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The relationship of seizure focus with depression, anxiety, and health-related quality of life in children and adolescents with epilepsy

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ABSTRACT

For youth with epilepsy, comorbid psychiatric conditions, such as depression and anxiety, require further examination as they carry increased risk for reduced health-related quality of life (HRQOL). The current study assessed whether rates of depression, anxiety, and withdrawal behaviors differed based on seizure location. Data included parental ratings on the Behavior Assessment System for Children (BASC-2) and the Quality of Life in Childhood Epilepsy (QOLCE) questionnaire for 132 children and adolescents (mean age = 11.34, *SD* = 3.95) with generalized or partial (i.e., frontal [FLE] or temporal lobe epilepsy [TLE]) epilepsy. Our results identified clinically significant internalizing psychopathology in nearly half of our sample (41%). Although rates of internalizing behavior were similar between generalized and partial groups, children and adolescents with TLE demonstrated higher rates of depression compared to youth with FLE. No effects of laterality on internalizing behaviors were identified between TLE and FLE groups. Finally, for youth with TLE, parental depression ratings along with current number of antiepileptic medications (AEDs) were found to be significant barriers to HRQOL above and beyond anxiety, withdrawal, and epilepsy-specific variables. Temporal lobe epilepsy was associated with a two-fold risk of clinically significant depression ratings. These findings highlight the high prevalence of internalizing psychopathology features in pediatric epilepsy and offer further support for the relationship between depression and TLE in children and adolescents with epilepsy.

1. Introduction

Epilepsy is one of the most common neurological disorders in childhood, and it is a condition that not only affects physical functioning but also cognitive, behavioral, and emotional functioning [1,2]. It has been established that children with epilepsy often have coexisting psychiatric conditions, which have been shown to be more prevalent in youth with complicated epilepsy versus uncomplicated epilepsy [3–6]. Existing studies report that 20–60% of children and adolescents with epilepsy also present with some form of psychopathology [3–8]. Psychiatric disturbance in childhood epilepsy can be related to psychosocial stressors imposed by chronic disease, but research indicates that specific epilepsy-related factors, including underlying brain dysfunction, can also play a role. Youth with epilepsy have been found to be at greater risk for psychopathology than children and adolescents dealing with other types of chronic conditions, such as diabetes mellitus and asthma [6].

Among psychiatric disorders, internalizing conditions, such as depression and anxiety, seem to be particularly common in youth with epilepsy [9,10]. In fact, depression symptoms alone have an estimated prevalence of 23–26%, based on self-report instruments [11,12]. The prevalence of anxiety, in comparison, is estimated to be between 15 and 20% [13]. Unfortunately, most cases of anxiety and depression go unrecognized and untreated in children with epilepsy [5,7,9,11,14–16]. This unrecognized psychopathology has been associated with negative quality-of-life outcomes [9,17,18] and higher rates of epilepsy-related stigma [19,20].

A number of predictive factors have been recognized that may impact the prevalence of both anxiety and depression (see Ekinci et al. [21], for a comprehensive review on this topic). Compared to younger children, adolescents with epilepsy are considered to be at higher risk for anxiety [22] and depression [23,24]. Despite the well-known female predominance for anxiety and depression in the general population, the majority of studies have found no relationship between gender and anxiety in children with epilepsy [10,11,24,25]. Studies examining the influence of gender on depression in childhood epilepsy reveal mixed findings [26–29]. The relationship of depression with seizure variables remains unclear in the literature, with some studies reporting no association with seizure variables [4,12,30–32] and others reporting an

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association with seizure frequency [24], polytherapy with antiepileptic drugs (AEDs) [10,24], type of AED [33–35], and duration of illness [24].

Recent population-based research suggests a bidirectional relationship between the presence of psychopathology, namely depression, and pediatric epilepsy. In a study by Austin et al. [36], approximately one-third of children with new-onset seizures had psychiatric symptoms prior to the onset of seizures. Similarly, Jones et al. [8] reported that 45% of children with new-onset-epilepsy exhibited symptoms of depression and anxiety before the first recognized seizure. Preliminary evidence from animal models and neuroimaging investigations indicate that depression and epilepsy may share a common pathogenic mechanism [37–40]. Zobel et al. [41] identified a hyperactive hypothalamic–pituitary–adrenal (HPA) axis in adults with TLE without depression, of comparable magnitude to that of patients with Major Depressive Disorder. These findings may partially explain why the presence of depression could facilitate the development of a seizure disorder either spontaneously or in the presence of an insult to the central nervous system [42]. It may also suggest that seizure foci particularly localized to the temporal lobe could be a salient risk factor given the potential for disrupted functional neuroanatomical architecture and neurochemical alterations in the limbic system [43–46].

