



Pattern of executive functioning in adolescents with epilepsy: A multimethod measurement approach

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ARTICLE INFO

Article history:

Received 23 October 2017

Revised 19 December 2017

Accepted 22 December 2017

Available online xxxx

Keywords:

Seizure

Neuropsychological

Teenagers

Measurement

NIH toolbox

Working memory

ABSTRACT

Youth with epilepsy demonstrate deficits in executive functioning (EF), the skills necessary for goal-directed behavior (e.g., problem-solving, initiating, monitoring, organization, planning, and working memory). Despite 30–50% of youth with epilepsy demonstrating EF deficits, no extant studies have utilized both performance and questionnaire-based measures to examine the pattern of EF deficits in adolescents with epilepsy. Study aims were to 1) identify the pattern of EF deficits in adolescents with epilepsy and 2) identify which assessment tools are most sensitive to EF deficits in this population (adolescents, ages 13–17, with epilepsy). An exploratory aim was to examine group differences on measures of EF by epilepsy type. Standard performance-based neuropsychological measures (Wechsler Intelligence Scale for Children – Version V or Wechsler Adult Intelligence Scale Working Memory Index-Version IV, Delis Kaplan Executive Functioning System, NIH Toolbox, Test of Everyday Attention for Children) and the Behavior Rating Inventory of Executive Functioning (BRIEF) comprised the multimethod assessment battery. Depending on the measure, 30% of adolescents with epilepsy had deficits in working memory, 17% in cognitive flexibility/problem solving, 6% in inhibition, and 18% in planning/organization. Attention was a significant problem for 15% of adolescents with epilepsy. Correlations among the various EF measures were quite poor.

Across various EF domains, results indicated that adolescents with localization-related epilepsy demonstrated better EF skills compared to adolescents with unclassified epilepsy. Overall, our findings suggest that executive functioning deficits are selective and different from those observed in other neurological populations (e.g., attention deficit hyperactivity disorder (ADHD), traumatic brain injury) where problems with self-regulation (i.e., inhibition, planning/organization) are more pronounced. These findings support utilizing multiple measures, including both performance-based neuropsychological tests and parent- and self-reports, to assess executive functioning difficulties in adolescents with epilepsy as they are uniquely sensitive to executive functioning domains. Adolescents with unclassified epilepsy also appear to be at higher risk for EF deficits and thus represent an important group to target for intervention.

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1. Introduction

Executive functioning (EF) is defined as the skills necessary for goal-directed and complex activities, includes problem-solving, initiating, monitoring, organization, planning, self-regulation and working memory [1]. Thirty to fifty percent of youth with epilepsy demonstrate significant EF deficits [2–8]. Even youth with newly diagnosed epilepsy and no significant medical or developmental comorbidities exhibited significant EF deficits compared to healthy controls [9]. Importantly, many EF deficits persist or worsen over time for youth with epilepsy [10–13], with the demands of adolescence constituting a period of increased

vulnerability [14–16]. Unfortunately, EF deficits can lead to significant academic underachievement [7,17], social difficulties [18], as well as health-related quality-of-life (HRQOL) impairments [19,20]. These data suggest that EF is an important mediator of social, academic, and HRQOL outcomes in this population [14–16].

The measurement of EF is commonly debated in the literature, with some proponents arguing for performance-based neuropsychological tests and others arguing for questionnaire-based methods (e.g., Behavioral Rating Inventory of Executive Function; BRIEF). Performance-based tests assess specific components of EF in isolation and have successfully identified deficits in youth with epilepsy compared to controls [21,22], while rating scales assess application of skills, and are more likely to reflect the demands of real-life settings. Performance-based neuropsychological tasks and questionnaire-based methods, such as the BRIEF are poorly correlated [23]. Questionnaires, such as the BRIEF, correlate highly with biological markers of EF (e.g., frontal

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lobe volume, cortical thinness [21,22,24]), have concurrent and predictive relationships with real-world functioning (e.g., academic skills), and can successfully be used to define intervention targets and outcomes [25–27]. However, questionnaire responses may be biased, with adolescents displaying less awareness of their EF deficits [28] and teacher report being difficult to obtain. More recently, new assessment tools, such as the National Institutes of Health (NIH) ToolBox [29,30], have been developed to measure a wide range of neurocognitive domains including EF. While use of the NIH ToolBox is beneficial due to its brevity and ability to standardize assessment across studies, it has not been evaluated in the context of other performance-based neuropsychological tasks or questionnaires in adolescents with epilepsy.

The pattern of EF deficits in adolescents with epilepsy has not been systematically examined, using a multimethod assessment battery. One study found that the most frequently elevated scales on the BRIEF [23] were Working Memory and Plan/Organize, with nearly half of their sample exhibiting significant deficits [8]. Youth with epilepsy are at 3.5 times higher risk for BRIEF Working Memory and Shifting deficits and about 2.5 times higher risk for Initiation and Plan/Organize deficits compared to healthy controls [31]. While these studies suggest that Working Memory is likely the most significant deficit based on the BRIEF, studies have not corroborated these findings using performance-based measures (e.g., Delis Kaplan Executive Functioning System [32]) in tandem with parent-reported questionnaires. Further, research suggests equivocal findings regarding differences in EF based on epilepsy type [33–35].

