Obligatory cortical auditory evoked potentials to speech and tonal stimuli in infants and adults with normal hearing

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Objective: To determine differences between infant and adult cortical auditory evoked potentials (CAEPs) for a range of speech and tonal stimuli.

Design: CAEPs were recorded at C3, Cz, and C4 electrode locations from 14 adults and 20 infants (aged 3-7 months) with normal hearing. Adults were tested using 500, 1k, 2k, and 4k Hz tonebursts and /t/, /k/, /d/, /g/ speech sounds presented at 65 dB SPL. Infants were tested with a subset of these stimuli (500 Hz, 2 kHz, /g/, /t/) plus an additional sound /m/ that was included to achieve greater spectral contrast across speech stimuli.

Results: CAEPs were reliably present for all subjects and all stimuli. There were substantial differences in the morphology of CAEPs between adults and infants. Adult waveforms showed the well-documented P1, N1 and P2 peaks that occurred at 57, 106, and 198 ms, on average, across stimuli and electrode montages. Infant waveforms showed a broad positivity "P1" at 202 ms following by a late negativity "N_{late}" at 367 ms, on average. Some infants had a double-peaked P1; the proportion infants with this morphology varied across stimuli. CAEP latencies and amplitudes differed significantly across stimuli for both adults and infants. Electrode montage affected N1/P2 in adults and P1 in infants. N1 was earlier and larger at Cz in adults and P1 was larger at C3 in infants.

Conclusions: CAEPs can be recorded reliably to a range of speech and tonal stimuli in both infants and adults. CAEP waveforms differ significantly across stimuli. Further work is needed to identify the specific effects of speech stimulus parameters on CAEPs.

KEYWORDS

cortical auditory evoked potential; neural encoding; speech stimuli; tones; infants; electrode montage

INTRODUCTION

The slow "obligatory" cortical P1-N1-P2 evoked potentials occur within about 300 ms after stimulus onset in adults. The slow cortical potential is referred to as obligatory because it is primarily determined by the physical properties of the stimulus and it invariably occurs when the sound is detected by the subject (Hyde, 1997; Stapells, 2002). Cortical potentials are affected by both arousal level and attention and are typically recorded when the subject is awake and alert or in a light sleep stage (Cody, Klass, & Bickford, 1967). Novak and Kushnerenko and colleagues have reported that cortical potentials are similar when infants are awake and in "active" sleep (Novak, Kurtzberg, Kreuzer, & Vaughan, 1989; Kushnerenko, Ceponiene, Balan, et al., 2002). Because of the difficulty of monitoring sleep stage, cortical recordings are typically made when subjects are awake, however.

Obligatory cortical auditory evoked potentials (CAEP) are routinely used by clinicians to estimate hearing sensitivity in adults because the P1-N1-P2 response thresholds agree very well with audiometric thresholds determined behaviorally (Cody et al., 1967; Davis, 1965; Tsui, Wong, & Wong, 2002). The auditory brainstem response (ABR) and auditory steady state response (ASSR) are widely regarded as more suitable for assessment of hearing sensitivity in infants (Sininger, 2003) because infants are usually tested when they are

asleep. As noted by Cone-Wesson and Wunderlich (2003), however, it may be possible to use CAEPs to obtain threshold in infants if subject state is closely monitored, and if age-appropriate normative data is available.

Kurtzberg, Hilpert, Kreuzer, and Vaughan (1984) reported that cortical potentials were present in 100% of well babies (n=17) and in 34 of 35 very low birthweight babies that they tested at age 2 months. Pasman and colleagues measured cortical potentials in preterm babies at 35-37 weeks conceptional age and also reported good (95%) detectability rates (Pasman, Rotteveel, de Graaf, et al., 1991). The cortical potentials reported in these studies differ from the adult P1-N1-P2 waveform. Up to about 7 years of age the vertex-recorded cortical potential often consists primarily of a single positive wave rather than a P1-N1-P2 complex, although there is some variability in CAEP morphology across studies (Wunderlich & Cone-Wesson, 2006). The developmental time course of the slow cortical potentials has been investigated in a number of studies (eg, Kurtzberg et al., 1984; Kushnerenko et al., 2002; Novak et al., 1989; Ponton, Don, Eggermont, Waring, & Masuda, 1996; Ponton, Eggermont, Kwong, & Don, 2000; Ponton, Eggermont, Khosla, et al., 2002; Sharma, Kraus, McGee, & Nicol, 1997). There are complex changes in the morphology, scalp distribution and amplitude and latency of the P1-N1-P2 waves with maturation (Ponton et al., 1996, 2000, 2002; Wunderlich & Cone-Wesson, 2006). This is not unexpected since the cortical potentials are generated by multiple brain regions including primary auditory cortex, auditory association areas, frontal cortex, and subcortical regions (Stapells, 2002) that mature at different rates.

Ponton et al. (2000) reviewed the evidence for generators of scalp-recorded CAEPs and concluded that, in adults, P1 originates from secondary auditory cortex and N1b reflects activation of primary auditory cortex resulting from intra- and inter-hemispheric activity, rather than the first volley of primary auditory cortex afferent activity. Ponton et al. (2002) investigated the maturational time course of the various CAEP peaks and found that P1 was robustly present in young children (aged 5 years+), but that its latency was not fully mature until very late (18-20 years). For children aged 5-6 years of age N1b was not consistently measurable in 5-6 year olds and became adult-like by 15-16 years of age.

Kushnerenko et al. (2002) found that infants aged 0 to 12 months have either a single or double positive peak cortical waveform. The cortical waveforms in the early publications of Kurtzberg and her colleagues also show both single and double-peaked positivities in the 150-350 ms latency region for infants aged 0-6 months, with differences in waveform morphology between stimuli (eg, Novak et al., 1989). The negativity following the positive peak in the immature cortical waveform is labeled differently in various publications as N1b (Sharma et al., 1997; Ponton et al., 2000), or N2 (Rapin & Graziani, 1967; Rotteveel de Graaf, Stegeman, et al., 1987; Pasman, Rotteveel, de Graaf, et al., 1999). The N1 peak recorded at the vertex has been referred to as N1b to distinguish it from the N1a and N1c negative peaks recorded from temporal regions (Picton, 1990). Kushnerenko et al. (2002) referred to the negativity following P1 as N250 and N450, depending on the latency. Pasman et al. (1991, 1999), Pang and Taylor (1999), and Sharma, Dorman, and Spahr (2002) recorded CAEPs in young children aged 0 to 4 years and obtained latencies in the approximate latency ranges of 150-200 ms for P1 and 300-350 ms for the late negativity

after P1. These latencies are considerably slower than those found in young school-aged children (eg, Gomes, Dunn, Ritter, et al., 2001; Ponton et al., 2002), indicating substantial maturational changes in the CAEP in the preschool years. This is consistent with Moore and Guan's (2001) finding of maturational changes in the cytoarchitecture of the deep cortical layers up to age 5 years.

