Case study: blood pressure drug reduces autistic symptoms

The drug spironolactone may be a safe and highly effective treatment for autistic children, according to a new study.

James Jeffrey Bradstreet and colleagues cite strong evidence showing a link between autism and immune system dysregulation. Many autistic children, they note, also exhibit gastrointestinal inflammation as well as evidence of inflammation in the brain. "In addition," they say, "a subset of autistic children exhibit higher than average levels of androgens." Androgens are "male" sex hormones, also present in smaller amounts in females.

The researchers note that spironolactone—currently prescribed for congestive heart failure, hormone abnormalities, high blood pressure, and a number of other conditions—has powerful anti-inflammatory and immune-enhancing properties. "In a recent study," they note, "Japanese researchers looking for a reduction in cardiovascular risk factors related to inflammation found spironolactone to be the most potent anti-inflammatory medication they studied." In addition, spironolactone is used as an anti-androgen treatment for disorders associated with high androgen levels. Bradstreet and colleagues note that spironolactone is very inexpensive, and appears highly safe after decades of widespread use.

The researchers say parents report anecdotally that spironolactone can cause "substantial and rapid improvements including cognitive gains, diminished obsessive-compulsive behaviors, improved spontaneous socialization, reduced aggression, and improved sleep." They report a case study of one 12-year-old patient with documented immune dysregulation, food allergies, and elevated testosterone levels. The boy exhibited a receptive language gain of 21 months within four weeks of starting on spironolactone (100 mg/day). In addition, the researchers report, tests revealed "a 79% improvement in irritability, an 83% decrease in lethargy, a 60% reduction of stereotypy, a 72% reduction of hyperactivity, and a 67% decrease in inappropriate speech."

The researchers conclude, "Spironolactone is a low-cost, easily available oral agent with a favorable safety profile, and with desirable immune and anti-inflammatory properties. Its secondary benefits as an anti-androgen might further enhance its appeal in autism, particularly in a definable subset of hyperandrogenic children."

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"Spironolactone might be a desirable immunologic and hormonal intervention in autism spectrum disorders," James Jeffrey Bradstreet, Scott Smith, Doreen Granpeesheh, Jane M. El-Dahr, and Daniel Rossignol, *Medical Hypotheses*, 2006, in press. Address: DrBradstreet@aol.com.

Diabetes drug reduces behavior problems in pilot study

A drug used to treat diabetes may reduce autistic symptoms, according to a pilot study.

In the open-label study, Marvin Boris and colleagues administered pioglitazone (Actos) to 25 autistic children, ranging in age from 3 to 17, who had not responded to biomedical, behavioral or educational therapies. Children under 6 received 30 mg per day, while older children received 60 mg per day. Parents rated the children's symptoms using the Aberrant Behavior Checklist (ABC), before treatment and at a follow-up either 12 or 16 weeks later.

The researchers report that participants showed significant decreases in 4 out of 5 subcategories of the ABC—irritability, lethargy, stereotypy, and hyperactivity. (No significant change occurred in the fifth subscore, inappropriate speech.) Seventy-six percent of the participants showed improvement on at least one subscale, while 56% showed improvement on two or more subscales and 40% showed improvement in three or more. More than half of the children showed improvement on the hyperactivity subscale. Younger children tended to benefit more than older ones, and no significant side effects occurred.

The researchers speculate that pioglitazone may reduce autistic symptoms because of its anti-inflammatory and immune-modulating properties. Autism is strongly linked to both immune system dysfunction and abnormal brain inflammation.

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"Effect of pioglitazone treatment on behavioral symptoms in autistic children," Marvin Boris, Claudia Kaiser, Alan Golblatt, Michael W. Elice, Stephen M. Edelson, James B. Adams, and Douglas L. Feinstein, *Journal of Neuroinflammation*, Vol. 4, No. 3, 2007, epub ahead of print publication. Address: Marvin Boris, mboris@pol.net.

Study links autism, toxins

(continued from page 1)

mercury excretion to 1/10 of normal levels), or a biological stressor such as illness.

The researchers conclude that some autistic children are selectively vulnerable to environmental insults such as heavy metal exposure, and "may be like the canary in the coal mine, exposing policy and/or environmental issues that need to be addressed."

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"Evidence of toxicity, oxidative stress, and neuronal insult in autism," Janet K. Kern and Anne M. Jones, *Journal of Toxicology and Environmental Health, Part B*, Vol. 9, 2006, 485-99. Address: Janet K. Kern, Department of Psychiatry, University of Texas Southwestern Medical Center at Dallas, 6363 Forest Park Road, Suite 13.354, Dallas, TX 75390-9119, janet.kern@UTSouthwestern.edu.

Infusion of hormone aids "social memory" in autistic adults

Adults with autism spectrum disorders (ASD) process and retain social information better after they receive infusions of the hormone oxytocin, according to a new study by Eric Hollander and colleagues.

In a randomized, double-blind crossover study, the researchers administered intravenous infusions of oxytocin or a placebo to fifteen adults with ASD. Before, during, and after the infusions, participants listened to pre-recorded sentences spoken with one of four emotional intonations (happiness, indifference, anger, or sadness) and pointed to the words that best matched the emotions they heard. Approximately two weeks later, participants initially given the placebo received an infusion of oxytocin and vice versa, and the researchers again administered the emotion recognition test.

Hollander and colleagues say, "All subjects showed improvements in affective speech comprehension from pre- to post-infusion; however, whereas those who received placebo first tended to revert to baseline after a delay, those who received oxytocin first retained the ability to accurately assign emotional significance to speech intonation on the speech comprehension task."

Earlier research by Hollander and colleagues showed that infusions of oxytocin reduce repetitive behaviors in autism. Other studies also indicate that children with autism have low plasma levels of oxytocin, and that levels of oxytocin in the blood do not increase with age as they do in non-disabled children.

In non-disabled individuals, intranasally administered oxytocin increases trust in social situations. Research suggests that oxytocin dampens the response of the amygdala (a brain region involved in fear responses) to threatening social situations, and animal studies indicate that oxytocin plays a role in social recognition and the processing of social cues.

Hollander and colleagues are now testing the effects of an intranasal spray of oxytocin on autistic behaviors. This formulation, they say, "may allow for better penetration of the blood brain barrier, and is easier to administer."

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"Oxytocin increases retention of social cognition in autism," Eric Hollander, Jennifer Bartz, William Chaplin, Ann Phillips, Jennifer Sumner, Latha Soorya, Evdokia Anagnostou, and Stacey Wasserman, *Biological Psychiatry*, August 10, 2006 (epub ahead of print publication). Address: Eric Hollander, Seaver and NY Autism Center of Excellence, Mount Sinai School of Medicine, Department of Psychiatry, One Gustave L. Levy Place, Box 1230, New York, NY 10029-6574, eric.hollander@mssm.edu.