Published in final edited form as:

Epilepsy Behav. 2011 October ; 22(2): 298–303. doi:10.1016/j.yebeh.2011.06.023.

Benign rolandic epileptiform discharges are associated with mood and behavior problems

Dean P. Sarco^{a,b,c,1}, Katrina Boyer^{b,c,d,*}, Shannon M. Lundy-Krigbaum^{b,c,d}, Masanori Takeoka^{b,c}, Frances Jensen^{b,c}, Matt Gregas^{b,c}, and Deborah P. Waber^{c,d}

^aDepartment of Neurology, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA, USA

^bDepartment of Neurology, Children's Hospital Boston, Boston, MA, USA

^cHarvard Medical School, Boston, MA, USA

^dDepartment of Psychiatry, Children's Hospital Boston, Boston, MA, USA

Abstract

Children with benign rolandic epilepsy (BRE) experience elevated rates of cognitive, behavioral, and affective problems. Frequent epileptiform spike discharges may impair behavioral functioning. To elucidate this relationship, we evaluated associations between the EEG spike frequency index (SI) and parental ratings of psychosocial adjustment and executive functioning in school-aged children with EEGs typical of BRE. Twenty-one children (6–12 years) participated. Parents completed validated questionnaires at a median of 5 months (range: 1–8) after a routine outpatient EEG. The EEG SI was calculated for wakefulness and sleep. The strength of association between the SI and behavioral variables was evaluated by simple and multivariate correlation. Higher awake and sleep SIs were associated with more symptoms of depression ($P < 0.001$), aggression and conduct problems ($P < 0.01$). Higher sleep SI was associated with executive dysfunction and anxiety ($P < 0.05$). Symptoms of hyperactivity and inattention had no correlation. Increased epileptiform activity in children with BRE may predict higher rates of mood and behavioral problems.

Keywords

Benign rolandic epilepsy; Neuropsychology; Mood; Epileptic encephalopathy; Interictal discharges; Depression

1. Introduction

Epilepsy is a common childhood neurological disorder that is often associated with impaired cognitive, emotional, and/or behavioral functioning. Learning disabilities, aggression, and

*Corresponding author at: Division of Epilepsy and Clinical Neurophysiology, Children's Hospital Boston, Fegan 9, 300 Longwood Avenue, Boston, MA 02115, USA. Fax: +1 617 730 0463. katrina.boyer@childrens.harvard.edu (K. Boyer).

¹These authors contributed equally to the article.

Conflict of interest statement

None of the authors has any conflict of interests to disclose.

attention-deficit/ hyperactivity disorder (ADHD), as well as mood and anxiety disorders, are far more prevalent in children with epilepsy than in typically developing children [1-7]. Up to 50% of children with epilepsy have school-related difficulties, and 20–30% have symptoms diagnostic of ADHD [2,8,9]. Likewise, approximately one-third have depressive disorders, and an estimated 16%, anxiety disorders [2,8-10]. These children with comorbid epilepsy and depression and/or anxiety have a heightened risk of suicide when disruptive behavioral problems, such as impaired impulse control, are also present [2,8,9,11,12]. Although associated to some extent with these comorbidities, epilepsy etiology, adverse effects of antiepileptic drugs (AEDs), psychological factors, and severity of seizures account only partially and inconsistently for the unusually high rates and severity of comorbid psychiatric disorders, suggesting that other, underappreciated factors may be contributory [13].

Data from animal models suggest another potentially important route to these observed comorbidities: interictal epileptiform discharges (IEDs). Though such discharges can disrupt the normal activity and function of the neuronal networks supporting cognitive and affective functioning [6,14], this mechanism has yet to receive significant attention in the clinical setting. A high frequency of IEDs is thought to contribute to the severe developmental problems experienced by children with devastating and rare epileptic encephalopathy syndromes, such as Landau–Kleffner syndrome (LKS) and epilepsy with continuous spike waves during slow sleep syndrome (CSWS). The majority of children with childhood epilepsy, however, experience less frequent IEDs, the functional significance of which in daily life is unclear. It is postulated that such activity has a cumulative, chronic impact on development, resulting in encephalopathy. To clarify, this state differs from the notion of *transient cognitive impairment*, an acute and transient cognitive dysfunction occurring only at the moment of an individual epileptiform discharge [15-17].