CAEPs have been recorded using a wide range of stimuli including tones, clicks, and speech stimuli. Several studies have shown differences in CAEP latencies for different tonal stimulus frequencies recorded using conventional evoked potential and magnetoencephalography techniques (Crottaz-Herbette & Ragot, 2000; Jacobson, Lombardi, Gibbens, et al., 1992; Roberts & Poeppel, 1996; Salajegheh, Elster, Burghoff, et al., 2004; Verkindt, Bertrand, Perrin, et al., 1995; Woods, Alain, Covarrubias, & Zaidel, 1993). There is some evidence that CAEPs in infants evoked by different speech phonemes differ in latency and morphology (eg, Kurtzberg, 1989). CAEP differences between speech stimuli are an indication of different underlying neural representations of speech sounds, and suggest that the information needed to differentiate the stimuli is available to the listener. There has been increasing interest in the use of cortical potentials to investigate the neural encoding of speech (Tremblay, Billings, Friesen, & Souza, 2006). Various studies have shown CAEP latency and/or amplitude differences with changes in voice onset time (Sharma et al., 1997; Sharma, Marsh, & Dorman, 2000; Tremblay, Friesen, Martin, Wright, 2003a; Tremblay, Piskosz, & Souza, 2003b), and differences between vowels (Obleser, Elbert, Lahiri, & Eulitz, 2003; Obleser, Eulitz, Lahiri, & Elbert, 2001; Obleser, Lahiri, & Eulitz, 2004; Shestakova, Brattico, Soloviev, et

al., 2004), and consonants (Gage, Poeppel, Roberts, & Hickok, 1998; Tremblay et al., 2003a).

Some years ago investigators showed that CAEPs can be used to compare unaided *versus* aided function in hearing impaired infants (Gravel, Kurtzberg, Stapells, et al., 1989; Rapin & Graziani, 1967). Objective tools are needed to evaluate hearing aid function in young infants who are difficult to assess behaviorally, especially now with the widespread implementation of universal newborn hearing screening programs. This was the motivation for the current study, which investigated CAEP characteristics in young infants with normal hearing to determine whether CAEPs can be reliably recorded to a range of stimuli at suprathreshold levels, and whether CAEP waveform characteristics differed across stimuli. Both adults and infants were tested.

METHOD

Subjects consisted of 14 adults (6 men, 8 women) aged 20-58 years (mean 36.7, SD 10.8 years) and 20 infants (8 boys, 12 girls), including two sets of girl twins (one identical set, one non-identical set). The age range of the infants was from 3 $^{1}/_{2}$ - 7 months (mean 5.0, SD 1.0 month). All the infants were full term except for a boy and a girl both aged 5 months at the time of testing who were born at 34 and 36 weeks gestational age, respectively. The infants were classified as normal hearing based on parental report and the presence of bilaterally normal transient click-evoked otoacoustic emissions (OAE). Adults had pure tone audiometric thresholds of 20 dB HL or better and normal Type A tympanograms.

During the testing infants were seated on a caregiver's knee in a soundproof room. The infants were awake and distracted by toys by a tester in the room who monitored the infant's state, while another tester conducted the CAEP testing from the adjoining control room. The infants listened binaurally to loudspeaker-presented sounds presented via a loudspeaker on the right hand side at 45 degrees azimuth, 1.5 m from the infant's head position. Due to the 1.5 m loudspeaker distance, latencies reported here are delayed by several milliseconds (4.4 ms, assuming a speed of sound of 345 m/s) compared to those obtained with earphones. Adults were tested via the same loudspeaker setup and watched a silent subtitled video during testing. Data collection was conducted over one or two test sessions each lasting up to an hour approximately. Testing of infants was terminated if they became unsettled, or fell asleep.

Stimuli were generated and CAEP were recorded using the Neuroscan STIM and SCAN evoked potential system. Interstimulus interval was 750 ms. Stimuli used to test adults consisted of 500, 1k, 2k, and 4k Hz tonebursts with 60 ms duration (20 ms rise/fall times, 20 ms plateau) and speech phonemes (/t/, /k/, /d/, /g/), presented at 65 dB SPL. Because of time constraints, infants were tested using a subset of the stimuli used to test adults. The adult subjects were tested first. After data collection was completed for the adults and preliminary analyses were performed on this data, an additional speech phoneme /m/ was added for infant testing, with the goal of ensuring a greater spectral contrast between speech stimuli. The five stimuli used when testing infants were 500 Hz, 2 kHz, /t/, /g/, and /m/.

The speech stimuli were natural speech tokens (initial consonants, followed by the vowel /ae/) extracted out of a recording of running speech digitized at 40 kHz, spoken by a native Australian male. The stops include the release and very little of the vowel transition. Stimulus durations were as follows: /t/ 79 ms, /g/ 32 ms, /m/ 141 ms, /k/ 82 ms, and /d/ 27 ms. Speech stimuli were gated off near a zero crossing to prevent audible clicks. Three recording channels were used to enable midline (Cz, vertex) and lateral (C3, C4) placement of electrodes. An additional electrode was placed above the eye to monitor eye blinks in the adults. The reference electrode was placed on the right mastoid and the ground electrode was placed on the forehead.

The order of stimulus runs was randomized in two blocks for the five stimuli used to test infants and the eight stimuli used to test adults. Each run lasted several minutes and was terminated when 100 artifact-free EEG samples were acquired. Artifact rejection was set at +/- 100 V in infants and +/- 75 V in adults (including the eyeblink channel in adults). The recording window was -100 to +500 ms relative to stimulus onset. On-line filtering was set at 0.1-100 Hz. Off-line analysis consisted of baseline correction, linear detrending, and 30 Hz low pass digital filtering.

