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# Neurobehavioral correlates of sleep-disordered breathing in children

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**SUMMARY** The effects of sleep-disordered breathing (SDB) on neurobehavioral function were examined in two matched groups of children from the general population. Thirty-five children with polysomnographically confirmed SDB were matched for ethnicity, age, gender, maternal educational attainment, and maternal smoking, to healthy children with no evidence of SDB. Children with SDB had significantly lower mean scores on the Differential Ability Scales for General Conceptual Ability (similar to IQ) and for the Non-verbal Cluster. On the neuropsychology assessment battery (NEPSY), children with SDB scored significantly lower than the control group on the attention/executive function domain and two subtests within that domain, one measuring visual attention and the other executive function. In addition, children with SDB scored significantly lower than the controls on one subtest from the NEPSY language domain: Phonological Processing. This subtest measures phonological awareness, a skill that is critical for learning to read. No differences in behavior, as measured by the Child Behavior Checklist (CBCL) or the Conners' Parent Rating Scale, were found between the two groups. Using a novel algorithm to assess sleep pressure, we found that children with SDB were significantly sleepier than controls. Furthermore, total arousal index was negatively correlated with neurocognitive abilities, suggesting a role for sleep fragmentation in pediatric SDB-induced cognitive dysfunction.

KEYWORDS neurocognitive function, sleep fragmentation, sleep-disordered breathing

## INTRODUCTION

Sleep-disordered breathing (SDB) is a common, albeit underdiagnosed, condition in children. Estimates of the prevalence of SDB in children range from 1 to 3% (Ali *et al.*, 1993; Blunden *et al.*, 2001; Brouillette *et al.*, 1984; Gislason and Benediktsdottir, 1995; Hulcrantz *et al.*, 1995); snoring, the hallmark symptom of SDB, affects as many as 27% (Ali *et al.*, 1993, 1994; Ferreira *et al.*, 2000; Gislason and Benediktsdottir, 1995; Hulcrantz *et al.*, 1995; Owen *et al.*, 1996; Teculescu *et al.*, 1992). SDB is characterized by repeated events of partial or complete upper airway obstruction during sleep, resulting in disruption of normal ventilation, hypoxemia, and sleep fragmentation. The primary symptom of SDB is snoring and the sequelae of SDB include growth impairment (Everett *et al.*, 1987), cardiovascular consequences (Amin *et al.*, 2002; Marcus *et al.*, 1998; Tal *et al.*, 1988), and neurobehavioral deficits (Chervin *et al.*, 1997; Gozal, 1998; Guilleminault *et al.*, 1982; Urschitz *et al.*, 2003).

In the adult literature there exists a body of information suggesting that SDB is associated with a wide range of neurocognitive deficits, which may be a consequence of the accompanying sleep fragmentation and/or hypoxemia. In adults, results of studies in which experimental sleep fragmentation was produced by inducing arousal with an auditory stimulus have indicated that participants aroused at various intervals during the night demonstrate performance

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decrements and increased sleepiness (Chugh *et al*., 1996; Rodin *et al*., 1962; Stepanski *et al*., 1984, 1987). Aggressive outbursts, irritability, anxiety and depression are all known manifestations of excessive daytime sleepiness (EDS) in adults, and appear to be fully reversible once sleep recovery is allowed (Chugh *et al*., 1996). However, in contrast to adults with SDB, EDS does not appear to be a major feature of childhood SDB (Carroll *et al*., 1995; Frank *et al*., 1983; Gozal *et al*., 2001a), although EDS-like morbidity is present in children.

