

## FULL-LENGTH ORIGINAL RESEARCH

# Cortical auditory dysfunction in benign rolandic epilepsy

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### SUMMARY

**Purpose:** To evaluate cortical auditory function, including speech recognition, in children with benign rolandic epilepsy (BRE).

**Methods:** Fourteen children, seven patients with BRE and seven matched controls, underwent audiometric and behavioral testing, simultaneous EEG recordings, and auditory-evoked potential recordings with speech and tones. Speech recognition was tested under multiple listening conditions.

**Results:** All participants demonstrated normal speech recognition abilities in quiet, as well as normal peripheral and subcortical auditory function. BRE patients performed significantly worse than controls when speech recognition was tested under adverse listening conditions, including background noise. Five BRE patients who were impaired on two or more tests had centrotemporal spiking on awake EEG. There were no significant group differences in the latency or amplitude of early N100

cortical responses to speech or tones. Conversely, the mismatch negativity, a preattentive index of cortical processing that is elicited passively, was absent or prolonged for speech, but not tones, in BRE patients as compared to controls.

**Discussion:** Children with BRE demonstrated specific speech recognition impairments. Our evoked potential findings indicate that these behavioral impairments reflect dysfunction of nonprimary auditory cortex and cannot be attributed solely to attention difficulties. A possible association between auditory impairments and centrotemporal spiking (> 1/min) on awake EEG was identified. The pattern of speech recognition impairments observed is a known risk factor for academic difficulties in school-age children. Our results underscore the importance of comprehensive auditory testing, using behavioral and electrophysiological measures, in children with BRE.

**KEY WORDS:** Benign rolandic epilepsy, Evoked potentials, Speech recognition, Auditory cortex.

Benign rolandic epilepsy (BRE), also known as benign epilepsy with centrotemporal spikes, is a common form of childhood epilepsy, accounting for 14–20% of cases (Holmes, 1993; Bouma et al., 1997). BRE is characterized by focal, predominantly nocturnal seizures with unilateral or bilateral centrotemporal diphasic spike waves. Seizures

typically begin between 3 and 12 years of age and resolve spontaneously by age 15–18 years (Holmes, 1993).

BRE has traditionally been considered benign, in part, because patients perform normally on global measures of cognition and language (Beaussart, 1972; Bouma et al., 1997). There is increasing evidence, however, that BRE is associated with subtle and specific impairments in language, attention, and visual-spatial processing (Piccirilli et al., 1994; Weglage et al., 1997; Staden et al., 1998; Yung et al., 2000; Baglietto et al., 2001; Monjauze et al., 2005; Riva et al., 2007). Children with BRE also have reported difficulty processing spoken speech in the presence of background noise despite normal hearing

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(Staden et al., 1998). This pattern of speech recognition abnormality is a known risk factor for decreased academic performance in school-age children (ASHA, 2005). The presence of speech recognition impairments in children with BRE, who have otherwise normal hearing, could reflect seizure-related dysfunction of temporal lobe auditory areas responsible for sound processing. Alternatively, impaired attention may make it more difficult for children with BRE to listen selectively under adverse listening conditions. It has been difficult to test these alternative explanations using behavioral methods because they are subject to attentional confounds.

Auditory-evoked potentials provide objective measures of auditory function and can be elicited without a behavioral response or overt attention. A recent study using a passive elicitation paradigm reported abnormal cortical-evoked responses to speech in children with BRE who had previously undergone language testing (Staden et al., 1998; Liasis et al., 2006). To date, no studies have attempted to correlate behavioral and electrophysiological results obtained concurrently in children with BRE. Moreover, it is not known whether speech recognition impairments associated with BRE reflect more global auditory dysfunction. To address these issues, we combined behavioral and electrophysiological methods to study multiple auditory functions in children with BRE and in age- and gender-matched normal controls. Continuous EEG recordings were obtained during behavioral testing of patients with BRE to determine whether changes in daytime EEG were associated with behavioral performance.

## METHODS

### Participants

Fourteen right-handed children (8 males) ages 7.5–11 years participated: seven consecutively recruited patients with BRE and seven matched controls (Table 1). The diagnosis of BRE was based on clinical findings that included infrequent, predominantly nocturnal or sleep-related seizures (partial or generalized) beginning 4–10 years of age following previously normal development (Fejerman, 2008). An EEG obtained within 4 months of beginning the study showed an interictal pattern characteristic of BRE for all seven patients that included the presence of high voltage (100–300  $\mu$ V), diphasic spikes with a centrotemporal distribution and no evidence of persistent focal slowing (Gregory & Wong, 1984; Fejerman, 2008). All had been seizure-free for at least 1 month before beginning the study and were not on anticonvulsant medication at the time of testing. Patients had normal MRI scans, full-scale IQ scores  $\geq 90$ , and no history of developmental delays, attention disorders, or speech-language impairments prior to onset of seizures. There was no history of language regression with the onset of seizures. Based on parental report, all

