



## Executive function and health-related quality of life in pediatric epilepsy



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### ABSTRACT

Children and adolescents with epilepsy often show higher rates of executive functioning deficits and are at an increased risk of diminished health-related quality of life (HRQOL). The purpose of the current study was to determine the extent to which executive dysfunction predicts HRQOL in youth with epilepsy. Data included parental ratings on the Behavior Rating Inventory of Executive Function (BRIEF) and the Quality of Life in Childhood Epilepsy (QOLCE) questionnaire for 130 children and adolescents with epilepsy (mean age = 11 years, 6 months; SD = 3 years, 6 months). Our results identified executive dysfunction in nearly half of the sample (49%). Moderate-to-large correlations were identified between the BRIEF and the QOLCE subscales of well-being, cognition, and behavior. The working memory subscale on the BRIEF emerged as the sole significant predictor of HRQOL. These results underscore the significant role of executive function in pediatric epilepsy. Proactive screening for executive dysfunction to identify those at risk of poor HRQOL is merited, and these results bring to question the potential role of behavioral interventions to improve HRQOL in pediatric epilepsy by specifically treating and/or accommodating for executive deficits.

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### 1. Introduction

Epilepsy is one of the most common neurological disorders in childhood and one that affects not only physical functioning but also cognitive, social, emotional, and behavioral functioning. In this regard, the presence of epilepsy during childhood and/or adolescence inevitably imposes unique challenges to patient well-being or health-related quality of life (HRQOL). Health-related quality of life (HRQOL) is an important metric in epilepsy because it acknowledges the complexity and subjectivity of health care treatment as well as the notion that psychological, social, and cognitive functioning can significantly impact the lives of patients who live with epilepsy [1–3].

Research has repeatedly shown that children and adolescents with epilepsy are at risk of diminished HRQOL compared with healthy controls and children with other chronic disorders such as asthma and diabetes [4–6]. When compared with other chronic illnesses, HRQOL in children with epilepsy tends to be more greatly and uniquely impacted by problems with psychological, social, and educational functioning [7–9]. These problems are likely compounded by social stigma, physical impact of medication, fear and uncertainty related to the unpredictability of seizures, and perceived cognitive slowing [10,

11]. Health-related quality of life in childhood epilepsy also appears to be dependent upon the degree to which children are able to socialize and participate in their environment. These variables seem to play an even more significant role than overall cognitive functioning (e.g., Full Scale IQ) or even some epilepsy-related variables (e.g., age at seizure onset) [12]. Psychiatric functioning further mediates HRQOL outcomes in childhood epilepsy [13], though the direction of the causal relationship between psychiatric symptoms, adaptive functioning, and HRQOL remains to be determined.

While factors such as psychiatric functioning and adaptive functioning influence HRQOL, both of these factors appear to be strongly impacted by executive functioning. Executive functions (EFs) have been defined as a set of interrelated skills often including one or more of the following constructs: (a) attentional control, (b) planning/goal setting and problem solving, (c) cognitive flexibility of thought and action, (d) concept formation/abstraction, (e) information processing, and (f) working memory [14–19]. These functions, or processes, are believed to be interrelated, and they are responsible for goal-directed or future-oriented behavior. Executive functions have been referred to as the “conductor” which controls, organizes, and directs cognitive activity, emotional responses, and behavior [20]. While EF deficits can come in many forms in children and adolescents, some common examples include the following: trouble following multistep instructions; difficulty adjusting to changes in routine; inefficient regulation of emotions and behavior; poor self-awareness; and problems initiating, following through, and completing tasks independently. Several prospective longitudinal studies on healthy

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children and young adults suggest that impairments in executive functioning can increase the likelihood of psychiatric symptoms [21–23]. In addition, deficits in executive functioning are known to negatively impact adaptive functioning [24], even when controlling for intelligence [25]. While adaptive and psychiatric impairments are well-known to impact HRQOL in the epilepsy literature, little information is known about how executive functioning relates to HRQOL in children with epilepsy.

Deficits in executive functioning have been well documented in the child and adolescent epilepsy literature [26–28] with executive dysfunction reported in 25–66% of cases [29,30]. Because executive deficits are related to psychiatric and adaptive functioning, it would be reasonable to suggest that children and adolescents with epilepsy may be at higher risk of lower HRQOL if they experience problems with executive functioning. However, this relationship has not been thoroughly examined in the literature. To date, Sherman et al. [31] offer the only investigation into this association with a study of 121 children with epilepsy. Comparing associations between parent ratings on both the Behavior Rating Inventory of Executive Function (BRIEF) [32] and the Impact of Child Illness Scale (ICI) [33], Sherman et al. [31], demonstrated that executive dysfunction exerted a broad adverse influence on HRQOL. The largest association was on the working memory scale of the BRIEF. Interestingly, the degree of association between executive functioning and HRQOL was equivalent to neurological predictors, such as the number of current and previous antiepileptic drugs (AEDs). This finding is important because it marks a potential avenue of intervention in pediatric epilepsy. While epilepsy-specific factors, such as AED treatment and intractability, cannot always be manipulated, the impact of cognitive concerns on a child or adolescent's life may be more readily manipulated through environmental accommodations or therapeutic interventions, thus providing a potential avenue to improve HRQOL [34,35].

