Clues point to impaired purine metabolism in autism

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to people who carry two copies of ADA1. (Reduced catalytic activity and resulting impaired purine metabolism could contribute to a build-up of toxic chemicals.)

The researchers report that ADA2 alleles were significantly more common in autistic subjects (17.6 percent) than in control subjects (7.9 percent), and more common in the fathers of autistic children as well. Their findings are consistent with those of an earlier study, which also found that ADA2 alleles were more common in autistic than in non-autistic subjects.

In earlier research, Ted Page and Mary Coleman reported that some autistic subjects with elevated levels of uric acid excretion exhibit unusually high rates of intracellular purine synthesis, indicating a purine metabolism defect. The researchers treated several subjects with uridine, a naturally occurring component of RNA and DNA, and report improvements in cognition and muscular function. They speculate that purine abnormalities may affect as many as 20 percent of autistic individuals.

An association between autism and abnormal purine metabolism was first reported in 1987 (see ARRI 1/2) by Harry Gruber and Paul Laikind. Gruber and Laikind identified a rare form of autism caused by a defect of the enzyme adenylosuccinate lyase, leading to a build-up of purines in the body.

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"Adenosine deaminase alleles and autistic disorder: case-control and family-based association studies," A. M. Persico, R. Militerni, C. Bravaccio, C. Schneider, R. Melmed, S. Trillo, F. Montecchi, M. T. Palermo, T. Pascucci, S. Puglisi-Allegra, K. L. Reichelt, M. Conciatori, A. Baldi, and F. Keller, *American Journal of Medical Genetics*, Vol. 96, No. 6, December 4, 2000, pp. 784-790. Address: A. M. Persico, Laboratory of Neuroscience, Department of Physiology and Neuroscience, Libera Universita Campus Bio-Medico, Rome, Italy.

—and—

"Purine metabolism abnormalities in a hyperuricosuric subclass of autism," Ted Page and Mary Coleman, *Biochimica et Biophysica ACTA*, Vol. 1500, No. 3, March 17, 2000, pp. 291-296. Address: Ted Page, Department of Neurosciences, University of California, San Diego, School of Medicine, 9500 Gilman Drive, La Jolla, CA 92093-0624.

Some seizures may be autoimmune phenomena

Most cases of epilepsy (a condition affecting up to a third of autistic individuals) are categorized as idiopathic—that is, of unknown origin. A new study by J. Palace and B. Lang, however, suggests that many cases of idiopathic epilepsy may be caused by autoimmune mechanisms.

Palace and Lang cite three lines of research that link epilepsy to autoimmune dysfunction:

• A number of childhood epilepsy syndromes show evidence of immune system involvement, and respond to immune system treatments. Among them is Landau-Kleffner syndrome (LKS) (see ARRI 13/2, 12/2, 11/1), which frequently causes autistic-like symptoms. The researchers note that "autoantibodies directed against brain endothelial cells and neuronal nuclear proteins have been reported" in LKS, and that there are case reports of LKS responding to IVIG (a treatment that helps ameliorate immune system disorders).

• Epilepsy is often associated with known autoimmune disorders. For instance, the incidence of epilepsy is raised in systemic lupus erythematosus, "stiff man" syndrome, and Hashimoto's encephalopathy, all of which involve autoimmune processes. *[Editor's note: while the authors do not mention autism, a large body of evidence indicates that autoimmune dysfunction plays a significant role in autism—see ARRI 14/3, 13/2, 13/1, 11/4.]*

• Studies of individuals with idiopathic epilepsy often show evidence of autoimmune abnormalities. One study, for instance, found that 13% of children with idiopathic epilepsy had high titers of antiphospholipid antibodies, compared to no subjects in control groups. In addition, the authors note, "immunotherapies seem to have efficacy above standard antiepileptic treatment in some groups of patients."

Palace and Lang conclude that additional study is needed to define the subgroups of epilepsy that may be linked to autoimmune dysfunction, and to assess the value of immune modulatory treatments in these patients.

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"Epilepsy: An autoimmune disease?" J. Palace and B. Lang, *Journal of Neurology, Neurosurgery & Psychiatry*, Vol. 69, No. 6, December 2000, pp. 711-714. Address: J. Palace, Department of Clinical Neurology, Radcliffe Infirmary, Oxford OX2 6HE, U.K.

Pica treated with vitamin supplements

Although pica (the eating of non-food items) is often considered a sign of nutritional deficiency in non-disabled individuals, it is common for pica in developmentally disabled individuals to be treated solely as a behavioral problem. However, a new study by Gary Pace and Edward Toyer indicates that pica in this population can also stem from nutritional deficiencies.

Pace and Toyer evaluated a nine-year-old girl with severe mental retardation, whose pica included eating cloth fragments and strings. The girl had required surgery to remove an intestinal blockage resulting from her pica. Before the study began, the girl's parents started her on a multivitamin supplement, and reported that no instances of pica occurred for three weeks—the longest pica-free period the girl had experienced in six years. (She was also continued on iron supplements, which she had taken for some time for previously diagnosed anemia.)

The researchers collected data during vitamin supplementation, after discontinuation of the supplements, and again when the supplements were reintroduced. They report that the girl's periods of non-pica behavior increased significantly during supplementation, both in situations where she was alone and when other people were present.

"The results of this investigation support the hypothesis that, in some cases, pica can be effectively and efficiently treated by implementation of a medical intervention," they say. They cite two earlier studies, one in which coprophagia (the eating of feces) by three developmentally disabled individuals decreased following nutritional supplementation, and one in which pica in a profoundly retarded woman was linked to zinc deficiency.

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"The effects of a vitamin supplement on the pica of a child with severe mental retardation," Gary M. Pace and Edward A. Toyer, *Journal of Applied Behavior Analysis*, Vol. 33, No. 4, Winter 2000, pp. 619-622. Address: Gary M. Pace, May Institute, 940 Main Street, Box 899, South Harwich, MA 02661, gpace@mayinstitute.org.

NIH creates alternative medicine database

The National Institutes of Health and National Center for Complementary and Alternative Medicine have created a free, online database offering access to more than 220,000 abstracts, references, and full-text articles on alternative medicine. The database is called CAM, and is part of PubMed, the National Library of Medicine's free medical database. To access the new database, go to www.nccam.nih.gov, and click on CAM.