

Abnormalities in central auditory maturation in children with language-based learning problems

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Abstract

Objective: To examine maturation of the central auditory pathways in children with language-based learning problems (LP).

Methods: Cortical auditory evoked potentials (CAEPs) recorded from 26 children with LP were compared to CAEPs recorded from 38 typical children. CAEP responses were recorded in response to a speech sound, /uh/, which was presented in a stimulus train with decreasing inter-stimulus intervals (ISIs) of 2000, 1000, 560, and 360 ms.

Results: We identified three atypical morphological categories of CAEP responses in the LP group. Category 1 responses revealed delayed P1 latencies and absent N1/P2 components. Category 2 responses revealed typical P1 responses, but delayed N1 and P2 responses. Category 3 responses revealed generally low-amplitude CAEP responses. A fourth sub-group of LP children had normal CAEP responses.

Conclusions: Overall, the majority of children with LP had abnormal CAEP responses. These children fell into distinct categories based on the abnormalities in maturational patterns of their CAEP responses.

Significance: We describe a rate sensitive stimulation paradigm which may be used to identify and categorize LP children who exhibit abnormal patterns of central auditory maturation.

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Keywords: Language impaired; Learning impaired; Auditory processing deficits; Cortical auditory evoked potential (CAEP); P1; N1; P2; Stimulation rate

1. Introduction

Many children identified with language-based learning problems (LP) also have difficulties encoding auditory inputs, such as rapidly changing acoustic cues (Tallal et al., 1993; Nagarajan et al., 1999; Nicol and Kraus, 2004; Kraus and Nicol, 2005). Evidence from behavioral and electrophysiological studies indicates that some children have abnormalities in neurophysiologic encoding that may contribute to the altered perception of these acoustic cues (Tallal et al., 1996; Nagarajan et al., 1999; King et al., 2002; Wible et al., 2004). Several differences in cortical auditory evoked response (CAEP) morphology have

been reported in children with LP when compared to typically developing children. Cunningham et al. (2001) investigated the CAEP in response to a speech sound in quiet and in the presence of background noise. Results from that study indicate a greater attenuation of the P1 and N1 CAEP in background noise in children with learning difficulties. Wible et al. (2002) studied CAEP responses to repeated stimuli in background noise, and revealed decreased RMS amplitudes to subsequent stimulus repetitions in children with LP when compared to typically developing children. These findings corroborate previous evidence of weaker auditory cortical responses to repeated stimuli in adult poor readers (Nagarajan et al., 1999). These results have been interpreted to suggest that abnormal auditory encoding may underlie some auditory processing deficits in children with LP.

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There is considerable evidence to suggest that many auditory encoding problems in children with LP originate in the auditory periphery and auditory brainstem pathways (King et al., 2002; Wible et al., 2004, 2005; Kraus and Nicol, 2005; Johnson et al., 2005), which show a remarkable ability to encode and differentiate linguistic and paralinguistic information within the acoustic signal (Russo et al., 2004). In some children with LP, brainstem response measures have shown delayed responses to transient acoustic cues (King et al., 2002; Wible et al., 2004, 2005; Johnson et al., 2005). Recently, Wible et al. (2005) have shown that abnormal brainstem responses are correlated with “weaker”, atypical cortical responses. In light of these findings, Wible et al. suggest that the relationship between brainstem and cortical responses may provide a marker for abnormal speech perception abilities in children with LP. Furthermore, these findings indicate that abnormal subcortical processing can influence the maturation of cortical responses (Kraus and Nicol, 2005).

