addition to subtle seizures, but not generalized tonic-clonic seizures, the type expected to result in brain injury.

Subtle seizures described as "breast-stroke swimming movements" were previously reported in studies of seizure patterns in newborn animals (Millichap JG. **Proc Soc Exp Biol and Med** 1957;96:125-129). Transient opisthotonus, tremors, and clonic movements were also characteristic of newborn seizure patterns, but in rats aged 1 to 15 days subjected to graded electroshock, a generalized tonic clonic seizure could not be elicited. Failure to induce convulsions in the newborn rat was associated with a low level of carbonic anhydrase in the brain. The maximal seizure pattern was correlated with increasing age and the higher maturational levels of carbonic anhydrase in the brain of older animals. Observation of the newborn seizure pattern in addition to seizure frequency and EEG discharges might permit closer correlation with severity of HIE and outcome. If neonatal seizures do contribute to HIE brain injury, inhibition of the development of brain carbonic anhydrase would be expected to lessen the severity of neonatal seizures and result in improved neurodevelopmental outcome. Detailed EEG monitoring is essential for confirmation of diagnosis of neonatal seizures, especially subtle seizures.

DEVELOPMENTAL CORRELATES OF MICROCEPHALY

Developmental and motor function at age 2 years of 958 children born before the 28th week of gestation were assessed at Boston and Harvard Universities and other centers, comparing those with microcephaly at birth or 2 years with children with normal head circumference. A total of 11% of infants in the sample had microcephaly at 2 years. Microcephaly at 2 years, but not at birth, was predictive of severe motor and cognitive impairments at 2 years. Of children with congenital microcephaly, 71% had normal head circumference at 2 years and similar neurodevelopmental outcomes to those with normal head circumference at birth and 2 years. Among children with microcephaly at 2 years, more than half had a Mental Developmental Index <70, and almost a third had cerebral palsy, rates 3 times greater than among children without microcephaly. Neonatal cranial ultrasound showing white matter damage increased risk of poor neurodevelopmental outcome. (Kuban KCK, Allred EN, O'Shea TM, et al. Developmental correlates of head circumference at birth and two years in a cohort of extremely low gestational age newborns. **J Pediatr** Sept 2009;155:344-349). (Response: Karl Kuban MD, SMEpi, One Boston Medical Center Place, Dowling 3 South, Boston, MA 02118. E-mail: karl.kuban@bmc.org).

COMMENT. Extremely low gestational age newborns (in the ELGANs epidemiological study) are at risk of neurodevelopmental dysfunction and autism (Kuban K. **J Pediatr** 2009;154:535-540). Microcephaly at 2 years, but not at birth, is associated with cognitive and motor impairment at age 2. Almost three-fourths of ELGANs with congenital microcephaly outgrow the problem by age 2 years. Congenital microcephaly is only a risk factor for CP or cognitive impairment if the microcephaly persists.

CAUSES OF NEONATAL HYPOGLYCEMIC BRAIN INJURY

Perinatal factors associated with hypoglycemic brain injury were studied by review of medical records in 60 hypoglycemic neonates at Tottori University, Yonago, Japan. Patients

were classified in 2 groups: Group I, 12 patients, abnormal, with mental retardation, developmental delay, cerebral palsy or epilepsy; and Group II, 48 patients, normal at follow-up. Proportion of infants small for gestational age (<10th percentile) was high in both groups (75% vs 58%) but was not associated with brain injury. Very low blood glucose levels (<15 mg/dl) occurred in 50% of Group I vs 14.6% of Group II (p=0.015). Duration of hypoglycemia was longer in Group I (median, 14 h) than in Group II (median, 1.75 h) (p<0.001). Associated factors more frequent in Group I than in Group II included toxemia (33.3% vs 8.3%, p=0.043), fetal distress (58.3% vs 14.5%, p=0.004), Apgar score <5 at 1 min (33.5% and 6.4%, p=0.025), neonatal seizures (53.8% vs 4.3%, p<0.001), and pathological jaundice (41.7% vs 6.4%, p=0.006). Eight of 9 patients in Group I had abnormal MRI at follow-up, showing cortical atrophy and white matter lesions, with occipital and parietal predominance. Apgar scores were partially correlated with the extent of brain lesions. Brain injury in neonates with prolonged hypoglycemia may be exacerbated by associated factors such as hypoxia, seizures, and jaundice. (Montassir H, Maegaki Y, Ogura K, et al. Associated factors in neonatal hypoglycemic brain injury. **Brain Dev** October 2009;31:649-656). (Respond: Dr Hesham Montassir, Tottori University, Yonago, Japan. E-mail: hishammontassir@gmail.com).

COMMENT. Neonatal seizures with hypoglycemia are correlated with duration of hypoglycemia and neurological outcome. Seizures may begin at onset of hypoglycemia but usually appear after 12 h of continuous hypoglycemia. (Pildes RS et al. A prospective controlled study of neonatal hypoglycemia. **Pediatrics** 1974;54:5-14).

Of 27 infants and children with seizures associated with hypoglycemia reported from the Mayo Clinic, only 2 had an onset of seizures in the neonatal period, and in 20 the etiology of hypoglycemia was unknown. Neurologic disease preceded the onset of symptoms in 50% of the 20 patients with cryptogenic hypoglycemia. Evidence for a primary neurological cause for seizures included birth injury, kernicterus, hydrocephalus, and cerebral dysgenesis. Level of blood sugar at time of seizure in patients with primary neurologic disorder was significantly lower than in patients with normal neurologic findings. Occurrence of seizures was not closely correlated with the level of blood sugar. A primary cerebral lesion should be considered as an etiologic factor in some neonatal and childhood hypoglycemic seizures. (Etheridge JE Jr, Millichap JG. Hypoglycemia and seizures in childhood. Etiologic significance of primary cerebral lesions. **Neurology** 1964;14:397-404).

SEIZURE DISORDERS

BRAIN SODIUM CHANNEL AND FEBRILE SEIZURE MECHANISM

Researchers at the University of Melbourne, Australia, measured the effect of temperature on brain sodium channel, $Na_v1.2$, properties, using a computer model of the dentate gyrus granule cell. In animal models thermogenic seizures are hippocampal in origin (Dube C et al. 2000). The voltage dependance of activation became 7.6mV more negative when the temperature was increased from 37C to 41C. The direct effect of heat caused an increase in gating rates of sodium ion channels and a more negative activation with increased neuronal excitability. This dramatic increase in excitability due to increased temperature may be an important factor in the mechanism of a febrile seizure. (Thomas EA, Hawkins RJ,