#### ORIGINAL RESEARCH

# The Association Between Sleep Problems and Attentional Network Functions in Patients with Self-Limited Epilepsy with Centrotemporal Spikes

Nan Jiang<sup>[],2</sup>, Chun Mei Yang<sup>1,2</sup>, Jia Le Wang<sup>1,2</sup>, Xiao Fei Ye<sup>1</sup>, Bin Yang<sup>1,2</sup>

<sup>1</sup>Children's Medical Centre of Anhui Medical University, Hefei, Anhui, People's Republic of China; <sup>2</sup>The Fifth Clinical College Affiliated to Anhui Medical University, Hefei, Anhui, People's Republic of China

Correspondence: Bin Yang, Children's Medical Centre of Anhui Medical University, The Fifth Clinical College Affiliated to Anhui Medical University, Hefei, People's Republic of China, Tel +86-13866127496, Email yangbin691202@163.com

**Purpose:** To investigate sleep problems in children with self-limited epilepsy with central temporal spiking (SeLECTS) and to assess the relationship between sleep problems and attention network dysfunction.

**Patients and methods:** 107 children 6–14 years of age with SeLECTS and 90 age- and sex-matched healthy controls were recruited for this study. The sleep status of these participants was evaluated using the Children's Sleep Habits Questionnaire (CSHQ), while attentional network function was assessed with the attention network function test (ANT).

**Results:** Together, these analyses revealed that children with SeLECTS exhibited higher total CSHQ scores and sleep disorder incidence relative to healthy controls (P< 0.001). Children with SeLECTS had higher scores in delayed sleep onset, sleep duration, night awakenings, parasomnias, daytime sleepiness and sleep anxiety (P<0.01). Total CSHQ scores were negatively correlated with average ANT correct rates ( $\rho$ = -0.253, P<0.01), while they were positively correlated with total reaction time ( $\rho$ =0.367, P<0.01) and negatively correlated with the efficiency of the alerting and executive control networks ( $\rho$ =-0.344 P<0.01;  $\rho$ =-0.418 P<0.01).

**Conclusion:** Children with SeLECTS face a higher risk of experiencing sleep disorders relative to age-matched healthy children, while also demonstrating that the magnitude of the impairment of attentional network function in these children is positively correlated with sleep disorder severity. Thus, the prognosis and quality of life of children with SeLECTS can be improved by interventions addressing sleep disorders.

Keywords: SeLECTS, attention network function, sleep disorders, CSHQ

#### Introduction

Self-limited epilepsy with centrotemporal spikes (SeLECTS) is the most frequently diagnosed form of self-limited epilepsy syndrome, and accounts for 6–7% of all childhood epilepsy. The disorder often manifests in children of early school age, with a peak age of SeLECTS onset of 7 years. The seizures experienced by the patients are closely associated with sleep.<sup>1</sup> Children with epilepsy tend to exhibit sleep problems at higher rates than age-matched healthy children owing to the close association between sleep and epilepsy.<sup>2</sup> This close pathophysiological link between sleep and epilepsy has been shown to be bidirectional, with sleep-related issues including nocturnal awakenings, shortened sleep duration, and excessive daytime sleepiness being particularly common in children suffering from epilepsy. The magnitude of the effects of sleep on seizures is highly variable, and there is strong evidence that sleep deprivation can impact seizure onset.<sup>3</sup>

Studies have also demonstrated that children with epilepsy often present with varying degrees of neuropsychological impairment and with certain cognitive deficits.<sup>4</sup> In children suffering from temporal lobe epilepsy, for example, attentional network impairment is often observed. Many potential mechanisms may underlie the relationship between epilepsy and such cognitive impairment in children, and efforts focused on exploring these mechanisms thus have the potential to improve cognitive outcomes in affected children.<sup>1,5</sup>

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Pediatric studies conducted to date have focused on the nature and frequency of sleep issues in children diagnosed with epilepsy, most often relying on retrospective reports to evaluate the history of this disease. However, relatively little is known regarding the association between sleep issues and seizures or the impact of these factors on the function of the attention network in children with SeLECTS. As such, the present study utilized questionnaires to explore sleep issues in children with SeLECTS and to better probe the relationship between sleep issues and various aspects of attentional network functionality.

