NMDAR ANTIBODIES AND NEW-ONSET EPILEPSY

The frequency and significance of antibodies to NMDAR were determined in 19 adolescents and young women, aged 15 to 45 years, with unexplained new-onset epilepsies, seen between Jan 2005 and June 2007 at the University of Bonn, Germany; Univ of Pennsylvania, Philadelphia; and John Radcliffe Hospital, Oxford, UK. Five (25%) patients had anti-NMDAR antibodies, and all 5 had a history of psychiatric symptoms, pleocytosis, seizures, and relapsing-remitting course. All recovered, either spontaneously or following corticosteroid or intravenous immunoglobulin treatment. Only 1 patient had a neoplasm (multiple neuroendocrine tumors including the ovaries). In a control series of 61 patients with other cryptogenic epilepsies and 11 surgically treated patients with epilepsy, one, a 22-year-old man, was NMDAR antibody positive and he had recovered from a severe encephalopathy. (Niehusmann P, Dalmau J, Rudlowski C, et al. Diagnostic value of N-methyl-D-aspartate receptor antibodies in women with new-onset epilepsy. **Arch Neurol** April 2009;66:458-464). (Respond: Christian G Bien MD, Department of Epileptology, University of Bonn, Sigmund-Freud-Str 25, 53105 Bonn, Germany.
E-mail:christian.bien@ukb.uni-bonn.de).

COMMENT. A significant proportion of unexplained new-onset epilepsies in adolescents and young women may be caused by anti-NMDAR encephalitis. Seizures are a common symptom in patients with anti-NMDAR encephalitis, reported in 76 of 100 cases (Dalmau J et al. 2008).

SEIZURE DISORDERS

LONG-TERM OUTCOME IN CHILDHOOD-ONSET EPILEPSY

The value of early seizure frequency and etiology in the prediction of long-term seizure and mortality outcome in a population-based cohort of 102 children was determined in a study at University of Turku, Finland, and Epilepsy Research Group, Berlin, Germany. Follow-up was a median of 40 years after the first seizure before the age of 16 years. One-year remission (1YR) had occurred in 95 (93%) of the group, and 7 (7%) never experienced a 1YR, their epilepsy considered drug-resistant. Patients with weekly seizures in the first year of treatment had a 8-fold risk of developing drug resistant epilepsy (P=0.0125), and a 2-fold risk of never entering a terminal 1YR (P=0.001). Weekly seizures prior to treatment carried a slight risk of never entering terminal 1YR (P=0.035). Mortality during follow-up was 13%, and long-term mortality was 9-fold higher for patients with symptomatic epilepsy (P=0.0071). Weekly seizures prior to or during the first year of treatment did not increase mortality. Virtually all (51/52, 98%) children with low seizure frequency and non-symptomatic etiology entered 1YR during 40 years follow-up, and almost all (49/52, 94%) entered 1-year terminal remission. A combination of frequent pretreatment seizures and symptomatic etiology is predictive of intractable epilepsy. (Sillanpaa M, Schmidt D. Early seizure frequency and aetiology predict long-term medical outcome in childhood-onset

epilepsy. **Brain** April 2009;132:989-998). (Respond: Prof Dr Dieter Schmidt, Epilepsy Research Group, Goethestr 5, D-14163 Berlin, Germany. E-mail: dbschmidt@t-online.de).

COMMENT. The long-term outcome of epilepsy in children may be predicted after one year of treatment. Patients with frequent seizures in the first year of treatment, especially those with symptomatic epilepsy, are at increased risk of intractable epilepsy, and should be considered for aggressive therapy.

INFLUENCE OF *SCN1A* GENE MUTATION ON AGE OF ONSET OF FEBRILE SEIZURES IN GEFS+

Twelve multigenerational families with the generalized epilepsy and febrile seizure plus (GEFS+) syndrome and a known clinically relevant epilepsy gene mutation were examined for age of onset of febrile seizures (FS or FS+), in a study at the University of Melbourne, Australia, and centers in the Netherlands and Israel. A total of 105 patients were identified with *SCN1A, SCN1B, or GABRG2* gene mutations. Sixty-two patients presented with a FS; 43 were excluded because the FS was atypical or age of onset was imprecise. The median age of onset of FS was 12 months in subjects with *SCN1A* and *GABRG2* mutations, and 24 months in those with *SCN1B* mutation. The median age of onset in children with an *SCN1A* mutation was significantly lower than for children with an *SCN1B* mutation ($p=0.001$). Age of onset of FS was not significantly different in children with *SCN1A* and *GABRG2* mutations. In 10 families reported in the literature that had mutations available, the findings were similar to the above; median age of onset of FS in patients with *SCN1A* mutations was 11 months compared to 30 months in those with *SCN1B* mutations ($p=0.033$). In patients with GABRG2 mutations, age of onset was 18 months. With all families combined, the median age of onset in those with *SCN1A* and *B* mutations was 12 months and 24 months, respectively ($p<0.001$); in those with *GABRG2* mutations it was 13 months and similar to *SCN1A* group. (Sijben AEJ, Sithinamsuwan P, Radhakrishnan A, et al. Does a *SCN1A* gene mutation confer earlier age of onset of febrile seizures in GEFS+? **Epilepsia** April 2009;50:953-956). (Respond: Prof Ingrid E Scheffer, Director of Paediatrics, Austin Health, Neurosciences, Heidelberg, Victoria 3081, Australia.
E-mail:scheffer@unimelb.edu.au).

COMMENT. The age of onset of febrile seizures is partly dependent on the underlying gene mutation involved. In two independent cohorts of subjects with FS or FS+ and *SCN1A* mutations, the median age of onset was 11-12 months compared with a population median of 18 months. The proceedings of an international symposium on febrile seizures and related conditions, edited by Fukuyama Y et al, are published in **Brain Dev** May 2009;31(5):331-404). Nakayama J reviews the search for FS susceptibility genes in **Brain Dev** 2009;31(5):359-365).

The phenotypic similarities of GEFS+ and autosomal dominant FS (ADFS) are reported in a multigenerational family with febrile and afebrile seizures (Hindocha N et al. **Epilepsia** April 2009;50:937-942). The two mutations identified in families with ADFS are in genes implicated in GEFS+ (*SCN1A* and *GABRG2*). The authors conclude that it is inappropriate to separate GEFS+ and ADFS, given the clinical and genotypic overlap.