Although the relationship of psychopathology with seizure focus has been extensively examined in the adult literature [47–52], there has been less work on this topic in the pediatric epilepsy literature. Titus et al. [53] reported significantly higher rates of depressive symptoms, measured by the BASC-2, in children and adolescents with TLE when compared with children and adolescents with FLE. No distinction, however, was found between TLE and generalized seizures [53]. More recently, in a sample of children and adolescents with refractory epilepsy, Salpekar et al. [54] reported significantly higher rates of behavioral disturbance, as measured by the CBCL, and higher rates of depression diagnoses, based on psychiatric interview, for children with TLE compared to children with extratemporal foci. Although several adult studies have found a relationship between depression and seizure focus lateralized to the dominant cerebral hemisphere (i.e., typically left) [50,55,56], findings from the pediatric literature regarding seizure laterality and depression are inconsistent [54,57].

In light of our limited understanding about the relationship of depression with seizure focus in children and adolescents with epilepsy, the current study was designed to address the following research questions: (1) What percentage of youth with epilepsy exhibits clinically significant internalizing psychopathology features on the BASC-2? (2) Do internalizing psychopathology features differ between youth with generalized versus partial epilepsies? (3) Do internalizing psychopathology features differ between youth with right- versus left-hemispheric seizure onset? (4) Does the lobe of seizure focus influence the presence of internalizing psychopathology features? (5) What types of internalizing psychopathology features uniquely predict lower HRQOL?

2. Methods

2.1. Participants

The study included 132 children and adolescents with epilepsy (56% male) aged 6 to 18 years (mean age = 11.30, *SD* = 3.97). Participants came from various ethnic backgrounds, with 61% Caucasian, 18% Hispanic, 12% African American, and about 8% identifying as Other. Children and adolescents were referred to pediatric neuropsychology services based upon clinical need as part of the comprehensive care protocol for the epilepsy program. Around 35% of the sample was referred as possible candidates for surgery to treat intractable seizures. The remainder of the sample was composed of children with chronic epilepsy who were experiencing cognitive difficulties that would warrant neuropsychological assessment.

Seizure focus was confirmed by board-certified epileptologists via clinical evaluation and EEG monitoring, yielding two groups based on classification: Generalized (n = 47) and Partial (n = 85). The partial epilepsy group included youth with frontal lobe (n = 42) and temporal lobe (n = 43) seizure foci. Seizure laterality was also recorded, and our partial epilepsy group consisted of approximately 35% (n = 30) with right-sided seizures, approximately 54% (n = 46) with left-sided seizures, and approximately 11% (n = 9) with independent, bilateral seizures. The youth with bilateral seizure foci were not included in the analyses regarding laterality. The demographic and clinical characteristics are presented in Table 1.

2.2. Measures

2.2.1. Internalizing psychopathology

The Behavior Assessment System for Children – 2: Parent Rating Scale (BASC-2: PRS) is a comprehensive measure of a caregiver's perceptions of their youth's emotional and behavioral functioning. Caregivers complete the four-choice response format on either the child (ages 6–11) or adolescent (ages 12–21 years) version. The BASC-2 provides validity scales that assess the reporter's pattern of item responding. Raw scores are converted to T-scores, making scales comparable across the developmental range of 6–21 years. T-scores of 60–69 are considered "at risk" and indicate behaviors that may warrant clinical attention, while T-scores ≥70 suggest clinical elevations and represent a high level of maladjustment warranting clinical attention. The BASC-2 has been deemed a "well-established" assessment tool in pediatric populations [58] and has demonstrated reliability and validity in pediatric epilepsy populations [18,53]. The present work examined clinical subscales across both developmental versions of the BASC-2, with specific focus on the Anxiety, Depression, and Withdrawal subscales. The Somatization subscale was not utilized for the current study, as somatic complaints in an epilepsy population are likely secondary to physical health problems related to having seizures. Instead, the withdrawal subscale was utilized for the current investigation. This subscale has been shown to significantly correlate with the Withdrawn/Depressed subscale on the CBCL, which is calculated as a contributor to the overall Internalizing Problems subscale of the CBCL [59].

Table 1
Demographic characteristics, (N = 132).

Mean age in years (*SD*)	11.34 (3.95)
Gender, male	74 (56.1%)
Full-Scale IQ (Mean/*SD*)	90.27 (17.23)
Racial ethnicity	
Caucasian/white	82 (62.1%)
Hispanic/Latina/Latino	24 (18.2%)
African-American/Black	16 (12.1%)
Other	10 (7.6%)
Age at seizure onset (years) (*SD*)	5.64 (4.23)
Duration of epilepsy (years) (*SD*)	5.69 (4.58)
Number of AEDs	1.54 (0.90)
Number of failed AEDs	1.70 (1.62)
Seizure frequency (at time of testing)	
Yearly	19 (14.4%)
Quarterly	27 (20.4%)
Monthly	36 (27.3%)
Weekly	26 (19.7%)
Daily	24 (18.2%)
Seizure focus	
Frontal lobe	42 (31.8%)
Temporal lobe	43 (32.6%)
Generalized	47 (35.6%)
Seizure lateralization for partial group	
Right	30 (35.0%)
Left	46 (54.0%)
Reason for referral	
Nonsurgical	85 (64.4%)
Surgical candidate/phase 1	47 (35.6%)