

# Sleep Disturbances in Chinese Children with Epilepsy: Associations with Behavioral Problems and Quality of Life

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**Objective:** To investigate the association between sleep disturbances and behavioral problems as well as quality of life (QOL) in Chinese children with epilepsy.

**Methods:** Caregivers of 167 epileptic children aged 3 to 12 years completed the Child Sleep Habits Questionnaire (CSHQ), the Strengths and Difficulties Questionnaire (SDQ), and the Pediatric Quality of Life Inventory (PedsQL™, 4.0 Core).

**Results:** The prevalence of sleep disturbances (CSHQ total score >41) in epileptic children was 73.7% [95% CI (66.9%-80.4%)]. Epileptic children with sleep disturbances demonstrated more behavioral problems and lower QOL compared to those without sleep disturbances. Sleep disturbances such as sleep anxiety and daytime sleepiness were associated with more behavioral problems and lower QOL ( $p < 0.05$ ). Linear regression analyses showed that higher disturbance in sleep duration domain were associated with more behavioral problems, while higher sleep disordered breathing domains was associated with lower QOL ( $p < 0.05$ ). The interaction between sleep disturbances and behavioral problems in predicting QOL was not significant. The sensitivity analysis using 48 as an alternative cutoff for CSHQ total score obtained consistent results.

**Conclusion:** Sleep disturbances occur frequently among Chinese children with epilepsy, and are associated with more behavioral problems and lower QOL. The sleep disturbance-QOL association is unlikely contingent on behavioral problems. This study highlights the necessity of evaluating and treating sleep disturbances multidimensionally among children with epilepsy to promote their whole health and wellbeing.

**Keywords:** sleep disturbances, behavioral problems, quality of life, epilepsy, children

## Introduction

Epilepsy is a common childhood neurological disease, affecting more than 10 million children worldwide.<sup>1</sup> Sleep disturbances are among the most prevalent comorbidities of epilepsy, with prevalence ranging 45–95% among children with epilepsy,<sup>2,3</sup> as compared with 25–40% among typically developing children.<sup>4</sup> The most common sleep disturbances in children with epilepsy include excessive daytime sleepiness (76%), sleep disordered breathing (65%), and parasomnia (53%).<sup>5</sup> The relationship between epilepsy and sleep disturbances is likely bidirectional and complex.<sup>6</sup> Sleep can modulate seizure occurrence or interictal epileptiform discharges, and sleep disturbances may worsen epileptic symptoms. Conversely, epileptic discharges have been shown to disrupt sleep-wake cycles.<sup>7</sup> Therefore, epilepsy with the added sleep disturbances likely exacerbates children's health and functioning.<sup>7</sup> Previous studies have independently reported high prevalence of sleep disturbances,<sup>7,8</sup>

behavioral problems,<sup>2,9</sup> and poor QOL,<sup>10</sup> in children with epilepsy. Yet, there lacks a systematic examination of the association among sleep disturbances, behavioral problems, and QOL.

Emerging evidence suggested the association between sleep disturbances and behavioral problems in children with epilepsy. A study regarding the Rolandic epilepsy reported higher level of behavioral problems in epileptic children with sleep problems than those without.<sup>11</sup> Byars et al also found that in children with epilepsy, sleep disturbances were correlated with increased behavioral problems.<sup>12</sup> However, existing studies focused predominantly on Western children with epilepsy, and thus the results may not be generalizable to Chinese children due to the social and cultural differences in sleep practice and behaviour.<sup>13</sup> What's more, for those having sleep disturbances or/and behavioral problems, impaired QOL may also be present. Yet, there are few studies on the relationship between sleep disturbance and QOL in children with epilepsy. A recent study showed that children with epilepsy and sleep disturbances had poorer QOL.<sup>14</sup> Given above evidence, it is possible that sleep disturbances may interact with behavioral problems in children with epilepsy to reduce QOL. However, such interaction has not been systematically investigated in empirical studies. Bridging such literature gap is crucial to furthering our understanding of the association among the three conditions and to inform clinical interventions.

Therefore, the current study was to explore the association among sleep disturbances, behavioral problems, and QOL in Chinese children with epilepsy. We hypothesized: 1) children with sleep disturbances would demonstrate more behavioral problems and poor QOL, 2) sleep disturbances would be associated with more behavioral problems and lower QOL, and 3) the sleep disturbance-QOL association would be contingent on behavioral problems in Chinese children with epilepsy.

