

Epilepsy and Attention Deficit Hyperactivity Disorder: Is There a Link?

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Abstract

The probability of developing attention deficit hyperactivity disorder (ADHD) increases in children with epilepsy. The two disorders may have common causative factors. A bidirectional association between ADHD and epilepsy has been suggested in previous studies. Causative factors, such as those that are genetics and environmental, may be common in both disorders and cause several transcriptional changes in the brain, thus, altering behavior or cognition prior to seizures.

Keywords: Epilepsy; Attention deficit hyperactivity disorder; Bidirectional

Epilepsy and attention deficit hyperactivity disorder (ADHD) significantly affect the social and behavioral development of children [1]. Epilepsy is characterized by spontaneous recurrent seizures [2] and can be a pervasive condition in which seizures are merely one expression [3]. Severe and persistent symptoms of ADHD, such as inattention, over-activity, and impulsiveness, are initially manifested during early childhood. ADHD is associated with long-term educational and social disadvantages [4]. In this review, the prevalence rates of ADHD and epilepsy among the general pediatric population are 3%–7% and 0.05%–1%, respectively [5–8]. The rate of the two occurring together increased over that expected by chance. ADHD and seizures may be comorbid conditions. Data revealed that part of this increase is due to a bidirectional relationship between ADHD and epilepsy [9].

A previous study reported that ADHD is the most common disorder among preschoolers and school-aged children with epilepsy [10]. Behavioral difficulties observed in children with epilepsy suggest a high risk of ADHD [11,12]. Similarly, 6.1% of children with ADHD exhibit an abnormal electroencephalograph (EEG), whereas only 3.5% of children in a study on healthy children exhibited an abnormal EEG [13]. Previous studies [14,15] on children with incidence of unprovoked seizures have determined that behavioral disturbances were more common before the onset of the first seizure, compared with the controls. A larger study on 148 children with first unprovoked seizures and 89 seizure-free sibling controls determined that attention problems before identification of the first seizure, as assessed using the Child Behavior Checklist, were 2.4-fold more common (8.1%) than in the controls (3.4%) [9].

The complex relationship between epilepsy and ADHD remains unclear. Several hypotheses on the possible pathophysiology of the comorbidity between ADHD and epilepsy have been proposed in the context of brain development, including the effects of chronic seizures, EEG epileptic form discharges, and AEDs [16,17]. Neurodevelopmental conditions may increase the vulnerability of children to epilepsy and ADHD. In a retrospective study, Austin et al. observed that attention and behavioral problems were increased in children with epilepsy, compared with their siblings, 6 months before the first diagnosed seizure. This finding agrees with the hypothesis that the possibility of acquiring ADHD increases in children with epilepsy, which is independent of the effects of seizures or their treatment [18]. Hesdorffer et al. evaluated the symptoms of ADHD in children prior to the onset of seizures and determined that ADHD was significantly more common in patients with new-onset epilepsy (31%) than in healthy controls (6%). ADHD antedated the diagnosis of epilepsy in 82% of cases [19].

Whether ADHD is a nonspecific symptom caused by antiepileptic drugs, non convulsive epileptic form discharges, or negative chronic seizure effects remains unknown. In addition, whether ADHD is associated with epilepsy because of overlapping pathophysiological mechanisms remains unclear. Comorbidity patterns revealing shared neurobiological mechanisms involved in multiple disorders may provide pathogenetic insights. In a recent study, ADHD was hypothesized to increase the risk of subsequent epilepsy and vice versa. Two separate cohort studies were conducted on the same population base to evaluate the bidirectional correlation between ADHD and epilepsy. In the current study, by contrast, the possibility of developing ADHD in patients with epilepsy was higher (adjusted HR = 2.54, 95% CI = 2.02–3.18). Comparably, ADHD increased the risk of subsequent epilepsy (adjusted HR = 3.94, 95% CI = 2.58–6.03), indicating that ADHD increases the risk of subsequent epilepsy and vice versa [9].

The pathogenesis of the relationship between epilepsy and ADHD remains unknown. Frontostriatal network dysfunction is related to ADHD without epilepsy [20–23]. Evidence of frontal lobe dysfunction was found in both the focal-onset and generalized-onset type of epilepsy. The frontal lobes may correlate epilepsy with ADHD. In addition, the comorbidity between ADHD and epilepsy is supported by animal models that can potentially be used to elucidate the common genetic defects underlying these disorders. In a previous study, rats were selectively bred to test amygdale kindling (a model for temporal lobe epilepsy) speed. The same rats were assessed for ADHD-like symptoms in subsequent generations. The fast kindling rats (genetically seizure-prone) were similar to humans with ADHD, compared with the slow kindling rats [24]. In another study, a seizure-induced rat simultaneously developed behavioral and physical characteristics similar to ADHD symptoms [25].

In conclusion, common neurobiological mechanisms may be present in epilepsy and ADHD. Identifying these conditions is crucial in clinically managing epilepsy. Future studies may focus on

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investigating genetic abnormalities that, through variable penetrance, can cause epilepsy alone, epilepsy with ADHD in others, and ADHD alone in some families. In addition, the effect of epileptic form activity in different neural network functions requires a more comprehensive understanding.

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