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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).

Keywords

Epilepsy; Children; Behavior; CBCL

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 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).

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.

Finally, to provide information regarding the potential clinical relevance of the results, we examined the distribution of scores indicating "at-risk" or "clinical" status defined as a T-score ≥ 65 for the behavioral problem scales and T-score ≤ 35 for the competence scales.

3. Results

Fig. 1 provides an overall schematic summary of the results for the LRE, IGE, and control comparisons, while Supplemental Fig. 1 provides a complementary schematic summary of the results for the specific LRE and IGE syndrome and control group comparisons. Fig. 2 provides a schematic summary of the mean CBCL scale scores for the groups with LRE and IGE and the controls, while Supplemental Fig. 2 provides a similar schematic summary of the mean CBCL scale scores for the groups with specific LRE and IGE syndromes and the controls. Supplemental Table 1 provides the mean CBCL scaled scores for the groups with LRE and IGE and the controls, while Supplemental Table 2 provides mean CBCL scaled scores for the groups with specific LRE and IGE syndromes and the controls.

3.1. LRE and IGE

3.1.1. Total Problems and Total Competence—Multivariate analysis of variance for Total Problems and Total Competence yielded a significant overall main effect, $F(4,398) = 6.78, p < 0.001$, partial $\eta^2 = 0.64$. Significant group differences were found for both Total Competence, $F(2,200) = 6.88, p = 0.001$, and Total Problems, $F(2,200) = 12.0, p < 0.001$. Group means are illustrated in Fig. 2 with means and standard deviations listed in Supplemental Table 1. Post hoc analysis revealed that both the groups with LRE and IGE had significantly lower Total Competence and significantly higher Total Problems scores compared with the controls, $p < 0.05$, with no significant LRE versus IGE differences for Total Competence and Total Problems.

3.1.2. Total Problems subscales—Multivariate analysis of variance for the component scales of Total Problems (Internalizing Problems and Externalizing Problems) yielded a significant overall main effect, $F(4,402) = 6.14, p < 0.001$, partial $\eta^2 = 0.58$. Follow-up ANOVAs showed significant group differences for both scales: Internalizing Problems,

$F(2,200) = 12.61, p < 0.001$ and Externalizing Problems, $F(2,200) = 4.83, p = 0.009$. Group means are shown in Fig. 2, and means and standard deviations are provided in Supplemental Table 1. Post hoc comparisons revealed significantly higher Internalizing and Externalizing Problems scores for the groups with LRE and IGE than for the controls, $p < 0.05$, with no LRE versus IGE differences for either scale.

3.1.3. Total Competence subscales—Multivariate analysis of variance for Total Competence scales (Activities, Social and School Competence) yielded a significant overall main effect, $F(6,396) = 5.27, p < 0.001$, partial $\eta^2 = 0.74$. Follow-up ANOVAs yielded significant group differences for Social, $F(2,200) = 3.66, p < 0.05$, and School Competence, $F(2,200) = 14.81, p < 0.001$, but not for Activities. Significant mean group differences are summarized in Fig. 2 and Supplemental Table 1. Post hoc group comparisons revealed significantly lower Social Competence for the group with IGE than for the controls, $p < 0.05$, but no significant differences between groups with LRE and IGE or between the group with LRE and the controls. Post hoc comparisons for School Competence showed significantly lower scores for both groups with LRE and IGE compared with controls, $p < 0.001$, with no significant LRE versus IGE differences.

3.1.4. Other Problems scales—Multivariate analysis of variance for “Other Problems” (Social, Thought, and Attention Problems scales) yielded a significant overall main effect, $F(6,400) = 4.30, p < 0.001$, partial $\eta^2 = 0.06$. Follow-up ANOVAs showed significant group differences for both Thought Problems, $F(2,202) = 8.91, p < 0.001$, and Attention Problems, $F(2,202) = 10.1, p < 0.001$ but not for Social Problems. Group means and standard deviations are summarized in Fig. 2 and Supplemental Table 1. Post hoc comparisons revealed that both groups with LRE and IGE had significantly more Thought and Attention Problems compared with the control group ($p = 0.001$), with no significant LRE versus IGE differences on Thought and Attention Problems.

3.2. Specific syndromes of LRE and IGE

3.2.1. Total Problems and Total Competence—Participants with specific LRE (BECTS, FLE/TLE, and Focal NOS) and IGE (JME, Absence, and IGE NOS) syndromes were compared with controls. Multivariate analysis of variance yielded a significant overall main effect, $F(12,390) = 3.20, p < 0.001$, partial $\eta^2 = 0.09$. Follow-up ANOVAs revealed significant group differences for both Total Problems, $F(6,196) = 5.5, p < 0.001$, and Total Competence, $F(6,196) = 3.1, p < 0.01$. Post hoc comparisons revealed significant group differences with lower Total Problems scores for controls compared with groups having JME ($p < 0.01$), Absence ($p = 0.01$), and FLE/TLE ($p < 0.01$). For Total Competence, there was a significant group difference with higher scores for controls compared with the group with JME ($p = 0.05$). Group means and standard deviations are illustrated in Supplemental Fig. 2 and Supplemental Table 2.

