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Sleep architecture and behavioral abnormalities in children and adolescents

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Abstract

Objective—wa to investigate the association between sleep disordered breathing (SDB) and parent report of attention and behavioral problems in children, as well as the association between sleep stage duration and measures of child functioning in a clinically referred sample.

Methods—A chart review was conducted of 95 children with clinical history of SDB who completed an overnight polysomnography study in a pediatric sleep laboratory. Child functioning was assessed at the time of the sleep study by parent report on the Child Behavior Checklist (CBCL). The apnea hypopnea index was used as a measure of SDB severity.

Results—The apnea hypopnea index was associated with externalizing behavior, but not attention problems on the CBCL. In children 2-3 years old, stage 4 sleep duration was associated with externalizing behavior. In children 4-16 years old, REM sleep duration was associated with externalizing behavior.

Conclusions—Children with increased SDB severity may be at greater risk for behavioral problems. Differences between the association of sleep stages and externalizing behavior in toddlers compared with older children suggests possible developmental differences in the association between sleep and behavior.

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Keywords

Sleep disordered breathing; pediatric behavior problems; child behavior checklist; apnea

INTRODUCTION

Sleep is an important barometer of pediatric wellness, as evidenced by the association between decreased sleep and a complex array of negative outcomes, including increased accidental injury (1,2), reduced academic performance (3,4), obesity (5) and increased parental stress (6,7). However, there are significant gaps in our understanding of the exact nature of the relation between sleep and neurobehavioral functioning of children (8). Research on children with sleep disordered breathing (SDB) may provide unique insights into this relationship. SDB ranges in clinical severity from snoring to obstructive sleep apnea. The underlying pathophysiology of SDB, including increased airway resistance, inflammation, sleep architecture changes, and gas exchange abnormalities; identifies possible mediators between sleep and child functioning. Previous studies of the association of SDB with child behavioral problems have yielded conflicting results. In this study, we investigated the relation between a) SDB severity and parent report of child functioning as well as b) the relationship between sleep architecture and functioning in children with clinical histories of SDB.

The association between parent report of SDB symptoms and child mood, behavior, and attention problems has been investigated. In a large sample of 3,019 five year olds from a birth cohort, children with parent report of frequent or loud snoring, observed apnea episodes, or noisy sleep breathing were significantly more likely to have parent ratings of hyperactivity and aggression compared to children without SDB symptoms (9). In a primary care clinic sample of 872 children 2-14 years old, parent report of child SDB symptoms children at high risk for SDB by parent report were two to three times more frequently identified by parents as having conduct behavioral problems (e.g. bullying, quarrelsome, destructive) on the Conners Parent Rating Scale compared to children at lower risk of SDB (10). In contrast, a comparison of 43 three to six year old children with parent report of snoring did not differ from 46 non-snorers in parent report of externalizing or behavioral problems on the Child Behavior Checklist (CBCL), but snorers did have higher ratings of internalizing or anxious/depressed mood (11). Differences between these two studies may be related to different measures used to assess behavior problems as well as true differences in the association of SDB with mood/behavior problems among different age ranges and cultures (US and Finnish) studied.

The above studies, however, did not include objective measurements of SDB. Overnight polysomnography studies and parent report of child functioning have been completed in community samples of children. The Tucson Children's Assessment of Sleep Apnea Study assessed 403 children ages 6-11 years old (approximately 40% Hispanic) by overnight polysomnography and parent report of behavior. Ratings of somatic complaints, social problems, and aggressive behaviors on CBCL as well as oppositional behaviors on Conners Parent Rating Scale were significantly associated with SDB (12). Similarly, significant

