COMMENT. Reading instruction in children with dyslexia is associated with changes in brain activation patterns during specific language processes that resemble those of control normal readers. Previous studies have demonstrated normalization of brain activation patterns in dyslexics during phonological tasks and following successful remedial training (Simos PG et al. Neurology 2002;58:1203-1213). The above study extends this treatment effect to morpheme mapping tasks, and shows that phoneme and morpheme language processes have different brain activation patterns. Treatment of dyslexia increases brain activation in circuits normally involved in processing language function.

Magnetic source imaging (MSI), a combination of MEG and MRI, has been used to study functional neuroanatomy during reading. Dyslexics failed to activate the left visual and receptive language cortical areas during word presentation, but instead, activated the left inferior frontal lobe (Salmelin R et al, 1996). The activation of the left posterior-temporal lobe during reading aloud or silently has been observed in PET studies of normal readers (Price CJ et al, 1994). The most critical area of dysfunction in dyslexic subjects is in the left posterior temporal lobe. A phonological-linguistic basis of dyslexia is most generally accepted (Denckla MB, 1994), and is preferred to the visual system deficit theory (Lehmkuhle S et al, 1993).

VISUOSPATIAL COGNITIVE DEFICITS AND SUBTLE CORTICAL ANOMALIES IN PRETERM ADOLESCENTS

Voxel-based morphometric analysis (VBM) of the MRI scans of a group of adolescents, born preterm with very low birth weights and with deficits in judgment of line orientation, was used to demonstrate anomalies of cortical gray matter in a study at the Institute of Child Health and Great Ormond Street Hospital, London, UK. Subjects were assigned to 2 groups, *deficit* and *no deficit*, 11 in each, based on their scores on the Benton Judgment of Line Orientation test. IQ scores were average in both groups, and Block Design was the only WISC-III subtest showing a significant difference between groups (Deficit group=7.8; No Deficit group=10.4; $p<0.05$). All were neurologically normal and the MRIs showed no consistent abnormalities (thinning of the corpus callosum in 2 of the No Deficit group and 1 of the Deficit group and small hippocampi in 4 of the Deficit group). VBM analysis of scans identified a decrease in gray matter density and increase in white matter density in the ventral extrastriate cortex in children with visuospatial deficits, most prominent in the right hemisphere. These anomalies of cortical architecture were situated close to a temporooccipital area previously implicated in the line orientation task. (Isaacs EB, Edmonds CJ, Chong WK, Lucas A, Gadian DG. Cortical anomalies associated with visuospatial processing deficits. Ann Neurol June 2003;53:768-773). (Respond: Dr Elizabeth B Isaacs, MRC Childhood Nutrition Research Centre, Institute of Child Health, University College London, 30 Guildford Street, London WC1N 1EH, UK).

COMMENT. Children born preterm may have cognitive deficits involving visuospatial processing of line orientation, despite normal neurologic examination and absence of specific abnormalities on conventional MRI. Subtle abnormalities of

extrastriate cortex can be identified by analysis of voxel-based morphometry of MRI scans.

CONGENITAL MALFORMATIONS

X-LINKED LISSENCEPHALY WITH ARX MUTATIONS, ABNORMAL GENITALIA, AND CORPUS CALLOSUM AGENESIS

The clinical and genetic findings of two X-linked lissencephaly with abnormal genitalia (XLAG) pedigrees with ARX mutations are reported from the University of Regensburg, Germany. Case 1 index patient had multifocal clonic seizures at birth and later developed generalized tonic-clonic seizures refractory to treatment. The head circumference at birth was in the 25th percentile and at 9 months, below the 3rd percentile. MRI showed lissencephaly, thick cortex, small basal ganglia, subependymal cysts, and absent corpus callosum (ACC) and septum pellucidum. Abnormal signs also included micropenis, hypospadius, cryptorchidism, and hypothermic episodes. Case 2 index patient developed microcephaly by 2 years and was born with a head circumference in the 25th percentile, myoclonic seizures, abnormal genitalia, and subsequent episodic hypothermia. MRI showed lissencephaly and ACC, and echocardiogram revealed a persistent patent ductus arteriosus and foramen ovale. Sequencing of the ARX gene showed in case 1 a single nucleotide deletion and in case 2 a missense mutation. Three known ARX mutations within the homeodomain are associated with a XLAG phenotype. Patients with XLAG show severe clinical deficits and cerebral malformations. Female carriers (mother of index case 1) with mutations leading to XLAG phenotype in males show partial or complete ACC. (Uyanik G, Aigner L, Martin P et al. ARX mutations in X-linked lissencephaly with abnormal genitalia. Neurology 22 July 2003;61:232-235). (Reprints: Dr Juergen Winkler, Department of Neurology, University of Regensburg, Universitatsstr, 84, D-93053 Regensburg, Germany).

COMMENT. XLAG is characterized by lissencephaly, complete agenesis of the corpus callosum, and hypogenitalism (Berry-Kravis, Israel, 1994). Posterior agyria, anterior pachygyria, and intermediate thickening of the cortex distinguish this syndrome from lissencephaly type 1, in which the cortex is thicker, and the corpus callosum is hypoplastic but not absent. Females related to boys with XLAG may be mentally retarded, and have epilepsy and agenesis of the corpus callosum (Bonneau D et al. see Ped Neur Briefs March 2002;16:22). ARX is a causative gene for X-linked mental retardation, X-linked infantile spasms, and X-linked lissencephaly with abnormal genitalia. Two different point mutations in the ARX gene are reported here in two pedigrees of XLAG. A report from Japan finds a polyalanine expansion of ARX associated with cryptogenic West syndrome in one of 8 patients tested (Kato M et al. Neurology 22 July 2003;61:267-268). The detection of this mutation is helpful in genetic counseling.