The Relationship Between Nocturnal Discharges and Language Dysfunction in Rolandic Epilepsy: Treat the Child, Not the Adage

Reading Performance in Children With Rolandic Epilepsy Correlates With Nocturnal Epileptiform Activity, but Not With Epileptiform Activity While Awake.


OBJECTIVE: An association between language impairment and rolandic epilepsy is frequently reported. This impairment could be correlated with the amount of nocturnal epileptiform activity. METHODS: We retrospectively analyzed 26 children with rolandic epilepsy and/or rolandic spikes. All had undergone a 24-hour EEG and neuropsychological assessment within 2 weeks. Reading performance (reading words and sentences) and intelligence were measured.

RESULTS: There was a significant negative correlation between amount of nocturnal epileptiform activity and reading sentences R= − 0.525 (P=0.008). There was a trend in this correlation for reading words R= − 0.398 (P=0.054). We found a negative correlation between amount of nocturnal epileptiform activity and Verbal IQ (R= − 0.51 P=0.08). No correlation was found between reading performance or Verbal IQ and amount of diurnal epileptiform activity. CONCLUSIONS: Reading performance is impaired in children with rolandic epilepsy and is correlated with the amount of nocturnal epileptiform activity.

Commentary

One of the most commonly cited “principles” of childhood epilepsy management is the concept of “treating the child, not the EEG.” The implied meaning is that treatment decisions should be made with the idea that the benefit of treatment should be greater than the potential adverse effects or that it is the overall quality of life that should be considered, not a diagnostic feature. However, there are some commonly accepted exceptions to this “rule” such as absence seizures as part of the childhood absence epilepsy syndrome, electrical status epilepticus during sleep (ESES), and hysparhythmia associated with epileptic spasms. The implication is that epileptiform abnormalities (spikes, sharp waves, electrographic seizures) are different than diagnostic features such as age of onset, sex, or etiology and different from a comorbidity such as attentional and behavioral problems. Rather, the implication is that the electrical abnormality is causal to an associated problem. The problems discussed include inducing more seizures (kindling), doing brain damage (excitotoxicity), and inducing a cognitive or behavioral decline or both (epileptic encephalopathy).

Impairments of the various domains of language can be considered a specific subset of the epileptic encephalopathies. The evidence that seizures and epileptiform discharges have a negative impact on language function, with an emphasis on rolandic epilepsy (RE), was recently the subject of a comprehensive review (1). It should be noted that the Landau-Kleffner syndrome (LKS) and ESES are also raised as examples of epilepsy syndromes that have epileptiform discharges while asleep and language/cognitive features as part of the syndrome definition.

The most relevant literature can be approached from at least two perspectives. The frequency of interictal, nocturnal epileptiform discharges in children with language impairment who do not have epilepsy has been reported to range from 13 to 94 percent (1), with the large variance likely explained by the specific language impairments, duration of EEG (routine with sleep versus prolonged), and degree of intellectual disability. The frequencies of nocturnal discharges reported are clearly elevated beyond general population numbers when compared with controls performed in some of the studies. Another approach is to consider the occurrence of language impairments in children with RE. This is set against the backdrop of the label “benign” applied to RE that was formerly considered a defining feature implying age-related resolution, few seizures, pharmaco-responsiveness, and lack of neurocognitive comorbidities. It has been clearly demonstrated that children with RE are subject to several types of language impairments, including problems with reading expression and comprehension, spelling, sound/phonologic, and vocabulary (2–7). These recent studies are methodologically sound with appropriate control populations.
The link between nocturnal discharges and language impairment has recently been provided by Ebus et al. in a study in which a well-defined population of 26 children (6–12 years old, IQ >70, no comorbid neurologic or MRI abnormalities) with seizures and EEG findings consistent with RE were studied. Approximately 75% had less than one seizure per 2-month period, and 65% were treated with a single antiepileptic drug (AED). The amount of epileptiform activity in the first sleep cycle of a 24-hour ambulatory EEG was put into the following categories: none, <1%, 1 to 10%, 10 to 50%, or 50 to 85%. Reading performance was measured by standardized Dutch tests of reading words and sentences. It was found that the extent of EEG abnormalities and language testing scores were significantly correlated (more discharges, lower language test scores) with a moderate degree of association (Spearman, $R = -0.525, p = 0.008$). Furthermore, a lower verbal IQ (WISC-RN, WISCIII) was associated with increased amounts of nocturnal epileptiform discharges. In contrast, there was no relationship between language measures and baseline seizure frequency, use of AEDs, or association with discharges in the awake state.