## Methods

### Participants and Procedure

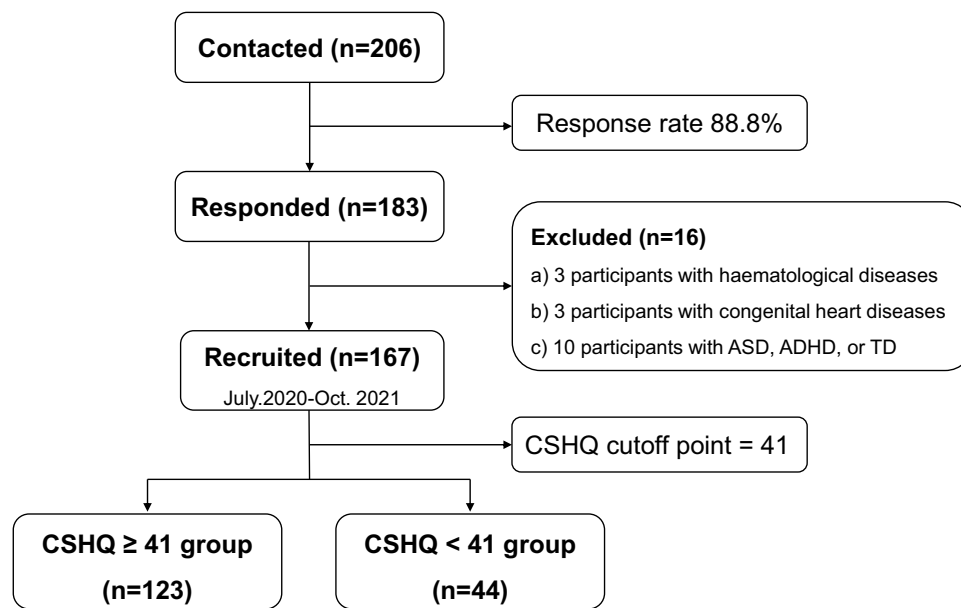
The current study is a cross-sectional design. We recruited children with epilepsy and their caregivers from a paediatric neurological clinic and inpatient ward in a tertiary children's hospital in Shanghai. Children aged 3 to 12 years who met the International League Against Epilepsy (ILAE) 2017 criteria<sup>15</sup> admitted for a diagnosis of epilepsy from July 2020 to October 2021. The exclusion criteria were: (1) children born at less than 37 weeks; (2) children with overt structural brain damage or cerebral palsy; (3) children with other confirmed physical and psychiatric diseases, such as haematologic tumours, congenital heart diseases, attention deficit hyperactivity disease (ADHD), autism spectrum disorder (ASD), and tic disorder (TD); or (4) parents unable to speak, read, and understand Chinese.

According to previous studies, sleep disturbances occurred 25–40% in typically developing children<sup>4</sup> and 45–95% of children with epilepsy.<sup>2,3</sup> Using the two lowest rates (25% vs 45%) by PASS software, we estimated that a sample size of at least 115 would provide an effect size of 0.9. A total of 206 children with epilepsy were contacted, and caregivers of 183 agreed to participate and signed informed consent (response rate 88.8%). Investigators on site supervised the caregivers of children with epilepsy while completing the questionnaires in person and independently in a quiet hospital setting. Three participants with haematologic tumours, three with congenital heart diseases, and ten with other clearly diagnosed neurodevelopmental disorders (ie, ADHD, ASD or TD) were excluded; data from 167 participants ultimately were included in the analysis (Figure 1).

The current study was approved by the Shanghai Children's Medical Center Ethics Committee (SCMCIRB-K2020030-1) in accordance with the guidelines of the Declaration of Helsinki (1964).

### Measures

Children's sleep disturbances were assessed by the Children's Sleep Habit Questionnaire (CSHQ), a 33-item parent-reported questionnaire initially designed for children aged 4 to 10 years.<sup>16</sup> More recent studies have extended its use to children aged 3–12 years.<sup>17,18</sup> Each item was rated on a 3-point scale ranging from "usually" to "rarely", reflecting sleep habits of children in the past week. The CSHQ evaluated sleep disturbances on eight subscales: bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night awaking, parasomnias, sleep disordered breathing, and daytime sleepiness. Higher total and subscale scores indicated more sleep problems. A total score of > 41 was suggested as the clinical cutoff for general sleep disturbance.<sup>16</sup> Considering the cutoff of 41 based on American children may



**Figure 1** Flowchart of study participants with data on inclusion, exclusion and distribution according to CSHQ.

**Abbreviations:** CSHQ, Children's Sleep Habits Questionnaire; ADHD, Attention Deficit Hyperactivity Disease; ASD, Autism Spectrum Disorder; TD, Tic Disorder.

overestimate sleep disturbances, especially for behavioral domains in Chinese children, a total score of 48 as an alternative cutoff point was utilized in the current study for a sensitivity analysis.<sup>4,19</sup> The Chinese version of the CSHQ<sup>20</sup> has been used in children with epilepsy.<sup>8</sup> The Cronbach's  $\alpha$  was 0.73 in the current study for the full questionnaire.

