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THE RELATIONSHIP BETWEEN SLEEP PROBLEMS AND NEUROPSYCHOLOGICAL FUNCTIONING IN CHILDREN WITH FIRST RECOGNIZED SEIZURES

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Abstract

Epilepsy is associated with sleep disturbance, but little is known about how early this relationship develops and how it affects neuropsychological functioning. This study documented the frequency and types of sleep problems and examined how sleep problems are associated with seizures and neuropsychological functioning in 331 children following their first recognized seizure (ages 6 to 14) and in 225 sibling controls. Formal neuropsychological batteries were administered to all subjects. Sleep was measured using the Sleep Behavior Questionnaire and the Child Behavior Checklist. Sleep problems were more frequent in the seizure sample relative to siblings and previously published norms; bedtime difficulties, daytime somnolence and parasomnias were the most frequently occurring sleep problems. In the seizure group, sleep problems were related to seizure parameters and to neuropsychological functioning. Seizure patients with significant sleep problems had worse neuropsychological functioning on all measures. Findings demonstrate the significant impact of sleep disturbance on children with newly recognized seizures.

Keywords

Sleep; Sleep Disturbance; Epilepsy; Seizures; First recognized seizures; Children; Pediatric; Cognition; Neuropsychology; Prevalence

Introduction

Sleep disturbances are one of the most common behavioral problems in childhood[1]. Sleep problems have an even greater prevalence in children with epilepsy[2] and are one of the most

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common comorbidities in childhood epilepsy[3]. The complex interaction between sleep and epilepsy is bi-directional[4]. A common example of this relationship is the observation that sleep deprivation lowers the seizure threshold in individuals with epilepsy[5]. Similarly, the sleep of children with epilepsy can be affected by the severity of their epilepsy. For example, children with generalized seizures and refractory epilepsy have relatively more severe sleep disturbances[6]. Alternatively, it has been found that sleep disorders may complicate seizure control. For example, a recent study demonstrated that effectively treating obstructive sleep apnea may result in improved seizure control in children with epilepsy[7].

It is also known that children with epilepsy are at an elevated risk for daytime behavioral problems such as inattention and hyperactivity[8]. Recent empirical evidence suggests that daytime behavioral dysfunction common in pediatric epilepsy could be attributed to interrupted sleep[9]. Similarly, neuropsychological deficits are prevalent in children with epilepsy[10]. Clinical and observational data suggest that compromised sleep may result in neuropsychological performance deficits in children[11]. Recent evidence has shown that sleep deprivation is associated with poorer neuropsychological performance on neurodevelopmental tests[12]. In addition, it has been observed in multiple studies that sleep disordered breathing (SDB), a continuum of respiratory conditions with high prevalence (estimated at 5 – 20%) in children[13], is associated with impaired behavioral and cognitive functioning[14–17]. Maganti and colleagues examined the presence of SDB in children with epilepsy and reported that nearly 40% of children with epilepsy had symptoms of SDB based on parent report[18–20]. Therefore, it is likely that neuropsychological factors are dually influenced by sleep disturbance and the underlying pathology of epilepsy.

To date, pediatric studies have characterized the frequency and nature of sleep problems in children with chronic epilepsy, often using retrospective report to obtain seizure history, but little is known about how early in the disorder sleep problems manifest or how they might affect neuropsychological functioning in this population. The study we report here examined the relationship between sleep problems and neuropsychological functioning in a well-characterized sample of children following the first recognized seizure using a prospective research design. This group of children is largely a new onset epilepsy group in that 76% of them had seizure recurrence within 36 months. The primary aims of this study were to (a) document parent-reported sleep patterns in children with first recognized seizures, (b) characterize the types and frequency of parent-reported sleep problems in children with first recognized seizures (c) examine the relationships between parent-reported sleep problems and specific seizure parameters including seizure type, age at first recognized seizure, the number of antiepileptic drugs (AEDs), and electroencephalography (EEG) findings, as well as magnetic resonance imaging (MRI) abnormalities, and (d) determine if parent-reported sleep problems are associated with neuropsychological functioning.

