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How do children with drug-resistant epilepsy sleep? A clinical and video-PSG study

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ABSTRACT

Aim: The aim of this study was to assess sleep architecture and sleep problems among three homogenous groups of children including children with drug-resistant focal epilepsy, children with newly diagnosed, drug-naïve focal epilepsy, and healthy children using overnight video-polysomnography (V-PSG) and a sleep questionnaire.
Methods: We compared sleep architecture among 44 children with drug-resistant focal epilepsy, 41 children with newly diagnosed, drug naïve focal epilepsy, and 36 healthy children. All children underwent an overnight V-PSG recording, and their parents completed the Children's Sleep Habits Questionnaire (CSHQ). Sleep recordings were scored according to the American Academy of Sleep Medicine criteria.
Results: Compared with children with newly diagnosed epilepsy and healthy controls, children with drug-resistant epilepsy receiving antiepileptic treatment showed disturbed sleep architecture, a significant reduction in time in bed, total sleep time, sleep efficiency, NREM3%, REM%, and a significant increase in awakenings, wake after sleep onset, and periodic leg movement. Children with drug-naïve, newly diagnosed focal epilepsy showed a statistically significant increase in sleep onset latency, rapid eye movement (REM) latency, N1%, awakenings, and a significant decrease in time in bed when compared with the controls. Children with drug-resistant epilepsy had the highest CSHQ total scores, while children with drug-naïve, newly diagnosed focal epilepsy had higher scores than healthy children.
Conclusion: This is one of the few polysomnographic studies adding to the limited research on the sleep macrostructure of children with drug-resistant epilepsy compared with children with drug-naïve, newly diagnosed focal epilepsy and healthy children by obtaining objective measurements of sleep concurrently with a validated questionnaire. Children with drug-resistant epilepsy had a greater incidence of sleep disturbance on the basis of qualitative aspects and architecture of sleep than children with newly diagnosed epilepsy, suggesting the need for referral of children with drug-resistant epilepsy for overnight sleep evaluation in order to improve the clinical management and optimize therapeutic strategies.
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1. Introduction

Although the intimate complex relationship between epilepsy and sleep had been known since antiquity, a scientific model could only be developed in the nineteenth century, and the last twenty years have seen a worldwide growing interest in the mutual interaction between sleep and epilepsy [1]. Seizures tend to occur mainly during sleep, and the epileptiform discharges can alter and/or disrupt the sleep architecture [1–4]. This suggests that similar mechanisms may be involved in seizure propagation and in the rhythmic activity of certain sleep stages [2].

In 1885, Gowers observed in institutionalized patients that 21% of epileptic seizures occur only during sleep (nocturnal), 42% only when awake (diurnal), and 37% when both awake and asleep (diffuse) [5]. Studies on the relationship between sleep and epilepsy in children are still scarce; however, this population is thought to have the greatest occurrence of these two comorbidities.

Approximately 10–20% children with epilepsy develop drug-resistant epilepsy, which is defined as at least one seizure per month, despite appropriate antiepileptic therapy with at least two antiepileptic drugs (AEDs), in maximally tolerated doses for 18 months, or adequate seizure control but with unacceptable

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drug-related side effects [6]. Drug-resistant epilepsy may have profound effects on the sleep organization of the child as well as other vital functions. Disrupted sleep architecture may negatively interfere with spike frequency and seizure control. In spite of this complex relationship, there is a paucity of data on the interaction between sleep and drug-resistant epilepsy in the pediatric population. Most of these studies are based on maternal or self-reported sleep data and sleep questionnaires [7–11]. However, little attention has been given to sleep organization throughout the night.

Polysomnography (PSG) remains the gold standard method for the assessment of sleep organization as well as diagnosis, classification, and analysis of the structure and quality of sleep, providing valuable information on the association between sleep and epilepsy in children. As PSG is expensive and time-consuming, it is not always available in day-to-day clinical practice. More recently, Pereira et al. evaluated sleep structure in drug-resistant epilepsies by PSG and addressed some of the more firmly established clinical relationships between sleep and drug-resistant epilepsy in children [11]. Therefore, further studies are warranted to fully elucidate this relationship. In pursuit of this goal, we investigated the macrostructure of sleep and sleep disorders in a considerable number of patients with drug-resistant epilepsy presenting to a tertiary sleep and video-electroencephalogram (EEG) center in Turkey and compared their data with those of children with drug-naïve, newly diagnosed epilepsy and healthy children.

