# Biomedical Update:

## LKS, autism: signs of autoimmune attack

A new study adds to evidence that some children with autism or Landau Kleffner Syndrome (a seizure disorder that begins in early childhood and can cause autistic symptoms) suffer from autoimmune disorders, in which the body attacks its own cells.

A.M. Connolly and colleagues studied 13 children with Landau Kleffner Syndrome (LKS) or variants of the disorder, 11 children with autism, 20 children with other neurological disorders, 22 children with non-neurological disorders, and 29 healthy controls. Levels of brain autoantibodies, an indication of autoimmune processes attacking the brain, were measured.

The researchers report that IgG anti-brain autoantibodies were found in 45% of the group with LKS variants, 27% of autistic subjects, and 10% of children with other neurological disorders. By comparison, the autoantibodies occurred in only 2% of healthy children or children with non-neurological disorders.

In addition, IgM autoantibodies were present in 36% of autistic children, 9% of children with LKS variants, and 15% of children with other neurological disorders, compared to none of the other subjects.

Connolly et al. conclude, "The presence of these antibodies raises the possibility that autoimmunity plays a role in the pathogenesis of language and social developmental abnormalities in a subset of children with these disorders."

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"Serum autoantibodies to brain in Landau-Kleffner variant, autism, and other neurologic disorders," *Journal of Pediatrics*, Vol. 134, No. 5, May 1999, pp. 607-613. Address: A. M. Connolly, Department of Neurology, Washington University, St. Louis Children's Hospital, St Louis, Missouri, USA 63110.

## Excess water drinking in autism, MR compared

"Polydipsia," or the excessive drinking of water, is common among mentally retarded individuals—but a new study suggests that it's even more common in autism.

K. Terai et al. studied the incidence of polydipsia in 49 autistic children and 89 mentally retarded, non-autistic children. The incidence of polydipsia was higher in the autistic children, the researchers say, and "the severity of water drinking behavior was significantly higher in autism than in mental retardation."

Polydipsia was not linked to the use of psychotropic drugs. The researchers suggest that the high incidence of the behavior in autistic children is "possibly due to some intrinsic factor in autism itself."

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***Editor's Note: Excessive thirst may indicate an essential fatty acid deficiency.***

"Excessive water drinking behavior in autism," K. Terai, T. Munesue, and M. Hiratani, *Brain and Development*, Vol. 21, No. 2, March 1999, pp. 103-106. Address: K. Terai, Noto Second Hospital, Division of Neuropsychiatry, Nanao, Ishikawa, Japan.

## More on L-carnitine for Rett syndrome

A new study supports earlier evidence that the amino acid L-carnitine is of some benefit for individuals with Rett syndrome. The progressive disorder, which almost exclusively affects girls, often mimics autism in its early stages.

C. Ellaway and colleagues recently conducted a randomized, placebo-controlled, double-blind crossover trial of L-carnitine on 35 girls with Rett syndrome. The researchers say that both parents and medical personnel noted improvements in the L-carnitine-treated subjects' well-being, and say, "In addition, medical review showed an improvement on the Hand Apraxia Scale for a higher proportion of girls on L-carnitine." (A prominent symptom of Rett syndrome is the loss of purposeful use of the hands.)

The researchers conclude, "While L-carnitine did not lead to major functional changes in ability, the type of changes reported could still have a substantial impact on the girls and their families."

This study's findings are similar to those of a 1996 case study (see ARRI 10/3), in which E. Plöchl and colleagues reported significant improvements in activity, sleep, and communication in a five-year-old Rett syndrome patient treated with L-carnitine.

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"Rett syndrome: randomized controlled trial of L-carnitine," C. Ellaway, K. Williams, H. Leonard, G. Higgins, B. Wilcken, and J. Christodoulou, *Journal of Child Neurology*, Vol. 14, No. 3, March 1999, pp. 162-167. Address: C. Ellaway, Western Sydney Genetics Program, the Royal Alexandra Hospital for Children, Westmead, Australia.



## Another study points to chromosome 15

A new report adds to evidence implicating a chromosome 15 defect, inherited through the maternal line, in some cases of autism.

To date, around two dozen cases of children with autism and duplications of a section of this chromosome have been reported. In 1997, Edwin Cook and colleagues reported that paternally inherited duplications of the chromosome region 15q11-q13 appear to cause no symptoms, while "maternally inherited duplications usually lead to autism or atypical autism." Cook et al. reported on a family with two autistic children, both of whom inherited the chromosome 15 defect from their mother, and one non-disabled child who did not inherit the defect (see ARRI 11/4).

Recently, Italian researchers F. Gurrieri et al. reported on a similar case. Their subject, a 12-year-old boy with atypical autism and seizures, exhibited a 15q11-q13 duplication which was inherited from his mother. The mother, in turn, had inherited the defective chromosome from her father, as a new mutation. Gurrieri et al. theorize that when the defect is inherited from fathers, it is "silenced" by genetic imprinting, and thus causes no harm. (A number of genes are imprinted, meaning that they are switched on or off depending on the sex of the parent from whom they are inherited.)

Interestingly, the researchers found that the defect seen in their subject was slightly different than that seen in his mother. "To the best of our knowledge," they say, "our patient is the first to demonstrate an instability in this region over two generations." They note that their patient, who had a simple duplication, had milder symptoms than some children with inverted-duplicated(15), in which three maternally derived copies of the critical region are duplicated, rather than just two.

The researchers conclude, "Together with data from the literature, our observation suggests that 1) there are genes for autism and possibly for some type of partial epilepsy in the chromosome 15q11-13 region that may act in a dose-dependent manner and 2) these genes are subject to imprinting, and only maternally derived alleles are active."

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"Pervasive developmental disorder and epilepsy due to maternally derived duplication of 15q11-q13," F. Gurrieri, A. Battaglia, L. Torrisi, R. Tancredi, C. Cavallaro, E. Sangiorgi, and G. Neri, *Neurology*, Vol. 52, No. 8, May 1999, pp. 1694-1697. Address: F. Gurrieri, Istituto di Genetica Medica, Università Cattolica del Sacro Cuore, Lgo. F. Vito, 1-00168 Rome, Italy, fgurrieri@rm.unicatt.it.