# Methods

## **Subjects**

This was a prospective, cross-sectional, hospital-based case-control study enrolling 107children who met the 2022 International League Against Epilepsy Syndrome SeLECTS diagnostic criteria in the Department of Neurology of Anhui Provincial Children's Hospital between December 2021 and April 2024. Of the enrolled children, 55 were untreated first-episode patients, while 30 and 22 were respectively undergoing oxcarbazepine(10mg/kg/d, bid) and levetiracetam(20mg/kg/d, bid) monotherapy. Children on medication were treated for 6 months. The hospital ethics committee approved this study, and all patients met with the following inclusion criteria:

- 1. Patients meeting the proposed 2022 ILAE criteria for SeLECTS diagnosis.
- 2. Children 6–14 years of age who were not medication-selected at initial diagnosis or who were currently undergoing oxcarbazepine or levetiracetam monotherapy.
- 3. Patients without any diseases known to impact sleep, any degree of substance abuse, or any medication use with the potential to impact sleep (other than antiepileptic medications).
- 4. Patients with normal auditory and visual function who were able to fully understand and perform the indicated experimental tasks.
- 5. Patients with normal brain imaging results.
- 6. Patients for whom informed consent was obtained from family members and guardians.

In addition, 90 age- and sex-matched healthy control subjects of similar socioeconomic and educational status were recruited from a primary school. All controls are subjected to the same tests, including the CSHQ and the Wechsler IQ test. These controls were eligible if they exhibited a Wechsler intelligence Test score >70, no family history of convulsions or epilepsy, and no history of drug use with the potential to impact sleep.

## **Baseline Analyses**

A structured evaluation was used to obtain data for each patient including age, sex, age at first seizure, seizure type, seizure frequency, disease course, family history of related neuropsychiatric disorders, antiepileptic drug use (type and dose), and disease control status. In addition, other data were collected including electroencephalogram (EEG) discharges, SWI, magnetic resonance imaging (MRI), and intelligence test results. Those participants exhibiting an IQ < 70 on the Wechsler Intelligence Scale for Children, fourth edition (WISC-IV) were not included in subsequent testing. Routine blood testing and electrocardiogram analyses were also performed, excluding patients with pronounced electrocardiogram abnormalities.

## Sleep Assessment

Sleep was assessed with the Children's Sleep Habits Questionnaire (CSHQ), which was completed by participants through discussion with the patient's guardian or caregiver. This questionnaire was developed to yield psychometric data based on the comprehensive assessment of the parent-reported sleep behaviors of school-aged children, with a focus on important behavioral and medical sleep disorders relevant to this age group.<sup>6</sup> This tool has previously been demonstrated to exhibit good validity and reliability,<sup>7</sup> and entails the assessment of sleep using eight subscales: bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night awakenings, parasomnia, sleep-disordered breathing, and daytime sleepiness. Total scores indicate overall sleep quality, with scores > 41 being indicative of the presence of sleep disorders.<sup>6</sup>

## Attention Network Test (ANT)

The ANT was developed by Fan et al<sup>8</sup> and was herein employed to assess overall attentional network function in SeLECTS patients with specific analyses of the functionality of the alerting, orientation, and executive control networks. The efficiency of the alerting network was computed based on the difference in reaction time between the cue and noncue conditions, while the efficiency of the orientation network was computed based on the difference in reaction time between the invalid and effective spatial cue conditions, and executive control network efficiency was calculated based on the difference in reaction times between directionally consistent and inconsistent conditions.

## Statistical Analysis

Data were analyzed with SPSS 26.0. Shapiro–Wilk tests and Q-Q plots were used for assessing the normality of data distribution, and Levene's test was used to test the homogeneity of variance of the samples. Continuous data are presented as mean  $\pm$  standard deviation (SD) or median and interquartile ranges (Q25, Q75). Independent-samples t-tests were used for assessing differences between groups when the data were normally distributed, and Mann–Whitney *U*-tests were used for comparisons of non-normally distributed data. Categorical data were presented as numbers (%) and compared with  $\chi^2$  tests. Spearman correlation analyses and logistic regression analyses were employed for correlation analysis. P < 0.05 served as the threshold to define significance.