**Table 1. Demographics for BRE patients and matched normal controls**

| Participant                  | Sex | Age (yrs)                      | VIQ                             | Seizure onset age (yrs)        |
|------------------------------|-----|--------------------------------|---------------------------------|--------------------------------|
| <i>Patients</i>              |     |                                |                                 |                                |
| 1                            | M   | 9                              | 121                             | 6                              |
| 2                            | M   | 10                             | 98                              | 8                              |
| 3                            | M   | 11                             | 108                             | 9                              |
| 4                            | M   | 11                             | 95                              | 6                              |
| 5                            | F   | 7.5                            | 127                             | 6                              |
| 6                            | F   | 11                             | 110                             | 8                              |
| 7                            | F   | 11                             | 106                             | 9                              |
| <i>Mean</i>                  |     | <i>10.07</i>                   | <i>109.28</i>                   | <i>7.25</i>                    |
| <i>(<math>\pm</math> sd)</i> |     | <i>(<math>\pm 1.36</math>)</i> | <i>(<math>\pm 11.51</math>)</i> | <i>(<math>\pm 1.38</math>)</i> |
| <i>Controls</i>              |     |                                |                                 |                                |
| 1                            | M   | 9                              | 99                              | NA                             |
| 2                            | M   | 10                             | 120                             | NA                             |
| 3                            | M   | 11                             | 91                              | NA                             |
| 4                            | M   | 11                             | 115                             | NA                             |
| 5                            | F   | 8                              | 121                             | NA                             |
| 6                            | F   | 11                             | NT                              | NA                             |
| 7                            | F   | 11                             | 110                             | NA                             |
| <i>Mean</i>                  |     | <i>10.14</i>                   | <i>109.33</i>                   |                                |
| <i>(<math>\pm</math> sd)</i> |     | <i>(<math>\pm 1.21</math>)</i> | <i>(<math>\pm 12.04</math>)</i> |                                |

NT, not tested; VIQ, verbal IQ score; NA, not applicable.

seven had experienced decreased academic performance with the onset of their seizures, including distractibility, reading comprehension difficulties, and difficulty following classroom directions. These observed changes were not sufficiently severe to require special education services or the diagnosis of learning disability. The other seven participants were age- and gender-matched controls with no history of academic difficulties, epilepsy, or other neurological or developmental disorders. All participants were enrolled in mainstream academic programs. Written parental consent was obtained for all participants. The study was approved by the Johns Hopkins Institutional Review Board.

### Procedures

All participants completed three sequential components of testing that included audiometric (hearing) screening, behavioral testing of auditory functions, and auditory-evoked potential recordings. BRE patients also underwent simultaneous EEG recordings during behavioral testing. Participants were tested individually in a sound-attenuated, electrically shielded room with measured ambient noise levels  $\leq 43$  dB sound pressure level. For each participant, testing was completed in a single morning session, with breaks provided between each test component.

### Audiometric screening

Pure tone air conduction thresholds were tested bilaterally at 500–4000 Hz (pass criterion  $\leq 20$  dB HL) with a two-channel, computer-based audiometric system (Noah v. 3.1, HIMSA; Aurical, Madsen, Schaumburg, IL, U.S.A.).

**Table 2. Behavioral tests of auditory function**

| Auditory function             | Test                                                                                        | Description                                                                                                                                      |
|-------------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Speech recognition in quiet   | CID-W22 Word recognition test (Katz, 1997)                                                  | 25 monosyllabic words presented monaurally.                                                                                                      |
| Speech recognition in noise   | Auditory figure ground: SCAN-C test (Keith, 2000)                                           | 40 monosyllabic words presented in +8dB S/N multispeaker noise.                                                                                  |
|                               | BKB – speech in noise (SIN) test (Etymotic Research, 2005)                                  | 10 sentences presented in multispeaker noise (+21 to –6 dB).                                                                                     |
| Acoustic filtering            | Filtered words: SCAN-C test (Keith, 2000)                                                   | 40 low-pass filtered words (1.0 kHz cut-off, 32 dB/octave roll-off).                                                                             |
| Dichotic listening            | Competing words: SCAN-C test (Keith, 2000)                                                  | 30 word pairs presented simultaneously (dichotically) to each ear.                                                                               |
| Auditory pattern sequencing   | Pitch pattern sequence test (Pinheiro & Ptacek, 1971)                                       | 20 triads of high-frequency (1430 Hz) or low frequency (880 Hz) tones. Listeners label triads (e.g., high-high-low).                             |
| Auditory selective attention  | Competing sentences: SCAN-C test (Keith, 2000)                                              | 20 phrase pairs presented dichotically. Listeners repeat right-ear phrases only for the 1st half of the test and left-ear only for the 2nd half. |
| Auditory continuous attention | The test of everyday attention for children (TEA-Ch) (Manly et al., 1999)                   | Listeners count beeps across 10 separate trials.                                                                                                 |
| Auditory verbal memory        | Digit span test: WISC III-R (Wechsler, 1991)                                                | Digit strings of increasing length presented for immediate recall (forward, backward).                                                           |
| Auditory verbal comprehension | Token test for children (DiSimoni, 1978)                                                    | Listeners implement verbal directions, of increasing complexity, by manipulating tokens of different colors and shapes.                          |
|                               | Understanding directions: Woodcock-Johnson III tests of achievement (Woodcock et al., 2001) | Listeners implement verbal directions, of increasing complexity, by pointing to pictures.                                                        |

