



Neuro UpdateSM

EXECUTIVE FUNCTIONING IN THE PRESENCE OF SLEEP-DISORDERED BREATHING: A CORRELATION OF NEUROCOGNITIVE SKILLS AND CORTICAL THICKNESS

Thomas G. Burns, Psy.D.; Greg Kirk, M.S.; Richard Jones, Ph.D.; Amy Sutton, M.A.; William G. Hamilton, Ph.D.; Gary Montgomery, M.D.

Sleep-disordered breathing represents a spectrum of upper airway conditions, ranging from mild, such as snoring, to severe, such as obstructive sleep apnea. Research has focused on the consequences of sleep-disordered breathing and reversibility of symptoms. Children with these problems may present with excessive sleepiness, failure to thrive and a variety of cognitive and behavioral dysfunctions, including impaired executive functioning.

The brain is described as an organization of specialized systems—each handling specific kinds of information, working relatively independently of each other to do routine tasks. When presented with a new task, however, these systems need to develop a responsive program. This process of defining the task, and designing a program to respond, is part of the brain's executive functions, which are believed to be mostly located in the anterior portion of the brain. These executive functions are responsible for purposeful, goal-oriented behavior. When trying to understand executive function, it is important to consider the relationships between these executive functions and the frontal lobes. Damage to the frontal lobe is thought to cause changes to executive function.

Beebe and Gozal developed a theoretical model to explain the impact of sleepiness and hypoxia on executive functioning. This model provides a framework for researchers to examine links between the medical disorder and the neuropsychological consequences. This study and its variables are driven by Beebe and Gozal's theory, using these constructs in their research design.

Children with sleep-disordered breathing are receiving increased attention, not only due to the large percentage of children affected, but also because of the growing evidence indicating the apparent cognitive and behavioral consequences of this condition. The outcomes of sleep-disordered breathing can be caused by general sleepiness, which is to be expected

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when sleep is continuously disrupted during a long period of time. It also can be caused by the effects of hypoxia—causing actual physiologic damage to sensitive parts of the brain. Through the use of imaging, some studies have identified actual tissue damage, supporting that cognitive and behavioral results of sleep-disordered breathing are due to hypoxia.

This study examined the relationship between executive function and cortical thickness of children with sleep-disordered breathing and matched controls. Each subject underwent a magnetic resonance imaging (MRI) scan of the brain (approximately 10 to 15 minutes) as well as an extensive neuropsychological evaluation. Cognitive capability and cortical thickness measures were examined.

Theoretical Methodology

Sleep-disordered breathing and obstructive sleep apnea have been a growing area of clinical interest at Children’s Healthcare of Atlanta. Using a collaborative model of research and clinical care, the Children’s Neuropsychology and Pulmunology departments are working together to further investigate the cognitive issues of patients diagnosed with sleep-disordered breathing.

The purpose of the research study was to investigate whether sleep-disordered breathing impairs executive functioning, e.g., problem solving skills, cognitive flexibility and multitasking of children compared to healthy controls. Additionally, the study sought to identify the executive functions at risk, the degree of sleep-disordered breathing required for dysfunction and the contribution of sleepiness and fatigue versus hypoxic injury.

Participants

- 48 participants
 - 27 children referred for sleep-disordered breathing (10 females, 17 males)
 - 21 matched controls (11 females, 10 males)
 - There were no significant differences in IQ or SES
- Clinical participant demographics
 - Ethnicity: six Black/African-Americans, 18 Caucasians, two Asian-Americans, one Hispanic
 - Age range: 8 to 18
 - Degree of sleep-disordered breathing: 18 mild, two moderate, seven none (based on polysomnography)

Assessment Procedure

Twenty-seven children with suspected sleep-disordered breathing were tested with a polysomnography and a neuropsychological battery. The children were referred to Children’s and ranged in age from 8 to 18, with no congenital or acquired brain damage. They were matched for age, gender and socioeconomic status with 21 healthy controls. The Wechsler Abbreviated Scale of Intelligence (WASI) and subtests of Woodcock-Johnson Academic Achievement Battery were administered to determine intellectual ability and academic skills. The executive function protocol included subtests

from the Delis-Kaplan Executive Function System (D-KEFS), the digit span subtest from the Wechsler Intelligence Scale for Children (WISCIV), the Tower of London-Drexel University, the Behavioral Rating Inventory of Executive Functioning (BRIEF) and the Conners’ Continuous Performance Test-II (CPT-II).

Twelve of the sleep-disordered breathing patients also underwent MRI scans of the brain to determine cortical thickness (morphometry). There have been many efforts to extract morphometric information from volumetric magnetic resonance imaging acquisitions of the brain. The efforts range from laborious manual editing of the volume with software tools to attempts to construct automated or semiautomated software tools to extract the region of interest. In all cases, the final endpoint of the study was to find a biological marker.

Statistical Analysis

Using the SPSS version 14 statistics package, Wilcoxon Rank-Sum nonparametric tests were used to compare the executive function performance of children referred for sleep-disordered breathing against healthy controls. This test is used in place of a two-sample t-test when the populations being compared are not normal. Due to the large number of variables generated by the neuropsychological battery and the relative small sample size, only variables thought to be sensitive to differences, based on theory, were included in the statistical analyses.

