Metabolite Concentrations Shed Light on Autistic Brain Structure

BY NORRA MACREADY
Los Angeles Bureau

IRVINE, CALIF. — Children with autism and pervasive developmental disorder show abnormalities in brain structure and chemistry early in their life, Seth Friedman, Ph.D., said at the annual conference of the EEG and Clinical Neuroscience Society.

Brain-volume increases in autism are likely not present at birth but begin to develop in infancy, grow most marked by 3-4 years of age, and level off somewhat by age 6-7 years, a theory championed by Eric Courchesne, Ph.D., of the University of California, San Diego. These changes may reflect deficits in cortical volume and organization relative to that seen in children who are developing more typically, said Dr. Friedman, of the University of Washington, Seattle.

These data contradict the idea that people with autism experience dense neuronal packing early in the life and may support other theories.

With his colleagues, Dr. Friedman compared magnetic resonance images from 45 children with autism or pervasive developmental disorder not otherwise specified (PDD-NOS) and from 14 children with other types of developmental delays (DD) with images from 26 typically developing (TD) children. All subjects were 3-4 years old.

The children in the autistic and PDD-NOS groups had significantly larger cerebral volumes than the other two groups. Their cerebellar, amygdala, and hippocampal volumes were also larger but were proportionate to the overall increase in cerebral size. However, the amygdala was disproportionately large in a subgroup of children with strictly defined autism. The findings were generally similar for boys and girls. Children with DD had smaller amygdalas (Neurology 2002;59:184-92).

Consistent with the findings of other studies, larger-than-average brains in the University of Washington autism sample leveled off in size over time, Dr. Friedman said. Some researchers have suggested that this early increase might be caused by a large number of neurons densely packed into the cortex.

To test this hypothesis, he and his associates evaluated regional brain chemistry in the same 45 children with autism and PDD-NOS, as well as 15 children with DD (the original 14 plus 1 more), and 13 of the original children in the TD group.

They used dual-proton echoplanar spectroscopic imaging to measure brain metabolite concentrations. They also measured each metabolite's relaxation time—the approximate time it takes a chemical system to return to its original state after being perturbed by an outside force, such as a change in temperature, pressure, or—in the case of magnetic resonance—radio waves. In this study, the relative measures of transverse relaxation (T_2r) were calculated from the paired echoes to provide a picture of the metabolic activity within the subjects' gray matter.

Compared with the TD children, those with autism and PDD-NOS had T_2r values of myoinositol, N-acetylaspartate, and creatine that were 13%, 10%, and 8% lower, respectively. These significant differences suggest there is a lower concentration of these metabolites in the gray matter. However, compared with those of the DD subjects, their T_2r values for choline and creatine were 10% and 9% higher, respectively (Neurology 2003;60:100-7).

These data contradict the idea that people with autism experience dense neuronal packing early in the life, Dr. Friedman said. They may support a theory advanced by Manuel F. Casanova, M.D., of the University of Louisville (Ky.), that cortical minicolumns, self-contained organizational neuronal units found throughout the brain, are more numerous but smaller and less organized in these patients. ■

Autism Commonly Treated With Stimulants

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Psychostimulants are commonly prescribed for children with autism, and that treatment is often continued for several years, according to results of a large new study, Katherine Nickels, M.D., reported at the annual meeting of the Society for Developmental and Behavioral Pediatrics.

Nearly two-thirds of children with autism in a population-based cohort received psychopharmacologic treatment, with more than half having been treated with psychostimulants.

'Some of these children were treated at a time when autism and autism spectrum disorders were not a very popular diagnosis.'

Previous studies have shown that 6.7%-20% of children with autism are treated with psychostimulants. But these studies were small or had biased subject populations, said Dr. Nickels, a pediatric resident at the Mayo Clinic, Rochester, Minn.

"What makes our research unique is that it is a large, population-based cohort of research-identified autism spectrum disorders," Dr. Nickels said.

"The patients were nonreferred and represent every case of autism spectrum disorders in a population at risk," she said.

Using data from the Rochester Epidemiology Project, Dr. Nickels and colleagues identified 124 patients that fulfilled the DSM-IV research criteria for autism. Ninety-five were male and 29 female, and the majority were cognitively impaired, as defined by an IQ of 70 or less.

