The Effect of Stimulus Duration and Inter-Stimulus Interval on Cortical Responses in Infants

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Cortical auditory evoked potentials (CAEP) were recorded from ten normal-hearing infants, aged 3 to 7 months, using the natural speech segments /m/ and /t/. The aim was to investigate the effect of selected stimulus durations and inter-stimulus intervals (ISIs) on infant responses. In the first experiment, various stimulus durations were used but the ISI was fixed. Results showed no significant difference in the latency of the first positive peak (P1) with changes in stimulus duration, but there was a minor increase in amplitude when duration increased from short to medium length. In the second experiment, medium length stimuli were presented with various ISIs. Results showed that as the ISI increased, P1 latency was constant but its amplitude increased nonlinearly for /t/ only. It appears therefore, that for the selected speech stimuli there was no clear advantage in using stimulus durations beyond 35 ms and ISIs beyond 1125 ms in infant assessments.

With the advent of infant screening programs, the identification of congenital hearing loss at an early age is achievable and desirable for optimum speech and language development. While recording the auditory brainstem response (ABR) has been invaluable in the identification process, a response arising from the brainstem does not guarantee detection of the stimulus at the level of the auditory cortex, which is necessary if speech understanding and language development are to occur (Stapells, 2002). Using speech stimuli to elicit cortical auditory evoked potentials (CAEPs) is likely to be far more instructive than ABR testing in monitoring the development of speech detection and perception. An association between cortical outcomes and receptive language has already been reported where the presence of cortical responses in the early months of life was correlated with normal receptive language at 1 year of age (Kurtzberg, Stapells, & Wallace, 1988).

The amplitudes and latencies of CAEP components are known to be highly stimulus-dependent with almost any perceptible change in any feature of the stimulus evoking a change in the response (Hyde, 1997; Martin & Boothroyd, 1999). Thus, changes to the stimulus frequency, changing from tonal stimuli to speech segments (Stapells, 2002), spectral changes at the transition from fricative to vowel in a consonant–vowel (CV) syllable (Ostroff, Martin, & Boothroyd, 1998) or manipulation of the temporal variations in the speech segments such as acoustic cues of voice-onset may all lead to changes in the resulting cortical response components (Kurtzberg, 1989).

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Tone burst stimuli have been commonly used to elicit CAEPs, particularly in adults, and a number of studies have investigated how the response may be optimised by the manipulation of the stimulus parameters. Several authors have reported that a constant 5–10 cycle rise/fall was required if frequency specificity and maximum response amplitude was to be achieved (Hyde, 1997; Onishi & Davis, 1968; Picton, 1990; Stapells, 2002). It has also been reported that varying the rise/fall and duration of tonal stimuli has complex implications for the amplitude and latency of the adult CAEP. When the rise/fall was brief (e.g., 3 ms), an increase in response amplitude and a decrease in latency was observed as the duration of the stimulus plateau varied from 0 to 30 ms (Onishi & Davis, 1968) and up to 70 ms (Alain, Woods, & Covarrubias, 1997). By contrast, when the rise/fall was longer (e.g., 30 ms or more) the duration of the plateau had no effect on the amplitude or latency of the response components, even though perceived loudness would increase (Davis & Onishi, 1969; Onishi & Davis, 1968). Alain, Woods and Covarrubias (Alain, Woods, & Covarrubias, 1997) however, reported that the latency of the CAEP components in response to low frequency stimuli (i.e., 250 Hz) was likely to increase with increased stimulus duration (and brief rise/fall) consistent with a longer integration time for lower frequencies.

Aside from the duration effects, manipulation of the inter-stimulus interval (ISI) (i.e., the period between stimulus offset and the following stimulus onset) or the stimulus onset asynchrony (SOA) (i.e., the difference in time between the onsets of two consecutive stimuli) is important in optimising the adult CAEP response to tonal stimuli. The amplitude of the adult N1–P2 late response was reported to increase as the ISI or SOA increased from 1 to 10 seconds, whereas the latency remained stable (Davis & Zerlin, 1965; Hyde, 1997; Nelson & Lassman, 1968). This predictable relationship was, however, modified by electrode site with an ISI less than 4 ms producing similar amplitude responses at frontal and central electrode sites, while a longer ISI resulted in enhanced response amplitude at the vertex (Hari, Kaila, Katila, Tuomisto, & Varpula, 1982). This difference may have arisen as different anatomic generators respond to stimuli presented with faster or slower ISIs (Hari, Kaila, Katila, et al., 1982). As the ISI increases however, test-time also increases and therefore an ISI of 1 or 2 seconds has been reported as a clinically satisfactory compromise (Hyde, 1997; Stapells, 2002).