Tympanometry (226 Hz probe, Madsen Zodiac 901) was performed to assess middle ear function with normal tympanograms defined as  $\pm 150$  daPa (Type A). Distortion product otoacoustic emissions were elicited for each ear at six frequencies (1.5, 2.0, 3.0, 4.0, 5.0, and 6.0 kHz). Emissions were measured in the 2f<sub>1</sub>-f<sub>2</sub> frequency band (f<sub>1</sub> intensity = 65 dB SPL, f<sub>2</sub> = 55 dB SPL), using a pass criterion of 5 dB or greater above the average noise level in adjacent frequency bands.

### Behavioral testing

Eleven standardized behavioral tests were administered to evaluate auditory function (Table 2). Tests measured speech recognition in quiet (1 test) and under adverse listening conditions (4), as well as auditory pattern sequencing (1), attention (2), verbal memory (1), and verbal comprehension (2). Speech recognition was tested under three adverse listening conditions: multispeaker background noise, acoustic filtering, and competing (dichotic) speech. An auditory sequencing task was administered to evaluate processing of nonverbal auditory information (tones). Two tests of auditory attention were included to assess selective and continuous attention skills. Auditory continuous attention was evaluated only in BRE patients.

Auditory verbal memory and comprehension were tested live-voice. All other tests were administered from CD through headphones (Seinheisser TDH-39, Old Lyme, CT, U.S.A.) at 50 dB HL presentation level. Participants responded orally and two practice items were given for each test. Interpretation of scores was based on published and

clinical norms. Test order was randomized across subjects. Percentage correct scores were converted to standard or scaled scores. A behavioral impairment was identified if a participant scored below the normal range on two or more tests. Impairments were further classified as mild (1–2 standard deviations below age norms) or severe (>2 standard deviations below age norms).

### Auditory-evoked potentials

Auditory-evoked potentials were recorded from 18 channels, using scalp electrodes placed according to the 10–20 system and a mid-forehead ground, with a Neuroscan System (Compumedics, El Paso, TX, U.S.A.). Electrodes were placed above each eye (Fp<sub>1</sub>, Fp<sub>2</sub>) to monitor ocular movement. Electrode impedances were <5 k $\Omega$ . Auditory stimuli were presented monaurally through insert earphones (ER-3, Etymotic Research, Elk Grove, IL, U.S.A.) at 70 dB nHL. During the recordings, participants watched a silent animated video on a small (3 × 5 inch) DVD screen.

#### Brainstem auditory-evoked potentials

Rarefaction clicks were presented (21/s) monaurally with 30 dB white noise masking in the contralateral ear. Recordings were made from vertex (Cz) using the mastoid ipsilateral to the stimulated ear as reference (A<sub>1</sub>, A<sub>2</sub>). Two runs of 1000 trials each were recorded for each ear. The EEG filter was set to band pass 0.01–3.0 kHz. Trials with ocular or movement artifact >50  $\mu$ V were rejected online. Waveforms were averaged using an analysis window of

5 ms prestimulus and 15 ms poststimulus. Waves I and V were identified visually. Peak latencies were corrected for a 1.0 ms delay associated with insert earphone presentation and compared to clinical norms.

#### *Cortical auditory-evoked potentials*

Cortical-evoked responses to 300 ms tones and speech were recorded using a passive oddball paradigm. For each stimulus type, 300 trials of standards (82%) and deviants (18%) were presented pseudo-randomly, with no two deviants occurring sequentially, to the right ear at 1.0 sec interstimulus intervals. Tone stimuli were 1000 Hz (standard) and 1200 Hz (deviant). Speech stimuli were digitized syllables /ba/ (standard) and /da/ (deviant). Continuous recordings were made using the right mastoid (A<sub>2</sub>) as reference, band-pass analog filtered online from 0.1–100 Hz, and sampled at 2.0 kHz. EEG epochs were created offline with –100 ms prestimulus and 300 ms poststimulus periods. The first three trials from each run and the first trial after each deviant stimulus were excluded from analysis. Before signal averaging, baseline correction was performed using the prestimulus waveforms and an artifact rejection algorithm (Neuroscan software, Compumedics, El Paso, TX, U.S.A.) was used to reject trials with peak amplitudes >70  $\mu$ V.

