Children with Epilepsy: Why Can't They Pay Attention?

The Frequency, Complications and Aetiology of ADHD in New Onset Paediatric Epilepsy. Hermann B, Jones J, Dabbs K, Allen CA, Sheth R, Fine J, McMillan A, Seidenberg M. *Brain* 2007;130(Pt 12):3135–3148. Recent studies suggest that Attention Deficit Hyperactivity Disorder (ADHD) is a common comorbid condition in childhood epilepsy, but little is known regarding the nature, frequency and timing of associated neurobehavioural/cognitive complications or the underlying aetiology of ADHD in epilepsy. This investigation examined: (i) the prevalence of ADHD and its subtypes; (ii) the association of ADHD with abnormalities in academic, neuropsychological, behavioural and psychiatric status and (iii) the aetiology of ADHD in paediatric epilepsy. Seventy-five children (age 8–18) with new/recent onset idiopathic epilepsy and 62 healthy controls underwent structured interview (K-SADS) to identify the presence and type of DSM-IV defined ADHD, neuropsychological assessment, quantitative MR volumetrics, characterization of parent observed executive function, review of academic/educational progress and assessment of risk factors during gestation and delivery. The results indicate that ADHD is significantly more prevalent in new onset epilepsy than healthy controls (31% vs 6%), characterized predominantly by the inattentive variant, with onset antedating the diagnosis of epilepsy in the majority of children. ADHD in childhood epilepsy is associated with significantly increased rates of school based remedial services for academic underachievement, neuropsychological consequences with prominent differences in executive function, and parent-reported dysexecutive behaviours. ADHD in paediatric epilepsy is neither associated with demographic or clinical epilepsy characteristics nor potential risk factors during gestation and birth. Quantitative MRI demonstrates that ADHD in epilepsy is associated with significantly increased gray matter in distributed regions of the frontal lobe and significantly smaller brainstem volume. Overall, ADHD is a prevalent comorbidity of new onset idiopathic epilepsy associated with a diversity of salient educational, cognitive, behavioural and social complications that antedate epilepsy onset in a significant proportion of cases, and appear related to neurodevelopmental abnormalities in brain structure.

COMMENTARY

Perhaps, the fact that the paper by Hermann et al. includes almost no references dated before 1995 is due to the constraints of a literature search by computer; however, the more likely cause is that serious attention paid to the psychosocial accompaniments of epilepsy began at about that time. Today, virtually all issues of epilepsy journals will include studies of psychiatric, cognitive, and social disorders that are overrepresented in populations with various types of epileptic disorders. Often these problems are described as "complications" of chronic epilepsy.

Yet, there is a growing body of observations suggesting that these other brain and behavioral disorders may not spring from the stresses and pathology related to chronic seizures but rather may be other symptoms of a common malady or maladies. In other words, a still unnamed disease or diseases may be manifested by a variety of symptoms and signs, including depression, attention deficit hyperactivity disorder (ADHD), a range of cognitive deficits, as well as seizures.

Hermann et al. have made a significant contribution to this field in their study of ADHD in children with recent onset of idiopathic epilepsy. The 75 children in this population were diagnosed with epilepsy within 12 months of entry into the study. These children, aged 8 to 18 years, superficially appeared to be completely healthy: normal neurological exam, normal MRI scan, no developmental disability, and no other neurological disorder. The control group consisted of age- and gender-matched first cousins.

Using careful parental interviewing, a broad range of neuropsychological testing, and quantitative MR volumetrics, investigators found that the apparently healthy children with idiopathic epilepsy had astonishingly high rates of abnormalities. Over 31% of them met DSM-IV diagnostic criteria for ADHD, compared with only 6.4% of the control group. Most of the children with ADHD (82%) had been symptomatic prior to their first seizure, ruling out medication or psychosocial stressors as etiological factors. In this study, the symptom profile of the epilepsy-associated ADHD seemed distinct from that seen in the general population, with the inattentive subtype predominating over the hyperactive or combined type.

Virtually all of the techniques used in the Hermann et al. study to characterize the children with epilepsy and ADHD point to the frontal lobe as the primary site of pathology. Neuropsychological testing as well as parental reports performed confirmed the high prevalence of symptoms and signs attributable to frontal lobe dysfunction in many of the children with epilepsy, but especially in those with ADHD. Neuropsychological test results included impairments in motor and psychomotor speed and in executive function. A parent-reported rating scale (Behavior Rating Inventory of Executive Function or BRIEF) revealed more abnormal scores in impulse control, attentional shifts, planning skills, executive function, and initiation of problem solving for those children with both epilepsy and ADHD. Finally, while MR volumetrics demonstrated that

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the epilepsy/ADHD group had significantly larger frontal lobes and smaller brainstem volumes, other brain areas showed no group differences, and interestingly, those children without ADHD showed no differences from the control group.

The educational histories of the children highlighted the clinical significance of these findings and showed them to be of more than theoretical interest. Of the children with epilepsy, over half of those with ADHD had already required a formal individual education plan (IEP) or other academic support services that frequently were begun before the first seizure occurred. Only 15% of the children with seizures but without ADHD needed such help.

The findings of Hermann et al. are important to the care of children without obvious features of symptomatic epilepsy, but with idiopathic epilepsy. How are such observations to be interpreted? After all, the 2001 International League Against Epilepsy (ILAE) classification proposal cited by the authors defines idiopathic epilepsy syndrome as one that is "only epilepsy, with no underlying structural brain lesion or other neurological signs or symptoms" (1). This definition is a moving target, since the same paper mentions other classification schemes for idiopathic epilepsy that would include "idiopathic focal epilepsies of infancy and childhood"—a definition that would embrace benign childhood epilepsy with centrotemporal spikes, for example. This syndrome has been shown to be accompanied by subtle attention and language deficits (2,3). Other "idiopathic" epilepsies such as childhood absence epilepsy and juvenile myoclonic epilepsy also have been associated with abnormal frontal lobe gray matter volumes (4). The designation of idiopathic as meaning no underlying structural brain lesion or other neurological signs or symptoms seems to be dissolving under increasingly sophisticated scrutiny of these patients. Hermann et al. enrolled study patients with both focal and generalized syndromes but gave no further specific diagnoses of subtypes.

The patient population studied by Hermann et al. presents further interpretive problems. The study group was defined as children with epilepsy with "no signs or symptoms indicative of neurological abnormality." Yet, many in the subgroup discovered to have ADHD already were dysfunctional enough to have earned IEPs at school and had symptoms of ADHD that preceded the onset of seizures. Furthermore, all subjects were recruited from pediatric neurology clinics. Could they have been referred to pediatric neurologists because their physicians or parents already suspected or recognized behavioral or cognitive problems? The proportion of children with epilepsy cared for by primary care doctors versus neurological specialists in their area are unknown or at least not provided. How generalizable are these findings?

This remains a valuable study, adding to a growing literature of similar findings. As the number of known and defined genetic epilepsies increases, the number of so-called idiopathic epilepsies appears to be shrinking, adding to the increasing suspicion that there are no true idiopathic epilepsies at all—simply epilepsy syndromes whose causes and other clinical and anatomic correlates are yet to be discovered.

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