Behavioral problems were assessed by Strengths and Difficulties Questionnaire (SDQ).<sup>21</sup> This 25-item questionnaire was designed for children aged 4 to 16 years, with later studies extending its use to children aged as young as 3 years.<sup>22</sup> Each response is rated on a 3-point Likert scale (0 for "not true", 1 for "partly true", or 2 for "very true"). The SDQ consists of five subscales: emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviors. Score ranged from 0 to 10 for each of the five subscales. The total difficulties score ranging from 0 to 40 was calculated by totalling all subscales except for prosocial behaviors. The internalizing score was a sum of emotional symptoms and peer relationship scales (ranges from 0 to 20) while the externalizing score was a sum of conduct problems and hyperactivity/inattention scales (ranges from 0 to 20). A higher score was indicative of more severe behavioral symptoms. Total score  $\geq 14$  was suggested as the clinical cutoff point for behavioral difficulties.<sup>21</sup> The SDQ had been used in children with epilepsy<sup>23</sup> and prior to this was used within the Chinese population with good psychometrics.<sup>24</sup> The Cronbach's  $\alpha$  for the total difficulties was 0.61 in current study.

The Paediatric Quality of Life Inventory (PedsQL™, 4.0 Core) scale was used to assess the QOL in children.<sup>25</sup> The PedsQL is a 23-item generic measure including four age-group scales specific to children aged 2–4, 5–7, 8–12, and 13–18 years. It assesses the following 4 domains: physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), and school functioning (5 items). Emotional, school, and social functioning can be combined into a psychosocial health domain. Each item was rated on a 5-point Likert scale from 0 to 4, subsequently reverse scored and linearly transformed to a 0 to 100 points scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0). Thus, a higher converted score was indicative of a better QOL. The reliability and validity of the Chinese translations of the PedsQL 4.0 scale have been reported for Chinese children.<sup>26</sup> The Cronbach's  $\alpha$  for the full scale was 0.94 in the current study.

In addition to the above assessments, caregivers also reported the sociodemographic characteristics including age, sex, the only-child status, caregivers' education level, family structure, family living environment, and their children's seizure history.

## Statistical Analysis

Descriptive statistics were used to characterize sociodemographic variables, and sleep and epilepsy-related variables. Continuous data were presented as mean  $\pm$  standard deviation (SD), and categorical data as frequencies (percentages). To test for sample distribution, we used a Shapiro–Wilk test. As most of data were not distributed normally, we used the Mann–Whitney test to compare continuous variables between groups. The categorical variables from the two groups were compared using chi-square test. Spearman correlation analyses were used to measure the association between sleep variables and behavioral problems as well as QOL. Stepwise linear regression analyses were performed to determine sleep and epileptic parameters predicting behavior problems or lower QOL. We conducted a two-way ANOVA to examine the interaction between sleep disturbance and behavioral problems in predicting QOL, including CSHQ total score (below or above cutoff) and SDQ total difficulties (below or above cutoff) as independent variables, and some sociodemographic variables (ie, sex, age, being the only child at home, family structure, education of caregiver, and family living environment) as covariates. We also used 48 as the alternative cutoff point of CSHQ total score for sensitivity analysis to examine the robustness of our findings. All analyses were performed using Statistical Package for the Social Sciences (SPSS<sup>®</sup>), version 26.0, with a significance level of 0.05.

## Results

### Sample Characteristics

Demographic and sleep characteristics of the samples are summarized in Table 1. Of the 167 children, 123 (73.7%) were rated as having sleep disturbances (CSHQ total score  $>$  41). There was a significant age difference between the group with sleep disturbances and the group without. As our preliminary analysis detected no difference in behavioral problems and QOL between children aged 3–6 years and 6–12 years, and thus we combined the age groups for all subsequent analyses. Children with epilepsy in the sleep disturbances group had significantly higher prevalence of bed-sharing and room-sharing than those without. Regarding epilepsy characteristics (Table 2), seizure duration of children with sleep

