Biomedical Update:

Unsociable voles: a clue for autism researchers?

Autism research takes many strange turns, but one of the most bizarre involves burrowing rodents called mountain voles.

Neuroscientists Thomas Insel and Lawrence Shapiro report in the *Proceedings of the National Academy of Sciences* that they have discovered a biological difference between mountain voles—which avoid other voles except to mate, and abandon their infants (who appear not to care)—and prairie voles, which are social and nurturing. Compared to mountain voles, the prairie voles have three times as many receptors for the reproductive hormone oxytocin in the prelimbic cortex, and seven times as many oxytocin receptors in a brain area called the nucleus accumbens.

Insel and Shapiro conclude that "oxytocin receptors may be very important for the social, 'affiliative' behaviors that make animals receptive to social attachments." The researchers plan to conduct postmortem studies of the brains of autistic individuals, to see if they too have reduced numbers of oxytocin receptors.

While Insel's and Shapiro's theory may seem far-fetched, autism researchers Charlotte Modahl and colleagues were already exploring the same idea. They note that "there is a growing body of evidence that oxytocin promotes emotional attachment behavior across the wide spectrum of activities in which it is involved," and that "higher oxytocin blood levels have been correlated with stronger human mother-infant bonding and with more social and outgoing personalities in men and nonpregnant women."

The oxytocin theory, the researchers say, ties in nicely with previous autism research and would explain why the drug naltrexone reduces autistic symptoms. Naturally produced opium-like hormones such as beta-endorphin, which some studies indicate are elevated in autism, *inhibit* the effects of oxytocin; and the opiate blocking drugs naltrexone and naloxone, which reduce self-injury and withdrawal in many autistic children, *increase* oxytocin levels. Further, noting that B6-magnesium treatment is helpful for many autistic children, Modahl and colleagues cite a 1990 Japanese study which found that magnesium enhances the effects of oxytocin. The researchers add that the brain's limbic system, which plays a primary role in social behavior, emotions, memory and motivation, contains the greatest concentration of oxytocin receptors.

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"Brain receptor shapes voles' family values," C. Ezzell, *Science News*, July 4, 1992, pp. 6-7.

—and—

"Does oxytocin deficiency mediate social deficits in autism?," Charlotte Modahl, Deborah Fein, Lynn Waterhouse and Niles Newton; *Journal of Autism and Developmental Disorders*, Vol. 22, No. 3, 1992, pp. 449-450.

Prozac: good, bad news

Fluoxetine (Prozac), used to treat obsessive compulsive disorder (OCD) and depression, is also being prescribed for autistic individuals with depressive symptoms or ritualistic and compulsive behaviors (see ARRI 5/4). A new study indicates that many autistic individuals improve significantly when taking Prozac, while another study warns that for some individuals the drug fails to relieve—and can actually cause—depressive symptoms.

Edwin Cook and colleagues studied the effects of Prozac on 23 autistic subjects (ages 7 to 28) and 16 retarded subjects (ages 7 to 52) who were treated with the drug between 1988 and 1990 at a University of Chicago clinic. Dosages ranged from 20 mg. every other day to 80 mg. per day.

The researchers report that 15 of the 23 autistic subjects, and 10 of the 16 retarded subjects, showed significant behavioral improvements including decreased aggression and self-injury, reduced obsessive thoughts and compulsive behaviors, better sleep, and fewer tantrums. They note, however, that six autistic subjects and three retarded subjects experienced significant side effects, "predominantly...restlessness, hyperactivity, agitation, decreased appetite, or insomnia."

Prozac and similar drugs, Cook and colleagues say, "do not address the core symptoms of either cognitive dysfunction or communication, but may be of use in adjunctive treatment of patients."

Eric Hollander et al. report on 10 non-autistic OCD patients for whom Prozac was ineffective in treating depression or actually brought on depressive episodes. In six cases, the onset of depressive symptoms followed a rapid increase in dosage levels of the drug.

Adding a tricyclic antidepressant to Prozac treatment relieved the depressive symptoms of eight of the patients, Hollander et al. report; however, in one case, combining Prozac with a tricyclic antidepressant resulted in the patient suffering a grand mal seizure. In five cases both OCD and depressive symptoms were alleviated when the patients were switched to clomipramine.

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"Fluoxetine treatment of children and adults with autistic disorder and mental retardation," Edwin H. Cook, Jr., Randall Rowlett, Catherine Jaselskis, and Bennett Leventhal; *Journal of the American Academy of Child and Adolescent Psychiatry*, 31:4, July 1992, pp. 739-745. Address: Edwin Cook, Department of Psychiatry, Box 411, 5841 S. Maryland Avenue, Chicago, IL 60637.

—and—

"Obsessive compulsive disorder, depression, and fluoxetine," Eric Hollander, Linda Mullen, Concetta DeCaria, Andrew Skodol, Franklin Schneier, Michael Liebowitz, and Donald Klein; *Journal of Clinical Psychiatry*, Vol. 52, No. 10, October 1991. Address: Eric Hollander, Dept. of Psychiatry, College of Physicians and Surgeons of Columbia University and The New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032.

Check for PKU

Tunisian researchers advise physicians that phenylketonuria (PKU) testing should be "part of an essential work-up of children with autism."

Najoua Miladi et al. recently diagnosed PKU in a seven-year-old autistic girl. Although the standard treatment (a diet low in the amino acid phenylalanine) was instituted, the child was too old to benefit significantly.

PKU—which can cause epilepsy, retardation, and autistic symptoms if treatment is not started within a few days after birth—occurs in about 1 in 16,000 live births. The disorder is caused by a metabolic defect that makes it impossible for the body to excrete excess amounts of phenylalanine. Because symptoms usually cannot be detected in the newborn without laboratory tests, many countries screen every infant for the disorder. Prenatal PKU testing also is available.

Many physicians recommend a repeat PKU screening for infants with autistic symptoms, a recommendation supported by recent research indicating that a small but significant percentage of PKU cases are missed by initial screenings.

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"Phenylketonuria: an underlying etiology of autistic syndrome. A case report," Najoua Miladi, Abdelmajid Lamaout, Neziha Kaabachi, Mohamed Helayem,and Mongi Ben Hamida; *Journal of Child Neurology*, Vol. 7, No. 1, January 1992, pp. 22-23. Address: Najoua Miladi, Institut National de Neurologie, La Rabta 1007 Tunis, Tunisia.

Autism and brain tumor

A case report of an autistic-like 3-1/2-year-old boy with a brain tumor adds to the evidence that defects of the temporal lobe may cause some cases of autism.

After the boy began having seizures, an MRI scan revealed a temporal lobe tumor which was removed, along with a large segment of the left temporal lobe. The boy showed somewhat more social awareness after the surgery, but continued to exhibit many autistic behaviors and developed hyperactivity.

Hoon and Reiss note that both human and animal studies offer "increasing evidence...that pathological processes affecting the temporal lobe, particularly the amygdala and hippocampus, are related to the development of autistic-like symptomatology." Their case, they say, indicates that damage even to only one temporal lobe—in this case, the left lobe—during early development "may lead to the development of a particular subset of autistic features."

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"The mesial-temporal lobe and autism: case report and review," Alexander H. Hoon, Jr., and Allan L. Reiss; *Developmental Medicine and Child Neurology*, 34, 1992, pp. 252-265. Address: Alexander H. Hoon, Jr., Department of Developmental Pediatrics, The Kennedy Institute, 707 North Broadway, Baltimore, MD 21205.