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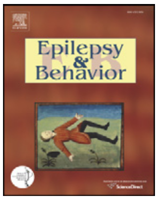

The social competence and behavioral problem substrate of new- and recent-onset childhood epilepsy

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ABSTRACT

This study examined patterns of syndrome-specific problems in behavior and competence in children with new- or recent-onset epilepsy compared with healthy controls. Research participants consisted of 205 children aged 8–18, including youth with recent-onset epilepsy (n = 125, 64 localization-related epilepsy [LRE] and 61 idiopathic generalized epilepsy [IGE]) and healthy first-degree cousin controls (n = 80). Parents completed the Child Behavior Checklist for children aged 6–18 (CBCL/6–18) from the Achenbach System of Empirically Based Assessment (ASEBA). Dependent variables included Total Competence, Total Problems, Total Internalizing, Total Externalizing, and Other Problems scales. Comparisons of children with LRE and IGE with healthy controls were examined followed by comparisons of healthy controls with those having specific epilepsy syndromes of LRE (BECTS, Frontal/Temporal Lobe, and Focal NOS) and IGE (Absence, Juvenile Myoclonic, and IGE NOS). Children with LRE and/or IGE differed significantly ($p < 0.05$) from healthy controls, but did not differ from each other, across measures of behavior (Total Problems, Total Internalizing, Total Externalizing, and Other Problems including Thought and Attention Problems) or competence (Total Competence including School and Social). Similarly, children with specific syndromes of LRE and IGE differed significantly ($p < 0.05$) from controls across measures of behavior (Total Problems, Total Internalizing, and Other Problems including Attention Problems) and competence (Total Competence including School). Only on the Thought Problems scale were there syndrome differences. In conclusion, children with recent-onset epilepsy present with significant behavioral problems and lower competence compared with controls, with little syndrome specificity whether defined broadly (LRE and IGE) or narrowly (specific syndromes of LRE and IGE).

1. Introduction

In the pediatric epilepsy literature, the Child Behavior Checklist (CBCL) has been an important and frequently utilized measure to characterize the social competence and behavioral problems exhibited by youth with epilepsy [1]. An extensive body of CBCL research has focused on comparing children with chronic epilepsy with normally developing children or youth with other neurological or nonneurological disorders in order to determine the degree of behavioral risk associated with epilepsy and its associated clinical seizure features (e.g., duration, seizure control, and severity), characterize the effects of living and dealing with a chronic illness, and examine the impact of other potential etiological factors (e.g., family integrity and family aggregation of behavioral problems).

A small number of investigations have examined children with epilepsy at or near the time of diagnosis [2–9]. This is a time during which the effects of chronic epilepsy, potential adverse social effects of epilepsy, and other complicating etiological effects are minimized. The majority of these investigations have detected increased behavioral problems in youth with new-onset epilepsy whether the observations are provided by parents [2,7] or teachers [2,5], suggesting that factors other than recurrent seizures, medications, and other epilepsy clinical variables underlie these complications.

The degree to which specific epilepsy syndromes are associated with the relative risk of problems in behavioral and social competence in children with new- or recent-onset epilepsy has not been comprehensively examined and represents the focus of the current investigation. In a recent study examining cognition in children with new- or recent-onset epilepsy across syndromes, we found a considerable degree of shared cognitive abnormality, despite the fact that the underlying pathophysiology of the idiopathic localization-related (LRE) and generalized epilepsies (IGE) is very distinct. Unique syndrome-specific contributions were identified such as dysexecutive function in IGE and language function in LRE, but these effects were comparatively minor relative to the shared cognitive morbidity observed across syndrome groupings [10]. Here, we undertake a companion investigation focusing on behavioral status as measured by the CBCL, comparing children first by broad

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syndrome groupings (LRE and IGE) followed by comparisons of children with specific syndromes of LRE and IGE with healthy controls. We hypothesized that, similar to the cognitive effects reported previously, there will be more similarities than differences in the pattern of identified behavioral complications, with relatively minor variance associated with specific LRE and IGE syndromes.

2. Methods

2.1. Participants

Research participants consisted of 205 children aged 8–18, including youth with recent-onset epilepsy ($n = 125$) and healthy first-degree cousin controls ($n = 80$). Participants attended regular schools with the exception of 6 (4 controls and 2 with epilepsy) who were homeschooled. Children with epilepsy were recruited from pediatric neurology clinics at three Midwestern medical centers (University of Wisconsin—Madison, Marshfield Clinic, Dean Clinic) and met the following inclusion criteria: (i) diagnosis of epilepsy within the past 12 months, (ii) no other developmental disabilities (e.g., intellectual disability or autism), (iii) no other neurological disorder, and (iv) normal clinical MRI. All children entered the study with active epilepsy diagnosed by their treating pediatric neurologists and confirmed by medical record review of the research study pediatric neurologist. We did not exclude children on the basis of psychiatric comorbidities (including ADHD) or learning disabilities. We did, however, exclude children with global intellectual disability and/or autism. In general, we tried to stay true to the concept of "epilepsy only" as defined broadly in the literature by normal neurological exams, intelligence, and attendance at regular schools [2].