Although neurobehavioral consequences in adults have been extensively investigated, the consequences in children have not yet been fully evaluated. There is emerging evidence that children with SDB show deficits in neurocognitive performance, behavioral impairments and reduced school performance (Blunden *et al*., 2000, 2001; Gozal, 1998; Lewin *et al*., 2002; Owens *et al*., 2000; Rhodes *et al*., 1995), which may be at least partially reversible with treatment (Ali *et al*., 1996; Friedman *et al*., 2003; Gozal, 1998; Lewin *et al*., 2002; Owens *et al*., 2000; Stradling *et al*., 1990; Tal *et al*., 1988). Problematic behaviors (Blunden *et al*., 2000; Lewin *et al*., 2002) have been reported in small numbers of children with SDB compared with matched controls. Conversely, Ali *et al*. (1996) found no difference in behaviors or in measures of attention and impulsivity for children with untreated SDB compared with controls, although improvements were observed in such measures following treatment in the SDB group. Such studies have been limited by the small number of participants and selected populations, i.e. children referred to a sleep disorders center (Lewin *et al*., 2002) or an ear, nose and throat (ENT) department (Blunden *et al*., 2000), and only one study has performed full polysomnography on both SDB and control children (Blunden *et al*., 2000). Thus, the effects of SDB on neurobehavioral function have yet to be reported in an unselected sample of children from the general population. The aim of the present study was to evaluate the relationship between SDB and neurobehavioral performance in a group of non-referred and matched control children from the local community.

## METHODS

Parents of children enrolling in the first grade of the local metropolitan school system completed a detailed sleep habits questionnaire (Gozal, 1998). In addition to demographic information and significant medical history of the child, the major questions addressed whether or not the child snored and if so, the severity of the snoring. The responses were graded as 'never', 'rarely' (once per week), 'occasionally' (twice per week), 'frequently' (three to four times per week) and 'almost always' ($>4$ times per week). families were subsequently contacted by telephone and children were recruited if they were reported to snore frequent or almost always. Non-snoring children were recruited in the same fashion as controls. All children were invited to the sleep laboratory for an overnight polysomnographic assessment, in order to identify those with SDB, and the following morning a battery of neurobehavioral tests was administered. Children were excluded if they had any chronic medical conditions or genetic or craniofacial syndromes, or if they had been diagnosed with developmental delay.

### Polysomnographic assessment

A full overnight polysomnographic assessment was performed and the following parameters were measured: chest and abdominal wall movement; heart rate; air flow and end-tidal carbon dioxide levels; arterial oxygen saturation ($SpO_2$); bilateral electro-oculogram (EOG); eight channels of electroencephalogram (EEG); chin and anterior tibial electromyograms (EMG); body position; tracheal sound. All measures were digitized using a commercially available polysomnography system (REMbrandt Systems, Medcare Diagnostics, Amsterdam, the Netherlands) and a digital time-synchronized video recording was performed. Analysis of the polysomnogram was performed using standard techniques. In brief, sleep staging was assessed using Rechtschaffen and Kales (1968) criteria. The obstructive apnea/hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of total sleep time (TST) and obstructive apnea was defined as the absence of airflow with continued chest wall and abdominal movement for a duration of at least two breaths (American Thoracic Society, 1996; Marcus *et al*., 1992). Hypopneas were defined as a decrease in nasal flow of $\geq$50% with a corresponding decrease in $SpO_2$ of $\geq$4% and/or arousal (American Thoracic Society, 1996). The mean $SpO_2$ together with $SpO_2$ nadir was determined. Arousals were defined as recommended by the American Sleep Disorders Association Task Force report (Sleep Disorders Atlas Task Force, 1992) and include respiratory-related (occurring immediately flowing an apnea, hypopnea or snore), technician-induced and spontaneous arousals. Arousals were expressed as the total number of arousals per hour of sleep time (arousal index). In addition, as a surrogate measure for sleepiness, the recently developed Sleep Pressure Score (SPS) (Tauman *et al*., 2004) was calculated for each subject's polysomnographic record using arousal indices as follows:

$$\mathrm{SPS} = (\mathrm{RAI}/\mathrm{ARtotI}) \times (1 - \mathrm{SAI}/\mathrm{ARtotI})$$

where RAI is the respiratory arousal index, SAI the spontaneous arousal index and ARtotI is the total arousal index.

A SPS score $\geq$0.25 was used as the threshold for evidence of increased sleepiness (Tauman *et al*., 2004).