Waveform peak latencies and amplitudes were measured by an EEG research technician blinded to subjects' status and behavioral results. Responses to standards and deviants were averaged separately for each stimulus condition. The N100 was identified on the averaged deviant waveform from Cz as the maximal negative peak occurring between 85–125 ms after stimulus onset. The mismatch negativity (MMN) was measured on the difference waveform for Fz, obtained by subtracting the standard waveform from the deviant waveform, as the maximal negativity occurring after the N100 and between 130 and 265 ms poststimulus. The MMN was considered absent if no measurable negativity was present. Because cortical response latencies for speech have been reported to be longer than those for tones (Tiitinen et al., 1999), we did not impose an upper limit on their latency.

#### **Simultaneous EEG recordings**

BRE patients underwent simultaneous 30-min continuous EEG recordings during behavioral testing using the same 18-channel montage used for the cortical-evoked potential recordings. The EEGs were reviewed independently by two pediatric epileptologists (EPV, WT). Interictal EEG patterns were examined visually to identify, lateralize, and localize spike discharges and quantify spike discharge frequency. Laterality of discharges was defined as unilateral (left or right) or bilateral with either bisynchronous discharges or independent discharges over the right and left sides. Diphasic spikes were localized in a longitudinal bipolar montage, based on either central (C3 or C4 phase reversals) or centrotemporal (simultaneous C3+T3 or si-

multaneous C4+T4 phase reversals) distributions. The rate of spike discharges was expressed as number of discharges per minute and coded using a four-point scale (1: no spikes; 2: <1 spike/min; 3: 1–5 spikes/min; 4: >5 spikes/min).

## STATISTICAL ANALYSIS

We used paired *t*-tests to compare behavioral test scores and auditory-evoked responses for the 14 BRE patients and matched controls. Statistically significant results were verified with nonparametric alternatives (e.g., Wilcoxon-matched pairs signed-ranks test). A kappa statistic was computed to assess interrater agreement in the four-point coding of EEG spikes for BRE patients.

## RESULTS

### **Audiometric screening**

All 14 participants had normal pure tone thresholds bilaterally at 500–4000 Hz ( $\leq 20$  dB HL) and normal tympanograms (Type A). All participants passed the otoacoustic emission screening for at least one ear and 12 participants (7 BRE, 5 controls) also passed the screening of the second ear. Testing could not be completed on the second ear of two of the controls because a seal was not obtained.

### **Behavioral testing**

All 14 participants had normal hearing and demonstrated normal speech recognition abilities in quiet ( $\geq 92\%$  correct). They also demonstrated age-appropriate auditory continuous attention skills (standard score norms:  $10 \pm 3$ ) and comprehension of verbal directions, as measured by the Token Test for Children (DiSimoni, 1978; standard score norms:  $500 \pm 5$ ) and the Woodcock Johnson III (Woodcock et al., 2001; standard score norms:  $100 \pm 15$ ). Statistical comparisons revealed no significant differences between patients and matched controls on these three behavioral measures ( $p \geq 0.103$ ).

All seven BRE patients were impaired on at least one test of auditory function (Table 3). Five patients (71%) were impaired on two or more tests. Three of these patients demonstrated severe impairments, performing more than two standard deviations below age norms. All patients demonstrated impaired speech recognition in noise; four patients also performed poorly under other adverse listening conditions (filtered speech, dichotic listening). Statistical comparisons were performed to determine whether BRE patients had more difficulty in background noise than normal controls and whether they performed worse than controls under other adverse listening conditions (filtered speech, dichotic listening). We applied a Bonferroni correction for multiple comparisons, yielding an alpha level for determining statistical significance of  $p = 0.025$ . Patients demonstrated significantly worse speech recognition in noise scores than controls, requiring higher signal-to-noise levels to recognize speech accurately ( $p = 0.020$ ,