Benign childhood epilepsy with centrotemporal spike discharges, or benign rolandic epilepsy (BRE), is the most common epilepsy syndrome of childhood, accounting for approximately 24% of epilepsy in school-aged children [18]. Onset typically occurs in middle childhood, and neurophysiological abnormalities resolve by mid-adolescence. Most children with BRE are either treated successfully with one AED or not medicated, requiring only monitoring [19]. Nonetheless, certain patients with BRE do not in fact have a “benign” course, demonstrating mild to moderate language, attention, and visual–motor problems, as well as learning disabilities, and possibly other educational impairments, with preserved general intelligence [20-24]. Elevated rates of affective disturbance are also reported [20,25,26].

Benign rolandic epilepsy provides an especially favorable model for evaluating potential associations between interictal EEG phenomena and comorbid behavioral symptoms because children with BRE typically lack significant neurological impairment and exhibit frequent interictal EEG activity but infrequent or less severe seizures. Thus, potential confounders, such as postictal and AED effects, are limited [18]. As children with BRE also, by definition, do not have known structural brain abnormalities that could account for both seizures and behavioral dysfunction, it is plausible that IEDs play a functional role. In addition, because BRE has a suspected genetic etiology, the population is likely to be

relatively homogenous etiologically, further minimizing potential confounding factors [27]. This homogeneity may also explain why the EEG features of BRE are relatively unique, well described, and readily identifiable to an experienced epileptologist. Finally, because children with BRE do not contend with the significant impairment of quality of life that can be associated with seizures, their mood and behavior problems are less likely to reflect a psychological response to the epilepsy itself. Few clinical studies have addressed potential links between the frequency of epileptiform activity in BRE and behavioral dysfunction, and even fewer such investigations have done so by quantifying both the behavioral variables and the epileptiform abnormalities. The latter is best accomplished through the Spike Index (SI), commonly quantified as spikes per minute. These studies, moreover, have focused largely on cognition [20-24,28], even though mood disorders are a prevalent and serious problem in individuals with epilepsy. Even without detailed quantification, though, previous work yielded promising results: a higher awake SI has been correlated with lower Full Scale and Performance IQ scores and language dysfunction, as well as with greater risk for educational and social-familial maladjustment [20,24,29,30].

The present study was undertaken as an initial proof of concept. We quantified the awake and sleep SI values of 21 children with BRE, and correlated these with well-standardized, quantitative questionnaires that assess psychosocial and executive functioning based on parent ratings. We hypothesized that higher SI values would be correlated with a higher prevalence of behavioral problems.

2. Methods

2.1. Design

The study design was cross sectional and correlational. The SI was derived from clinical EEG studies and correlated with parent ratings on standard behavioral questionnaires targeted to be obtained within the 6-month period after the EEG had been completed, the time span for which the authors of the questionnaires deem the behavioral ratings valid. The study was approved by the Childrens Hospital Boston (CHB) institutional review board, which viewed completion of the questionnaires as implied consent.

2.2. Subjects

Subjects were otherwise healthy children with BRE, with clinical EEG studies performed during 2008 and 2009 at CHB. *Inclusion criteria* were: (1) age 6–11 years; (2) awake and sleep outpatient EEGs in the 5 months prior to recruitment as part of routine clinical care, with findings suggestive of BRE (see below); (3) clinical course suggestive of BRE, including localization-related epilepsy, with or without generalized convulsive seizures; (4) normal neurological examination; (5) typical early development (prior to 4 years); (6) parent sufficiently fluent in English to complete questionnaires. *Exclusion criteria* were: (1) acquired disease or developmental disorder independently impairing cognition or behavior, such as developmental delay, autistic spectrum disorder, meningoencephalitis, prior brain injury, and progressive neurological disorders; (2) previously diagnosed Axis I psychiatric disorders, including psychosis, major mood disorder, disruptive behavior disorder, and ADHD under current psychopharmacological treatment; (3) treatment with more than two

AEDs; (4) more than eight seizures in the month prior to enrollment; and (5) abnormal neuroimaging study obtained during the course of normal clinical care (not routinely obtained for BRE). Our exclusion criteria were designed primarily to limit comorbid neurological or psychiatric disorders that might confound interpretation of the questionnaire measures.