Empirical data for the definition of SDB in children have yet to be fully delineated. As oxyhemoglobin desaturations in the presence of an AHI $>$ 1 are associated with morbidity (Goodwin *et al*., 2003) a composite score incorporating desaturations would better represent SDB than a conventional but arbitrary threshold of AHI $>$ 5. Furthermore, as sleep fragmentation may be also associated with morbidity, respiratory arousal indices were included in the composite score. Children were assigned composite scores according to the severity of the sleep disturbance (Table 1). Children were identified as having SDB if the composite score was $\geq$5.

**Table 1** Composite scores for sleep disturbance

| | *0* | *1* | *2* | *3* |
|---|---|---|---|---|
| Apnea/hypopnea index | 0–0.9 | 1.0–4.9 | 5–9.9 | ≥10 |
| Respiratory arousal index | 0–0.9 | 1.0–4.9 | 5–9.9 | ≥10 |
| $SpO_2$ nadir | ≥90 | 85–89 | 80–84 | ≤80 |

Composite score maximum = 9 with a threshold of ≥5.

Children with SDB were matched for ethnicity, gender, maternal education level, and maternal smoking to non-snoring children with a composite score ≤1 (control children). Children were matched for maternal smoking as the latter is known to significantly increase the risk of snoring in children (O'Brien *et al.*, 2003).

### Neurobehavioral assessments

A battery of neurobehavioral tests was administered the morning following polysomnographic assessment. The parent completed the long form of the Conners' Rating Scales-Revised (Conners, 1997) while the child was undergoing neurocognitive assessment. The Conners' is used to identify behavioral problems in children. The long version yields seven factors: Oppositional, Cognitive Problems/Inattention, Hyperactivity, Anxious-Shy, Perfectionism, Social Problems, and Psychosomatic and several summary indices, all with a mean T-score of 50 and a standard deviation (SD) of 10. The CBCL (Achenbach, 1991) is the most well developed, empirically derived behavior rating scale available for assessing psychopathology and social competence in children (Barkley, 1990). The parent-report version of the questionnaire yields eight factors: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior, and Aggressive Behavior and three summary indices, all with a mean T-score of 50 and a SD of 10.

The neurocognitive assessment included the Preschool Form of the Differential Ability Scales (DAS; Elliott, 1990) and the NEPSY (Korkman *et al.*, 1998). The DAS is a battery of cognitive tests designed to measure verbal, reasoning, and spatial ability. Individual DAS subtests are designed to measure separate and distinct areas of cognitive functioning and thus have high specificity. The ability score for a subtest is expressed as a T score with a mean of 50 and a SD of 10. The sum of the core subtest T-scores is converted to a total standard score, with a mean of 100 and a SD of 15. In addition to the six core subtests, two diagnostic subtests were administered (Matching Letterlike Forms and Recall of Digits). The NEPSY (Korkman *et al.*, 1998) is a relatively new neurobehavioral test battery and was designed to assess neurocognitive development in five functional domains: attention/executive functions, language, sensorimotor functions, visuospatial processing, and memory and learning. Domain and subtest standard scores have a mean of 100 and SD of 15. The sensorimotor domain was not assessed. In addition to the core subtests, two supplemental subtests were administered: Design Fluency and Sentence Repetition.

### Data analysis

Data are presented as mean ± SD unless otherwise indicated. For questionnaire-derived responses comparisons of the distribution of demographic and risk factors according to group membership were made with independent *t*-tests (continuous variables) with *P*-values adjusted for unequal variances when appropriate (Levene's test for equality of variances), or Fisher's exact test (dichotomous outcomes). Paired *t*-tests were used for comparisons of polysomnographic and neurobehavioral variables. Correlation and regression analyses were performed to evaluate potential relationships between sleep measures and neurobehavioral scores for the study groups. All *P*-values reported are two-tailed with statistical significance set at $< 0.05$.