# Results

## Sample Characteristics

The cases consisted of 107 participants, 59 (55.14%) males and 48 (44.86%) females, with a mean age of (8.99±1.84) years. There were 90 healthy controls, 50 (55.56%) males and 40 (44.44%) females with a mean age of (8.87±2.05) years. There were no significant differences in age or sex between these two groups. The average age of onset in SeLECTS patients was 7.36±1.56 years old (range: 5–12 years), while the average disease course was 20.22±19.99 (range: 1–90) months. Generalized and partial seizures respectively affected 61 (57.01%) and 46 (42.99%) SeLECTs patients, and 41, 42, and 24 patients respectively experienced seizures < 1, 1–3, and  $\geq 4$  times in a 6-month period. In addition, 19 patients (17.76%) experienced seizures during wakefulness (within 30 minutes before falling asleep/within 30 minutes after awakening in the morning), while 88 (82.24%) experienced seizures during sleep. Of the enrolled children, 55 were not undergoing antiepileptic drug treatment (51.40%), while of the remaining 52 children (48.60%), 30 (57.69%) were treated with oxcarbazepine alone and 22 cases (42.31%) were treated with levetiracetam alone.

## Sleep Problems in Children with SeLECTS

### Comparisons of Sleep Duration and CSHQ Between Children with and without SeLECTS

(Table 1) Children in the SeLECTS group exhibited significantly higher (p < 0.01) scores on delayed sleep onset, sleep duration, night awakenings, parasomnias, daytime sleepiness, and sleep anxiety, total CSHQ score, and frequency of sleep disturbances compared to children in the healthy control group. There was no significant difference between the two groups in terms of total sleep duration, Sleep disordered breathing and bedtime resistance (P > 0.05).

### Identification of Factors Influencing Sleep Disorders in Children with SeLECTS

(Table 2) The sleep quality of children with SeLECTS differed significantly in terms of age of onset onset (years) (P<0.001), duration (months) (P=0.022), seizure type (P=0.003), seizure frequency (P=0.006), and seizure phase (P=0.001). The mean age of SeLECTS onset was  $7.36\pm1.56$  years, while the age of onset of of no sleep disorder was  $8.28\pm1.45$  years and the age of onset of sleep disorders was  $6.74\pm1.32$  years. The mean duration of SeLECTS was  $20.22\pm19.99$  months, and the mean seizure duration was  $2.75\pm3.34$  minutes.

In the SeLECTS study, children without sleep disorders demonstrated the following results: Twenty-four cases (55.81%), 14 cases (32.56%), and 5 cases (11.63%) experienced <1, 1–3, and  $\geq$ 4 episodes within 6 months, respectively. Of these, 17 cases (39.53%) had generalized seizures and 26 cases (60.47%) had focal seizures. Twenty patients (46.51%) did not receive antiepileptic drugs, 15 patients (34.88%) received oxcarbazepine alone, and 8 patients (18.60%) received levetiracetam alone. The mean duration was 14.37±13.84 months, and the mean seizure duration

Parameter	SeLECTS Group	Healthy Control Group	<b>Ζ</b> /χ²	Р
Daily sleep duration, h	9.08±0.90	9.25±1.36	-0.546 <sup>a</sup>	0.585
Bedtime Resistance	7.37±2.85	6.57±2.57	1.941 <sup>a</sup>	0.052
Sleep Onset Delay	1.49±0.98	0.71±0.71	5.701 <sup>a</sup>	<0.001
Sleep Duration	3.50±1.41	2.80±0.93	3.511ª	<0.001
Night Waking	3.93±1.57	2.99±1.16	4.164 <sup>a</sup>	<0.001
Parasomnias	9.09±2.09	6.90±1.88	6.821 <sup>a</sup>	<0.001
Sleep Disordered Breathing	2.77±2.93	2.64±1.01	0.164 <sup>a</sup>	0.869
Daytime Sleepiness	11.79±2.25	9.19±2.25	6.958 <sup>a</sup>	<0.001
Sleep Anxiety	4.51±1.16	3.39±1.41	5.735 <sup>a</sup>	<0.001
Total CSHQ score	44.45±6.65	35.19 ±7.83	7.639 <sup>a</sup>	<0.001
Sleep disorders	64 (59.81)	20(22.22)	28.242 <sup>b</sup>	<0.001