Method

Participants

Children were prospectively recruited from July 2000 through March 2004 as part of a larger ongoing longitudinal study to identify factors that predict children's adaptation to seizures. Families were requested to participate at two large academic medical centers located in Cincinnati, Ohio, and Indianapolis, Indiana. At the Indianapolis site fliers were also sent to physicians in private practice and to school nurses requesting them to forward the fliers to appropriate families. Children ages 6 to 14 years who had experienced a first-recognized seizure within the past 3 months were included. Children were excluded if their seizure resulted from an acute situational etiology such as toxin, infection, or trauma. They were also excluded if they had a chronic illness or a functional impairment (e.g., cerebral palsy) that limited their activities of daily living. Children were not excluded if it was determined that they had had a

prior seizure that had not been previously recognized as such. A comparison group of healthy siblings of the children with first recognized seizures was also recruited. This study was approved by the institutional review boards at both participating institutions. Parents signed consent forms, and children signed assent forms before participation.

The sample consisted of 349 children with seizures and 226 sibling controls. We collected sleep questionnaire and behavior rating data on 331 children with seizures and behavior rating data on 225 siblings. Demographic and clinical characteristics of this sample are presented in Table 1. The seizure diagnosis was made by history and EEG. Age of onset is distributed across the specified age range (ages 6 to 14 years). There were roughly equal numbers of boys and girls. IQ was estimated from the Kaufman Brief Intelligence Test (K-BIT)[21], a brief screening instrument that correlates highly ($r = .80$) with a Full Scale IQ obtained on the Wechsler Intelligence Scale for Children-Revised in children spanning the age range of this study. IQ estimates in this sample covered a broad range spanning from mild deficiency to the superior range; the mean and median IQs fall in the middle of the average range, which has been observed in other studies[22]. The sample represents a relatively broad sampling of onset ages and seizure types; the majority of children (91%) had only one seizure type. Children with partial seizures slightly outnumbered those with generalized seizures, which is characteristic of this population[23] and slightly less than half (45%) had idiopathic epileptic syndromes. The proportion with symptomatic syndromes was low (<10%) but not unexpected for onset at age 6 and above. Among children with symptomatic epilepsy syndromes, there were roughly equal proportions of common causes (malformation, neonatal, trauma, infection), which is consistent with population estimates[24].

Neuropsychological Examinations

Children underwent neuropsychological examination an average of 2.8 months after the first recognized seizure. Testing was administered in a neurology or neuropsychology clinic by psychometrists who were trained, observed, and certified on the test battery by a pediatric neuropsychologist. The specific tests comprising the three-hour battery are listed in Table 2. All of the instruments were administered according to the standardized procedures for each test; scores were converted to age-corrected standardized scores using the best available national norms for all tests except WRAML Design Copy, for which no norms are available. The many scores obtained from the test battery were subjected to factor analysis, which yielded Language, Processing Speed, Attention/Executive/Constructional, and Verbal Memory & Learning factors, described elsewhere[25].

Sleep Assessments

The parent or guardian of each child with a first recognized seizure completed the Sleep Behavior Questionnaire (SBQ)[26], a set of six questions having to do with the sleep timing and quantity of sleep (e.g., bedtime; wake time; sleep latency; nap duration) as well as a 29-item Likert-type rating scale designed to assess sleep problems. The SBQ total score is considered a global index of sleep problems with higher scores representing more sleep problems. The SBQ has five subscales (Bedtime Difficulties, Parent/Child Interaction During the Night, Sleep Fragmentation, Parasomnias, and Daytime Drowsiness) that measure specific sleep problems. The SBQ has one question related to sleep-disordered breathing (item 24: snores while sleeping). This item was used as a measure of sleep-disordered breathing in children with a first recognized seizure. The SBQ was not obtained for sibling controls. Cortesi and colleagues[26] have published SBQ scores for a group of 321 healthy children as well as for a group of 89 children with epilepsy (with duration of illness longer than one year) and a group of 48 of their healthy siblings. The 321 healthy children (154 boys, 167 girls with a mean age of 9.6 years) were recruited from five randomly-selected primary and middle public schools in Rome. They were equally distributed for age, sex, and SES. The age and gender distribution

for our sample of children with first recognized seizures and the Cortesi healthy control group are nearly identical. Because we did not obtain the SBQ from our sibling control group, we used these normative data for statistical comparisons with our seizure sample.

