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Targeted Review

Treating anxiety disorders in children and adolescents with epilepsy: What do we know?

Jana E. Jones *

University of Wisconsin School of Medicine & Public Health, Department of Neurology, 1685 Highland Ave., Medical Foundation Centennial Building, Room 7229, Madison, WI 53705, USA

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ABSTRACT

Children with epilepsy are at significant risk of psychiatric disorders, which can in turn negatively impact social skills development, academic achievement, and quality of life. The most commonly reported psychiatric comorbidities in pediatric epilepsy are ADHD, depression, and anxiety. The prevalence rates of anxiety disorders in pediatric epilepsy range from 5 to 49%, and in the general population, anxiety disorders are the most common psychiatric disorder in childhood. For the purposes of this review, anxiety disorders will be examined in order to 1) examine rates of anxiety disorders in children and adolescents with epilepsy, 2) review treatment options for anxiety disorders in children with epilepsy, and 3) identify future avenues for the development of evidence-based practices for the treatment of anxiety disorders in youth with epilepsy.

Key questions

1. What are the most common anxiety disorders in children and adolescents with epilepsy?
2. What are the recommended treatments for anxiety disorders in youth with epilepsy?
3. What are the future avenues for research and development of evidence-based anxiety treatment for youth with epilepsy?

1. Introduction

Epilepsy in childhood carries with it a number of psychosocial burdens including cognitive impairments, academic underachievement, social skills problems, and behavioral and psychiatric disorders [1–4]. In particular, children with epilepsy are at significant risk of psychiatric disorders, which can in turn negatively impact social skills development, academic achievement, and quality of life. The Isle of Wight study utilized a population-based cohort in the United Kingdom [5] and reported that 26% of children with epilepsy had a psychiatric disorder. The most recent update of the Isle of Wight study by Davies et al. [6] indicated that 36% of the sample had a psychiatric condition, and among children with more complicated (structural brain abnormalities) epilepsy, this rate jumped to 56%. More recently, in a large population-based cohort in the United States, Berg et al. [2] reported somewhat lower rates of psychiatric comorbidity, with 27% in the group with uncomplicated (no lesions and IQ > 80) epilepsy and 36% in the group with complicated (lesion with IQ < 80) epilepsy. Much higher rates of psychiatric disorders have been reported in clinical samples. Ott et al. [7] identified psychiatric diagnoses in 60% of the sample recruited from a tertiary care center and community-based clinics, and only one third of these individuals were receiving treatment for their psychiatric conditions. In Brazil, Thome-Souza et al. [8] reported that among children with epilepsy who were referred from a tertiary care center, 71% of the sample met criteria for a psychiatric disorder.

The most commonly reported psychiatric comorbidities in pediatric epilepsy are attention deficit hyperactivity disorder (ADHD), depression, and anxiety. Berg et al. [2] reported that in the overall sample (complicated and uncomplicated), the most common diagnoses were ADHD (20.8%), depression (13.4%), and anxiety (5%). In adults with epilepsy, depression is quite common; however, anxiety disorders have gained more attention in recent years because of the fact that anxiety and depression often co-occur, and a number of studies utilizing psychiatric interviews have reported higher rates of anxiety disorders in children and adolescents when compared with depression [9]. Adewuya and Ola [10] utilized a psychiatric interview (Diagnostic Interview Schedule for Children Version IV [DISC-IV]) [11] and reported that 31% of adolescents in Nigeria met criteria for an anxiety disorder compared with 28% with depression. Among adolescents in Jordan, Alwash et al. [12] found that nearly half of the sample had clinically elevated

* Tel.: +1 608 262 5481; fax: +1 608 265 0172.
E-mail address: jejones@neurology.wisc.edu.

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symptoms of anxiety based on the DSM-IV criteria, and 23% met criteria for depression. In the United States, Caplan et al. [13] found that among children with epilepsy and an affective disorder, two thirds met criteria for an anxiety disorder based on a psychiatric interview (Kiddie Schedule for Affective Disorders and Schizophrenia [KSADS-PL]) [14]. In a study of children with new-onset epilepsy, Jones et al. [15] reported that 36% of the sample had a lifetime anxiety disorder compared with 22% of controls. Depression was identified in 23% of the children with epilepsy and only 4% of controls. For the purposes of this review, anxiety disorders will be examined in order to elucidate rates of anxiety disorders in children and adolescents with epilepsy, and secondly, to review treatment options for anxiety disorders in children with epilepsy since there is a dearth of literature examining this topic in epilepsy despite evidence-based treatments in pediatric anxiety disorders in the population at large. Finally, opportunities in the research and development of evidence-based practices for treating anxiety disorders in youth with epilepsy will be discussed.

2. What are the most common anxiety disorders in childhood and adolescence?

2.1. What are the differences in prevalence rates of anxiety disorders in youth overall compared with youth with epilepsy?

