Biomedical Update:

Brain size and autism

A recent report in *The Lancet* suggests that many autistic children have "megalencephaly," or brain overgrowth.

British researchers Anthony Bailey et al. say post mortem measurements of the brains of four autistic children revealed that three "were heavier than the means for the normal population." Bailey and colleagues cite two earlier studies showing that more than a third of autistic subjects had increased head circumferences.

The researchers note that the density of brain cells appears normal in autistic subjects, "suggesting that there may be an excessive number of neurons."

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"Autism and megalencephaly," Anthony Bailey, Phillip Luthert, Patrick Bolton, Anne Le Couteur, Michael Rutter, and Brian Harding; *The Lancet*, Vol. 341, May 8, 1993. Address: Anthony Bailey, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK.

New naltrexone study discouraging

The largest controlled study to date of the drug naltrexone indicates that it reduces hyperactivity markedly, but does not significantly affect self-injury or core autistic symptoms.

Naltrexone blocks the effects of opioids, opium-like chemicals produced by the body. Several researchers theorize that autistic children have high levels of these chemicals, which can cause autistic-like symptoms including aloofness, poor bonding, and reduced pain sensitivity. Earlier studies indicated that the drug might reduce self-injury and aggression, and increase social responsiveness.

The new study of 41 children by Magda Campbell et al., however, offered only a "suggestion that [naltrexone] had a beneficial effect" in reducing self-injury. The researchers note, however, that none of the children in their study had very severe self-injurious behaviors, and that the dose they used (1 mg/kg/day) might have been too low to be effective against self-injury. The drug did not cause changes in aggressive behavior or learning.

The researchers say side effects were minimal and included sedation, decreased appetite, and vomiting. They add that "all laboratory studies including ECG and liver function tests remained within normal limits."

Campell et al. conclude that "based on our findings, the clinical superiority of naltrexone versus placebo has not been demonstrated," and add that "at present, use of naltrexone as a first line treatment is not recommended for autistic persons and for those with self-injurious behavior."

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"Naltrexone in autistic children: behavioral symptoms and attentional learning," Magda Campbell, Lowell Anderson, Arthur Small, Phillip Adams, Nilda Gonzalez, and Monique Ernst; *Journal of the American Acad. of Child and Adolescent Psychiatry*, 32:6, November 1993, pp. 1283-1291. Address: Magda Campbell, Dept. of Psychiatry, New York Univ. Med. Ctr., 550 First Avenue, New York, NY 10016.

Research notes in brief...

Swedish researchers report that cerebrospinal fluid levels of a protein associated with chronic nerve cell damage were three times normal levels in a group of 47 autistic individuals they tested. Gunilla Ahlsen et al. say the high levels of this substance, glial fibrillary acidic protein (GFA), could indicate either gliosis (an excess of glial cells seen in damaged areas of the brain and central nervous system) or an increased turnover of synaptic membranes.

In related research in the U.S., Nancy Minshew et al. report that their findings from a preliminary study of 11 subjects "are consistent with a hypermetabolic energy state and undersynthesis of brain membranes." Their research, which used a new technology called magnetic resonance spectroscopy (MRS), supports the Swedish researchers' theory that autism may involve an enhanced turnover of synaptic membranes.

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"Glial fibrillary acidic protein in the cerebrospinal fluid of children with autism and other neuropsychiatric disorders," Gunilla Ahlsen et al., *Biological Psychiatry*, 1993, 33, pp. 734-743. Address: Christopher Gillberg, CNC, Annedal Clinics, 413 45 Goteborg, Sweden.

—and—

"A preliminary ^{31}P MRS study of autism: evidence for undersynthesis and increased degradation of brain membranes," Nancy J. Minshew et al., *Biological Psychiatry*, 1993, 33:762-773. Address: Nancy Minshew, Univ. of Pittsburgh School of Med., Dept. of Psychiatry, 3811 O'Hara St., Iroquois Bldg., #208, Pittsburgh, PA 15213.

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A study of 18 autistic children with food and/or chemical intolerances revealed that all showed evidence of a disturbance in sulphate metabolism, according to British researchers B.A. O'Reilly and R.H. Waring. Every subject had low levels of the enzyme phenol-sulphotransferase-P and/or a low capacity for oxidizing sulphur compounds. The researchers say these defects indicate the children have difficulty fully metabolizing foods and chemicals containing phenols. In addition, they say, the enzyme deficiency would increase levels of serotonin, a brain chemical which is found in elevated levels in about a third of autistic children.

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"Enzyme and sulphur oxidation deficiencies in autistic children with known food/chemical intolerances," B.A. O'Reilly and R.H. Waring, *Journal of Orthomolecular Medicine*, Vol. 8, No. 4, 1993. Address: R.H. Waring, Dept. of Biochemistry, Birmingham University, Edgbaston, Birmingham, B15 2TT, UK.

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Fragile X syndrome, caused by a mutation on the X chromosome, is a leading cause of mental retardation and autistic-like behaviors. The defective gene that causes fragile X, discovered in 1991, involves repetitions of a nucleotide sequence, but the number of repetitions varies from person to person—and that variation, Louise Staley et al. say, may determine the severity of the disorder.

Staley and colleagues examined the gene variation in 116 individuals with the fragile X mutation, and compared the size of the gene mutation to the severity of symptoms. In males, they found, physical abnormalities did not correlate with the size of the nucleotide sequence, but the highest IQ was seen in males with a "mosaic" genotype (in which several variations of the mutation were present). In females, the researchers say, "those with the smallest nucleotide sequence had the fewest fragile X syndrome physical attributes," as well as the highest IQs.

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"Molecular-clinical correlations in children and adults with fragile X syndrome," Louise Staley et al., *American Journal of Diseases of Children*, Vol. 147, No. 7, pp. 723-726. Address not listed.

No chromosome damage seen in Leominster children; study disputed

Concern over a cluster of autism cases in the Massachusetts town of Leominster has prompted researchers to investigate a possible link between the town's autism rate and residents' exposure to toxins from nearby plastics manufacturing sites. Recently, Donna Spiker et al. reported that chromosome tests on 14 autistic children from the Leominster area showed no abnormalities, "thus failing to support the hypothesis that toxic exposure in parents of autistic children is accompanied by cytogenetic abnormalities in the children."

However, the researchers caution that the current findings "do not address questions about the epidemiology of autism in this particular geographic area," and that the test they performed may not detect some abnormalities.

Lori Altobelli, the mother who first called attention to the Leominster pollution problem, expressed great disappointment with the Stanford report. "We thought they were going to do an up-to-date DNA analysis to see if there was any damage at the gene level," Altobelli said. "instead they used 40-year-old technology to do only a gross visual examination of the chromosomes. Since the kids look normal, we never suspected chromosome damage. We are making arrangements with another laboratory to do the kind of analysis we had in mind originally, which will employ 1990s technology rather than 1950s methods."

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"Failure to find cytogenetic abnormalities in autistic children whose parents grew up near plastics manufacturing sites," Donna Spiker, Linda Lotspeich, Joachim Hallmayer, Helena Kraemer, and Roland Ciaranello; *Journal of Autism and Developmental Disorders*, Volume 23, Number 4, December 1993, pp. 681-682. Address: Donna Spiker, Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305.