

# Biomedical Update:

## French SPECT studies suggest delayed development of cortex

French researchers report evidence that development of the frontal cortex of the brain is delayed in autistic individuals.

Mônica Zilbovicius et al. performed SPECT studies to investigate the cerebral blood flow of autistic children at two different times: when the children were 33-52 months of age, and three years later. Five children participated in the first stage of the study, and four in the second stage. Their test results were compared to those of age-matched children with normal development.

The researchers found that "at three to four years, the autistic children had a regional cerebral blood flow pattern...similar to the pattern reported for normal children about two years younger." By the time the second tests were performed, the autistic children's results were similar to controls'.

Zilbovicius et al. suggest that a transient period of abnormal frontal cortical development may alter later development of the cortex in autistic individuals. This is consistent, they say, with findings that autistic children are impaired in developing a "theory of mind"—that is, an understanding of the mental states of others. "In normal children," they say, "theory of mind develops simultaneously with the development of other high-order cognitive tasks that depend on frontal lobe maturation."

The researchers note that other studies have revealed defects in a different area of the brain, the cerebellum. The connection (if any) between cerebellar and frontal cortical abnormalities in autistic individuals, they say, is not yet understood.

*Editor's note: see related article in column 3.*

"Delayed maturation of the frontal cortex in childhood autism," Mônica Zilbovicius, Bernard Garreau, Yves Samson, Philippe Remy, Catherine Barthélémy, André Syrota, and Gilbert Lelord; *American Journal of Psychiatry*, 152:2, February 1995. Address: Mônica Zilbovicius, Service Hospitalier Frédéric Joliot, C.E.A., 4 Place du Général Leclerc, 91406 Orsay, France.

## R-THBP: Japanese researchers report new findings

Researchers in Japan have reported improvement in autistic subjects receiving R-tetrahydrobiopterin (R-THBP), an enzyme vital in the synthesis of neurotransmitters (brain "messenger" chemicals). A new Japanese study, by Yoshihiro Tani et al., suggests that this treatment may correct abnormally low levels of R-THBP in autistic individuals.

Tani and colleagues, who studied 20 autistic subjects and 10 non-disabled controls, found that cerebrospinal fluid levels of R-THBP and a related compound (NH2)

were significantly lower in the autistic group than in the controls. Further reduction of these two substances was seen in the youngest children studied.

"These results," the researchers say, "could well explain the results of a clinical study [Naruse et al.] in which 53.7% of autistic subjects receiving [R-THBP] treatment showed significant improvement, and particularly in which marked improvement was seen in the group under the age of 5 years old."

*Editor's note: This is the fourth article in our continuing coverage of research on R-THBP. R-THBP is not currently being used as a treatment for autism in the United States.*

"Decrease in 6R-5,6,7,8-tetrahydrobiopterin content in cerebrospinal fluid of autistic patients," Yoshihiro Tani, Elisabeth Fernell, Yasuyoshi Watanabe, Tadashi Kanai, and Bengt Långström; *Neuroscience Letters*, 181, 1994, pp. 169-172. Address: Yoshihiro Tani, Suntory Institute for Biomedical Research, 1-1-1 Wakayamadai, Shimamoto-cho, Mishima-gun, Osaka 618, Japan.

## Desipramine: are current dosage levels dangerous?

A recent ARRI (8/4) reported warnings from researchers about several cases of sudden death linked to desipramine, a popular drug which has been used to treat autistic individuals as well as individuals with Tourette's syndrome, attention deficit disorder, anxiety, and depression. Now another group of researchers suggests that currently recommended doses of the drug may be too high.

Yona Amitai et al. note that "desipramine hydrochloride has been associated with a disproportionately high fatality rate," both in cases involving overdoses and in cases where the drug was administered in amounts considered to be therapeutic.

Noting that desipramine is chemically similar to another drug, nortriptyline, the researchers point out that mortality from nortriptyline is not as high as from desipramine.

The researchers say this difference may be due to the lower standard dose of nortriptyline. "The largest preparation of nortriptyline... is limited to 75 mg.," they point out. "In contrast, the recommended dose for desipramine... has not been scaled down, and tablets containing 100 mg. and 150 mg.... are available." Studies suggest, they say, that doses of desipramine lower than commonly prescribed may be therapeutic, indicating that a "downscaling" of recommended desipramine dosages might be called for.

"The toxicity and dose of desipramine hydrochloride," Yona Amitai, Henri Frischer, and John Mann; *Journal of the American Medical Association*, Vol. 272, No. 22, Dec. 14, 1994, pp. 1719-1721. Address not listed.

## Odd behaviors in autism: a new theory

Studying the stereotypical behaviors of autistic individuals, two British researchers have concluded that they show similarities to the behaviors of patients with dysfunction of the frontal lobes of the brain.

Nicola Fox and Frank Tallis say patients with frontal lobe lesions often show a symptom called "utilization behavior"—that is, they immediately attempt to grasp and use objects given to them, even if such use is not appropriate. Thus, a patient handed a tea bag might immediately make tea, and a patient standing next to kitchen cabinets might continually open and close them.

Fox and Tallis designed an experiment, involving 28 autistic subjects and 24 retarded controls, to determine if autistic subjects exhibited similar utilization behaviors. Each subject was interviewed by an investigator in a room with a table on which the researchers placed a tray containing paper, a pen, a comb, a mug, a tea bag, a cassette player and tape, and other objects. The researchers, who made no reference at all to the objects, interviewed each subject while observing how many of the objects each subject picked up and used.

"Half of the subjects with autism showed at least one demonstration of utilization behavior," the researchers say, "while only one subject from the control group did." Behaviors included "stirring" the empty mug with a spoon, combing hair, writing on the papers, and switching the cassette player on and off. Several autistic subjects also switched the lights in the room on and off, or opened and closed the door repeatedly. In all, the researchers say, autistic subjects displayed 139 incidents of utilization behaviors, while controls displayed only nine.

"The results of this study," they say, "appear to be consistent with research suggesting that frontal-limbic dysfunction may be important in the understanding of autism."

"Utilization behaviour in adults with autism: a preliminary investigation," Nicola S. Fox and Frank Tallis; *Clinical Psychology and Psychotherapy*, Vol. 1, No. 4, 1994, pp. 210-218. Address: Nicola S. Fox, Department of Clinical Psychology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK.

### SCHOOLS & SERVICES:

The Autism Research Institute maintains a list of schools and services for autistic individuals. If your service should be on our list and you believe it may not be, please send a self-addressed, stamped envelope to receive our referral list questionnaire.