CAEPs have also been reliably elicited to a variety of speech segments when presented to normal-hearing adults and infants at conversational levels (Cone-Wesson & Wunderlich, 2003; Pang & Taylor, 2000; Tremblay, Friesen, Martin, & Wright, 2003). While studies have examined the nature of cortical responses evoked by voiced and unvoiced speech stimuli (Kurtzberg, 1989; Ostroff, Martin, & Boothroyd, 1998; Sharma, Marsh, & Dorman, 2000; Simos & Molfese, 1997; Steinschneider, Kurtzberg, & Vaughan, 1992; Tremblay, Friesen, Martin, et al., 2003), the effect of the duration of the speech stimulus on the amplitude and latency of the CAEP components has not been systematically examined. In fact, the stimulus duration of speech segments has varied widely across studies to date, from 90 ms (for /ba/) (Sharma, Kraus, McGee, & Nicol, 1997) to 484 ms through 756 ms (for /bi/, /pi/, /shi/ and /si/) (Tremblay, Friesen, Martin, et al., 2003). Variations in the ISI with the speech stimulus /uh/, have been recently shown to impact on the components of the CAEP in children from 3 to 12 years in a highly complex manner (Gilley, Sharma, Dorman, & Martin, 2005), but the impact of ISI change in infants has not been widely reported.

CAEPs have a prolonged period of maturation with changes in component shape and latency occurring over the first two decades of life (Pasman, Rotteveel, Maassen, & Visco, 1999; Sharma, Kraus, McGee, et al., 1997). At birth, the cortical response is dominated by a broad positive wave with a latency around 200 ms–300 ms (Kushnerenko, Ceponiene,

Balan, et al., 2002; Wunderlich & Cone-Wesson, 2006) but this latency decreases rapidly over the first 12 months. The morphological changes in the CAEP from infancy to adult years are complex and not completely understood (Kushnerenko, Ceponiene, Balan, et al., 2002; Wunderlich & Cone-Wesson, 2006) and therefore understanding how speech stimuli may be manipulated to optimise the maturing response in the normal-hearing infant is critical to the application of these techniques in evaluating infants and children with hearing impairment.

While the ISI and stimulus duration are known to be critical determinants of the adult cortical response amplitude and latency when tonal stimuli are used, it is not known how these features affect the infant cortical response to speech stimuli. The purpose of the present study was, therefore, to identify the most robust effects on the latency and amplitude of the infant cortical response that arise from systematic variation in speech stimulus duration (Experiment 1) and ISI (Experiment 2). As the study was part of a clinical test procedure development for infants, we limited the range of ISIs and stimulus durations.

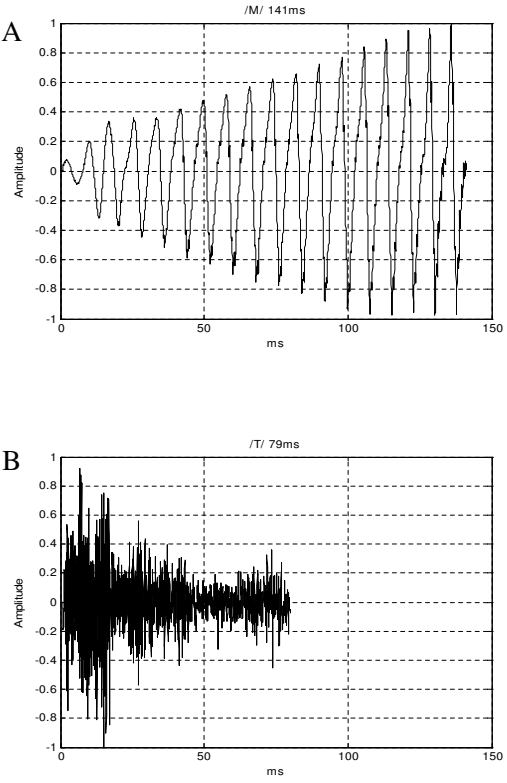

FIGURE 1
Time/intensity spectra are shown for maximum stimulus durations of (A) /m/ at 141 ms and (B) /t/ at 79 ms.

EXPERIMENT 1 (STIMULUS DURATION)

Method

Participants. Infants were screened for normal outer hair cell function and middle ear pathology using transient evoked otoacoustic emissions prior to cortical testing. There were 6 female and 4 male infants, aged 3 to 7 months (mean = 4.8 months, *SD* = 1.0 months) in this experiment.

