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Comparing sleep profiles between patients with juvenile myoclonic epilepsy and symptomatic partial epilepsy: Sleep questionnaire-based study

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ABSTRACT

Objectives: Patients with epilepsy commonly report excessive daytime sleepiness and daytime fatigue, which may be attributed to the direct effect of seizures, a side effect of antiepileptic drugs or a combination of the two. The aim of the study was to compare sleep profiles in patients with juvenile myoclonic epilepsy (JME) and symptomatic partial epilepsy (PE) in drug naïve and treated patients using standardized sleep questionnaires.

Methods: Three study groups: - 1) juvenile myoclonic epilepsy (N = 40) [drug naïve (N = 20); On sodium valproate (SVA) (N = 20)]; 2) symptomatic partial epilepsy (N = 40) [drug naïve (N = 20); On carbamazepine (CBZ) (N = 20)]; 3) healthy controls (N = 40) completed 3 standardized sleep questionnaires – Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index, and NIMHANS Comprehensive Sleep Disorders Questionnaire. Scores were compared using *t*-test and Chi-squared tests ($P \leq 0.005$).

Results: The mean PSQI scores as well as the proportion of subjects with abnormal PSQI scores were higher in patients with JME and PE compared to controls. Although the mean ESS scores were comparable between patients with epilepsy and controls, the percentage of patients with partial epilepsy having abnormal ESS scores was higher. No significant differences were present between drug naïve and treatment monotherapy groups. Excessive daytime somnolence was reported more often by patients with JME compared to patients with partial epilepsy and controls.

Conclusion: This study found that patients with epilepsy have a higher prevalence of poor sleep quality compared to controls. Moreover, a significantly higher percentage of patients with partial epilepsy had higher ESS scores compared to healthy controls. However, there was no difference between ESS and PSQI scores between drug naïve and treated patients with JME or PE.

Significance: Poor sleep quality is more prevalent in patients with epilepsy irrespective of the use of antiepileptic medications. Excessive daytime somnolence is more commonly seen in patients with partial epilepsy when compared to the general population.

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1. Introduction

Epilepsy and sleep have a complex bidirectional relationship. Epilepsy and antiepileptic drugs (AEDs) known to cause sleep disruption and exacerbate some sleep disorders. Seizures in some of the epilepsies occur exclusively during wakefulness, like absence seizures, while others occur exclusively or primarily during sleep, such as benign rolandic epilepsy and nocturnal frontal lobe epilepsy. Some seizure types are exacerbated by drowsiness and sleep/wake transition, such as infantile spasms and generalized tonic-clonic seizures (GTCS) on awakening [1]. Epileptic seizures and interictal discharges can cause sleep fragmentation and alteration in sleep architecture [2,3]. The sleep state, alternatively, provides an opportunity for clinicians to better diagnose and treat epilepsy. For many patients with epilepsy, the interictal and sometimes ictal manifestations are best observed during specific sleep states [4].

In a sleep questionnaire-based study assessing subjective sleep disturbance in a large cohort of patients with partial epilepsy [5], 38.6% of the adults with partial epilepsy had sleep complaints compared with 18% in the control group. Another study [6] surveyed 100 patients

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with epilepsy and found that 30% had sleep complaints compared to 10% of the control population, and patients with epilepsy also had a higher prevalence of sleep maintenance insomnia symptoms (52% vs 38%).

Data from the literature concerning the frequencies of sleep disturbances in patients with epilepsy are contradictory. In all studies, the frequency in patients is higher than in controls, yet the difference is significant in some, but not in all. This discrepancy may be attributed to differences in patient samples (such as patients referred to a sleep center, patients with drug-resistant seizures, unselected patients) and possibly differences in treatment, given that a number of drugs acting on the central nervous system (CNS) are positively associated with excessive daytime sleepiness (EDS). Data on predictors of sleep disturbances in patients with epilepsy are not clear. Sleep deprivation is known to worsen seizures [7–10]. Hence this aspect of treatment has to be addressed and evaluated. It is known that sleep disturbance can result in worsening memory and deteriorating seizure control [11]. In some patients, recognition and treatment of a coexisting sleep disorder can be the difference between complete seizure control and refractory epilepsy [12]. Sleep disorders can coexist with epilepsy, leading to errors in diagnosis and worsening of seizures. Besides, patients with epilepsy are treated with AEDs, some of which can have adverse (or beneficial) effects on sleep [13].

Carrying out further studies would allow us to improve understanding as to how epilepsy and AEDs affect sleep and to understand how sleep and its events affect epileptiform activity and seizures. The aim of the study was to study and compare sleep profiles using sleep questionnaires in patients with idiopathic generalized epilepsy (IGE) specifically juvenile myoclonic epilepsy (JME) and symptomatic partial epilepsy and to compare sleep profiles in drug naïve vs treated patients in this cohort.

