Biomedical Update:

Postmortem study shows brain damage from self-injury

Severe self-injury—a behavior seen in many autistic individuals—may cause brain damage similar to that seen in professional boxers, according to Swiss and U.S. researchers.

P. R. Hof and colleagues conducted a postmortem study on the brain of a 24-year-old autistic woman who died of a massive pulmonary embolism. The woman's behaviors had included years of head-banging, eye-gouging (which had left her blind), hair-pulling, and self-biting.

The researchers report finding "numerous neurofibrillary tangles"—a symptom also seen in Alzheimer's disease and a form of dementia frequently suffered by boxers—in cortical areas of the temporal lobe, as well as in some subcortical areas.

Hof et al. say their findings indicate that violent impacts can affect specific groups of cells, "resulting in the disruption of specific elements of the cortical circuitry."

"Moreover," they say, "chronic self-injurious behavior may cause long-term brain lesions which could be related to the progressive deterioration observed in our patient."

Editor's note: the use of harmless short-term aversives could possibly have saved this woman. See SIB story, page 1.

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Neuropathological observations in a case of autism presenting with self-injury behavior," P.R. Hof, R. Knabe, P. Bovier, and C. Bouras; *Acta Neuropathologica*, 1991, 82:321-326. Address: P.R. Hof, Fishberg Research Center for Neurobiology, Mount Sinai School of Medicine, Box 1065, New York, NY 10029.

Sweetener linked to sound sensitivity, other symptoms

More than 500 people have complained to the Food and Drug Administration about adverse reactions to the popular artificial sweetener aspartame, according to researcher Hyman Roberts.

Some of the most common complaints involved hypersensitivity to noise (a problem common in autistic children), tinnitus (ringing or buzzing in the ears), and hearing impairment. Additional symptoms reported after aspartame ingestion included vision problems, headaches, dizziness, gastrointestinal problems, and psychological symptoms including irritability and depression. Seventy individuals reported suffering grand mal epileptic seizures after ingesting aspartame, while 18 reported petit mal epilepsy episodes.

Parents of autistic children who exhibit any of these symptoms may want to eliminate aspartame from their children's diets to see if they are sensitive to the chemical. Roberts suggests "a brief trial of abstinence for several days or weeks."

Roberts notes that laboratory tests showing that aspartame is safe may be inaccurate, since they did not take into consideration the chemical changes aspartame undergoes when heated or stored for long periods of time.

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"Reactions attributed to aspartame containing products: 551 cases," Hyman J. Roberts, *Natural Food & Farming*, , March 1992, pp. 23-28.Reprinted from the *Journal of Applied Nutrition*.

Fragile X: defect seen in brain cell dendrites

Dendrites are the receiving ends of neurons: tree-like branches on the cells that accept incoming messages from other cells. Researchers conducting postmortem studies on three mentally retarded males with Fragile X syndrome (a genetic disorder linked to many cases of autism) report that dendrites of brain cells in the neocortex were malformed in all three subjects—a finding which could help explain the cognitive and behavioral problems associated with Fragile X.

According to Veronica Hinton and colleagues, analysis showed that the men's brain cell dendrites had "irregularly thin, very long, tortuous dendritic spines" interspersed with normal short, stubby spines. The men's ages ranged from 15 to 62, indicating that the long, thin spines (which are normal in some stages of fetal development but should mature into short spines) "persist throughout the adult life span" in Fragile X syndrome.

Subtle defect may lead to severe problems

The researchers say that while the abnormality appears subtle, "the effects . . . may be quite profound." They cite a theory by W. Rall that normal short thick spines transmit electrical messages along dendrite branches more efficiently than long, thin spines.

No gross brain defects were seen in any of the subjects, and all appeared to have normal numbers of neurons in the areas examined. There was no evidence, the researchers said, of abnormal migration or differentiation of brain cells during fetal development.

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"Analysis of neocortex in three males with the fragile X syndrome," V.J. Hinton, W.T. Brown, K. Wisniewski, and R.D. Rudelli; *American Journal of Medical Genetics*, 41:289-294, 1991. Address: Raoul Rudelli, New York State Institute for Basic Research, 1050 Forest Hill Road, Staten Island, NY 10314-3803.

Dopamine gene implicated in autism, other disorders

While much evidence points to a genetic basis for many cases of autism, most research suggests that autism is "multifactorial"—that is, it is caused by a combination of genetic factors, possibly in conjunction with environmental factors such as viral infections. David Comings et al. believe that one of the genes involved in autism is an allele of the dopamine D_2 receptor (DRD2) gene. (Alleles are the different variations of a gene at a particular location on a chromosome—for instance, an allele for blue eyes or for brown eyes. The A1 allele of the DRD2 gene is a variation of that gene occurring only in some members of the population.)

Comings et al. examined the prevalence of the A1 allele in individuals with a variety of physical and psychological disorders. They found that the gene was more prevalent in individuals with autism, Tourette's syndrome, attention deficit hyperactivity disorder, and alcoholism than in non-disabled control groups.

The researchers believe the A1 allele is not a direct cause of these disorders since it was usually seen in less than half of the individuals in each group. Also, in several cases one affected family member showed the allele while another affected family member did not. They suggest, rather, that "other yet-to-be-discovered genes are the primary cause [of these disorders]," but the A1 allele may result in more severe symptoms.

"The similar prevalence of the A1 allele in TS, ADHD, autism, alcoholism, and drug abuse [linked to a somewhat elevated frequency of the A1 allele] is consistent with our proposal that these are part of a spectrum of disorders that share common pathophysiologic genetic mechanisms," Comings et al. say. "One feature these disorders appear to have in common is a substrate of impulsive-compulsive-addictive behaviors." They note that abnormalities of the dopamine system have been implicated in all of these disorders.

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"The dopamine D_2 receptor locus as a modifying gene in neuropsychiatric disorders," David E. Comings et al.; *Journal of the American Medical Association*, October 2, 1991, Volume 266, No. 13. Address: David Comings, Dept. of Medical Genetics, City of Hope National Medical Center, 1500 E. Duarte Rd., Duarte, CA 91010-0269.