## RESULTS

A total of 11 983 questionnaires were mailed with an overall response rate of 5728 achieved (47.6%). Contact was made with 576 families and of these, 438 agreed completed the sleep study and neurobehavioral evaluations. There were no significant differences in demographic information for those families who declined to participate and thus the sample studied was representative of the local population. Of the 438 children, 43 were found to meet the criteria for SDB. However, due to the stringent matching criteria only 35 children (17 boys) could be matched to a control child. Data is presented, therefore, on these 35 pairs. Demographic information on these two groups is given in Table 2.

### Polysomnographic characteristics

The results of the overnight assessment are shown in Table 3. Children with SDB had fewer spontaneous arousals ($P = 0.004$), increased respiratory arousals ($P < 0.001$) and total arousals ($P < 0.001$), increased AHI ($P < 0.001$), a

**Table 2** Demographic information for 35 children with SDB and matched controls

| | *SDB (n = 35)* | *Controls (n = 35)* |
|---|---|---|
| Mean age in years | 6.7 ± 0.6 | 6.7 ± 0.5 |
| Male gender | 17 (49%) | 17 (49%) |
| Body mass index (kg $m^{-2}$ ) | 19.8 ± 4.3 | 17.7 ± 3.5 |
| Ethnicity | | |
| African-American | 21 (60%) | 21 (60%) |
| White Non-Hispanic | 14 (40%) | 14 (40%) |
| Maternal educational attainment | | |
| College or higher | 21 (60%) | 21 (60%) |
| High school or lower | 14 (40%) | 14 (40%) |
| Maternal smoking | | |
| Yes | 13 (37%) | 13 (37%) |
| No | 22 (63%) | 22 (63%) |

**Table 3** Results of the overnight sleep study for 35 children with SDB and matched controls

| | *SDB (n = 35)* | *Control (n = 35)* |
|---|---|---|
| TST (min) | 472.4 ± 47.2 | 474.7 ± 46.1 |
| Sleep efficiency (%) | 90.8 ± 8.9 | 88.8 ± 8.5 |
| Sleep latency (min) | 18.6 ± 18.6 | 28.4 ± 36.0 |
| REM latency (min) | 130.0 ± 49.0 | 125.8 ± 54.6 |
| Stage 1 (%TST) | 9.8 ± 8.1 | 8.0 ± 7.4 |
| Stage 2 (%TST) | 45.2 ± 9.0 | 46.8 ± 8.6 |
| SWS (%TST) | 22.9 ± 6.4 | 23.5 ± 7.3 |
| REM (%TST) | 22.2 ± 7.3 | 21.7 ± 6.1 |
| Spontaneous arousal index | 5.4 ± 4.4** | 8.3 ± 3.1 |
| Respiratory arousal index | 9.8 ± 9.4*** | 0.2 ± 0.3 |
| Total arousal index | 14.7 ± 6.1*** | 9.2 ± 3.2 |
| Sleep Pressure Score | 7.1 ± 7.1*** | 0.0 ± 0.1 |
| Apnea/hypopnea index ($h^{-1}$ TST) | 9.8 ± 7.2*** | 0.4 ± 0.3 |
| Mean $SpO_2$ | 97.1 ± 1.6* | 97.9 ± 0.7 |
| $SpO_2$ nadir | 82.0 ± 7.7*** | 94.0 ± 1.7 |

TST, total sleep time; SWS, slow wave sleep; REM, rapid eye movement sleep. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

lower mean baseline oxygen saturation ($P = 0.009$) and a significantly lower $SpO_2$ nadir ($P < 0.001$) than the matched control group. Furthermore the SPS, a novel numerical factor as a surrogate measure of sleep fragmentation, was significantly higher in children with SDB ($P < 0.001$). Using 0.25 as the threshold value for increased sleep pressure (Tauman *et al.*, 2004), 34 of the 35 children in the index group had an elevated sleep pressure, compared with only one child in the control group (97% versus 3%, respectively; $P < 0.001$).

