Impact of Apnea on Cognition Highly Variable

BY DAMIAN McNAMARA
Miami Bureau

FORT LAUDERDALE, FLA. — Some children with sleep-disordered breathing experience significant cognitive deficits, but not all do, and identification of those at risk remains a clinical challenge, according to a sleep medicine expert.

The range of individual susceptibility is wide, Dr. David Gozal said. "A child can have a mild [sleep] disturbance and be affected or have severe sleep apnea and be unaffected cognitively." Together with apnea severity and environmental factors, individual differences in susceptibility complete the triple-risk model of obstructive sleep apnea morbidity, said Dr. Gozal, professor and vice chair of research, department of pediatrics, University of Louisville (Ky.).

In general, increased apnea severity is associated with greater impairments in cognition. For example, the Louisville study investigators, including Dr. Gozal, found significant neurocognitive deficits with higher apnea/hypopnea index (AHI) scores among snoring children (J. Sleep Res. 2004;13:165-72).

With increases in AHI severity, a child's IQ can decrease, Dr. Gozal said at a pediatric pulmonology meeting sponsored by the American College of Chest Physicians. For children with an AHI of 5 or more, for example, there is average loss of 6-8 IQ points. "If you are born with an IQ of 100, that can be the difference between going to college or not."

Together with apnea severity and environmental factors, individual differences in susceptibility complete the triple-risk model of OSA morbidity.

At any AHI level in the study, however, there were children without any cognitive deficit, again pointing to the individual variability, said Dr. Gozal, who is also a respiratory/sleep physiologist in the division of sleep medicine at Kosair Children's Hospital Research Institute, also in Louisville.

Specifically, significantly higher impairments in phonological processing, visual and auditory attention, and social problems were found among children with an AHI greater than 5, compared with those scoring 5 or less. High scorers also had significantly worse thought problems, delinquent or oppositional behavior, aggressiveness, externalizing of problems, and deficits in verbal comprehension ability.

In another study of 297 poorly performing first graders, there was a 6- to 9-fold increase in sleep apnea, compared with the general population (Pediatrics 1998;102:616-20).

In terms of potential misdiagnosis, there is some overlap between children with attention-deficit/hyperactivity disorder (ADHD) symptoms and those with obstructive sleep apnea (OSA) who demonstrate intrinsic daytime sleepiness. These patients can benefit from stimulant treatment, Dr. Gozal said.

The diagnosis of sleep apnea may be completely overlooked, since these patients improve with stimulants, similarly to children with ADHD who also are intrinsically sleepy. However, children with a formal diagnosis of ADHD-inattentive type who are not sleepy will be more likely to improve with addition of a norepinephrine reuptake inhibitor to treat their prefrontal cortex executive dysfunction, he said.

The way a child lives affects the way the sleep-disordered breathing affects them, Dr. Gozal said. "Physical activity is actually protective of our children when they have sleep apnea."

Given such individual variability in risk of adverse cognitive outcomes in these children, Dr. Gozal and his associates are searching for a prognostic marker. They found that elevated plasma C-reactive protein levels, an indicator of increased systemic inflammation, might indicate children with OSA are at greater neurocognitive risk (Am. J. Respir. Crit. Care Med. 2007;176:188-93).

They assessed 278 children and found high-sensitivity C-reactive protein (hsCRP) levels almost triple among children with cognitive deficits, compared with those without. Participants were 5- to 7-year-old children recruited from the community.

The mean hsCRP was 0.48 plus or minus 0.12 mg/dL in children with OSA and cognitive deficits, compared with 0.21 plus or minus 0.08 mg/dL in children with the condition and normal cognitive scores. This difference was statistically significant.

Dr. Gozal and his associates wrote, "We show in a community-based study of snoring and nonsnoring school-aged children, that children with OSA have increased levels of hsCRP and also exhibit decreased cognitive performances compared with control children." ■

Extremely Preterm Birth Linked to Later Autism

BY ROBERT FINN
San Francisco Bureau

HONOLULU — Children born at less than 26 weeks' gestation are significantly more likely to have symptoms indicative of autism spectrum disorders at school age than are their classmates, according to a study of 219 children born extremely preterm matched with 153 children born at term.

