Biomedical Update:

Disordered metal metabolism common in autistic individuals

Studying 503 autistic individuals, William Walsh and colleagues report that 428 exhibited "severely elevated" copper-to-zinc ratios in their blood, and 30 had severe zinc deficiency. Of the remaining 45, 41 were undergoing aggressive zinc therapy at the time of sampling. The researchers say their findings may point to a metallothionein disorder as "a fundamental cause" of autism.

Metallothionein is a protein involved in the detoxification of heavy metals, as well as in nervous system development and immune function. "Many classic symptoms of autism may be explained by a metallothionein defect in infancy," Walsh and colleagues say, "including GI tract problems, heightened sensitivity to toxic metals, and abnormal behaviors."

Editor's Note: Dr. Walsh's findings may help explain why mercury toxicity is important in autism. He will be a speaker at our Dan! Conference in October.

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"Disordered metal metabolism in a large autism population," William J. Walsh, Anjum Usman, and Jeffrey Tarpey, presentation to the Annual Meeting of the American Psychiatric Association, New Orleans, May 2001. Abstract available at http://www.hriptc.org/APA_abstract.htm.

Risperidone reduces behavioral symptoms in mildly retarded subjects

A new double-blind study concludes that risperidone (Risperdal) is useful in treating behavior problems of children with mildly reduced IQs.

In a four-week study, Marc Van Bellinghen and C. De Troch of Belgium treated 13 children, ages 6 to 14, with IQs between 66 and 85. Subjects received either a placebo or risperidone (at an average dose of .05 mg/kg). The researchers report that children taking risperidone showed improved social behavior and significant decreases in irritation, hyperactivity, and other behavioral symptoms. No significant side effects were seen, although weight gain and other side effects have sometimes been reported in patients *(see article below)*.

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"Risperidone in the treatment of behavioral disturbances in children and adolescents with borderline intellectual functioning: a double-blind, placebo-controlled pilot trial," M. Van Bellinghen and C. De Troch, *Journal of Child and Adolescent Psychopharmacology*, Vol. 11, No. 1, Spring 2001, pp. 5-13. Address: Marc Van Bellinghen, Psychotherapeutisch Centrum, Department of Child Psychiatry, A.Z.H. Hart. Asse, Belgium, marc.van.bellinghen@skynet.be.

...but drug frequently causes prolactinemia

Risperidone (Risperdal) is a "potent inducer" of hyperprolactinemia, according to new research on schizophrenics taking the drug.

Hyperprolactinemia (elevated levels of the hormone prolactin) causes a wide range of symptoms. In women, these include abnormal milk production, breast engorgement, absence of periods, and an increased risk of osteoporosis and cardiovascular disease. In men, hyperprolactemia can cause breast milk production and impotence.

A. E. Kearns and colleagues measured prolactin concentrations in 68 schizophrenic outpatients taking risperidone, clozapine, or typical antipsychotic drugs. They report that among female subjects, 100 percent taking risperidone had elevated prolactin levels, compared to 25 percent of clozapine users and 83 percent of those taking typical antipsychotic drugs. Among male patients, 94% of those taking risperidone had elevated prolactin levels, compared to 18 percent of those taking clozapine and 27 percent of those taking typical antipsychotics. Mean prolactin concentrations also were higher in risperidone users of both sexes than in subjects taking clozapine or traditional antipsychotics.

Although risperidone is generally considered safer and more effective than most antipsychotic drugs, Kearns and colleagues caution that "the higher and more frequently increased prolactin concentrations caused by risperidone [in comparison to other drugs] could adversely affect patient health and compliance."

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Risperidone-associated hyperprolactinemia," A. E. Kearns, D. C. Goff, D. L. Hayden, and G. H. Daniels, *Endocrine Practice*, Vol. 6. No. 6, November 2000, pp. 479-481. Address: A. E. Kearns, Endocrine Unit, Department of Medicine, Massachusetts General Hospital, Boston, MA 02114.

Fragile X: more dendrite abnormalities reported

Individuals with fragile X syndrome, the most common inherited form of mental retardation, frequently exhibit autistic behaviors. A new study suggests that one reason for the behavioral problems seen in fragile X is abnormal development of dendrites (branch-like protrusions from neurons which receive incoming messages from surrounding cells) in several cortical areas.

In post-mortem studies, S. A. Irwin and colleagues examined the temporal and visual cortices of individuals with fragile X and non-disabled control subjects, and found that the fragile X subjects had a significantly larger number of longer dendritic spines, and fewer short spines, than control subjects. They also exhibited more immature dendritic spines and a lower number of mature spines. The researchers note that other studies of fragile X subjects report abnormal dendrite spine lengths and shapes in the parietal and occipital lobes, and that mice genetically engineered to have fragile X show similar dendrite abnormalities.

"Long dendritic spines with immature morphologies and elevated spine numbers are characteristic of early development or a lack of sensory experience," the researchers say. "The fact that these characteristics are found in fragile X patients throughout multiple cortical areas may suggest a global failure of normal dendritic spine maturation and/or pruning during development that persists throughout adulthood."

Fragile X syndrome occurs when a defective FMR1 gene on the X chromosome results in the absence of a protein known as FMRP. Symptoms vary but often include mental retardation, attention deficits, hand-biting and hand-flapping, tactile defensiveness, poor eye contact, perseverative speech, large testicles, long face, and prominent ears.

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"Abnormal dendritic spine characteristics in the temporal and visual cortices of patients with fragile X syndrome: a quantitative examination," S. A. Irwin, B. Patel, M. Idupulapati, J. B. Harris, R. A. Crisostomo, B. P. Larsen, F. Kooy, P. J. Willems, P. Cras, P. B. Kozlowski, R. A. Swain, I. J. Weiler, and W. T. Greenough, *American Journal of Medical Genetics*, Vol. 98, No. 2, January 15, 2001, pp. 161-167. Address: S. A. Irwin, Neuroscience Program, University of Illinois, Urbana, IL 61801.

ARI maintains a list of physicians who use drugs only as a last resort, and who are interested in the Defeat Autism Now! (DAN!) approach to diagnosis and treatment. If you are a physician who should be on that list, send a self-addressed, stamped envelope with a request for our "Doctor Referral List Questionnaire."