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showed well-organized background activity; paroxysmal abnormalities disappeared. This inborn biotinidase deficiency is one of the first treatable neurometabolic diseases in children.

Thursday, September 5, 1996

Parallel Session 3: Principles of Treatment

9:30 a.m. to 12:00 noon

High-Dose Gabapentin is Absorbed and Can Be Effective. E. A. Wilson, G. Forrest, and M. J. Brodie (Epilepsy Research Unit, Western Infirmary, Glasgow, Scotland).

Oral absorption of gabapentin (GBP) has been suggested to begin to saturate at >1,800-mg daily doses. Patients with refractory epilepsy, in whom GBP was introduced, were started on 400 mg daily for the first week of treatment, with further increments of 400 mg until seizures were controlled or to the limit of tolerability. All patients had three-times-daily regimens. When possible, concomitant antiepileptic drug (AED) therapy was reduced. Plasma GBP levels were measured by high-performance liquid chromatography at the same time after dosing after every increment of 1,200 mg daily. Mean circulating GBP concentrations (mg/L) at each dose level were as follows: 1,200 mg, 4.1; 2,400 mg, 8.6; 3,600 mg, 13.2; 4,800 mg, 15.5; and 6,000 mg, 17.2. In 3 patients receiving GBP in $\leq 6,000$ -mg doses daily, concentrations continued to increase at each increment. However, the curves were not completely linear, indicating some reduction in relative bioavailability at high dosage. So far, 8 patients receiving 2,400–6,000 mg GBP daily have shown improvement in seizure control >50%, with 2 becoming seizure-free. Their plasma GBP concentrations varied from 5.9 to 21.0 mg/L. Side effects most commonly reported included tiredness, dizziness, headache, and diplopia. Some patients developed flatulence and diarrhea, and a few others myoclonic jerks at GBP >3,600 mg/day. These problems responded rapidly to dosage reduction. High-dose GBP is absorbed and can be effective in controlling seizures in patients with refractory epilepsy.

Use of Intravenous Gammaglobulin in Drug-Resistant Epilepsy. P. Tyomin, V. Perminov, A. Krapivkin, B. Belousova, and A. Ermakov (Institute of Pediatrics, Moscow, Russia).

Eight children aged 8 months to 6 years with resistant forms of epilepsy [Lennox-Gastaut syndrome (LGS), infantile spasms (IS)] and adequate anticonvulsant therapy received intravenous injections of Sandoglobulin (Sandoz). The course consisted of three injections (on days 1, 15, and 36 of therapy); the single dose varied from 200 to 400 mg/kg per injection.

Improvement was noted in all 8 patients (100%), 5 children had complete seizure control, (62, 5%), and duration of remission was 3–10 months. During the control period (3–10 months), we observed no seizures recurrence in these children. Three patients (37.5%) had 50% reduction in number of seizures; this reduction was stable throughout the same control period. We noted no adverse reactions due to Sandoglobulin. Sandoglobulin treatment did not cause changes in immune status. The positive anticonvulsant effect observed in our study confirms the possibility of use of Sandoglobulin in drug-resistant epilepsy.

Effects of Chronic Diazepam on Absence-Like Phenomena and on the EEG on the WAG/Rij Rat. Clementina M. Van Rijn, Marijtje L. A. Jongsma, Peter M. Edelbroek, and Ris Dirksen (Departments of Psychology/NICI and Anaesthesiology, University of Nijmegen, The Netherlands).

We evaluated the effects of chronic diazepam (DZP) treatment for 21 days on spike-wave discharges (SWD) and on the spectral

content of the EEG of the WAG/Rij rat; a model for absence epilepsy. Permeable silastic tubes either empty or filled with DZP were implanted subcutaneously. The dose the animals received was ~50 mg/kg/day, resulting in sustained constant blood concentrations. EEGs were recorded before implantation, during treatment, and 9 days after tube removal.

DZP reduced both the incidence and the duration of SWD. The magnitude of these effects decayed during the treatment: The incidence of the SWDs increased again with a half-life ($t_{1/2}$) of 3 days; baseline values were not reached, however. The mean duration increased slowly with a $t_{1/2}$ of ~20 days. The posttreatment measurement showed no group differences. DZP caused an increase in the power of the high-frequency band (21–40 Hz). This change persisted during the 21-day treatment and was no longer evident on the ninth day after tube removal.

The results show tolerance development to the antiabsence effect of DZP, but different $t_{1/2}$ values for different parameters. No tolerance developed to the effect of DZP on the spectral content of the EEG. These observations suggest that different molecular mechanisms underlie the genesis and the termination of the epileptic phenomena and that the incidence and the duration of the SWD are independent of changes in the spectral content of the EEG.

Behavior Seizure Control: Biofeedback and Behavior Therapy of Partial Epilepsy. Carmen Uhlmann, N. Birbaumer, and W. Fröscher (Zentrum für Psychiatrie, Abteilung, Neurologie, Ravensburg, Germany).

In patients with partial seizures, drug resistance unfortunately is common. One possible strategy to help patients may be clinical-psychological treatment. Birbaumer et al. (1991) successfully treated patients with epilepsy, mostly with complex partial seizures, with biofeedback of slow cortical potentials. In a multicenter study, we wish to verify the results of this first study in a greater number of patients and to determine the patients in whom the biofeedback method is most promising. Drug resistance was defined as ineffectiveness of two standard antiepileptic drugs administered as mono- or combination therapy in 2 years.

In our center, 10 patients were recruited in the past year, with 5 in the slow-wave group and 5 in the control group. The verum group is treated with slow-wave biofeedback and behavioral modification elements. The controls receive breathing biofeedback (percentage of end tidal- CO_2 and respiration rate) and behavior therapy. All patients are treated for 3 months.

The study design and treatment elements are presented, and preliminary results of biofeedback acquisition and changes in seizure frequency (in both groups) in ≤ 1 -year follow-up are reported. The results are encouraging in some patients. (Supported by Deutsche Forschungsgemeinschaft Fr 645/3-1.)

Assessment of Antiepileptic Drug Interaction by Ictal Behavior Analysis. O. E. Della Paschoa, R. Hamstra, R. A. Voskuyl, M. R. Kruk, and M. Danhof (Division of Pharmacology, Leiden/Amsterdam Center for Drug Research, Leiden, The Netherlands).

Reports on pharmacodynamic antiepileptic drug (AED) interaction in vivo are scarce and conflicting. The current approaches for the assessment of anticonvulsant effect are not focused on the exact discrimination of drug action on the clinical patterns of seizure activity. Recently, quantitative behavioral analysis was shown to be a useful tool for the characterization of ictal and postictal seizure components in the cortical stimulation model. We applied this approach to identify drug-induced changes in the pattern of overt motor seizure, characterizing the interaction between phenytoin (PHT) and valproate (VPA) by ictal behavior analysis, in parallel with determination of the concentration-anticonvulsant effect profile. Eighteen male Wistar-derived rats were allocated to three groups according to a parallel-group de-