Abnormal Brain Growth Starts Early in Autism, Then Slows

**STANFORD, CALIF.** — Increasing evidence suggests that children with autism have a normal head circumference at birth, but that many develop macroencephaly in childhood. Dr. Antonio Hardan said at a recent pediatric update sponsored by Stanford (Calif.) University.

Distinguishing features within the brain are evident in utero, with abnormal neural migration and a decrease in cerebellum size seen as early as the first trimester.

Both findings have important implications for research into the causes, and one day perhaps the prevention, of autism.

The first suggestion of abnormal head circumference in children with autism appeared in 1943, with Dr. Leo Kanner’s groundbreaking description of 11 children with what would come to be known as autistic features. He noted that five had “relatively large heads,” and one had “markedly prominent” occipital and frontal regions.

Since the advent of modern neuroimaging techniques, nine studies have found increased brain size in individuals with autism, but four studies have had negative findings, said Dr. Hardan, director of the autism and developmental disabilities clinic at Stanford’s Lucile Packard Children’s Hospital at Stanford (Calif.) University.

The trial is small and incomplete, and the results should be interpreted with caution, he said. “But what is nice about this is it opens up a whole group of medications to study.”

The use of donepezil (Aricept) in autism was first studied by Dr. Hardan at the University of Pittsburgh in an open-label study of eight children, half of whom demonstrated improvement on the Auer Tot Behavior Checklist and Clinical Global Impressions Scale. Improvements were seen on the Ex- ercise One-Word Vocabulary Test, which measures language skills.

“We didn’t see magic improvement or large improvements,” emphasized Dr. Hardan, director of the Autism and Developmental Disabilities Clinic at Lucile Packard Children’s Hospital of Stanford (Calif.) University.

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Another novel study of an existing drug in autism is ongoing at Indiana University Health, Indianapolis, where a broad-spectrum antibiotic once used to treat tuberculosis led to apparent improvement in social withdrawal in a pilot study. A randomized, double-blind study is currently underway, said Dr. Hardan.

Another study of a medication is currently underway, the use of donepezil (Aricept) in autism. Although these are small studies, it is encouraging to see research into existing drugs to determine whether they might be effective in treating children with autism spectrum disorders, he said.

It took 15 years for risperidone (Risperdal) to be approved for treatment of autism-related irritability, noted Dr. Hardan, who published an early case study suggesting the drug’s efficacy in 1996. “That’s why [parents] jump at any opportunity [to use a drug’s efficacy in 1996].” He stressed that research must be driven by theories that make scientific sense, followed by proof-of-concept studies to see whether evidence exists that an agent may be helpful.

He pointed to “the [high] price of short-cuts,” citing as an example secretin, which was hailed as a possible treatment based on one uncontrolled observational study that hinted it may have improved behavioral problems in children undergoin gastroenterological procedures.

No verification was made to determine whether the children actually met diagnostic criteria for autism, he noted. “Based on this, secretin was unfortunately the most studied medication in autism.”

Fifteen randomized, double-blind studies eventually produced uniformly negative results. “You can’t find anything consistent like that in medicine,” he said.

**Is Autism Prevalence Rising, or Is the Diagnosis Expanding?**

**STANFORD, CALIF.** — A preliminary analysis of a randomized, double-blind, placebo-controlled study of donepezil suggests that the Alzheimer’s drug may slightly improve some neuropsychologic functions in children with autism, Dr. Antonio Hardan said at a pediatric update sponsored by Stanford University.

At the halfway point in a 20-week trial, improvements were seen in scores on some, but not all, neuropsychologic tests in 10 autistic children aged 7-17 years receiving the drug, compared with 10 receiving placebo. Specifically, children somewhat improved their performance on tests aimed at measuring spatial executive functioning (the Design Fluency Test), selective attention (the Color-Word Interference Test), and the California Verbal Learning Test. No improvement was seen on the Expressive One-Word Vocabulary Test, which measures language skills.

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