Abnormal Brain Anatomy Found With ADHD

Diffusion tensor imaging shows abnormalities in pathways between the frontal lobe, cerebellum.

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," she said.

Dr. Ashtari was also colead 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 naïve.

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 re-myelinating the axons."

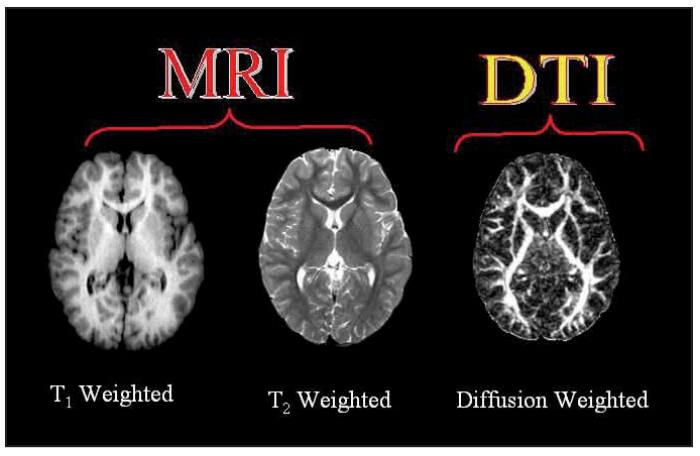
However, she cautions against jumping to the conclusion that the study shows stimulants can reverse, or partially correct, the brain abnormalities seen in ADHD.

"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.

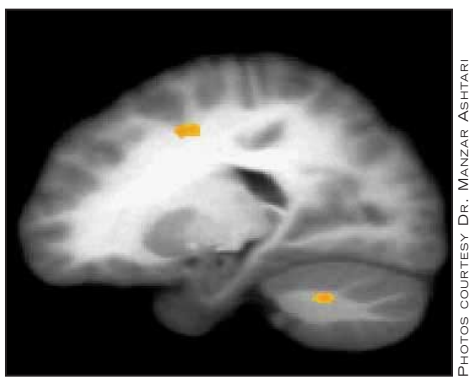
"So could the improvement be just an effect of age—as the brain grows?" she said in an interview.

"The more conclusive study will be to follow drug-naïve children prospectively and then see what happens when you medicate them," she said.

Dr. Ashtari added that her team has received funding to start such a study of drug-naïve children. ■



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.

Psychiatric Conditions Common in Child Epilepsy

WASHINGTON — Comorbid psychiatric conditions appear to be very common among children with medically refractory epilepsy, Jay A. Salpekar, M.D., said at the annual meeting of the American Academy of Child and Adolescent Psychiatry.

In a study of 24 children (16 boys and 8 girls) recommended for epilepsy surgery, 22 were diagnosed with at least one psychiatric disorder, said Dr. Salpekar of Children's National Medical Center in Washington. Seven children were diagnosed with two or more psychiatric disorders

The patients ranged in age from 6 to 17 years and had an average IQ greater than 70. After undergoing clinical psychiatric evaluations, 12 children were diagnosed with anxiety disorders, 11 with attention deficit hyperactivity disorder, and 7 with mood disorders.

Parents completed the Child Behavior Checklist (CBCL) for their children, and 19 children had at least one CBCL subcategory T score above 65—1.5 standard deviations above normal. The most common problems were in the somatic, social, and attention subcategories. Thirteen children had at least one T score above 70—2 standard deviations above normal. The most common problems for these children were also in the somatic, social, and attention subcategories.

The 14 children with temporal lobe foci appeared to have more psychiatric problems than the 10 children with extratemporal foci. Among the children with temporal lobe foci, six were diagnosed with anxiety, eight with ADHD, and five with mood disorders. Each of these children averaged about two CBCL subcategory T scores greater than 65, and those with extratemporal lobe foci averaged one CBCL subcategory T score greater than 65, Dr. Salpekar reported.

Children with extratemporal lobe epilepsy also had fewer clinical psychiatric diagnoses. "There is something, not only about chronic epilepsy, but about temporal lobe chronic epilepsy" in particular, that leads to greater psychiatric comorbidity, he said.

—Kerri Wachter

Long-Acting Investigational ADHD Treatment Promising in Children

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.

"What's coming out well with this particular medication is that you get twice the effect at half the amount in terms of what you are delivering," Dr. Lopez said during the poster presentation. "It's got a rapid onset, very smooth, and so far in this preliminary study, the effect was seen carrying out over 12 hours, which is a very nice thing."

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 for the study 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, he reported.

Overall, 67.3% 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 13.3% of patients in the placebo group, Dr. Lopez said.

Of d-MPH-ER patients, 49% reported an adverse event, compared with 25.5% of patients in the placebo group. The most frequently reported adverse events associated with d-MPH-ER were decreased appetite (28.3%), headache (9.4%), and insomnia (7.6%). One patient in the placebo group and no one in the d-MPH-ER group discontinued use because of adverse events. ■