The primary caregiver completed the Child Behavior Checklist (CBCL)[27] for each child with a first recognized seizure as well as for each sibling control participant in order to provide a direct comparison between the children with seizures and their healthy siblings. There are seven items on the CBCL that are specific to sleep (nightmares, overtired, sleeps less than most children, sleeps more than most children, walks or talks in sleep, has trouble sleeping, and wets the bed) that were the basis for the comparison.

Statistical Analysis

Sleep Patterns—Descriptive statistics for total nighttime sleep on weeknights and weekends, naps, and sleep latency (how many minutes it takes to fall asleep at bedtime) were computed. Sleep latency in children with first recognized seizures was compared with the normative data provided by Cortesi et al.[26] using a one-sample *t*-test. Statistical comparisons were not made for total sleep time and nap duration because Cortesi et al. did not report comparable data for their normative sample[26].

Frequency and Types of Sleep Problems—We examined sleep problems in children with first recognized seizures by comparing their SBQ total and subscale scores with normative data[26]. Because the SBQ total and subscale scores were not normally distributed, non-parametric analyses were used when possible. However, because Cortesi et al.[26] reported mean and not median values, we were unable to compare our SBQ subscale medians to normative data. One sample *t*-tests were used for these comparisons. In order to ensure that correct statistical inferences would be drawn with one-sample *t*-tests, bootstrap analyses were carried out to verify that the sampling distributions of the SBQ means were normally distributed.

In addition, we constructed two subgroups of children with seizures by using the mean and standard deviation from the healthy control group data provided in Cortesi et al.[26]. A cutoff score of >2 standard deviations above the mean for the SBQ total score was considered indicative of significant sleep disruption.

We also examined the difference between children with first recognized seizures and their siblings on the seven CBCL scores. Because the CBCL difference scores between children with first recognized seizures and their siblings were normally distributed, we used paired *t*-tests for these comparisons.

We examined the frequencies of each of the five possible ratings for “snores” on the SBQ. The item is rated on a Likert scale from 1 to 5; nearly half of the responses were “1” or “never.” We also computed Spearman’s correlation coefficients between the snoring score and the neuropsychological factor scores.

Sleep and Demographic/Clinical Variables—Spearman’s rank correlation coefficient was calculated to test for an association between age and the SBQ scores. Mann-Whitney tests were used to investigate the association between the SBQ scores and gender, anti-epileptic drugs (yes/no), significant MRI abnormality (presence vs. absence), and EEG findings (presence vs. absence of slowing and presence vs. absence of epileptiform discharges).

A Kruskal-Wallis test was used to examine the association between primary seizure type (generalized tonic-clonic, AAM, complex partial, simple partial, partial with secondary generalization and absence) and the SBQ scores.

Sleep and Neuropsychological Function—Spearman's rank correlation coefficients were calculated to test for an association between IQ and the four neuropsychological factor scores with the SBQ scores. A one-sample *t*-test was used to test for a difference in neuropsychological factor scores between children whose SBQ total score was more than two standard deviations above the control mean vs. children whose SBQ total score was not above this cutoff.