**Notes:** P < 0.05 is marked in bold and is the critical value defining significance. <sup>a</sup>Mann–Whitney U-test was used for statistical analysis. <sup>b</sup>Chi square test was used for statistical analysis.

Characteristics	Valuea					
	Total Samples (n = 107)	CSHQ ≤ 41 (n = 43)	CSHQ>41 (n = 64)	Ρ		
Age at seizure onset, years (mean, SD)	7.36 (1.56)	8.28 (1.45)	6.66 (1.32)	<0.001		
Duration of epilepsy, month (mean, SD)	20.22 (19.99)	14.37 (13.84)	24.16 (22.49)	0.022		
Seizure type(n, %)				0.003		
Generalized seizures	61 (57.01)	17 (39.53)	44 (68.75)			
Partial seizures	46 (42.99)	26 (60.47)	20 (31.25)			
Seizure frequency(n, %)	41 (38.32)	24 (55.81)	17 (26.56)	0.006		
<1 time in a 6-month period						
I~3 times in a 6-month period	42 (39.25)	14 (32.56)	28 (43.75)			
≥4 times in a 6-month period	24 (22.43)	5 (11.63)	19 (29.69)			
Seizure phase(n, %)				0.001		
During sleep	88 (82.24)	29 (67.44)	59 (92.19)			
During wakefulness	19 (17.76)	14 (32.56)	5 (7.81)			
Current AED(n, %)				0.434		
Non-antiepileptic Drug group	55 (51.40)	20 (46.51)	35 (54.69)			
Oxcarbazepine	30 (28.04)	15 (34.88)	15 (23.44)			
Levetiracetam	22 (20.56)	8 (18.60)	14 (21.88)			
Seizure duration (min)	2.75 (3.34)	3.36 (4.60)	2.34 (2.06)	0.157		
Family history(n)						
Febrile convulsion	4	2	2			
Siblings have SeLECTS	3	I	2			

Table 2 Demographic Characteristics of Children with SeLECTS

**Notes:** P < 0.05 is marked in bold and is the critical value defining significance. The Mann–Whitney *U*-test were used for continuous variables. Chi-square tests for categorical data.

was  $3.36\pm4.60$  minutes. In the SeLECTS study, children with sleep disorders demonstrated the following results: 17 cases (26.56%), 28 cases (43.75%), and 19 cases (29.69%) experienced <1, 1–3, and ≥4 episodes within 6 months, respectively. Of these, 44 cases (68.75%) had generalized seizures and 20 cases (31.25%) had focal seizures. Thirty-five patients (54.69%) did not receive antiepileptic drugs, 15 patients (23.44%) received oxcarbazepine alone, and 14 patients (21.88%) received levetiracetam alone. The mean duration was 24.16±22.49 months, and the mean seizure duration was 2.34±2.06 minutes.

#### Multivariate Logistic Analyses of Factors Associated with Sleep Disorders in Children with SeLECTS

Binary logistic regression analyses were next conducted for the five factors that were significantly associated with sleep disorder incidence in children with SeLECTS (age of onset, course of the disease, seizure type, seizure frequency, seizure phase). The results of these analyses are presented in Table 3.

The results showed that the type of epilepsy, seizure phase, seizure frequency and the age of onset were significantly associated with the incidence of sleep disorders. The probability of sleep-disorder occurrence in children with SeLECTS with generalized seizures was 4.464 times higher than that in children who experienced partial seizures (OR=4.464,95% CI: 1.559-12.777) (P<0.05). Compared with children with a younger age of onset, those with an older age of onset were less likely to have sleep disorders (OR=0.472, 95% CI: 0.323-0.691)(P<0.01). Children who had seizures while awake were less likely to have a sleep disorder (OR=0.198, 95% CI: 0.048-0.816) compared to children who had seizures while sleeping (P<0.05). Children with 1–3 seizures per 6 months were 5.708 times more likely to have a sleep disorder than children with less than 1 seizure per 6 months (OR=5.708, 95% CI: 1.309-24.897) (P<0.05).

