

## SEIZURE DISORDERS

### SEX HORMONES AND PROGNOSIS OF NEONATAL SEIZURES

The influence of testosterone on the development of the substantia nigra pars reticulata (SNR), a brain region involved in the control of seizures, was investigated in male rats castrated at birth, in experiments at Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY. Neonatal castration alters the maturation of the muscimol (GABA-A)-sensitive SNR effect on seizures. Microinfusions of muscimol in the SNR in neonatal rats castrated at 15 days postnatally (PN15) had no effect on seizures, irrespective of the infusion site within the SNR. In PN25 and 30 neonatally castrated rats, muscimol infusions had an anticonvulsant effect when injected into the SNR anterior but not posterior locations. The expression of a proconvulsant region in the SNR occurs only in the presence of testosterone in the immediate postnatal period. The development of the proconvulsant region at PN15 is triggered by restoring testosterone levels in neonatally castrated rats or by artificially increasing testosterone levels in females. The demonstration of sex-related differences in the SNR points to postnatal testosterone as a critical factor in the development of pro- or anticonvulsant circuits in the developing brain. (Veliskova J, Claudio OI, Galanopoulou AS et al. Seizures in the developing brain. *Epilepsia* December 2004;45 (Suppl 8):6-12). (Reprints: Dr J Veliskova, Department of Neurology, K312, Albert Einstein College of Medicine, 1410 Pelham Parkway South, Bronx, NY 10461).

COMMENT. A research agenda for epilepsy, developed by the NINDB, included proposals regarding the maturation of the brain and hormonal status. The above studies address the issues raised by the NINDB/White House conference held in March 2000.

**Effects of seizures and their treatment on fetal brain** are reviewed by LaJoie J and Moshe SL. (*Epilepsia* December 2004;45(Suppl 8):48-52). Generalized tonic-clonic seizures can have adverse effects on the fetus, but the effect of complex partial or absence seizures is unclear. AEDs have potentially adverse effects on the fetus and its subsequent development, and monotherapy is encouraged. Despite potential risks of adverse effects of seizures and AEDs on the fetus during pregnancy, most epileptic women have normal, healthy children.

**Prognosis of neonatal seizures** is reviewed by Verrotti A et al. (*J Pediatr Neurol* December 2004;2:191-197). Well-organized major seizures may be associated with a relatively favorable outcome whereas subtle neonatal seizures are more commonly encountered in infants with cerebral dysfunction (Lombroso, 1983). Prolonged seizures are associated with a poor outcome; tonic seizures occur in infants with cerebral palsy, mental retardation, and epilepsy, whereas myoclonic seizures are correlated only with mental retardation (Gururaj et al, 2003). The etiology of seizures is the most important factor in determining outcome: poor prognosis is associated with malformations and hypoxic-ischemic lesions, while a favorable outcome is expected with neonatal seizures caused by subarachnoid hemorrhage and hypocalcemia. In long-term follow-up studies, children who recovered from neonatal seizures with an early favorable outcome were found to have spelling, arithmetic, and memory problems, despite normal IQ, as teenagers. Post-neonatal seizures and abnormal interictal EEG are important predictors of adverse outcome.