Each child's epilepsy syndrome was defined in a research consensus meeting by the research pediatric neurologist who reviewed all available clinical data (e.g., seizure description and phenomenology, EEG, clinical imaging, and neurodevelopmental history) while blinded to all research cognitive, behavioral, and neuroimaging data. Two levels of epilepsy syndrome classification were undertaken and confirmed by two board-certified pediatric neurologists who were blinded to all research data. Children with epilepsy were first classified into broad syndrome groups of IGE and LRE, followed by classification into specific IGE (juvenile myoclonic epilepsy [JME], childhood and juvenile absence [Absence], and IGE not otherwise specified [NOS]) and LRE (benign epilepsy with centrotemporal spikes [BECTS], temporal lobe epilepsy [TLE], frontal lobe epilepsy [FLE], and focal epilepsy NOS). The groups with temporal and frontal lobe syndrome were combined into one group (FLE/TLE) because of their small sample size, lack of ictal confirmation of true frontal versus temporal lobe onset, and the fact that group comparisons revealed no significant CBCL differences between them.

First-degree cousins were used as controls, and exclusion criteria were as follows: (i) history of any initial precipitating insult (e.g., simple or complex febrile seizures, cerebral infections, or perinatal stroke); (ii) any seizure or seizure-like episode; (iii) diagnosed neurological disease; (iv) loss of consciousness for more than 5 min; and (v) other family history of a first-degree relatives with epilepsy or febrile convulsions. We used cousin controls rather than siblings or other potential control groups for the following reasons: (i) first-degree cousins are more genetically distant from the participants with epilepsy and, thus, less predisposed than siblings to shared genetic factors that may contribute to anomalies in brain structure and cognition; (ii) a greater number of first-degree cousins are available than siblings in the target age range; and (iii) the family link was anticipated to facilitate participant recruitment and especially retention over time (which is our intent) compared with more general control populations (e.g., unrelated schoolmates). Demographic characteristics of the participants are provided in Table 1.

This study was reviewed and approved by the Institutional Review Boards of all institutions. On the day of study participation, families and children gave informed consent and assent, and all procedures were consistent with the Declaration of Helsinki (1991).

Table 1
Sample demographics.

	Group with LRE	Group with IGE	Control group
Group N	64	61	80
Age in years	11.35 (2.62)	13.34 (3.43)	12.69 (3.16)
Gender	36 (34.0%) male	29 (27.4%) male	41 (51.3%) male
Grade	5.30 (2.58)	7.20 (3.47)	6.56 (3.10)
Full Scale IQ	101.80 (12.61)	101.51 (14.28)	107.65 (12.01)
Age of onset in years	10.42 (2.68)	12.53 (3.56)	–
0 AED/>1 AED	19/45	1/60	–

Note. LRE (31—BECTS, 18—FLE/TLE, and 15—Focal NOS); IGE (32—JME, 16—Absence, and 13—IGE NOS).

2.2. Procedures

As part of their study visit, the children completed a comprehensive battery of neuropsychological tests, questionnaires, a clinical interview, and an MRI. Each participating child was accompanied to their study visit by a parent who underwent a clinical interview and completed questionnaires characterizing the child's gestation, delivery, neurodevelopment, and seizure history. All pertinent medical records were obtained after signed release of information was obtained from the parent.

Parents completed the Child Behavior Checklist for children aged 6–18 (CBCL/6–18) from the Achenbach System of Empirically Based Assessment (ASEBA) [1]. The dependent variables of interest included the following: a) overall CBCL/6–18 summary scales (Total Competence, Total Problems, Internalizing Problems, and Externalizing Problems); b) CBCL/6–18 Total Competence subscales (Activities, Social Competence, and School Competence); and c) the "Other Problems" scales which are part of the configuration of Total Problems and, therefore, appropriate for examination in the attempt to understand the source of the Total Problems effects.

The time from diagnosis to CBCL completion was approximately 7 months (LRE = 7.1 months and IGE = 7.5 months). The time from first seizure leading to the onset of the medical evaluations for epilepsy to CBCL completion was of course a little longer (LRE = 11.1 months and IGE = 9.9 months). The CBCL was completed by the parent accompanying the child to the study visit. For information pertaining to the validity and reliability of the CBCL, please visit: http://www.aseba.org/ordering/reliabilityvalidity.html.

2.3. Data analyses

Analyses were conducted using IBM SPSS Statistics Software 21.0. The initial focus of our analyses was the effect of group (LRE, IGE, and controls) on CBCL summary scales (Total Problems and Total Competence). Significant effects for these summary scales led to subsequent examination of group effects for pertinent component scales (e.g., Externalizing Problems and Internalizing Problems for Total Problems). This analytic plan was pursued using MANOVA and follow-up ANOVA with post hoc Tukey's tests to adjust for multiple pairwise comparisons. The remaining scales (Social, Thought, and Attention Problems), referred to collectively as "Other Problems", underwent similar analysis. For those analyses where there was a significant syndrome effect, a subsequent set of analyses examined the effects of specific syndromes of LRE and IGE (i.e., BECTS, FLE/TLE, Focal NOS, Absence, JME, and IGE NOS) and control groups. Using this analytic approach, we computed a total of 8 MANOVAs (4 examining IGE versus LRE effects and 4 examining specific IGE/LRE syndromes) with an adjusted overall p-value (.05/8 or 0.006) for MANOVAs as well as use of Tukey's tests (with adjusted family-wise error) for multiple pairwise comparisons.