**Table 3. Behavioral results as percentage correct with standard or scaled scores (SS) in parentheses**

| Subjects (norms) | Words in quiet % ( $\geq 92\%$ ) | Words in noise % (SS 10 $\pm$ 3) | Sentences in noise SNR loss (0–2 dB) | Filtered words % (SS 10 $\pm$ 3) | Dichotic words % (SS 10 $\pm$ 3) | Competing sentences % (SS 10 $\pm$ 3) | Pitch pattern % ( $\geq 86\%$ ) | Digit span (SS 10 $\pm$ 3) |
|------------------|----------------------------------|----------------------------------|--------------------------------------|----------------------------------|----------------------------------|---------------------------------------|---------------------------------|----------------------------|
| <b>Patients</b>  |                                  |                                  |                                      |                                  |                                  |                                       |                                 |                            |
| 1                | 100%                             | 85%<br>(10)                      | 3.5 dB <sup>+</sup>                  | 80%<br>(8)                       | 82%<br>(13)                      | 95%<br>(14)                           | 100%                            | (10)                       |
| 2                | 96%                              | 75% <sup>+</sup><br>(6)          | 6.5 dB <sup>++</sup>                 | 60% <sup>++</sup><br>(2)         | 40% <sup>++</sup><br>(3)         | 60% <sup>+</sup><br>(6)               | 90%                             | (12)                       |
| 3                | 96%                              | 62% <sup>++</sup><br>(3)         | 7.5 dB <sup>++</sup>                 | 50% <sup>++</sup><br>(1)         | 33% <sup>++</sup><br>(2)         | 20% <sup>++</sup><br>(2)              | 40% <sup>++</sup>               | (5) <sup>+</sup>           |
| 4                | 92%                              | 72% <sup>+</sup><br>(5)          | 9.5 dB <sup>++</sup>                 | 70% <sup>+</sup><br>(4)          | 58% <sup>+</sup><br>(6)          | 55% <sup>+</sup><br>(5)               | 100%                            | (7)                        |
| 5                | 92%                              | 65% <sup>+</sup><br>(6)          | 3.5 dB <sup>+</sup>                  | 55% <sup>+</sup><br>(5)          | 53%<br>(9)                       | 45%<br>(8)                            | 100%                            | (9)                        |
| 6                | 100%                             | 95%<br>(14)                      | 3.5 dB <sup>+</sup>                  | 95%<br>(10)                      | 72%<br>(10)                      | 95%<br>(13)                           | 100%                            | (7)                        |
| 7                | 92%                              | 92%<br>(12)                      | 5.5 dB <sup>+</sup>                  | 95%<br>(13)                      | 53% <sup>+</sup><br>(5)          | 70%<br>(7)                            | 70% <sup>+</sup>                | (9)                        |
| Mean ( $\pm$ sd) | 95.42%<br>( $\pm$ 3.60)          | 78%<br>( $\pm$ 12.94)            | 5.64 dB<br>( $\pm$ 2.34)             | 72.14%<br>( $\pm$ 18.45)         | 55.86%<br>( $\pm$ 17.02)         | 62.86%<br>( $\pm$ 26.90)              | 85.71%<br>( $\pm$ 22.99)        | 8.43<br>( $\pm$ 2.30)      |
| <b>Controls</b>  |                                  |                                  |                                      |                                  |                                  |                                       |                                 |                            |
| 1                | 100%                             | 85%<br>(10)                      | 1.0 dB                               | 92%<br>(13)                      | 70%<br>(10)                      | 60%<br>(7)                            | 86%                             | (8)                        |
| 2                | 100%                             | 87%<br>(10)                      | 2.0 dB                               | 87%<br>(11)                      | 62%<br>(7)                       | 70%<br>(7)                            | 90%                             | (6) <sup>+</sup>           |
| 3                | 92%                              | 85%<br>(10)                      | 1.0 dB                               | 80%<br>(8)                       | 97%<br>(8)                       | 50% <sup>+</sup><br>(5)               | 90%                             | (7)                        |
| 4                | 96%                              | 85%<br>(9)                       | NT                                   | 77%<br>(7)                       | 83%<br>(13)                      | 80%<br>(9)                            | 96%                             | (8)                        |
| 5                | 100%                             | 85%<br>(11)                      | 2.2 dB <sup>+</sup>                  | 92%<br>(13)                      | 63%<br>(10)                      | 55%<br>(8)                            | 90%                             | (8)                        |
| 6                | 100%                             | 75% <sup>+</sup><br>(6)          | 0.9 dB                               | 82%<br>(9)                       | 65%<br>(8)                       | 80%<br>(9)                            | 90%                             | (7)                        |
| 7                | 96%                              | 90%<br>(11)                      | 0.5 dB                               | 85%<br>(10)                      | 80%<br>(12)                      | 85%<br>(10)                           | 90%                             | (8)                        |
| Mean ( $\pm$ sd) | 97.71%<br>( $\pm$ 3.15)          | 84.57%<br>( $\pm$ 4.61)          | 1.27 dB<br>( $\pm$ 0.67)             | 85%<br>( $\pm$ 5.77)             | 74.29%<br>( $\pm$ 12.96)         | 68.57%<br>( $\pm$ 13.76)              | 90.29%<br>( $\pm$ 2.93)         | 7.43<br>( $\pm$ 0.79)      |

<sup>+</sup>, mild impairment (1–2 standard deviations below the mean); <sup>++</sup>, severe impairment (>2 standard deviations below the mean); NT, not tested.