While there is evidence of decreased cortical activity in children with LP in some listening situations, there have been only a few studies that have examined maturation of the auditory system in this population. One measure of maturational changes in the central auditory system is the age-related change in morphology of the cortical auditory evoked potential (CAEP) (Tonnquist-Uhlen et al., 1995; Ponton et al., 1996, 2000; Sharma et al., 1997; Cunningham et al., 2000; Ceponiene et al., 2002; Gilley et al., 2005). In a series of papers, Tonnquist-Uhlen (1996a,b,c) described a comprehensive evaluation of scalp topography and peak morphology of the CAEP, including the T-complex (Wolpaw and Penry, 1979), in children with severe language impairments. Results from those studies revealed delayed CAEP latencies, but little difference in topographic distribution when compared to normal-hearing controls. Analysis of electroencephalographic (EEG) activity unrelated to auditory specific events revealed a high degree of abnormal EEGs in the learning impaired children. Overall, the findings from those studies suggest that some children with language impairments may have both an auditory processing deficit and a more global developmental delay in cortical processing. More recently, Bishop and McArthur (2004) described immature CAEP morphologies in response to tone pairs in children with LP. Results from that study also indicate delayed development of the central auditory system in children with LP.

Taken together, the studies reviewed thus far suggest that children with LP may have auditory processing deficits stemming from an abnormal and/or immature central auditory system. Recently, Gilley et al. (2005) showed that it is important to account for rate dependent properties of the CAEP when assessing central auditory maturation. Gilley et al. (2005) investigated the developmental changes in morphology of the CAEP using a stimulus paradigm that revealed rate sensitive development of the P1, N1, and P2 CAEP in normal-hearing children aged 3–12 years. In that study, the CAEP was recorded in response to a stimulus

train designed to examine the refractory properties of the CAEP (without regard to long-term habituation that may occur during the test session). Results from that study showed that the detectability, morphology, and amplitude of the N1 and P2 CAEP components were significantly altered as a function of both age and stimulation rate. Gilley et al. (2005) suggested that the morphological changes in the N1/P2 seen as a function of age and rate reflected the development of neuronal refractoriness of the generators underlying the N1/P2. Based on their findings, Gilley et al. (2005) concluded that the complex maturational patterns of the CAEP components are best understood when the effects of both age and rate on waveform morphology are considered. Therefore, it would be reasonable to investigate maturation in LP children with specific focus on the rate sensitive development of the CAEP.

In the present study, we recorded CAEP responses in a group of school-age children, who were clinically diagnosed with LP, using the rate sensitive paradigm described by Gilley et al. (2005). Responses were recorded from the vertex, Cz, as we are able to compare these responses to an extensive set of normative data (Gilley et al., 2005). Our goal was to examine patterns of CAEP maturation in children with language and learning difficulties.

2. Methods

2.1. Subjects

CAEPs were recorded in 26 children ranging in age from 6 to 13 years diagnosed with LP at the UTD Callier Center for Communication Disorders. All of the children were diagnosed by a professional clinician and referred to us after clinical testing. Referring clinicians reported using a variety of auditory and language materials in their diagnoses, which included the SCAN-C Test for Auditory Processing Disorders in Children, the Hearing in Noise Test for Children (HINT-C), the Staggered Spondaic Word Test (SSW), the Auditory Continuous Processing Test (ACPT), the Goldman–Frostoe–Woodcock Test of Auditory Discrimination (GFW-TAD), the Test of Auditory Processing Skills – Revised (TAPS-R), and/or the Test of Language Development (TOLD).

CAEP recordings from 38 typical children ranging in age from 5 to 12 years were taken from a previous study (Gilley et al., 2005). All subjects received informed consent prior to participation in any of the experimental procedures. All procedures and protocols, including informed consent procedures used in the present study received prior approval by the University of Texas at Dallas and its Institutional Review Board.

2.2. Stimulus paradigm

The stimuli used in this study were identical to those described by Gilley et al. (2005). CAEPs were recorded in response to a natural speech syllable [uh] with a 23 ms

duration. The speech sound was presented in a sequence of four presentations with sequentially decreasing inter-stimulus intervals (ISIs) of 2000, 1000, 560, and 360 ms preceding each presentation. In this approach, the ISI just preceding the stimulus eliciting the CAEP response was varied within the stimulus train. The stimulus was delivered via a loudspeaker placed at a 45° angle to the right of the subjects at a constant level of 70 dB SPL measured at the head location in the sound booth.

