

Biomedical Update:

Synthetic hormone improves autistic behaviors

A Dutch research group has announced new findings supporting its earlier report that synthetic adrenocorticotrophic hormone (ACTH) reduces some symptoms of autism.

In a double-blind placebo study of 20 autistic children and a control group, J. K. Buitelaar and colleagues found that eye contact and verbal initiations improved in autistic children given 40 mg per day of the synthetic hormone for eight weeks. The researchers say additional ratings by parents, teachers, a child psychiatrist and a psychologist "substantiated an effect of [the hormone] treatment, mainly as a lessening of social withdrawal behavior at home."

Buitelaar et al. note that ORG 2766, the synthetic ACTH analog used, has been shown to influence the social behavior of rats, to counteract declines in social attention in aging rats, and to improve the social behavior of elderly people. "Furthermore," they note, "ORG 2766 beneficially influenced attentional and motivational processes in animal and human studies."

In their 1990 study, Buitelaar and colleagues found that the hormone caused autistic subjects to become more talkative and appropriately active, while showing less stereotyped behavior.

"Deficits in social behavior in autism and their modification by a synthetic adrenocorticotrophic hormone (4-9) analog," J.K. Buitelaar, H. van Engeland, C. H. de Kogel, H. de Vries, J. A. R. A. M. van Hooff and J. M. van Ree; *Experientia* 48, 1992, pp. 391-394. Address: J. K. Buitelaar, Department of Child and Adolescent Psychiatry, Utrecht University Hospital, P.O. Box 85 500, NL-3508 GA Utrecht, The Netherlands.

Antibiotic use for ear problem questioned

Editor's Note: The following report, while not addressing autism per se, is particularly interesting in the light of mounting evidence that antibiotic-caused *Candida* yeast infections may play a part in some cases of autism. (See editorial in *ARRI* 2/2, and *ARI* Publication 65. For copy, send \$1.00 and SASE marked "candida.")

The antibiotic amoxicillin "is not effective for the treatment of persistent asymptomatic middle-ear effusions," Erdem Cantekin and colleagues state, in a report that has touched off a heated debate over the politics of scientific research.

Cantekin's paper, based on a study of the effects of amoxicillin treatment on secretory otitis media (painless accumulation of fluid in the middle ear, resulting from obstruction of the eustachian tube), was a dissenting opinion written after his co-researchers—

who were funded by the pharmaceutical industry—had interpreted their data as favorable to amoxicillin, and had published their conclusions in the *Journal of the American Medical Association (JAMA)* in 1987. *JAMA* originally rejected Cantekin's dissenting paper, but—in a surprising turnaround—published it in 1991, saying that the journal had erred in rejecting it earlier.

Cantekin criticized the diagnostic and statistical methods used by his co-researchers, and said objective measures showed that at four-week follow-up, "only 30.7% of the [460] children treated with amoxicillin or amoxicillin with decongestant-antihistamine had improved hearing, compared with 32.8% of those in the placebo group." Further, while fluid accumulation decreased in children treated with amoxicillin and decongestants, Cantekin et al. note, "four weeks after treatment...the recurrence of effusion in children treated with the antibiotic treatment was two to six times higher than in children treated with placebo." They add that side effects such as diarrhea, rashes, irritability or sedation were much more common among those receiving antibiotics (especially when combined with decongestants and antihistamines) than in the placebo group.

Cantekin et al. note that another large-scale study found that the antibiotics Pediazole and cefaclor also were ineffective in treating secretory otitis media.

Cantekin notes in the June 1992 issue of *JAMA* that while his findings related only to non-acute otitis media, "several recent studies (Dutch, Danish, Swedish, Israeli, and multinational) show that antibiotic treatment for acute otitis media is not effective." In addition, he says, "the acute otitis media study conducted at the Otitis Media Research Center in Pittsburgh [published in 1985] showed that amoxicillin was not effective in clearing severe episodes of acute otitis media."

In a letter in *JAMA*, John Wilson, Jr., says that "Cantekin confirm[s] what many of us in primary care have observed: namely, that chronic and recurrent otitis media does not respond to antibiotics." He cites studies indicating that children with chronic secretory otitis media who were treated for food and inhalant allergies showed significant improvement, and suggests that "the common practice of prescribing antibiotics freely for children...be replaced by a more thoughtful approach that addresses and treats the initial environmental triggers causing this condition."

"Antimicrobial therapy for otitis media with effusion ('secretory' otitis media)," Erdem Cantekin, Timothy McGuire, and Terri Griffin; *Journal of the American Medical Association*, December 18, Vol. 266, No. 23, 1991. See also: "The Cantekin affair" (editorial), *JAMA*, December 18, 1991; and "Secretory otitis media: the Cantekin affair" (letters and replies), *JAMA*, June 10, 1992, Vol. 267, No. 22.

SPECT study shows unusual patterns

English, Kuwaiti and U.S. researchers using a new brain imaging technology—high-resolution brain single photon emission tomography, or SPECT—report finding decreased blood flow in the brains of autistic subjects.

Mark S. George and colleagues performed SPECT studies on four young autistic adults and four age-matched control subjects. They found that total brain blood flow was significantly decreased in autistic subjects, and that "the autism group also had regionally decreased flow in the right lateral temporal and right, left, and midfrontal lobes" compared with the controls.

George et al. note that two other groups of researchers using SPECT—Lelord et al. in 1991, and Sherman et al. in 1984—reported similar results. Researchers using PET scans (a similar technology) have reported mixed findings.

"Cerebral blood flow abnormalities in adults with infantile autism," Mark S. George, Durval C. Costa, Kypros Kouris, Howard A. Ring, and Peter J. Eli; *Journal of Nervous and Mental Disease*, 1992, Vol. 180, No. 7, 1992, pp. 413-417. Address: Mark S. George, Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Building 10, Room 3N 212, Bethesda, MD 20892.

Possible gene linkage?

Although it has been clear for at least three decades that some cases of autism are genetic in origin, the search for the gene or genes involved in these cases has been difficult. A research team at the medical school of the University of Tours in France has come up with what may prove to be an important candidate gene: HRAS, located on chromosome 11.

The researchers, led by Gilbert Lelord, have been investigating the biochemistry of autism since the 1970s, and have conducted many of the studies on vitamin B6 and magnesium which have established these nutrients as the biological treatment of choice for autism. Recently, J. Herault, Lelord and colleagues compared 50 autistic patients with 50 non-autistic controls, using as markers genes coding for DBH, TH, TpH, and HRAS. Only the HRAS marker was found to be associated with autism.

While this finding is of considerable significance to researchers, is not yet considered to be firmly established, and cannot be applied in individual cases to determine if a person carries a gene for autism.

"Genetic abnormalities associated with infantile autism," J. Herault, A. Perrot, C. Barthelémy, D. Sauvage, M. Leboyer, J. Mallet, J.P. Muh, and G. Lelord; presented at the Association Française de Psychiatrie Biologique, November 17, 1992.