Psychiatric Comorbidity in Children with Epilepsy . . . or Is It: Epilepsy Comorbidity in Children with Psychiatric Disorders?

Psychiatric Comorbidity in Children with New Onset Epilepsy. Jones JE, Watson R, Sheth R, Caplan R, Koehn M, Seidenberg M, Hermann B. *Dev Med Child Neurol* 2007;49(7):493–497. The aim of this study was to characterize the distribution, timing, and risk factors for psychiatric comorbidity in children with recent onset epilepsy. Children aged 8 to 18 years with recent onset epilepsy (<1 year in duration) of idiopathic etiology ($n = 53$) and a healthy comparison group ($n = 50$) underwent a structured psychiatric diagnostic interview to characterize the spectrum of lifetime-to-date history of comorbid psychiatric disorder. There was no significant difference between the children with recent onset epilepsy and healthy comparison children in sex (31 males, 22 females vs 23 males, 27 females) or mean age 12.7y [SD 3.3] vs 12.7y [SD 3.2]). Children with recent onset epilepsy exhibited an elevated rate of lifetime-to-date Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) Axis I disorders compared with the comparison group. They showed significantly higher rates of depressive disorders (22.6 vs. 4%, $p = 0.01$), anxiety disorders (35.8 vs 22%, $p<0.05$), and attention-deficit-hyperactivity disorder (26.4 vs 10%, $p = 0.01$) with elevated but less prevalent rates of oppositional defiant and tic disorders. A subset of children with epilepsy (45%) exhibited DSM-IV Axis I disorders before the first recognized seizure, suggesting the potential influence of antecedent neurobiological factors that remain to be identified. The increased prevalence of psychiatric comorbidity antedating epilepsy onset may be consistent with the presence of underlying neurobiological influences independent of seizures, epilepsy syndrome, and medication treatment.

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COMMENTARY

Typically, it is assumed that the relationship between psychiatric and seizure disorders is one in which psychiatric comorbidities are a complication of the seizure disorder and/or of the underlying neurological insult that caused the epilepsy. Thus, in one of the most important population-based studies of childhood psychopathology, Rutter et al. found evidence of psychiatric disease in 29% of children with uncomplicated epilepsy and in 58% of children with epilepsy and structural abnormalities of the brain (1). In another population-based study, Austin et al. compared the behavior profile of 224 children (ages 4–14 years) with new-onset seizures and 159 siblings (4–18 years) without seizures, using the diagnostic instrument Child Behavior Check List (CBCL) (2). Data were obtained at baseline and at 6, 12, and 24 months, during which 163 (73%) children had at least one additional seizure. On average, all children with new-onset epilepsy had higher CBCL scores, indicative of greater psychopathology across all times when experiencing recurrent seizures than when not experiencing recurrent seizures.

Accordingly, children with new-onset epilepsy who entered remission early in the course of their disease would be expected to display prevalence rates of psychosocial disturbances comparable to that of healthy children when they enter adolescence or early adulthood. Yet, the evidence does not always support such suppositions. For example, in a Finish population-based study, Sillanpaa et al. found worse social and educational outcomes in 66 neurologically normal adults with idiopathic or cryptogenic childhood-onset epilepsy that had remitted and in whom antiepileptic medication was discontinued, than in a control group matched for age and gender (3). Similarly, in a population-based study in Canada, Camfield et al. studied the social outcome of 337 normally intelligent children with onset of epilepsy between 1977 and 1985 (4). After a follow-up averaging 7.5 years (subjects were 7–28 years old at last follow-up), 34% were reported to have failed in school, 34% had to be referred for special educational resources (vs 11.7% of healthy children with normal intelligence in Nova Scotia), 22% had undergone psychiatric consultation (vs 12% of children of 4–16 years of age in the province of Ontario), 20% were unemployed (vs 14% of females and 17% of males aged 19–24), 27% showed signs of social isolation, 12% had an unplanned pregnancy, and 2% were convicted of a criminal offense (comparative rates were not available for the latter three variables in the general population). The authors failed to find an association between the social outcome and the many variables related to epilepsy, seizure control, and electroencephalographic findings.

Thus, what accounts for the declining performance of these patients? The existence of psychiatric pathology at the time of the onset of the seizure disorder may provide an explanation for the findings. For example, the previously described study by Austin et al. identified higher rates of behavior disturbances in 32% of the children with new-onset epilepsy than in the siblings in the 6 months preceding the first recognized seizure. The psychopathology included symptoms of mood and anxiety disorders, attention disturbances, as well as thought and somatic complaints (5). In recent years, other studies have confirmed these observations: in the study by Jones et al., 45% of the children with new-onset epilepsy already presented with a psychiatric disorder (according to DSMIV-TR diagnostic criteria) at the time of the diagnosis of epilepsy. Furthermore, in a prospective community-based study of 613 children with new-onset epilepsy (mean age at time of first seizure was 5 years, 11 months), Berg et al. found that 15% of 66 children with idiopathic or cryptogenic epilepsy had been referred for special education services before the first seizure (6).

Recent studies have suggested that psychiatric pathology could be a risk factor for the development of unprovoked nonfebrile seizures and epilepsy in children. For example, McAfee et al. conducted a retrospective cohort study of 133,440 pediatric patients (ages 6–17 years) without a history of seizures or prior use of anticonvulsant medications (7). The data source for this study was a research database containing pharmacy and medical claims for members of a large US-based managed healthcare organization. The incidence rate of seizures among children without psychiatric diagnoses was 149 per 1,00,000 person-years, while that among children with psychiatric diagnoses, other than ADHD, was 513 per 1,00,000 person-years. In a population-based, case-control study of all newly diagnosed, unprovoked seizures among Icelandic children, ages 3–16 years, Hesdorffer et al. found that a history of ADHD was 2.5-fold more common among children with newly diagnosed seizures than among control subjects (8). The investigators used the Diagnostic Interview Schedule for Children to make a DSM-IV diagnosis of ADHD in a standardized fashion among cases and controls, who were the next two same-sex births listed in the population registry. The association was restricted to ADHD of the predominantly inattentive type and was not seen with ADHD of the predominantly hyperactive–impulsive or combined types. Seizure type, etiology, sex, and seizure frequency at diagnosis ($\geq$1) did not have any impact on the findings. These data suggest that epilepsy shares common pathogenic mechanisms with ADHD, mood, and anxiety disorders, which facilitates the occurrence of the seizure disorder in the presence of the psychiatric disorder and vice versa. The possible implications of common pathogenic mechanisms between depression and epilepsy have been reviewed in great detail in this journal (9).

Yet, the negative impact of psychiatric disorders at the time of epilepsy onset is not restricted to potential risks of future psychosocial maladjustments; it also may herald a worse response to treatment with antiepileptic drugs. Indeed, in a study of 780

patients with new-onset epilepsy, Hitiris et al. found that those with a history of psychiatric disorders, detected at the time of diagnosis of the seizure disorder, were almost 2.5 times more likely to develop refractory epilepsy (10). What is the moral of this story? The evaluation of patients with epilepsy cannot be restricted to seizure-related data but must include a careful investigation of previous psychiatric and cognitive disturbances . . . even in patients with new-onset epilepsy!

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