2.3. Data collection

Electroencephalograms with typical BRE findings obtained in the 5 months prior to recruitment were identified from our institutional database and confirmed by chart review. First, clinically obtained EEGs reported as being suggestive of BRE from 2008 and 2009 were identified from our database. Each of these reports was reviewed by a board-certified pediatric epileptologist (D.P.S.) to screen for those potentially fulfilling EEG inclusion criteria (see below). D.P.S. was blinded to questionnaire results. One hundred twelve potential subjects had EEG impressions suggestive of BRE. Review of these 112 medical records yielded 73 potential subjects. These potentially eligible families were initially invited by mail to participate. Those not responding within 2 weeks received a phone invitation. Twenty-seven of the 73 eligible families expressed willingness to participate. Brief phone interviews and EEG review yielded 21 subjects fulfilling clinical and EEG inclusion/exclusion criteria. Two were excluded for pharmacological therapy for ADHD and one for a diagnosed anxiety disorder. One subject was excluded from this analysis as the clinical history was consistent with BRE trait but not BRE because of a lack of observed clinical seizures. Two EEGs were uninterpretable for technical reasons. Although significant EEG SI change within 6 months was not anticipated, we sought to minimize the time between EEG completion and survey administration. The median elapsed time from the EEG to the questionnaire completion was 5 months (range: 1–8). One EEG per subject was used, and for most, only one EEG had been obtained within our 2008–2009 time period of review. When more than one was available, the study that would minimize the EEG to questionnaire completion time frame was chosen. Families who endorsed sufficient symptoms to place the child in the clinical range for psychiatric disorder were notified and advised on how to obtain help.

2.4. Electroencephalographic analysis

Clinical outpatient sleep-deprived EEGs were obtained in our laboratory using the standard international 10–20 system of EEG lead placement with Bio-Logic Systems Corporation software (presently Natus Medical Inc, San Carlos, CA, USA). Recording durations ranged from 20 to 60 minutes. Digital EEG recordings were visually inspected using an anterior–posterior bipolar montage using Bio-Logic software. EEG inclusion criteria for characteristic central-midtemporal discharges included: (1) bilateral or unilateral, independent or synchronous, central-midtemporal spike and sharp wave discharges; (2) sleep potentiation or activation; (3) maximal voltage in the central (C3–C4) and midtemporal (T7–T8) regions; (4) di- or triphasic spike or spike–wave morphology; (5) amplitude of at least 70 μ V and discernable from the EEG background. Discharges with a field involving electrodes adjacent to the central and midtemporal electrodes were included as long as a central-midtemporal voltage maximum was present. As the presence of a tangential dipole is not a necessity for a rolandic discharge, discharges without a dipole were included in the SI.

The SI was defined as the absolute number of spike discharges per EEG recording time (minutes) and calculated for awake, sleep, and total EEG times. Centrotemporal epileptiform discharges meeting the above criteria were identified by visual inspection and included in the SI. Because these were routine outpatient studies, only Stage I and II sleep was recorded. The onset of sleep was marked by the disappearance of the posterior dominant rhythm, and the end of sleep was marked by an arousal pattern. Independent generalized discharges, which may be present in about 5–7% of children with BRE, and any other epileptiform discharges were not included in the SI [31,32].

2.5. Behavioral assessment

Parents completed two widely used and well-standardized questionnaires chosen because of previously described behavioral problems in children with BRE, specifically executive dysfunction and mood and behavioral dysregulation [23].

2.5.1. Behavioral Assessment System for Children-Second Edition—Parent—

This 160-item Behavioral Assessment System for Children-Second Edition—Parent (BASC-2) is used to assess adaptive and maladaptive behaviors in children and adolescents [33]. The subscales are organized into an Externalizing Composite (Aggression, Hyperactivity, Conduct Problems); Internalizing Composite (Anxiety, Depression, Somatization); and Adaptive Skills Composite (Adaptability, Social Skills, Leadership). The BASC-2 also provides subscales for Atypicality and Withdrawal. The Behavioral Symptoms Index combines the central scales from the clinical composites and reflects overall level of problem behaviors. Although a higher score generally denotes more problems, the Adaptive Skills Composite is reversed, with a higher score indicating better adaptive skills. Internal consistency of this questionnaire is very high and test–retest reliability is high. In terms of validity, parent ratings on this measure correlate highly with other commonly used measures of child emotional and behavioral function.