The two replications and the grand average waveform were printed for peak picking by two independent observers. Adult waveforms consisted of P1, N1, and P2 peaks at about 50, 100, and 200 ms, respectively. The waveform in the infants consisted of a large positivity at about 200 ms and a broad late negativity, which we refer to here as P1 and

N_{late}, respectively. Peak latencies and amplitudes were identified using the following criteria in infants: P1 was defined as the first large positive peak, with amplitude picked at the highest peak and latency taken in the middle of the peak (generally these two points coincided but not always). The infant P1 was described as a "double peak" if there were two peaks in the region from about 100 ms to 350 ms, and the amplitude of the negative trough between two peaks was less negative (ie, smaller) than the amplitude of the negative trough following the double peak. In this case the amplitude of P1 was taken as that of the higher peak and the latency was taken as the mid-point of the double-peaked P1. N_{late} was defined as the first major negative trough after P1. School aged children can show both an early and a late "N1" negativity (Sharma et al., 1997; Ceponiene et al., 1998; Kushnerenko et al., 2002). The late negativity at about 250 ms ("N250") seen in school-aged children is not as late as the negativity seen in infants in the current study, hence the use of the term N_{late} rather than N250.

RESULTS

CAEPs in adults

Adult grand average waveforms are shown in Figure 1, and peak latencies and amplitudes are shown in Tables 3 and 4 respectively. Repeated measures analyses of variance (ANOVA) were performed to determine whether latencies or amplitudes of P1, N1, and P2 were affected by stimulus and electrode montage. Significance levels for the statistical results obtained for adult data are shown in Table 1. There were significant differences in

N1 and P2 peak latencies and P1, N1, and P2 amplitudes across stimuli, and there was a significant effect of electrode montage on N1 latency and amplitude and P2 amplitude.

N1 amplitudes were generally larger and N1 was earlier on average for the tonal stimuli compared to speech stimuli in adults. Figure 2 shows that N1 amplitude was maximal for the 1 kHz tonal stimulus. Posthoc analyses showed that N1 amplitudes were significantly larger for 1 kHz tones than for all other tonal stimuli ($p<0.05$), across electrode montages.

Overall, when comparing the speech *versus* tonal stimuli for adults, P1 was bigger, and P2 was later and bigger for speech. There was a significant stimulus by electrode montage interaction for the amplitude of N1. Figure 2 shows a consistent Cz (vertex) electrode montage advantage for N1 amplitude that is evident across stimuli for the adults. When comparing responses to speech stimuli, P1 and N1 peaks were largest and latest, and P2 was smallest for /t/. Posthoc analyses showed that N1 and P2 latencies and P1, N1 and P2 amplitudes differed significantly for /t/ and /k/ compared to the tonal stimuli.

CAEPs in infants

All infants had repeatable CAEP waveforms for each of the stimuli. There were no obvious CAEP morphology differences across infants within the 3-7 month range, consistent with Novak et al.'s (1989) finding that CAEP wave shape (morphology) and scalp topography were similar in infants aged 3 and 6 months. Figure 3 shows that the infant CAEP grand average waveforms have very different morphology to those recorded

in adults. The infant waveforms also show significant differences across stimuli for both P1 and N_{late} (see Table 2). In adults N1 amplitudes were greatest at Cz. In contrast, infants showed no systematic amplitude differences across electrodes for N_{late}, and P1 was consistently larger at C3 for all stimuli (see Table 6). There was a statistically significant effect of electrode montage on P1 amplitude.

When the infants' P1 is compared for the different stimuli, we see that P1 is larger in amplitude and earlier for speech. Across speech stimuli, N_{late} was similar for /g/ and /t/, and larger and later for /m/. Posthoc analyses showed statistically significant differences between /m/ and /t/ and between /m/ and /g/ latencies and amplitudes for P1 and N_{late}, for all three electrode montages. There were fewer significant differences between /t/ and /g/. P1 amplitudes were significantly greater for /t/ across electrode montages and N_{late} latencies were significantly earlier at Cz for /t/ compared to /g/, however. For the N_{late} peak, comparing speech *versus* tones, /m/ produced a larger and later N_{late}. For tones, N_{late} was smaller and earlier for 2 kHz *versus* 500 Hz. Posthoc comparisons showed that these amplitude and latency differences were significant at Cz and C4.

The early negativity immediately prior to P1 in the infant CAEP waveform contains post auricular muscle response (PAMR) for the /g/ and /t/ speech stimuli, and hence the latencies and amplitudes of this peak was not analyzed statistically. To verify that the early biphasic waveform occurring at about 20-50 ms in the cortical waveforms was the PAMR, several infants (n=7) were tested using an additional recording montage that optimizes PAMR amplitude (O'Beirne & Patuzzi, 1999). This involved placing an

additional non-inverting electrode on the back of the pinna, referenced to the inverting electrode on the mastoid. The mastoid to pinna recording montage produced an inverted PAMR waveform, enhanced PAMR amplitude and absent cortical responses in all seven infants tested using this additional electrode montage (Purdy, Katsch, Dillon, et al., 2005).

A double peak was present in 65% (N=13) of 2 kHz recordings (see Figure 5). This response morphology was not seen as commonly in the infants for the other stimuli (≤30%). The speech stimulus that produced a double-peaked waveform most commonly (30% of infants, N=6) was /g/. Figure 5 shows that the early part of the CAEP waveform (containing PAMR and P1) is very similar for infants with single- and double-peaked waveforms, with the differences arising after about 250 ms.

DISCUSSION

Adult versus infant CAEP morphology

As expected there were substantial differences in the CAEP waveforms recorded from adults and infants. Infant CAEP amplitudes are larger than those recorded in adults, and the latencies of the major P1 and N_{late} peaks are considerably later. P1 occurs at about 200 ms in infants *versus* about 60 ms in adults. P1 latencies obtained for tonal and speech stimuli were consistent with those shown in previous studies of CAEPs in infants aged

less than 12 months (Rapin & Graziani, 1967; Gravel et al., 1989; Kurtzberg et al., 1989; Pasman et al., 1999; Sharma et al., 2002).

The current consensus is that P1 is generated in deeper cortical layers, in the lateral portion of Heschl's gyrus (secondary auditory cortex). N1 is thought to have several generators in upper cortical layers including primary and secondary auditory cortex sources in or near the supratemporal plane (Ponton et al., 2002). Ponton et al. (2002) suggested that CAEP maturational changes reflect developmental changes in the cortical layers. The auditory cortex has fewer neuro-filaments in young children, especially in more superficial cortical layers thought to generate N1 (Moore, 1999; Moore & Guan, 2001). Auditory cortex has a laminar structure with layers distinguished by the predominance of different cell types and different cellular connections (Linden & Schreiner, 2003). Recent studies using functional imaging and molecular techniques suggest a more detailed laminar structure than the traditional six-layer view (Zilles, Palomero-Gallagher & Scheicher, 2004) and there is increasing interest in the role of these laminar differences in auditory processing in the cortex (Linden & Schreiner, 2003). The most superficial "marginal" layer, also known as layer I, appears mature at birth (Moore, 1999; Ponton et al., 1999). Layer I is thought to have an important intra-cortical role that may stimulate the development of deeper cortical layers, but cells in this layer do not carry information about external stimuli (Moore, 1999). The thalamo-cortical pathway ends in the middle layers III and IV.