Results

Sleep Patterns

Parent-reported mean total nighttime sleep during the week and on weekends for children with first-recognized seizures was $9.8 \pm .9$ hours and 10.1 ± 1.3 hours, respectively. Because Cortesi et al.[26] presented nighttime sleep (mean = $9.3 \pm .68$ hours) and did not differentiate between weekday and weekend nighttime sleep, we did not make formal statistical comparisons. Visual comparisons between our data and the Cortesi et al.[26] data show that parent-reported total sleep time during the week and on weekends was greater for children with first-recognized seizures by 30 minutes and 48 minutes, respectively. Mean sleep latency for first recognized seizure patients was 23.3 ± 24.2 minutes. Comparisons between the normative data[26] and our seizure sample demonstrated significantly longer sleep latency ($t = 10.7$, mean difference = 14.3, $p < 0.001$) in children with first-recognized seizures. Parents of 47 (14.2%) children with first-recognized seizures reported that their child napped during the day. Parent-reported nap duration in the seizure sample ranged from 15 to 180 minutes (mean = 76.7 ± 37.3 minutes).

Frequency and Types of Sleep Problems

Children with first-recognized seizures had significantly higher mean SBQ total scores than the normative comparison group ($t = 21.6$, mean difference = 16.0, $p < 0.001$) (see Table 3). Almost half (45%) of the sample ($n = 124$) had SBQ total scores >2 standard deviations above the mean for the SBQ total score, which was considered indicative of significant sleep disruption.

With regard to the types of sleep problems reported, children with first-recognized seizures had significantly higher scores on the Bedtime Difficulties ($t = 6.2$, mean difference = 1.3, $p < 0.001$), Daytime Drowsiness ($t = 28.0$, mean difference = 4.2, $p < 0.001$), and Parasomnia ($t = 13.9$, mean difference = 3.3, $p < 0.001$) subscales. Children with first-recognized seizures had significantly lower scores on the Parent-Child Interaction subscale ($t = -4.1$, mean difference = -1.0, $p < 0.001$). Children with first-recognized seizures did not differ from the normative data[26] on the Sleep Fragmentation subscale ($t = 0.6$, mean difference = 0.1, $p = 0.569$) (see Table 3).

With regard to sleep-disordered breathing, 48% of our sample of children with first recognized seizures was rated as "never" snoring during the previous six months. Another 12% were rated as snoring "a few times" and 25% were rated as snoring "sometimes." In contrast, 5% snored "often" and 9% "always" snored during the previous six months.

Compared to their siblings, children with first-recognized seizures had significantly more sleep problems as measured by each of the seven CBCL sleep items except bedwetting (see Table 4).

Sleep and Demographic/Clinical Variables

There were no significant associations between gender and any of the SBQ scores. Age at seizure onset was associated with the SBQ total score ($r = -0.19$, $p < 0.001$), Bedtime Difficulties ($r = -0.21$, $p < 0.0001$) and Parent-Child Interaction ($r = -0.31$, $p < 0.001$)

subscales of the SBQ. The negative correlation coefficient indicates that younger age of seizure onset was associated with more sleep difficulties.

The number of antiepileptic drugs (AEDs) required was associated with the Parasomnia subscale ($\chi^2 = 9.4, p = 0.009$). Almost half (48%) of the children were not taking an AED; half (50%) were taking one AED; and seven children (2%) were taking two AEDs. The median parasomnia score for children taking at least one AED was 12.0, compared to a median of 11.0 for children not taking an AED.

Although there was a significant association between primary seizure type and Daytime Drowsiness ($\chi^2 = 11.1, p = 0.049$), no pair-wise comparisons were significant at the 0.01 level of significance. There was a significant association between seizure type and Sleep Fragmentation ($\chi^2 = 14.3, p = 0.014$). Pair-wise comparisons indicated that children who had partial seizures with secondary generalization had significantly higher Sleep Fragmentation scores than did children with primarily generalized tonic-clonic seizures (median 11.0 vs. 9.0, $\chi^2 = 8.5, p = 0.004$). Children with idiopathic/familial seizures had significantly higher Sleep Fragmentation scores than did children with symptomatic/cryptogenic seizures (median 12.0 vs. 10.0, $\chi^2 = 4.2, p = 0.040$).

