Language function in childhood idiopathic epilepsy syndromes


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ABSTRACT

Purpose: To examine the impact of diverse syndromes of focal and generalized epilepsy on language function in children with new and recent onset epilepsy. Of special interest was the degree of shared language abnormality across epilepsy syndromes and the unique effects associated with specific epilepsy syndromes.

Methods: Participants were 136 youth with new or recent-onset (diagnosis within past 12 months) epilepsy and 107 healthy first-degree cousin controls. The participants with epilepsy included 20 with Temporal Lobe Epilepsy (TLE; M age = 12.99 years, SD = 3.11), 41 with Benign Epilepsy with Centrotemporal Spikes (BECTS; M age = 10.32, SD = 1.67), 42 with Juvenile Myoclonic Epilepsy (JME; M age = 14.85, SD = 2.75) and 33 with absence epilepsy (M age = 10.55, SD = 2.76). All children were administered a comprehensive test battery which included multiple measures of language and language-dependent abilities (i.e., verbal intelligence, vocabulary, verbal reasoning, object naming, reception word recognition, word reading, spelling, lexical and semantic fluency, verbal list learning and delayed verbal memory). Test scores were adjusted for age and gender and analyzed via MANCOVA.

Results: Language abnormalities were found in all epilepsy patient groups. The most broadly affected children were those with TLE and absence epilepsy, whose performance differed significantly from controls on 8 of 11 and 9 of 11 tests respectively. Although children with JME and BECTS were less affected, significant differences from controls were found on 4 of 11 tests each. While each group had a unique profile of language deficits, commonalities were apparent across both idiopathic generalized and localization-related diagnostic categories.

Discussion: The localization related and generalized idiopathic childhood epilepsies examined here were associated with impact on diverse language abilities early in the course of the disorder.

1. Introduction

Examination of the cognitive effects of epilepsy often, but not always, focuses on specific epilepsy syndromes and on the cognitive abilities that would appear most likely to be adversely affected by the underlying abnormal pathophysiological processes associated with the syndrome under consideration (Braakman et al., 2011; Helmsmeder & Witt, 2012; Hommet, Sauerwein, De Toffol, & Lassonde, 2006; Lin, Mula, & Hermann, 2012; MacAllister & Schaffer, 2007). However, it has become clear that cognitive abnormalities may extend beyond narrow syndromic boundaries. Perhaps the best example is temporal lobe epilepsy (TLE), in which relatively widespread cognitive effects can be observed that are often at least as severe as the memory deficits typically associated with TLE (Oyegbile et al., 2004). These findings are not unexpected in the context of associated neuroimaging findings that have included widespread cortical thinning both ipsilateral and contralateral to the side of seizure onset, volumetric abnormalities of subcortical structures (e.g., caudate, thalamus) and cerebellum, and disruptions in ipsi- and contralateral connectivity relative to side of seizure onset (Bernasconi et al., 2004; Bernhardt, Bonilha, & Gross, 2015; Bonilha et al., 2004; Dabbs, Jones, Seidenberg, & Hermann, 2009; Keller & Roberts, 2008; Lin et al., 2007; McDonald et al., 2008; Mueller et al., 2009; Oyegbile et al., 2004). These consequences may be due to the effects of epilepsy and its treatment on typical neurodevelopmental processes, harmful effects of seizures, or untoward effects of medications.

In pediatric epilepsy, there are a large number of investigations focusing on memory in TLE (e.g., Martins et al., 2015), executive
function in JME (e.g., Pulsipher et al., 2011) and frontal lobe epilepsy (FLE) (e.g., Braakman et al., 2011), language in benign epilepsy with centrotemporal spikes (BECTS) or Rolandic epilepsy (e.g., Datta, 2015; Overvliet, Aldenkamp, Klinkenberg, Vles, & Hendriksen, 2011; Overvliet et al., 2013; Smith, Bajomo, & Pal, 2015), and attention in absence epilepsy (e.g., Masur et al., 2013; Mirsky, Duncan, & Myelobodsky, 1986). Taking a broader view of the neuropsychological consequences of the epilepsies, especially childhood epilepsies, one open question is the degree of shared cognitive abnormality that is evident across diverse epilepsy syndromes and the degree or added contribution of specific syndromes either in nature or severity of affected cognitive domains (Jackson et al., 2013; Jambaque, Pinabiaux, & Lassonde, 2013; Loughman, Bowden, & D’Souza, 2014).

Here we focus specifically on language dependent abilities and compare performance across multiple childhood epilepsy syndromes including both localization related epilepsies (BECTS and TLE) and genetic generalized epilepsies (absence and JME). Only children with new- and recent-onset epilepsy were included in the current study, so that language function could be assessed before the possible deleterious effects of years of seizures and/or anti-epileptic medications. All groups were compared to healthy controls for age and gender. This comparison facilitated the characterization of spared and adversely affected language skills within and between epilepsy syndromes, as well as the degree of shared impairment when present. While we expected to find some degree of language impairment in all groups, we hypothesized that participants with BECTS would have language deficits across multiple functional areas, particularly expressive naming and vocabulary (Jackson, 2015), while verbal memory deficits would be particularly associated with TLE. We predicted that children with juvenile myoclonic and absence epilepsy would be the least affected in the language domain.

