

Cognitive Effects of Sleep Apnea and Narcolepsy in School Age Children

David E. Hansen, Ph.D. and Brian Vandenberg, Ph.D.

To evaluate the effects of disordered sleep upon children's attention and memory skills, before and after treatment. Prior to polysomnographic evaluation and following treatment, apnea and narcolepsy patients completed measures of auditory attention, visual attention, and general memory. Pretreatment scores of apneic and narcoleptic children were compared with standardized norms; following treatment their performance was compared with pretreatment scores. Participants were fourteen school-age children referred for polysomnographic evaluation. Seven children received the diagnosis of obstructive apnea and seven were diagnosed with narcolepsy. Sleep-disordered patients performed lower than standardized norms on measures of attention and memory prior to treatment. Further, subjects' overall cognitive performance significantly improved following successful intervention. Separate posttreatment analyses revealed substantial improvement for both apnea and narcolepsy groups on overall measures of cognitive ability. The findings suggest that additional emphasis should be placed upon the clinical recognition, diagnostic accuracy, and early treatment of pediatric sleep disorders in order to avoid unnecessary diurnal complications. (*Sleep and Hypnosis* 2001;3(2):73-80)

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INTRODUCTION

Although there exist numerous pediatric sleep disorders as defined by the DSM-IV and the American Sleep Disorders Association, the majority of these problems are transient in nature and/or present problems primarily at night (e.g. insomnia, enuresis, nightmares, night terrors, somnambulism). Sleep apnea and narcolepsy, conversely, are often chronic, potentially lifelong disorders that give rise to the daily experience of excessive hypersomnolence and numerous diurnal complications. The pathological components of apnea and narcolepsy are unrelated and each disorder is characterized by a distinctly different pattern of diagnostic features. Yet, recent research among adult populations indicates that sufferers of apnea and narcolepsy may

experience numerous daytime difficulties.

Associated Daytime Symptoms

Apnea

The most frequent complaint associated with apnea is constant, unrelenting fatigue (1). Such fatigue frequently manifests in additional symptoms such as depression, increased irritability, and volatility (2). Symptoms of depression among apnea patients are so frequent, in fact, that some researchers argue that obstructive sleep apnea should be routinely screened in cases of chronic or unremitting depression (3). Additionally, apnea patients commonly report decreased occupational and social functioning, reduced ability to maintain attention and focus, more physical and emotional difficulties, decreased energy, and worse mental health than controls (4). Other reports indicate an increased frequency of headaches and concentration difficulties (5,6).

Address reprint requests to: Brian Vandenberg, Ph.D., University of Missouri-St. Louis, Department of Psychology-Stadler Hall, 8001 Natural Bridge Road, St. Louis, MO. 63121, USA
Phone: ++314-516-5476 e-mail: BVANDEN@UMSL.EDU

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Neuropsychological tests generally support the subjective complaints of apnea sufferers and, in fact, suggest numerous cognitive deficits of which patients may be unaware. Neuropsychological performance decrements have been consistently demonstrated for adult sufferers of apnea compared to healthy control subjects, especially on tasks that require sustained attention and concentration; immediate and delayed recall of visual or verbal information; higher cognitive (e.g. problem solving) or executive functions (e.g. planning, sequential thinking); manual dexterity and motor speed; and learning of new material (7-10). Pre-post treatment designs also indicate a direct relationship between apnea and reported neuropsychological complications, as hypersomnolence (11), cognitive functioning (12,13), and levels of depression and fatigue (14) generally improve following successful interventions.

Narcolepsy

Compared with the adult apnea literature, evaluations of neuropsychological deficits associated with narcolepsy have found less conclusive evidence of impaired functioning (15-17). However, many sleep professionals and narcolepsy sufferers report numerous cognitive difficulties similar to those experienced by hypersomnolent apnea patients. Included in these reports are poor memory functioning, inability to sustain attention and concentration, difficulty learning new information (18), decreased occupational and social functioning (19,20), increased automobile and household accidents, and a variety of psychosocial difficulties (19).

Several researchers have demonstrated that while overall performance levels do not appear significantly different from normals, continuous plots of narcolepsy subjects' performances reflect distinct, intermittent lapses in their abilities (21,22). These lapses may occur as a result of brief "microsleeps" that intrude into the wakeful state, presumably providing minimal amounts of restoration in response to narcolepsy patients' chronic experience of fatigue. Providing further indication of narcolepsy's adverse effects, several studies have found improvements in performance and levels of alertness following behavioral treatments (i.e. napping schedule) and pharmacological interventions (23,24).