### Behavioral measures

Table 4 presents the mean and SD for the Conners' Rating Scales-Revised and the CBCL. No differences were found between the children with SDB and the controls for any measures from the Conners' Parent Rating Scales-Revised or the CBCL.

### Neurocognitive measures

Table 5 presents the mean and SD for the DAS and the NEPSY. For the DAS, mean scores in the SDB group were significantly lower for General Conceptual Ability (GCA; $P = 0.016$), which is similar to IQ, and for the Non-verbal Cluster ($P = 0.03$) Effect sizes were moderate (0.6 for each). Between-group differences approached significance for the non-verbal Pattern Construction subtest, a measure of spatial construction ($P = 0.06$) and the Auditory Attention subtest ($P = 0.08$) with effect sizes of 0.5 and 0.4, respectively. On the NEPSY, the SDB group performed significantly worse than the controls on the Attention/Executive Function domain ($P = 0.026$) with a moderate effect size of 0.6. Significant differences were found on two of the three subtests in this domain: the Tower subtest, which measures the executive functions of planning, monitoring, and self-regulation; and Visual Attention subtest ($P = 0.035$ and 0.046, respectively)

**Table 4** Results of the behavioral assessments for 35 children with SDB and matched controls

| | *SDB (n = 35)* | *Control (n = 35)* |
|---|---|---|
| Conners Parent Rating Scale | | |
| Oppositional | 56.2 ± 13.2 | 55.1 ± 14.7 |
| Cognitive problems/Inattention | 59.6 ± 14.3 | 59.6 ± 14.5 |
| Hyperactivity | 60.8 ± 13.5 | 61.1 ± 14.9 |
| Anxious/Shy | 55.0 ± 12.3 | 55.6 ± 13.8 |
| Perfectionism | 51.0 ± 9.9 | 51.9 ± 11.4 |
| Social Problems | 52.2 ± 11.9 | 52.4 ± 12.3 |
| Psychosomatic | 59.7 ± 16.2 | 56.8 ± 14.9 |
| ADHD Index | 60.4 ± 12.2 | 58.3 ± 14.7 |
| DSM-IV Inattentive | 58.7 ± 13.9 | 56.7 ± 13.8 |
| DSM-IV Hyperactive – Impulsive | 62.9 ± 13.9 | 61.9 ± 14.4 |
| DSM-IV Total | 61.3 ± 13.6 | 59.7 ± 14.7 |
| CBCL | | |
| Withdrawn | 55.7 ± 6.5 | 57.2 ± 8.4 |
| Somatic Complaints | 61.7 ± 9.1 | 61.0 ± 9.7 |
| Anxious/depressed | 56.3 ± 8.9 | 58.3 ± 9.6 |
| Social Problems | 60.3 ± 9.4 | 59.8 ± 9.0 |
| Thought Problems | 57.9 ± 8.6 | 57.6 ± 8.8 |
| Attention Problems | 61.4 ± 9.4 | 60.5 ± 9.4 |
| Delinquency | 59.1 ± 8.6 | 57.8 ± 8.7 |
| Aggression | 59.2 ± 9.6 | 60.5 ± 12.0 |
| Internalizing Behaviors | 56.0 ± 11.9 | 57.8 ± 12.2 |
| Externalizing Behaviors | 56.8 ± 13.1 | 56.8 ± 13.5 |
| Total | 59.8 ± 11.8 | 59.9 ± 13.1 |

Values are given as mean ± SD. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

with moderate effect sizes. Group differences for the Language domain approached significance ($P = 0.084$); a significant difference with a moderate effect size was found for one subtest in this domain: Phonological Processing, which measures phonological awareness, a linguistic skill that is crucial for learning to read ($P = 0.047$).