2. Methods

2.1. Participants

Research participants consisted of 243 youth aged 8–18, including 136 with new and recent-onset epilepsy and 107 healthy first-degree cousin controls (see Table 1). The groups did not differ in terms of age or sex. Full-scale IQ was lower in children with epilepsy (M = 102.07, SD = 13.28) than in controls (M = 109.35, SD = 11.31; p < .001; see Table 1 for demographic and clinical variables presented by specific epilepsy syndrome). At baseline, all participants attended regular schools. 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 impairment, autism); (iii) no other neurological disorder, and (iv) normal routine brain MRI scan. All children had active epilepsy as diagnosed by their treating pediatric neurologists and confirmed by medical record review by the research study pediatric neurologist. We did not exclude children on the basis of common comorbidities such as attention deficit hyperactivity disorder (ADHD) or learning disabilities, in an effort to increase the generalizability of our results. We did however exclude children with intellectual disability, autism, and other neurological disorders, given the developmental language impairments often found with these disorders. Details regarding the subject selection process have been described in detail in previous publications (Hermann et al., 2006). In general, we tried to adhere to the concept of “epilepsy only” as defined broadly in the literature: normal neurological exam, average intelligence, and attendance at regular schools. 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, neurodevelopmental history) while blinded to all research cognitive, behavioral, and neuroimaging data.

Exclusion criteria for control participants were as follows: (i) history of any initial precipitating insult (e.g. simple or complex febrile seizures, cerebral infections, perinatal stroke); (ii) any seizure or seizure-like episode; (iii) diagnosed neurological disease; (iv) loss of consciousness for a period greater than 5 min; and (v) history of other 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 pre-disposed 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 was our intent) compared to more general control populations (e.g. unrelated school mates).

Participants with epilepsy were diagnosed with specific syndromes by the pediatric epileptologists blinded to all cognitive and psychiatric data. The following syndromes and their operational definitions (Berg et al., 2010) are as follows:

- **BECTS:** (1) the presence of nocturnal hemifacial seizures that may secondarily spread to involve clonic movements on the same side or bilaterally, (2) EEG revealing spikes with maximal negativity in centrotemporal regions and maximal positivity in frontal regions that activate with drowsiness and sleep, (3) EEG with otherwise typical background, (4) normal neurological exam, (5) if obtained, normal routine brain MRI.
- **CAE:** (1) age of onset 2–12 years, (2) multiple daily seizures with

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>HC</th>
<th>BECTS (n = 41)</th>
<th>TLE (n = 20)</th>
<th>Absence (n = 33)</th>
<th>JME (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.46 (3.00)</td>
<td>10.32 (1.67)</td>
<td>12.99 (3.11)</td>
<td>10.55 (2.76)</td>
<td>14.85 (2.75)</td>
<td></td>
</tr>
<tr>
<td>Gender (#/% female)</td>
<td>53 (50%)</td>
<td>15 (37%)</td>
<td>11 (55%)</td>
<td>21 (64%)</td>
<td>25 (60%)</td>
</tr>
<tr>
<td>FSIQ</td>
<td>109.35 (11.31)</td>
<td>104.44 (15.08)</td>
<td>98.90 (8.53)</td>
<td>100.67 (13.60)</td>
<td>102.38 (12.99)</td>
</tr>
<tr>
<td>Academic problems</td>
<td>19 (18%)</td>
<td>22 (54%)</td>
<td>11 (55%)</td>
<td>16 (48%)</td>
<td>19 (45%)</td>
</tr>
<tr>
<td>Age of seizure onset (yrs)</td>
<td>–</td>
<td>9.55 (1.68)</td>
<td>12.13 (3.06)</td>
<td>9.70 (2.87)</td>
<td>14.03 (2.88)</td>
</tr>
<tr>
<td>Epilepsy duration (mos.)</td>
<td>–</td>
<td>7.49 (3.33)</td>
<td>7.05 (3.66)</td>
<td>7.97 (3.81)</td>
<td>8.36 (3.44)</td>
</tr>
<tr>
<td>Antiepileptic drugs (0/1/2+)</td>
<td>–</td>
<td>17/24/0</td>
<td>4/14/2</td>
<td>2/29/2</td>
<td>1/39/2</td>
</tr>
</tbody>
</table>

HC: Healthy controls.

BECTS: Benign epilepsy with centro-temporal spikes.

TLE: Temporal lobe epilepsy.

Absence: Childhood (n = 23) and Juvenile (n = 10).

JME: Juvenile myoclonic epilepsy.

FSIQ: Full-scale intelligence quotient.

Academic problems: School or parent provided resources because of child academic difficulty (e.g., IEP, grade retention, summer school, tutors).

* Significantly different across groups (for pairwise comparisons see text).
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