## Sleep Problems and Attentional Network Function in Children with SeLECTS Comparisons of Sleep Quality and ANT Parameters in SeLECTS Patients

Patients with SeLECTS were separated into those with and without sleep disorders. The average correct rate for the ANT was lower for patients with sleep disorders relative to those without sleep disorders (t= 4.116, P< 0.05), with a corresponding increase in total average reaction time (t=4.283, P< 0.05), and reduced efficiency on the executive control network test (Z=3.273, P< 0.05). Lower alerting network efficiency was also observed in these patients (Z=2.796, P< 0.05), whereas no difference in orientation control network efficiency was noted between groups. The analysis of the ANT results between the groups of children with and without sleep disorders on unmedicated SeLECTS yielded results consistent with all SeLECTS enrolled. For further details, see Table 4.

#### Correlations Between Total CSHQ Scores and ANT Parameters in Children with SeLECTS

Spearman correlation analyses were utilized to examine the association between total CSHQ scores and individual ANT parameters in patients with SeLECTs. Total CSHQ scores were found to be negatively correlated with the average correct rate for the ANT ( $\rho$ =-0.364, P<0.05), whereas they were positively correlated with total reaction time ( $\rho$ =0.527, P<0.05), and negatively correlated with alerting network efficiency and executive control network efficiency ( $\rho$ =-0.344, P<0.05,  $\rho$ =-0.447, P<0.05). Total CSHQ scores were not significantly associated with the efficiency of the directed network (P>0.05). The same results were observed in unmedicated children with SeLECTS. Total CSHQ scores were found to be negatively correlated with the average correct rate for the ANT ( $\rho$ =-0.305, P<0.05), whereas they were positively correlated with alerting network efficiency and executive control network efficiency of the directed network (P>0.05). The same results were observed in unmedicated children with SeLECTS. Total CSHQ scores were found to be negatively correlated with the average correct rate for the ANT ( $\rho$ =-0.305, P<0.05), whereas they were positively correlated with alerting network efficiency and executive correlated with alerting network efficiency and negatively correlated with total reaction time ( $\rho$ =0.489, P<0.05), and negatively correlated with alerting network efficiency and

Factors		B value	S.E.	Wald	df	Р	OR	95% CI	
								Lower	Upper
Seizure type	Partial seizures								
	Generalized seizures	1.496	0.537	7.774	Т	0.005	4.464	1.559	12.777
Seizure phase	During sleep								
	During wakefulness	-1.621	0.723	5.025	Т	0.025	0.198	0.048	0.816
Seizure	<1 time in a 6-month period			5.677	2	0.059			
frequency	I~3 times in a 6-month period	1.742	0.751	5.373	Т	0.020	5.708	1.309	24.897
	$\geq$ 4 times in a 6-month period	0.872	0.725	1.448	Ι	0.229	2.392	0.578	9.904
Age at seizure onset		-0.750	0.194	14.922	Ι	<0.001	0.472	0.323	0.691
Duration of epileps	Ŷ	-0.191	0.133	2.058	Ι	0.151	0.826	0.636	1.073

Table 3	Multivariate	Logistic Analyses	of Factors A	Associated with	Sleep	Disorders i	n Children	with SeLECTS
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**Notes:** Binary logistic regression analyses were conducted for the five factors that were significantly associated with sleep disorder incidence in children with SeLECTS. P < 0.05 is marked in bold and is the critical value defining significance. **Abbreviations:** SE, standard error; df, degree of freedom.