mean difference 4.73, 95% CI = 2.67, 6.80). Because of the relatively small sample size, this result was verified with a nonparametric alternative, the Wilcoxon-matched pairs signed-ranks test, which yielded a test statistic ( $z = 2.20$ ) that was borderline significant when using an alpha level adjusted for multiple comparisons ( $p = 0.028$ ). Although BRE patients also demonstrated poorer speech recognition than controls under other adverse listening conditions (filtered speech, dichotic listening), these differences did not reach statistical significance ( $p \geq 0.10$ ). On dichotic word listening, only one patient demonstrated an age-appropriate (right) ear advantage for speech (patient 1). Six patients showed either an atypically large right-ear advantage (patients 3, 4, 5, 6) or an atypical left-ear advantage for speech (patients 2, 7). Auditory selective attention was impaired in three patients (patients 2, 3, 4). Two patients had difficulty with tone (pitch) sequencing

(patients 3, 7); one had impaired auditory verbal memory (patient 3). However, BRE patients' scores were not significantly worse than those of normal controls on tests of auditory selective attention, tone sequencing, or auditory verbal memory ( $p \geq 0.530$ ).

None of the matched controls met criteria for impairment of auditory function on behavioral testing: three performed within normal limits on all behavioral tests; four scored in the mildly impaired range on a single test, with otherwise normal scores. All but one control (control 2) demonstrated an age-appropriate right-ear advantage for speech under dichotic listening conditions.

#### Auditory brainstem responses

For all participants, wave I and V peak latencies were within normal limits, ranging from 1.65 to 1.90 ms for wave I and from 5.50 to 5.75 ms for wave V, suggesting

**Table 4. Auditory evoked latencies (ms) and amplitudes ( $\mu\text{V}$ ): tones and speech**

| Subject         | Tones          |               |                |               | Speech         |               |                |               |
|-----------------|----------------|---------------|----------------|---------------|----------------|---------------|----------------|---------------|
|                 | NI latency     | NI amplitude  | MMN latency    | MMN amplitude | NI latency     | NI amplitude  | MMN latency    | MMN amplitude |
| <i>Patients</i> |                |               |                |               |                |               |                |               |
| 1               | 97.28          | -1.89         | 168.20         | -12.01        | 114.26         | 1.59          | 228.63         | -5.28         |
| 2               | 94.28          | -7.44         | 141.73         | -9.06         | 104.77         | -9.30         | -              | -             |
| 3               | 121.75         | -2.61         | -              | -             | 139.73         | -6.25         | -              | -             |
| 4               | 89.29          | -9.12         | 184.18         | -2.43         | 93.29          | -0.41         | -              | -             |
| 5               | 94.28          | 8.29          | 221.64         | -6.82         | 106.77         | 4.05          | 253.11         | -7.20         |
| 6               | 109.27         | -2.98         | 174.20         | -1.93         | 112.26         | -1.73         | 174.69         | -0.21         |
| 7               | 107.77         | 5.35          | 245.62         | -3.83         | 95.78          | -2.56         | 202.16         | -5.40         |
| Mean            | 101.99         | -1.48         | 189.26         | -6.01         | 109.55         | -2.09         | 214.65         | -4.52         |
| ( $\pm$ sd)     | ( $\pm$ 11.40) | ( $\pm$ 6.32) | ( $\pm$ 37.89) | ( $\pm$ 4.0)  | ( $\pm$ 15.41) | ( $\pm$ 4.54) | ( $\pm$ 33.80) | ( $\pm$ 3.0)  |
| <i>Controls</i> |                |               |                |               |                |               |                |               |
| 1               | 105.77         | -1.56         | 189.68         | -3.68         | 109.77         | -4.90         | 217.15         | -12.30        |
| 2               | 105.78         | -2.12         | 136.74         | -2.70         | 116.76         | -0.07         | 135.24         | -5.11         |
| 3               | 120.75         | -7.32         | 162.21         | -10.79        | 119.26         | -6.85         | 206.66         | -7.33         |
| 4               | 96.78          | 0.08          | 134.24         | -1.31         | 91.79          | -0.70         | 170.70         | -6.88         |
| 5               | 99.28          | 4.80          | 181.19         | -3.59         | 100.28         | 6.57          | 195.67         | 0.98          |
| 6               | 106.27         | -9.64         | 191.68         | -8.49         | 109.27         | -7.34         | 206.66         | -4.43         |
| 7               | 99.78          | -0.73         | 207.16         | -1.22         | 111.78         | -2.37         | 251.61         | -6.53         |
| Mean            | 104.91         | -2.35         | 171.84         | -4.54         | 108.42         | -2.24         | 197.67         | -5.94         |
| ( $\pm$ sd)     | ( $\pm$ 7.94)  | ( $\pm$ 4.79) | ( $\pm$ 28.24) | ( $\pm$ 3.68) | ( $\pm$ 9.52)  | ( $\pm$ 4.81) | ( $\pm$ 36.70) | ( $\pm$ 3.97) |

-, Absent.

normal subcortical transmission of auditory information from the periphery to the level of the inferior colliculus in the brainstem.