2.3. Evoked response recording procedures

During the recording procedure participants sat in a comfortable chair and watched a DVD movie of their choice. Audio from the DVD movie was kept below 40 dB SPL (Kraus et al., 1995). This testing environment has been found to be effective in engaging young subjects without interfering with the CAEP recordings (Sharma et al., 2002; Gilley et al., 2005). CAEP responses were collected using the vertex, Cz, as the active recording electrode referenced to the right mastoid. Eye movements were monitored using a bipolar electrode montage (lateral outer canthus referenced to superior orbital). The common ground electrode was placed on the forehead.

EEG responses were collected in response to each stimulus presentation with a recording window of 371 ms, including a 5 ms pre-stimulus interval. Incoming evoked responses were analog filtered from 0.1 to 100 Hz (12 dB/octave). EEG epochs containing eye blink activity were automatically marked for rejection during the recording procedure. The recording session was stopped when the number of EEG epochs acceptable for averaging reached approximately 1200. The test session, including electrode application and evoked response recording lasted about 45 min.

2.4. Data analysis

All data analysis procedures were performed offline after the recording session took place. EEG epochs with activity greater than $\pm 100 \mu\text{V}$ were rejected from further analysis. The remaining epochs were then baseline corrected to the average amplitude of the waveform, and averages were generated for each of the four ISI conditions. The averaged waveforms were then subjected to a digital, band-pass filter from 4 to 30 Hz (FIR, bi-directional zero phase shift, 12 dB/oct, 60 ms filter width) to enhance detection of the N1 and P2 CAEP responses (Ceponiene et al., 2002; Kavanagh and Franks, 1989; Sharma and Dorman, 2000). P1, N1, and P2 peak detection procedures were identical to those of a previous study using this stimulus design and recording procedure (Gilley et al., 2005). P1, N1, and P2 peaks were identified visually and independently by two experienced testers (authors PG and KM). The P1 was defined as the first robust positivity in the waveform in the time window of 50–300 ms. The N1 was defined as the first negativity

occurring after the P1 response, and only if the negativity appeared as a deflection with an amplitude apparently larger than the noise floor of the response. An additional criterion for the identification of the N1 component was the presence of a positive peak immediately following the negativity, defined as P2. The N1 and P2 peaks were not labeled if agreement between the two independent testers was not met, or if the components were not discernable from extraneous EEG noise. Within subject comparisons of the waveforms for each ISI condition were compared to differentiate peak components from possible noise. Latency and amplitude values were determined for each component (P1, N1, and P2) when present without regard to subject, age, or ISI condition. Amplitude values were measured from the baseline to peak of each component, and latency values were measured relative to the onset of the stimulus presentation.

3. Results

3.1. CAEP morphology

CAEP responses from the normal-hearing participants were subjected to two separate group-averaging procedures for comparison. First, normal-hearing participants were divided into four separate age groups of 5–6 years, 7–8 years, 9–10 years, and 11–12 years; and group averages and standard deviations were computed for each age group (Fig. 1). These four age groups were based on typical CAEP development as described by Gilley et al. (2005), and used to compare responses from age-matched children in the LP. Second, group averages and standard deviations were computed for all normal-hearing children irrespective of age to allow a more conservative comparison of CAEP morphology to children with LP.

In the LP group, each CAEP response was compared to the average responses for normal-hearing children, matched for age and ISI condition (Fig. 2). Morphologic patterns, which appeared abnormal when compared to normal-hearing children, were identified visually for further comparison. Fig. 2 shows CAEP responses from representative participants in each age category, compared to the average and standard deviations for age-matched, normal-hearing children. Morphologic patterns revealed three distinct categories of atypical CAEP responses. These categories include children with no evidence of N1 or P2 development, and a delayed P1 latency (Category 1); children with a normal P1 response, and delayed N1 and P2 responses (Category 2); and children considered to have generally low-amplitude responses when compared to normal-hearing children (Category 3). Children with morphologic patterns that did not appear abnormal were considered to have typical responses. Group averages were then computed for each of the response categories, and compared to the group averages for normal-hearing children irrespective of age (Fig. 3).

