CONGENITAL CEREBRAL MALFORMATIONS

CORPUS CALLOSUM SIZE AND VERBAL INTELLIGENCE

Quantitative MRI measurements of the sagittal surface area of the corpus callosum (CC) in 72 preterm individuals tested at adolescence (14-15 years) were compared with verbal skills on neuropsychological tests in a study at the Institute of Psychiatry, De Crespigny Park, London, UK. Total CC area in very preterm adolescents was 7.5% smaller than in controls (p=0.015). In preterm individuals who had a periventricular hemorrhage in the neonatal period, the decrease in CC area was greater. Verbal IQ and verbal fluency scores were lower in male adolescents with reduced total mid-sagittal CC size and mid-posterior surface area. (Nosarti C, Rushe TM, Woodruff PWR, et al. Corpus callosum size and very preterm birth: relationship to psychological outcome. **Brain** September 2004;127:2080-2089). (Respond: Chiara Nosarti PhD, Division of Psychological Medicine, Section of General Psychiatry, PO Box 63, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, UK).

COMMENT. The development of the corpus callosum (CC), especially the posterior quarter adjacent to the periventricular region, is adversely affected by very preterm birth. The decreased size of the CC is correlated with lower verbal IQ and verbal fluency scores in preterm boys at adolescence.
A decrease in size of the splenium of the corpus callosum is reported in ADHD children compared to controls (Semrud-Clikeman et al. 1994; see **Ped Neur Briefs** July 1994).

CAUSES, TYPES, AND OUTCOME OF HOLOPROSENCEPHALY

Recent advances in genetics and neuroimaging of children with holoprosencephaly (HPE) are reviewed from Stanford University School of Medicine, CA. Four major types of HPE are delineated by MRI findings: alobar, semilobar, lobar, and middle interhemispheric (MIH) variant, the lobar and MIH types being most prevalent. In etiology, both genetic and environmental factors are identified. *Chromosomal anomalies* account for 40% and include trisomies (> half of these cases), duplications, deletions, and ring arrangements. Outcome in HPE cases with cytogenetic abnormalities is very poor, only 2% surviving beyond 1 year, compared to 30-54% for those without genetic causes. Smith-Lemli-Opitz syndrome carries an increased risk of HPE. Mutations have been identified in 15% to 20% of HPE cases with normal karyotypes. In the autosomal dominant form of HPE, *SHH* is the most frequently identified gene defect. *Environmental causes* include antiepileptic drugs, alcohol, smoking, statins, gestational diabetes, and cytomegalovirus infection. Some teratogens interfere with sonic hedgehog signaling pathways by disturbing cholesterol metabolism. *Neuroimaging abnormalities* include non-separation of deep gray nuclei, especially thalamus, monoventricle, dorsal cyst, hydrocephalus, Sylvian fissure abnormalities, and cortical dysplasia. *Clinical manifestations* include mental and developmental retardation, epilepsy, spasticity, dystonia, choreoathetosis, and endocrine disorders (diabetes insipidus, growth hormone deficiency). Craniofacial malformations are severe (cyclopia, midline cleft lip and

palate and flat nose), moderate (midface hypoplasia, hypotelorism), or mild (single central incisors, iris colobomas, anosmia). Feeding and swallowing difficulties are common. Microcephaly occurs in 75% of classic HPE cases, while one sixth require CSF shunting for hydrocephalus, especially in the alobar type and those with a dorsal cyst. Motor dysfunction varies and is most prevalent in the alobar and semilobar types of HPE. *Outcome.* This varies with the type and severity of HPE, and early mortality is expected in those with severe craniofacial or chromosomal abnormalities. Of 104 surviving cases evaluated at the Carter Centers, mean age was 4 years, and 15% were between 10 and 19 years of age. The recurrence risk of HPE is estimated at 6%, and is highest in familial forms. A thorough family hstory is advised. Prenatal diagnosis attempted by ultrasound in 93% was positive in only 22% of cases. Fetal MRI may prove effective in characterizing the malformation in cases with positive ultrasound. (Hahn JS, Plawner LL. Evaluation and management of children with holoprosencephaly. **Pediatr Neurol** August 2004;31:79-88). (Respond: Jin S Hahn MD. Department of Neurology, A343, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305).

COMMENT. Holoprosencephaly is a congenital malformation caused by a defect in patterning of the basal forebrain in the first 4 weeks of embryogenesis, and characterized by incomplete separation of the cerebral hemispheres and basal ganglia. The mainly topographical classification of CNS malformations is being replaced by a classification based on integration of morphological and molecular genetic criteria (Sarnat and Sarnat, 2001; see **Ped Neur Briefs** 2001;15:57). The middle interhemispheric variant of HPE has previously been described as a distinct clinico-neuroradiologic subtype (Lewis et al, 2002; see **Ped Neur Briefs** Jan 2003;17:1-2). It differs from the lobar subtype by the absence of endocrine abnormalities and choreoathetosis. A delay in white matter maturation is described in 25 of 47 patients with HPE, a defect most evident in the MRI of infants and in severe subtypes (Barkovich et al, 2002; see **Ped Neur Briefs** Jan 2003;17:2-3).

FOCAL CORTICAL DYSPLASIA AND HOT WATER EPILEPSY

A 4-year-old girl with complex partial seizures triggered by bathing in hot water and found to have a left parietal focal cortical dysplasia on MRI is reported from the University of Siena, Italy. The interictal EEG showed spikes and spike-and-wave epileptiform discharges in the left parietal region. Spontaneous non-reflex complex partial seizures recurring at 3 months after the first HWE seizure at 6 months were resistant to carbamazepine and gabapentin and controlled by topiramate. This is the second patient with hot water epilepsy (HWE) rported in association with a cortical malformation. MRI is advised in patients with HWE. (Grosso S, Farnetani MA, Francione S, et al. Hot water epilepsy and focal malformation of the parietal cortex development. **Brain Dev** Sept 2004;26:490-493). (Paolo Balestri, Department of Pediatrics, University of Siena, Viale M Bracci, Le Scotte, 53100 Siena, Italy).

COMMENT. HWE accounts for 6.9% of all epilepsies in the Indian community, it is also common in Turkey but rare in other ethnic groups. Children are affected more frequently than adults. First reported in an Australian patient (Lenoir et al, 1989), HWE is classified as a benign reflex epilepsy with a good prognosis, usually occurring when hot water is poured on