### Correlational results

Correlation analyses were performed between affected sleep variables and neurobehavioral variables. To correct for the number of correlations computed between a particular sleep measure and a particular neurobehavioral or neurocognitive measure, correlations were only considered significant if $P \leq 0.005$. Total arousal index was found to be negatively correlated with DAS GCA ($r = -0.42$, $P = 0.001$), the standard score for the DAS Non-verbal Cluster ($r = -0.42$, $P = 0.001$), and the DAS Pattern Construction subtest ($r = -0.40$, $P = 0.001$). The negative correlation between total arousal index and the NEPSY Attention/Executive Function domain approached significance ($r = -0.34$, $P = 0.007$) with the correlation for the Tower subtest reaching significance ($r = -0.43$, $P = 0.001$).

## DISCUSSION

The main finding of this study is that children with polysomnographically defined SDB showed significant neurocognitive deficits relative to control children matched for gender,

**Table 5** Results of the DAS and NEPSY neurocognitive assessments for 35 children with SDB and matched controls

| | *SDB (n = 35)* | *Control (n = 35)* | *Effect size* |
|---|---|---|---|
| **DAS domains** | | | |
| Verbal Cluster | 91.2 ± 12.2 | 93.7 ± 11.2 | |
| Non-verbal Cluster | 93.3 ± 14.7* | 101.3 ± 13.0 | 0.6 |
| GCA (General Conceptual Ability) | 90.8 ± 12.2* | 97.8 ± 10.9 | 0.6 |
| *Subtests* | | | |
| Verbal Comprehension | 40.6 ± 7.6 | 42.1 ± 7.3 | |
| Naming | 49.1 ± 10.1 | 50.7 ± 8.7 | |
| Picture Similarity | 47.9 ± 9.5 | 50.0 ± 11.1 | |
| Pattern Construction | 49.1 ± 9.0¶ | 53.1 ± 8.3 | 0.5 |
| Copying | 45.2 ± 12.7 | 48.8 ± 7.9 | |
| Early Number Concepts | 43.9 ± 8.4¶ | 47.6 ± 8.4 | 0.4 |
| Recall of Digits | 51.7 ± 9.7 | 49.6 ± 7.8 | |
| Matching Letter-Like Forms | 47.9 ± 7.3 | 50.9 ± 7.3 | |
| **NEPSY domains** | | | |
| Attention/Executive | 98.7 ± 18.0* | 107.3 ± 12.3 | 0.6 |
| Language | 90.0 ± 14.4¶ | 96.9 ± 15.2 | 0.5 |
| Visuospatial | 95.4 ± 15.9 | 98.3 ± 15.6 | |
| Memory | 104.8 ± 17.9 | 106.1 ± 12.0 | |
| *Subtests* | | | |
| Tower | 10.2 ± 3.3* | 11.8 ± 2.2 | 0.6 |
| Auditory Attention and Response Set | 9.2 ± 2.9¶ | 10.2 ± 2.5 | 0.4 |
| Visual Attention | 9.5 ± 3.0* | 10.9 ± 2.5 | 0.5 |
| Design Fluency | 7.6 ± 2.6 | 8.0 ± 3.0 | |
| Phonological Processing | 7.8 ± 3.9* | 9.7 ± 3.4 | 0.5 |
| Speed Naming | 8.4 ± 3.2 | 8.6 ± 3.4 | |
| Comprehension of Instructions | 8.9 ± 3.3 | 9.9 ± 2.9 | |
| Design Copying | 9.2 ± 3.5 | 9.8 ± 3.3 | |
| Arrows | 9.0 ± 2.6 | 9.6 ± 2.6 | |
| Memory for Faces | 11.9 ± 3.2 | 11.6 ± 2.8 | |
| Memory for Names | 9.8 ± 3.4 | 10.0 ± 2.7 | |
| Narrative Memory | 10.2 ± 3.2 | 10.8 ± 3.3 | |
| Sentence Repetition | 10.0 ± 2.7 | 9.8 ± 2.6 | |

Values are given as mean ± SD. *$P \leq 0.05$; ¶$P \leq 0.09$.

ethnicity, age, maternal educational level (as a surrogate for socioeconomic status), and maternal smoking. Deficits were found in both overall cognitive ability (DAS GCA; similar to IQ), non-verbal ability (DAS Non-verbal Cluster standard score), Attention and Executive Function (NEPSY), and phonological awareness (NEPSY Phonological Processing subtest). One sleep parameter, Total Arousal Index, was significantly correlated with neurocognitive function on both the NEPSY and the DAS. Furthermore, results from use of a novel algorithm, which accounts for the reciprocal relation between spontaneous and respiratory related arousals in children and that is thought to represent a measure of sleepiness, indicated that children in the SDB group were significantly sleepier than controls. These data suggest a significant role for sleep fragmentation in neurocognitive dysfunction and raise important questions about the mechanisms by which SDB may lead to neurocognitive deficits.