The presence of a clinically relevant finding on MRI of the brain was associated with the SBQ total score ($\chi^2 = 5.1, p = 0.024$), Sleep Fragmentation ($\chi^2 = 5.4, p = 0.020$) and Parent-Child Interaction ($\chi^2 = 4.2, p = 0.042$) subscales. For all three scores, children with a significant MRI abnormality had significantly higher sleep problem scores. Finally, EEG findings (i.e., epileptiform discharges or slowing) were not associated with any of the SBQ subscales.

Sleep and Neuropsychological Function

Estimated intellectual function (K-BIT score) was associated with the SBQ total score ($r = -0.25, p < 0.001$), Bedtime Difficulties ($r = -0.20, p = 0.001$), Daytime Drowsiness ($r = -0.14, p = 0.013$), Sleep Fragmentation ($r = -0.16, p = 0.006$), and Parasomnia subscales ($r = -0.14, p = 0.013$). The negative correlation coefficient indicates that lower K-BIT scores were associated with more sleep difficulties.

Multiple associations between the SBQ scores and the neuropsychological factor scores for the children with seizures were observed and are shown in Table 5. All correlation coefficients were negative, indicating that more sleep difficulties were associated with worse neuropsychological functioning. The SBQ total score and the Bedtime Difficulties and Sleep Fragmentation subscale scores from the SBQ were significantly associated with all four neuropsychological factors. The Parasomnia subscale was significantly associated with both the Language and Attention/Executive/Constructional factor scores. The Parent-Child Interaction subscale score was significantly associated with the Attention/Executive/Constructional factor score. Children with seizures and significant sleep disturbances scored significantly worse on all measures of cognitive functioning than children with seizures without significant sleep disturbances (see Table 6).

Given that some of our sample of children with first-recognized seizures had recurrent seizures, we compared the association between sleep and neuropsychological function in children with recurrent seizures and those with only a single seizure using regression models. There was no significant difference in the association of these factor scores with any of the sleep problem subscales from the SBQ for those children with recurrent seizures compared to those with a single seizure.

With regard to sleep-disordered breathing, children who never, a few times, or sometimes snored did not differ from those who often or always snored on any of the neuropsychological

factor scores. Similarly, the ratings for snoring did not correlate with neuropsychological performance (Spearman's r ranged from $-.10$ to $-.02$).

Discussion

Early Onset of Sleep Disturbances in Children with Seizures

These findings document that sleep disturbances in children with seizures are already present at onset, and these sleep problems were associated with lower neuropsychological functioning. The detection of sleep problems in children with seizures is consistent with previous findings in chronic populations[2,6,26], but it is remarkable that they appear so early in the course of the disorder (especially considering that 26% of these children have not even had a second unprovoked seizure). Furthermore, the degree of sleep problems was more severe than might be expected at this early stage: nearly half of the children had sleep problem scores that were more than two standard deviations higher than normative group data[26]. Thus, as we have previously shown with behavior problems[28], sleep problems are present at the onset of seizures in a considerable number of children. The exception to this was the frequency of snoring, assumed to reflect sleep-disordered breathing, in our sample: only 14%, generally consistent with estimates of 5 to 20% in children[21] and considerably less than the 40% in children with epilepsy reported by Maganti et al.[19].

Our observation that children with first recognized seizures have worse sleep patterns than their healthy siblings is consistent with two prior studies[2,26]. With respect to specific types of sleep disturbance, our data showed convergence with previous findings in that our sample was characterized by higher levels of symptoms indicative of sleep onset problems[26], daytime somnolence[2,26] and parasomnias[2,26] as measured by the SBQ factor scores. We did not replicate the previous findings that children with seizures have more difficulty maintaining sleep during the night[2,26] (i.e., fragmented sleep) and have more problems with parent-child interactions during the night[2]. We are not able to make definitive conclusions regarding this discrepancy; however, it is possible that sleep consolidation was unaffected at the onset of illness (seizures), when our sample was studied. It may be that issues contributing to sleep fragmentation and parent-child interactions during nocturnal awakenings are influenced by learning and environmental factors that become more pronounced in children with chronic epilepsy and persistent sleep difficulties.