**Table 1** Demographic Characteristics of Children with Epilepsy

Characteristics	Value <sup>a</sup>			
	Total Samples (n = 167)	CSHQ > 41 (n = 123)	CSHQ $\leq$ 41 (n = 44)	p <sup>b</sup>
Age, years	7.56 $\pm$ 2.40	7.27 $\pm$ 2.36	8.38 $\pm$ 2.34	< 0.05
Female	65 (38.9%)	49 (39.8%)	16 (36.4%)	n. s.
BMI	21.31 $\pm$ 5.73	20.97 $\pm$ 5.59	22.27 $\pm$ 6.06	n. s.
The education of caregiver				n. s.
High school or less	85 (50.9%)	63 (51.2%)	22 (50.0%)	
College	72 (43.1%)	53 (43.1%)	19 (43.2%)	
Graduate school	10 (6.0%)	7 (5.7%)	3 (6.8%)	
The only-child status	80 (47.9)	63 (51.2%)	17 (38.6%)	n. s.
Family structure				n. s.
Nuclear family	92 (55.1%)	64 (52.0%)	28 (63.6%)	
Extended family	73 (43.7%)	58 (47.2%)	15 (34.1%)	
Single parent or other	2 (1.2%)	1 (0.8%)	1 (2.3%)	
Family living environment				n. s.
Quiet	105 (62.9%)	73 (59.3%)	32 (72.7%)	
Noisy	62 (37.1%)	50 (40.7%)	12 (27.3%)	
Sleeping arrangement pattern				< 0.01
Child-adult bed-sharing	117 (70.1%)	96 (78.0%)	21 (47.7%)	
Child-adult room-sharing	28 (16.8%)	17 (12.8%)	11 (25.0%)	
Others	22 (13.2%)	10 (8.1%)	12 (27.3%)	
Total sleep time per 24h (hours)	10.06 $\pm$ 1.38	10.16 $\pm$ 1.49	9.78 $\pm$ 0.97	n. s.

**Notes:** Percentages may not total to 100% due to rounding. <sup>a</sup>Data are presented as mean  $\pm$  standard deviation (SD) or n (%). <sup>b</sup>The Mann–Whitney U-test were used for continuous variables. Chi-square tests or Fisher's exact tests for categorical data.

**Abbreviations:** CSHQ, Children's Sleep Habits Questionnaire; BMI, body mass index; n. s., non-significant.

**Table 2** Epilepsy Related Characteristics

Characteristics	Value <sup>a</sup>			
	Total Samples (n = 167)	CSHQ>41 (n = 123)	CSHQ ≤ 41 (n = 44)	p <sup>b</sup>
Age at seizure onset, years	5.13 ± 2.56	5.03 ± 2.46	5.40 ± 2.82	n. s.
Duration of epilepsy, months	23.70 ± 26.57	20.92 ± 23.87	31.48 ± 32.01	n. s.
Duration of epilepsy ≤ 1 month	51 (30.5%)	38 (30.9%)	13 (29.5%)	n. s.
Seizure frequency (in last 6 months)				n. s.
Daily	16 (9.6%)	13 (10.6%)	3 (6.8%)	
Weekly	14 (8.4%)	11 (8.9%)	3 (6.8%)	
Monthly	9 (5.4%)	7 (5.7%)	2 (4.5%)	
Less than 1 per month	47 (28.1%)	37 (30.1%)	10 (22.7%)	
None	81 (48.5%)	55 (44.7%)	26 (59.1%)	
Seizure type				n. s.
Focal	83 (49.7%)	61 (49.6%)	22 (50.0%)	
Generalized	64 (38.3%)	43 (35.0%)	21 (47.7%)	
Both	10 (6.0%)	9 (7.3%)	1 (2.3%)	
Unclassified	10 (6.0%)	10 (8.1%)	0	
Seizure diurnal pattern				n. s.
Day	48 (28.7%)	38 (30.9%)	21 (52.5%)	
Night	77 (46.1%)	54 (43.9%)	10 (22.7%)	
Both	42 (25.1%)	31 (25.2%)	11 (25.0%)	
Epileptic discharge in EEG				n. s.
Normal	42 (25.1%)	34 (27.6%)	8 (18.2%)	
Unilateral discharge	59 (35.3%)	42 (34.1%)	17 (38.6%)	
Bilateral discharge	66 (39.5%)	47 (38.2%)	19 (43.2%)	
Seizure duration (min)				< 0.01
< 5	110 (65.9%)	73 (59.3%)	37 (84.1%)	
5–15	25 (15.0%)	19 (15.4%)	6 (13.6%)	
16–30	14 (8.4%)	14 (11.4%)	0	
>30	4 (2.4%)	4 (3.3%)	0	
Time inconsistency	14 (8.4%)	13 (10.6%)	1 (2.3%)	
The Status epilepticus	48 (28.7%)	44 (35.8%)	4 (9.1%)	< 0.01
Family history	23 (13.8%)	18 (14.6%)	5 (11.4%)	n. s.
Specific diagnosis				< 0.01
BECTS	59 (35.3%)	35 (28.5%)	24 (54.5%)	
Childhood Absence epilepsy	11 (6.6%)	9 (7.3%)	2 (4.5%)	
Occipital epilepsy	3 (1.8%)	2 (1.6%)	1 (2.3%)	
ADNFLE	2 (1.2%)	2 (1.6%)	0	
Unclassified	92 (55.1%)	75 (61.0%)	17 (38.6%)	
Current AED				n. s.
Monotherapy	132 (79.0%)	95 (77.2%)	37 (84.1%)	
OXC	52 (39.4%)	38 (40.0%)	15 (40.5%)	
LEV	58 (43.9%)	41 (43.2%)	17 (45.9%)	
VPA	19 (14.4%)	14 (14.7%)	5 (13.6%)	
TPM	3 (2.3%)	2 (2.1%)	0	
Polytherapy	29 (17.4%)	22 (17.9%)	7 (15.9%)	
None	6 (4.2%)	6 (5.7%)	0	

**Notes:** Percentages may not total to 100% due to rounding; <sup>a</sup>Data are presented as mean ± standard deviation (SD) or n (%); <sup>b</sup>The Mann–Whitney *U*-test were used for continuous variables. Chi-square tests or Fisher's exact tests for categorical data.