Several aspects of this study merit comment. First, both SDB and control children were recruited from non-selected samples and were closely matched not only for age, gender, and socioeconomic status, but also for ethnicity and exposure to maternal smoking. Parental smoking has been shown to be a risk factor for snoring in children and has a dose–response effect (O'Brien *et al*., 2003). As it can be assumed that children spend most of their time with their mother, we only matched for the presence of maternal smoking. Moreover, all children underwent identical assessments of sleep and neurobehavioral function and children were categorized by strict criteria. This rigorous process lends credence to our findings. In addition, this is the first study to include a large number of African-American children.

We found no differences in behavior between children with SDB and controls. This is in agreement with those findings of Blunden *et al*. (2000), who did not find significant behavioral differences between SDB and control groups, despite a tendency for the parents of the SDB children to report more problems. However, our findings differ from Lewin *et al*. (2002), who found that children with SDB had significantly higher CBCL scores (indicating more problem behavior) than healthy controls for attention problems, anxiety/depression, social problems, and aggressive behaviors. Since problem behaviors are frequently associated with SDB in children (Ali *et al*., 1993; Chervin and Archbold, 2001; Chervin *et al*., 1997, 2002; Guilleminault *et al*., 1982; Owens *et al*., 2000) it may seem somewhat surprising that we did not uncover behavioral differences in the present study. The power for detecting behavioral disturbances may have been reduced due to the comparatively small number of subjects studied. Indeed, although the SDB group had mildly elevated scores on many subtests of both the Conners' and the CBCL questionnaires, the scores of the control population were also mildly elevated compared with published means. Nonetheless, a strength of this present study is that these subjects were closely matched and thus many potential confounding variables were well controlled. Furthermore, the children were drawn from a community sample rather than from children who were referred for evaluation and are therefore more representative of the general population.

The DAS was used in one previous study of children with SDB (Lewin *et al*., 2002). Lewin *et al*. compared a clinically referred sample with SBD to a healthy control group. Our findings replicate theirs, this time for a community sample with SDB rather than a clinically referred sample. An additional difference between the two studies is that our sample includes a large number of African-American children. Results of both studies indicated significant differences between the SDB and control groups for DAS GCA and for DAS Non-verbal Cluster standard score. Effect sizes also were similar in the two studies.

Blunden *et al*. (2000) found that a group of 5–10-year-olds with either obstructive sleep apnea or primary snoring scored significantly lower than a healthy control group on overall IQ, performance IQ, and verbal IQ as measured by the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) or the Wechsler Intelligence Scale for Children 3rd edition (WISC-III). In contrast, neither the findings of Lewin *et al*.

(2002) nor the results of the present study indicated the presence of verbal deficits in children with SDB relative to healthy controls. However, in the present study, the SDB group performed significantly lower than the controls on the NEPSY Phonological Processing subtest, which is part of the language domain. A deficit on this subtest, which measures an ability that is not assessed by the DAS, WPPSI, or WISC-III, is particularly concerning because phonological awareness is a key skill underlying the ability to read well (McBride-Chang and Kail, 2002).

