Metabolite Levels Reveal Autistic Brain Structure

Data contradict the idea that people with autism experience dense neuronal packing early in life.

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 clinical course, 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.

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. ■

Symptomatic Generalized Epilepsy Deters Development

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

NEW ORLEANS — The long-term social outcome for children with symptomatic generalized epilepsy is usually disappointing, with only 6% having normal intelligence and becoming seizure-free off medication and financially and socially independent.

"Twenty years after the onset of symptomatic generalized epilepsy, the outcome is usually death or complete dependence," Carol Camfield, M.D., said at the annual meeting of the American Epilepsy Society. "Only a tiny fraction of these children are seizure-free and independent."

Dr. Camfield of Dalhousie University, Halifax, Nova Scotia, examined outcomes for the 75 children with symptomatic generalized epilepsy (SGE) who were included in the Nova Scotia Childhood Epilepsy Cohort. The cohort includes 692 children diagnosed with epilepsy from 1977 to 1985. The outcomes assessment took place in 2003.

About 11% of the cohort had SGE. Of these 75 children, 45 (60%) developed seizures before 1 year of age. Undefined SGE was present in 28 (37%), 32 (43%) had West's syndrome, 4 (5%) had Lennox-Gastaut syndrome, and 9 (12%) had myoclonic astatic epilepsy. One child had Dravet's syndrome, and one child had partial complex seizures.

By the end of the follow-up period, 25% of the group (19) had died. The mean age at death was 11.6 years; the mean duration of epilepsy was 10.5 years. Of the 56 children who survived, the mean follow-up was more than 19 years.

Of the cohort of 75 patients, 25% were in remission off antiepileptic drugs, 5% were in remission on antiepileptic drugs, 8% were having seizures on antiepileptic drugs, and 37% were considered to have intractable epilepsy. Information was not available on the remaining survivors.

Social outcomes were almost universally poor for the survivors, who were an average of 23 years old at the time of assessment. Of the 46 survivors who were evaluated, almost half were unable to walk, three-quarters had mental handicap, and half had neurologic handicap. Only three were mentally and neurologically normal.

More than half of the group was living with a parent or guardian, and one-third lived in a group home or institution. Only three individuals were living independently, although another five were judged capable of independent living by their caretakers. Of the 46, 41 (89%) were completely financially dependent on their parents or the government.

Functional literacy—reading at about a fifth-grade level—had been achieved by one-quarter of the group. Another 18 (39%) had safety literacy; they could interpret an exit or stop sign and find appropriate bathrooms by looking at the picture on the door.

A good outcome (the ability to live independently) was seen in 8 (17%) of the group. A fair outcome (not capable of independent living, but not needing total care) occurred in 10 (22%). A bad outcome (requiring assistance with all activities of daily living) occurred in 28 (61%).

Almost all of the group (94%) were considered by their caregiver to have satisfactory overall health. Problematic sexual behavior occurred in 6 (11%), 13 (29%) were judged aggressive, and 10 (22%) were socially isolated. Some of the group had more than one problematic behavior. ■

Maternal Issues May Predispose Desire for Gender Change in Boys

BY ANNE SCHECK
Contributing Writer

SAN FRANCISCO — Boys who say they want to become girls may be trying to win a lost mother's love rather than expressing a true desire to switch gender, Judith Fingert Chused, M.D., said at the annual meeting of the American Psychoanalytic Association.

One of the most challenging psychotherapeutic dilemmas is treating young patients who believe they are "biologically incongruent" to their birth gender. Why? "Because the wish to be a different gender may have to do with something else that is going on," said Dr. Chused of the department of psychiatry and behavioral sciences at George Washington University, Washington.

Early maternal loss and parental intolerance of aggressive behavior can underlie a boy's repeated assertion that he wants to be a girl.

Although there is growing recognition that some people correctly identify themselves as being a different gender from a very early age, when it comes to children there is every reason to question such self-assessment, she said. In her practice, she has found that early maternal loss—between 12 and 24 months of age—and parent intolerance of aggressive behavior can underlie a boy's repeated assertion that he wants to be a girl.

Treatment of children needs to take into account the role of unconscious fantasies, which can be tough to discern in children, but this aspect may be particularly influential for those who express the wish to be a different gender, Dr. Chused stressed.

In her experience of treating several boys who said they wanted to be girls, she found that they had a universal longing to become like their mothers. "It was to try to find a way to be close to her, by becoming her themselves," she suggested.

In the cases she has encountered, maternal deprivation seemed to go hand in hand with the expressed desire, although the loss of the mother occurred in different ways, she pointed out. Of course, she added, not all boys who have lost their mothers wish to change into girls, just as a male having feminine traits is not necessarily a sign of pathology.

Dr. Chused speculated that variations of maternal loss may be an underrecognized etiology for certain cases of gender identity disorder. In the panel discussion of the issue, she reiterated that concern, saying, "My sense from this [experience] and from reading the material on it, is that very few boys actually want to be a girl."

In one case, she concluded that a boy had nothing more than a craving for maternal affection and that his mother had shown disdain for men. "This is different from wanting to be a girl. This is wanting to be loved," she said. The reverse also seems to be true, according to the literature. When girls have mothers who don't like themselves as women, or who have a strong bias against their own gender, they may express the desire to be boys, believing that if they were male, they would be more acceptable to their parents, she said.

"The way I address such gender issues is to ask, 'Why is this child not comfortable with himself?' and to look at the whole individual within his environment—who is he or she," she advised. ■