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SEIZURE AND OTHER PAROXYSMAL DISORDERS

DRUG-TRANSPORTER GENE AND REFRACTORY EPILEPSY

The drug-transporter gene ABCB1 polymorphism (C to T) at position 3435 was typed in 315 patients with epilepsy, classified as drug-resistant in 200 and drug-responsive in 115, and 200 controls without epilepsy, in a study at the Institute of Neurology, London, UK. Drug resistance was defined as at least 4 seizures in 1 year with more than 3 appropriate antiepileptic drugs at maximal tolerated doses. Drug responsiveness was complete freedom from seizures for at least a year. Compared with the drug-responsive patients, those with drug-resistant epilepsy were more likely to have the CC genotype at ABCB1 3435 than the TT genotype ($p=0.006$). The frequency of the CT genotype did not differ between the two groups. The C polymorphism was overrepresented among drug-resistant as compared with drug-responsive patients ($p=0.008$). (Siddiqui A, Kerb R, Weale ME, et al. Association of multidrug resistance in epilepsy with a polymorphism in the drug-transporter gene ABCB1. *N Engl J Med* April 10, 2003;348:1442-1448). (Reprints: Dr Sanjay M Sisodiya, Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London WC1N 3BG, UK).

COMMENT. A genetic basis for refractory epilepsy and resistance to antiepileptic drugs (AED) is identified. Most AED are planar lipophilic agents and substrates for the ABCB1 drug-transporter gene. Multidrug-resistance proteins such as ABCB1 are important in the development of refractory epilepsy, and over-expression of these proteins has been demonstrated in the temporal-lobe tissue from patients with epilepsy. By restricting the entry of lipophilic molecules into the brain, the ABCB1 protein may lessen the effective concentration of AED (Pedley TA, Hirano M. Is refractory epilepsy due to genetically determined resistance to antiepileptic drugs? *N Engl J Med* 2003;348:1480-82).

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Both Siddiqui and Pedley and their colleagues caution that the polymorphism in the ABCB1 gene may not be the specific cause of drug resistance, and other associations may be uncovered in different populations. Pharmacogenomics opens a new approach to the development of therapeutic agents in epilepsy.

A loss of Na⁺ channel drug sensitivity is proposed as a novel mechanism underlying drug, specifically carbamazepine (CBZ), refractory epilepsy (Remy S, Gabriel S, Urban BW, et al. *Ann Neurol* April 2003;53:469-479). Researchers at the University of Bonn Medical Center, and Charite, Berlin, Germany, studied cellular mechanisms underlying drug resistance in resected hippocampal tissue from patients with temporal lobe epilepsy. The mechanism of action of CBZ, use-dependent block of voltage-dependent Na⁺ channels, is completely lost in CBZ-resistant patients.

EEG IN PANAYIOTOPOULOS SYNDROME

The sequential changes in localization of EEG foci with age, and the relation between the clinical manifestations and EEG pattern in Panayiotopoulos syndrome (PS) were analyzed in a study of 76 children (37 boys and 39 girls) followed for >2 years at Tokyo Woman's Medical University, Japan. PS syndrome (early-onset benign occipital seizure susceptibility syndrome) is characterized by the following: onset of epilepsy between ages 1 and 8 years; attacks of ictal vomiting and eye deviations, with or without secondary generalization; normal development before seizure onset; normal neuroimaging; occipital EEG foci, at times shifting to centrottemporal or frontal regions with age; and remission before age 12 years. In this study, the EEG findings were excluded from the criteria for inclusion. A history of febrile convulsions was recorded in 33 (43.4%) patients, and a family history of seizure disorder in 21 (27.6%). The age at onset of epilepsy ranged from 14 to 118 months (average 48 months). Seizures recurred from 0 to 139 months (median 70 months); the total number in each case was 1 to 27 (mean 4.8). Status epilepticus occurred in 45 (61.6%) cases.

The EEG occipital spike focus (12 cases) was seen most frequently at 2 to 5 years of age; independent and synchronous frontopolar and occipital spikes (Fp-O spikes) (14 cases) at 4 to 7 years; and centroparietotemporal (CPT) spike foci (21 cases) at 6 to 10 years. EEG foci showed frequent shifting, multiplications, and generalization with age. The Fp-O group showed the latest age at onset of epilepsy. The generalized EEG pattern (19 cases) had the highest frequency of seizures and status epilepticus, and the longest active seizure period. The prognosis was favorable regardless of the EEG pattern. (Ohtsu M, Oguni H, Hayashi K, et al. EEG in children with early-onset benign occipital seizure susceptibility syndrome: Panayiotopoulos syndrome. *Epilepsia* 2003;44:435-442). (Reprints: Dr H Oguni, Department of Pediatrics, Tokyo Woman's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162, Japan).

COMMENT. EEG foci in Panayiotopoulos (PS) syndrome do not persistently localize to occipital regions but tend to shift location, multiply, and become generalized with age. The various EEG patterns tend to appear at different ages and to be associated with certain clinical characteristics. For example, the generalized EEG pattern group has the highest frequency of seizures, status epilepticus (SE), and longest active