2. Materials and method

For this study, children were recruited at the Sleep and Video-EEG Monitoring Unit of Gazi University Hospital, Turkey. Forty-four consecutive children with drug-resistant focal epilepsy (27 boys and 17 girls; mean age, 9.6 years; SD ± 2.4) (Group 1), 41 children with newly diagnosed, drug-naïve focal epilepsy (26 boys and 15 girls; mean age, 9.1 years; SD ± 1.6) (Group 2), and 36 healthy, nonsnoring children (19 boys and 17 girls; mean age, 10.2 years; SD ± 2.2 years) (Group 3) underwent an overnight video-PSG (V-PSG) recording after one night of adaptation in order to avoid the first-night effect in all children.

Group 1 consisted of children with drug-resistant epilepsy. The inclusion criteria were as follows: (1) age range of 2–18 years, (2) failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom; we recruited those with seizures persisting at a frequency of >1 per month for at least 6 months prior to assessment, on optimal doses of >2 AEDs with good compliance, and (3) all children were on polypharmacological treatment and were receiving at least three or more AEDs (Table 1).

Forty-one children with newly diagnosed, drug-naïve focal epilepsy were recruited at the Gazi University, Department of Pediatric Neurology. They all met the inclusion criteria: one unprovoked (or reflex) seizure with a probability of further seizures (epileptiform activity on EEG or a potential epileptogenic abnormality on brain imaging) similar to the general recurrence risk after two unprovoked seizures, occurring in a 10-year period [12] and no medication at the time of the study. Eighteen of these children had two unprovoked seizures; others had an epileptiform activity on EEG.

The control group consisted of healthy children with no history of severe organic and mental illness and, in particular, without any neurological or psychiatric disorder who were retrospectively enrolled from our sleep recording database. Children with a history suggestive of sleep-disordered breathing, paroxysmal nocturnal events, a previous diagnosis of sleep disorder, or those taking any pharmacotherapy were excluded from the control group of the study.

Patients with a comorbid neurological illness, which can affect sleep such as stroke, encephalitis/meningitis, metabolic encephalopathy; coexisting medical conditions including hypothyroidism and chronic respiratory diseases or known primary sleep disorders such as obstructive sleep apnea (OSA) or narcolepsy were excluded from the study group. None of the children had adenotonsillectomy before V-PSG.

All children were from a similar socioeconomic background. All parents were asked to sign informed consent form, and the project was approved by the local ethics committee.

A study design based on the assumption of independent distribution among three groups was planned. According to this design,

Table 1
Demographic and clinical characteristics of patients in Groups 1 and 2.

	Group with drug-resistant epilepsy (Group 1) (*n* = 44)	Group with newly diagnosed epilepsy (Group 2) (*n* = 41)	Control group (Group 3) (n = 36)	p-Value
Age (mean ± SD) (years)	9.6 ± 2.4	9.1 ± 1.6	10.2 ± 2.2	0,43
Gender (M/F)	27/17	26/15	19/17	0,72
Age at onset, duration and frequency of seizures (mean and range)				
Age of onset of seizures (years)	3.8 (0–9.8)	8.4 (3–12)		**0.02**
Duration of Seizures (years)	7.6 (1–8.5)	2.6 (0.5–5.2)		**0.03**
Frequency (per month)	41.5 (8–340)	0.50 (0.2–1)		**<0.01**
Type of seizures (number and percentage)				
Focal aware seizure	0 (0%)	19 (46%)		**<0.01**
Focal impaired awareness	19 (42%)	3 (7%)		0.07
Focal impaired awareness to bilateral tonic–clonic	30 (%67)	7 (17%)		**0.001**
Generalized	0 (%)	11 (27%)		**0.02**
AEDs				
Number of AEDs, median (range)	3 (2–5)	–	–	
Duration of AEDs, median (range) (years)	7 (1–12)	–	–	
VLP	19 (43%)	–	–	
CBZ	15 (34%)	–	–	
OxCBZ	9 (20%)	–	–	
SUL	5 (11%)	–	–	
LEV	34 (77%)	–	–	
LMT	3 (7%)	–	–	
CLB	27 (61%)	–	–	
ZNS	2 (4%)	–	–	
TPM	8 (18%)	–	–	
LCM	4 (9%)	–	–	

Abbreviations: AEDs — antiepileptic drugs; VLP — sodium valproate; CBZ — carbamazepine; OxCBZ — oxcarbamazepine; SUL — sulthiame; LEV — levetiracetam; LMT — lamotrigine; CLB — clobazam, ZNS — zonisamide; TPM — topiramate; LCM — lacosamide.
The bold values represent statistically significant p values.

we recruited patients based on the 'purposeful sampling method' with 1:1 age and sex-matched controls depending on the availability of PSG appointments for research purposes during the study period. The sample size was calculated based on the sample size table published by Cohen [13]. It was estimated that a minimum of 35 subjects in each group would be required for a study design with a type 1 error rate of 0.05, 80% power, and medium effect size (0.25). In total, 44 children with drug-resistant focal epilepsy, 41 children with drug-naïve, newly diagnosed focal epilepsy, and 36 controls meeting the study requirements were included in the study.