The aims of the current study were to 1) identify the pattern of EF deficits in adolescents with epilepsy using a multimethod assessment approach (e.g., performance-based neuropsychological tests, NIH toolbox, and parent and self-reported questionnaires) and 2) identify which assessment tools are most sensitive to EF deficits in adolescents with epilepsy. We hypothesized that adolescents with epilepsy would have significant EF deficits for all measurement approaches. We also hypothesized that the BRIEF-Parent report would identify a higher proportion of EF deficits in adolescents with epilepsy compared to other measures, as it has greater ecological validity. The final exploratory aim was to examine differences on measures of EF by seizure type (e.g., localization-related, generalized, and unclassified).

2. Methods

2.1. Participants

Participants included adolescents with epilepsy seen at a large tertiary pediatric medical center within the Comprehensive Epilepsy Center. Participants were part of a larger neuroimaging study focused on identifying biomarkers of executive functioning in adolescents with epilepsy and healthy controls. Inclusion/exclusion criteria for adolescents with epilepsy included the following: 1) being 13–17 years of age, 2) English as the primary language, 3) meeting magnetic resonance imaging (MRI) safety criteria (e.g., no braces), 4) body mass index between the 5th and 99th percentile for age and sex, 5) no significant developmental disorders (e.g., Autism spectrum disorder), 6) no previous history of head trauma, 7) negative screening for pregnancy (verbal), 8) no symptomatic etiology or brain lesions detected on clinical MRI, and 9) no use of psychoactive medications, with the exception of stimulants for attention-deficit hyperactivity disorder (ADHD).

2.2. Measures

2.2.1. Wechsler Intelligence Scale for Children, 5th edition (WISC-V)/Wechsler Adult Intelligence Scale, 4th edition (WAIS-IV)

The Wechsler Intelligence Scale for Children, 5th edition (WISC-V) [36] and Wechsler Adult Intelligence Scale, 4th edition (WAIS-IV) [37] are measures of various domains of intellectual ability based on the youth's performance. The WISC-V measures domains in children and

adolescents, aged 6 to 16 years, while the WAIS-IV measures these in individuals aged 17 to 90 years. The two measures of intelligence were used based on the participant's age at the time of testing. The Digit Span and Picture Span subtests of the WISC-V and Digit Span and Arithmetic subtests of the WAIS-IV were utilized as measures of working memory. Raw scores for these subtests were converted to scaled scores to create the Working Memory Index (WMI). Scores <80 were considered as a significant deficit in working memory [36,37].

2.2.2. Delis-Kaplan Executive Functioning System (D-KEFS)

The Delis-Kaplan Executive Functioning System (D-KEFS) [32] is a reliable and valid measure of EF skills for individuals ages 8 through 89 years. The Trail Making (cognitive flexibility), Color-Word Interference (verbal inhibition), and Tower (planning and reasoning, impulsivity) subtests were used to measure various aspects of EF for each adolescent. Raw scores for each of the three subtests were converted to scaled scores normed for the participant's age. Lower scores indicated greater EF deficits and scores <4 were considered clinically impaired [32].

2.2.3. Test of Everyday Attention (TEA-Ch)

The Test of Everyday Attention (TEA-Ch) [38] is a measure of attentional and memory capacities for youth ages 6 to 15 years. In the current study, only participants less than 16 years of age completed the Code Transmission subtest. Raw scores (0–40) were converted to scaled scores based on the child's age and gender, with higher scores indicating greater attentional capacity and working memory. Scores <4 were considered clinically impaired [38].

2.2.4. NIH Toolbox

The NIH Toolbox [29,30] is a set of measures assessing cognitive, emotional, motor, and sensory function in individuals ages 3 to 85 years. It was designed to measure skills in a brief, easily administered, and more widely acceptable way offering options of administration online [39]. Dimensional Change Card Sorting (cognitive flexibility), Flanker Inhibitory Control and Attention (attention and inhibition), List Sorting (working memory), and Pattern Comparison (processing speed) subtests were administered via computer. Aged-normed scaled scores were generated as part of the NIH Toolbox website functionality. Higher scaled scores indicated greater functioning in the corresponding EF domains. Scores <2 standard deviations (e.g., scores <70) were considered to be indicative of clinical impairment [29,30].

2.2.5. Behavioral Rating Inventory of Executive Function (parent and self-report)

The 80-item, BRIEF-Parent report and 80-item BRIEF-Self Report were administered to assess executive functioning in school and home [23] environments. Both versions have eight scales, two broader indices (Behavioral Regulation and Metacognition), and the Global Executive Composite. Scales in common between the parent and self-report forms include the following: Inhibit, Shift, Emotional Control, Working Memory, Plan/Organize, Organization of Materials, and Monitor. The parent scale assesses Initiation whereas the self-report scale assesses Task Completion. Two additional subscales assessing Behavioral Shift and Cognitive Shift are also on the Self-report version. Raw scores were converted to T scores, with scores of 65 or higher classified as clinically significant.

2.2.6. Child Behavior Checklist (CBCL)

The Child Behavior Checklist (CBCL) [40] is a 113-item parent-reported measure of child behavioral and emotional functioning for youth ages 6 to 18 years. While a variety of subscales are calculated for this measure (e.g., Anxiety, Depression, Somatic Complaints, Social problems), the variable of interest was the Attention subscale. Raw scores were converted to T scores, with scores between 60 and 64 considered "At-risk" and scores ≥ 65 in the "Clinically Elevated" range.

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