Brain Anatomy Differs in Children With ADHD

It may become possible to diagnose ADHD using a new technique called diffusion tensor imaging.

BY KATE JOHNSON
Montreal Bureau

CHICAGO — Children with attention-deficit hyperactivity disorder have anatomical brain abnormalities that can be seen with a novel technique called diffusion tensor imaging.

"Our hope is, in the future, to be able to diagnose ADHD with this technique," said lead investigator Manzar Ashtari, Ph.D., of North Shore–Long Island Jewish Health System in New Hyde Park, N.Y.

Speaking at a press conference at the annual meeting of the Radiological Society of North America, Dr. Ashtari explained that until now, imaging of the brain in patients with ADHD has revealed mostly macroscopic findings.

"For example, we know that the frontal lobe and cerebellum are smaller in these patients."

But she said her work with diffusion tensor imaging (DTI) looks deeper—at a more microscopic level—showing abnormalities in the corticopontocerebellar circuit, the fiber pathways that communicate between the frontal lobe and the cerebellum.

The study compared DTI of the brain in 18 children with ADHD, aged 7-11 years, and 15 healthy controls matched for age, sex, and socioeconomic status.

"We found abnormalities in the fiber pathways in the frontal cortex, basal ganglia, brain stem, and cerebellum in the ADHD patients," she said, explaining that these areas of the brain regulate attention, impulsive behavior, motor activity, and inhibition. "These findings suggest that the circuit which connects the frontal lobe and the cerebellum is not efficient in ADHD."

Dr. Ashtari was also co–lead investigator on a second study that used DTI to compare the brain anatomy of 20 children with ADHD, half of whom were medicated for their condition, and half of whom were medication naive.

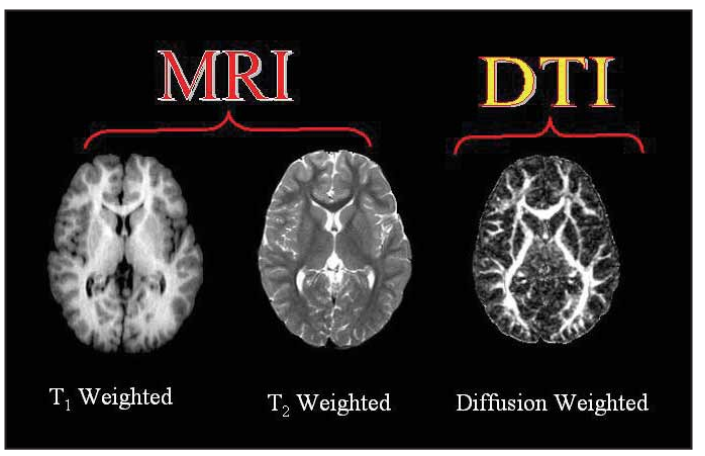
Fiber pathway abnormalities are less pronounced in children who have been treated with stimulant medication, compared with those who have not.

"These results are definitely very exciting," said Dr. Ashtari. "They suggest that perhaps the medication is doing something to normalize the brain abnormalities, such as remyelinating the axons."

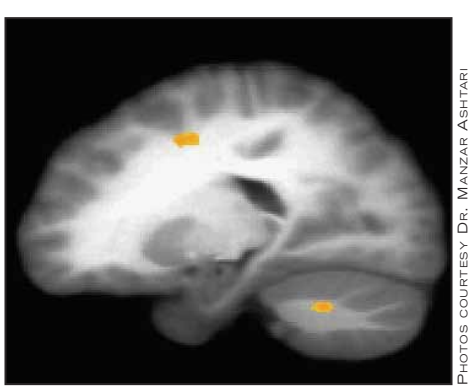
However, she cautions against jumping to the conclusion that the study shows stimulants can reverse, or partially correct, the brain abnormalities seen in ADHD.

"Other studies into the effect of medication have shown that the white matter of the brain increases to close to normal in medicated children. But medicated children also are usually older. So could the improvement be just an effect of age—as the brain grows?" Dr Ashtari discussed with FAMILY PRACTICE NEWS.

"The more conclusive study will be to follow drug-naive children prospectively and then see what happens when you medicate them," she said, adding that her team has received funding to start this study. ■



While brain imaging using MRI has mostly revealed macroscopic findings, DTI shows a more microscopic view.



PHOTOS COURTESY DR. MANZAR ASHTARI

DTI shows frontal cortex and cerebellum abnormalities in an ADHD patient.

Long-Acting ADHD Treatment Improved Core Symptoms

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — A long-acting formulation of dexmethylphenidate is safe and effective in children and adolescents with attention-deficit hyperactivity disorder, according to data presented at the annual meeting of the Society for Developmental and Behavioral Pediatrics.