After signing informed consent prior to V-PSG recording, parents were interviewed for the sleep history of the children. Medical records of all children were reviewed, and a detailed history including age, sex, age at onset, duration of epilepsy, frequency and semiology of seizures, and medications (e.g. AEDs) was taken using a structured questionnaire. Children in both groups were examined before overnight V-PSG recording, and only children without an acute illness underwent the recording. Before overnight V-PSG, children with drug-resistant epilepsy were allowed to take their prescribed medication.

The Children's Sleep Habits Questionnaire (CSHQ) was used to examine children's sleep problems, as reported by the parent or caregiver. The CSHQ is a 45-item parent questionnaire that has been used in a number of studies to examine sleep behavior in young children [14]. The CSHQ includes items relating to a number of key sleep domains that encompass the major presenting clinical sleep complaints in this age group: bedtime behavior and sleep onset; sleep duration; anxiety around sleep; behavior occurring during sleep and night wakings; sleep-disordered breathing; parasomnias; and morning waking/daytime sleepiness. Parents are asked to recall sleep behaviors occurring over a "typical" recent week. Items are rated on a three-point scale: "usually" if the sleep behavior occurred five to seven times/week; "sometimes" for two to four times/week; and "rarely" for zero to one time/week. Some items were reversed in order to consistently make a higher score indicative of more disturbed sleep [14]. A total CSHQ score of 41 has been reported to be a sensitive cutoff for clinically significant sleep problems [14]. The validity and reliability of the Turkish version of the scale were demonstrated by Perdahlı et al. [15]. In the present study, CSHQ scores of 56 and above were labeled as "moderate to severe sleep problems" in line with the approach used in the aforementioned study [15].

Sleep macrostructure was assessed by overnight V-PSG. The V-PSG was performed in a dedicated sleep lab with a maintained comfortable temperature, and a hypnogram was obtained for each case. The V-PSG recording was carried out using a digital system that consisted of at least 19 EEG channels (Fp1, Fp2, F7, F8, F3, F4, C3, C4, T3, T4, T5, T6, P3, P4, O1, O2, Fz, Cz, and Pz) referenced to the contralateral mastoid, electrooculography, electromyography, electrocardiography, nasal airflow, measures of thorax and abdominal effort, peripheral oxygen saturation, and pulse and position sensors. None of the patients had seizures during the night of the recording. Sleep was subdivided into 30-second epochs, and sleep stages were visually scored according to the standard American Academy of Sleep Medicine (AASM) criteria [16]. All recordings were visually scored, and the sleep parameters derived were tabulated for statistical analysis.

The following conventional sleep parameters were evaluated:

1. Time in bed (TIB);
2. Sleep period time (SPT): the time from sleep onset to sleep end;
3. Total sleep time (TST): the time from sleep onset to the end of the final sleep epoch minus time awake;
4. Sleep onset latency (SOL): time from lights out to sleep onset, defined as the first of two consecutive epochs of sleep stage 1 or one epoch of any other stage, in minutes;
5. Rapid eye movement (REM) latency (RL): the time from sleep onset to the first REM sleep epoch; in minutes;
6. Number of awakenings/h (AWN/h);
7. Sleep efficiency (SE%): the percentage ratio between total sleep time and time in bed (TST / TIB $*$ 100);
8. Percentage of SPT spent in wakefulness after sleep onset (WASO%), i.e., the time spent awake between sleep onset and end of sleep;
9. Percentage of SPT spent in sleep stages 1 (N1%), 2 (N2%), slow-wave sleep (N3%), and REM sleep (REM%);
10. Apnea/hypopnea index (AHI);
11. Leg movements (LMs); and
12. Periodic limb movement index (PLMI).

All recordings were started at the subject's usual bedtime and continued until spontaneous morning awakening.