	project	Without Sleep Disorders	With Sleep Disorders	t/Z value	P value
The average correct rate (100%)	SeLECTS Children	97.98±1.57	96.44±2.08	4.116	<0.001ª
	Children with unmedicated SeLECTS	98.15±1.44	96.75±2.04	2.688	0.010 <sup>a</sup>
Total average reaction time (ms)	SeLECTS Children	925.19±116.90	1030.41±129.45	4.283	<0.001ª
	Children with unmedicated SeLECTS	926.18±112.77	1027.40±152.59	2.586	0.012 <sup>a</sup>
Executive control network efficiency	SeLECTS Children	55.98 (32.00, 77.00)	75.52 (61.10, 88.85)	3.273	<0.001 <sup>b</sup>
(ms)	Children with unmedicated SeLECTS	46.86 (18.03, 67.25)	79.00 (65.00, 100.00)	4.113	<0.001 <sup>b</sup>
Alerting network efficiency (ms)	SeLECTS Children	33.00 (9.00, 75.22)	75.72 (42.50, 88.23)	2.796	0.005 <sup>b</sup>
	Children with unmedicated SeLECTS	33.49 (3.24, 78.26)	75.23 (43.00, 89.00)	2.380	0.017 <sup>b</sup>
Orientation control network	SeLECTS Children	35.00 (7.50, 76.00)	40.55 (3.75, 73.00)	0.124	0.901 <sup>b</sup>
efficiency (ms)	Children with unmedicated SeLECTS	43.00 (4.00, 73.50)	48.00 (6.00, 80.00)	0.324	0.746 <sup>b</sup>

#### Table 4 Comparisons of Sleep Quality and ANT Parameters in SeLECTS Patients

**Notes**: <sup>a</sup>Normal distribution data: represented by  $x \pm s$ , independent sample *t* test was used for comparison between groups. <sup>b</sup>Skewed distribution data: represented by M (Q25, Q75), the non-parametric Mann–Whitney *U*-test was used for comparison between groups. P < 0.05 is marked in bold and is the critical value defining significance.

Table 5	<b>Correlations</b>	Between To	tal CSHQ	Scores and	ANT	Parameters i	n Children	with	SeLECTS
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Value		Alerting Network Efficiency	Orientation Control Network Efficiency	Executive Control Network Efficiency	Total Average Reaction Time	The Average Correct rate
SeLECTS Children	Correlation coefficent (p)	-0.344	-0.146	-0.418	0.367	-0.253
	Р	<0.001	0.133	<0.001	<0.001	<0.001
Children with unmedicated SeLECTS	Correlation coefficent (ρ)	-0.329	-0.175	-0.682	0.489	-0.305
	Р	0.014	0.202	<0.001	<0.001	0.023

Notes: Spearman correlation analyses was employed for multivariate assessments. P < 0.05 is marked in bold and is the critical value defining significance.

executive control network efficiency ( $\rho$ =-0.329, P<0.05,  $\rho$ =-0.682, P<0.05). Total CSHQ scores were not significantly associated with the efficiency of the directed network (P>0.05). For further details, see Table 5.

# Discussion

SeLECTS is an age-dependent form of epilepsy that tends to occur during sleep and is generally associated with a good prognosis. Seizures in children with SeLECTS often result in the disruption of sleep. The present data, however, suggest that sleep disorders already exist in these children at the time of SeLECTS onset, and that these sleep issues are associated with altered attentional network function.

# Sleep Problems in Children with SeLECTS

The present analyses revealed that the total CSHQ scores of children with SeLECTS were generally more than one standard deviation higher than those for control subjects, and these patients exhibited significantly higher rates of sleep disorders as compared to healthy age-matched controls. SeLECTS children scored higher on delayed sleep onset, sleep

duration, night waking, parasomnia, daytime sleepiness, and sleep anxiety, consistent with the findings of previous studies.<sup>9,10</sup> No difference in total sleep duration was observed between SeLECTS patients and controls, in contrast to prior evidence indicating that children with epilepsy exhibit a reduction in total sleep duration as compared to healthy children.<sup>9</sup> This difference is likely attributable to the fact that most children with SeLECTS were school-aged children, most of whom were newly diagnosed with a relatively short disease course. Most patients included in the study had a short disease duration. On the other hand, children in this age group in China are subject to significant academic pressure, and most parents of children in the control group said they had to shorten their children's sleep time to make concessions for learning. Thus, the healthy group also had shorter total sleep times.

