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Differentiation of Attention-Related Problems in Childhood Absence Epilepsy

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Abstract

The current study examined the specific types of attention-related problems CAE children experience and the role of disease factors on the development of attention-related problems. Thirty-eight subjects with CAE and 46 healthy controls, ages 6 to 16 participated in the study. The Behavior Assessment System for Children (BASC) was completed by parents, and the Attention Problems and Hyperactivity subscales were used to characterize CAE children's problems. Item analysis within the subscales revealed that CAE children demonstrated higher rates of hyperactive (overactivity and fidgetiness) and inattentive (forgetfulness and distractibility) problems, and required more supervision. Within CAE analyses revealed that those who were actively having seizures were more impatient and those with a longer duration of illness were less proficient in completing homework. Children with CAE are at risk for certain inattentive and hyperactive problems, which can differ depending on duration of illness and active seizure status.

Keywords

Childhood Absence Epilepsy; Attention; Hyperactivity; Seizures; Behavior

Introduction

Childhood Absence Epilepsy (CAE) accounts for 10 to 15 percent of pediatric epilepsy diagnoses [1]. Prior studies point toward the presence of interictal attention problems, which can interfere with academic performance and daily functioning [2–4]. The current study

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investigates attention-related problems that might differentiate children with CAE from their healthy peers, and the role of disease on attention-related problems in this group.

Williams et al. [5] investigated the ADDES-HV sensitivity in correctly classifying children with seizures compared to ADHD. Two items differentiated the groups; remain on task and complete homework, showing 79% sensitivity and 92% specificity however both groups shared staring behaviors. In another study, Williams et al. [6] examined the prevalence of ADHD symptoms in newly diagnosed pediatric epilepsy using the ADDES-HV, and compared changes following attainment of seizure control. Nineteen percent of their sample met clinical diagnostic criteria for ADHD, combined type, based on parent report. They also found the severity of inattention or hyperactivity/impulsivity symptoms was unchanged despite good seizure control on medication. Further, there was no difference in symptom severity based on seizure type or medication prescribed. Despite unequivocal data of higher incidence of ADHD symptoms in pediatric epilepsy including CAE, to our knowledge, no prospective study has identified the specific symptom characteristics of inattention and hyperactivity in CAE that might differentiate them from healthy controls.

Within the literature, findings are mixed as to whether interictal attention problems are a consequence of seizures or are part of the disease [7–8]. Clarification of the role of disease factors on attention-related problems will help improve identification of behavior problems, leading to earlier diagnoses and/or accommodations in the academic setting.

The current study investigates attention and hyperactive symptoms in children with CAE, testing the hypotheses: (1) CAE would have higher report of attention and hyperactive problems compared to healthy controls, and (2) those with CAE having a longer duration of illness, younger age of onset, and active seizures would have higher report of problems.

Method

Subjects

The sample consisted of 38 CAE and 46 healthy controls (HC), ages 6 to 16. Following Institutional Review Board approval, CAE were recruited from area neurologists and electroencephalographic laboratories, and HC from postings at university and in newspapers. Subjects with a history of psychiatric (including ADHD) or medical (including other epilepsies) disease were excluded. CAE diagnosis was confirmed by the principal investigator.

Procedure

The study was staffed by trained bachelor and/or doctoral research assistants. Subjects and parents provided informed consent and assent.

Parents completed a series of forms including the *Seizure History Form* developed by study investigators. They reported on Age of Diagnosis and Duration of Illness was calculated (age of diagnosis – current age). Current Seizure Status was coded categorically as controlled (no seizures for six months) or active (seizure occurrence). Current medication was obtained. Attention-related symptoms were identified with the Behavior Assessment System for Children [9] (BASC) Attention Problems (ATT) and Hyperactivity (HYP) subscales and their items. Subscale scores are continuous and subscale items are ordinal variables. Socioeconomic status (SES) was obtained using the *Hollingshead Four-Factor Scale* [10]. Study children were administered the two-subtest *Wechsler Abbreviated Scale of Intelligence* [11] (WASI) to obtain an estimate of IQ.

Data Analyses

Data was analyzed in SPSS 17.0 (www.spss.com). Frequency and descriptive statistics are provided. Chi-square and Analysis of Variance (ANOVA) were used to assess for potential confounds of age, gender, SES, or IQ. Since there were significant group differences in age and IQ, these were used as covariates during hypotheses testing. Statistics were performed to determine group differences on ATT and HYP subscales and items. Discriminant function analysis were used to determine sensitivity and specificity of ATT and HYP subscale items in classifying the two groups, using significant items at the bivariate level.

Analyses within the CAE group that assessed Seizure Status were performed using ANOVA or Mann-Whitney test. Pearson's and Spearman-rank correlations assessed the relationship between Duration of Illness and Age of Disease Onset with subscales and items.