Although the mechanism(s) by which SDB may contribute to deficits in neurobehavioral function remains unknown, the impaired performance in verbal abilities as well as the decrease in attention/executive function observed in SDB is consistent with dysfunction of the prefrontal cortex (PFC) regions of the brain (Beebe and Gozal, 2002; Harrison and Horne, 1998, 1999). Executive dysfunction, i.e. the inability to develop and sustain an organized, future-oriented, and flexible approach to problem solving, appears to be a prominent area of cognitive impairment in untreated SDB in adults (Beebe *et al*., 2003; Greenberg *et al*., 1987; Naegele *et al*., 1995) and our results have now extended these findings to the pediatric age. Our finding that the SDB group performed significantly worse than the control group on the NEPSY Visual Attention subtest provides further support to Blunden *et al*.'s (2000) finding that children with SDB had impairments in both selective attention and sustained attention, as measured by a continuous performance task. Indeed, a recent meta-analysis of adult studies has revealed a strong effect of SDB on vigilance (Beebe *et al*., 2003). It is possible that disruption of the sleep process, either via the sleep fragmentation or episodic hypoxia that characterize SDB, may lead to alterations in the neurochemical substrate of the PFC and result in executive dysfunction.

Although traditional measures of EDS in children (e.g. Multiple Sleep Latency Test) are relatively insensitive and cannot detect subtle changes in sleep propensity (Gozal *et al*., 2001b), we have utilized a novel algorithm to show that the SDB group had significantly more sleep propensity than the control group, thus supporting a role for sleep fragmentation in neurocognitive morbidity. Furthermore, in 10–14-year-old children, a single night of sleep restriction has been shown to impair higher cognitive functions, particularly verbal creativity (Randazzo *et al*., 1998). Sadeh *et al*. (2002) reported that fragmented sleep, as measured by actigraphic recordings, was associated with reductions in the ability to perform more complex neurobehavioral tasks involving executive control in children aged 7–12 years. These associations were strongest among 7-year-old children, i.e. the age group included in the present study. This is concerning, particularly given the high prevalence of SDB and objectively measured sleep fragmentation in school children (Sadeh *et al*., 2000).

In addition to sleep fragmentation, hypoxia may play a key role in neurobehavioral performance decrements in SDB. Some studies have shown that intermittent hypoxemia is associated with reduced neurocognitive function in adults (Berry *et al*., 1986; Findley *et al*., 1986; Naegele *et al*., 1995). Findley *et al*. (1986) found that patients with sleep apnea and hypoxemia had mean performance scores in the impaired range on measures of attention, concentration, complex problem-solving, and short-term recall of verbal and spatial information. In contrast, patients who had sleep apnea without hypoxemia had no mean performance score in the impaired range. Findley *et al*. also found that degree of hypoxemia was significantly correlated with degree of overall cognitive impairment. Nonetheless, not all studies of SDB in adults have found associations between hypoxemia and cognitive morbidities. Frequent oxygen desaturations during sleep are common in children with SDB (Gislason and Benediktsdottir, 1995; Stradling *et al*., 1990) and the present study supports this observation. A potentially serious consequence of intermittent hypoxia may involve its long-term deleterious effects on neuronal and intellectual function. Although $SpO_2$ nadir was significantly lower in the SDB group than in the control group in the present study, such desaturations were only transient and did not correlate with neurobehavioral function. It is possible that such short-lasting desaturations did not induce significant changes in brain tissue oxygenation. Alternatively, it is possible that even mild and infrequent transient oxyhemoglobin desaturations may impose adverse effects, particularly at a critical age for brain development. Indeed, studies in animals have recently unveiled a developmental period of neuronal susceptibility to episodic hypoxia during sleep (Gozal *et al*., 2001b), and postnatal ages equivalent to the peak prevalence of SDB in children were associated with more severe disruption in the acquisition of spatial tasks (Row *et al*., 2002).

In summary, we have demonstrated that children with SDB who have not been referred for evaluation of snoring have significant neurobehavioral morbidities compared with matched controls, particularly on tasks related to higher cognitive functioning. These impairments are associated with nocturnal sleep fragmentation and may or may not be fully reversible with appropriate treatment. Early identification and treatment of children with SDB is therefore a critical component in preventing the occurrence of substantial morbidities in this highly prevalent pediatric condition.

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