NEUROCUTANEOUS SYNDROMES

FREQUENCY OF COGNITIVE DEFICITS IN NEUROFIBROMATOSIS

The frequency and severity of specific cognitive deficits in 81 children with neurofibromatosis type 1 (NF1), ages 8 to 16 years, compared to 49 unaffected sibling controls, were assessed in a study at the University of Sydney, New South Wales, Australia. Specific learning disabilities, defined by IQ-achievement discrepancies, occurred in 20% (37% in males and 5% females), but 51% showed impairments in reading, spelling, and mathematics, and 81% had moderate to severe impairments in cognitive functioning. Mental retardation was present in 6 – 7%. Attention deficit hyperactivity disorder was diagnosed in 38%, while 63% had sustained attention difficulties. Compared with their siblings, ADHD was 3 times more common in NF1 children, with similar frequencies in males and females. An NF1 neuropsychological profile shows deficits in visuo-spatial and –perceptual skills, executive functioning, attention, and expressive and receptive language. Verbal and visual memory was preserved. (Hyman SL, Shores A, North KN. The nature and frequency of cognitive deficits in children with neurofibromatosis type 1. **Neurology** October (1 of 2) 2005;65:1037-1044). (Reprints: Dr KN North, Children's Hospital at Westmead, Clinical Sciences Building, Locked Bag 4001, Westmead, NSW 2145, Australia).

COMMENT. A neuropsychological profile for neurofibromatosis type 1 is characterized by weaknesses in visuospatial and visuoperceptual skills and strengths in verbal and visual memory. Specific learning disabilities are particularly prevalent in males, and girls are relatively spared. Comorbidity with ADHD is prevalent, both in males and females with NF1.

COGNITIVE AND BEHAVIORAL DEFICITS IN NEUROCUTANEOUS SYNDROMES

Cognitive and behavioral features of Sturge-Weber syndrome, tuberous sclerosis, and neurofibromatosis are summarized by a literature review (113 references) at the New York University, New York. *Sturge-Weber syndrome* is associated with mental retardation in 50 to 60% of cases, correlated with the extent of unilateral cerebral calcification and atrophy. The occurrence of seizures in up to 90% of cases is associated with leptomeningeal angiomatosis, and predicts a poorer prognosis. Hemispherectomy provides an 80% rate of seizure freedom; mean age of surgery was 2 years for patients left with a mild disability compared to 3 years for those with moderate or severe disability. A progressive neurological and developmental deterioration may be explained by venous occlusions and hypoxia, and is sometimes correlated with a worsening of seizures and EEG abnormalities. Psychiatric symptoms in Sturge-Weber syndrome include irritability, social problems, ADHD, oppositional defiance disorder, self-abuse, aggressive behavior, and depression, often correlated with occurrence of seizures.

Tuberous sclerosis (TS) presents with seizures in 80 – 90% of cases, often developing in the first year of life, and manifesting as infantile spasms in one-third. An IQ below 70 was

found in 44% of one sample of 108 patients (a DQ below 21 in 31%); 55% had a normal IQ. In studies of children with TS and near-normal IQ, 50% had ADD or hyperkinetic syndrome, and 25% had ODD. Infantile spasms and low IQ are significantly related. Cognition is also correlated with *tuber burden* (tuber number, size, and location). Genetic factors correlate with developmental outcome: *TSC1* cases have lower rates of mental retardation, seizures, and autism than *TSC2.* TS is linked to autistic spectrum disorder in 50 to 60% of cases (the rate is higher in those with infantile spasms), and these patients do not show the characteristic male preponderance seen in idiopathic autism cases. Temporal lobe tubers and EEG abnormalities increase the risk of autism.

Neurofibromatosis type 1 (NF-1) patients have an average mean IQ, despite earlier reports of an increased incidence of mental retardation, but learning disabilities, especially visual-perceptual deficits, occur in 30-60% of cases. ADHD is reported in 33%. Some studies show a resolution of childhood cognitive dysfunction in adults with NF-1. Cognitive deficits are correlated with the occurrence, number, and location of UBO's. Macrocephaly shows no correlation with cognitive functioning in NF-1. Adolescents with NF-1 and learning difficulties had social-skill problems, when compared to unaffected siblings. ADHD was the major risk factor for social problems. (Zaroff CM, Isaacs K. Neurocutaneous syndromes: behavioral features. **Epilepsy Behav** Sept 2005;7:133-142). (Respond: Charles M Zaroff MD, Comprehensive Epilepsy Center, New York University, 403 East 34th Street, New York, NY 10016).

COMMENT. Neurocutaneous syndromes are associated with an increased rate of mental retardation or learning disabilities. Problems in cognition and behavior are related to the underlying neurological disorders, especially seizures, and in tuberous sclerosis the genotype contributes to clinical heterogeneity. An increased prevalence of ADHD in all three syndromes is noteworthy, and tuberous sclerosis is strongly linked with autism.

SEIZURE DISORDERS

ETHOSUXIMIDE-INDUCED PSEUDOLYMPHOMA

A first case of pseudolymphoma induced by ethosuximide treatment in a 12-year-old boy is reported from the University of Sao Paulo, Brazil. He presented with a 2-month history of fever, weight loss, and non-painful lympadenopathy in the neck, axillae, and inguinal regions. He had taken ethosuximide (30 mg/kg/day) for 3 months for absence epilepsy. The liver and spleen were not palpable. Blood count revealed a leucopenia of $3.6x10^3$ /mcl (48% neutrophils, 3% eosinophils, 40% lymphocytes, and 9% monocytes), and decreased platelets of $119x10^3$ /mcl. Cytomegalovirus, Epstein-Barr, herpes simplex virus, and toxoplasmosis were excluded. Biopsy of a cervical gland confirmed a diagnosis of lymphoma. After discontinuing ethosuximide, fever disappeared within 1 day, and lymph nodes decreased in size in 2 weeks and completely regressed in 2 months. Leukocyte and platelet counts normalized after 2 weeks of drug withdrawal. Fever and enlargement of lymph nodes recurred after 1 week following rechallenge with ethosuximide treatment. (Masruha MR, Marques CM, Vilanova LCP et al. Drug induced pseudolymphoma secondary to ethosuximide. **J Neurol Neurosurg Psychiatry** November 2005;76:1610). (Respond: Dr