Biomedical Update:

Eccentric diets of autistic children may have serious consequences

The bizarre and restricted food preferences of many autistic children can cause severe health problems, according to a new report by gastroenterologist Joseph Clark and colleagues.

Clark et al. found that one of their patients, an eight-year-old autistic boy with a limp and swelling around the eyes, was suffering from rickets (a potentially crippling disorder caused by vitamin D deficiency). He also had physical signs of vitamin A deficiency, which can lead to blindness if not corrected. The boy had eaten only french fries and water for two years, refusing other foods as well as vitamin supplements.

The boy's doctors were able to reverse his symptoms by hospitalizing him and administering supplements through a nasogastric tube. He continues to receive nasogastric nutrient supplementation in his care facility.

"Because autism is frequently associated with abnormal eating practices," Clark et al. say, "close attention should be paid to specific intake of individual nutrients so proper supplementation can be initiated before the development of a clinical deficiency state." They note that the boy they treated "had been seen episodically for several years by many different caregivers who falsely reassured his mother that his dietary intake would be adequate."

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"Symptomatic vitamin A and D deficiencies in an eight-year-old with autism," Joseph H. Clark, Donna K. Rhoden, and Denece S. Turner, *Journal of Parenteral and Enteral Nutrition*, Vol. 17, No. 3, 1993. Address: Joseph H. Clark, Pediatric Gastroenterology and Nutrition, Medical College of Georgia, Augusta, GA 30912.

New twist to theory linking "attachment" hormone to autism

The hormone oxytocin appears to play a major role in "attachment" behaviors including maternal bonding, sexuality, and social relationships. Recently, several researchers (see ARRI 6/3) have speculated that low levels of oxytocin could cause autistic behavior. But Jaak Panksepp, one of the first researchers to explore the link between levels of "social peptides" (such as oxytocin and opioids) and autism, suggests that the opposite may be true: autistic behaviors may result from levels of oxytocin that are abnormally *high*.

Oxytocin, Panksepp notes, reduces vocal activity and alters pain sensitivity. Also intriguing, he says, is research showing "the ability of centrally administered oxytocin to produce stereotypical wing-flapping in birds which is strikingly similar to the arm/wrist flapping of many autistic children."

Panksepp cites evidence indicating that oxytocin has different effects on sociability in different areas of the brain, and that oxytocin receptor areas in the brain are very changeable. "Perhaps these fields fail to shift from infantile to more mature patterns in autistic children," he speculates, "yielding the puzzling failure to develop commonly seen in autistic children at two to three years of age."

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"Commentary on the possible role of oxytocin in autism," Jaak Panksepp, *Journal of Autism and Developmental Disorders*, Vol. 23, No. 3, 1993. Address: Jaak Panksepp, Bowling Green State University, Bowling Green, OH 43404-0228.

Fenfluramine: helpful for ADHD but not autism?

A new study joins dozens of earlier ones in concluding that the drug fenfluramine has little usefulness in the treatment of autism.

Bennett Leventhal et al., who administered fenfluramine to 15 autistic children in a double-blind study, say that drug treatment resulted in small decreases in parent ratings of hyperactivity and sensorimotor abnormalities, but that no improvements were seen in cognition. Small decreases in abnormal social and affectual responses were seen, but could not be attributed conclusively to the drug treatment. "Overall," they say, "no significant advantage for the use of fenfluramine could be established."

By contrast, two studies (both by Michael Aman and colleagues) of children with mental retardation and attention deficit hyperactivity disorder (ADHD)—but without autism—concluded that fenfluramine caused improvements in a variety of symptoms including conduct disorders, hyperactivity, and irritability.

Aman et al. compared fenfluramine to methylphenidate (Ritalin), the drug most commonly administered to children with ADHD. Teachers rated methylphenidate as more effective, while parent ratings favored fenfluramine slightly. In a second study of the same subjects, fenfluramine was found to cause "significant improvement" in attention, activity level, and mood.

Fenfluramine, most commonly used as an appetite suppressant for overweight individuals, reduces levels of the natural brain chemical serotonin. Abnormal serotonin levels have been linked to autism and other behavioral disorders.

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"Clinical and neurochemical effects of fenfluramine in children with autism," Bennett Leventhal, Edwin Cook, Marolyn Morford, Alan Ravitz, Wendy Heller, and Daniel Freedman; *Journal of Neuropsychiatry*, Vol. 5, No. 3, Summer 1993. Address: Bennett Leventhal, Dept. of Psychiatry, MC 3077, University of Chicago, 5841 S. Maryland Ave., Chicago, IL 60637.

—and—

"Fenfluramine and methylphenidate in children with mental retardation and attention deficit hyperactivity disorder: laboratory effects," Michael Aman et al., *Journal of Autism and Developmental Disorders*, Vol. 23, No. 3, 1993, and "Fenfluramine and methylphenidate in children with mental retardation and ADHD: clinical and side effects," Michael Aman et al., *Journal of the American Academy of Child and Adolescent Psychiatry*, 32, 4, July 1993. Address for both: Michael Aman, The Nisonger Center, Room 175, Ohio State University, 1581 Dodd Drive, Columbus, OH 43210-1296.

How blind is a blind study? Some surprising answers

The double-blind, placebo-controlled study is considered the most scientific of drug testing methods. The procedure involves assigning subjects to groups receiving either an active drug or a placebo, without letting either the study subjects or the patients' evaluators know which group a subject is in. Supposedly, such a procedure rules out the effects of bias on the part of the researchers, or false expectations on the part of the subjects.

Not so, say Seymour Fisher and Roger Greenberg, who argue that "there is now a substantial reservoir of data discrediting the integrity of the double-blind." In fact, Fisher and Greenberg go so far as to say that "most past studies of psychotropic drugs are to unknown degrees scientifically untrustworthy" because of limitations of the double-blind procedure.

The biggest problem, Fisher and Greenberg say, is that both researchers and subjects in "blind" studies frequently can tell whether the drug or placebo is being given. This happens, they say, because the drug's effects — either good or bad — are obvious compared to the placebo's lack of effect. "A major defect in the double-blind design, as currently practiced," they say, "is the fact that the placebo is almost invariably an inert substance that simply does not arouse the variety and intensity of body sensations instigated by the active drug." Once such "cues" are detected, a study can be influenced by the hopes or biases of those involved.

Evidence that double-blind studies are unreliable, Fisher and Greenberg say, includes:

—post-study surveys of researchers and subjects. Most such surveys show that a high percentage of both groups were able to guess when placebos or drugs were being given.

—the widely noted phenomenon in which the effects reported during placebo phases mimic those caused by the real drug. This could only occur, the researchers say, "if patients were somehow surreptitiously identifying the properties of the active drug."

Fisher and Greenberg say it is time for researchers to develop study designs less open to bias. One approach, they say, would be to use active placebos which will match the side effects of active drugs but have no therapeutic effects. Other strategies include using independent assessment teams with no personal stake in study results, using at least two active drugs, or employing complex crossover designs to make it more difficult to breach the blind design.

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"How sound is the double-blind design for evaluating psychotropic drugs?," Seymour Fisher and Roger P. Greenberg; *Journal of Nervous and Mental Disease*, Vol. 181, No. 6, 1993. Address: Seymour Fisher, Department of Psychiatry, State University of New York Health Science Center, 750 East Adams Street, Syracuse, New York 13210.