Children taking the investigational treatment showed improvements in core symptoms both at school and at home, compared with patients taking placebo.

The treatment, currently known as dexmethylphenidate extended-release capsules (d-MPH-ER), is a once-daily formulation of Focalin, which was introduced in 2002. D-MPH-ER is in phase III trials.

Focalin and d-MPH-ER contain only the active isomer of racemic methylphenidate (Ritalin), said lead investigator Frank Lopez, M.D., of Children's Developmental Center, Maitland, Fla. "You get twice the effect at half the amount in terms of what you are delivering," Dr. Lopez said during the poster presentation.

Sustained medications are often preferable to immediate-release drugs because they improve compliance and decrease the stigma of having to take medications at school.

In the double-blind, parallel-group study, 103 patients (aged 6-17 years) with a previous diagnosis of ADHD of any type were randomized to receive d-MPH-ER 5-30 mg or placebo once daily for 7 weeks. A flexible dosing schedule was used during weeks 1 through 5 to determine optimal therapeutic levels, and patients were then maintained on their optimal dosages for the remaining 2 weeks.

A total of 97 patients were evaluated for efficacy, and a total of 100 patients were evaluated for safety, he said. The primary efficacy end point was change from baseline to final visit in the total subscale score of the Conners ADHD/DSM-IV Scale for Teachers (CADS-T).

At the final visit, scores on all primary and secondary efficacy end points, except the Child Health Questionnaire physical component score, were statistically superior for d-MPH-ER, compared with placebo. The differences between groups emerged early and increased over time.

The adjusted mean change from baseline to final visit in the CADS-T total score was 16.3 in the d-MPH-ER group vs. 5.7 in the placebo group. The adjusted mean change in the CADS for Parents (CADS-P) total subscale scores from baseline was 17.6 in the d-MPH-ER group vs. 6.5 in the placebo group.

Overall, 67% of patients treated with d-MPH-ER were rated as "very much improved" or "much improved" on the Clinical Global Impressions-Improvement (CGI-I) scale at the final visit, compared with 13% of patients in the placebo group.

Of d-MPH-ER patients, 49% reported an adverse event, compared with 26% in the placebo group. The most frequently reported adverse events associated with d-MPH-ER were decreased appetite (28%), headache (9%), and insomnia (7%). ■

Sleep Problems and Attention Difficulties in Adults Intertwined

BY DOUG BRUNK
San Diego Bureau

SEATTLE — Many adults with obstructive sleep apnea or insomnia also have attention-deficit disorder as well as neuromuscular and psychiatric conditions, results from a detailed analysis suggest.

"The sleep specialist isn't done when he says, 'It's sleep apnea. Use continuous positive airway pressure,' or 'It's insomnia; take a sleeping pill,' " Clifford G. Risk, M.D., said at a press briefing during the annual meeting of the American College of Chest Physicians. "He has to work out what the concurrent conditions are at the same time he's trying to improve the insomnia or sleep apnea. The assessment of patients with a sleep disorder and impaired daytime cognition may represent a complex interlay between the sleep disorder and comorbid dual diagnoses."

He and his associates at a sleep disorder center in Marlborough, Mass., evaluated 58 patients who presented with sleep apnea or insomnia. Investigators administered a wide battery of standardized tests to assess the severity of obstructive sleep apnea, attention-deficit problems, depression, and insomnia.

All patients received treatment for their respective conditions, including continuous positive airway pressure (CPAP) treatment for obstructive sleep apnea, cognitive-behavioral therapy and/or hypnotic medication for insomnia, and psychiatric evaluation and possible medication for primary ADD.

Of the 34 patients who were found to have sleep apnea, 16 had baseline Adult Self-Report Scale (ASRS) symptom checklist scores that suggested moderate or severe impairment of attention. After CPAP treatment, 60% of these patients substantially improved their attention scores. "However, 40% continued to report serious attention deficits following treatment, and required further neuropsychiatric evaluation and specific interventions," said Dr. Risk, who directs the sleep disorder center.

Of the 24 patients who had insomnia, 54% had baseline ASRS scores that suggested moderate or severe impairment of attention. Nine patients suffered from a primary muscular disorder, including fibromyalgia, chronic fatigue, multiple sclerosis, peripheral neuropathy, and postpolio syndrome; 15 suffered from a primary psychological disorder, including depression, bipolar disorder, and anxiety.

There were serious rheumatologic and neurologic diseases causing sleep disturbances in patients with insomnia, Dr. Risk said.

He concluded that a multidisciplinary approach to patients with sleep difficulties "may be necessary in order to isolate additional comorbidities that are causing persistent impairment." ■