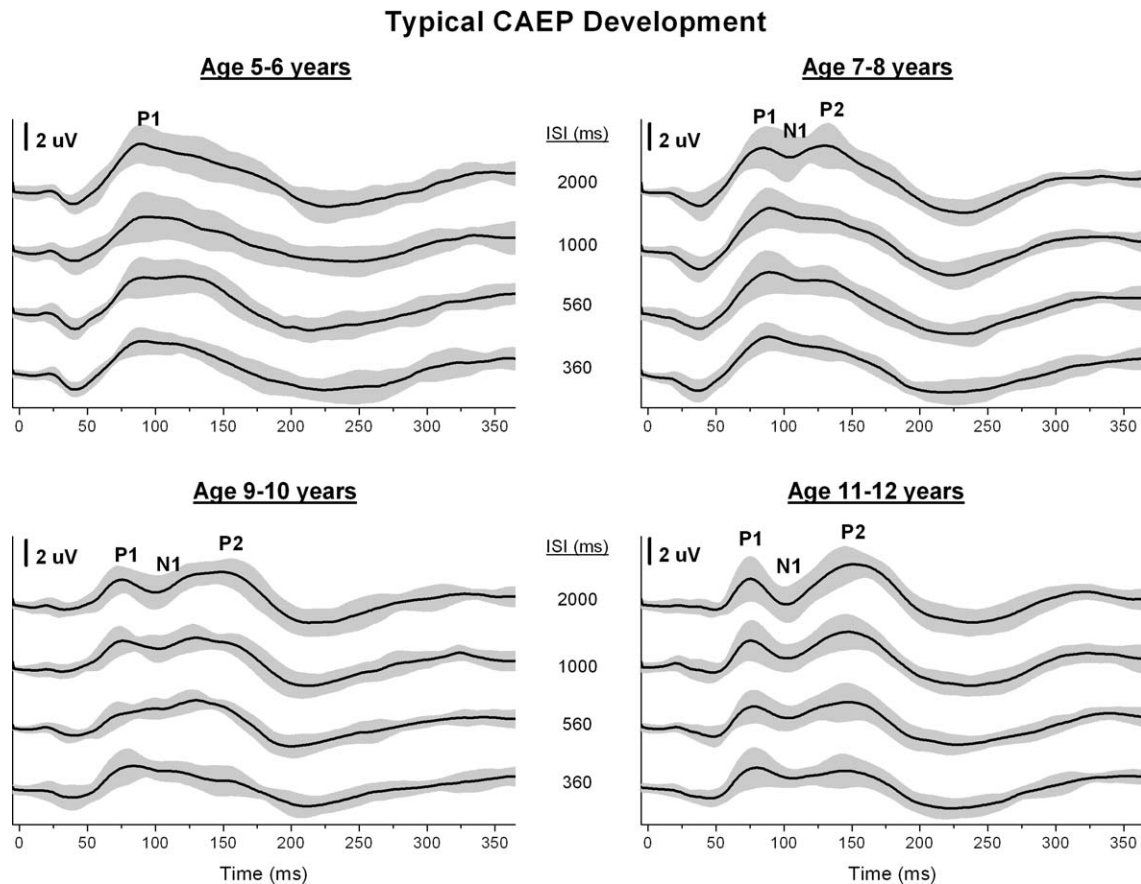


Fig. 1. Grand average CAEPs in four groups of normal-hearing children aged 5–6 years, 7–8 years, 9–10 years, and 11–12 years. CAEPs for each of four ISI conditions are represented for each age group (black line) plotted over the ± 1 standard deviation regions (shaded) for each condition.

3.2. Statistical analysis

Absolute latency and amplitude values for the P1, N1, and P2 CAEP components were each treated as dependent variables in separate analyses. Table 1 details the mean and standard deviations of peak latency and amplitude for each LP group. The data were treated as a partially repeated measures, analysis of variance (ANOVA) design. In this manner, each atypical response category, the typical response category, and the normal-hearing responses were each treated as separate groups for comparison, and the ISI condition was treated as a within-subject variable. Each group was then subjected to a *post hoc* analysis including a pair-wise comparison (Bonferroni correction for multiple comparisons) and a group comparison using Duncan's multiple-comparison test.