Ponton et al. (2002) suggested that the relatively early appearance of P1 in the CAEP waveform reflects the more mature state of cortical layers III and IV in young children, compared to more superficial cortical layers thought to generate N1. Moore (1999) reported that neurofilaments with axons radiating into the deeper cortical layers IV, V, and VI first appear between 4-12 months of age. Axonal density in layers III to VI increases until about 5 years (Moore & Guan, 2001).

It is generally agreed that cortical potentials recorded at the surface of the scalp arise from postsynaptic potentials of pyramidal neurons (Novak et al., 1989). Pyramidal cells make up the majority of the neurons in auditory cortex (Hall, Hart, & Johnsrude, 2003). Layers II and III contain many pyramidal cells. Layer IV is dominated by small pyramidal cells but also contains spiny stellate cells and is referred to as the granular layer (Meyer, Gonzalez-Hernandez & Ferres-Torres, 1989; Hall, Hart, & Johnsrude, 2003). Layer V has relatively few cells and contains large pyramidal cells (Linden & Schreiner, 2003). Ponton and Eggermont (2001) suggested that positive EEG deflections recorded on the surface of the scalp, relative to an ear reference, result from excitation in the deeper cortical layers IV and lower III and negative EEG deflections reflect excitation in more superficial layers. Based on this, N_{late} recorded in the 3-7 month old infants in the current study is likely to reflect activity in more superficial cortical layers, but it is not clear whether it has the same sources as the N1b recorded at the vertex in young school-aged children.

Stimulus effects

Latency differences of up to 20 ms have been reported with frequency changes in the 100-5000 Hz range (Jacobson et al., 1992; Woods et al., 1993; Verkindt, et al., 1995; Roberts & Poeppel, 1996). With frequency changes in the 500-4000 Hz range, Roberts and Poeppel (1996) found smaller latency changes of about 10 ms. In the current study P1 and N1 latencies varied by only 5 ms on average across tonal stimuli for the adult subjects, and these differences were not statistically significant. This discrepancy may reflect differences in stimuli, recording electrode site, and subjects between studies. Latency differences were more evident for the infants for tonal stimuli, with significant differences in P1 and N_{late} latencies between 500 and 2 kHz tones.

The main reason for including tonal stimuli in the current study was to determine how speech-evoked CAEPs differ from more conventional tone-evoked recordings. In adults P1 latencies did not differ across stimuli but N1 latencies did show a significant stimulus effect, with longer latencies overall for the speech stimuli. The longest latencies were recorded for the voiceless stop consonants /k/ and /t/. The differences were relatively minor however, in the order of 10 ms. P1 amplitudes were generally greater and N1 amplitudes were smaller for speech compared to tonal stimuli in adults. Durations varied across stimuli in the current study, but this is unlikely to account for differences between stimuli since durations longer than approximately 30 ms produce similar CAEP amplitudes (Davis & Zerlin, 1966; Skinner & Jones, 1968; Onishi & Davis 1968; Picton, Woods, Baribeau-Braun & Healey, 1976; Gage & Roberts, 2000; Alain, Woods, & Covarrubias, 1997).

In the adults' grand average waveforms P1 has a bifid peak for the speech stimuli, which was not evident for the tonal stimuli. A double-peaked N1 has been reported previously for stimuli with longer voice onset times (VOT) in a synthesized /ba/-/pa/ continuum, but not for a /ga/-/ka/ continuum (Sharma et al., 2000). Because of this difference between stimulus contrasts, Sharma et al. (2000) concluded that N1 morphology does not reliably predict phonetic identification of stimuli varying in VOT. Consistent with Sharma et al.'s /ba/-/pa/ findings, Oates et al. (2002) found N1 latency differences for /ba/ *versus* /da/ synthetic speech stimuli. As in the current study, Tremblay et al. (2003a) used naturally produced speech rather than synthetic speech. Tremblay et al. found some differences in VOT effects on CAEP morphology compared to earlier studies using synthetic stimuli. Although /bi/ and /pi/ (differing in VOT by about 60 ms) evoked CAEPs with significantly different N1 and P2 amplitudes, there were no significant latency differences. This result was in contrast to Sharma et al.'s (2000) finding of N1 and P2 latency differences for voiced *versus* voiceless stimuli. Since they were not able to replicate this finding of N1 latency differences with changes in VOT, Tremblay et al. suggested that natural and synthetic speech stimuli may evoke different CAEP patterns.

Previous studies of CAEPs in infants have used a range of stimuli including tones, clicks, and speech sounds and generally have not systematically explored the effect of stimulus characteristics on the CAEP. One exception is Novak et al. (1989) who used synthetic speech stimuli and found consistent morphological differences in infants' CAEP waveforms for /da/ *versus* /ta/. Both produced a double peaked "P1"; the first peak was

consistently larger for /ta/ than for /da/. Novak et al.'s stimuli differed from those in the current study in that they were longer duration, synthetic speech stimuli that included the vowel /a/. In the current study a double peak was seen in only one infant for /t/, but in six infants for /g/, and 13 infants for the 2 kHz tonal stimuli. Only 3 out of 20 infants had a double peak for the 500 Hz tone. Thus, it is not clear what causes this waveform morphology in the infants. Since it was relatively common for 2 kHz tones and for /g/ that has a spectral peak at approximately 3 kHz, this waveform may be associated with spectral rather than temporal or linguistic characteristics of the stimuli. This would be consistent with Crottaz-Herbette and Ragot's (2000) finding that the "central frequency of the passband" (rather than simply pitch) for complex stimuli influenced CAEP amplitude and dipole orientation in adults.