2.1. Statistical analysis

All statistical analyses were performed using the SPSS, version 21. Descriptive statistics were presented as mean and standard deviation or frequencies and percentages for continuous and categorical data, respectively. p values less than 0.05 were considered statistically significant. Comparisons between the control group and subgroups of patients with epilepsy (drug-resistant and newly diagnosed) were performed using the nonparametric Kruskal–Wallis analysis of variance (ANOVA) for unpaired datasets. A Tukey post hoc test was applied for multiple comparisons. The Mann–Whitney test was used for comparisons between the group with newly diagnosed epilepsy and the group with drug-resistant epilepsy. One-way analysis of variance was used to test the differences between the groups for CSHQ scores.

3. Results

During the study period, a total of 85 patients were recruited and completed the study. Of these, 44 had drug-resistant focal epilepsy and 41 had drug-naïve, newly diagnosed focal epilepsy. Thirty-six healthy children served as the control group. The groups did not differ significantly in age and gender distribution. The age at onset of seizures, duration and frequency of seizures, and number and duration of AEDs were significantly greater in Group 1. The most common seizure type was focal impaired awareness to bilateral tonic–clonic seizure (67%) in Group 1 and focal onset motor seizures with awareness (39%) in Group 2. All patients in Group 1 were receiving benzodiazepines in combination with other AEDs. The demographic and clinical characteristics of the children in Groups 1 and 2 are shown in Table 1.

Table 2 shows the comparison of CSHQ scores among children with drug-resistant epilepsy, drug-naïve, newly diagnosed focal epilepsy, and the control group. Except for parasomnias, all CSHQ scores were significantly different between groups. Total CSHQ score ($p < 0.001$) and subscores for bedtime resistance ($p = 0.003$), sleep onset delay ($p \leq 0.001$), sleep anxiety ($p < 0.001$), and night wakings ($p = 0.006$) were higher in Group 1 when compared with Groups 2 and 3. When Group 1 and Group 2 were compared, the total CSHQ score ($p = 0.030$) and subscores for bed time resistance ($p < 0.001$), sleep onset delay ($p < 0.001$), sleep anxiety ($p < 0.001$), and night wakings ($p = 0.0020$) subscores of CSHQ were higher in Group 1. When Group 2 and Group 3 were compared, the total CSHQ score ($p = 0.001$) and sleep onset delay ($p < 0.001$) subscores were higher in Group 2. The frequency of clinically significant sleep problems (CSHQ >41) was high in Groups 1 and 2 versus Group 3 (100% ($n = 44$) in Group 1, 60% ($n = 25$) in Group 2, and 22.2% ($n = 8$) in Group 3). The frequency of moderate-to-severe sleep problems (CSHQ >56) was 72% ($n = 32$) in Group 1 and 35% ($n = 21$) in Group 2 ($p = 0.003$).

Table 2
CSHQ scores among the study groups.

CSHQ	Group 1 (N = 44) Mean (SD)	Group 2 (N = 41) Mean (SD)	Group 3 (N = 36) Mean (SD)	p
Total score	61.23 (6.54)	56.34 (9.18)*	41.45 (6.43)†	<0.001
Bedtime resistance	14.26 (3.45)	9.54 (3.24)*	6.34 (1.26)	0.003
Sleep onset delay	9.34 (3.52)	5.24 (2.13)*	2.36 (1.49)†	<0.001
Sleep anxiety	8.36 (3.46)	4.38(2.42)*	2.34 (1.16)†	<0.001
Night wakings	7.23 (2.14)	3.85 (1.74)*	2.39 (1.39)	<0.001
Daytime sleepiness	19.48(4.37)	13.67(3.39)*	8.94 (2.56)	<0.001
Parasomnias	8.63 (2234)	8.36 (2.84)	7.13 (2.41)	NS
Sleep-disordered breathing	5.23 (1.49)	3.49 (1.23)*	2.57 (1.35)	0.003

p values according to one-way ANOVA; NS: nonsignificant (p > 0.05).
* p < 0.05 versus Group 1.
† p < 0.05 versus Group 2.

Table 3
Comparison of polysomnographic data among patients with drug-resistant epilepsy, newly diagnosed focal epilepsy, and control subjects.