The P1 CAEP component was detected in all individuals in all ISI conditions. ANOVA results revealed a significant main effect of group for P1 latency [$F(4, 59) = 6.95$, $p = 0.00012$] and for P1 amplitude [$F(4, 59) = 3.67$, $p = 0.00974$]. A main effect of ISI was found for P1 amplitude [$F(4, 42) = 4.42$, $p = 0.00506$], but not for P1 latency. Results revealed no significant interaction effects of group and ISI for P1 latency or amplitude. *Post hoc* analyses of the P1 component revealed a significantly delayed P1 laten-

cy for Category 1 and Category 3 CAEP responses ($p < 0.05$), and significantly decreased P1 amplitudes for Category 3 responses ($p < 0.05$).

The N1 and P2 CAEP components were detected in 27 of 38 normal-hearing participants, 8 of 9 LP participants with typical responses, 0 LP participants with Category 1 responses, 6 of 6 participants with Category 2 responses, and 1 of 5 participants with Category 3 responses. The 1 Category 3 participant with an N1 response only revealed the components in the slowest ISI condition. The detectability of the N1 and P2 components in normal-hearing children is discussed in detail by Gilley et al. (2005). ANOVA results revealed a significant main effect of group for N1 latency [$F(3, 42)$, $p = 0.000035$] and for N1 amplitude [$F(3, 42)$, $p = 0.033$]. No significant main effects for ISI were found for N1 latency or amplitude, and no significant interaction effects of group and ISI were found for N1 latency or amplitude. ANOVA results revealed a significant main effect of group for P2 latency [$F(3, 42)$, $p = 0.000003$], but no main effect for ISI and no interaction effect of group and ISI. Additionally, there were no significant effects for P2 amplitude. *Post hoc* analyses of the N1 and P2 components revealed significantly delayed N1 and P2 latencies for Category 2 CAEP responses ($p < 0.01$), but no significant differences for N1 or P2 amplitude when detected.