3.2.2. Total Problems subscales—Participants with specific LRE (BECTS, FLE/TLE, and Focal NOS) and IGE (JME, Absence, and IGE NOS) syndromes were compared with controls. Multivariate analysis of variance yielded a significant overall main effect, $F(12,394) = 3.29, p < 0.001$, partial $\eta^2 = 0.09$. Follow-up ANOVAs revealed significant group differences for both Internalizing Problems, $F(6,198) = 5.54, p < 0.001$, and Externalizing Problems, $F(6,198) = 3.2, p = 0.005$. Post hoc comparisons revealed no significant pairwise group differences for Externalizing Problems using the adjusted p -value for multiple corrections. For Internalizing Problems, there were significant mean differences between controls and the group with JME ($p < 0.05$), Absence ($p < 0.001$), FLE/TLE ($p = 0.010$), and Focal NOS ($p < 0.05$). In all cases, the controls exhibited lower (fewer problems) scores. There were no significant differences between any of the groups with

specific syndromes. Group means and standard deviations are illustrated in Supplemental Fig. 2 and Supplemental Table 2.

3.2.3. Total Competence subscales—Multivariate analysis of variance yielded a significant overall main effect, $F(12,390) = 2.98$, $p = 0.001$, partial $\eta^2 = 0.84$, and follow-up ANOVA revealed a significant group effect for School Competence $F(6,196) = 5.28$ ($p < 0.001$) but not for Social Competence. Post hoc comparisons for School Competence revealed significantly higher scores for the controls compared with the groups having BECTS ($p = 0.002$), JME ($p = 0.009$), Absence ($p < 0.05$), and Focal NOS ($p = 0.008$). There were no significant differences between any of the groups with specific syndromes. Group means and standard deviations are illustrated in Supplemental Fig. 2 and Supplemental Table 2.

3.2.4. “Other Problems” scales—Multivariate analysis of variance for Thought and Attention Problems yielded a significant overall effect, $F(12,394) = 3.54$, $p < 0.001$, $\eta^2 = 0.10$. Follow-up ANOVAs showed significant group differences for both Thought Problems, $F(6,198) = 6.24$, $p < 0.001$, and Attention Problems, $F(6,198) = 4.73$, $p < 0.001$. Post hoc comparisons for Thought Problems showed significant group differences between controls and FLE/TLE, $p = 0.002$, and JME, $p < 0.001$, groups, with the controls exhibiting lower (fewer problems) scores. There were two syndrome-specific differences with the group with IGE NOS showing lower scores compared with the groups with JME, $p = 0.007$, and FLE/TLE, $p < 0.05$. For Attention Problems, significant group differences were found between the controls and the groups with JME, $p < 0.001$, and FLE/TLE, $p = 0.013$, with the controls showing lower scores. There were no significant differences between any of the groups with specific syndromes. Group means and standard deviations are illustrated in Supplemental Fig. 2 and Supplemental Table 2.

Significantly more children with epilepsy were in the “at-risk” or “clinical” range compared with controls across the main summary scales of Total Competence ($p < 0.001$) and Total Problems ($p = 0.034$). Across specific CBCL scales, the same pattern was evident on the following scales: School Competence ($p < 0.01$), Withdrawn/Depressed ($p < 0.001$), Somatic Complaints ($p = 0.001$), Thought Problems ($p = 0.002$), and Attention Problems ($p = 0.002$).

4. Discussion

Consistent with the small number of published papers examining CBCL performance in youth with new-onset epilepsy (e.g., [2,5,7]), significantly more behavioral problems and lower social competence scores were observed in the children with epilepsy compared with healthy controls. Specifically, both the groups with LRE and IGE exhibited significantly worse scores compared with control participants, with no LRE versus IGE differences, across 7 of 10 CBCL scales (Total Problems, Total Competence, Total Internalizing, Total Externalizing, School Competence, Thought Problems, and Attention Problems). On 2 of the 10 scales, the groups with LRE and IGE did not differ from controls or each other (Activities and Social Competence). The only dissociation between the groups with LRE and IGE was found for Social Competence, where only the group with IGE was different from controls but not LRE. Therefore, while there was evidence of more parent-reported behavioral and competence concerns in the children with new-onset epilepsy, there was minimal evidence of syndrome-specific behavioral differences.