2.5.2. Behavior Rating Inventory of Executive Function—Parent—The 86-item Behavior Rating Inventory of Executive Function—Parent measures the regulation of behavior and emotions as well as the cognitive aspects of executive functions, including planning, working memory, organization, and self-monitoring [34]. BRIEF comprises eight scales organized within two major indices: Behavior Regulation (includes Inhibition, Shifting, and Emotional Control scales) and Metacognitive (includes Initiation, Working Memory, Planning and Organization, Organization of Materials, and Monitoring scales). The Global Executive Composite combines the two major indices. Higher scores indicate more problems.

2.6. Statistical methods

The primary analytical method was simple correlation. Preliminary analysis indicated that 21 subjects would provide 80% power to detect a moderate size correlation ($r=0.36$), assuming a 5% level of significance. Exploratory multiple regression analyses were subsequently performed to evaluate potential moderating effects of age, as the impact of BRE declines as children age into adolescence.

In this pilot study we did not have hypotheses on the correlations of specific behavioral measures with specific EEG measures; therefore, we obtained many estimates of the correlation coefficient. When calculating the significance level we did not correct for multiple comparisons. The small sample size does not yield enough power to detect Bonferroni-adjusted significance levels. Therefore we have an inflated chance of observing false-positive results, and significant results will need to be replicated. The purpose of this phase of the study was to generate hypotheses for a second phase of the study.

3. Results

3.1. Sample characteristics

Table 1 summarizes the demographic and medical characteristics of the sample, typical of children reported in the literature with a diagnosis of BRE, including age, a slight male predominance, and monotherapy for most [19,35]. Bilateral and unilateral IED profiles were approximately equal in prevalence. Sleep potentiation was prominent overall. The mean duration of epilepsy for this group of children was 2.35 years. The socioeconomic status of the sample tended to be high, with most parents reporting at least some post-high school education and many holding college or graduate school degrees.

Table 2 lists descriptive statistics for the behavioral variables. These were entirely within the average range. The range of scores did, however, indicate that there were individuals with scores in the clinical range (>65) on each measure.

3.2. Psychosocial adjustment and Spike Index

Table 3 demonstrates the correlation of the spike indices with the actual BASC-2 and BRIEF subscale scores, revealing robust associations for mood and behavior problems as measured by the BASC-2. Large correlations were detected for the Depression scale, in both the awake and sleep states and, thus, for the total SI. Anxiety symptoms were moderately associated with the SI in the sleep state. Moderate to large correlations were seen for two of the three externalizing scales; the SI was correlated with Aggression and Conduct Problems, but not Hyperactivity. These correlations were of comparable magnitude for the awake, sleep, and total SIs. Fig. 1 is the scatterplot depicting the correlation between total SI and the Depression scale. It illustrates importantly that the observed correlation was not accounted for by a few outliers, but that the association was well distributed across the range.

As the prevalence and severity of BRE decline with age, we evaluated potential moderating effects of age. The depression outcome was most striking, and so we evaluated it in the context of a multivariate model that included age, gender, and all interactions.

There was no effect of gender, but there were main effects of total SI ($P=0.0001$), age ($P<0.0090$), and an age $\times$ SI product ($P<0.00312$), the latter indicating that the association becomes attenuated with age.

3.3. Executive function and spike index

Table 3 also displays correlations between the SI and the BRIEF summary indices, as well as scales that yielded statistically significant correlations. A moderate-sized correlation was

observed for Behavioral Regulation Index (sleep but not awake SI). Specific scales affected were Emotional Control (sleep SI only), Initiation (sleep and awake SI), and Organization (sleep SI only). Thus, the associations were moderate in magnitude and more prevalent in the sleep state than the awake state.

4. Discussion

We found substantial and reliable correlations between the frequency of interictal phenomena in children with benign rolandic discharges and parent-reported problems with mood, externalizing behaviors, and, to a lesser extent, executive functioning. The correlations with depression and externalizing behaviors (aggression, conduct) were striking, suggesting that mood is especially sensitive to the frequency of interictal discharges in children with BRE. A moderate association was also seen for executive functioning, particularly behavioral regulation, which likely reflects the mood problems highlighted by the BASC-2. The key associations were well distributed across the range and not attributable to a categorically different subset of individuals with significant impairment. It is also noteworthy that correlations were smaller for anxiety, attention, and hyperactivity, the latter two being cardinal features of ADHD. Approximately three otherwise eligible subjects on current pharmacological treatment for ADHD, anxiety, and mood disorders were ineligible to participate because they fulfilled the exclusion criteria for this study. Such exclusions likely attenuated our variability on scales of attention, impulse control, mood, and anxiety.