In the population at large in childhood and adolescence, anxiety disorders are quite common. Prevalence rates range from 10% to 32% [16–18], with higher rates reported for lifetime prevalence rates (9%–32%) compared with current or 12-month prevalence rates (8%–21%) [16–18]. When identifying age at anxiety onset, preschool-age children aged 4–5 years have higher rates of anxiety compared with children aged 2–3 years (11% vs. 8%, respectively) [16]. According to Kim-Cohen et al. [19], half of adults with anxiety or depression had a history of anxiety onset before age 15. In the general population, it is increasingly understood that anxiety disorders occur at particular time points in childhood. Specific phobias, for example, occur first at around age 6 with social phobia appearing around age 8, and panic disorder often does not appear until late adolescence or early adulthood (Fig. 1) [17,20,21]. In terms of frequency in adolescence, the anxiety disorder with the highest lifetime prevalence rate is specific phobia (19.9%), with social phobia (8.5%) and separation anxiety (7.6%) coming in at a close second and third (Fig. 1) [20].

In the pediatric epilepsy literature, very little is known regarding the prevalence rates of specific anxiety disorders or the timing or appearance of anxiety disorders in childhood in the context of epilepsy. Additionally, when anxiety disorders are evaluated, they are typically reported aggregately instead of reporting the specific types of anxiety disorders. Notably, Berg et al. [2] reported that 3% of the sample had been diagnosed with obsessive–compulsive disorder (OCD). Alwash et al. [12] utilized the DSM-IV criteria for generalized anxiety disorder (GAD) and reported that 49% of the sample met criteria for the disorder. Additionally, Jones et al. [15] reported several subtypes of anxiety disorders: OCD (11%), specific phobia (8%), social phobia (8%), overanxious disorder (6%), separation anxiety (2%), and PTSD (2%).

2.2. What is the relationship between anxiety disorders and epilepsy? Psychological and neurobiological perspectives

Hamid et al. [22] and Mula [23] discussed the coexistence of epilepsy and anxiety in terms of psychological pathogenesis. Based on more contemporary conceptualizations of anxiety as a reaction to real or imagined threats, seizures might potentially be viewed as a threat to the individual and result in a "seizure fear" that may impact the individual's well-being [24]; however, there is very little research to shed light onto this potential development of a seizure phobia. Additionally, based on learning and cognitive behavioral theoretical perspectives, seizures could potentially prime an individual for developing anxiety as the individual may overestimate the risk of harm and underestimate one's ability to manage life-threatening or stressful situations as a result of seizures [22]. Again, these fear-based responses have not been studied thoroughly in epilepsy, and how this theoretical perspective applies to cognitive behavioral interventions for anxiety disorders in the context of seizures has not been examined.

In terms of neurobiological perspectives on the development of anxiety in the context of epilepsy, there are shared pathogenic mechanisms including the following: a) neurotransmitter disturbances in serotonin, norepinephrine, glutamate, and gamma-aminobutyric acid (GABA); b) inflammatory process in the central nervous system; c) neuroendocrine disturbances; and d) similar brain regions and brain circuitry in both disorders (i.e., amygdala and hippocampus) [22,23,25,26]. For further review, Kanner [26] examined the bidirectional relationship between epilepsy, anxiety, and depression, and their common co-occurrence provides support for common pathogenic mechanisms.

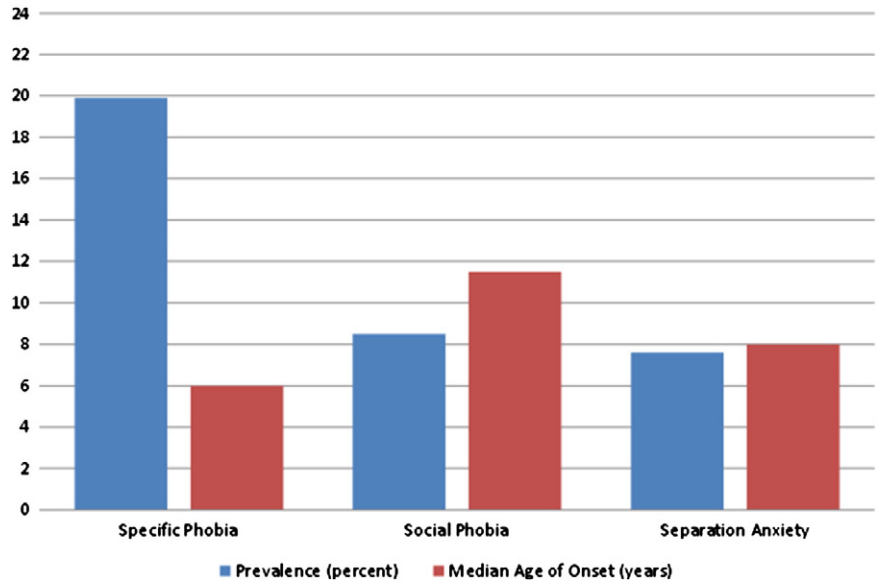

Fig. 1. Common anxiety disorders in childhood: prevalence and age at onset. Kessler et al. [20].