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SEIZURE DISORDERS

EPILEPSY AND BEHAVIOR

Investigators at Georgia Regents University, Augusta, GA, and multiple centers (25) in the USA and UK, studied the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD Study) in 195 children of pregnant women with epilepsy who had received AED monotherapy (carbamazepine, lamotrigine, phenytoin, or valproate) from 1999 to 2004. Epilepsy was localization-related in 59%, idiopathic generalized in 31%, and GTCS in 10%. Adaptive and emotional/behavioral functioning at 6 years of age were evaluated by parental and teacher completion of Adaptive Behavior Assessment System (ABAS-II) and Behavior Assessment System for Children (BASC). BASC clinical symptoms included hyperactivity, conduct, anxiety, depression, withdrawal, and attention disorders.

Adjusted mean scores for the four AED groups were in the low average to average range for parent rating of ABAS-II and for parent and teacher ratings of BASC. Children of mothers taking valproate during pregnancy had significantly lower General Adaptive Composite scores than the lamotrigine and phenytoin groups. The significant decline in performance was dose related for both valproate and phenytoin. Children exposed to fetal valproate exhibited significantly more atypical behaviors and inattention than those in the lamotrigine and phenytoin groups. BASC parent and teacher ratings of attention span and hyperactivity showed that children of mothers who took valproate during pregnancy had a significantly greater risk of a diagnosis of ADHD by age 6 years. (Cohen MJ, Meador KJ, et al. Fetal antiepileptic drug exposure: Adaptive and emotional/behavioral functioning at age 6 years. **Epilepsy Behav** 2013 Nov;29:308-315).

COMMENTARY. Cohen and associates [1] examine the behavioral effects of prenatal AED exposure, and especially valproate, on adaptive and behavioral functioning of children at age 6 years. In the NEAD prospective study of children at 3 years of age,

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fetal valproate exposure was shown to significantly impair cognitive function [2], and verbal and nonverbal abilities [3]. At the completion of the study, six-year cognitive outcome of valproate fetal-exposed children continued to exhibit significantly lower IQ than those exposed to other AEDs examined [4].

Adverse outcomes in children born to mothers with epilepsy may be caused by AEDs, maternal epilepsy, socioeconomic or genetic factors, maternal cigarette smoking, alcohol consumption, folate deficiency, or may occur by chance. Even after adjustments for these potential confounders, a follow-up study of a Danish National Birth Cohort found that preschool children exposed prenatally to AEDs had a behavioral disorder [5]; 133 children (age 4-5 years) whose mothers had received AEDs were compared to 304 unexposed and 1193 whose mothers did not have epilepsy.

References

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3. Meador KJ, et al. Brain. 2011 Feb;134(Pt 2):396-404.
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EPILEPSY AND FINE MOTOR FUNCTION

Investigators at Kocaeli University, Pediatric Neurology OP Clinic, Turkey, studied the relationship between fine motor skills and seizure and treatment parameters in 44 children with rolandic epilepsy (RE) and compared to 44 healthy controls. The children were aged 8 to 14 years, mean age 10 years, 64% males and 36% females, matched in age, gender and level of education in each group. WISC-R total scores were normal in both groups but the mean score in the RE group was lower than controls ($p<0.006$). Fine motor skills as measured by the Purdue Pegboard Test (PPT) were lower in the RE group than in controls. Epileptic focus, treatment, type of treatment, age at onset of seizures, time since last seizure, and total number of seizures did not affect motor skills. RE negatively affected fine motor skills regardless of level of IQ. (Ayaz M, Kara B, Soylu N, Ayaz AB. Fine motor skills in children with rolandic epilepsy**. Epilepsy Behav** 2013 Nov;29(2):322-5).

COMMENTARY. Although RE is regarded as a benign disorder, several reports emphasize development of cognitive, behavioral and psychiatric disorders during the active seizure phase, sometimes persisting after the epilepsy remits [1]. Early seizures in RE may interfere with brain development, causing deficits in executive function despite a normal IQ. Cognitive and behavioral abnormalities may outlast the RE [2].

Month to month fluctuations in cognitive abilities and the frequency and lateralization of interictal EEG spikes are reported, potentially impacting academic performance [3]. Clinical seizure remission was achieved 4-5 years earlier than the recovery of cognitive function. No significant correlations were found between lateralization of EEG changes and the character of the cognitive dysfunction, although age-related lateralization of focal epileptiform activity was present [4]. One study suggests that valproate, ethosuximide or levetiracetam is effective in treatment of transitory cognitive disorders [4] whereas one other found that medication and duration