Pediatric Considerations

There is ample anecdotal and empirical evidence of significant diurnal difficulties associated with

apnea and narcolepsy among adults, including chronic hypersomnolence and fatigue, affective dysfunction, neuropsychological impairment, and decreased psychosocial functioning. Yet, the nature and extent to which these symptoms affect pediatric populations remains unclear. Despite the lack of empirical data pertaining to children, many pediatric specialists have long speculated that disordered sleep may contribute to daytime complications (25). This speculation has been based largely upon clinicians' direct observations and descriptive accounts.

In one of the earliest reports regarding daytime difficulties associated with pediatric apnea, Guilleminault and colleagues (26) documented that among eight children diagnosed with apnea, five experienced academic difficulties, poor attention spans, morning headaches, abnormal blood pressure, and periods of hyperactivity, while four required individual or family counseling for mood and personality changes. Similarly, a second group of researchers described 71 children selected from a clinic population due to their common experience of behavioral, developmental, and academic problems. Upon evaluation, this group of children was found to have greater rates of snoring and labored nocturnal breathing than did a randomly selected group of 355 clinic-referred children (27). In addition to such clinical reports, a seminal effort to empirically evaluate potential cognitive difficulties associated with pediatric apnea found apneic children to have markedly lower scores on measures of general memory, verbal memory, visual memory, learning abilities, and vocabulary compared to a non-apneic, clinic-referred, control group (28).

As with apnea research, the majority of published information regarding associated symptoms of pediatric narcolepsy is descriptive in nature. Such descriptions, nevertheless, provide dramatic accounts of children's struggle with narcolepsy symptoms. Among the case studies is the account of a 7 year old boy whose mother described as sleeping all the time-during school, while watching TV, while eating, and even at the physician's office. Additionally, he had scheduled naps of two to three hours a day. When he expressed emotions, such as laughing, he often fell to the floor from cataplexy. He reported seeing faces upon going to sleep, including the face of the devil; yet, he was generally unable to escape these images due to sleep-onset paralysis (29). A second account of a nine year old child describes similar experiences, as well as decreased academic performance and loss of social relationships as his need for daytime naps interfered with

social functions (30).

Despite compelling clinical information and preliminary research suggesting impairment of children's daytime functioning associated with disordered sleep, few empirical evaluations have focused upon diurnal complications unique to pediatric populations. Considering the adult literature, which documents a variety of adverse diurnal effects, there is ample reason to believe that children also experience numerous difficulties secondary to disordered sleep. In an effort to clarify the nature and severity of such deficits, the present study examines the effects of apnea and narcolepsy upon the cognitive abilities of children. Specifically, attention and memory functions of children with apnea and narcolepsy were investigated using standardized outcome measures, before and after treatment. It was hypothesized that children with apnea or narcolepsy would perform significantly lower than the standardized norms on each of the attention and memory measures. It was also hypothesized that, following treatment, apnea and narcolepsy subjects' attention and memory scores would significantly improve compared to pre-treatment performances.

METHOD

Subjects

The study consisted of ten male and four female children who were referred for polysomnographic evaluation of daytime hypersomnolence. Following polysomnographic evaluation, seven of the fourteen children were diagnosed with obstructive sleep apnea syndrome and seven were found to have narcolepsy. Patients with other medical conditions that commonly affect cognitive functioning (e.g. head injury, Down's Syndrome, asthma, seizure disorder) were not recruited for study participation. Urban and rural areas were similarly represented by the overall sample. Subjects age ranged from 7 to 16 years, with a mean age of 10.7 years. There were no significant differences between the ages of apnea or narcolepsy subjects (10.96 vs. 10.51). Regarding ethnicity, the sample included ten Caucasian (71%) and four African-American (29%) children.

Measures

Polysomnographic Measures

Included in the polysomnograph (PSG) were measures of respiratory effort, air flow, oxygen satu-

ration, and sleep stage. Cessation of breathing for a period of 10 seconds or more, a greater than 50% reduction in airflow or respiratory effort, or decreases in oxygen saturation below 90% were each considered to represent an obstructive respiratory event (31). Having more than 5 respiratory episodes (e.g., apnea/hypopnea) per hour was established as the cutoff criteria for identifying apneic children.

