

Biomedical Update:

Another study finds large head size common in autism

Mounting evidence suggests that a high percentage of autistic children have larger-than-normal head sizes, although the cause and significance of this finding are unclear.

The most recent study on head size in autism was conducted by Michael Davidovitch et al., who studied the charts of 148 autistic children with no co-existing conditions known to affect head size. The researchers found that 18.2 percent of their autistic subjects had head circumferences at the 98th percentile or above (the researchers' criteria for "macrocephaly"), while the expected percentage would be 3%. Furthermore, they note, "the incidence of head circumference at the 50th percentile and above (82%) was also significantly above the expected."

In addition, the researchers found that the children with head sizes above the 98th percentile were significantly taller and heavier than the other autistic children they studied. The ratio of boys to girls was also higher in this group than among non-macrocephalic subjects, and the macrocephalic children had significantly lower adaptive behavior scores than the other children.

Davidovitch et al. note that their findings are supported by earlier studies, including:

—A study by A. Bailey et al., who found that 37% of the autistic children they studied had head circumferences above the 97th percentile.

—A study of autistic twins, also by Bailey et al., which found that 9 of 21 subjects (42%) had head circumferences above the 97th percentile.

—Magnetic resonance imaging studies by Joseph Piven et al., which found that autistic subjects had greater total brain, total tissue, and total lateral ventricle volumes than control subjects.

Given the increased height and weight measurements seen in macrocephalic subjects, Davidovitch et al. suggest the presence of "a common factor that influences all somatic and brain growth indices."

"Head circumference measurements in children with autism," Michael Davidovitch, Bonnie Patterson, and Peter Gartside; *Journal of Child Neurology*, Vol. 11, No. 5, Sept. 1996, pp. 389-393. Address: Michael Davidovitch, University Affiliated Cincinnati Center for Dev. Disorders, Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229-3039.

Tuberous sclerosis offers clues about cause of autism

Tuberous sclerosis is a genetic disorder that affects the skin and nervous system, causing noncancerous tumors of the brain, kidney, heart, and retina. (Tumors that form

in the brain are called "tubers.") Individuals with the disorder usually are mentally retarded and have seizures.

Many but not all individuals with tuberous sclerosis also are autistic, a finding which led Patrick Bolton and Paul Griffiths to investigate whether or not the location of tubers in the brain influenced the development of autistic symptoms. The researchers examined the brain scans of 18 patients with tuberous sclerosis—nine with autism or atypical autism, and nine with various other psychiatric disorders—to determine the number of tubers each subject exhibited, and the areas of the brain in which they occurred.

The researchers found that "the number of tubers was significantly greater in individuals with a diagnosis of autism or atypical autism than in those without this diagnosis." Of the nine autistic or autistic-like patients, eight had tubers located in the temporal lobes. In contrast, no subjects in the non-autistic group had tubers in the temporal lobes.

This finding, the researchers say, "suggest[s] that temporal lobe neurodevelopmental abnormalities may create a risk for autism or atypical autism."

Bolton and Griffiths note that some research supports a link between autism and temporal lobe abnormalities. "Primates that have had surgical ablation [destruction] of the medial temporal lobes in the neonatal period," they say, "develop autistic-like behavioral, social, and emotional deficits." A positron emission tomography (PET) study of children with infantile seizures, they add, found that children with perfusion abnormalities in the temporal lobes were much more likely to develop autism later, and some magnetic resonance imaging (MRI) studies indicate that the temporal lobes are enlarged in some autistic subjects.

Bolton and Griffiths also found that subjects with mental retardation had significantly more tubers than those with normal intelligence, and that the degree of retardation was correlated with the number of tubers.

"Association of tuberous sclerosis of temporal lobes with autism and atypical autism," Patrick F. Bolton and Paul D. Griffiths; *The Lancet*, Vol. 349, February 8, 1997. Address: Patrick F. Bolton, Section of Developmental Psychiatry, Douglas House, 18b Trumpington Road, Cambridge, CB2 2AH, UK.

More concerns about movement disorders caused by SSRIs

A relatively new class of drugs called selective serotonin reuptake inhibitors (SSRIs) is gaining popularity for the treatment of autistic aggression and self-injury (see ARRI 10/4). New reports, however, suggest that the SSRIs—while apparently safer than older neuroleptics such as Hal-dol—can occasionally cause movement disorders, particularly when combined with other medications.

ARRI 10/4 summarized a report by Steven Dubovsky and Marshall Thomas, who found that Prozac (fluoxetine) can sometimes cause tardive dyskinesia, a neurological disorder resulting in involuntary muscle movements such as chewing, swallowing, and lip smacking. Similarly, a new literature review by Raphael Leo found a number of reports associating Prozac and other SSRIs with tardive dyskinesia. In addition, the researchers report that the drugs can cause other serious movement disorders including:

—akathisia (motor restlessness that causes quivering, anxiety, and an inability to sit still);

—dystonia (including symptoms such as muscle spasms, jaw tightness, or twisting of the neck); and,

—parkinsonism symptoms including rigidity, tremor, gait disturbances, and a mask-like appearance.

Leo used MEDLINE searches to identify physician reports of movement disorders associated with SSRIs. He found 71 cases reported, with akathisia being the most common condition. Leo notes that the literature of Eli Lilly and Company, which manufactures Prozac, reports "375 cases of akathisia, 218 cases of dystonia, and 76 cases of tardive dyskinesia" associated with the drug as of December 1995, and that the World Health Organization has received 438 reports of movement disorders associated with Prozac. "Although these side effects are infrequent," he says, "clinicians should be alert to the possibility of their occurrence."

Leo's own research suggests that individuals most at risk for SSRI-linked movement disorders include older patients, those with Parkinson's disease, and those taking multiple drugs. Although side effects are most often reported with Prozac, he says, it is not clear if this is due to the drug's popularity or to pharmacological differences among the SSRIs.

"Movement disorders associated with the serotonin selective reuptake inhibitors," Raphael J. Leo; *Journal of Clinical Psychiatry*, 57, 10, October 1996, pp. 449-454. Address: Raphael J. Leo, Department of Psychiatry, State University of New York at Buffalo, Erie County Medical Center, 462 Grider Street, Buffalo, NY 14215.

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