Within this sample, mean standard scores on measures of depression and other scales assessing mood and behavior problems were not in the clinical range. Whereas 5.5% of the general population (i.e., approximately 1 of the 21 participants) would be expected to obtain scores in the clinical range on these measures, 2 subjects obtained Internalizing Behavior Problems scores in the clinical range and 2 obtained scores in the clinical range on the Externalizing Behavior Problems scale of the BASC-2 in this study. A closer review indicated that these were not the same children across measures, suggesting that our findings were not due to a few children with significant problems, but were more broadly representative. Moreover, although cognitive function was not a focus of this study, nearly half of our participants were enrolled in special education. In most school systems, approximately 15% of children qualify for special education.

The magnitude of the observed association between SI and mood, especially depressive symptoms, was unanticipated based on the prior literature on BRE, which has been focused primarily on cognition. These findings raise the central question of why interictal discharges should be so strongly and specifically linked to mood. Similar anatomic hippocampal changes may be seen in both depression and epilepsy, suggesting a relation between the two disorders and a common functional role for the temporal lobe [36]. The central-midtemporal locus of the characteristic discharges in BRE, however, could disrupt neural circuits involving the temporal lobe, thus causing greater dysregulation of mood [37]. This hypothesis merits further investigation as it could have direct implications for clinical management. Furthermore, it is an unproven assumption that depression should be treated in the same manner in all children regardless of whether they have epilepsy [38]. Therapies typically implemented to treat depression in children without epilepsy might be less

effective for children with BRE than therapies aimed at controlling abnormal epileptic activity, particularly because depressive symptoms may differ between children with and those without epilepsy.

Another consideration is the relative contribution of the SI during the awake and sleep states. Within the epileptic encephalopathies, most work has focused on the sleep SI, with relatively few studies examining the functional impact of waking discharges. In our study, both the awake and the sleep SIs were highly correlated with symptoms of depression, aggression, and conduct problems, with comparable levels of association. In LKS and CSWS, the sleep SI is thought to result in greater impairment when the discharges are most frequent during the course of the disorder. The same may be true for BRE, with executive function more sensitive to discharges in sleep rather than waking. As our study was powered to detect medium effect sizes, the correlations observed for the awake state, although present, were not large enough to achieve statistical significance. Prior work, though, has reported an association between the awake SI and language as well as Full Scale and Performance IQ scores [20,39,40].

4.1. Limitations

This study, intended as an initial proof of concept, has several limitations. We relied on parent report rather than direct neuropsychological or psychiatric evaluation of the children. Well-constructed questionnaires, however, can often be highly sensitive in detecting problems that may not be evident under the controlled conditions of a clinical evaluation. This being a cross-sectional investigation we cannot make assumptions about causality. Assessing mood and cognition before and after the development of IEDs would allow the testing of a causality hypothesis, though this would not be practical in most settings. Another issue is that a single rater derived the SI, and so we were unable to evaluate interrater reliability. Most BRE discharges are fairly stereotypical, however, and are readily identifiable to an experienced epileptologist. Moreover, EEG parameters were defined at the outset to standardize interpretation, and the rater was blinded to the behavioral data, providing greater confidence in the reliability of his ratings. Another limitation is that we had a mixture of patients treated with different medications and untreated patients. Medication side effects, therefore, may have affected the behavioral ratings or contributed to suppression of spike discharges. If the spikes themselves are largely responsible for the symptoms, however, a lower SI should result in less morbidity, even if it is the result of medication. Exclusion of children with previously diagnosed mood and anxiety disorders and ADHD under pharmacotherapy was perhaps an overzealous effort to have a pure sample and restricted our ability to appreciate the full behavioral range of children with BRE. The participation rate (24 of 73 invited responding, with 21 ultimately participating) may possibly have biased our results, though our data provide no indication of the source of any potential bias. Also, because we did not correct for experiment-wise error, some statistically significant correlations could actually be due to chance.