association between externalizing behavior problems and SDB were noted in the Cleveland Children's Sleep and Health Study, which assessed children 8 – 11 years old from a birth cohort designed to overrepresent African American and premature birth children (13). In both of these studies, PSG was conducted unattended in a home based setting, and SDB was determined either by a) parent report of habitual snoring and/or objectively measured apnea-hypopnea index or b) respiratory distress index, respectively. A clinical referred sample of 235 children ages 3-18 years was evaluated by overnight PSG in a sleep laboratory for assessment of suspected SDB (14). This sample did not include a control group without symptoms of SDB. There were no significant associations between SDB severity and CBCL internalizing or externalizing scores. In this sample with a spectrum of SDB, the strongest predictor of behavioral problems was presence of at least one additional sleep diagnosis. The lack of association between SDB severity and behavioral problems was also noted in the Tucson Children's Assessment of Sleep Apnea Study (13), in which behavioral scores were not progressive across respiratory index categories. In another study, 35 children with PSG confirmed SDB were compared with 35 control children matched for ethnicity, age, gender, maternal education, and maternal smoking (15). Children were designated as having SDB based on a composite score including apnea hypopnea index, respiratory arousal indices, and desaturation. There were no significant differences on parent report of behavior on CBCL or Conners Parent Rating scale, but children with SDB scored significantly lower on an attention subtest completed as part of a neuropsychology assessment battery.

In summary, studies investigating the relationship between behavior and SDB have differed in terms of age range of child, ethnic/racial demographic composition, and method of assessing sleep disordered breathing problems. The contradictory findings may be due to possible developmental differences in the association of SDB with child functioning as well as methodological issues in terms of threshold for determination of SDB. The above studies also focused on relation between measures of SDB or SDB severity and child functioning. They did not report on possible associations between measures of sleep architecture (e.g. duration of sleep stages) and behavior or attention in the samples studied, and did not report on the relation between SDB severity and attention measures. We hypothesize that REM and slow wave sleep duration would be inversely correlated with parent report of behavior problems because of the important role these sleep stages play in memory consolidation, a cognitive process that impacts learning and by extension the acquisition of prosocial behaviors. We also anticipate that measures of SDB severity would be associated with measures of attentional problems, as there is growing evidence of overlap between cognitive and behavioral symptoms of SDB and attention deficit hyperactivity disorder.

In this study, we tested the following hypotheses about the possible relation between sleep parameters and parent report of child functioning: We hypothesized that a) a measure of sleep disordered breathing severity (the apnea hypopnea index) would correlate positively with parent report of child inattention and b) both REM and slow wave sleep duration would correlate negatively with measures of externalizing behavior.

METHODS

We conducted a chart review of 95 children ages 2-16 years old, who were clinically referred for an overnight polysomnography sleep study because of symptoms consistent with SDB. Children with co-morbid medical conditions, with the exception of asthma, were excluded. This study was conducted with IRB approval at University of Maryland. We analyzed the relationship between apnea severity (AHI) and parent report of child functioning (CBCL); as well as the relationship between sleep stage duration and child functioning.

Measures

Polysomnography standard overnight monitoring was accomplished with the Alice 4 diagnostic system (Respironics, Murrysville, PA, USA). The patient slept in a quiet darkened room up to seven hours with a parent or guardian present. The montage included EEG leads O1A2, O2A1, C1A2, C2A1, LOC, ROC, submental EMG, EKG, measurements of airflow (oronasal thermistor) and end tidal CO₂ (ETCO₂), chest and abdominal impedance using strain gauges, and oxyhemoglobin saturation using a Nellcor pulse oximeter. Respiratory events were described as: 1) obstructive apneas, with cessations of airflow with continued thoracic and/or abdominal respiratory effort lasting two respiratory cycles in duration; or 2) hypopneas, with reductions of airflow >50% associated with ≥4% fall in oxygen saturation or post-event arousal. The severity of OSA was defined by the apnea-hypopnea index (AHI; number of obstructive apneas and hypopneas per hour of sleep). The arousal index included respiratory and non-respiratory arousals per hour of sleep. Baseline and nadir oxyhemoglobin saturation, baseline and peak ETCO₂ in addition to sleep stage were recorded. No patient was acutely ill on the night of the study. Polysomnographic scoring was performed in 30 s epochs according to the Rechtschaffen-Kales criteria by the same technician and reviewed by one of two pulmonologists, who were blinded to CBCL score.