The infants in the current study were similar to the adults in that both showed differences in CAEPs for speech *versus* tones. For the infants, P1 amplitudes were larger for the speech *versus* tonal stimuli, and larger for /t/ *versus* /g/, consistent with the adults. In infants N_{late} did not differ for /g/ and /t/, but was significantly larger for /m/. The /m/ stimulus was not used in the adults and so the infant data cannot be compared to see if the same trend was found. It is not surprising that such large differences were evident in the infants' cortical waveforms for /t/ *versus* /m/ since these stimuli are spectrally and temporally very different. Larger CAEP amplitudes for /t/ *versus* /m/ in infants are consistent with Gage et al.'s (1998) magnetoencephalography study that showed larger cortical responses to stops than no-stops in adults. Gage et al. also found shorter latencies for stops *versus* no-stops. The stop consonant /t/ is characterized by a very fast (a few ms)

onset of peak energy in the temporal waveform which contrasts with the slower rise in energy over approximately the first 100 ms for the /m/ nasal consonant. As noted by Phillips, Hall, and Boehnke (2002) in their review of central auditory onset responses, the available evidence from animal studies suggests that it is the rate of change of sound pressure at sound onset that determines the strength and latency of cortical neural responses. This is consistent with the earlier and larger CAEP to /t/ *versus* /m/ seen in the infants. Despite the very different temporal characteristics of these two stimuli, both generated robust cortical potentials, however, indicating that abrupt rise times are not essential for CAEP generation.

Electrode montage effects

CAEPs were recorded in adults and infants using electrodes located at C3, Cz, and C4. These three montages were selected based on Novak et al.'s (1989) finding that CAEP morphology showed some differences in young infants depending on whether the midline vertex electrode, or laterally placed electrodes over the temporal regions were used. CAEPs at these different sites showed a different maturational time course in the first few months of life. They found that differences between Cz, C3, and C4 were not as evident at 3-6 months as they were in newborns. This is consistent with our finding that CAEP morphology was similar across electrodes in the 3-7 month old infants.

For infants in the current study there was a significant electrode montage effect on P1 amplitudes, with greater amplitudes at C3 and C4 compared to Cz, consistent with Novak et al.'s (1989) results. The greatest P1 amplitudes were seen at C3 (left temporal

electrode), which may reflect a test ear effect. The right ear should have contributed more than the left since stimuli were delivered via a right-sided loudspeaker. Verkindt (1995) found that CAEPs were earlier and larger in adults when recorded from the hemisphere contralateral to the ear of stimulation. Other investigators have also reported amplitude advantages for CAEPs recorded over the hemisphere contralateral to the test ear (Paavilainen, Alho, Reinikainen, et al., 1991; Ponton et al., 2002).

The adults showed the expected Cz amplitude advantage for N1 and P2 (Picton, 1990). There was also a significant electrode montage effect for N1 latency. N1 latencies did not differ between electrode locations for the tones, but were consistently earlier for speech stimuli at C3 compared to C4, especially for /d/ and /g/. This left hemisphere latency advantage for some of the speech stimuli could reflect hemispheric differences in processing of these stimuli or could be due to a contralateral/ipsilateral recording electrode difference, due to the stimuli being presented from the right side. Jacobson et al. (1992) found that the latency of tone-evoked N1 was earlier when recorded from temporal electrode sites contralateral to the test ear.

Several studies (Gage et al., 1998; Rosburg, Kreitschmann-Andermahr, Emmerich, et al., 1998; Crottaz-Herbette & Ragot, 2000; Obleser et al., 2001; Maakinen, May, & Tiitenen, 2004) suggest that, in adults, there may be hemispheric differences in CAEP generators that are distinct from the ipsilateral/contralateral differences. These hemispheric differences appear to be influenced by stimulus type, tonal frequency, and gender. Novak et al. (1989) found a right hemisphere amplitude advantage in 3 and 6 month old infants

tested binaurally with a frontal loudspeaker for both /da/ and /ta/ speech stimuli. Further research is needed to determine whether hemispheric differences in CAEP occur in infants, and how these might be influenced by test ear and stimulus characteristics.

Summary and Conclusions

Infant CAEP waveforms differ substantially from those of adults, and consist primarily of a large positivity "P1" followed by a late negativity. The morphology and latency of these peaks are consistent with physiological evidence that the more superficial cortical layers thought to generate N1 contain very few axonal neurofilaments in children aged two years and younger. Both adults and infants showed significant differences in CAEP latencies and amplitudes across stimuli. The most robust stimulus differences were seen in infants for /t/ *versus* /m/, two stimuli with very different spectral and temporal characteristics. The finding of significant CAEP differences between speech stimuli is consistent with earlier studies indicating that cortical potentials provide objective evidence of the neural encoding of speech characteristics. There were differences in electrode montage effects between adults and infants, consistent with the Ponton et al.'s (2000) finding that the pattern of CAEP maturational changes is influenced by electrode location. Overall, however, the latency and amplitude differences between C3, Cz, and C4 were relatively minor and hence any of these locations appears to be appropriate for CAEP recording in young infants. Regardless of electrode location, robust CAEP waveforms were recorded to a range of speech stimuli in both adults and infants, indicating that obligatory cortical potentials can be used to indicate the detection, and perhaps discrimination, of speech by young infants.

Peak	Measure	Stimulus	Montage	Stimulus by Montage
P1	latency	p>.05	p>.05	p>.05
	amplitude	p=.0011	p>.05	p>.05
N1	latency	p=.0167	p=.0185	p>.05
	amplitude	p<.0001	p=.0084	p<.0001
P2	latency	p<.0001	p>.05	p=.0448
	amplitude	p<.0001	p<.0001	p>.05

Table 1. Significance values for repeated measures ANOVA of adult peak amplitudes and latencies.

Peak	Measure	Stimulus	Montage	Stimulus by Montage
P1	latency	p<.0001	p>.05	p=.0223
	amplitude	p<.0001	p=.0006	p>.05
N_{late}	latency	p<.0001	p>.05	p>.05
	amplitude	p=.0002	p>.05	p>.05

Table 2. Significance values for repeated measures ANOVA of infant peak amplitudes and latencies.

		C3		Cz		C4	
		Mean	SD	Mean	SD	Mean	SD
P1	500 Hz	58.9	9.3	54.3	10.4	58.4	11.0
	1 kHz	53.5	8.9	53.2	9.3	54.4	8.8
	2 kHz	56.1	9.5	55.1	8.1	52.6	7.9
	4 kHz	56.0	15.7	55.4	17.4	57.6	17.4
	/d/	57.4	10.0	57.6	12.0	55.5	11.7
	/g/	58.9	10.4	57.9	11.1	57.6	10.6
	/k/	63.3	20.9	59.2	23.7	58.4	23.1
	/t/	57.0	11.9	57.7	13.1	56.8	10.5
N1	500 Hz	103.7	9.2	105.1	8.0	105.4	8.3
	1 kHz	100.9	8.7	100.7	7.2	100.0	7.2
	2 kHz	100.9	11.3	100.4	7.5	100.4	11.0
	4 kHz	105.7	10.6	105.0	10.1	106.1	10.4
	/d/	106.7	17.6	108.0	15.3	109.6	14.4
	/g/	106.4	17.5	105.6	17.0	114.5	18.3
	/k/	110.7	20.0	108.1	19.5	110.8	18.6
	/t/	111.9	15.8	112.0	15.3	113.8	15.7
P2	500 Hz	187.0	17.3	188.0	17.7	189.7	13.4
	1 kHz	180.5	22.6	180.3	24.0	182.5	18.9
	2 kHz	185.6	27.3	183.6	25.4	190.8	25.2
	4 kHz	180.5	25.5	174.9	18.9	190.5	26.7
	/d/	201.7	15.0	199.7	12.8	203.0	17.3
	/g/	211.4	20.0	202.4	16.5	216.2	21.5
	/k/	212.0	30.3	201.8	27.9	201.5	28.4
	/t/	226.9	42.3	223.5	42.6	227.4	48.4