Results

Descriptive Statistics

Sample characteristics are presented in Table 1. The majority of subjects, CAE and HC were female, had middle or higher SES. There was a significant mean difference between the groups in age and estimated IQ, although both IQ group means fall within the average range.

Within the CAE group, there was a mean Age of Seizure Onset of approximately 7-years, ranging from 2 to 13. The Duration of Illness was approximately 3-years, and ranged from 0 to 11 years, with 13% of the sample diagnosed less than one year prior to the assessment. Most subjects were on monotherapy (66%) and approximately 42% had been seizure free for at least six months. Seven subjects were not taking medication. No differences were found between subjects on monotherapy, polytherapy, and no medication therapy, and no individual medication effects within monotherapy subjects were present, although it should be noted that our sample size was not sufficiently large to directly examine medication effects as in recent multicenter studies [12]. The remaining subjects had seizures ranging from > 1 to 20 per day.

Hypothesis Testing

ANOVA revealed significant differences between CAE and HC on the ATT subscale, which remain after covarying for age and IQ (see Table 2 and 3). The HYP subscale showed significant mean differences between the groups at the bivariate level, but lost significance after covarying. CAE had higher means compared to HC.

Item-analysis for the ATT subscale revealed group differences on A1 that lost significance after controlling for age and IQ, and A5 that remains significant following covariate analysis. From the HYP subscale, there were group differences at the bivariate level on the following items: H1, H5, and H7. H1 remains significant after covarying. Higher means were found in the CAE group.

Discriminant function classification statistics were used to determine sensitivity and specificity of ATT and HYP items in differentiating the CAE and HC groups. A1 and A5 were significant as a single function ($X^2_{(df = 2, 76)} = 14.8$, $p = 0.001$). Their classification of CAE and HC had a sensitivity of 58.3% and specificity 76.2%. H1, H5, and H7 were also significant as a single function ($X^2_{(df = 3, 76)} = 10.9$, $p = 0.01$). Their group classification of CAE and HC had a comparable sensitivity of 51.4% and specificity of 73.8%.

Within the CAE group, analyses were performed to determine attention and hyperactive symptoms that may be related to disease factors. ANOVA revealed no significant differences between the children that were well-controlled or actively having seizures and the ATT

subscale ($F_{(df = 1, 15)} = 0.37$, $p = 0.55$), HYP subscale ($F_{(df = 1, 15)} = 2.36$, $p = 0.15$), age ($F_{(df = 1, 15)} = 0.44$, $p = 0.52$), and IQ ($F_{(df = 1, 15)} = 0.41$, $p = 0.53$). Similarly, no difference on Mann-Whitney test between this disease factor and ATT items ($p > 0.05$); one HYP item, H4 yielded significant results ($U_{(df = 1, 19)} = 20.50$, $p = 0.03$).

Using Pearson correlation, no significant relationships between Duration of Illness and Age of Disease Onset with subscales, ATT and HYP were found ($p > 0.05$). Spearman-rank correlations with these disease factors and ATT items revealed a significant negative relationship with Duration of Illness and A4 ($r = -0.32$, $p = 0.05$), reflecting that lengthier Duration of Illness is associated with less proficiency with homework (reverse score item). Age of Disease Onset and A1 (forgets things) approached significance ($r = 0.30$, $p = 0.08$). With the HYP items, Age of Disease Onset and H6 approached significance ($r = -0.30$, $p = 0.07$).

Discussion

The current study supports previous literature suggesting that children with CAE are at greater risk for attention-related problems [2–4,13] and contributes new information by identifying real-world symptoms (forgetfulness and distractibility) that may differentiate CAE children from their peer counterparts. An interesting finding at the bivariate level is that CAE children are at increased risk for hyperactive symptoms (overactivity and fidgetiness). While this relationship did not remain significant after controlling for IQ, it does provide direction for future studies that have increased sample size and may give rise to CAE as a potential risk factor for additional behavior problems associated with hyperactivity such as impulsivity and risk taking. In addition, impatience and less homework proficiency show a trend association with lengthier and active disease. This preliminary information will enhance early identification of behavior problems, and thereby influence the time and course of intervention and treatment.

Study results also provide insight into an ongoing debate regarding whether behavior problems are a part of pediatric epilepsy syndromes or develop as a consequence of disease factors [8]. This provides preliminary evidence for consideration of a multidimensional perspective, as inattentive and hyperactive symptoms may be part of the disease (CAE), while a differing pattern of symptoms could evolve as a consequence of poor disease management.

A larger sample size would improve the study's ability to detect differences between the CAE and healthy controls, as there were a number of attention-related symptoms that approached significance. A greater sample size could also increase the number of subjects falling in each seizure subgroup assisting in better characterization of disease. It would be important to explore the differences in behavioral presentation of CAE and other pediatric epilepsies, as well as ADHD in future studies. Finally, a semi-structured interview with the parent and child, as well as collaborative information from a teacher via completion of a teacher report scale would be a useful tool to clarify attention-related deficits in CAE. The measure used to assess behavior symptoms (BASC) in the current study may be limited by parent report, which can be susceptible to over or under-reporting. In addition, while the BASC provides subscales that assess inattention and hyperactivity, some items have limited specificity, thus the scale does not serve as an independent ADHD diagnostic tool.