Child behavioral/emotional functioning

Versions of the caregiver-completed CBCL were used to assess child behavioral/emotional functioning: the CBCL/2-3 (16) for toddlers and preschoolers and the CBCL/4-18 (17) for older children. The CBCL is a widely used and reliable behavior symptom checklist that records child behavior problems along with areas of competency. Consistent evidence over 4 decades on content validity supports the ability of the CBCL to discriminate significantly between demographically matched (age, gender, SES, ethnicity) referred and non-referred youth. Parents or parent surrogates are asked to rate the degree to which they believe each item on the CBCL is true of their child within the past 2 months, for the CBCL/2-3 or 6 months, for the CBCL/4-18, on a scale from 0 (not true) to 2 (very true or often true).

According to the scale authors, the CBCL can be completed independently by parents with at least a 5th-grade reading skill level. Both versions yield scores on three broadband scales: Internalizing, Externalizing, and Total Problems, syndrome scales and DSM-IV oriented scales. Percentiles and standardized T scores are used to estimate a child's level of impairment relative to the population, and cut points have been prescribed for children with scores falling into the "borderline" (93rd percentile) and "clinical" (98th percentile) ranges

that do not differ by child gender, SES, or racial/ethnic background. The 99 items on the CBCL/2-3 cluster into six empirically-derived syndrome scales (anxious/depressed, withdrawn, sleep problems, somatic problems, aggressive behavior and destructive behavior). The Internalizing scale consists of two syndrome subscales (anxious/depressed, withdrawn). The Externalizing scale consists of two syndrome subscales (destructive behavior and aggressive behavior). The CBCL/4-18 consists of 113 items. Syndrome scales consist of social withdrawal, somatic complaints, anxiety/depression, social problems, thought problems, attention problems, delinquent behavior, aggressive behavior and sex problems. The internalizing scale comprises the social withdrawal, somatic complaints and anxiety/depression scales, while the externalizing scale comprises the delinquent behavior and aggressive behavior scales.

Data analysis

Descriptive statistics include means for continuous data and percents for dichotomous variables. Because age was found to be highly associated with both behavior and sleep variables, associations between these variables are expressed as partial Pearson correlations, age-adjusted. We used t-tests to compare medicated with nonmedicated patients.

RESULTS

Clinical records from 95 children who presented for evaluation of possible obstructive sleep apnea were reviewed for this study. Table 1 presents characteristics of the sample, which includes 15 boys, 8 girls in the 2-3 year age range, and 35 boys, 37 girls in the 4-16 year range. About 82% were African American, 18% Caucasian, and 7 with race data missing. The majority of patients (76%) were on Medical Assistance, while 24% had private insurance. Among the 95 patients, 72 were completely unmedicated, 23 were on some medication. Only two children in the 2-3 year old group were on medication (corticosteroids). In the 4-16 year group, 15 were taking corticosteroids (1 systemic, 14 nasal corticosteroids) and 6 were on psychotropic medications (5 stimulants and 1 antidepressant).

Table 2 presents age-adjusted correlations among the sleep variables and results on the behavioral instruments for all subjects combined. No significant correlations were observed between sleep variables and internalizing behavior or problems with attention. Stage 1 sleep duration was significantly positively associated with externalizing behavior ($r = .28$, $p = .007$). Stage 4 sleep, slow wave sleep duration, and REM sleep duration were significantly negatively associated with externalizing behavior; age-adjusted correlations ranged from $-.21$ to $-.25$. REM sleep duration was also negatively associated with total behavior problems ($r = -.25$, $p = .03$). In terms of children meeting CBCL threshold for clinically abnormal functioning, only 8 children had externalizing scores ≥ 70 , and only 6 with internal scores ≥ 70 .