5. Conclusion

This study provides evidence for a potential functional role for interictal epileptiform discharges in the etiology of behavioral comorbidity in benign rolandic epilepsy. Our results confirm that greater frequency of benign rolandic epileptiform activity in children is associated with an increased likelihood of depression and behavioral disturbance, in some cases dramatically so. It thus constitutes an initial proof of concept.

Even though the EEG preceded the behavioral measurement in our study, the correlational design precludes firm conclusions about causation. Our primary hypothesis, of course, is that the interictal events are causally related to the adverse behavioral outcomes. It is also possible that a common underlying, presumably genetic or epigenetic, etiology results in both epileptiform discharges and behavioral symptoms that may not be related to one another in a causal fashion. In addition to the common underlying cause hypothesis, it is also conceivable that the pathophysiology associated with depression and related psychiatric disorders may contribute to the presence of IEDs as depression is a risk factor for epilepsy. Treatment studies are needed to demonstrate causality. Recent genetic advances and future related work continuing to integrate epilepsy and neuropsychological function will allow further examination of whether genotype may predispose children to a benign rolandic epilepsy course that is not “benign.”

Acknowledgments

The authors thank the families who participated in our study, Lorraine Sardano for her administrative support, and Jonathan Girard for his editorial assistance.

References

1. Smith DB, Craft BR, Collins J, Mattson RH, Cramer JA. Behavioral characteristics of epilepsy patients compared with normal controls. *Epilepsia*. 1986; 27:760–8. [PubMed: 3780614]
2. Aldenkamp AP, Alpherts WC, Dekker MJ, Overweg J. Neuropsychological aspects of learning disabilities in epilepsy. *Epilepsia*. 1990; 31(Suppl 4):S9–S20. [PubMed: 2279487]
3. Helmstaedter C, Elger CE. The phantom of progressive dementia in epilepsy. *Lancet*. 1999; 354:2133–4. [PubMed: 10609823]
4. Besag FM. Cognitive and behavioral outcomes of epileptic syndromes: implications for education and clinical practice. *Epilepsia*. 2006; 47(Suppl 2):119–25. [PubMed: 17105481]
5. Cornaggia CM, Beghi M, Provenzi M, Beghi E. Correlation between cognition and behavior in epilepsy. *Epilepsia*. 2006; 47(Suppl 2):34–9. [PubMed: 17105457]
6. Holmes GL, Lenck-Santini PP. Role of interictal epileptiform abnormalities in cognitive impairment. *Epilepsy Behav*. 2006; 8:504–15. [PubMed: 16540376]
7. Austin JK, Caplan R. Behavioral and psychiatric comorbidities in pediatric epilepsy: toward an integrative model. *Epilepsia*. 2007; 48:1639–51. [PubMed: 17565593]
8. Devinsky O. Psychiatric comorbidity in patients with epilepsy: implications for diagnosis and treatment. *Epilepsy Behav*. 2003; 4(Suppl 4):S2–S10. [PubMed: 14654422]
9. Pellock JM. Understanding co-morbidities affecting children with epilepsy. *Neurology*. 2004; 62:S17–23. [PubMed: 15007160]
10. Dunn DW, Austin JK. Differential diagnosis and treatment of psychiatric disorders in children and adolescents with epilepsy. *Epilepsy Behav*. 2004; 5(Suppl 3):S10–7. [PubMed: 15351341]
11. Caplan R, Siddarth P, Gurbani S, Hanson R, Sankar R, Shields WD. Depression and anxiety disorders in pediatric epilepsy. *Epilepsia*. 2005; 46:720–30. [PubMed: 15857439]