	Group 1 Drug-resistant epilepsy (n:44) Mean ± SD	Group 2 Newly diagnosed epilepsy (n:41) Mean ± SD	Group 3 Control (n:36) Mean ± SD	p value	Post hoc Tukey		
					Group 1 vs Group 3	Group 2 vs Group 3	Group 1 vs Group 2
TIB (min)	435.57 ± 84.52	498.74 ± 83.78	548.5 ± 61.24	<0,001	<0,001	0,003	0,004
SPT (min)	445.87 ± 48ç21	501.78 ± 28	532.19 ± 60.34	<0,001	<0,001	NS	NS
TST (min)	350.6 ± 23 ± 14	498.2 ± 34.15	524.5 ± 52.24	<0,001	<0,001	NS	<0,001
SOL (min)	16.5 ± 13.50	22.4 ± 31.45	15.25 ± 12.35	NS	NS	0,04	0,033
RL (min)	224.6 ± 126.30	152,5 ± 86.9	121.6 ± 42.05	<0,001	0,002	0.02	<0,001
AWN/h	1,30 ± 0,62	0,85 ± 0,36	0,5 ± 0,24	<0,001	<0,001	0,04	0,002
WASO (%)	22.3 ± 18.9	12.3 ± 6,42	2,1 ± 1,9	<0,001	<0,001	0,033	NS
SE (%)	68.6 ± 24.8	89.5 ± 19.48	92.8 ± 6,24	<0,001	<0,001	NS	<0,001
N1 (%)	19.8 ± 17.8	7.3 ± 4.91	3,2 ± 2,3	<0,001	0,003	0,04	0,042
N2 (%)	54.6 ± 34.8	58.2 ± 32.5	62.8 ± 24.5	NS	NS	NS	NS
N3 (%)	7.2 ± 5.85	20.5 ± 8.72	22.35 ± 4.26	<0,001	<0,001	NS	<0,001
REM (%)	5.8 ± 4,5	19.2 ± 11.56	22.8 ± 6.35	<0,001	<0,001	NS	<0,001
AHI	1.1 ± 1,84	0.88 ± 0,46	0,45 ± 0,21	NS	NS	NS	NS
AHI ≥ 5 (number, %)	6 (14)	2(5)	0	NS	NS	NS	NS
LMs	6.4 ± 5,6	2.1 ± 1,5	1,8 ± 1,2	<0,001	0,003	NS	0,002
PMLI	3,42 ± 2,52	0,8 ± 0,4	0,6 ± 0,2	<0,001	0,0012	NS	0,003

3.1. V-PSG findings

Compared with the control group, patients with drug-resistant focal epilepsy showed a significant reduction of TIB, TST, SPT, sleep efficiency, NREM3%, REM%, and a significant increase in AWN/h, WASO, LM, and PLMI (Table 3). When compared with children with newly diagnosed epilepsy, children with drug-resistant epilepsy had a significant reduction in TIB, SE, and REM (%) and a significant increase in AWN/h, LMs, and PLMI (Table 3). Patients with drug-resistant epilepsy showed significantly higher numbers of LMs and a high PLMI when compared with patients with newly diagnosed epilepsy and control subjects. Respiratory events were observed more frequently in Group 1, although not reaching statistical significance. Compared with the control group, children with drug-naïve, newly diagnosed epilepsy showed a statistically significant increase in SOL, RL, AWN/h WASO (%), and N1% and a significant decrease in TIB (min). A trend for reduction in SPT, SE, N2, N3, and REM sleep and a trend for increase in AHI, LM, and PLMI were observed, but the differences were statistically nonsignificant (Table 3).

4. Discussion

In this study, we aimed to examine the macrostructure of sleep and sleep quality in children with drug-resistant epilepsy in comparison with children with newly-diagnosed epilepsy and healthy children. The sleep architecture was markedly disturbed in children with drug-resistant focal epilepsy. Our main findings were as follows: When compared with children with drug-naïve, newly diagnosed focal epilepsy and healthy children, 1) sleep efficiency was poorer; 2) there was a considerable decrease in TST, SPT, sleep efficiency, NREM3%, and REM%; 3) there were more frequent awakenings after sleep onset, leg movements, and periodic leg movements; 4) total CHSQ score and certain subscores were significantly higher; and 5) clinically significant sleep problems were more prominent in children with drug-resistant epilepsy group. Many studies are available that provide a subjective analysis of sleep patterns by questionnaires in pediatric patients with different types of epilepsy [17–22]. Published studies on the sleep organization of children with drug-resistant epilepsy in comparison with controls involved small sample sizes. Studying on a larger sample of children with epilepsy, we evaluated the quality of sleep using objective polysomnographic features including sleep efficiency and sleep architecture and analyzed sleep habits in a more subjective manner using a standardized questionnaire.