Associations Between Sleep and Neuropsychological Functioning

A number of relationships between sleep problems and neuropsychological functioning were observed. The significant negative correlation between the SBQ total score and all of the neuropsychological factor scores indicates that sleep disruption is broadly related to neuropsychological functioning in children with seizures. The relationships between sleep problems and neuropsychological performance were not different for those children with only a single seizure at the time of the assessment and those children with recurrent seizures.

Bedtime difficulties appeared to have the most extensive relationship to neuropsychological functioning in that they were significantly correlated with all of the neuropsychological factor scores. Sleep fragmentation was also associated with a number of neuropsychological domains, including Language, Processing Speed, and Verbal Memory & Learning. In contrast, symptoms of parasomnia were associated with Language and Attention/Executive/Construction, but not with Verbal Memory & Learning factor scores, demonstrating some specificity in the relationship between varying types of sleep disturbance and neuropsychological function.

The relationship between sleep problems and neuropsychological performance was also evident when we compared the children with first-recognized seizures with significant sleep disturbance to those without significant sleep disturbance. Those who had significant sleep disturbance had lower performance in all neuropsychological domains. Those without significant sleep disturbance had mean factor scores that were positive and close to zero; those with significant sleep disturbance had mean factor scores that were negative. Thus, there was a clear separation between the two groups with respect to their neuropsychological performance. It may be that sleep disturbance, as well as potential seizure-related variables, accounts for some of the differences in neuropsychological status among children with first-recognized seizures.

Relationships Between Sleep and Illness Factors

We found a number of interesting relationships between sleep and illness factors in children with first-recognized seizures. The association between the number of AEDs and level of parasomnia symptoms suggests that polytherapy may exacerbate sleep related arousal due to parasomnia. Previous research conducted by Batista and colleagues[6] demonstrates that children on polytherapy had worse sleep habits than children on monotherapy. Taken together, these data suggest that polytherapy may affect both intrinsic (e.g., partial arousal parasomnia) and extrinsic (e.g., sleep behavior) features of sleep. The negative correlation between age at onset of seizures and the global index of sleep problems, the presence of bedtime difficulties and parent-child interaction problems during the night indicates that the younger children had more problems in these areas. Cortesi and colleagues[26] studied a group of children with idiopathic epilepsy similar in age to our sample and reported that similar problems (i.e., bedtime difficulties and parent-child interaction) on the SBQ were worse in children of younger age.

There were some findings relating seizure type and syndrome to sleep fragmentation but not to any of the other aspects of sleep disturbance captured by the SBQ. Children with partial seizures with secondary generalization or idiopathic seizures had more difficulty with sleep fragmentation than children with generalized tonic-clonic seizures or symptomatic/cryptogenic seizures. Given that this observation was made in children with first recognized seizures, some of whom had only one seizure, it may be that sleep fragmentation is more susceptible to the short-term effects of seizures than behavioral aspects of sleep disturbance such as bedtime difficulties or parent-child interaction, which are likely to evolve over time in the context of a risk factor such as epilepsy.

An interaction between nocturnal EEG abnormalities (e.g., paroxysmal activity) and sleep disturbance has been previously reported[26]. Such a relationship has been cited as evidence that epileptiform discharges have an important role in arousal disorders of sleep[26]. We did not make any observations to support or refute the hypothesized relationship between EEG abnormalities and disorders of arousal. This may be because most of the EEG data we had was from routine (i.e., not sleep-deprived) studies.

We are not aware of any previous research that has attempted to examine the relationship between MRI findings and sleep problems in children with seizures or epilepsy. The observed association between the presence of a clinically relevant finding on MRI and the global index of sleep problems, fragmented sleep, and problematic parent-child interactions during the night suggests that greater neurological pathology may lead to worse sleep.

