Biomedical Update:

Too few neurons in the autistic amygdala?

The amygdala, a brain region involved in emotions and memory, contains fewer neurons in males with autism than in non-disabled males, according to a recent study.

Cynthia Mills Schumann and David Amaral counted the neurons in representative samples of postmortem amygdala tissue from nine males who had autism (ranging in age from 10 to 44 years at the time of their death) and samples from ten males without autism. The autistic individuals had not had epilepsy or other major neurological disorders.

Using a technique called "unbiased stereological analysis," the researchers found significantly fewer neurons in the whole amygdala, and in one amygdala region called the lateral nucleus, in the samples from individuals with autism.

Previous studies revealed that the amygdala is actually enlarged in young children with autism. "The autistic amygdala appears to undergo an abnormal pattern of postnatal development that includes early enlargement and ultimately a reduced number of neurons," Schumann and Amaral say. "It will be important to determine in future studies whether neuron loss in the amygdala is a consistent characteristic of autism and whether cell loss occurs in other brain regions as well." (See related article on page 7.)

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"Stereological analysis of amygdala neuron number in autism," Cynthia Mills Schumann and Davis Amaral, *Journal of Neuroscience*, Vol. 26, No. 29, July 19, 2006, 7674-9. Address: Cynthia Mills Schumann, Department of Psychiatry and Behavioral Sciences and the M.I.N.D. Institute, University of California, Davis, Sacramento, CA 95817.

—and—

"UC Davis M.I.N.D. Institute researchers find fewer neurons in the amygdala of males with autism," news release, UC Davis, July 18, 2006.

Key substance in brain formation low in autism

Levels of IGF-1—a substance that stimulates cell proliferation and differentiation both before and after birth—are low in young autistic children, according to a new study.

Raili Riikonen and colleagues measured levels of IGF-1 (insulin-like growth factor-1) and IGF-2 (insulin-like growth factor-2) in the cerebrospinal fluid of 25 children with autism and 16 age-matched children without disabilities. The researchers found significantly reduced IGF-1 levels in autistic children under five years of age, but not in older children. No differences in IGF-2 levels were seen between autistic children and controls, except that IGF-2 concentration was correlated with age in controls but not in the autistic children

Riikonen et al. note that cerebellar abnormalities are a consistent finding in autism, and that IGF-1 is crucial to the survival of Purkinje cells in the cerebellum. "Low concentrations might mean that the important survival factor IGF-1 during the critical brain spurt period is insufficient for normal Purkinje cell development," they say.

No autistic children in this study had abnormally large heads, a common finding in autism. However, head circumferences correlated with IGF-1 levels in autistic children, but not in the control children.

The researchers note that IGFs increase the numbers of cells called oligodendrocytes, which make up most of the cells in the white matter of the brain. "We expected a correlation between... head growth (head circumferences) and IGF concentrations in children with autism but not in the comparison group," they say. "We speculate that this might help explain the abnormal brain size in autism."

Their findings, the researchers speculate, may have implications for treatment. "In theory," the researchers say, "IGF-1 administration might increase the brain IGF-1 concentrations and perhaps be of therapeutic importance" if administered early in development.

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"Cerebrospinal fluid insulin-like growth factors IGF-1 and IGF-2 in infantile autism," R. Riikonen, I. Makkonen, R. Vanhala, U. Turpeinen, J. Kuikka, and H. Kokki, *Developmental Medicine & Child Neurology*, Vol. 48, No. 9, September 2006, 751-5. Address: Raili Riikonen, Kuopio University Central Hospital, P.O. Box 1627, FI-70211 Kuopio, Finland, raili.riikonen@kolumbus.fi.

Blood vessel study points to oxidative stress

Scientists are increasingly focusing on oxidative stress—which occurs when unstable molecules called "free radicals" damage cells—as a factor in autism (see related article on page 4). A new study of blood vessel function in autistic children reveals more clues supporting this association.

Domenico Pratico et al. studied urinary samples from 26 autistic children and 12 non-disabled controls. The researchers measured three substances in the samples: isoprostane, a marker for oxidative stress; thromboxane, an index of platelet activation; and prostacyclin, a measure of blood vessel activation.

The researchers report that autistic children's levels of isoprostane, a byproduct generated when free radicals attack fat cells, indicated oxidative stress levels nearly double those of the control children. This is consistent, they say, with earlier findings indicating that autistic children exhibit higher free radical production and impaired antioxidant defenses, and that a number of autistic children improve when taking antioxidants. (Antioxidants are substances—for instance, a number of vitamins, minerals, and carotenoids—that deactivate free radicals.)

In addition, the samples from autistic children revealed elevations of thromboxane and prostacyclin, which work together to maintain proper blood vessel function. These elevations correlated directly with levels of oxidative stress.

"In general," Pratico says, "it is known that abnormalities in blood vessels can be clinically reflected by an abnormal blood flow. In this regard, it is interesting that earlier neuroimaging studies of autistic children have demonstrated a reduced amount of blood reaching the brain."

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"Altered vascular phenotype in autism: correlation with oxidative stress," Y. Yao, W. J. Walsh, W. R. McGinnis, and D. Pratico, *Archives of Neurology*, Vol. 63, No. 8, August 2006, 1161-4. Address: Domenico Pratico, Department of Pharmacology, School of Medicine, University of Pennsylvania, 3620 Hamilton Walk, Philadelphia, PA 19104.

—and—

"Link between autism and abnormal blood-vessel function and oxidative stress," news release, University of Pennsylvania, August 15, 2006.

—In Memoriam—
Katie Dolan

The autism world mourns the passing of Katie Dolan, a tireless advocate for autistic individuals, at the age of 82.

When Katie Dolan's autistic son was born in 1950, there were almost no options for educating developmentally disabled children. Dolan and a group of other parents founded the Northwest Center in Seattle in 1965 to address this need. Not content to win this battle solely for their own children, they also authored the Education for All Act, which mandated public schooling for developmentally disabled children in Washington. The act was a model for the 1975 federal Education for All Handicapped Children Act.

Up to the time of her death, Katie Dolan continued to battle for the rights of the developmentally disabled. ARI sends condolences to her family; she will be deeply missed.