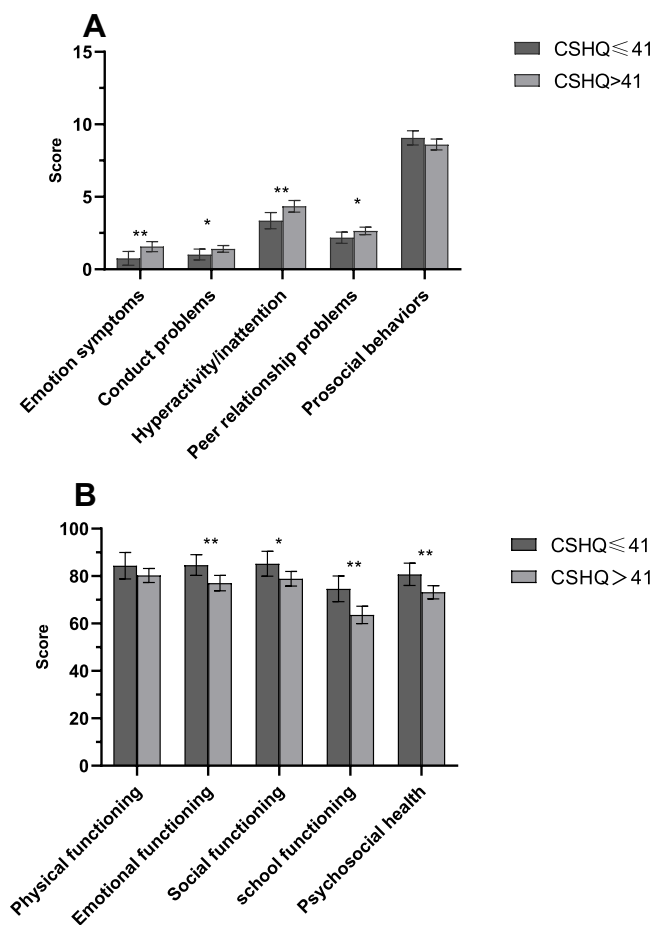
**Abbreviations:** CSHQ, Children's Sleep Habits Questionnaire; AED, anti-epileptic drug; EEG, electroencephalogram; BECTS, Benign Epilepsy with Centrotemporal Spikes; ADNFLE, Autosomal Dominant Nocturnal Frontal Lobe Epilepsy; OXC, oxcarbazepine; LEV, levetiracetam; VPA, valproic acid; TPM, topiramate; n. s., non-significant.

disturbances were significantly longer than those without, and children with sleep disturbances had significantly more epileptic status during the duration of epilepsy than those in the other group. And significant difference in specified diagnosis was observed between the two groups, with a higher proportion of Benign Epilepsy with Centrotemporal Spikes (BECTS) in the group without sleep disturbance.

### Differences of Behavioral Problems and QOL Between CSHQ > 41 Group and CSHQ ≤ 41 Group

Compared with children without sleep disturbances, those with sleep disturbances had significantly higher score in SDQ total difficulty as well as the domains of emotional symptom, conduct problems, hyperactivity/inattention, and peer relationship ( $p < 0.05$ ). The domain of prosocial problems was not significantly different between the two groups (Figure 2A). Regarding QOL, children in the sleep disturbances group had significantly lower scores in emotional, social, and school functioning and psychosocial health domains ( $p < 0.05$ ). Significant differences were not observed in physical functioning (Figure 2B).

In the sensitivity analysis, consistent results showed that epileptic children with CSHQ total score > 48 had significantly higher SDQ total score and lower QOL total score.



**Figure 2** Differences of SDQ subscale (A) and QOL subscale scores (B) between CSHQ > 41 group and CSHQ ≤ 41 group. Number of samples in each group are as follows: children with epilepsy in CSHQ ≤ 41 score group (n =44) and in CSHQ > 41 score group (n =123). Each column shows SDQ subscale scores and QOL subscale scores and error bar represent 95% confidence interval. \* $p < 0.05$ , \*\* $p < 0.01$ .