Table 3 presents bivariate correlations for children in the 2-3 year old age group only. For these young children, stage 4 sleep duration was strongly negatively associated with externalizing scores ($r = -.53$, $p = .01$) and total problems ($r = -.50$), while slow wave sleep duration had a negative association with externalizing behavior ($r = -.41$, $p = .06$) at a

borderline level of significance. In the older age group (4-18 years), REM stage sleep duration was found to be negatively correlated with externalizing, internalizing, and total behavior problems (see table 4). The apnea-hypopnea index (AHI) and stage 1 sleep duration were both significantly positively correlated with externalizing behavior. Because of possible confounding effects of medications, we analyzed the data in a subsample of unmedicated individuals in the older age group (only 2 children were medicated in the younger age group). In this subsample, REM stage sleep duration was negatively associated with total behavior problems and there was a tendency towards a negative correlation with internalizing and externalizing problems. Stage 1 sleep duration was positively associated with internalizing and externalizing problems, and somewhat with total problems. We also assessed correlations with children on corticosteroids and psychotropics omitted, respectively. Results were similar to those where all medicated children were omitted, although associations for REM sleep duration are stronger when psychotropic medications are omitted.

DISCUSSION

Our first hypothesis concerned the relation between a measure of SDB severity and inattention. There was no significant association between AHI and attention problems for children 4-16 years old. We anticipated a positive association between AHI and inattention since sleep impairment leads to daytime sleepiness and individuals with the more severe form of SDB, obstructive sleep apnea. The lack of association may be due to the lack of observer data from a structured school setting. Teachers may be more able to accurately report inattention problems in comparison to same age peers. However, other studies suggest that the relation between inattention and SDB may be less robust in children than adults. A comparison of 19 children with moderate to severe obstructive sleep apnea to 12 control subjects reported similar inattention scores on continuous performance task, but lower performance on measures of verbal working memory and word fluency in the apnea group (18). Differences between children and adults in measures of inattention may be due to differences in daytime sleepiness. In a multiple sleep latency test conducted with 54 children with obstructive sleep apnea compared with 14 children with primary snoring and 24 control participants, mean daytime sleep latencies did not differ between the obstructive sleep apnea and primary snoring group and sleep latency was significantly but mildly reduced in apnea patients compared to controls (23.7 minutes $\pm$ 3.1 minutes compared to 20.0 $\pm$ 7.1 minutes)(19). Further, only 4 parents indicated observation of daytime sleepiness and only 13% of children with obstructive sleep apnea had mean sleep latencies <10 minutes.

In our sample, there was a positive correlation between the AHI and externalizing score among 4-16 year old children. Although the association between SDB and daytime sleepiness may be less strong in children than adults, sleep fragmentation caused by apnea episodes/arousals may be associated with greater impulsivity and hyperactivity symptoms. There was no significant association between AHI and externalizing behavior in 2-3 year old children. The difference between these two age groups may be due to the higher level of supervision and structured activity for toddlers compared to school age children. Because young children also have less exposure to a large number of peers and adults, their

environment may be better adapted to their needs and less likely to introduce interpersonal conflict.

In testing our second hypothesis about the relation between slow wave sleep and REM sleep duration with externalizing problems, we found a significant negative correlation between stage 4 sleep duration and parent report of externalizing problems in 2-3 year old children, and a trend towards a significant association between total slow wave sleep and externalizing problems. In 4-16 year olds, there was a significant negative correlation between REM duration and externalizing problems. The differences between the specific sleep stages associated with behavior problems in toddlers compared to older children raises an interesting question about whether there are true developmental differences in these associations. A meta-analysis of quantitative sleep parameters across development in healthy individuals reported a modest but significant increase in REM sleep from childhood to the end of adolescence and a negative correlation of slow wave sleep with age(20). Surprisingly, the total sleep time did not change significantly from age five through adolescence for healthy children studied on non-school days. Changes in sleep stages time without changes in total sleep time suggest that sleep functions may change across development. In our study, there was no association between externalizing behavior and total sleep time for either age group; the correlation appeared to be specific to REM sleep in school age children and stage 4 sleep in toddlers.

