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Intraindividual variability in attentional vigilance in children with epilepsy

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ABSTRACT

Attentional vigilance, the ability to maintain focus over time, is frequently impaired in childhood epilepsy. Typically, indices of Omissions (failure to detect a target) and Commissions (responding to a nontarget) are considered primary indices of attentional vigilance. Recently, the concept of intraindividual variability (IIV) has been identified as an important measure of attentional vigilance in several pediatric and adult clinical populations, but has not yet been systematically examined in childhood epilepsy. Here, we examined IIV on the Connors Continuous Performance Task-II (CCPT-II) for 144 newly diagnosed children with epilepsy (age 8–18 years) and a matched age group of healthy children (n = 82). Intraindividual variability showed a large effect size difference (d = 0.68) between groups. In addition, IIV significantly predicted both intellectual functioning and academic achievement. These findings support the utility of examining IIV in the assessment of attentional ability in childhood epilepsy.

1. Introduction

Impairment in attention is a common cognitive comorbidity in childhood onset epilepsy [1,2]. It is evident in several childhood seizure syndromes that, at the time of epilepsy diagnosis or shortly after, a negative impact is exerted on cognitive and social development, even when seizures are properly controlled [3–8]. Given the presence and impact of attentional difficulties in childhood epilepsy, it is important to identify and manage attentional problems.

However, the domain of attention is a complex and heterogeneous construct, and several component processes have been identified. Mirsky et al. proposed an influential model that identified four different attentional "elements": 1) *focus-execute*, the ability to select target information from groups and use it in enhanced procession, 2) *sustain*, the capacity to maintain focus and alertness over time, 3) *shift*, the ability to flexibly change focus in an adaptive manner, and 4) *encode*, a diverse process of attention that depends on the ability to receive and manipulate data, equivalent to working memory [9]. Mirsky's model has proven to be a useful framework from which to investigate attentional dysfunction in several clinical populations including childhood epilepsy [10].

Mirsky and Duncan added *stabilize* as a fifth attentional process to their model; the ability to maintain consistency and stability of attention while individuals are responding to target stimuli over time [10]. In childhood epilepsy, increased response variability has been reported for children with complex partial seizures (CPS), absence seizures, and benign rolandic epilepsy (BRE) [11–13]. However, these studies included children with diagnosed epilepsy for several years. As a result, it is difficult to disentangle the impact of several interrelated seizure-related factors (e.g., frequency of seizures, age of onset, antiepileptic drug (AED) use, comorbid psychiatric disorders). In addition, there is little currently known about the relationship between intraindividual variability (IIV) and performance on measures of intellectual functioning and performance in school.

The IIV, or response variability, is a measure of the consistency of an individual's response to a stimulus. More specifically, in this study, it is a measure of the consistency of response time to targets in a continuous performance test. Intraindividual variability is a useful tool in determining more subtle fluctuations of attention than mean response time. The objective of this study was to examine the performance of a group of children with recently diagnosed epilepsy on four commonly used indices of attentional ability: Omissions, Commissions, mean Hit RT, and IIV. We also examined the relationship between these indices and measures of intellectual functioning and academic achievement.

2. Material and methods

2.1. Participants

One hundred and forty-four children between the ages of 8 and 18 years with a recent diagnosis of epilepsy were recruited from pediatric

Abbreviations: IIV, intraindividual variability; CCPT-II, Conner's Continuous Performance Test-II; WASI-II, Wechsler Abbreviated Scale of Intelligence-Second Edition; WRAT-3, Wide-Range Achievement Test-3.

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neurology clinics at three midwestern medical centers. Inclusion criteria included a diagnosis of epilepsy within the past year (mean = 8.3 months, SD = 3.7), normal neurological examination, and normal clinical Magnetic Resonance Imaging (MRI). All children obtained a minimum Wechsler Abbreviated Scale of Intelligence-Second Edition (WASI-II) Full Scale Intelligence Quotient (IQ) of 70. These children did not have another diagnosed neurological disorder. Medical records were reviewed blind to cognitive testing by an independent board-certified pediatric neurologist to establish the epilepsy diagnosis and classification. The healthy control group (HC) was comprised of 82 first-degree cousins of the children with epilepsy between the ages of 8 to 18 years. Inclusion criteria included no history of seizures, no clinical diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD), no signs of neurological disease, and no loss of consciousness longer than 5 min.

2.2. Procedure and consent

Written informed consent was obtained from legal guardians of the children and adolescents in the study. Participants aged 18 years gave their own written informed consent, and participants age 8 to 17 years provided written informed assent. University of Wisconsin School of Medicine and Public Health provided approval to conduct this study through their health sciences institutional review board. After informed consent and assent was obtained, participants underwent neuropsychological testing while parents underwent clinical interviews and completed questionnaires about their child's developmental history. Medical information regarding participant's epilepsy and treatment was obtained after parent's signed release of information.