In addition to the night-time PSG, patients suspected of narcolepsy completed a Multi-Sleep Latency Test (MSLT) the following day, consisting of four monitored, daytime napping opportunities. Children were considered to have narcolepsy if they evidenced sleep latencies less than 19 minutes for one or more naps, accompanied by REM onset sleep, and displayed clinical symptoms consistent with narcolepsy, including excessive daytime somnolence, cataplexy, sleep paralysis and hypnagogic hallucinations.

Neuropsychological Measures

WISC-R Digit Span (Auditory Attention). Subjects are instructed to attend to and repeat a series of random number sequences (forward and backward) from two to nine digits immediately after they are read by the examiner. Raw scores are converted to standardized scale scores with a mean of 10 and standard deviation of three. Factor analyses indicate a substantial loading of this test upon the Freedom from Distractibility factor (Mdn loading = .56) and it is commonly employed as a measure of auditory attention. Test-retest reliability ranged from .73 to .80 depending upon the child's age (33).

WRAML Finger Windows (Visual Attention). Subjects must visually attend to a plastic board with randomly spaced holes, as the examiner indicates certain holes by pointing. The subject is then asked to reproduce the visual array in the same order. Raw scores are converted to standardized scale scores with a mean of 10 and standard deviation of three. The normative statistics for this subtest suggest high internal consistency with a median alpha coefficient of .81 across the 5 to 17 year old age groups (34). A second measure of reliability, the Person Separation Index, was also high at .91. Test-retest reliability was not provided for this specific subtest, although the WRAML as a whole has a stability coefficient of .84. General Memory. To account for both verbal and visual memory skills, four subtests (two verbal and two visual tasks) were administered from the Wide Range Assessment of Memory and Learning (WRAML), and an overall composite score for the

four tests was derived. Given limited sample size and reduced power, the single composite score, rather than the four separate subtests, served as the dependent measure of general memory ability. Raw scores for each of the four subtests were converted to scale scores with a mean of 10 and standard deviation of three, which were then added together and converted to a standard score with a mean of 100 and standard deviation of 15.

Correlations of overall WRAML scores with other measures of children's memory skills provide estimates of criterion referenced validity. Sheslow and Adams (34) found six and seven year old children's scores to correlate with the McCarthy Memory Index at .72 overall, while ten and eleven year olds' WRAML scores correlated at .80 with the Stanford Binet Short Term Memory test. The WRAML scores of 16 and 17 year olds correlated with the Wechsler Memory Scale at a .54 level; however, the authors raised concerns that the Wechsler Scale may not provide an appropriate criterion reference given the Wechsler scores that were obtained. Specifically, the Wechsler scale indicated a significant 19 point difference between mean verbal and visual memory scores (Verbal < Visual) while the WRAML scores suggested average performance in both modalities, with a difference of only seven tenths of one point. Given the random selection of high school students, the WRAML scores appear more consistent with the expectation and probability of obtaining average scores from such a sample. Separate measures of reliability for the four General Memory subtests ranged from .78 to .87 (coefficient alphas) and .79 to .92 (Person Separation Statistics).

Procedure

Completion of the neuropsychological measures occurred approximately two hours prior to the PSG. As a standard procedure of the sleep laboratory, in order to avoid potential medication effects on the PSG, all medications were discontinued at least two weeks prior to testing. PSG evaluation employed a standard montage, including the attachment of electrodes to the scalp (EEG), temple area (EOG), legs and chin (EMG), thoracic region (EKG), as well as thermistor (airflow), respiratory belts, and oximetry placement. Children who presented with signs of narcolepsy also completed a multisleep latency test the following day. Formal diagnoses of apnea and narcolepsy were rendered by a treating physician who was blind to the results of neuropsychological testing.

Children that were treated for apneic or narcoleptic conditions were rescheduled for follow-up evaluation approximately five months subsequent to their original PSG. Apnea treatments included surgical and CPAP interventions. Treatment of narcolepsy included prescriptions of stimulant medications and behavioral management of napping opportunities. Post-treatment testing for all subjects paralleled the pre-treatment protocol.

RESULTS

In order to compare baseline cognitive scores with normative data, it was necessary to determine that demographic and statistical characteristics of the present sample reasonably approximated those of the dependent measures' standardization samples. Regarding demographics, data pertaining to age, gender, ethnicity, and urban-rural residence was previously summarized in the description of subjects' characteristics. Inspection of this data revealed that the overall sample (n=14) was similar to standardization samples that were proportionally based upon U.S. Census information. Analyses of apnea and narcolepsy subjects' age and ethnicity indicated no significant differences between groups. Children in the apnea condition averaged 13 respiratory events/hour with an average oxygen desaturation to 86 percent SaO₂.