Table 3. Means and standard deviations (SD) for adult P1, N1, and P2 latencies for the eight tonal and speech stimuli, at the three electrode montages.

		C3		Cz		C4	
		Mean	SD	Mean	SD	Mean	SD
P1	500 Hz	0.85	1.01	0.92	1.08	0.94	1.14
	1 kHz	0.67	0.71	0.72	0.66	0.68	0.59
	2 kHz	0.53	0.60	0.52	0.62	0.49	0.55
	4 kHz	0.53	0.33	0.52	0.51	0.36	0.42
	/d/	0.93	0.95	0.84	1.04	0.82	0.90
	/g/	0.91	0.80	0.90	0.73	0.87	0.59
	/k/	1.27	0.96	1.28	0.91	1.13	0.81
	/t/	1.36	0.86	1.42	0.81	1.32	0.84
N1	500 Hz	-2.19	1.47	-2.72	1.90	-2.34	1.69
	1 kHz	-3.25	1.78	-4.03	2.27	-3.33	1.98
	2 kHz	-2.48	1.17	-3.16	1.51	-2.57	1.30
	4 kHz	-1.77	1.15	-2.23	1.41	-1.69	1.24
	/d/	-1.34	1.23	-1.71	1.50	-1.50	1.16
	/g/	-1.27	1.23	-1.58	1.59	-1.38	1.37
	/k/	-1.47	1.48	-1.66	1.96	-1.57	1.69
	/t/	-1.83	1.38	-2.11	1.82	-1.92	1.75
P2	500 Hz	2.22	1.16	2.87	1.41	2.30	1.13
	1 kHz	2.03	1.02	2.79	1.22	2.15	0.99
	2 kHz	1.48	0.91	1.97	1.07	1.63	0.72
	4 kHz	0.91	0.58	1.25	0.57	0.92	0.51
	/d/	2.28	1.04	2.76	1.30	2.10	0.95
	/g/	2.03	0.98	2.76	1.46	2.00	0.71
	/k/	2.30	1.09	2.90	1.38	2.27	1.05
	/t/	1.61	0.92	2.26	1.21	1.71	0.72

Table 4. Means and standard deviations (SD) for adult P1, N1, and P2 amplitudes for the eight tonal and speech stimuli, at the three electrode montages.

		C3		Cz		C4	
		Mean	SD	Mean	SD	Mean	SD
P1	500 Hz	203.9	23.1	199.6	22.8	204.1	21.7
	2 kHz	215.4	39.2	203.0	42.2	208. 7	36.8
	/m/	233.1	25.1	239.3	27.4	232.5	30.1
	/g/	181.1	16.7	187.2	20.6	181.1	20.1
	/t/	185.0	10.2	185.4	11.5	184.7	12.1
N_{late}	500 Hz	371.9	49.2	361.6	51.2	366.8	48.9
	2 kHz	350.1	75.7	333.5	79.5	339.2	86.5
	/m/	424.7	47.3	421.1	47.7	422.5	56.0
	/g/	358.7	55.2	368.5	55.7	351.1	58.5
	/t/	343.3	43.6	346.1	52.3	347.3	44. 5

Table 5. Means and standard deviations (SD) for infant latencies for the five tonal and speech stimuli, recorded at the three electrode montages.

		C3		Cz		C4	
		Mean	SD	Mean	SD	Mean	SD
P1	500 Hz	7.64	3.63	6.41	3.15	7.40	3.65
	2 kHz	5.66	2.63	4.52	2.89	4.95	2.58
	/m/	7.39	2.29	5.66	1.80	6.21	2.54
	/g/	10.06	3.93	9.19	4.17	9.65	3.95
	/t/	13.03	4.69	12.18	5.16	12.46	5.63
N_{late}	500 Hz	-1.94	1.53	-1.87	1.27	-1.94	1.67
	2 kHz	-1.33	1.43	-1.64	1.43	-1.57	1.09
	/m/	-3.21	1.93	-2.82	1.81	-3.17	1.92
	/g/	-1.46	1.75	-1.54	1.81	-1.49	1.59
	/t/	-0.98	2.15	-1.34	1.83	-0.78	1.69

Table 6. Means and standard deviations (SD) for infant amplitudes for the five tonal and speech stimuli, recorded at the three electrode montages.

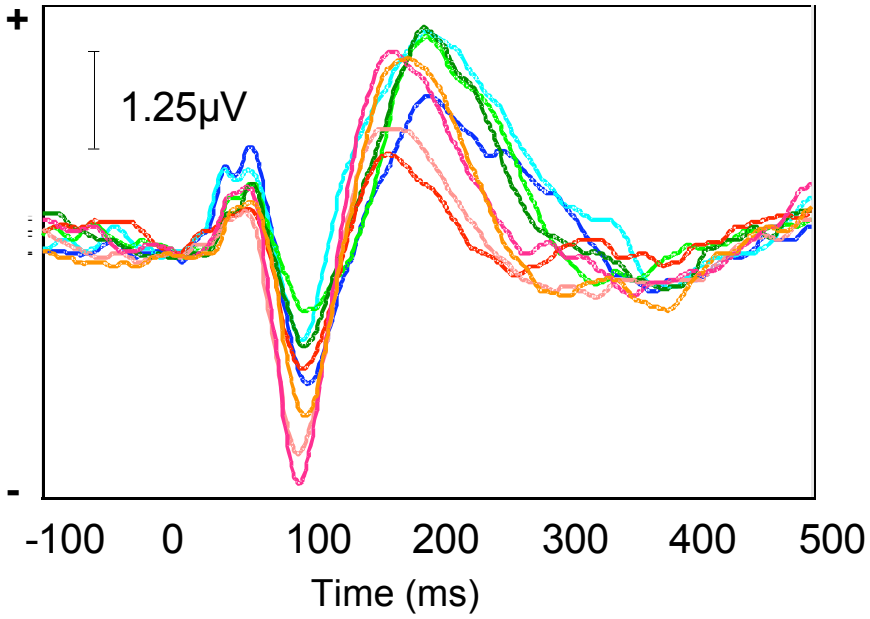

Figure 1. Grand average adult (N=14) CAEP waveforms for the eight tonal and speech stimuli, recorded at Cz. 500 Hz = orange, 1 kHz = dark pink, 2 kHz = light pink, 4 kHz = red, /k/ = aqua /t/ = dark blue, /d/ = dark green, /g/ = light green.

