Volume 11, No. 1 1997

Autism Research Review INTERNATIONAL

A quarterly publication of the Autism Research Institute

Reviewing biomedical and educational research in the field of autism and related disorders

LKS patient responds to gamma globulin

Researchers at the American University of Beirut report that Landau-Kleffner syndrome (LKS), a disorder whose symptoms sometimes mimic autism, may respond to IV- gamma globulin treatment.

M. Fayad and colleagues tested gamma globulin therapy, an approach used to treat autoimmune disorders and immune deficiency syndromes, on an eight-year-old female LKS patient. "Over one and a half years," they say, "she received three courses of IV-globulin... followed each time by remarkable clinical and electrographic improvement lasting a few months each time, followed by recurrence of the spikes [abnormal EEG patterns] and worsening of language." The researchers note that the girl's cerebrospinal fluid IgG index, which was abnormal before treatment (an indication of altered immune system function), "dropped to normal after the first IV-globulin infusion."

LKS is characterized by normal development followed, in early childhood, by the loss of receptive and then expressive language. Children with LKS may exhibit aloofness, unusual responses to sound, aggression, monotonic voices, compulsions, and other autistic symptoms. The disorder is characterized by a particular EEG pattern (although children may not have overt seizures), and is diagnosed with sleep EEGs. Although the prognosis for individuals with LKS generally is poor, a number of patients have improved dramatically following surgery to stop their seizures (see ARRI 10/2).

Fayad et al. say the effectiveness of gamma globulin therapy "supports the possibility of an autoimmune pathophysiology of Landau-Kleffner syndrome in our patient." Similarly, researchers have recently reported improvement in autistic children (see ARRI 10/3) and individuals with Tourette syndrome or obsessive-compulsive disorder (see ARRI 10/3) following immunoglobulin therapy, implicating autoimmune processes in these disorders as well.

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"Landau-Kleffner syndrome: consistent response to repeated IV gamma globulin doses: a case report," M. N. Fayad, R. Choueiri, and M. Mikati, American University of Beirut, Lebanon, 1996. Abstract available on the Internet at http://www.aub.edu.lb/aub-online/research/medicine/pediatrics_projects.html.

Researchers call for studies on pentoxifylline's effects on autism

In a recent article in the *Journal of Child Neurology*, Sudhir Gupta, Bernard Rimland, and Paul D. Shilling note that a number of clinical trials, most by Japanese researchers, suggest that the drug pentoxifylline—commonly used to treat symptoms caused by blocked blood vessels—can reduce autistic symptoms and/or improve language and social skills. Among the studies:

—S. Sogame treated 36 children with autism or other biologically-based behavioral abnormalities with pentoxifylline. Within one month of beginning treatment, 34 of the children showed a positive response to the drug. Sogame reported the drug to be "remarkably effective" with 10 of 23 subjects, "fairly effective" with eight others, and "slightly effective" with three. Improvements were seen in language, relatedness, insistence on sameness, and self-image. In addition, Sogame reported that no case of intractable epilepsy in the group failed to respond to the drug.

—A. Nakane reported that of 30 autistic children given pentoxifylline, six showed marked behavioral improvement and 14 showed slight improvement.

—M. Shimoide reported improvements in 7 of his 20 male autistic subjects given pentoxifylline. Most of the subjects who improved were under 6 years of age.

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More evidence of autistic brain defects

Sixteen magnetic resonance imaging (MRI) and autopsy studies of autistic individuals have reported abnormalities (usually under-development, but sometimes over-development) of the cerebellum, a brain region that coordinates motor activity and is involved in speech, learning, attention, and autonomic functions. In addition, MRI scans indicate that nearly half of autistic individuals have defects of the parietal lobe, one of the four lobes of each hemisphere of the cerebrum.

In new research that strongly supports these findings, Richard Haas and colleagues performed neurological evaluations on autistic and non-disabled subjects and found that "in groups of tests that reflect cerebellar and parietal function, the neurologic abnormalities detectable by clinical examination were significantly greater for autistic subjects than for normal controls." In contrast, they say, no differences were seen between autistic and control subjects on several tests measuring the function of other brain areas.

The researchers tested 28 autistic patients between the ages of 6 and 18, and 24 non-disabled controls. They found that 96% of the autistic subjects had abnormal scores on at least one category of the tests measuring cerebellar function, and that 75% had abnormal scores on two or more categories. "In contrast," they report, "only five of the 24 normal controls had abnormal scores on *any* category of cerebellar testing." Forty-four percent of the autistic subjects who were able to perform the tests of parietal lobe functioning had abnormal scores on at least one category, and 20% had abnormal scores on two or more categories. Only one non-disabled subject had an abnormal score on a single test of parietal lobe functioning.

The researchers also note that abnormal scores on tests of cerebellar functioning in normal subjects occurred almost entirely in subjects under the age of eight. But among autistic subjects, they note, "abnormalities of cerebellar function were observed throughout the age range." This indicates, they say, "a permanent loss in structure and function" in the cerebellar region in autistic subjects.

In addition, both retarded and non-retarded autistic subjects exhibited cerebellar and parietal abnormalities (although retarded subjects had a higher proportion of abnormal scores). This finding, Haas et al. say, suggests that mental retardation alone cannot explain the abnormalities seen in the autistic subjects.

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"Neurologic abnormalities in infantile autism," Richard H. Haas, Jeanne Townsend, Eric Courchesne, Alan J. Lincoln, Laura Schreibman, and Rachel Yeung-Courchesne; *Journal of Child Neurology*, Vol. 11, No. 2, March 1996, pp. 84-92. Address: Eric Courchesne, Autism and Brain Development Research Laboratory, Children's Hospital, 8110 La Jolla Shores Drive, La Jolla, CA 92037.