Given the goal of optimizing HRQOL among children and adolescents with epilepsy, the identification of potentially modifiable risk factors associated with HRQOL above and beyond demographic and epilepsy-specific characteristics is important. The present study focused upon replicating and expanding upon the findings of Sherman et al. [31] by utilizing a multidimensional measure of HRQOL. The Quality of Life in Childhood Epilepsy (QOLCE) [36] scale is a psychometrically sound measure specifically designed for use with parents of children with epilepsy. The QOLCE scale offers a quantifiable assessment of HRQOL across five domains (i.e., physical function, emotional well-being, cognitive function, social function, and behavior), and it includes evaluation of perceived stigma and subjective experiences of general health and overall HRQOL. The purpose of the current study was to determine the extent to which executive deficits predict HRQOL across multiple domains, while simultaneously considering epilepsy-specific variables. Additionally, we sought to determine those executive functioning variables that best predicted HRQOL above and beyond epilepsy variables.

The current study addressed the following research questions:

- (1) What percentage of clinically referred children and adolescents with epilepsy demonstrates executive functioning problems on the BRIEF?
- (2) While epilepsy-specific variables are known to be associated with lower HRQOL and deficits in executive functioning, what is the relationship between HRQOL and executive functioning?
- (3) Are executive functioning deficits related to specific aspects of HRQOL, and if so, do they predict lower HRQOL above and beyond epilepsy variables?

## 2. Methods

### 2.1. Participants

Participants in the present study included 130 children and adolescents between the ages of 6 years, 0 months and 18 years, 4 months

(mean age = 11 years, 6 months; SD = 3 years, 6 months) who were referred for epilepsy treatment at a tertiary care health system. All epilepsy diagnoses were confirmed by board-certified epileptologists via clinical evaluation and EEG monitoring, and the patients were referred to the pediatric neuropsychology service based upon the presence of cognitive concerns or as part of a presurgical epilepsy evaluation. Because epilepsy-specific variables and their impact on HRQOL were of particular interest in this study, children and adolescents were not excluded on the basis of specific epilepsy characteristics. However, children were excluded if caregivers could not speak or read English. The demographic and clinical characteristics of the sample are shown in Table 1.

### 2.2. Measures

#### 2.2.1. Health-related quality of life

The Quality of Life in Childhood Epilepsy (QOLCE) questionnaire is a 91-item parent-rated measure designed to assess the HRQOL of children with epilepsy [36]. It was developed to assess the HRQOL of children aged 6–18 years. Caregiver ratings are measured on a 5-point Likert scale ranging from “very often” or “all of the time” to “never” or “none of the time”. Some questions ranged from “yes, limited a lot” or “very often” or “excellent” to “no, not limited” or “N/A” or “poor” depending on the item content. The present study followed scoring procedures recommended by the authors, which included a linear transformation of raw scores to a 0- to 100-point scale (1 = 0, 2 = 25, 3 = 50, 4 = 75, 5 = 100) to aid with interpretation [36,37]. Higher scores indicate a higher level of HRQOL. The advantage of this instrument over other

**Table 1**

Demographics and seizure characteristics (n = 130).

Age	
Mean	11 years, 6 months
SD	3 years, 6 months
Gender	
Male	73 (56.2%)
Female	57 (43.8%)
Ethnicity	
Caucasian/white	80 (61.5%)
Hispanic/Latina/Latino	24 (18.5%)
African-American/black	19 (14.6%)
Other	7 (5.4%)
Full Scale IQ	
Mean	83.44
SD	18.17
Age at seizure onset	
Mean	6 years, 3 months
SD	4 years, 0 months
Duration	
Mean	5 years, 2 months
SD	4 years, 2 months
Number of AEDs (at time of testing)	
None	9 (6.9%)
1	77 (59.2%)
2	33 (25.4%)
3	7 (5.4%)
≥4	3 (2.3%)
Number of ineffective AEDs	
Mean	1.58
SD	1.48
Seizure frequency (at time of testing)	
None	8 (6.2%)
Yearly	18 (13.9%)
Quarterly	26 (20.0%)
Monthly	28 (21.5%)
Weekly	22 (16.9%)
Daily	28 (21.5%)
Reason for referral	
Nonsurgical	84 (64.7%)
Surgical candidate/phase 1	33 (25.3%)
Postsurgical	13 (10.0%)

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