Correlation analyses suggested that sleep disorder incidence was higher in children with SeLECTS exhibiting generalized seizures, more seizures, and seizures occurring during sleep. EEG results from SeLECTS patients exhibit normal background and high-amplitude centrotemporal spike-slow wave complexes that are activated during sleepiness and sleep.<sup>1</sup> The sleep spindle is a typical sleep-related EEG pattern, and a reduction thereof is generally associated with increased seizure activity. Relative to focal seizures patients, individuals with secondary generalized seizures typically exhibit a greater sleep spindle reduction together with increased sleep wakefulness, particularly in those with rolandic epilepsy.<sup>11–13</sup> Better seizure control and fewer seizures have previously been linked to greater sleep efficiency and fewer awakenings.<sup>14</sup> A higher incidence of sleep disorders was also detected in children whose seizures occurred during sleep. Seizures during sleep may contribute to worsening sleep quality and the disturbance of sleep structure, thereby contributing to daytime sleepiness.<sup>15</sup> Patients have been found to exhibit greater daytime sleepiness following seizures,<sup>16</sup> as measured via the maintenance arousal test, with this relationship being more significant in cases of nocturnal seizures.

Different antiepileptic drug types and doses have been shown to have a range of impacts on sleep issues.<sup>17,18</sup> The present data suggest that there are no significant differences in the incidence of sleep problems when comparing newly diagnosed untreated children with SeLECTS and patients undergoing oxcarbazepine or levetiracetam monotherapy, potentially owing to the limited number of drugs included in this study and the absence of any combined treatment regimens. Indeed, one prior study similarly found that oxcarbazepine and levetiracetam failed to impact sleep deterioration.<sup>19</sup> Lacosamide has additionally been reported to reduce the number of awakenings, while perampanel has no impact on some aspects of sleep. Lamotrigine may contribute to a higher risk of insomnia among children, and patients undergoing sodium valproate monotherapy reportedly exhibit prolonged N1 stage sleep together with the shortening of REM sleep and a greater number of awakenings.<sup>20</sup> Prior studies have demonstrated that polytherapeutic regimens tend to be associated with worse sleep habits than those associated with monotherapeutic regimens.<sup>21</sup>

## Sleep Disorders and Attentional Network Function

The present data highlight a close association between impaired sleep and attentional network function in children with SeLECTS. The incidence of sleep problems in these children was associated with slower total reaction time values in the ANT, with consistent reductions in the efficiency of the alerting and executive control networks. However, the strength of the correlation was not high. In children with SeLECTS who were not taking medication, consistent results were obtained. Attentional function is a key aspect of cognition that generally entails both simple sustained attention as well as more complex selective and distributive forms of attention important for daily function. Sleep has long been shown to be related to behavioral self-regulation and a wide range of cognitive processes associated with inhibitory control, working memory, shifting attention, and executive function.<sup>22–24</sup> Sustained attention can be impaired by sleep deprivation, contributing to slower reaction times and higher error rates, with attentional decline worsening with the prolongation of task duration.

It can be concluded that sleep disturbances are strongly associated with reduced efficiency of the alarm network in SeLECTS children. Sustained or alert attention refers to the ability of a given individual to steadily maintain focused attention over a given time period. Vigilant attention has been shown to be the aspect of cognitive function most sensitive to loss of sleep,<sup>25</sup> with insufficient sleep having a significant adverse effect on vigilant attention. This may be attributable to changes in functional activity and network connectivity among various regions of the brain. Shared physiological and neural causes are believed to underlie the negative impacts of sleep deprivation and time-on-task studies on sustained attention, as evidenced by prior functional neuroimaging experiments.<sup>26</sup> Sleep deprivation has been posited to increase the variability of cognitive performance owing to interactions between the homeostatic stresses of sleep and the increases

and decreases in awake circadian stress and the compensatory efforts that people continue to perform. Owing to the priming effects of sleep on the endogenous maintenance of alertness and attention, performance while in a state of sleep deprivation tends to become increasingly unstable The significant increases in psychomotor vigilance test performance variability observed during sleep deprivation provide support for this "state instability" hypothesis.<sup>27</sup> Owing to the accumulation of homeostatic stress during sleep, alertness-related attentional deficits are positively correlated with the duration of wakefulness.