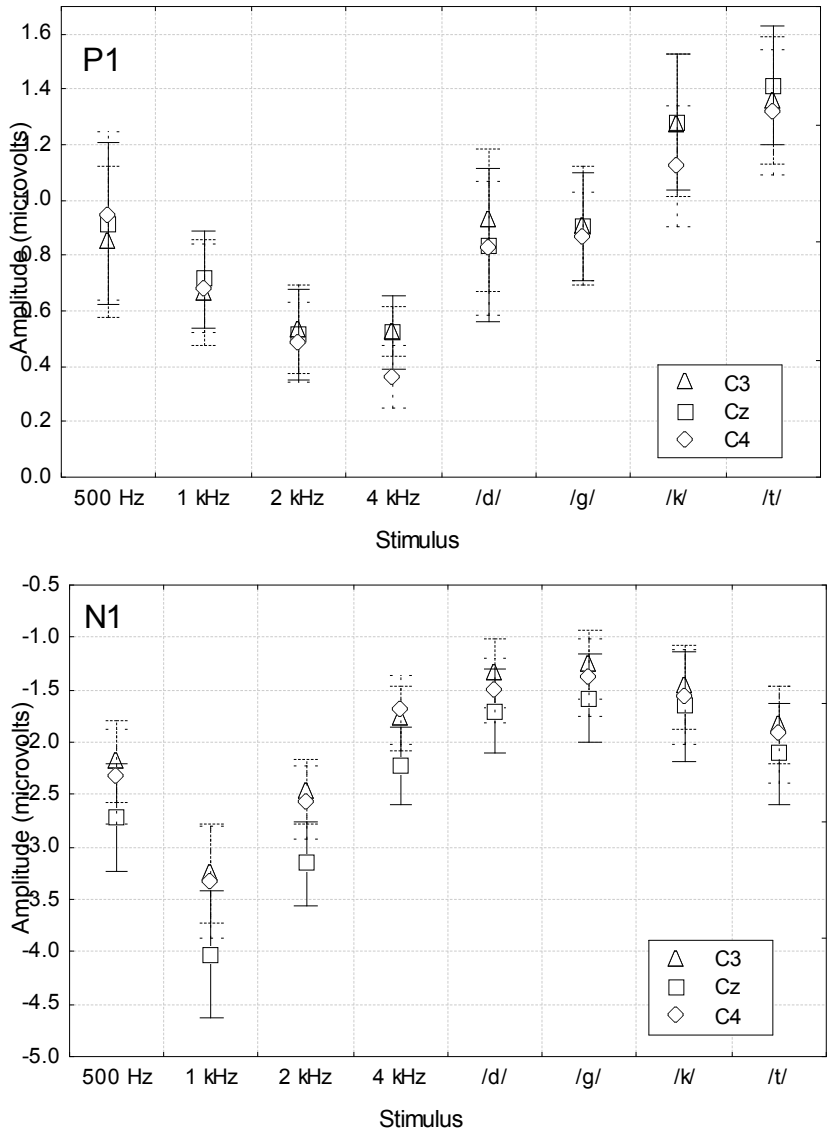

Figure 2. Average P1 and N1 amplitudes for adult subjects (N=14) for the eight stimuli and three electrode montages (C3, Cz, C4). Error bars show standard errors of the means.

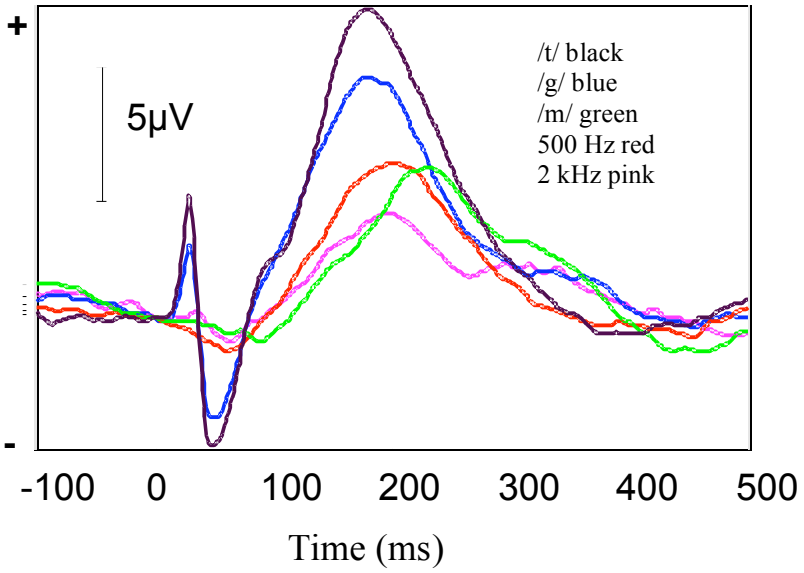

Figure 3. Grand average (N=20) infant cortical waveforms recorded at Cz. /t/ = black, /g/ = blue, /m/ = green, 500 Hz = red, 2 kHz = pink. Responses to /t/ and /g/ show a large post auricular muscle response in the early part of the waveform.

