding NREM parasomnias, it is well known that they are common in childhood, being present in up to 80 % of preschool-age children [27], with a significant association with epilepsy [14]. In adults, the lifetime prevalence of various parasomnia ranges from 4 % to 67 % [28]. It seems that the presence of DoA in patients with epilepsy may reflect the destabilizing effect of epileptiform activity on sleep stability leading to a greater tendency to arousals and arousal disorders [5]. The previous studies found an increased prevalence of DoA, especially in patients with mesial temporal lobe epilepsy or SHE [6,12,16,29]. In particular, NREM arousal disorders were reported to be more frequent in SHE, being present in the personal history of about 34 % of SHE patients, in accordance with the theory that the two phenomena share a common pathophysiological substrate [30–32]. In our sample we only found a positive association between DoA and younger age as described in the general population [28]. However, being a retrospective study, we were not able to reconstruct the anamnestic data of DoA in childhood and we could only rely on PSG findings which are rarely able to record the more complex behaviors of DoA, especially in adults [33]. Regarding sleep-related movement disorders, except for PLM which has been extensively studied, the other disorders have been poorly investigated in relation with epilepsy [13]. PLM and RLS prevalence among epilepsy patients varies between 10 % and 33 % in different studies [34,35] with values comparable with our case series (20 %). In our sample we found a significant association of PLM with epilepsy. This comorbidity appears to be frequent, yet highly variable, in different cohorts of epilepsy patients [13]. Moreover, the protective effect of levetiracetam on PLM that we found in our population has been already described in other case series [36], but not confirmed by a subsequent metanalysis [37]. The positive association of topiramate use with PLM has been reported only in one case report, in a patient affected by focal epilepsy [38].

Bruxism is a quite common sleep disorder, but its link with epilepsy has not been specifically explored. In a recent questionnaire-based study about sleep disorders in patients with epilepsy, the frequency of bruxism was 23.7 % in patients and 5.4 % in controls [39]. Some other studies report a prevalence of about 8% in the general population [40]. In our study we found a significant higher prevalence in patients (20 %) than controls (4.8 %). However, it should be underlined that patients with mesial temporal lobe epilepsy have been reported to have minor motor events during sleep [41]. Among these, oroalimentary automatisms were significantly more frequent than in healthy controls [41], with a pattern that can be similar to chewing movements, thus resembling bruxism. Nonetheless, in our sample, bruxism was equally distributed in all types of epilepsy and we differentiated simple oral automatisms from the typical tooth grinding of bruxism, following the AASM scoring rules [22].

Physiological sleep variants are controversial phenomena which are frequently overlooked by physicians or misinterpreted by researchers, thus usually considered not clinically relevant entities. Some of them, such as NM, are not even included in the ICSD3, and little is known about their prevalence and significance.

ALMA was present in 17 % of our patients with epilepsy and 14.5 % of controls, with no significant differences. In a previous study a frequency of 33 % was found among healthy controls investigated with polysomnography [42] but the authors considered all high frequency leg movements, comprising not only ALMA but also hypnagogic foot tremor. However, even if the frequency is comparable in patients and controls, its significant association with the phenotype of SHE, being present in 50 % of subjects, opens to an intriguing pathophysiological hypothesis: the disinhibition of innate motor behaviors due to the activation of the so-called 'central pattern generators', can produce stereotypical rhythmic motor sequences such as ambulatory behaviours, or bipedal activity, as the one found in ALMA, both in patients and healthy subjects [43,44].

Neck myoclonus is a quite new sleep related motor phenomenon firstly described as a "short stripe-shaped movement-induced artifact" visible vertically over the polysomnographic traces [25]. It has been initially considered as a physiological phenomenon since it was found in 35 %–54.6 % of normal subjects undergoing PSG [25,35]. Following reports confirmed NM as an incidental finding in routine VPSG, but with a negative impact on sleep, possibly through sleep fragmentation [45]. The higher prevalence found in our patients compared to controls, could possibly be explained as an epiphenomenon of sleep instability with frequent arousals that can lead to the most frequent appearance of physiological sleep events. Indeed, in our patients group, the quality of sleep was significantly lower than controls, with significant less total sleep time, longer sleep latency and less REM sleep, possibly due to both the sleep alterations of epilepsy itself and the use of ASMs [46]. Nonetheless, our findings add new insights in the pathogenesis of NM and give a drive to new research on the subject.

Finally, the prevalence of EFM in our study population, both patients and controls, was lower than the prevalence found in the general population (9 %) [42] in a VPSG study where it was confirmed its age-dependent association, with the highest values in the group of subjects older than 60 years [35].

Our study certainly has some limitations. In particular, due to its the retrospective nature, we were not able to give accurate anamnestic data on previously reported sleep disorders in our patients, which is a limit in the interpretation of our results. However, we excluded patients and controls with a current sleep complaint at the time of the recording, in order to avoid a selection bias. The choice of excluding patients with sleep apnea from the entire study population, which may be a possible limit of our study, has been made to leave out the well-known influence of apneas on sleep stability and on the comorbidities with other sleep disorders, which could have biased our results [47].

Besides, being a retrospective study, we were able to include as controls only subjects referred to our center for which a neurological disease has been reasonably excluded, after a complete diagnostic assessment. This could have been a source a bias in our study, but the

comparison with previous studies on sleep of healthy subjects [40,42] seems to support the reliability of our data. On the other hand, the retrospective nature of the study also limited the homogeneity between the two groups since the video recording was available for all patients and only the majority of controls. At any rate, the lack of video for a minority of subjects could not be considered as a major issue since for the sleep disorders studied, except from RBD, the polygraphic recording is sufficient to make a correct diagnosis [18,22].

Moreover, even if large, our sample could not have been sufficient to evaluate the possible associations between the single sleep disorders and the different epilepsy etiologies, such as hippocampal sclerosis or focal cortical dysplasia.

Nevertheless, this is one of the largest study so far evaluating physiological sleep variants together with other sleep disorders in patients with focal epilepsy and controls by means of PSG recordings.

5. Conclusions

In our study we explored the presence of sleep disorders and physiological sleep variants in adult patients with focal epilepsy by means of PSG. The results of our study showed a high frequency of PLM, bruxism and NM in patients with focal epilepsy as compared to controls. The presence of these sleep disorders in patients with focal epilepsy could be overlooked, with a possible negative impact on the clinical management of these patients. However, further prospective studies are needed to confirm our findings and to shed light on their significance.

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Transparency document

The Transparency document associated with this article can be found in the online version.

Declaration of Competing Interest

None.

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