The Future Risks of Childhood Sleep-Disordered Breathing

Comment on Chervin RD; Ruzicka DL; Archbold KH et al. Snoring Predicts Hyperactivity 4 Years Later. SLEEP; 28(7); 885-890

Daniel J. Gottlieb, MD, MPH

Boston University School of Medicine, Boston, MA

THE PAST DECADE HAS SEEN INCREASING AWARENESS OF THE IMPORTANCE OF SLEEP-DISORDERED BREATHING (SDB) IN CHILDREN. AS THE EPIDEMIC OF OBESITY extends to ever younger ages, the obesity-related SDB typical of adults will become increasingly prevalent in childhood. Its management will likely be similar to that of obesity-related SDB in adults, albeit with greater urgency due to possible effects on growth and development and with likely greater difficulty in achieving adherence to therapy. In young children, however, adenotonsillar hypertrophy remains a more important cause of SDB and its management presents a different set of issues. Adenotonsillectomy may be curative in a majority of cases but is not without significant morbidity. When polysomnography reveals overt obstructive sleep apnea in a symptomatic child with adenotonsillar hypertrophy, the decision to perform adenoidectomy or tonsillectomy is not difficult. There is increasing evidence, however, that SDB symptoms in children are associated with problem behaviors, sleepiness, and poorer cognitive function even in the absence of obstructive sleep apnea. If mild SDB, characterized by snoring and increased airway resistance in the absence of gas exchange abnormalities, is indeed a cause of behavioral and cognitive impairment, then its public health impact may be quite large.

Important questions about the behavioral and cognitive consequences of mild SDB in children remain to be answered, however, before embarking on major public health or medical treatment initiatives. First, the causal nature of the association remains uncertain. Several small studies have demonstrated improvements in behavior, cognitive function, and academic performance following adenotonsillectomy in children with obstructive sleep apnea. These studies indicate that overt obstructive sleep apnea does cause behavioral and cognitive impairment that is at least partially reversible, but provide limited evidence regarding children with “primary” snoring. Cognitive impairment in SDB is commonly attributed to the effects of hypoxemia. An important effect of hypoxemia is supported by recent experiments demonstrating increased cortical and hippocampal neuron apoptosis and impaired spatial learning in rats exposed to intermittent hypoxia, effects which are greatest at an age corresponding to early childhood in humans. However, experimental sleep fragmentation and sleep deprivation studies, mostly conducted in adults, provide unequivocal evidence that sleep disruption has behavioral and cognitive consequences that are not dependent on gas exchange abnormalities (recently reviewed in reference 10). Neither the numerous observational studies of the correlates of SDB in humans, nor the interventional studies conducted to date, are able to distinguish the relative contributions of sleep disruption and gas exchange abnormalities to the behavioral and cognitive consequences of SDB.

Second, even if the association is causal, what are its long-term consequences? Unfortunately, little is known about the natural history of SDB or its consequences in young children. One large survey study suggests spontaneous resolution of snoring in 50% of habitually snoring 4- to 5-year-old children over a two-year period. If the cognitive and behavioral effects of SDB are similarly reversible, specific therapeutic interventions such as adenotonsillectomy may not be warranted in large numbers of children simply to hasten their natural resolution. Conversely, early childhood is a period of rapid development of executive brain function. It is plausible that sleep disturbance during this critical period might lead to permanent impairment of executive function, as suggested by one retrospective study that found a stronger association of poor academic performance at age 13 to 14 years with early childhood snoring than with current snoring. If impairment of executive function is persistent, then identification and treatment of children at risk for such impairment would be of major public health importance.

The study by Chervin et al in this issue of SLEEP begins to address this question. Although based on a fairly small number of observations, this study provides prospective evidence that the presence of SDB symptoms in children age 2-13 years is associated with an approximately 3-fold increase in the prevalence of hyperactive behaviors 4 years later. Although baseline and follow-up SDB symptoms were highly correlated, fewer than 1/2 of children with habitual snoring at baseline were habitual snorers 4 years later. While both baseline and follow-up SDB symptoms are included in logistic regression models, the association with hyperactive behaviors is stronger for baseline symptoms and is little affected by adjustment for symptoms at follow-up. While the authors considered 5 separate measures of SDB symptoms, the concordance of findings across these measures should allay concerns regarding multiple comparisons. The sole outcome measure is the Hyperactivity Index of the Conners’ Parent Rating Scale, a well-validated and widely used measure of childhood behavior problems. The definition of hyperactive behavior used in this study, a score of 60 or more on the Hyperactivity Index, is only 1 standard deviation above the normal mean for this measure and would not be considered a diagnostic clinical abnormality. Given the high prevalence of SDB symptoms in young children, however, even modest decrements in executive function may have impacts on learning and performance that are quite important at the population level.

Disclosure Statement
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Address correspondence to: Daniel J. Gottlieb, MD, MPH, Boston University School of Medicine, 715 Albany Street, R-304, Boston, MA 02118-2394; Tel: (617) 638-4470; Fax: (617) 638-5298; Email: dgottlieb@lung.bumc.bu.edu

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The major threat to the validity of the study is the low response rate. Follow-up data were available in only 26% of subjects from the original cross-sectional study. This raises questions of potential bias in the respondents, which cannot be assessed analytically, although the included subjects were of similar age and sex to non-responders and had somewhat fewer baseline SDB symptoms. The small sample size of children under age 8 years yielded effect estimates too unstable to conclude whether the association was stronger at younger ages, as might be expected if SDB were causing impairments in development of executive function. Finally, no adjustment is made for sociodemographic or health variables such as recurrent respiratory infections or asthma that might confound the association of SDB symptoms with problem behaviors.

As the children in this study did not have polysomnography, it is unknown whether sleep studies would have identified the children at increased risk for hyperactive behaviors, although overt obstructive sleep apnea is likely to have been present in only a small fraction of the nearly 13% of children with baseline habitual snoring.

Despite these limitations, the study by Chervin and colleagues should raise concern that highly prevalent, mild childhood SDB may have persistent cognitive and behavioral consequences. At present, it would be premature to recommend adenotonsillectomy as a routine treatment for early childhood snoring associated with adenotonsillar hypertrophy. Further study is needed to confirm the persistence of problem behaviors, cognitive impairment and academic performance deficits in children with early childhood SDB symptoms and to determine whether there is a critical age at which children are at risk for development of persistent impairment. In order to effectively target therapeutic interventions, it will be important to identify predictors of subsequent impairment, including both sociodemographic and health factors and physiologic markers of children at risk. In addition to conventional polysomnographic measures, markers might include measures of respiratory effort, acoustic characteristics of snoring or EEG characteristics such as the respiratory cycle-related changes in EEG spectral power that Chervin and colleagues have preliminarily demonstrated to correlate with sleepiness in both children and adults. Finally, if SDB symptoms are associated with persistent cognitive and behavioral impairments, clinical trials are needed to demonstrate that these effects can be prevented with treatment. Such treatment might include not only adenotonsillectomy but alternative therapies aimed at reducing adenotonsillar hypertrophy, as was recently reported for montelukast in children with SDB considered too mild to warrant adenotonsillectomy. That said, in young children with adenotonsillar hypertrophy, snoring and daytime behavioral problems, including age-inappropriate hyperactivity, inattentiveness or excessive sleepiness, failure to thrive or unexplained hypertension, adenotonsillectomy may be a reasonable therapeutic option even in the absence of polysomnographic abnormalities.

REFERENCES