Significance and Limitations

This study advances the previous research in this area in a few important ways. First, the published pediatric studies to date have used samples of children with chronic epilepsy (i.e., time since diagnosis of at least one year or greater). We are not aware of any other published

studies that have investigated sleep problems in children with newly recognized seizures and documented the existence of sleep problems at this early stage. Second, we have taken additional steps to better clarify the extent of sleep problems in children with first recognized seizures by applying a cut-off criterion relative to healthy control subjects. Finally, we observed a significant relationship between sleep problems and neuropsychological functioning, one facet of daytime functioning that had not previously been assessed using an extensive neuropsychological battery. Our data on sleep and cognition shed light on an area that was previously lacking and necessitated further investigation[9].

Limitations of this study should be considered when interpreting the results. It is well-known that rater bias can influence self-report measures. The measurement of sleep is not immune to this methodological issue. We chose the SBQ because it was developed specifically for use with children and has been used as a sleep outcome variable in several investigations of pediatric epilepsy. There are data to suggest that some paper-and-pencil sleep questionnaires show correlation with sleep diaries and objective sleep recording[29,30].

Our assessment of sleep-disordered breathing was limited to parent report on one item of the SBQ. Because there is a known relationship between sleep-disordered breathing and daytime cognitive and behavioral function, future studies examining the relationship among cognition, behavior, and sleep in patients with epilepsy should include more rigorous measures of sleep-disordered breathing.

Two studies[20,31] have objectively measured differences in sleep architecture (e.g., stage I density; REM latency) and sleep continuity measures (e.g., total sleep time; time in bed) in children with epilepsy using polysomnography. Although the use of polysomnography as an outcome measure in sleep research might be the most comprehensive and objective measurement tool, it will likely continue to be cost-prohibitive in large scale studies. Future studies should attempt to use an integrated measurement methodology that includes both retrospective paper-pencil measures and objective indices of sleep. Actigraphy, for example, should be considered as a cost effective objective sleep measure when polysomnography is impractical.

Conclusions

In summary, our findings support the accumulating evidence that documents a higher prevalence of sleep problems in children with epilepsy and the role that compromised sleep has on health and behavioral outcomes in this population. It has been reported that even in cases of children with mild epilepsy, sleep problems occur frequently and lead to complications such as parent and child distress and psychological dysfunction (e.g., behavioral problems such as inattention)[32]. Our data suggest that even in the earliest stage of seizure diagnosis, sleep problems exist and are associated with important health and neuropsychological outcomes. Thus, clinicians working with children with seizures should place a high priority on evaluating for sleep disturbances and intervening early to help prevent and/or minimize the impact of sleep problems in their patients. There are some aspects of sleep disturbance that may be considered difficult to manage (e.g., arousal disorders) or even an untreatable associated symptom. However, the observation that children with new seizures have greater bedtime problems and issues related to parent-child interactions, suggest that behavioral intervention may have an important role in the overall management of pediatric epilepsy. Evidence-based behavioral interventions have been demonstrated to be effective for treating bedtime problems and night wakings in children[33,34]. Use of such interventions in the pediatric epilepsy population is ripe not only for clinical application but also for intervention and outcomes research.

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Table 1
Demographic and Clinical Characteristics of the Samples

	Total Sample (N = 332) Mean (SD)	Siblings (n=225) Mean (SD)
Age	9.6 (2.5)	9.6 (2.4)
IQ (Estimated from K-BIT)	100.9 (15.3)	103.6 (13.2)
	Percent	Percent
Gender (% Female)	51%	51%
Handedness (% Left-Handed)	11%	11%
Race		
White/Non-Hispanic	84%	86%
African-American	14%	12%
Hispanic	1%	1%
Other	1%	1%
Primary Seizure Type		
Generalized Tonic-Clonic	23%	
Atonic, Akinetic, Motor	1%	
Complex Partial Seizures	26%	
Simple Partial	6%	
Partial with Secondary Generalization	29%	
Absence	13%	
Unknown/Unclassified	2%	
Etiology of Seizures		
Idiopathic	45%	
Partial Cryptogenic	39%	
Partial Symptomatic	8%	
Generalized Cryptogenic/Symptomatic	3%	
Unknown	5%	
Neurological Exam		
Normal	94%	
Abnormal	5%	
Not Done/Missing	1%	
Number of anti-epileptic drugs		
0	48%	
1	50%	
2	2%	
Significant MRI abnormality	14%	
EEG slowing	11%	
EEG epileptiform discharges	61%	