We propose that associations of NREM and slow wave sleep duration with externalizing problems are mediated by effects of sleep impairment on cognitive processes that promote learning during development. Sleep has been associated with explicit learning processes (21). REM sleep is characterized by psychophysiological properties that allow for optimum cognitive flexibility compared to brain states while awake, including increased prefrontal lobe function, decreased aminergic dominance, and increased weak associative memory networks (22). Both REM and slow wave sleep have been shown to contribute to the consolidation of complex, emotionally salient declarative memories (23). Further, a MRI study of untreated adults with OSA compared to control subjects also indicates alterations in white matter, including axonal connections to the hippocampus and amygdale, centers critical for learning and memory (24).

Our study participants included predominately African American children. A study that compared PSG studies of non-clinically referred Caucasian and African American children ages 5-7 years old found similar sleep architecture between the two racial groups, except periodic limb movements were more prevalent among the Caucasian children (25). However, African American youth have higher prevalence of sleep disordered breathing compared to other ethnic groups (26).

Limitations

Data on childhood functioning were limited to one time parent report of child functioning on the CBCL. Comprehensive assessment of child mood and behavior functioning requires synthesis of data from multiple sources, including child, parent, teacher report as well as direct observation of the child. However, an advantage of utilizing the CBCL is that, unlike

the DSM, which utilizes the same criteria for disruptive behavior disorders across the lifespan, the CBCL is normed for each gender within specific age groups.

Sleep data in this study were obtained from a single overnight polysomnography study conducted in a sleep lab. REM sleep has been shown to increase during a second consecutive sleep study (27), and children have higher ratings of sleep efficiency during home based monitoring than in a sleep laboratory. Also, data were obtained from a clinically referred sample during one time encounters. We did not adjust for body mass index. It is unclear if associations between externalizing problems and slow wave or REM sleep differ in a non-clinical sample or if the associations would persist after intervention/improvement of SDB.

Childhood externalizing behaviors are concerning in the long run because of their association with future mood and behavior problems. Parent report of elevated, persistent child aggressive behaviors over childhood is positively associated with both teacher report of externalizing behavior problems in early adolescence and adolescent self report of poorer quality friendships (28). Also, parent report of child externalizing behaviors has been demonstrated in a longitudinal sample to be predictive of early adult depression (29).

CONCLUSIONS

In summary, this study provides evidence of possible associations of externalizing problems with stage 4 sleep in toddlers and REM sleep in older children from a clinically referred sample. Future studies are needed to assess associations between externalizing problems and sleep parameters in non-referred samples, as well as the associations between sleep alterations and externalizing problems. Specifically, future studies should test for specific respiratory, architectural, molecular (e.g. cytokines) aspects of sleep changes in relation to specific aspects of cognitive development such as memory, language, and learning that may mediate these relations. More extended periods of ambulatory monitoring would also be needed to assess consistency of these associations within an individual. Ultimately, intervention studies which modify sleep architecture (e.g. increase REM sleep duration in children with disruptive behavior) are needed to further understand whether sleep changes mediate, modulate, or are the consequence of childhood behavior problems.

