

# PEDIATRIC NEUROLOGY BRIEFS

## A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

---

Vol 18, No.12

December 2004

---

### AUTISTIC DISORDERS

#### NEUROPATHOLOGY OF AUTISM

The neuropathological literature and the prospects for future research in the genetics and pathology of autism are outlined in an inclusive review article from the University Medical Center Utrecht, The Netherlands. Increased head circumference, brain weight and brain volume in children with autism are well documented. The limbic system shows increased cell packing density and smaller neuronal size in 9 of 14 autism cases reported; the cerebellum shows a decreased number of Purkinje cells in 21 of 29 cases studied, and the cerebral cortex has features of dysgenesis. Small sample size, inconsistent findings, and comorbid conditions, including mental retardation in 70% and epilepsy in 40%, diminish the significance of the reports in regard to the pathogenesis of autism. Future neuropathological studies should include larger sample sizes, younger subjects free of comorbidities, and new techniques such as stereology, that permits precise measurement of number, size and spatial distribution of cells, and the study of gene expression, to uncover the molecular and cellular basis of the neuropathology of autism. (Palmen SJMC, van Engeland H, Hot PR, Schmitz C. Neuropathological findings in autism. **Brain** December 2004;127:2572-2583). (Respond: Saskia Palmen MD, Department of Child and Adolescent Psychiatry, HP A01.468, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands).

COMMENT. Autism is a neurodevelopmental, genetically determined, disorder characterized by impairments in social interaction and communication skills, cognitive rigidity, abnormal language development, and repetitive, stereotypical behaviors. The prevalence of autistic spectrum disorders (ASD) in studies published before 1985 was 4-5 per 10,000 children. After 1990, the prevalence began to rise to as high as 50-70 per 10,000 in the USA (Wing L, Potter D. 2002, cited by Bale JF. Autism: the search for the missing link. **Lancet Neurology** Dec 2004;3:706-707). Causative factors proposed for the apparent

---

PEDIATRIC NEUROLOGY BRIEFS (ISSN 1043-3155) © 2004 covers selected articles from the world literature and is published monthly. Send subscription requests (\$68 US; \$72 Canada; \$75 airmail outside N America) to **Pediatric Neurology Briefs - J. Gordon Millichap, M.D., F.R.C.P.-Editor**, P.O. Box 11391, Chicago, Illinois, 60611, USA.

The editor is Pediatric Neurologist at Children's Memorial Hospital and Northwestern University Medical School, Chicago, Illinois. PNB is a continuing education service designed to expedite and facilitate review of current scientific information for physicians and other health professionals. Fax: 312-943-0123.

increase in prevalence of ASD have included more inclusive definitions, improved recognition of the symptoms, greater parental concern, and possible epigenetic factors and modifications of gene expression. The theory that the measles-mumps-rubella (MMR) vaccine and thimerosal were responsible for the apparent increased prevalence of autism has largely been put to rest (Madsen KM et al. **Pediatrics** 2003;112:604-606; Smeeth L et al. **Lancet** 2004;364:963-969). ASD has a strong genetic basis, and a specific medical cause or environmental trigger is found in only 6-10% of cases, eg. prenatal insult, metabolic and toxic disorders, tuberous sclerosis, and postnatal encephalitis (Baird G et al. **BMJ** 2003;327:488-493; see **Ped Neur Briefs** October 2003;17:79-80). The study of the etiology of autism is multifaceted, and future research will involve pediatric neurologist, psychiatrist, pathologist, and geneticist.

**Oculomotor studies in autism.** Pursuit eye movement deficits were observed in a study of 60 high-functioning autistic young adults compared to 94 normal control subjects, at the University of Illinois, Chicago (Takarae Y et al. **Brain** Dec 2004;127:2584-2594). The authors conclude that their findings are consistent with reduced functional connectivity within the visual pursuit system caused by abnormalities in brain maturation in autism.

## **BROCA'S AREA ASYMMETRY AND LANGUAGE DEFICITS IN AUTISM**

The asymmetry of frontal language cortex in boys with autism, previously reported, was investigated further in a sample of 22 boys with autism compared to 9 boys with specific language impairment (SLI) and 11 normal controls, in a study at Massachusetts General Hospital and Harvard Medical School, Boston. Of the boys with autism, 16 were language impaired (ALI) and 6 had normal language ability (ALN). Their ages ranged from 6.2 to 13.4 years; they were all right-handed. As predicted, MRI brain scans showed group differences in volumetric asymmetry in language-related regions in inferior lateral frontal (Broca's area) and posterior superior temporal cortex. Language impaired boys with autism (ALI) and boys with SLI both had significant reversal of asymmetry in frontal language-related cortex. Language-related areas were larger on the right side in both ALI and SLI groups and larger on the left in both normal language groups. The boys with unimpaired language and autism (ALN) had similar asymmetry to that of control groups. Broca's area asymmetry reversal is correlated more with language impairment than with autism. The findings strengthen a proposed phenotypic link between ALI and SLI in boys. (De Fosse L, Hodge SM, Makris N, et al. Language-association cortex asymmetry in autism and specific language impairment. **Ann Neurol** December 2004;56:757-766). (Gordon J Harris PhD, RAD CADx LAB, MGH, Zero Emerson Place #3A, Boston, MA 02114).

**COMMENT.** The abnormal asymmetry in language-related brain areas in boys with specific language impairment (SLI) or language impairment and autism is more closely related to language impairment than to autism. The authors conclude that their findings support the hypothesis of a common neurobiological basis of language impairment in autism and SLI. Language function is variable but is often impaired in autism. Autistic children with impaired language have a similar profile of language impairment to that of SLI, and a common genetic linkage is likely (Kjelgaard MM, Tager-Flusberg H, 2001).