Our study is one of the few studies to compare PSG and clinical sleep characteristics between drug-resistant epilepsy and newly diagnosed, drug naïve focal epilepsy in the largest number of patients available thus far. Assessment of sleep patterns among pediatric patients with different types of epilepsy is important but challenging. There are multiple factors that can contribute to sleep abnormalities. Sleep can be influenced by neurobiological correlates of epilepsy, the type of epilepsy, brain lesion, AEDs, or the cognitive status of the child [18].

Drug-resistant epilepsy is related to sleep abnormalities more often than controlled epilepsy. Zanzmera et al. reported markedly disturbed sleep architecture, poor sleep efficiency, more frequent arousals, and awakenings in patients with refractory epilepsy [23]. Kaleyias et al. observed decreased sleep efficiency, a higher arousal index, and an increased percentage of REM sleep in chil-

dren with poor seizure control in comparison with children who were seizure-free or exhibited good seizure control [10]. Their findings seem to be in line with those of previous studies reporting that children with symptomatic partial epilepsy show permanent modifications in sleep architecture, including an increased number of stage shifts, reduced number of REM periods, and percentage of sleep stage 2 and REM sleep. In a recent study, Pereira et al. underscored the important role of structural cerebral abnormalities in disrupting sleep architecture in children with drug-resistant epilepsies [11]. In the present study, we observed a greater reduction in TST, sleep efficiency, REM%, and NREM3% and a marked increase in N1%, AWN/h, WASO, RL, LMs, and PLMI in children with drug-resistant focal epilepsy. As opposed to previous studies, we found reduced N3/SWS (slow wave sleep), which has been previously mentioned in only one study in children [9]. Perreira et al. attributed the reduction of NREM3 to the antiepileptic therapy or the cognitive status of the child [9]. Marzec et al. reported a mild reduction in SWS, probably associated with the first night effect [24]. Reduced SWS, as found in our study, might be related to the use of antiepileptic therapy since all patients were receiving benzodiazepines.

We also evaluated sleep problems in children with epilepsy using the validated CSHQ. Children with epilepsy in our study had poor sleep, with up to 60% of children with epilepsy having clinically significant sleep disturbance scores in comparison with the 22.2% of the control group. Our findings are consistent with those of prior studies suggesting that children with epilepsy are more likely to have problematic sleep than the general pediatric populations [25,26]. Chan B et al. have shown more irregular bedtimes and rise times in children with epilepsy compared with healthy children [26]. Given that there is a high prevalence of sleep disturbances in children with epilepsy, this clearly merits further clinical research in different groups of epileptic syndromes aiming to investigate sleep at various timepoints in epilepsy and the longitudinal effects of sleep disturbance.

Except for parasomnias, all of the CSHQ subscores were significantly different between groups. In line with our findings, two previous studies reported more sleep problems in children with refractory epilepsy based on parent-rated questionnaires [27,28]. Batista et al. noted that increased epilepsy severity and AED polytherapy were linked with sleep problems [27]. In contrast with Batista's findings, Maganti et al. did not find an association between daytime sleepiness and epilepsy syndrome, AEDs used, and seizure severity [28].

Sleep architecture was also disturbed in children with newly diagnosed, drug-naïve focal epilepsy in our study. This is mainly because epilepsy and/or seizures themselves aggravate sleep disruption and significantly affect both the quality, quantity, and the architecture of sleep. Our results regarding sleep in drug-naïve, newly diagnosed epilepsy are consistent with those of the studies showing that focal epilepsy may cause permanent modifications in sleep architecture [17–22].

The strengths of this study include enrollment of patients with epilepsy at the time of the diagnosis before AED treatment is initiated and inclusion of healthy children as the control group to compare PSG and questionnaire data. However, a number of limitations of the study should be noted: (1) all patients with drug-resistant epilepsy were treated with AEDs including benzodiazepine, and we cannot rule out the influence of AEDs on sleep in these patients; (2) we did not include the interictal EEG abnormalities that could be in part responsible for the changes in sleep microstructure; and (3) we included epilepsies with different etiologies, and the underlying brain lesions may also have influenced sleep structure.

5. Conclusion

In conclusion, this study adds to the limited research on sleep architecture and sleep disturbance in children with drug-resistant epilepsy in comparison with children with newly diagnosed, drug-naïve epilepsy and healthy controls by obtaining objective measurements of sleep using V-PSG concurrently with the validated CSHQ. Our findings demonstrate the need to gain further understanding of the relationship between epilepsy and disruption of sleep architecture in order to break the vicious cycle and control the seizures more effectively.

Declaration of competing interest

All authors declare that they have no conflict of interest.

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