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### J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

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## SEIZURE DISORDERS

## EPILEPSY TWIN STUDIES BY LENNOX COMPARED TO MODERN SERIES AND SYNDROME CLASSIFICATION

Lennox's original files of twins with seizures from 1934 through 1958 were reviewed, and the International League Against Epilepsy (ILAE) classifications of seizures and epileptic syndromes were applied to 143 (71 monozygous [MZ], 72 dizygous [72]) twin pairs, in a study at the University of Melbourne, Australia; the Montreal Neurological Institute, Canada; Harvard Medical School, and Beth Israel Medical Center, Boston, USA. The Lennox data that included personal records and EEGs allowed classification of 75% of cases according to contemporary ILAE epilepsies and epileptic syndromes. "Petit mal" corresponded to the contemporary absence seizures, and "psychomotor seizures" equated with simple and complex partial terminology. For MZ and DZ twin pairs, concordance for seizures was 59% and 14%, respectively. Casewise concordance estimates for MZ and DZ twin pairs showed a strong genetic influence in idiopathic generalized epilepsies. High MZ concordances also supported a genetic etiology in symptomatic generalized epilepsies and febrile seizures. In the Lennox data 86% of MZ twin pairs and 60% of DZ twin pairs were concordant for both seizures and epilepsy syndromes. The Australian data showed 94% of MZ and 71% of DZ twin pairs were concordant for epilepsy syndromes. Also, a genetic contribution to partial epilepsy was evident although weaker than that for generalized epilepsies. (Vadlamudi L, Andermann E, Lombroso CT et al. Epilepsy in twins. Insights from unique historical data of William Lennox. **Neurology** April (1 of 2) 2004;62:1127-1133). (Reprints: Professor Samuel F Berkovic, Epilepsy Research Centre, First Floor, Neurosciences Building, Repatriation Campus, Austin Health, Banksia Street, Heidelberg West, Victoria, Australia 3081).

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COMMENT. Despite the differences in epilepsy terminology, the earlier Lennox and recent Australian twin studies provide similar and valuable evidence of a genetic basis for generalized epilepsies and febrile seizures and further support the concept of specific genes for epilepsy syndromes. A genetic factor in symptomatic generalized epilepsies demonstrated in the twin studies is also apparent in a current Japanese study of family history rates of epilepsy and consanguinity. (Wakamoto H et al. **Brain Dev** 2004;26:184-189). In 311 probands with childhood-onset epilepsy, a family history of epilepsy (within second-degree relatives) occurred in 19% and consanguinity (within first-degree relatives) in 6%. A positive family history was more common with generalized than localization-related epilepsies, and more common with idiopathic/cryptogenic epilepsy than symptomatic epilepsy. However, the data suggest that a genetic susceptibility could play a role in the etiology of pre- or perinatal symptomatic generalized epilepsy and in postnatal symptomatic localization-related epilepsy. Also, a genetic factor through consanguinity may influence the etiology of idiopathic/cryptogenic and symptomatic generalized epilepsies.

## SCN2A MUTATIONS AND BENIGN FAMILIAL NEONATAL-INFANTILE SEIZURES

*SCN2A* sodium channel gene was analyzed in 2 families with probable benign familial neonatal-infantile seizures (BFNISs), 9 with possible BFNIS, 10 with benign familial infantile seizures, and in 93 additional families with various early childhood epilepsies, in a study at the University of Melbourne, Australia, and other international centers. Six different SCN2A mutations were found in 8 families and 56 affected individuals with BFNIS, and in no other family in the study. BFNIS is an autosomal dominant disorder that presents from day 2 to 7 months of age (mean, 11.2 +/- 9.2 weeks) with afebrile secondarily generalized partial seizures of varying frequency, from a few to clusters of many per day. Seizures completely remit by 12 months of age, with no recurrences in later childhood or adolescence. Interictal EEGs in the active phase were either normal or showed focal epileptiform discharges in posterior or central regions. Brain imaging was normal in 8 cases; one patient had a choroid plexus papilloma. SCN2A mutations are specific for BFNIS. (Berkovic SF, Heron SE, Giordano L, et al. Benign familial neonatal-infantile seizures: Characterization of a new sodium channelopathy. **Ann Neurol** April 2004;55:550-557). (Respond: Dr Berkovic, Epilepsy Research Centre, Neurosciences Building, Repatriation Campus, Heidelberg West, Victoria 3081, Australia).

COMMENT. Benign familial neonatal-infantile seizure disorder (BFNIS) with onset around 3 months is an intermediate variant of autosomal dominant benign epilepsies in the first year. Benign familial neonatal seizures (BFNS) begin around day 3 and benign familial infantile seizures (BFIS) begin around 6 months. BFNIS has now been linked to mutations in the sodium channel gene SCN2A (Heron et al, 2002; Berkovic 2004), BFNS is caused by defects in potassium channel genes KCNQ2 and KCNQ3 (Singh et al, 1998), and BFIS in one family is associated with a mutation in the ATP1A2 gene (Vanmolkot et al, 2003). BFNIS has characteristic clinical manifestations that allow early diagnosis and an excellent prognosis.

A total of 13 genes have been identified in human idiopathic epilepsies since 1995 (Steinlein OK. Genes and mutations in human idiopathic epilepsy. **Brain Dev** June