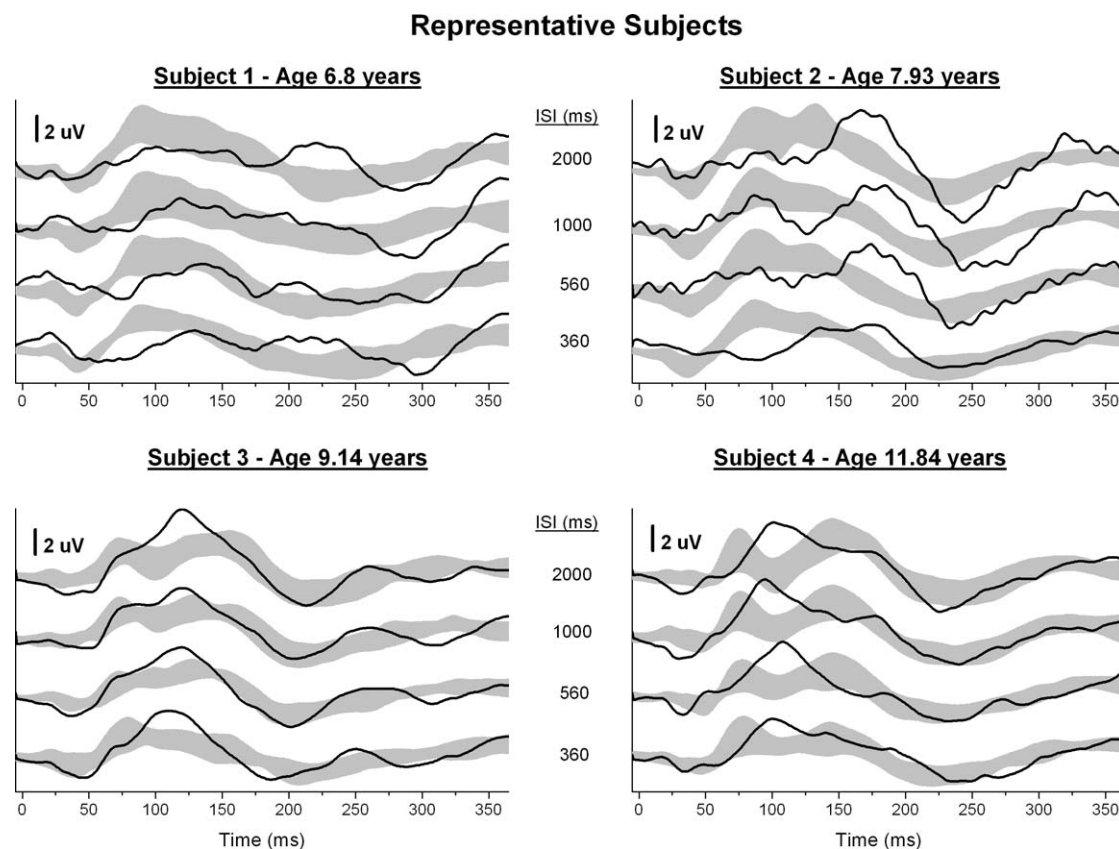


Fig. 2. CAEPs from four representative LP subjects (black lines) plotted over the standard deviation regions for age-matched, normal-hearing controls (shaded). CAEPs for each of four ISI conditions are represented. Categories for the representative subjects are: Subject 1—Category 3, Subject 2—Category 2, Subject 3—Category 1, and Subject 4—Category 1.

4. Discussion

The focus of this study was to examine patterns of CAEP maturation in a group of children with language based learning problems. We compared, individually, the CAEP responses from each LP participant to a group of normal-hearing controls matched for age and ISI condition. Overall, we found that the majority (17 out of 26) LP showed abnormal CAEP responses. In further analysis, we identified four categorical groups of children based on the morphological pattern of the CAEP in each condition. Results from the ANOVA and *post hoc* group comparisons verify the categorical groups identified by the age and ISI matched normal-hearing controls.

Children identified with Category 1 responses (6 out of 26) revealed waveform morphologies that consisted of a delayed P1 response, and no evidence of N1 or P2 responses. The P1 CAEP response is primarily generated from thalamic input to auditory cortex and auditory association areas (Erwin and Buchwald, 1986; McGee et al., 1991; Liegeois-Chauvel et al., 1994). In studies of humans and animals with auditory deprivation, delayed P1 responses have been attributed to immature development of the primary central auditory pathways (Kral et al., 2001; Sharma et al., 2002). Bishop and McArthur (2004) examined CAEP responses to rapid tone sequences in children with LP, and

found that older LP children revealed CAEP morphologies more similar to younger controls than to age-matched controls. The authors interpreted their findings to indicate that some children with LP may have generally delayed central auditory development. In the present study, children identified with Category 1 responses support the previous findings of Bishop and McArthur. The present findings, coupled with our results from studies of central auditory maturation in children who experience deprivation (Sharma et al., 2002), suggest that children with Category 1 responses may have delayed maturation of the auditory pathways that provide input to the auditory cortex.

Children identified with Category 2 responses (6 out of 26 children) revealed waveform morphologies with normal P1 latencies, but delayed N1 and P2 latencies. Because CAEP latencies reflect the sum of synaptic delays along the auditory pathways, latency changes as a function of age are typically attributed to synaptic development (Arezzo et al., 1986; Eggermont, 1988; Courchesne, 1990). Our findings are similar to those of Tonnquist-Uhlen (1996b) who found delayed P2 latencies in LP children, and attributed those delays to slower processing mechanisms. Although N1 and P2 latencies were delayed in Category 2 children, the overall pattern of N1 and P2 amplitude decrements with increased stimulation rate were similar to the normal-hearing group. These typical patterns