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Table 1

Characteristics of study patients

	All children	2-3 years [*]	4-16 years
	N=95 (100%)	N=23 (24%)	N=72 (76%)
Age, mean (range)	6.7 (1.6-16.0)	2.8 (1.6-3.8)	7.9 (4.0-16.0)
Gender n (%)			
Male	50 (52.6)	15 (65.2)	35 (48.6)
Female	45 (47.4)	8 (34.8)	37 (51.4)
Race n (%)			
Caucasian	16 (18.2)	5 (23.8)	11 (16.4)
African-American	72 (81.8)	16 (76.2)	56 (83.6)
Insurance n (%)			
Medical Assistance	72 (75.8)	14 (60.9)	58 (80.6)
Private	23 (24.2)	9 (39.1)	14 (19.4)
Medications n (%)			
Unmedicated	72 (75.8)	21 (91.3)	51 (70.8)
Medicated	23 (24.2)	2 (8.7)	21 (29.2)
Corticosteroid	17 (18.1)	2 (8.7)	15 (21.1)
Psychotropic	6 (6.3)	0 (0)	6 (8.3)

^{*} 3 children were between 1.6 and 2 years of age

Table 2

Age-adjusted correlations between sleep variables and child behavior scores in children ages 2-16 (n=95)

Sleep Variable	Internalizing Problem n=95		Externalizing Problem n=95		Total Problems n=81		Attention problem ** n=72	
	r*	p	r	p	r	p	r	p
AHI	0.081	0.435	0.152	0.142	0.033	0.770	0.053	0.658
Stage 1	0.136	0.191	0.278	0.007	0.116	0.305	0.104	0.388
Stage 2	0.146	0.160	0.153	0.141	0.153	0.173	0.125	0.300
Stage 3	-0.029	0.775	0.045	0.141	0.006	0.957	0.161	0.179
Stage 4	-0.137	0.187	-0.244	0.018	-0.189	0.094	-0.170	0.155
SWS	-0.149	0.151	-0.212	0.041	-0.179	0.112	-0.069	0.570
REM	-0.154	0.138	-0.247	0.017	-0.252	0.034	-0.179	0.135
Total sleep time	-0.061	0.557	-0.138	0.187	-0.137	0.228	0.037	0.762

*
r = age-adjusted partial correlation, with associated p-value

**
Attention not measured in 2-3 year olds

Table 3

Age-adjusted correlations between sleep variables and child behavior scores in children 2-3 years old only (n=23)

Sleep Variable	Internalizing Problem n=23		Externalizing Problem n=23		Total Problems n=23	
	r [*]	p	r	p	r	p
AHI	−0.012	0.957	−0.111	0.622	−0.108	0.631
Stage 1	−0.127	0.572	−0.014	0.950	−0.072	0.752
Stage 2	0.221	0.324	0.222	0.321	0.249	0.263
Stage 3	0.085	0.704	0.306	0.166	0.220	0.326
Stage 4	−0.329	0.135	−0.534	0.010	−0.489	0.021
SWS	−0.293	0.186	−0.406	0.061	−0.397	0.068
REM	0.073	0.747	−0.111	0.624	−0.038	0.865
Total sleep time	−0.086	0.705	−0.329	0.136	−0.252	0.259

* r = age-adjusted partial correlation, with associated p-value

Table 4

Age-adjusted correlations between sleep variables and child behavior scores in children 4-16 years old only (n=72)

Sleep Variable	Internalizing Problem n=72		Externalizing Problem n=72		Total Problems n=72		Attention problem n=72	
	r [*]	p	r	p	r	p	r	p
AHI	0.102	.398	0.237	0.047	−0.012	0.927	0.053	0.658
Stage 1	0.166	0.167	0.313	0.008	0.151	0.262	0.104	0.388
Stage 2	0.082	0.496	0.101	0.401	0.066	0.625	0.125	0.300
Stage 3	−0.033	0.785	0.018	0.879	−0.027	0.843	0.161	0.179
Stage 4	−0.064	0.598	−0.176	0.141	−0.076	0.573	−0.171	0.155
SWS	−0.082	0.498	−0.160	0.182	−0.090	0.508	−0.069	0.570
REM	−0.264	0.026	−0.323	0.006	−0.421	0.001	−0.179	0.135
Total sleep time	−0.070	0.565	−0.115	0.342	−0.136	0.318	0.037	0.762

*
r = age-adjusted partial correlation, with associated p-value