12. Jones JE, Austin JK, Caplan R, Dunn D, Plioplys S, Salpekar JA. Psychiatric disorders in children and adolescents who have epilepsy. *Pediatr Rev.* 2008; 29:e9–e14. [PubMed: 18245299]
13. Deonna, T.; Roulet Perez, E. Cognitive and behavioral disorders of epileptic origin in children. London: MacKeith Press; 2005. p. 28-43.
14. Kleen JK, Scott RC, Holmes GL, Lenck-Santini PP. Hippocampal interictal spikes disrupt cognition in rats. *Ann Neurol.* 2010; 67:250–7. [PubMed: 20225290]
15. Binnie CD, Marston D. Cognitive correlates of interictal discharges. *Epilepsia.* 1992; 33(Suppl 6):S11–7. [PubMed: 1486830]
16. Deonna T. Rolandic epilepsy: neuropsychology of the active epilepsy phase. *Epileptic Disord.* 2000; 2(Suppl 1):S59–61. [PubMed: 11231227]
17. Binnie CD. Cognitive impairment during epileptiform discharges: is it ever justifiable to treat the EEG? *Lancet Neurol.* 2003; 2:725–30. [PubMed: 14636777]
18. Cavazzuti GB. Epidemiology of different types of epilepsy in school age children of Modena, Italy. *Epilepsia.* 1980; 21:57–62. [PubMed: 6766394]
19. Bouma PA, Bovenkerk AC, Westendorp RG, Brouwer OF. The course of benign partial epilepsy of childhood with centrottemporal spikes: a meta-analysis. *Neurology.* 1997; 48:430–7. [PubMed: 9040734]
20. Weglage J, Demsky A, Pietsch M, Kurlemann G. Neuropsychological, intellectual, and behavioral findings in patients with centrottemporal spikes with and without seizures. *Dev Med Child Neurol.* 1997; 39:646–51. [PubMed: 9352724]
21. Saint-Martin AD, Seegmuller C, Carcangiu R, et al. Cognitive consequences of rolandic epilepsy. *Epileptic Disord.* 2001; 3(Spec No 2):S159–65. [PubMed: 11827848]
22. Metz-Lutz MN, Filippini M. Neuropsychological findings in rolandic epilepsy and Landau–Kleffner syndrome. *Epilepsia.* 2006; 47(Suppl 2):71–5. [PubMed: 17105467]
23. Nicolai J, Aldenkamp AP, Arends J, Weber JW, Vles JS. Cognitive and behavioral effects of nocturnal epileptiform discharges in children with benign childhood epilepsy with centrottemporal spikes. *Epilepsy Behav.* 2006; 8:56–70. [PubMed: 16263335]
24. Nicolai J, van der Linden I, Arends J, et al. EEG characteristics related to educational impairments in children with benign childhood epilepsy with centrottemporal spikes. *Epilepsia.* 2007; 48:2093–100. [PubMed: 17645539]
25. Connolly AM, Northcott E, Cairns DR, et al. Quality of life of children with benign rolandic epilepsy. *Pediatr Neurol.* 2006; 35:240–5. [PubMed: 16996395]
26. Volk-Kernstock S, Bauch-Prater S, Ponocny-Seliger E, Feucht M. Speech and school performance in children with benign partial epilepsy with centrottemporal spikes (BCECTS). *Seizure.* 2009; 18:320–6. [PubMed: 19249229]
27. Strug LJ, Clarke T, Chiang T, et al. Centrottemporal sharp wave EEG trait in rolandic epilepsy maps to elongator protein complex 4 (ELP4). *Eur J Hum Genet.* 2009; 17:1171–81. [PubMed: 19172991]
28. Stephani U, Carlsson G. The spectrum from BCECTS to LKS: the rolandic EEG trait—impact on cognition. *Epilepsia.* 2006; 47(Suppl 2):67–70. [PubMed: 17105466]
29. Staden U, Isaacs E, Boyd SG, Brandl U, Neville BG. Language dysfunction in children with rolandic epilepsy. *Neuropediatrics.* 1998; 29:242–8. [PubMed: 9810559]
30. Massa R, de Saint-Martin A, Carcangiu R, et al. EEG criteria predictive of complicated evolution in idiopathic rolandic epilepsy. *Neurology.* 2001; 57:1071–9. [PubMed: 11571336]
31. Blume, WT.; Kaibara, M. Atlas of pediatric electroencephalography. 2. Philadelphia: Lippincott–Raven; 1999. Abnormal electroencephalogram: epileptiform potentials; p. 159-60.
32. Pedley, TA.; Mendiratta, A.; Walczak, TS. Seizures and epilepsy. In: Ebersole, JS.; Pedley, TA., editors. Current practice of clinical electroencephalography. Philadelphia: Lippincott Williams & Wilkins; 2003. p. 506-87.
33. Reynolds, CR.; Kamphaus, RW. Behavior Assessment System for Children. 2. Circle Pine, MN: American Guidance Service; 2004.
34. Gioia GA, Isquith PK, Guy SC, Kenworthy L. Behavior rating inventory of executive function. *Child Neuropsychol.* 2000; 6:235–8. [PubMed: 11419452]

