

TEACHING THE TEACHERS: DATA TO BENEFIT SCHOOL SYSTEMS AND DOCTORS ABOUT CHILDREN WITH NEWLY DIAGNOSED EPILEPSY

Neuropsychological Status at Seizure Onset in Children: Risk Factors for Early Cognitive Deficits. Fastenau PS, Johnson CS, Perkins SM, Byars AW, deGrauw TJ, Austin JK, Dunn DW. *Neurology* 2009;73(7):526–534. **OBJECTIVE:** This large, prospective, community-based study characterized neuropsychological functioning and academic achievement at the time of the first recognized seizure and identified risk factors for cognitive deficits. **METHODS:** We compared 282 children (ages 6–14 years, $IQ \geq 70$) with a first recognized seizure to 147 healthy siblings on a battery of well-standardized and widely used neuropsychological and academic achievement tests and examined relationships with demographic and clinical variables. **RESULTS:** In this intellectually normal cohort, 27% with just one seizure and up to 40% of those with risk factors exhibited neuropsychological deficits at or near onset. Risk factors associated with neuropsychological deficits included multiple seizures (i.e., second unprovoked seizure; odds ratio [OR] = 1.96), use of antiepileptic drugs (OR = 2.27), symptomatic/cryptogenic etiology (OR = 2.15), and epileptiform activity on the initial EEG (OR = 1.90); a child with all 4 risks is 3.00 times more likely than healthy siblings to experience neuropsychological deficits by the first clinic visit. Absence epilepsy carried increased odds for neuropsychological impairment (OR = 2.00). **CONCLUSIONS:** A subgroup of intellectually normal children with seizures showed neuropsychological deficits at onset. Academic achievement was unaffected, suggesting that there is a window early in the disorder for intervention to ameliorate the impact on school performance. Therefore, the risk factors identified here (especially if multiple risks are present) warrant swift referral for neuropsychological evaluation early in the course of the condition.

COMMENTARY

Cognitive and behavioral comorbidities have long been recognized among patients with epilepsy, although the timing of their appearance has been difficult to research because of a number of methodological issues. Several reports have suggested that cognitive impairment may present at or even predate the appearance of the initial seizure (1,2). However, these studies typically have been limited in value as a result of small sample sizes, gross measures of neuropsychological outcomes, absence of appropriate controls, or exclusion of seizure types and seizure etiologies that decrease the ability to generalize the findings.

Many of these drawbacks were overcome by Fastenau et al. in a relatively large-scale, community-based prospective study of children with newly diagnosed epilepsy. In this report, 292 children with epilepsy were identified at the time of diagnosis or soon thereafter; their neuropsychological and achievement profiles were compared to sibling controls ($n = 147$), using a battery of well-recognized measures. Although children with new onset epilepsy performed more poorly than their siblings on most of the neuropsychological tests administered, they did not differ on measures of academic achievement, suggesting that poorer cognitive abilities had not yet begun to negatively affect school performance. Because the child cohort enrollment was community-based, rather than recruited from specialized epilepsy clinics, the results are relatively representative of the population of new onset pediatric epilepsy cases.

While neuropsychological impairment at the time of epilepsy diagnosis has been reported previously, the size, overall representation of the subjects enrolled, and sibling controls make this an important study, confirming the risk of decreased cognitive abilities at the time of epilepsy diagnosis—a risk that is not limited to patients with the severe epilepsy syndromes. However, even stronger findings would have been achieved if the sample had not been restricted to children with so-called normal IQ estimates (i.e., $IQs \leq 70$). Just as previous studies that excluded children based on seizure type or etiology limited the clinical usefulness of the data, exclusion of patients based on IQ restricts the generalizability of these results. An exclusion criterion based on IQ, when cognitive performance is a primary outcome variable, biases the sample such that the frequency and magnitude of any observed effect will be underestimated. Thus, the true frequency of cognitive impairment in new onset pediatric epilepsy will be higher than the 27 to 40 percent reported.

This study employed the Kaufman Brief Intelligence Test (K-BIT) for the IQ estimate, rather than the Wechsler Intelligence Scale for Children-IV (WISC-IV), which is considered the gold standard for IQ assessment of children in North America. However, the K-BIT yields scores that may range from as many as 25 IQ points *lower* to as many as 24 point *higher* than the WISC-III (3). Thus, in creating a sample of children with normal IQ by excluding those with IQ estimates below 70, unnecessary noise has been introduced, given the poor relationship between WISC-IV and K-BIT IQ scores on the individual patient level.

Despite these limitations, the study highlights that cognitive impairment is a core feature of many pediatric epilepsy

syndromes, including the so-called benign epilepsy syndromes, and cannot solely be attributed to the effects of recurrent seizures or side effects of pharmacotherapy. Although neuropsychological impairment may be present in many children at the time of epilepsy diagnosis, academic achievement appears normal, suggesting that there is a window of opportunity during which appropriate interventions might decrease the burden of cognitive loss. This assessment raises the question of whether all newly diagnosed children with epilepsy should be referred for neuropsychological testing. At a minimum, these findings indicate that the referral threshold should be sufficiently low to prevent appropriate patient evaluations from being missed. Another approach to assess intervention needs could be a two-stage process, similar to what is used to identify dementia in many geriatric clinics, in which patients receive brief cognitive screening and neuropsychological referrals are made based on that screening.

Although a focus on noncognitive behavioral abnormalities is apparent, the study did not report other neurobehavioral conditions, such as Attention Deficit Hyperactivity Disorder (ADHD) or mood disturbances, which also may be present at the time of initial epilepsy diagnosis (4,5). Thus, the degree to which cognitive and psychiatric comorbidities overlap or exist independently among children with new onset epilepsy remains unanswered. When considered together, the actual incidence of neurobehavioral comorbidities at the time of initial diagnoses—defined as either cognitive impairment, ADHD, or mood disturbance—is remarkably high and remains to be properly assessed. A paper by Hermann and colleagues addresses the issue of whether combined or single comorbidities lead to poorer neurobehavioral prognosis. The authors studied children with new onset epilepsy and found that children with either ADHD or academic problems were not only worse neuropsychologically at baseline but also had a poorer 2-year cognitive trajectory across all cognitive domains, particularly for executive functioning (6). In contrast, those children who did not present with neuropsychological and/or neurobehavioral comorbidities not only had normal neuropsychological status at baseline but also displayed a normal rate of cognitive development over the 2-year interval, as compared to controls. This finding suggests the benefits of early identification of children with neuropsychological deficits, so that appropriate interventions can be performed to maximize long-term cognitive outcomes.

The findings of Fastenau et al. have significant implications for schools, since important neuropsychological impairment in areas necessary for academic success (e.g., attention/executive function) are seen prior to development delays in achievement performance, even in the absence of an effect on gross neuropsychological measures, such as full-scale IQ measures. Thus, schools that approach children with epilepsy in a manner similar to students who have sustained traumatic brain injury, for which neuropsychological evaluation is suggested, will benefit these students by facilitating the development and implementation of Individual Education Plans as well as by identifying children who may require tutoring or additional time for test taking (7). Such an approach, in turn, can provide greater awareness of cognitive comorbidities in the larger educational community, so that queries, such as how the diagnosis of complex partial seizures disorder is related to the need for extra time on standardized tests, no longer arise and parents and teachers of children with epilepsy can work closely together to allow these children to realize their full academic potential.

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