Table 2
Neuropsychological Tests Administered

Kaufman Brief Intelligence Test (K-Bit)[21]
Clinical Evaluation of Language Fundamentals, Third Edition[35]
Comprehensive Test of Phonological Processing[36]
Conners' Continuous Performance Test, 2 nd Edition v5.0[37]
Coding and Symbol Search subtests of the Wechsler Intelligence Scale for Children, 3 rd Edition[38]
Wide Range Assessment of Memory and Learning – Verbal Learning, Story Memory, Design Memory subtests and Design Copy[39]
Wisconsin Card Sorting Test[40]

Table 3
Sleep Behavior Questionnaire Total and Subscale Scores

SBQ Score	Our Seizure Sample		Cortesi et al. Sample[26]	
	Mean	S.D.	Mean	S.D
Total	54.2	13.5	38.2	7.8
Bedtime difficulties	7.7	3.8	6.4	2.9
Daytime drowsiness	9.7	2.7	5.5	1.5
Sleep fragmentation	9.0	3.1	8.9	2.7
Parasomnia	12.2	4.3	8.9	2.5
Parent-child interaction	7.4	4.4	8.4	2.8

Table 4

CBCL Sleep Items

Item	Children with seizures		Siblings		t-statistic	p-value
	Mean (Median)	SD (Range)	Mean (Median)	SD (Range)		
47) Nightmares	0.4 (0)	0.6 (0–2)	0.2 (0)	0.5 (0–2)	3.6	<0.001
54) Overtired	0.4 (0)	0.6 (0–2)	0.3 (0)	0.6 (0–2)	2.1	0.039
76) Sleeps less than most children	0.3 (0)	0.7 (0–2)	0.2 (0)	0.6 (0–2)	2.1	0.040
77) Sleeps more than most children	0.3 (0)	0.6 (0–2)	0.1 (0)	0.4 (0–2)	2.5	0.015
92) Walks or talks in sleep	0.4 (0)	0.6 (0–2)	0.3 (0)	0.5 (0–2)	2.4	0.017
100) Has trouble sleeping	0.4 (0)	0.7 (0–2)	0.2 (0)	0.5 (0–2)	2.8	0.005
108) Wets the bed	0.1 (0)	0.4 (0–2)	0.1 (0)	0.4 (0–2)	0.4	0.697

Note. Numbers immediately preceding the Item Description refers to the item number on the CBCL.

Table 5

Spearman correlations between neuropsychological factor scores and SBQ Total Sleep Score and subscale scores for children with seizures

	Language	Processing Speed	Attention/Executive Construction	Verbal Memory & Learning
Total Sleep Score	-0.19 **	-0.18 **	-0.26 **	-0.18 **
Bedtime Difficulties	-0.14 *	-0.14 *	-0.23 **	-0.18 **
Daytime Drowsiness	-0.06	-0.10	-0.01	-0.09
Sleep Fragmentation	-0.15 *	-0.18 **	-0.12 *	-0.13 *
Parasomnia	-0.12 *	-0.11	-0.18 **	-0.10
Parent-Child Interaction	-0.03	0.01	-0.18 **	-0.09

* $p < .05$

** $p \leq .01$

One-sample t-tests examining differences on neuropsychological factor scores between sleep problem sub-groups for children with seizures

Table 6

	≤ 2 SD above		> 2 SD above control		t-statistic	t-test p-value
	MEAN	STD	MEAN	STD		
Language	0.07	0.87	-0.22	0.91	2.72	0.0069
Processing speed	0.07	0.90	-0.17	0.91	2.21	0.0280
Attention/Executive/Construction	0.05	0.82	-0.28	0.81	3.39	0.0008
Verbal memory	0.03	0.85	-0.18	0.81	2.19	0.0296