#### Auditory cortical responses

Cortical auditory N100 response latencies to tones and speech were compared for patients and matched controls (Table 4). For patients, N100 latencies were 89.29–121.75 ms (mean 101.99) for tones and 93.29–139.73 ms (mean 109.55) for speech. For matched controls, N100 latencies were 96.78–120.75 ms (mean 104.91) for tones and 91.79–119.26 ms (mean 108.42) for speech. A Bonferroni correction for multiple ERP comparisons was applied, yielding an alpha level for determining statistical significance of  $p = 0.0125$ . Statistical comparisons revealed no significant differences between patients and controls in N100 response latencies for tones ( $p = 0.315$ , mean difference  $-2.93$ , 95% CI =  $-9.46$ , 3.60) or speech ( $p = 0.813$ , mean difference 1.13, 95% CI =  $-10.08$ , 12.35). BRE patients had slightly smaller N100 amplitudes than matched controls that did not differ significantly for tones ( $p = 0.719$ , mean difference 0.87, 95% CI =  $-4.77$ , 6.51) or speech ( $p = 0.942$ , mean difference 0.15, 95% CI =  $-4.71$ , 5.00).

Measurable MMN responses to tones were evident for all but one BRE patient and for all normal controls (Table 4). MMN tone latencies were 141.73–245.62 ms (mean 189.26) for BRE patients and 134.24–207.16 ms (mean 171.84) for controls. Although mean MMN response latencies for tones were longer and larger for BRE patients compared with controls, these differences did not

reach significance ( $p \geq 0.271$ ). MMN responses to speech were absent in three patients. The four remaining patients had MMN speech latencies of 174.69–253.11 ms (mean 214.65). In contrast, all seven controls had measurable negativities in the expected latency range for the MMN: 135.24–251.61 ms (mean 197.67). The absence of an MMN for speech in close to half of the BRE patients precluded statistical comparisons.

#### EEG recordings

EEG spike rate, lateralization, and location for the seven BRE patients are listed in Table 5. The EEG for six of the seven patients showed high voltage, diphasic spikes with peak negativities in the central or centrottemporal region and fields that, in two patients, extended anteriorly to the frontal lobe, as reported previously (Gregory & Wong, 1984). Interrater agreement in the coding of EEG spike rate yielded a kappa score of 0.816. Six patients showed evidence of spiking on their EEG, with spike rates ranging from 0 to  $>5$ /min. Five patients had unilateral spike waves: four with left hemisphere spiking (patients 1, 2, 4, 5); one with right hemisphere spiking (patient 7). One patient had bilateral spikes (patient 3) and one patient showed no evidence of spiking on EEG (patient 6).

## DISCUSSION

All BRE patients demonstrated impaired speech recognition abilities under one or more adverse listening conditions despite normal hearing, cognition, and language comprehension. This finding is consistent with previous

**Table 5. Analysis of spikes in continuous EEG recordings from BRE patients**

| Patient | Spike rate | Spike                       |                | Speech recognition |
|---------|------------|-----------------------------|----------------|--------------------|
|         |            | lateralization (hemisphere) | localization   |                    |
| 1       | <1/min     | Left                        | Central        | WNL                |
| 2       | >5/min     | Left                        | Centrotemporal | ++                 |
| 3       | 1–5/min    | Bilateral                   | Centrotemporal | ++                 |
| 4       | >5/min     | Left                        | Centrotemporal | ++                 |
| 5       | 1–5/min    | Left                        | Centrotemporal | +                  |
| 6       | 0/min      | NA                          | NA             | WNL                |
| 7       | <1/min     | Right                       | Centrotemporal | +                  |

WNL, within normal limits; NA, not applicable; +, mild impairment; ++, severe impairment.

reports of subtle and specific functional impairments in children with BRE, including speech recognition difficulties in noise (Piccirilli et al., 1994; Weglage et al., 1997; Staden et al., 1998; Yung et al., 2000; Baglietto et al., 2001; Monjauxe et al., 2005; Riva et al., 2007). All of our patients had difficulty repeating phrases in high levels of background noise (e.g., 0 to –6 dB S/N) and four patients had impaired word recognition even in relatively low levels of noise (+8 dB S/N). The decrease in speech recognition scores cannot be attributed to stimulus length effects (words vs. phrases) as only one patient had impaired auditory verbal memory and none of the controls showed similar difficulties. Our relatively small sample size precludes generalization of these findings. Additional studies with larger numbers of BRE patients are needed to verify these findings.

Five BRE patients demonstrated impaired speech recognition under multiple adverse listening conditions, including background noise, acoustic filtering, and competing (dichotic) speech. This suggests that their speech recognition difficulties are not limited to background noise and may occur in a variety of real world listening environments including mainstream classrooms that often have high levels of reverberation and background noise resulting in degradation and masking of the speech signal (Nabelek & Pickett, 1974). Moreover, these speech recognition difficulties may go largely undetected since routine hearing evaluations rarely assess speech recognition under listening conditions other than quiet.

