Abnormal Brain Anatomy Found With ADHD

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

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WASHINGTON — 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, M.D., 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 10 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 category 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 few 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.

“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,” Dr. Ashtari said. “So could the improvement be just an effect of age—at the brain grows?” she said in an interview.

The more conclusive study will be to follow drug-naive 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-naive children.

LONG-ACTING INVESTIGATIONAL ADHD TREATMENT PROMISING IN CHILDREN

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, Miami, 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 (ages 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 ADH/D-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.