

cognitive functions involved in goal-directed behavior are impaired, including inhibition, planning, set-shifting, working memory, and fluency, and reflect a dysfunction of fronto-subcortical pathways. The neuropsychological deficits in ADHD are heterogeneous. Although the majority of ADHD children have a deficit on at least one EF measure, the same is true for nearly half a control group (Nigg JT et al, 2005). Different populations of children with neuro-developmental disorders have deficits in EF similar to those found in children with ADHD (Sergeant JA et al, 2002). The EF deficits with ADHD are nonspecific and not diagnostic. In the Multimodal Treatment Study of Children with ADHD, a 14-month trial of treatment strategies (1999), 40% of the sample (n=579) had a comorbid ODD that could modulate or interact with the intellectual and executive profile. The role of IQ in prognosis of ADHD alluded to in this review is well known. Risk factors for a poor prognosis include a low average or borderline IQ, and comorbid oppositional and conduct disorders.

ATTENTION DEFICITS FOLLOWING ADEM RELIEVED BY GUANFACINE

Neuroscientists at the Institute of Cognitive Neuroscience, London, UK report the case of a 38-year-old male with severe deficits in arousal and sustained attention, associated with hemispatial neglect, secondary to acute disseminated encephalomyelitis. Treatment with the noradrenergic agonist guanfacine was associated with significant improvements in both sustained attention and spatial neglect. Presenting with a right hemiparesis following a prodrome of headache and fever, he developed tonic-clonic seizures soon after admission. MRI revealed signal changes in the thalamus, cerebellum, and temporal and occipital lobes. CSF was normal, and EEG was consistent with encephalopathy and ADEM. Following courses of iv methylprednisolone, immunoglobulin, plasma exchange and antibiotics, seizures at first refractory to AEDs were stabilized after 4 months. Neuropsychological testing revealed severe cognitive impairments and left-sided neglect. At a 2-year follow-up, he had persistent left hemiparesis with severe left hemispatial neglect, and impairments in sustained attention and arousal. MRI showed lesions localized to the right thalamus and pulvinar, areas linked to the mechanism of neglect. This is the first demonstration of a persistent amelioration of spatial neglect following treatment with guanfacine. General level of alertness and arousal also improved. (Singh-Curry V, Malhotra P, Farmer SF, Husain M. Attention deficits following ADEM ameliorated by guanfacine. *J Neurol Neurosurg Psychiatry* June 2011;82:688-690). (Response: Professor Masud Husain, Institute of Cognitive Neuroscience, 17 Queen Square, London WC1N 3AR, UK. E-mail: m.husain@ion.ucl.ac.uk).

COMMENT. Impairments of arousal or maintained alertness are considered a component of the neglect syndrome, and arousal is dependent on noradrenergic input, responsive to guanfacine. Guanfacine, as a sustained release formulation, Intuniv, is effective in the treatment of ADHD (Biederman J et al. *Pediatrics* 2008;121:E73-84).

Hemispatial neglect is usually reported following stroke involving the medial thalamus and pulvinar in the right hemisphere. ADEM is a rare cause of neglect but is associated with impaired arousal and sustained attention, components of the neglect

syndrome. A study comparing cognitive profiles of children aged 7-16 years with MS (n=9) to those with ADEM (n=9) found impairments across all cognitive domains with differences in severity and spread. The transient white matter disruption in ADEM results in subtle cognitive impairments, while the multiple white matter insults in childhood MS are associated with more severe cognitive sequelae (Deery B et al. *Dev Neuropsychol* 2010;35(5):506-521).

CONGENITAL MALFORMATIONS

MAJOR BIRTH DEFECTS AND NEWER ANTIEPILEPTIC DRUGS

The association between fetal exposure to newer-generation antiepileptic drugs during the first trimester of pregnancy and the risk of major birth defects was studied by researchers at the Statens Serum Institut, Copenhagen, Denmark. Cases of birth defects diagnosed within the first year of life following fetal exposure to AEDs were identified through the National Patient Registry, Jan 1996 through March 2009. Dispensed AEDs to mothers were ascertained from nationwide registries. Of 1532 infants exposed to lamotrigine, oxcarbazepine, topiramate, gabapentin, or levetiracetam during the first trimester, 49 (3.2%) were diagnosed with a major birth defect compared to 2.4% of unexposed infants. The prevalence of major birth defects following exposure to individual AEDs was 3.7% following lamotrigine, 2.8% with oxcarbazepine, 4.6% with topiramate, 1.7% with gabapentin, and 0 following levetiracetam. First-trimester exposure to newer-generation AEDs compared to no exposure was not associated with an increased risk of major birth defects diagnosed in the first year of life. (Molgaard-Nielsen D, Hviid A. Newer-generation antiepileptic drugs and the risk of major birth defects. *JAMA* May 18, 2011;305(19):1996-2002). (Response: Ditte Molgaard-Nielsen, MSc, Artillerivej 5, 2300 Copenhagen 5, Denmark.. E-mail: dnl@ssi.dk).

COMMENT. The authors comment that unadjusted estimates did show a significant association between exposure to any newer AED or lamotrigine alone during the first trimester and risk of major birth defects. A significantly increased risk of eye defects was observed for lamotrigine, but only 4 infants were exposed and affected. After adjustment for older-generation AED use and epilepsy, no associations remained. Older-generation AEDs are associated with a 2- to 3-fold increased risk of major birth defects, and some of the mothers were treated with both older and newer generation AEDs. In this study, maternal epilepsy was associated with a moderately increased risk of birth defects and was regarded as a confounder. A meta-analysis shows that untreated women with epilepsy are not at increased risk of having infants with birth defects compared with healthy women (Fried S et al, 2004).

MALFORMATIONS AFTER FETAL EXPOSURE TO AED IN UTERO ASSESSED AT BIRTH AND 12 MONTHS LATER

Researchers at Universities of Melbourne and Queensland, Australia, compared the incidence and natures of fetal malformations (FMs) recognized at birth with those