Executive function is a key aspect of cognitive function that refers to a range of high-level cognitive processes engaged by individuals through which they control their thoughts and behaviors.<sup>28</sup> One review article based on functional neuroimaging data found that the primary neural substrates associated with executive function are concentrated in the prefrontal, particularly in the lateral prefrontal cortex.<sup>29</sup> A lack of sufficient sleep can injure the prefrontal cortex in a manner proportional to the duration of sleep deprivation such that the prefrontal cortex serves as a key physiological mediator of the relationship between sleep and executive function. Functional MRI signals in the dorsolateral prefrontal cortex and parietal sulcus are decreased when attention tasks are performed while sleep-deprived, reaffirming this correlation between sleep insufficiency and impaired executive function.<sup>30</sup> This relationship between sleep and executive function, sleep does does relationship between sleep disorders and executive function, the exacerbation of sleep problems. concluded that sleep disorder symptoms were closely related to the executive function of adolescents. Children at risk of sleep-disordered breathing and exhibiting poor sleep hygiene also face impairment when performing daily tasks.<sup>32</sup>

Attention deficit-like cognitive deficits have been shown to occur in a number of less severe epilepsy syndromes including SeLECTS, catatonic epilepsy, and frontal lobe epilepsy.<sup>33</sup> It is therefore important for clinicians to be aware of the concept of "cognitive epilepsy", which can assist them in guiding life with epilepsy, especially in children and adolescents. By identifying specific types of cognitive impairment that correspond to epilepsy syndromes, remedial assistance can be provided to children to minimise their negative impact on, for example, their academic performance.

The study has several limitations. The sample size was not sufficiently large, and the enrolled patients were mostly from the same province as those in the healthy control group, representing a limitation. Only two drugs, oxcarbazepine and levetiracetam, were used by the majority of the patients on medication; thus, the effects of other antiepileptic drugs on sleep in children with SeLECTS could not be evaluated. Although the reliability of the CSHQ has been well established, it is possible that sleep quality could be more effectively reflected by a sleep-monitoring instrument, which would increase the reliability of the results. This was a cross-sectional study, and we will continue to follow up the sleep quality and attention network functioning of newly diagnosed children after symptom relief.

## Conclusion

The present results suggest that children with SeLECTS face a higher risk of sleep problems as compared to age-matched healthy controls. Sleep quality in SeLECTS children is negatively affected by younger age at the onset of the first seizure, higher seizure frequency, seizures during sleep and the incidence of generalized seizures. The degree of sleep disorder in children with SeLECTS was also found to be positively correlated with the impairment of attention network function. This study is the first to our knowledge to systematically evaluate sleep disorders in SeLECTS patients using a combination of sleep questionnaires and functional analyses of the attention network. These results emphasize the pronounced changes in sleep quality and sleep disorder prevalence in SeLECTS patients, while also highlighting the effects that seizures and treatment strategies can have on sleep. Attentional network function was also found to be strongly affected by sleep disorders. These results were observed despite the fact that most enrolled patients were newly diagnosed or reported well-controlled seizures, emphasizing the close functional relationships that comprise this sleep-epilepsy-attention network. These results have demonstrated that administering sleep interventions during hospitalization in children with epilepsy can lead to improvements in the duration and quality of sleep.<sup>34</sup> Future studies focused on sleep interventions in children with SeLECTS are thus warranted in an effort to reduce the incidence of sleep problems in these individuals while also mitigating damage to attentional networks and other aspects of neurocognitive function.

## **Data Sharing Statement**

The data sets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

## **Ethics Statement**

Consent was obtained from all study participants before the start of the study. This study adheres to the tenets set forth in the Declaration of Helsinki.

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# **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

# Disclosure

This is not an industry-supported study. None of the authors have potential conflicts of interest to be disclosed.

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