Samantha Johnson, Ph.D., who is a psychologist at the University of Nottingham (England), and her colleagues compared these extremely preterm children with term classmates matched for age, sex, and ethnic group.

The mean age of children in both groups was 11 years, the researchers wrote in a poster presentation at the annual meeting of the Pediatric Academic Societies.

Parents completed the Social Communication Questionnaire (SCQ), which evaluates autism spectrum symptoms, and psychologists administered the Kaufman Assessment Battery for Children (K-ABC), an IQ test.

Compared with the control group, the extremely preterm children had significantly higher total scores on the SCQ as well as significantly higher scores on each of the three component scales: social interaction, communication, and repetitive behavior. These significant differences persisted even after adjustments for both IQ and sex.

A total score of 15 or above on the SCQ is often used to define a threshold for autism spectrum disorders, and a score of 22 or above is used to define a threshold for autism. Of the preterm children, 8% had SCQ scores between 15 and 21, and another 8% had scores of 22 or above.

In contrast, only 3% of their term classmates passed the threshold for autism spectrum disorders, and none passed the threshold for autism. Compared with their classmates, the extremely preterm children were 6.3 times more likely to have scores of 15 or above.

In an interview, coinvestigator Dr. Neil Marlow, professor of neonatal medicine at the University of Nottingham, emphasized that it would not be appropriate to interpret the results as indicating that extreme prematurity is associated with a formal diagnosis of autism. The results show an association between prematurity and autism spectrum disorder symptoms, not autism itself.

Although other studies have found associations between prematurity and autism spectrum disorder symptoms at the age of 2 years, the investigators stated that this is the first study to find that association among school-age children. The investigators reported that they had no relevant conflicts of interest. ■

Identifying Endophenotypes Can Help Guide Treatment of Autism

BY HEIDI SPLETE
Senior Writer

BALTIMORE — Identifying shared endophenotypes might help clinicians characterize neurobehavioral syndromes and plan treatment, said a specialist in neurobehavioral development.

An endophenotype is a subset of features of a syndrome that are more highly correlated with a genetic mechanism than the whole syndrome, and grouping syndromes that share common features can help target and simplify treatment strategies, said Travis Thompson, Ph.D., also a professor in the department of pediatrics at the University of Minnesota, Minneapolis.

Some genetic evidence suggests that there might be shared inherited traits between autism and Prader-Willi syndrome (PW), and Dr. Thompson presented important behavioral similarities and differences between these two conditions at a meeting on developmental disabilities sponsored by Johns Hopkins University.

"Identifying clinically relevant endophenotypes can be more helpful than trying to figure out exactly which genes cause autism," he said.

Phenotypic features that differ might be just as informative as those that are the same in understanding genetic and associated brain differences in clinical syndromes, Dr. Thompson said. "The fact that they are alike in some ways but different in a specific way tells you that there is probably a different genetic mechanism," he said.

Candidates for a common genetic lesion include the γ-aminobutyric acid (GABA) receptor 3 (GABRB3), which might be absent or reduced in children with either autism or PW. And research has shown that both conditions might be associated with genes in the 15q11-q13 region of chromosome 15.

Features that are common to both autism and PW include compulsive behavior, social processing deficits (including facial processing deficits), and self-injury, Dr. Thompson said.

Compulsive behavior in children with either condition might be associated with overactive dopamine due in part to the missing or suppressed GABA-3 receptor. But some differences emerge within these categories. For example, compulsive behavior in children with PW often involves excessive overeating, which might be due to an overproduction of GABA. And skin picking is a common compulsive behavior in children with either condition, although in PW skin picking can start as early as 2 years of age, he said.

Studies have shown that face perception is limited in children with either autism or PW. This problem might be linked to a common genetic defect that might cause hypoactivation of the amygdala and fusiform face area—parts of the brain that recognize facial features.

More research is needed on common behavior phenotypes in neurobehavioral syndromes to determine which individuals show the maximum improvement to different treatments, and what characteristics of those individuals make them responsive to a specific intervention, he added. "That has to be the future of research in this area." ■