

## Biomedical Update:

### MRI study links abnormal asymmetry to language problems

An MRI study indicates that the communication deficits of autistic children may stem in part from an abnormal asymmetry of two brain regions involved in language.

Martha Herbert and colleagues performed scans on 16 autistic boys between the ages of 7 and 11, comparing them to 15 control children matched for age and handedness. All of the autistic subjects had nonverbal IQs over 80.

The researchers found that in control subjects, the language-related cortex was 17 percent larger on the left than on the right, while in autistic subjects the region was 27 percent larger on the right than on the left.

In addition, the researchers found that asymmetry of the posterior temporal fusiform gyrus—a brain region involved in visual face processing—was more left-sided in autistic subjects than controls.

The researchers conclude, "In boys with autism, language and social/face processing-related regions displayed abnormal asymmetry. These structural abnormalities may be related to language and social disturbances observed in autism."

"Abnormal asymmetry in language association cortex in autism," M. R. Herbert, G. J. Harris, K. T. Adrien, D. A. Ziegler, N. Makris, D. N. Kennedy, N. T. Lange, C. F. Chabris, A. Bakardjiev, J. Hodgson, M. Takeoka, H. Tager-Flusberg, and V. S. Caviness, Jr., *Annals of Neurology*, Vol. 52, No. 5, November 2002, 588-96. Address: Martha Herbert, Center for Morphometric Analysis, Massachusetts General Hospital, Boston, MA 02114.

### More signs of immune system dysfunction in autism reported

New evidence linking autism to abnormal immune system function is reported in a recent study from the Netherlands.

J. Croonenberghs et al. found "significantly increased concentrations of total serum protein (TSP) in autistic subjects, which were attributable to increased serum concentrations of albumin and gamma globulin." In addition, they say, serum IgG, IgG2 and IgG4 were markedly increased. They also found significant correlations between TSP and serum gamma globulin concentrations and social impairment, and between TSP, serum albumin, and IGG levels and social withdrawal.

The researchers conclude, "The increased serum concentrations of IgGs in autism may

point towards an underlying autoimmune disorder and/or an enhanced susceptibility to infections resulting in chronic viral infections, whereas the IgG subclass skewing may reflect different cytokine-dependent influences on autoimmune B cells and their products."

"Increased serum albumin, gamma globulin, immunoglobulin IgG, and IgG2 and IgG4 in autism," J. Croonenberghs, A. Wauters, K. Devreese, R. Verkerk, S. Scharpe, E. Bosmans, B. Eged, D. Deboutte, and M. Maes, *Psychological Medicine*, Vol. 32, No. 8, November 2002, 1457-63. Address: J. Croonenberghs, University Center of Child and Adolescent Psychiatry, A. Z. M. and Department of Medical Biochemistry, University of Antwerp, Wilrijk, Clinical Laboratory A. Z. Middelheim, Antwerp, The Netherlands.

### Seizure drug may work as monotherapy

The anticonvulsant drug Levetiracetam (LEV, sold under the brand name Keppra), generally used as an adjunct to other medications, may work well as a single-drug therapy, according to a recent study. If so, some patients currently taking multiple anti-seizure drugs may be able to reduce their medications and thus experience fewer side effects.

Taoufik Alsaadi and colleagues evaluated the effectiveness of LEV for 37 patients with epilepsy. Of these patients, 28 had difficult-to-control seizures and were placed on LEV after other drugs failed to control their seizures. The researchers report that nearly 80 percent of these individuals experienced seizure reductions of 50 percent or more, and one-third became seizure-free. For the remaining nine patients, LEV was the first anticonvulsant drug administered. Four patients in this group became seizure-free, and three experienced seizure reductions of at least 75 percent.

"Compared with other treatments," study co-author Katy Thieman says, "patients in the study reported fewer side effects such as grogginess, poor cognition and memory loss that can hinder the ability to work and maintain relationships." The researchers note, however, that their study is preliminary and that a double-blind study is needed to confirm their results.

(Editor's note: while only minor side effects were seen in this study, reported LEV side effects include dizziness, clumsiness, crying, depression and other mental changes, memory loss, anger outbursts, shortness of breath, and headaches.)

"UC Davis study identifies promising epilepsy treatment," press release, UC Davis Health System, October 28, 2002.

### Nutrients beneficial for children with PDD, OCC

Extending their earlier research on the effects of nutrients on bipolar disorder, Bonnie Kaplan and colleagues now report that high-dose vitamins, minerals and amino acids can dramatically reduce rage and mood problems in children with pervasive developmental disorder (PDD) and obsessive-compulsive disorder.

In a pilot study, the researchers administered a supplement containing three dozen nutrients to two boys whose symptoms included explosive rage and wild mood swings. One subject was a 12-year-old diagnosed with PDD, and the other was an eight-year-old with atypical obsessive-compulsive disorder.

The researchers report that both boys benefited from the supplement. "Mood, angry outbursts, and obsessional symptoms improved when initially treated," they say, "returned when not taking the supplement, and remitted when the micronutrient supplement was reintroduced." The researchers have followed both boys for more than two years, and say that their behaviors are stable.

Earlier (see ARRI 16/1), the researchers reported on a study of 11 adults diagnosed with bipolar disorder and unresponsive to drug treatment (or unable to take drugs due to side effects). In this six-month study, subjects experienced symptom reductions of 55 to 66 percent, and Kaplan et al. reported that "need for psychotropic medications decreased by more than 50 percent."

"Treatment of mood lability and explosive rage with minerals and vitamins: two case studies in children," B. J. Kaplan, S. G. Crawford, B. Gardner, and G. Farrelly, *Journal of Child and Adolescent Psychopharmacology*, Vol. 12, No. 3, Fall 2002, 205-19. Address: Bonnie Kaplan, Department of Paediatrics, University of Calgary, Calgary, Alberta, Canada AB T2T 5C7.

#### SECRETIN STUDY:

Repligen Corporation and more than a dozen medical centers in the United States are currently enrolling children in a Phase 3 clinical trial to evaluate the effectiveness of synthetic human secretin. Autistic children between the ages of 2 years 8 months and 4 years 11 months are eligible to participate. The study involves 11 clinical visits over a five month period. Information about clinical sites currently enrolling study participants may be obtained at [www.repligen.com](http://www.repligen.com) or by calling 1-800-622-2259 and selecting option 5.