2.3. IQ and academic achievement

All participants were administered the Wide-Range Achievement Test-3 (WRAT-3) and the WASI-II. Both tests are commonly used in clinical and research with pediatric populations and have excellent psychometric properties [14]. The WRAT-3 subtests include reading, spelling, and arithmetic [14]. The WASI includes an abbreviated measure of Verbal and Performance IQ based on subtest scores on Block Design, Matrix Reasoning, Similarities, and Vocabulary [14].

2.4. Conner's Continuous Performance Test-II (CCPT-II)

The CCPT-II is considered a hallmark test of attentional vigilance with excellent discriminative and convergent validity, and has been used extensively in both research and clinical assessment of child and adult populations including children with epilepsy [14–16]. The CCPT-II is a computerized task lasting 14-minutes in duration which is divided into six subblocks of twenty trials with letters presented at varying speeds. Subjects are asked to press a computer key when any stimulus appears on the computer screen other than a specific symbol ('x'). Four variables of interest were selected: (1) *Omission errors*, *which* represent the failure to respond to nontargets (i.e., failure to respond to letters other than "x"), (2) *Commission errors*, *which* indicate targets that were responded to in error (i.e., respond to "x"), (3) *Standard hit rate reaction time* (Hit RT), a gauge of inattention when reaction time is slow and impulsivity when it is fast, and (4) *Variability* (IIV), which is calculated as the standard deviation of the standard error values for reaction times for each of the 18 subblocks.

2.5. Statistical analyses

Raw scores were converted to t-scores based on the CCPT-II standardization sample [14]. All distributions were examined for normality allowing for kurtosis. In cases where the assumption of normality was violated, a Mann–Whitney *U* test was used. First, independent between group *t*-tests were conducted to examine group differences for the four CCPT-II indices: errors of Omission, errors of Commission, IIV, and Hit RT. We also examined group differences on the Verbal (VIQ) and Performance (PIQ) sections of the WASI-II, and the three subtests of the WRAT (word recognition, spelling, and arithmetic). Subsequently, hierarchical multiple regression models were conducted with the IQ and academic measures serving as the dependent variable and the CCPT-II indices as predictor variables. In all the regression models, age at diagnosis (months), seizure syndrome (generalized, localized), and gender were entered on step one, and on step two each of the four CCPT-II variables were included in separate models. Of importance is the amount of increased variance produced by each of the CCPT-II indices after accounting for the seizure variables. In addition, we examined the relationship between the clinical seizure variables, age of diagnosis and epilepsy syndrome, and IIV. We did not include AED in these analyses because over 93% were being treated with a single AED, and only nine children were being treated with two or more AEDs.

3. Results

Table 1 provides descriptive demographic and clinical seizure characteristics for the epilepsy and healthy control groups (HC). No significant group differences for age, education, or gender (p's > 0.05) were found. The group with epilepsy performed significantly lower than HC on all measures of academic and intellectual functioning (p's < 0.001), however, performance was within the generally "average" range for both groups on all measures.

3.1. Group differences

Scores in Table 2 show that the group with epilepsy performed more poorly than HC on all CCPT-II measures examined: Omissions ($z = 2.36$, $p < 0.01$, $d = 0.41$), Hit RT ($t = 3.62$, $p < 0.001$, $d = 0.51$), and IIV ($t = 4.93$, $p < 0.001$, $d = 0.68$), and Commissions approached significance ($t = 1.90$, $p = 0.06$, $d = 0.26$).

3.2. Multiple regression analysis

Findings examining the relationship between the CCPT-II indices and WASI IQ and academic achievement are presented in Table 3. In all analyses, the demographic and seizure variables were entered in a single block followed by entry of one of the four CCPT-II indices resulting in a total of four distinct models. Similar analyses were conducted including ADHD diagnosis as a predictor variable on block, and results were similar to findings presented below. When more than one CCPT-II score added a significant increase in predicted variance, a

Table 1
Demographic and clinical seizure variables for children with recent onset epilepsy and healthy controls.

Demographic Variable	Epilepsy N = 144 M (SD)	Healthy controls N = 82 M (SD)	t-Score	p-Value
Age (years)	11.91 (3.12)	12.20 (2.93)	0.68	0.50
Education (grade)	6.28 (3.12)	6.51 (2.84)	0.55	0.59
Gender (M/F)	68/76	38/44		1.00
Full scale IQ	102.06 (13.76)	108.27 (11.56)	3.45	<0.01
Performance IQ	100.13 (14.07)	107.15 (11.85)	3.81	<0.001
Verbal IQ	103.23 (14.31)	107.62 (12.98)	2.29	0.02
Word recognition	101.25 (12.46)	104.55 (10.70)	2.01	0.05
Spelling	100.63 (13.15)	104.79 (12.31)	2.33	0.02
Arithmetic	97.10 (12.96)	107.20 (12.17)	5.76	<0.001
Localized/generalized syndrome	70/69			
Duration of illness (months)	8.33 (3.74)			
Age of diagnosis (months)	140.14 (37.52)			
Number of medications (multiple/one or less)	9/135			