35. Callenbach PM, Bouma PA, Geerts AT, et al. Long term outcome of benign childhood epilepsy with centrottemporal spikes: Dutch Study of Epilepsy in Childhood. *Seizure*. 2010; 19:501–6. [PubMed: 20688544]
36. Shamim S, Hasler G, Liew C, Sato S, Theodore WH. Temporal lobe epilepsy, depression, and hippocampal volume. *Epilepsia*. 2009; 50:1067–71. [PubMed: 19054394]
37. Kondziella D, Alvestad S, Vaaler A, Sonnewald U. Which clinical and experimental data link temporal lobe epilepsy with depression? *J Neurochem*. 2007; 103:2136–52. [PubMed: 17887964]
38. Kanner AM. Depression in epilepsy: prevalence, clinical semiology, pathogenic mechanisms, and treatment. *Biol Psychiatry*. 2003; 54:388–98. [PubMed: 12893113]
39. Croona C, Kihlgren M, Lundberg S, Eeg-Olofsson O, Eeg-Olofsson KE. Neuropsychological findings in children with benign childhood epilepsy with centrottemporal spikes. *Dev Med Child Neurol*. 1999; 41:813–8. [PubMed: 10619279]
40. Fonseca LC, Tedrus GM, Tonelotto JM, Antunes Td Tde A, Chiodi MG. School performance in children with benign childhood epilepsy with centrottemporal spikes. *Arq Neuropsiquiatr*. 2004; 62:459–62. [PubMed: 15273844]

Fig. 1. Scatterplot displaying correlation between BASC-2 Depression scale (*T* score) and total Spike Index (spikes per minute) ($N=21$).

Table 1Demographic characteristics of children with BRE ($N=21$).

Mean (range) age, years	9.38 (7–12)
Gender	
Male	52.3%
Female	47.7%
Mean (range) duration of epilepsy, years	2.35 (0–8)
AED treatment	
Monotherapy	76%
No treatment	24%
Interictal epileptiform discharges	
Unilateral	47.6%
Bilateral	52.4%
Mean (range) Spike Index, spikes/min	
Awake	11.50 (4.37–35.78)
Sleep	36.64 (0–123.30)
Total	21.90 (1.68–87.75)

Table 2

Descriptive statistics and probability levels (difference from normative expected value) for primary summary scales of BASC-2 and BRIEF.

	<i>T</i> score		<i>T</i> scores > 65, <i>N</i> (%) in clinical range
	Mean (SD)	Median (range)	
BASC-2			
Externalizing Problems Composite	51.1 (12.0)	49.0 (37–85)	2 (9.5%) ^a
Internalizing Problems Composite	53.43 (11.9) ^b	52.0 (35–90)	2 (9.5%)
Behavioral Symptoms Index	51.57 (11.1)	49.0 (38–86)	2 (9.5%)
Behavioral Regulation Index	54.43 (11.6) ^c	53.0 (37–81)	1 (4.7%)
BRIEF			
Metacognitive Index	52.9 (12.5) ^c	49.0 (34–87)	3 (14.3%) ^c
Global Executive Composite	55.0 (14.4) ^b	51.0 (36–92)	1 (4.7%)

^a $P < 0.05$.

^b $P < 0.001$.

^c $P < 0.0001$.

Table 3

Pearson correlations between the total, awake, and sleep Spike Indices and Behavioral Rating Scale subgroup scores ($N=21$).

	Total SI	Awake SI	Sleep SI
BASC-2 Internalizing	0.58^b	0.41^a	0.56^a
Depression	0.63^c	0.53^b	0.76^b
Anxiety	0.32	0.26	0.40^a
BASC-2 Externalizing	0.53^a	0.40^a	0.43^a
Aggression	0.65^b	0.48^a	0.50^a
Hyperactivity	0.10	0.08	0.26
Conduct	0.59^b	0.57^b	0.54^b
BASC-2 Attention	0.08	0.18	0.12
BRIEF Metacognitive	0.35	0.27	0.35
BRIEF Behavioral Regulation	0.45	0.16	0.41^a

^a $P < 0.05$.

^b $P < 0.01$.

^c $P < 0.001$.