New understandings of absence seizure pathophysiology complements the current work, as the cortical-subcortical networks identified during seizures are associated with attention [14]. Recent findings reject the traditional assumption that CAE affects primarily subcortical structures, and propose that seizures disrupt anterior interhemispheric regions in the frontal cortex, cingulate, and thalamus [14]. Future research focusing on structural and functional

neuroanatomical differences in conjunction with behavior measures may help better identify the etiology of attention-related problems in CAE. By acknowledging that inattentive and hyperactive symptoms are part of the CAE behavior spectrum, irrespective of disease severity, practitioners can anticipate effects on cognitive development and advocate for academic support services.

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Table 1

Demographic Data for the Study Subjects

	Group			
Sociodemographic Variables	**CAE**	**Control**	**Statistic**	**P**
N, n (%)	38 (46.3)	44 (53.7)		
Age, M ± SD	10.5 ± 2.3	11.8 ± 2.3	4.37	0.04 *a*
WASI Full-Scale est. IQ, M ± SD	100.8 ± 17.2	111.2 ± 16.4	5.02	0.03 *a*
Gender, n (%)			1.54	0.22
Male	13 (34.2)	21 (47.7)		
Female	25 (65.8)	23 (52.3)		
SES, n (%)			4.59	0.10
Low	1 (2.6)	1 (2.3)		
Middle	18 (47.4)	11 (25.0)		
Middle-High	19 (50.0)	32 (72.7)		
Seizure Variables				
Age of Disease Onset, M ± SD *b*	6.9 ± 2.8	---		
Duration of Illness, M ± SD *b*	3.4 ± 2.7	---		
Current Seizure Status, n (%) *c*				
Controlled	8 (42.1)	---		
Active (range daily – monthly)	11 (57.9)	---		
Antiepileptic Medication, n (%)				
None	5 (13.2)	---		
Monotherapy	24 (63.2)	---		
Duotherapy	8 (21.1)	---		
Polytherapy (3 or more)	1 (2.6	---		

a p = .05

b n = 37

c n = 19

Categorical data has X^2 statistic and Continuous data has F-statistic

Table 2

Mean Differences between CAE and Healthy Controls on the BASC items

	Group M ± SD		Bivariate			Covariate		
BASC Subscales	**CAE**	**Control**	**df**	**Statistic**	**P**	**df**	**Statistic**	**P**
Attention Problems	58.2 ± 12.7	48.8 ± 9.3	1	9.04	0.004 *b*	1	8.68	0.005 *b*
A1	2.5 ± 0.8	2.0 ± 0.7	1	485.50	0.001 *c*	1	70.92	0.31
A2	2.8 ± 1.0	2.9 ± 0.9	1	697.50	0.41			
A3	2.9 ± 0.8	3.0 ± 0.8	1	713.00	0.50			
A4	2.4 ± 1.2	2.5 ± 0.9	1	699.00	0.42			
A5	2.6 ± 0.9	1.9 ± 0.7	1	424.50	0.0001 *c*	1	375.07	0.0001 *c*
Hyperactivity	50.8 ± 12.2	44.6 ± 9.7	1	4.05	0.05 *a*	1	2.27	0.14
H1	1.7 ± 0.9	1.2 ± 0.4	1	548.00	0.006 *b*	1	602.25	0.0001 *c*
H2	1.4 ± 0.6	1.2 ± 0.5	1	668.00	0.17			
H3	1.7 ± 0.8	1.4 ± 0.5	1	645.00	0.13			
H4	1.7 ± 0.8	1.8 ± 0.7	1	694.50	0.37			
H5	1.7 ± 0.7	1.4 ± 0.7	1	559.50	0.01 *b*	1	0.15	0.70
H6	2.1 ± 0.6	1.9 ± 0.7	1	673.00	0.25			
H7	1.9 ± 0.8	1.5 ± 0.8	1	560.00	0.02 *a*	1	0.96	0.33

a p = .05

b p = .01

c p = .001

Categorical data has U statistic and continuous data has F-statistic.

Covariate analysis included age and estimated IQ in the model.

Table 3

Items corresponding to the Attention and Hyperactivity subscales from the BASC.

Hyperactivity (HYP)	Attention Problems (ATT)
H1 Needs too much supervision	A1 Forgets things
H2 Is restless during movies	A2 Completes work on time *
H3 Throws tantrums	A3 Listens to directions *
H4 Cannot wait to take turn	A4 Completes homework from start to finish *
H5 Is overly active	A5 Is easily distracted
H6 Interrupts others when they are speaking	
H7 Fiddles with things while at meals	

* reverse score item