The children were drawn from all 0- to 21-year-old residents of Olmsted County, Minn., who received either inpatient or outpatient care at all sites providing medical care from 1976 to 1997.

Information on all psychopharmacologic medications ever used was abstracted, including name, dose, and dates at which treatment was started and stopped. Duration of follow-up was defined as the time between the first and last documented medical visits. Treatment outcomes were not assessed.

Psychopharmacologic treatment of any kind was used for 82 cases (66%). Among these, 65 patients (79%) were treated with psychostimulants. Overall, 53% of the 124 patients with research-identified autism were treated with stimulants.

There was no difference in stimulant use by gender (53% male vs. 52% female). The median age at which treatment began was 8 years.

The most commonly prescribed stimulant was methylphenidate (80%), followed by dextroamphetamine (54%), and mixed amphetamine salts (20%).

The median time between the first and last documented psychostimulant treatment was 4.3 years. Median duration of follow-up was 12.5 years overall for autism cases and 13.9 years for cases treated with stimulants.

The study did not look at the difference in treatment preference by decade. But, some children were diagnosed after treatment began.

"Some of these children were treated at a time when autism and autism spectrum disorders were not a very popular diagnosis," Dr. Nickels said. "I remember reading through charts of children, who very obviously fit all DSM-IV criteria, and yet their symptoms were still blamed on their mothers."

The study was limited in that it was retrospective, although the investigators were able to apply the DSM-IV criteria to all patients given the detailed records available on this medically well-served population.

Additionally, the racial demographics of the study (96% white) suggest caution in generalizing the findings to the U.S. population, Dr. Nickels said. However, a recent population-based study demonstrated that the rate of autism spectrum disorders is comparable between African American and white children. ■

CAM Use High Among Autism Patients

CHICAGO — The use of complementary and alternative medicine is very common among children with autistic spectrum disorders, according to two poster presentations at the annual meeting of the Society for Developmental and Behavioral Pediatrics.

Seventy-four percent of the 112 families of children with autistic spectrum disorders (ASDs) from Children's Hospital in Boston reported having used some type of complementary and alternative medicine (CAM). A Canadian study showed 91% of 183 families surveyed had used a CAM of any type.

"People are doing a lot of things that they aren't telling their doctor about, unless they ask," Leonard Rappaport, M.D., director of the developmental medicine center at Children's Hospital, Boston, said. "This is something that needs to be reinforced continually."

The most common CAM therapies were modified diet (38%), vitamins/minerals (30%), food supplements (23%), and prayer/shaman (16%), according to the Boston study, led by Ellen Hanson, Ph.D.

The most frequently used interventions were conventional therapies such as educational techniques (89%), sensory therapies (71%), and prescription drugs (50%).

CAM use was associated with having a more severe form of ASD. There was some suggestion that CAM use was associated with longer time since diagnosis, and with higher education level in mothers.

Very few families reported that any of the interventions were harmful. Most families reported that their chief motivations for choosing CAM were unacceptable side effects, concern about the side effects, and safety of prescription medications.

In a separate presentation, a cross-sectional survey of a study population of children aged 3-18 years (mean 8.9 years) diagnosed with any ASD in southern Alberta showed that the most common types of CAM used were vitamins and minerals (63%), mind-body therapies (51%), dietary-nutritional therapies (48%), natural therapies such as St. John's wort, Kava, and homeopathy (39%), and anti-yeast therapies (31%).

The most common reasons for CAM use were: to improve symptoms of autism (43%), to improve mental and emotional well being (39%), to improve health (36%), a belief it could not hurt (28%), a belief that conventional medicine did not have any answers (22%), and a belief in holistic health (20%).

"Only 10% of families used CAM because they wanted to heal their child of ASD, so this is a pretty aware population," said lead investigator W. Ben Gibbard, M.D., of the University of Calgary (Alt.). "If you go online you'll find 20-30 sites that say there is a potential cure," Dr. Rappaport said.

The mean number of therapies used was 10, but "some patients are up to 80 therapies that they've tried," Dr. Gibbard said.

—Patrice Wendling