2. Materials and methods

This cross-sectional hospital-based study was carried out in a university teaching hospital in south India from November 2012 to January 2016. The study protocol was approved by the Institute's Ethics Committee. Informed consent was obtained. Patients satisfied the ILAE criteria with JME and partial epilepsy [14]. Forty patients of JME, 40 patients with symptomatic partial epilepsy, and 40 healthy controls were recruited. Patients were divided into a) drug naïve JME (n = 20)/drug naïve partial epilepsy (n = 20) group – not on any AEDs for at least last one month and b) treated JME group (n = 20) – on sodium valproate (SVA) monotherapy for at least last one month; treated partial epilepsy group (n = 20) – on carbamazepine (CBZ) monotherapy for at least last one month. Treatment in drug naïve patients was initiated within 24 h of recruitment.

Among the 379 patients with epilepsy who were screened [mean age: 23.67 ± 8.36; M:F = 191:188] during the study period, 71 met the inclusion criteria for JME, 95 met the inclusion criteria for TLE, and 104 met the inclusion criteria for extra-temporal lobe epilepsy (Ex-TLE). The remaining patients had other epileptic subtypes. Further, among them, 44 patients with JME, 57 with TLE and 55 with Ex-TLE were included for the study after excluding the rest due to a) taking AEDs other than SVA or CBZ, b) taking other medications affecting sleep, c) presence of space occupying lesion on brain imaging causing mass effect, or d) not providing informed consent. Among them, 40 patients were selected from each group - JME (mean age: 21.53 ± 4.1 years; M: F = 20:20), TLE (mean age: 25.00 ± 8.34 years; M: F = 22:18) and Ex-TLE (23.53 ± 8.23 years; M: F = 20:20) for the final data analysis. Age- and gender-matched healthy volunteers/friends of the patients who consented were included. Those with history of seizures, any neurologic disorder/systemic disorder known to affect sleep, substance abuse/addiction, and on any medications known to affect sleep were excluded.

All study subjects underwent a structured evaluation according to a predefined study protocol, including a detailed clinical, family and treatment history, neurological examination, routine digital EEG, and neuroimaging. Age of onset of epilepsy was determined as the age at which the patient developed habitual and recurrent seizures, whereas the duration was the interval between age of onset and time of current evaluation. Estimation of the frequency of seizures was based on review of seizure calendars and specific questioning of the patient and family members.

Assessment of sleep was done in all the study subjects using standard sleep questionnaires: Epworth Sleepiness Scale (ESS) [15], Pittsburgh Sleep Quality Index (PSQI) [16], and NIMHANS Comprehensive Sleep Disorders Questionnaire (NCSDQ) [17].

The data were entered in a predesigned proforma and incorporated into R software version 3.2.2 for analysis. The sample size calculation was performed based on information obtained from a previous study by Krishnan et al. [21]. The mean differences and threshold of ESS and

Table 1
Profiles of patients with juvenile myoclonic epilepsy and symptomatic partial epilepsy.

JME	Drug naïve (n = 20)	SVA monotherapy (n = 20)	P value
Mean age at onset (years)	16.20 ± 4.0	14.05 ± 4.3	0.10
Mean disease duration (months)	60 ± 49.2	82.8 ± 56.76	0.18
Absence seizures	1 (5.0%)	2 (10.0%)	1.00
Myoclonic jerks	20 (100.0%)	20 (100.0%)	1.00
Nocturnal myoclonus	10 (50%)	5 (25%)	0.19
Worsening with sleep-wake transition	19 (95%)	19 (95%)	1.0
Worsening with sleep deprivation	17(85%)	19 (95%)	0.60
Generalized tonic clonic seizures	17 (85.0%)	18 (90.0%)	1.0
Nocturnal generalized tonic clonic seizures	9 (52.9%)	10 (55.5%)	1.0
Worsening with sleep-wake transition	14 (82.3%)	10 (55.5%)	0.33
Worsening with sleep deprivation	7 (41.1%)	14 (77.8%)	0.05
Partial epilepsy	**Drug naïve (n = 20)**	**CBZ monotherapy (n = 20)**	**P value**
Mean age at onset (years)	18.30 ± 8.8	15.68 ± 7.9	0.32
Mean disease duration (months)	86.17 ± 99.1	86.00 ± 103.7	0.99
Contralateral tonic posturing	8 (40.0%)	13 (65.0%)	0.20
Contralateral clonic jerks	7 (35.0%)	10 (50.0%)	0.52
Aura	8 (40.0%)	8 (40.0%)	1.00
Oroalimentary/extremity automatisms	5 (25.0%)	11(55.0%)	0.1
Somatosensory	3 (15.0%)	0	0.23
Psychic phenomena	4 (20.0%)	1 (5.0%)	0.34
Worse with sleep deprivation	1 (5.0%)	1 (5.0%)	1
Loss of consciousness/altered sensorium	18 (90.0%)	11 (55.0%)	0.03

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