Given the particular susceptibility of small samples to the effects of outlying scores, an initial screening of each group's test scores was conducted using frequency plots, descriptive statistics (e.g. means, standard deviations), and measures of skewness. Additionally, each group's distribution of scores on the three dependent measures was separately evaluated using the Shapiro-Wilks test of normality. Each of these analyses failed to indicate significant outliers or deviations from normality. Thus, although the sample size was small, the data was normally distributed, allowing for the use of parametric statistics. Furthermore, since standardized scores were used, this allows for comparison with normative data.

Pretreatment Cognitive Functioning

The apnea and narcolepsy groups were initially combined to examine the effects of diagnosable sleep disorders on children's cognitive abilities. Using z-tests analyses, comparisons to normative data found sleep disordered children's performance significantly below established norms on all three

cognitive measures. Impaired performances were indicated on tasks of auditory attention (Digit Span), $z=-2.76$, $p<.01$, visual attention (Finger Windows), $z=-2.14$, $p<.05$, and general memory, $z=-1.92$, $p<.05$ (see Table 1).

Examining the performances of apnea and narcolepsy groups separately, a clear trend of below average performance was apparent for both groups, across cognitive measures. Apnea subjects scored significantly below normative values on the measure of auditory attention (Digit Span), $z=-2.27$, $p<.01$, and their general memory performance approached levels of statistical significance, $z=-1.56$, $p=.06$. Visual attention (Finger Windows) was also below normative values, but did not reach levels of statistical significance. Children with narcolepsy scored significantly below normative values on auditory attention (Digit Span), $z=-1.64$, $p<.05$, and visual attention (Finger Windows), $z=-1.89$, $p<.05$. General memory, while also below normative values, was not statistically significant (see Table 1). There were no differences between the apnea and narcolepsy groups.

Post-Treatment Cognitive Functioning

As with pretreatment comparisons, narcolepsy and apnea subjects were combined to form a general sleep disordered group in order to examine the post-treatment cognitive performances of diagnosed and treated hypersomnolent children. One-tailed, paired t-tests were employed to evaluate pretreatment to posttreatment changes on each of the cognitive measures. Results indicated that the overall sleep disordered group's general memory performance significantly improved following treatment, $t(13)=1.91$, $p<.05$. Further, improved performance on the visual attention measure approached statistical significance, $t(13)=1.41$, $p=.09$. Only the measure of verbal attention failed to show noticeable improvement, $t(13)=.40$, $p=.35$ (see Table 2).

Considering the small sample sizes and the inherent limitations of statistical power, an additional t-test was conducted to compare pretreatment to posttreatment changes on the cognitive measures considered as a whole. This cognitive index score consisted of the verbal attention, visual attention,

Table 1. Baseline attention and memory functioning of apnea, narcolepsy, combined sleep disorder, and control groups

	Apnea (n=7)	Narcolepsy (n=7)	Combined (n=14) (Apnea & narc.)
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)
Digit Span	7.43**(0.98)	8.14* (1.68)	7.78**(1.37)
Finger Windows	8.71 (3.20)	7.86* (3.80)	8.29* (3.41)
General Memory	91.14 (16.75)	93.43 (14.89)	92.29*(15.27)

Normative values for Digit Span and Finger Windows are a mean of 10, standard deviation of three. General memory normative values are a mean of 100, standard deviation of 15.

* $p < .05$ compared to normative data

** $p < .01$ compared to normative data

Table 2. Pretreatment and posttreatment cognitive functioning, combined apnea & narcolepsy group

COMBINED APNEA AND NARCOLEPSY GROUP (n = 14)						
	Baseline		Post-Treatment		t-value	p
	Mean	(S.D)	Mean	(S.D)		
Digit Span	7.79	(1.37)	8.07	(3.47)	.40	.35
Finger Windows	8.29	(3.41)	9.23	(3.65)	1.41	.09
General Memory	92.29	(15.27)	99.29	(17.64)	1.91	<.05
Cognitive Index*	8.63	(1.81)	9.50	(2.17)	2.30	<.05

Normative values for Digit Span and Finger Windows are a mean of 10, standard deviation of three. General memory normative values are a mean of 100, standard deviation of 15.