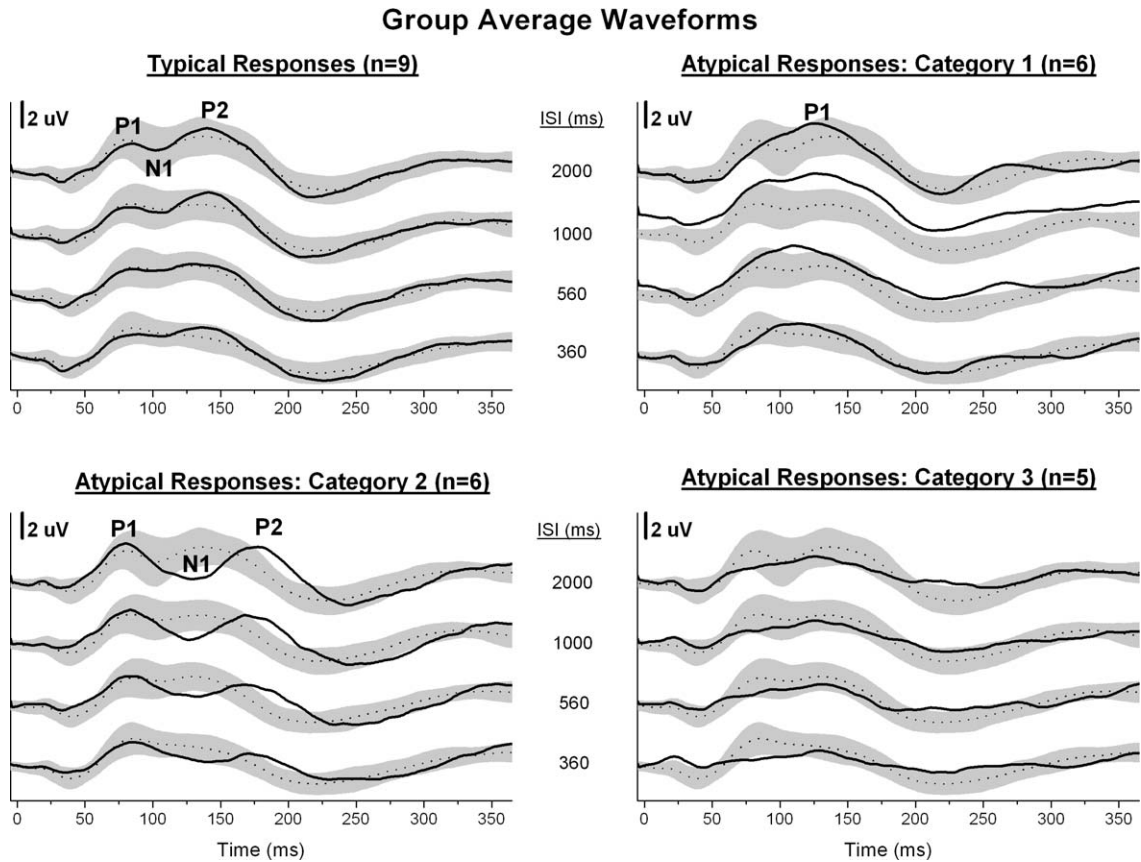


Fig. 3. Group average CAEPs for each of the atypical categories and the typical CAEP responses (black lines) are plotted over the cumulative standard deviation regions for normal-hearing children across all age groups tested (shaded). CAEPs for each of four ISI conditions are represented.

of amplitude changes in the N1 may reflect the normal aspects of axonal development in layers II and III of the auditory cortex (Eggermont and Ponton, 2003; Gilley

et al., 2005). Overall the findings from Category 2 present a more complex response pattern, and suggest that while primary input to the auditory cortex (P1) may be mature,

Table 1
Means and standard deviations (parentheses) for latency and amplitude of the CAEP components

