Update: Biomedical

New evidence of link between autism, CMV

Cytomegalovirus (CMV) is a common virus that is generally harmless to healthy children and adults, although it can be fatal to newborns. About 80 percent of adults over 35 have antibodies to CMV, indicating past infection, but most CMV infections go unnoticed and are thought to cause no symptoms.

When CMV attacks unborn babies, however, it can disrupt development, causing brain damage and physical malformations. A new report by Swedish researchers S. A. Ivarsson et al. adds evidence that prenatal CMV infections also may cause autism.

The possible CMV-autism link was noted more than a decade ago by researcher Gene Stubbs, and several cases of prenatal CMV and autism have been reported since then. Ivarsson and colleagues report on two children with autistic symptoms who had contracted CMV before birth; one mother had a new infection, while the other apparently had a reactivated old infection. (CMV can remain latent in the body after initial infection and become reactivated by pregnancy.) One child also was deaf and had seizures and strabismus, while the other had cerebral palsy.

Ivarsson et al. note that a Swedish study of infants infected by CMV before birth has found that one of the 72 infants followed for more than three years developed autistic symptoms. "As the central nervous system is not fully developed at birth," they comment, "and owing to the immaturity of the brain even after birth, fetuses and infants are at special risk for viral damage to the central nervous system."

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"Autism as one of several disabilities in two children with congenital cytomegalovirus infection," *Neuropediatrics*, 21, 1990, pp. 102-103. Address: S.A. Ivarsson, Dept. of Pediatrics, Malmo Gen. Hospital, S-214 01 Malmo, Sweden.

Naltrexone reports: one positive, one cautious

"Opiate blockers appear to be very powerful tools for treatment of SIB [self-injurious behavior]," according to Curt Sandman and colleagues, who recently tested the opiate blocking drug naltrexone on four retarded adults in a state hospital.

Each participant in the double-blind study received fixed doses (0, 25, 50 and 100 mg) of naltrexone on different occasions, with intervening days of no treatment. Sandman et al. report that "all patients had decreased SIB when treated with naltrexone," and that three of the patients showed greater improvement as the dosage increased.

The researchers say that overall, no consistent improvement was seen in stereotyped behaviors, and naltrexone did not appear to either sedate or arouse the study subjects.

Many researchers suspect that self-injury involves a defect in the body's opioid system, the system that makes and metabolizes natural substances similar to opium. In particular they are studying b-endorphin, the most powerful of the opioids, a substance that has strong pain-relieving properties and may underlie the addictive process. "The results of this study in concert with similar findings suggest that b-endorphin and the opioid receptor are involved in SIB," Sandman and colleagues conclude.

Sandman et al. note that there are two hypotheses as to why self-injury might be linked to a faulty opioid system: the "addiction" hypothesis (that self-injurious behavior results in the body delivering a "fix" of opioids), and the "pain" hypothesis (that a defect in the opioid system causes self-injurious individuals to feel less pain, and less sensory input in general, than other people).

One potentially significant finding of the Sandman et al. study was that the most self-injurious study subject was the most sensitive to naltrexone. In addition, that individual's other behaviors improved during drug treatment. The implication, they say, "is that the degree of therapeutic response to opiate blockers is related to the extent of opioid disregulation."

Other research involving naltrexone offers "only a suggestion" that the drug reduces hyperactive behavior and alleviates overall symptoms, according to a preliminary report by Magda Campbell et al.

After administering naltrexone to 18 autistic patients (ages 3-7) at a treatment center for 21 days, Campbell and colleagues found that the children's scores on one rating scale (Clinical Global Consensus Ratings) improved, while scores on other behavior rating scales did not change significantly. Older children seemed to benefit more from the drug than younger children.

"According to staff [at the treatment center]," they report, "the most consistent symptom changes during naltrexone administration in each child were decreases of withdrawal and increases of verbal production and communicative speech." It is possible, they say, that "global clinical judgments on an inpatient ward take into account more factors" than any single rating scale.

The double-blind, placebo-controlled study also offered evidence that naltrexone appears safe and does not seem to affect discrimination learning.

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"An orally administered opiate blocker, naltrexone, attenuates self-injurious behavior," Curt A. Sandman, Jennifer L. Barron, and Howard Colman; *American Journal on Mental Retardation*, Vol. 95, No. 1, 1990, pp. 93-102. Address: Curt A. Sandman or Jennifer Barron, Fairview Developmental Center, Costa Mesa, CA 92626.

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"Naltrexone in autistic children: a double-blind and placebo-controlled study," Magda Campbell, Lowell T. Anderson, Arthur M. Small, Joseph J. Locascio, Nona S. Lynch, and Milagros C. Choroco; *Psychopharmacology Bulletin*, Vol. 26, No. 1, 1990, pp. 130-135. Address: Magda Campbell, Dept. of Psychiatry, New York Univ. Med. Center, 550 First Ave., New York, NY 10016.

Rett drug promising

Two of ten girls with Rett syndrome showed impressive gains in gross and fine motor development, social and cognitive skills, and independence after receiving the drug bromocriptine, according to Italian researcher Michele Zappella.

"The [developmental] improvements these two girls made in a few months . . . corresponded to improvements which normal children make in much longer periods of time," Zappella reports. "In addition, their sleep became regular, their attention and exploration improved, their 'hand-washing' stereotypic activities decreased, and periods of relaxation of up to half an hour were often seen almost daily."

One other girl improved slightly, while no change was seen in the other seven study subjects. The two girls who improved greatly had developed Rett syndrome at a later age than the others, and had slightly better hand use, indicating, Zappella says, that bromocriptine—a drug which binds to the same cell receptors as the brain "messenger" substance dopamine—may only be effective "where damage to the dopaminergic system is not as profound as in most girls affected by this syndrome."

Earlier studies by Zappella and French researchers Simon-Soret and Borenstein showed encouraging results with bromocriptine (see ARRI 2/3). Since that time there has been some concern over the safety of the drug, which was linked in 1988 to several deaths.

Amino acids tested

Danish researchers Jytte Nielsen et al. are investigating possible abnormalities of brain chemical synthesis in Rett's. Recently they administered tyrosine and tryptophan (two biological building blocks of neurotransmitters) to nine girls with Rett's, and found that byproducts of the neurotransmitters dopamine and serotonin increased in spinal fluid samples. This, they say, "supports the hypothesis of a compromised neurotransmitter synthesis." Treatment of 11 girls with the tyrosine and tryptophan, however, did not affect symptoms.

Rett syndrome causes severe growth and motor problems, loss of speech and mobility, chronic hand-washing or hand-wringing motions, seizures, and many other symptoms. The progressive disorder, which occurs (possibly with rare exceptions) only in girls, often causes withdrawal and other autistic-like symptoms in its early stages.

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"A double blind trial of bromocriptine in the Rett syndrome," Michele Zappella; *Brain and Development*, Vol. 12, No. 1, 1990, pp. 148-150. Address: Michele Zappella, Department of Child Neurology and Psychiatry, Regional Hospital, USL 30, Via Mattioli 10, 53100 Siena, Italy.

-and-

"Biochemical and clinical effects of tyrosine and tryptophan in the Rett syndrome," Jytte B. Nielsen, Hans C. Lou, and Jente Andresen; *Brain and Development*, Vol. 12, No. 1, 1990, pp. 143-147. Address: Jytte Nielsen, Department of Neuropediatrics, The John F. Kennedy Institute, G1 Landevej 7, DK-2600 Glostrup, Denmark.