**Abbreviations:** CSHQ, Children’s Sleep Habits Questionnaire; SDQ, the Strengths and Difficulties Questionnaire; QOL, quality of life.

## Association Among Sleep Disturbances, Behavioral Problems, and QOL

A series of significant correlations were detected between sleep disturbances and behavioral problems or QOL in children with epilepsy (Table 3). Bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night waking, parasomnias, and daytime sleepiness were significantly correlated with SDQ total score (all  $r_s < 0.5$ ,  $p < 0.05$ ). Sleep anxiety, sleep disordered breathing, daytime sleepiness, and total sleep disturbance scores were correlated significantly with QOL total score (all  $|r_s| < 0.3$ ,  $p < 0.05$ ). Sleep disordered breathing and daytime sleepiness were significantly correlated with both physical functioning and psychosocial health scores ( $p < 0.05$ ).

In the regression analyses (Table 4), the multicollinearity test found that the tolerance of each variable was between 0.81 and 0.98, and the variance expansion factor ranged between 1.01 and 1.23, indicating no multicollinearity. The SDQ total score was significantly associated with the CSHQ subscale score on sleep duration ( $\beta = 0.43$ ,  $p < 0.001$ ) and sleep anxiety ( $\beta = 0.16$ ,  $p < 0.05$ ), while QOL total score was significantly associated with the CSHQ subscale scores on sleep disordered breathing ( $\beta = -0.17$ ,  $p < 0.05$ ). In epilepsy-related parameters, diagnosis of BECTS was significantly correlated both higher SDQ total score ( $\beta = -0.17$ ,  $p < 0.05$ ) and lower QOL total scores ( $\beta = 0.24$ ,  $p < 0.05$ ). Duration of epilepsy  $\leq 1$  month ( $\beta = -0.18$ ,  $p < 0.05$ ) was only significantly correlated with SDQ total score, while the  $\geq 2$  anti-epileptic drugs (AEDs) was only significantly correlated lower QOL total score ( $\beta = -0.20$ ,  $p < 0.01$ ).

There was a strong correlation between sleep disturbances and behavioral problems, but the results of two-way ANOVA showed no significant interaction between CSHQ total score and SDQ total score ( $F_{(1,163)} = 0.71$ ,  $p > 0.05$ ).

## Discussion

Our study provided first evidence for the association among sleep disturbances, behavioral problems, and QOL among Chinese children with epilepsy. Sleep disturbances were highly prevalent in children with epilepsy (73.7%). Among children with epilepsy, sleep disturbances were significantly associated with more behavioral problems and lower QOL, and the sleep disturbance-QOL association was unlikely contingent on behavioral problems. The sensitivity analysis using an alternative cutoff of 48 for CSHQ total score obtained consistent results, ensuring the robustness of our findings. Results of the current study suggested that sleep disturbances, behavioral problems, and QOL should be integrated as part of a comprehensive assessment of overall life functioning for epileptic children to enhance clinicians' awareness and promote children's health.

The current study showed that sleep disturbances were common and severe in epileptic children, with a prevalence of 73.7% and a mean CSHQ total score of 45.92. In Hong Kong, CSHQ total score was 48.89 from a sample of epileptic children aged 4 to 12 years old.<sup>8</sup> A study among American children with epilepsy aged 2 to 10 years reported a CSHQ total score of 48.25.<sup>7</sup> The relatively lower severity level of sleep disturbances in the current sample compared to earlier

**Table 3** Spearman Correlation Between Sleep Subscales and Behavioral Problems as Well as QOL

CSHQ Domains	Behavioral Problems			Quality of Life		
	Internalizing Problems	Externalizing Problems	SDQ Total Score	Psychosocial Health	Physical Functioning	QOL Total Score
Bedtime resistance	0.19*	0.12	0.22**	-0.15	-0.02	-0.09
Sleep onset delay	0.03	0.12	0.16*	-0.05	-0.07	-0.12
Sleep duration	0.41**	0.34**	0.41**	-0.11	0.08	-0.05
Sleep anxiety	0.20**	0.05	0.19*	-0.25**	-0.13	-0.18*
Night waking	0.18*	0.08	0.17*	-0.04	-0.01	-0.04
Parasomnias	0.13	0.16*	0.16*	-0.16*	-0.06	-0.07
Sleep disordered breathing	0.07	0.12	0.13	-0.19*	-0.16*	-0.20**
Daytime sleepiness	0.13	0.17*	0.23**	-0.19*	-0.18*	-0.16*
CSHQ total score	0.30**	0.24**	0.37**	-0.30**	-0.19*	-0.25**

Notes: \* $p < 0.05$ ; \*\* $p < 0.01$ .

Abbreviations: SDQ, Strengths and Difficulty Questionnaire; QOL, Quality of Life; CSHQ, Children's Sleep Habits Questionnaire.