Syndrome specificity of parent-reported behavioral issues was further investigated by comparison of specific syndromes of LRE (BECTS, FLE/TLE, and Focal NOS) and IGE (JME, Absence, and IGE NOS). Across 5 of the 6 behavioral measures examined

(Internalizing, Externalizing, School Competence, Social Competence, and Attention Problems), there were no unique specific syndrome effects. On the Thought Problems scale, there were significant specific syndrome differences with the group with IGE NOS exhibiting lower scores compared with the groups with JME and FLE/TLE.

In summary, the behavioral differences identified here appear to be largely independent of epilepsy syndrome whether defined broadly (IGE versus LRE) or narrowly by specific syndromes of LRE and IGE, suggesting that behavioral and competence complications do not necessarily respect traditional syndrome groupings in children with new- or recent-onset epilepsy. Overall, there appears to be more shared than syndrome-specific behavioral findings—at least at the level of behavioral analysis provided by the CBCL. This pattern of results is similar to the neuropsychological findings observed in this same group of children [10], where there were broad similarities in cognitive abnormalities among children with IGE and LRE, with both groups notable for the degree of shared abnormalities overall, with a smaller number of syndrome-specific findings, where children with IGE showed more widespread executive function deficits and children with LRE exhibited more difficulty with memory and language tests. In both studies, even at the level of specific syndromes of IGE and LRE, there were more similarities than differences. This lack of syndrome-specific pathology has been examined in children with established and chronic epilepsies (e.g., [11]), and our findings here in children with new- or recent-onset epilepsies are consistent with those reports.

It may be that phenotypes of the behavioral complications of epilepsy should be derived on the basis of factors other than seizure type or syndrome. An initial step would be the characterization of the actual nature and distribution of behavioral groups, or behavioral phenotypes, followed by understanding of their correlates (e.g., neuroimaging, family history/aggregation, and neurodevelopmental history) and prospective course. The same holds true for competence problems. In that regard, it should be noted that the Social Competence scale consists of items that assess the child's involvement in social activities (e.g., number of organization they are part of such as sports or clubs, how many friends they have, and the amount of time they spend together). The Social Problems scale focuses on specific target problems (e.g., dependent, lonely, jealous, bullied/teased, not liked, clumsy, prefers younger children, and has speech problems).

5. Limitations

There are several limitations associated with this investigation. First, we used only the parent report version of the CBCL, and in the future, it would be useful to incorporate reports from teachers and child self-report to assess the generalizability of these findings. The use of the parent form has been a very frequent form of investigation in this literature. Second, the pattern of results presented here applies just to the CBCL. It is possible that other behavioral measures and more formal psychiatric diagnoses will show greater syndrome separation and should be investigated. Third, this investigation involved only baseline assessment, and it is possible that behavioral changes may evolve over time in syndrome-specific ways—an issue which we are currently examining. Fourth, the number of participants in some syndromic groups was limited, and it remains to be determined whether results will differ in a meaningful way with a larger sample size. Fifth, it should be noted that the overall *mean scores* of the epilepsy sample were not elevated to the clinically significant range, typically falling in the broad range of normal, although significantly different from controls. However, secondary analyses examined the distribution of behavioral problem and competence scale scores falling in the “at-risk” and/or clinical range. The results revealed a statistically significantly higher proportion of children with epilepsy than controls with scores that fell in the “at-risk”/clinical range compared with

controls across the overall Total Competence and Total Problems scales as well as several behavioral problem and competence scales as described. For the summary scales mentioned above, there were between 20 and 30% of the epilepsy group at risk. Information from other sources (e.g., teachers and child self-report) and other methods of assessment (e.g., K-SADS) are needed to confirm this general pattern. Finally, the relative strengths and limitations of the CBCL deserve mention. On the positive side, the CBCL is a widely used measure in the general pediatric and pediatric epilepsy literature. This is an instrument with demonstrated reliability and validity, providing an efficient screen of diverse behavioral and competence problems, facilitating a shared methodology and language with which to compare behavioral findings. That said, when interested in specific behavioral issues (e.g., social competence, depression, and ADHD), there are advantages to using other measures and procedures specifically tailored for the assessment of those issues, either alone or in combination with the CBCL [12–14].

6. Conclusion

The fundamental conclusion of this investigation is that there are few syndrome-specific differences across the behavioral problem and competence scales of the CBCL whether one considers epilepsy syndrome broadly (e.g., LRE and IGE) or narrowly (e.g., specific syndromes of LRE and IGE). There appear to be more shared than unique epilepsy syndrome effects across measures of behavior and competence in children with new- and recent-onset epilepsy. While behavioral complications are significantly elevated in children with epilepsy as assessed by the CBCL, this elevation appears to have little to do with epilepsy syndrome as investigated here.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Analysis summary for controls and groups with LRE and IGE. Each cluster of boxes represents a MANOVA: dark blue—main effects, light blue—significant pairwise comparisons, gray—no significant pairwise comparison.

Fig. 2.
Mean CBCL scores for controls and groups with LRE and IGE.

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/N1 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).