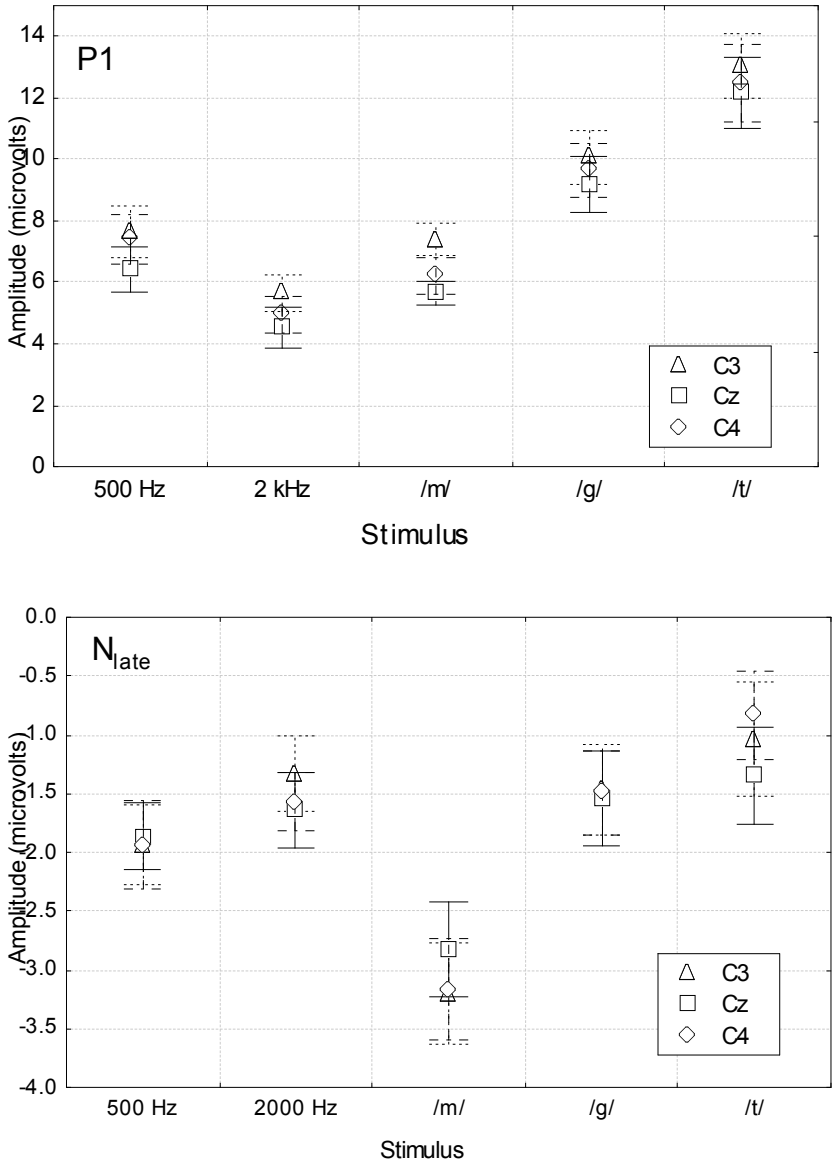

Figure 4. Average P1 and N_{late} amplitudes for infant subjects (N=20) for the five tonal and speech stimuli and 3 electrode montages (C3, Cz, C4). Error bars show standard errors of the means.

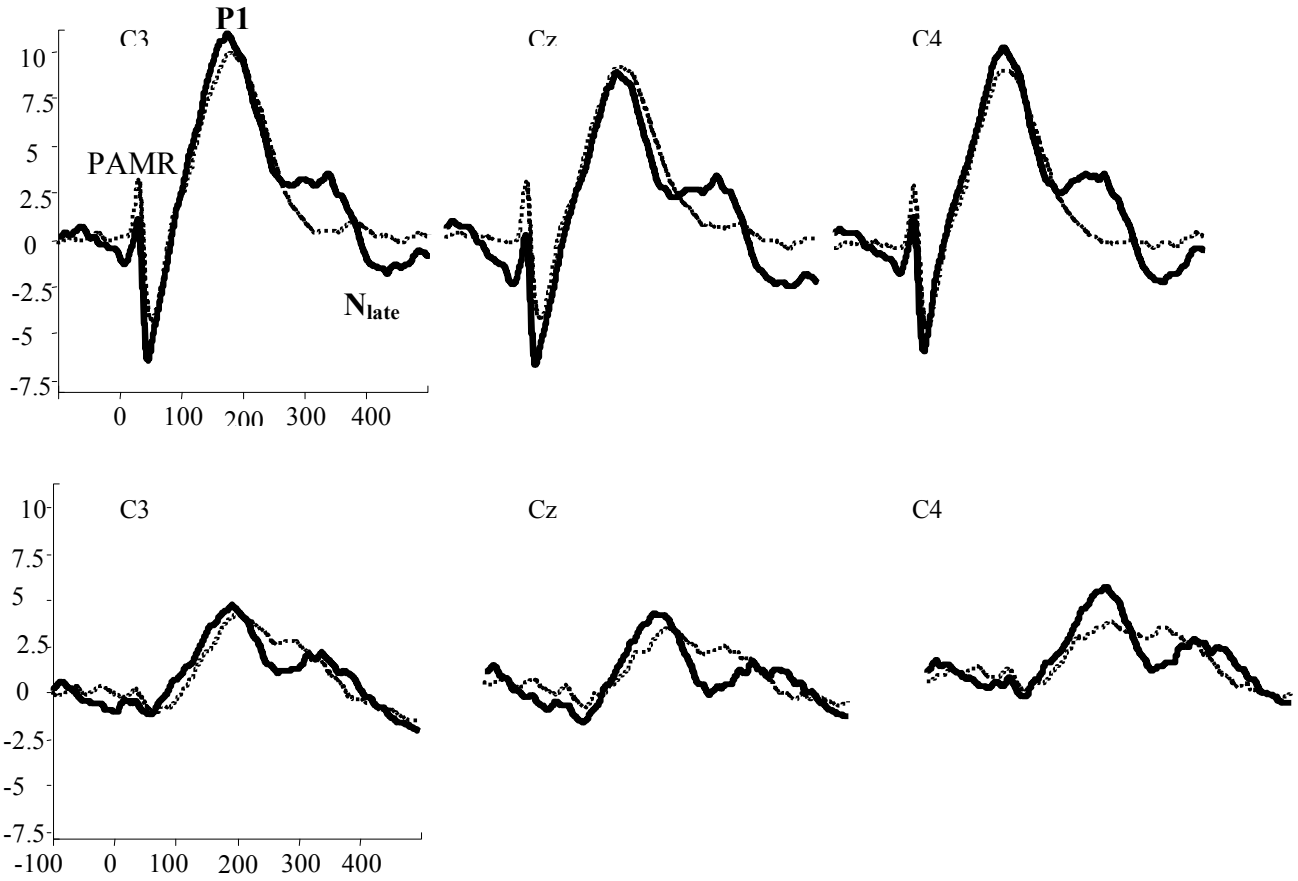

Figure 5. Grand average waveforms for the infants with single- (solid line) *versus* double-peaked (dotted line) cortical waveforms for the /g/ (top) and /2 kHz/ (bottom) stimuli. PAMR=post auricular muscle response.

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