**Table 4** Linear Regression Models for Epileptic and Sleep Parameters on Behavioral Problems and QOL in Children with Epilepsy

Parameters	Behavioral Problems			Quality of Life		
	SDQ Total Scores	Internalizing Problems	Externalizing Problems	QOL Total Scores	Psychosocial Health	Physical Health
	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$
Sex	-	-	-0.18**	-	0.19**	0.15*
The only-child status	-	-	0.14*	-	-	-
Family structure	0.17*	0.17*	0.16*	-	-	-
Duration of epilepsy $\leq$ 1 month	-0.18*	-0.16*	-0.34***	-	0.19*	-
Seizure diurnal pattern	-	-	-	-	-0.19*	-
Seizure type	-	-	0.18**	-	-	-
BECTS	-0.17*	-	-	0.24**	-	0.19*
$\geq$ 2AEDs	-	-	-	-0.20**	-0.21**	-0.19*
CSHQ	-	-	-	-	-	-
Sleep anxiety	0.16*	0.24**	-	-	-0.24**	-
Sleep duration	0.43***	0.44***	0.29***	-	-	-
Parasomnia	-	-	0.14*	-	-	-
Daytime sleepiness	-	-	0.17*	-	-0.22**	-
Sleep disordered breathing	-	-	-	-0.17*	-	-
Adjust R <sup>2</sup>	0.33	0.29	0.38	0.18	0.26	0.11
F	15.57	16.72	10.56	11.57	9.42	7.00

Notes: \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

Abbreviations: SDQ, Strengths and Difficulty Questionnaire; QOL, Quality of Life; BECTS, Benign Epilepsy with Centrottemporal Spikes; CSHQ, Children's Sleep Habits Questionnaire; AEDS, Anti-epileptic drugs.

reports in Hong Kong and US may due to sample's heterogeneity and cross-cultural differences. In our study, nearly half of epileptic children reported no seizures within the last six months, which was higher than 41% in the Hong Kong study.<sup>8</sup> A prior study reported higher seizure frequency was related to higher scores for excessive sleepiness and disorders of sleep-wake transition.<sup>11</sup> Also, a polysomnographic study did not identify difference in sleep structures between epilepsy patients without seizures and healthy controls,<sup>27</sup> which may partially explain the lower prevalence of sleep disturbances in our sample. Additionally, the effect of antiepileptic drugs on sleep should be acknowledged. For example, benzodiazepines and barbiturates may reduce sleep latency, valproate may increase the stage 1 sleep, and lamotrigine may decrease slow wave sleep and insomnia.<sup>28</sup> Further, children on polytherapy presented with worse sleep problems than children on monotherapy.<sup>28</sup> In our study, 79% of the children with epilepsy took the monotherapy, which was higher than the American sample (50%)<sup>7</sup> and the Hong Kong sample (62%).<sup>8</sup> Regarding cross-cultural difference, unique school schedules and sleep practices may contribute to the differences in the sleep disturbances of children from different regions.<sup>29</sup> For example, previous studies showed that Chinese children had significantly later bedtimes, earlier morning wake time, and shorter sleep duration compared with those from the United States,<sup>29</sup> and Hong Kong children had significant later bedtime and shorter sleep duration than Shanghai children.<sup>30</sup> These factors may account for the lower prevalence of sleep disturbances in our study.

Consistent with previous studies,<sup>11,12</sup> the current study showed that epileptic children with sleep disturbances presented with higher emotional symptoms, conduct problems, hyperactivity/attention, and peer relationship problems than those without.<sup>12</sup> The mechanisms of this relationship may involve the prefrontal cortex and its associated neurocognitive and neurobehavioral processes.<sup>31</sup> Additionally, our results revealed that epileptic children with sleep disturbances had lower scores on emotional, school, social functioning and psychosocial health of QOL, which corroborated with previous studies.<sup>14</sup> It is worth noting that discrepancies in the specific domain of QOL also existed. For instance, as previous studies reported significant differences in physical functioning of QOL between epileptic



children with and without sleep disturbances,<sup>14,32</sup> the current study did not. It may be possible that, as children in the current sample experienced shorter duration of illness, its deleterious influence on physical functioning has yet to manifest. Another conjectural reason may be that the low rate of seizure within the last six months may decrease the positive moderating role of active epileptic seizures on the relationship between sleep disturbances and physical functioning.<sup>33</sup> Also, patients with CHSQ > 41 in our study had more status epilepticus in which the massive epileptic discharges releasing from brain might have a different impact on physical and psychosocial health of QOL.<sup>34</sup>

More importantly, we found an independent association of sleep disturbances and behavioral problems with QOL in children with epilepsy, without detecting a significant interaction effect. This finding expands our understanding of the complex relationship among sleep disturbances, behavioral problems, and QOL in children with epilepsy, and underlines comprehensive management of these comorbidities.