Thus, the relationship between nocturnal epileptiform discharges and language dysfunction in RE has become increasingly difficult to deny. The question now is what, if anything, to do about it? Should an attempt be made to decrease the nocturnal discharges, and if the answer is “yes,” then to what degree? Also, “yes” implies the requirement of repeating the EEG and language testing to determine the effect of therapy. An overnight EEG study may not be required as the frequency of discharges noted during a routine EEG with sleep onset compares favorably to recording all stages of sleep (8). Although the frequency of nocturnal epileptiform discharges was not the primary outcome measure, a small number of studies have suggested that AEDs may improve language function in RE with use of valproic acid (9) and levetiracetam (10). However, one study demonstrated a decrease in central temporal discharges and language skills with the use of sulthiame (11).

There is now significant evidence that the nocturnal interictal discharges, which are a defining feature of RE, may have a direct relationship to the language impairment found in many children with this common epilepsy syndrome. An alternative hypothesis is that the discharges are a manifestation of an underlying process that gives rise to the electrical and functional abnormalities. Further studies that carefully examine the functional consequences of epileptiform discharges in RE and the response to treatment are required. We should consider adding RE to the list of exceptions to the adage “Treat the child, not the EEG.” It may be that the EEG should be thought of as a part of the child that provides a unique window into functional activity of the brain and not simply a contributory laboratory finding.

by Jeffrey R. Buchhalter, MD, PhD

References

Instructions
The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in four parts.

1. Identifying information.
   Enter your full name. If you are NOT the main contributing author, please check the box “no” and enter the name of the main contributing author in the space that appears. Provide the requested manuscript information.

2. The work under consideration for publication.
   This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking “No” means that you did the work without receiving any financial support from any third party – that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check “Yes”. Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

3. Relevant financial activities outside the submitted work.
   This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. For example, if your article is about testing an epidermal growth factor receptor (EGF) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

   Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work’s sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

   For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Other relationships
   Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.
American Epilepsy Society

Epilepsy Currents Journal
Disclosure of Potential Conflicts of Interest

Section #1 Identifying Information

1. Today’s Date: 11/15/2012

2. First Name Jeffrey   Last Name Buchhalter  Degree MD, PHD

3. Are you the Main Assigned Author? ☑ Yes   ☐ No

   If no, enter your name as co-author:

4. Manuscript/Article Title: The Relationship between Nocturnal Discharges and Language Dysfunction in Roland Epilepsy: Treat the Child, Not the Adage

5. Journal Issue you are submitting for: Epilepsy Currents 12.5

Section #2 The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

<table>
<thead>
<tr>
<th>Type</th>
<th>No</th>
<th>Money Paid to You</th>
<th>Money to Your Institution*</th>
<th>Name of Entity</th>
<th>Comments**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Grant</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Consulting fee or honorarium</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Support for travel to meetings for the study or other purposes</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Fees for participating in review activities such as data monitoring boards, statistical analysis, end point committees, and the like</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Payment for writing or reviewing the manuscript</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Provision of writing assistance, medicines, equipment, or administrative support.</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Other</td>
<td>☑</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This means money that your institution received for your efforts on this study.
** Use this section to provide any needed explanation.
Section #3 Relevant financial activities outside the submitted work.
Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the “Add” box. You should report relationships that were present during the 36 months prior to submission.

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

<table>
<thead>
<tr>
<th>Type of relationship (in alphabetical order)</th>
<th>No</th>
<th>Money Paid to You</th>
<th>Money to Your Institution*</th>
<th>Name of Entity</th>
<th>Comments**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Board membership</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Consultancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Expert testimony</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Grants/grants pending</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Payment for lectures including service on speakers bureaus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Payment for manuscript preparation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Patents (planned, pending or issued)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Royalties</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Payment for development of educational presentations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Stock/stock options</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Travel/accommodations/meeting expenses unrelated to activities listed.**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Other (err on the side of full disclosure)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Section #4 Other relationships
Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☒ No other relationships/conditions/circumstances that present a potential conflict of interest.
☐ Yes, the following relationships/conditions/circumstances are present:

Thank you for your assistance.
Epilepsy Currents Editorial Board