SIGNIFICANCE OF FOCAL EEG ABNORMALITIES IN PERVASIVE DEVELOPMENTAL DISORDER AND ADHD

Researchers at University of Fukui, Japan analyzed the relation between EEG abnormalities and PDD or ADHD, and assessed the clinical utility of EEG in the differential diagnosis of these disorders. The study involved 64 PDD children and 22 ADHD children with no history of epilepsy or progressive neurological or psychiatric disease. Paroxysmal discharges at the frontopolar-frontal brain regions and background EEG abnormalities were detected preferentially in the PDD group expressing persistence or hypersensitivity, whereas central-temporal discharges were detected preferentially in the ADHD group expressing impulsivity. No significant differences in the laterality of paroxysmal discharges were found between PDD and ADHD. Patients classified as inattentive subtype ADD showed no EEG abnormality. A combination of EEG abnormalities, including background abnormalities and paroxysmal discharges at Fp-F and C-T regions, might be useful diagnostic hallmarks to distinguish PDD with ADHD from ADHD alone. Dysfunction of specific brain areas associated with EEG abnormalities might explain characteristics of PDD and ADHD symptoms. (Kawatani M, Hiratani M, Kometani H, et al. Focal EEG abnormalities might reflect neuropathological characteristics of pervasive developmental disorder and attention-deficit/hyperactivity disorder. **Brain Dev** 2012 Oct;34(9):723-30). (Respond: Dr Masao Kawatani, Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Eiheiji, Yoshida, Fukui 910-1193, Japan. E-mail: kawatani@u-fukui.ac.jp).

COMMENT. The utility of the EEG in ADHD is previously documented, especially in relation to choice of medication (stimulant vs. non-stimulant) in patients with lack of awareness and transient cognitive impairment. (Millichap JJ, Stack CV, Millichap JG. **J Child Neur** 2011 Jan;26(1):6-11; idem. **Clinical EEG and Neuroscience** 2011 Jul;42(3):180-4). Of 624 EEG recordings in non-epileptic children evaluated for ADHD, 26% were abnormal. Of 163 abnormal recordings, 55% were focal epileptiform discharges, localized predominantly in the central region, less frequently in frontal and temporal regions, and infrequently in parietal and occipital areas; 41.7% had generalized epileptiform discharges. Hemispheres were equally affected, but in frontal areas, the left side had more frequent spikes. Only 3 patients had background slowing and 3 had focal slowing. None had a primary diagnosis of PDD.

ANTIEPILEPTIC DRUGS AND SEIZURES

EFFECT OF NEONATAL EXPOSURE TO AED ON SYNAPTIC MATURATION

Pharmacologists at Georgetown University, Washington, DC examined functional synaptic maturation in striatal medium spiny neurons from neonatal rats exposed to antiepileptic drugs (AED) with proapoptotic action (phenobarbital, phenytoin, lamotrigine) and without proapoptotic action (levetiracetam). Phenobarbital-exposed rats were also assessed for reversal learning at weaning. Compared to control animals that

showed increased inhibitory and excitatory synaptic connectivity between postnatal day P10 and P18, rats exposed at P7 to a single dose of phenobarbital, phenytoin, or lamotrigine had impaired maturation of synaptic connectivity. Phenobarbital exposure also impaired striatal-mediated behavior on P25. Neuroprotective pretreatment with melatonin, which prevents drug-induced neurodevelopmental apoptosis, prevented the drug-induced disruption in maturation. Synaptic development was not disrupted by levetiracetam. (Forcelli PA, Janssen MJ, Vicini S, Gale K. Neonatal exposure to antiepileptic drugs disrupts striatal synaptic development. **Ann Neurol** 2012 Sep;72(3):363-72). (Respond: Dr Forcelli or Dr Gale, Department of Pharmacology and Physiology, Georgetown University, Washington, DC. E-mail: Paf22@georgetown.edu).

COMMENT. Protection from experimental seizures in small, laboratory animals is the backbone of development of new potentially effective and less toxic antiepileptic drugs, beginning with the introduction of phenytoin in 1937 (Putnam TJ, Merritt HH. **Science** 1937 May 28;85(2213):525-6). Phenobarbital, introduced as an anticonvulsant by Hauptmann in 1912, has a troublesome sedative side effect. Phenytoin was the first AED to show anticonvulsant activity without sedation. Various laboratory methods to elicit seizures have been employed in the testing of new drugs, and major advances were made in the mid 1900s, particularly in the pharmacology department at the University of Utah, under the direction of Louis S Goodman, Ewart A Swinyard, Dixon M Woodbury and others. The current laboratory study from Georgetown University should increase concern regarding the potential hazard of continuing use of phenobarbital and phenytoin in the neonate and young infant, and should lead to the introduction of alternative therapies that control seizures without compromising synaptic maturation, cognition and behavior.

Epileptologists in a Catch-22 situation. Whereas this pharmacological study cautions the epileptologist against overuse of AEDs in the control of neonatal seizures, the following clinical study emphasizes the need for early aggressive treatment and seizure control in infants and young children.

AGE AT ONSET OF EPILEPSY AND EFFECT OF UNCONTROLLED SEIZURES ON COGNITIVE OUTCOME

Researchers at the Epilepsy Center and Department of Psychiatry at Lurie Children's Hospital of Chicago examined the association of cognitive scores and age at onset of epilepsy, pharmacoresistance, and interaction between the two in a prospective community-based study of 198 children, aged <8 years, with new-onset epilepsy. The range of epilepsy syndromes reflected those seen in this age group. The average age at the first unprovoked seizure was 3.7 years. Full-scale IQ (FSIQ) assessed with the WISC for Children (WISC-III) after 8-9 years follow-up (mean IQ 94.2) was not correlated with age at onset. In 38 (19.2%) patients meeting the study criteria, pharmacoresistance was associated with an 11.4-point lower FSIQ ($p=0.002$) and similar decrements in each WISC-III domain. Pharmacoresistance lessened with increasing age. IQ was strongly correlated with age at onset in the pharmacoresistant group ($p<0.0001$) but not in the non-pharmacoresistant group ($p=0.61$). Impairment of cognitive function associated with uncontrolled seizures is most severe in infancy and lessens with increasing age at onset.