In analysing specific domains of sleep disturbances, we found sleep disordered breathing was significantly associated with QOL, but not with behavioral problems. However, previous studies have reported that children with sleep-disordered breathing displayed worse behavioral functioning and lower QOL.<sup>35</sup> It is possible that sleep-disordered breathing symptoms can affect QOL initially, but behavioral functioning over time. A prior study showed that remission of sleep breathing symptoms after adenotonsillectomy frequently improved QOL in short time but did not improve behavioral outcomes.<sup>36</sup> Hence, it is imperative to routinely screen for sleep disturbances and refer epileptic children for polysomnography (PSG) studies if necessary, particularly for those with sleep complaints and symptoms of sleep-disordered breathing.

Finally, the current study found that the diagnosis of BECTS was associated with both behavioral functioning and QOL. As a benign epilepsy, BECTS had lower seizure frequency than other epilepsy and seizures usually disappeared after puberty, so it had subtle impact on sleep, behavior, and QOL.<sup>37</sup> When viewed in combination with the studies of BECTS, behavioral problems may be slighter but more persistent in children with BECTS than in children with epilepsy in general, though direct comparisons between epilepsy syndromes are not available.<sup>38</sup>

In our study, shorter duration of epilepsy was also correlated with more behavioral problems. Consistently, an Italian study suggested that the longer duration of the epilepsy was associated with behavioral problems and children with enduring epileptic manifestations were at higher risk for social failures.<sup>39</sup> Furthermore, epileptogenic networks with enduring changes in brain function and structure, may have resulted in emotional and behavioral alterations.<sup>40</sup> We also found the number of antiepileptic drugs was associated with lower QOL, which was similar with that being reported in previous studies.<sup>41</sup> The reason may be that the treatment of epilepsy may cause significant side effects, such as drowsiness, irritability, nausea, and headache, which had particular risk for diminished QOL.<sup>41</sup>

Our study was strengthened by using validated instruments, covering a wide range of relevant factors, and conducting a sensitivity analysis. Nevertheless, the findings should be interpreted with caution due to the following limitations. Firstly, with the current sample being recruited from the same site, nearly half reported no seizures within the last six months, and the majority being on monotherapy, our findings may lack generalizability. Future studies with larger samples from multiple sites are encouraged to confirm and expand our findings. Secondly, the study did not include objective sleep measurements such as actigraphy or polysomnography, and thus the findings may be subject to reporting bias. Nevertheless, the CSHQ is a well-validated tool for screening sleep problems in children with neurodevelopmental disorders,<sup>42</sup> providing measurements that correspond moderately well with objective measurement results.<sup>43</sup> Similarly, the study could be enhanced by including clinical evaluation of sleep disorders, psychopathology, and neurodevelopmental disorders by experienced psychiatrist or developmental and behavioral pediatricians, which would provide more accurate information such as detecting more children with ADHD and ASD. Thirdly, parents, teachers and children (particularly for old children) might have different perspectives in terms of sleep disturbances, emotional and behavioral problem, and QOL, and thus future studies would better consider multiple informants. Fourthly, the small sample size of the group without sleep disturbances could potentially produce the type 2 error when comparing to the group with sleep disturbances. However, our sensitivity analysis using an alternative cutoff of 48 for CSHQ total score increased the sample size of the group without sleep disturbances, but still demonstrated consistent results, which ensured the robustness of our findings. Finally, we could not establish a causal relationship due to the cross-sectional design. Thus, longitudinal and intervention studies are warranted to fully unveil the relationship among sleep disturbances, behavioral problems and QOL in children with epilepsy.

## Conclusion

In conclusion, sleep disturbances are prevalent in Chinese children with epilepsy. Among the epileptic children, sleep disturbances are significantly associated with worse behavioral functioning and lower QOL, and the sleep disturbance-QOL association is unlikely contingent on behavioral problems. Our study highlights the necessity of evaluating and treating sleep disturbances multidimensionally among children with epilepsy to promote their whole health and well-being. Future studies should investigate whether effective sleep interventions can improve behavioral functioning and QOL in children with epilepsy.

## Abbreviations

QOL, quality of life; CSHQ, Children's Sleep Habits Questionnaire; SDQ, the Strengths and Difficulties Questionnaire; PedsQL™, the Pediatric Quality of Life Inventory; ILAE, the International League Against Epilepsy; ADHD, Attention Deficit Hyperactivity Disease; ASD, Autism Spectrum Disorder; TD, Tic Disorder; AEDs, antiepileptic drugs; PSG, polysomnography; BECTS, Benign Epilepsy with Centrotemporal Spikes; ADNFLE, Autosomal Dominant Nocturnal Frontal Lobe Epilepsy.

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## Disclosure

The authors report no conflicts of interest in this work.

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