ISI (ms) by group	P1 latency (ms)	N1 latency (ms)	P2 latency (ms)	P1 amp (μV)	N1 amp (μV)	P2 amp (μV)
<i>Typical</i>						
360	85.4 (11.2)	111.3 (11.6)	141.6 (12.4)	2.1 (0.9)	0.8 (0.7)	2.3 (0.9)
560	88.8 (12.2)	109.4 (12.9)	140.1 (14.3)	2.0 (0.7)	1.0 (0.8)	2.5 (1.0)
1000	89.9 (15.8)	106.9 (8.3)	147.1 (9.6)	2.1 (0.7)	0.5 (0.6)	3.1 (1.4)
2000	85.8 (10.7)	106.5 (7.8)	141.9 (10.0)	1.9 (1.0)	0.8 (0.8)	3.2 (1.4)
<i>Category 1</i>						
360	119.7 (35.5)	–	–	3.1 (1.2)	–	–
560	120.8 (29.4)	–	–	3.5 (0.9)	–	–
1000	123.8 (33.9)	–	–	3.8 (1.0)	–	–
2000	124.0 (29.6)	–	–	4.4 (1.6)	–	–
<i>Category 2</i>						
360	100.0 (35.2)	138.2 (12.3)	177.8 (6.3)	2.3 (1.2)	–0.5 (0.3)	0.7 (0.7)
560	84.2 (7.9)	130.0 (11.2)	171.9 (11.1)	2.2 (1.6)	0.1 (0.8)	1.6 (0.9)
1000	83.8 (7.7)	136.0 (19.3)	175.8 (11.8)	2.5 (1.4)	–0.4 (1.1)	2.1 (1.1)
2000	80.5 (8.1)	132.2 (11.9)	177.7 (10.5)	2.9 (2.1)	–0.8 (0.9)	2.6 (1.3)
<i>Category 3</i>						
360	117.6 (19.7)	–	–	1.1 (0.5)	–	–
560	106.0 (28.0)	–	–	1.4 (0.6)	–	–
1000	103.2 (23.8)	–	–	1.2 (0.6)	–	–
2000	111.2 (26.3)	95 ()	159 ()	1.6 (1.1)	–1.7 ()	1.5 ()

Note: –, indicates no observation for that condition; (), indicates no SD due to only one data point.

generators associated with N1 and P2 development may be immature in these children.

Children identified with Category 3 responses (5 out of 26 children) revealed waveform morphologies with generally low-amplitudes when compared to normal-hearing controls. Additionally, all of the children in this group showed some evidence of decreased amplitude with increased stimulation rate, although no statistical significance was found for this trend. N1 and P2 components could be identified reliably in only one of the children in this group. It is possible that the N1 and P2 components were present with very low amplitudes but the signal-to-noise ratios were too small to identify the N1 or P2 components with any confidence in most of the children with Category 3 responses (H. Neville, personal communication). The findings described for Category 3 responses appear to corroborate previous findings of decreased response amplitudes in children with LP (Cunningham et al., 2001; Wible et al., 2002) and of adults with poor reading abilities (Nagarajan et al., 1999). The studies by Cunningham et al. and Wible et al. both examined CAEP responses in the presence of background noise. Results from those studies indicate that some children with LP may have impairments of synchronous response activity in the presence of a masking noise. In the present study, however, a masking noise was not used when presenting the stimuli. The findings in the present study may suggest a general decrease in synchronous activity, indicating an immature development of the central auditory pathways in this respect.

In addition to the three atypical response categories described, nine of the LP children revealed typical CAEP responses, consistent with Cunningham et al. (2000). The N1 and P2 components do not begin to appear until about 7 years of age, and not in all ISI conditions until about 11 years of age (Gilley et al., 2005). Therefore, some children without evidence of the N1 or P2 components at all stimulation rates were considered to have typical responses if no other atypical morphologies were identified. One disadvantage of this categorization is that some of these children may show atypical development at later ages. For example, (Giraud et al., 2005) describe at least two different topographic response patterns in adult poor readers when comparing responses from stimuli with different temporal acoustic cues. Therefore, in light of these recent findings, it is important to consider the possibility of late emerging abnormalities when interpreting any findings from younger children. Further studies of CAEP responses to varying stimulus conditions may be necessary to determine if other patterns of abnormal maturation may exist in this group of children.

We have described a rate sensitive stimulation paradigm which can be used to identify and categorize LP children who exhibit abnormal patterns of central auditory maturation. Our results suggest that LP children fall into different categories based on the abnormalities exhibited in the development of their CAEP responses as a function of stimulation rate. Future studies should examine whether

the children who fall into these abnormal categories also exhibit deficits in brainstem processing, psychoacoustic and behavioral perception of acoustic cues that have been previously documented in LP children.

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