*The Cognitive Index is an average of Digit Span, Finger Windows, and the four subscales that compose the General Memory Index. Normative values for the cognitive Index are a mean of 10, standard deviation of three.

p-values are based upon 13 degrees of freedom, one-tail t-test

and four general memory subtests combined. Comparison of pretreatment with posttreatment performance on the cognitive index indicated statistically significant improvement, $t(13)=2.30$, $p<.05$ (See Table 2). Separate consideration of the apnea and narcolepsy groups' pretreatment to posttreatment cognitive index scores indicated results that approach statistical significance $t(13)=1.52$ and 1.62 , $p=.09$ and $.07$, respectively.

DISCUSSION

The adult apnea and narcolepsy literature indicates a host of associated daytime complications, including chronic hypersomnolence and affective, cognitive, and psychosocial difficulties. Yet, despite clinical descriptions of similar problems among children, empirical efforts to document and clarify children's experience of these symptoms have been slow to develop. The findings of the present study substantiate clinical concerns and preliminary reports regarding the effects of sleep disorders upon children's cognitive functions and emphasize the need for additional study.

Pretreatment Cognitive Deficits

The findings of the present study indicate decreased cognitive functioning associated with the disordered sleep of children, as all three performance measures were significantly below normative values for the combined apnea/narcolepsy group. Further, mild performance decrements were found among apnea and narcolepsy subjects when each group was separately compared to normative values. In comparison with previous studies of sleep apnea, these results provide preliminary indications of mild cognitive difficulties among pediatric populations similar to those that have been found among adults with apnea (7-9,35). Although limited in severity, the obtained results are also consistent with the case studies, anecdotal information, and clinical speculation that predominate the pediatric literature (26,27). Yet, consideration of previous research suggests that the current results may only partially reflect the effects of apnea upon cognitive skills.

Rhodes and colleagues (28) obtained measures of vocabulary, verbal memory, and general memory that each fell within the deficient range for a group of five children diagnosed with apnea. The discrepancy between the severely impaired cognitive functions of these five children compared to the mild declines of the present sample may relate to differ-

ences in apnea severity. In the present study, the majority of children experienced mild levels of apnea, averaging 13 respiratory events/hour with an average oxygen desaturation to 86 percent SaO₂. Conversely, Rhodes' sample experienced an average of 32.8 respiratory events every hour, with a low oxygen saturation of 64.6 percent, indicating much more severe breathing problems. Thus, it appears that the present sample may best describe the nature of cognitive difficulties associated with mild levels of apnea, whereas increased respiratory disturbances may give rise to more severe cognitive deficits.

The present results also suggest mild cognitive difficulties among children with narcolepsy. Again, two of the three cognitive measures were performed significantly below standardized norms, with the third measure reaching significantly low levels in analyses of the overall (apnea/narcolepsy combined) sleep disorder group. Although such difficulties have long been reported by adult narcolepsy patients (18), empirical evaluations have generally failed to substantiate these complaints (15-17). Similarly, anecdotal accounts of pediatric narcolepsy have described symptoms of impaired vigilance and academic difficulties (29,30), yet supportive empirical evidence is absent from the literature. The current findings offer preliminary support to clinicians' and patients' claims regarding cognitive symptoms.

Posttreatment Cognitive Performances

Posttreatment findings provide confirmation of the link between disordered sleep and children's cognitive difficulties, as subsequent to treatment, subjects' overall performance significantly improved. Further, when viewed separately, both the apnea and narcolepsy groups' general level of posttreatment performance substantially improved. These findings generally support the efficacy of current treatment modalities and emphasize the need for early and accurate diagnosis and intervention in order to avoid the prolonged and unnecessary experience of diurnal complications. In fact, considering the mounting evidence of cognitive difficulties associated with disordered sleep, several researchers have called for an increased emphasis on diagnostic and treatment efforts (25,36).

Despite the difficulties of clinical research, especially with pediatric populations, continued efforts to overcome such obstacles and limitations are necessary in order to further clarify the diurnal effects of children's sleep disorders. Evaluation of sleep fragmentation, hypoxia, and REM deprivation effects

among children with apnea would provide important information regarding divergent symptom presentations, symptom severity, and associated cognitive effects. Similarly, the daytime difficulties of narcoleptic children who only experience the symptoms of EDS may significantly differ from those who experience the full tetrad of symptoms. Additionally, broadening the scope of dependent variables to include

measures of perception, psychomotor skills, problem solving, language and visuospatial functioning, and other performance abilities would better delineate the full range of cognitive effects. Improved clinical training, diagnostic accuracy, and the provision of treatment are dependent upon such empirical investigations that will further delineate both the breadth and severity of associated sleep disorder symptoms.

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