Our behavioral and evoked potential results further suggest that attention difficulties cannot account for the speech recognition impairments observed. All BRE patients demonstrated age-appropriate auditory continuous attention skills. The results are less clear for auditory selective attention, with three BRE patients and one normal control performing in the impaired range. However, the abnormal ERP results obtained from BRE patients provide further evidence against the auditory attention explanation. A passive oddball paradigm was used with a visual dis-

tracter to elicit the MMN, a preattentive index of cortical processing (Näätänen, 1990). Three patients showed no measurable MMN for speech and the mean MMN latency for the four remaining patients was prolonged. The three patients who showed no speech MMN responses also had the most severe speech recognition impairments on behavioral testing (patients 2, 3, 4). In contrast, the MMN was evident for all seven normal controls. The presence of an MMN for tones in all but one BRE patient suggests that the abnormality may be specific to speech or similarly complex sounds and not tones. This view is supported by the concurrent presence of the N100 response to tones in all BRE patients that did not differ statistically in latency or amplitude from those of the matched controls. The neural generators of the N100 include primary auditory cortex where frequency information is coded tonotopically (Vaughan & Ritter, 1970; Scherg & Von, 1986) in contrast to nonprimary auditory areas located on the lateral superior temporal gyrus, which have been identified as generators of the MMN and are associated with processing of complex sounds (Giard et al., 1990; Näätänen, 1990).

EEG recorded simultaneously during behavioral testing revealed spiking in six BRE patients, five of whom had impaired speech recognition abilities. The presence of spiking in the awake EEG of children with BRE has been reported previously (Metz-Lutz et al., 1999; Riva et al., 2007). However, another recent study reported no EEG spiking during wakefulness in children with BRE (Liasis et al., 2006). One possible explanation for the lack of spiking is that EEG abnormalities may have largely resolved by the time the recordings were made (Liasis et al., 2006), which was well after the initial diagnosis and identification of language abnormalities (Staden et al., 1998). In our study, EEG recordings and language testing were performed concurrently and both occurred within an average of 2.5 years of the initial diagnosis. It is unlikely that the EEG spiking observed affected our auditory-evoked potential findings since the spikes were relatively large (>100  $\mu$ V) and trials with such spikes would have been rejected automatically by our analysis protocol (rejection cut-off >70  $\mu$ V). Because EEG was recorded only during the first 30 min of behavioral testing and test order differed across patients, we cannot determine from our data whether spike activity was associated with impaired performance on a particular test. Future studies recording EEG during the entire behavioral test session using additional trigger channels to correlate spike activity with individual behavioral tests and test trials will be helpful in further clarifying this association. Similarly, longitudinal studies, combining behavioral and electrophysiological measures, are needed to determine if speech recognition impairments associated with BRE are transiently associated with EEG spiking or if they resolve once the EEG becomes normal.

In contrast to the four patients who had left hemisphere spiking (unilateral or bilateral) and impaired speech

recognition, one patient showed no EEG spiking and no behavioral impairments (patient 6). This suggests a possible relationship between EEG spiking and behavioral performance. However, another patient with left hemisphere spiking showed no behavioral impairments (patient 1). Interestingly, this patient had a very low spike rate (<1/min) and predominantly central distribution. One possibility is that low spike rate and/or less temporal lobe involvement may have resulted in the sparing of speech recognition. However, the sample size was too small for statistical comparisons by spike rate or location. Larger studies are needed to investigate a possible relationship between spike localization and rate.

Two patients had right hemisphere spiking: one unilateral (patient 7) and one bilateral (patient 3). These two patients were the only ones who performed poorly on the tone sequencing test and either had no MMN for tones (patient 3) or prolonged MMN tone latencies (patient 7). This pattern is consistent with the well-established role of the right temporal lobe in processing nonspeech auditory information, including pitch (Belin et al., 2000; Zatorre et al., 2002).

Interestingly, both patients also demonstrated speech recognition difficulties. This finding is consistent with studies suggesting that listeners require both hemispheres to process speech under adverse listening conditions (Shtyrov et al., 1999; Boatman et al., 2006).

In summary, our results indicate that children with BRE experience subtle and specific impairments in speech recognition. These impairments emerge under adverse listening conditions and cannot be attributed solely to attention effects. EEG results suggest a possible association with the presence of daytime spikes in either temporal lobe that warrants further study. One implication of our findings is that children with BRE are likely to experience speech recognition difficulties in their everyday listening environments, including classrooms, putting them at risk for academic difficulties. Comprehensive testing of auditory functions using behavioral and electrophysiological methods is important to identify children with BRE who could benefit from interventions, including assistive listening devices designed to improve signal-to-noise levels in the classroom.

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Conflict of interest: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that our report is consistent with those guidelines and that the authors have no conflicts of interest to disclose.

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