The brain surfaces are reconstructed automatically to produce topologically correct versions. Small topological errors arising from the finite resolution of the images and noise from the measurement process are fixed by an automated procedure. The surfaces are registered to a spherical atlas, maximizing the sulcal and gyral pattern alignment. The registration to the spherical representation allows the application of an automated method for cortical parcellation. The parcellation is accomplished using an atlas of statistical data from a manually labeled brain and a statistical algorithm (Markov Random Field) to label all sulci and gyri. In validation studies, the labeling has been shown to be of comparable accuracy to a manual labeling by a trained neuroanatomist. A manual labeling by a trained neuroanatomist for a single subject takes an average of one week of effort, making it impractical for large studies. The software automatically computes the cortical thickness at each point on the cortex by computing for each point on the pial surface, the distance to the closest point on the white matter surface. Statistics about cortical thickness for each of the 84 labeled regions of the entire brain are generated.

Results

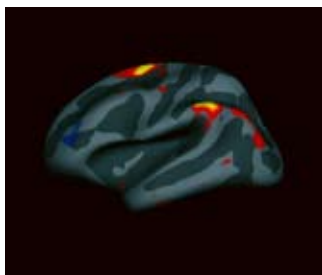
Results of the Wilcoxon Rank-Sum tests demonstrate comparable intelligence scores between the sleep-disordered breathing group and the control group. However, poorer academic performance was found in the sleep-disordered breathing group—despite similar IQ scores. Several of the executive function measures appeared sensitive to group differences, including the D-KEFS subtests and the parent report measure, the BRIEF (see table).

Table 1. Sample Neurocognitive Findings

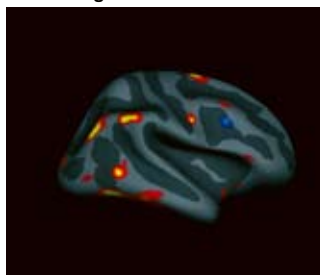
Test Administered Wilcoxon	Sleep-Disordered Breathing Group		Control Group		
	Mean	SD	Mean	SD	p
WASI IQ	108.54	15.45	108.73	13.75	.0139
Woodcock-Johnson Academic	98.96	12.61	108.64	9.27	.0083
WISC IV-Digit Span	9.21	2.5	10.36	2.46	.1113
DKEFS-Color-Word Switching	8.18	3.65	11.64	1.64	.0007
DKEFS-Verbal Fluency Switching	10.00	2.76	12.59	2.52	.0033
DKEFS-Trail-making Switching	8.14	4.62	10.55	3.12	.1269
BRIEF-Planning/Organization	57.96	12.42	49.23	8.86	.0047
BRIEF-Behavioral Regulation	56.43	14.21	48.14	10.18	.0287
BRIEF-Inhibition	54.25	10.78	50.14	8.58	.2180
BRIEF-Global Composite	58.43	13.18	49.23	8.86	.0055

Tests with bold text denote significant differences of frontal lobe measures. Patients with sleep-disordered breathing performed poorer on tests measuring planning and organization. Further comparison of morphometry demonstrated organic differences between the sleep patients. The children with sleep-disordered breathing had thinner cortices when compared with the controls. The areas of difference are shown below:

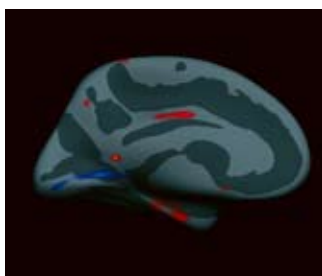
Left Lateral Surface



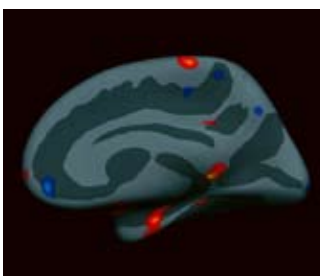
Right Lateral Surface



Left Medial Surface



Right Medial Surface



This morphometric comparison delineates the left hemilateral surface, which shows posterior superior frontal thinning, and the areas involving the supramarginal gyrus and inferior parietal cortex. The right hemilateral surface map shows the thinning of the inferior parietal and middle temporal cortices. Additionally, there is thinning found at the inferior temporal region, representing the fusiform gyrus.

Discussion

The results of the study suggest children suspected of having sleep-disordered breathing performed poorer than control participants on some tests of executive function and academic skills despite comparable IQ scores. Moreover, using parent report measures, parents of children with sleep-disordered breathing endorsed overall problems with executive functioning skills at home, compared to the normal sample. The findings support previous research, suggesting sleep-disordered breathing impairs cognitive and academic functioning.

The results of this study implicate executive function as an area of cognitive function especially susceptible to sleep disturbances. It is interesting that not all aspects of executive function have significant differences between sleep-disordered breathing and control groups. For example, the Drexel Tower measures various aspects of planning, initiation and inhibition, but no between-group differences emerged. Although, the findings show significant group differences. Often times, these differences remained within the acceptable range of normal.

Future studies should focus on the post-treatment cognitive function of those children who demonstrate cognitive deficits prior to a sleep-disordered breathing treatment. It seems a likely conclusion that sleep-disordered breathing has a negative impact on the higher-level cognitive function in children, which is a critical component of academics and life success. Further research is needed to correlate these findings and suggest the mechanisms for how these differences are caused, helping scientists to further explore problem with children's sleep.

References

Beebe, D.W., & Gozal, D. (2002). Obstructive sleep apnea and the prefrontal cortex: Towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *Journal of Sleep Research*, 11, 1-16.

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