Stimuli. The speech segments /m/ and /t/ were extracted from running speech that was spoken by an average male Australian and recorded at digitisation rates of 40k Hz. A speech spectrogram of the utterances was used to identify the beginning point of the consonant, as well as the point of transition to the following vowel /ae/. These utterances were truncated to create speech segment durations of 79 ms for /t/ and 141 ms for /m/, which equalled the maximum duration for each consonant with very little of the vowel transition. These speech segments were gated off near/at a zero crossing to avoid audible clicks, but no further modifications of the onset or offset characteristics were made. The time/intensity functions for these maximum durations are shown in Figure 1. These stimuli were chosen because they had a spectral emphasis in the low and high frequency regions respectively and thus had the potential to give diagnostic information about the perception of speech sounds in different frequency regions.

For the purpose of this experiment, the ends of these stimuli were further truncated to create shorter stimuli with durations of 32 ms for /t/, and 31 ms plus 79 ms for /m/. There

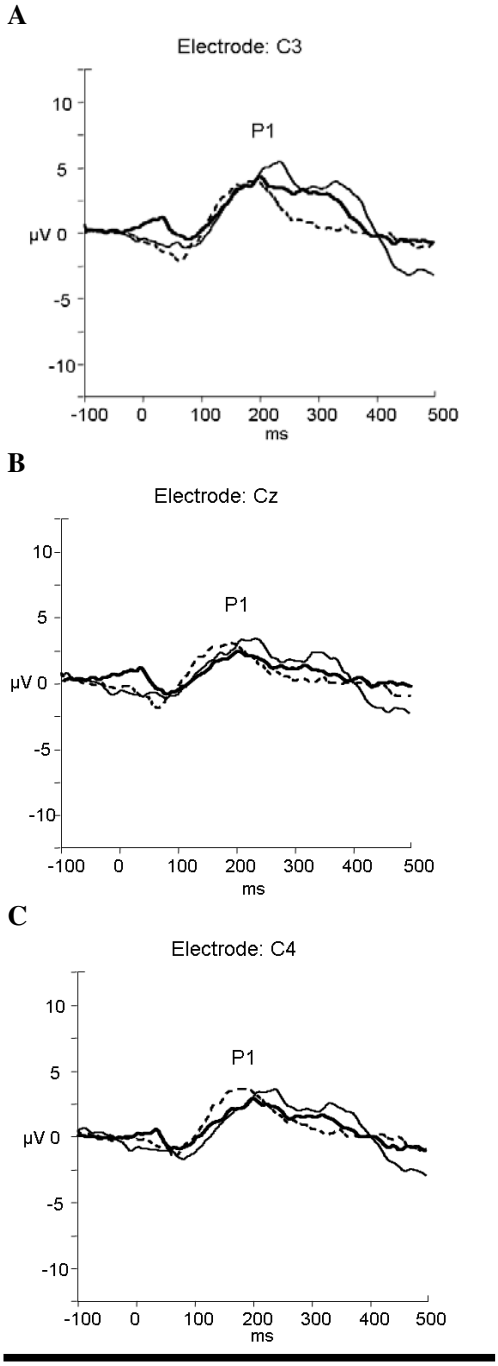

FIGURE 2
The grand average waveforms for 10 infants in response to the stimulus /m/ with a short duration of 31 ms (— – -), medium duration of 79 ms (———) and long duration of 141 ms (———) recorded at (A) C3, (B) Cz, and (C) C4.

were therefore two stimulus durations for /t/ (i.e., 79 ms and 32 ms) and three stimulus durations for /m/ (i.e., 31 ms, 79 ms and 141 ms). The durations selected for the experiment, which were described as short, medium or long, thus represented the maximum possible vowel-free duration, plus shorter durations chosen to approximately match the duration of the other consonant. In this experiment, all stimuli were presented with an ISI of 750 ms.

Procedure

Stimuli were delivered via a loudspeaker positioned on the right-hand side at 45 degrees azimuth relative to the nominal position of the infant's head, with no attempt to control for lateral bias. The stimulus output was measured as 65 dB SPL, using an impulse time constant, at the chair by means of a microphone suspended from the ceiling and connected to a measuring amplifier in the observation room. The microphone was then retracted to a point above the head height of the parent and child for continuous monitoring of the signal in the sound-field.

Brain electrical activity was recorded using the Neuroscan^{TM} system with electrodes positioned at Cz, C3 and C4 referenced to the right mastoid with forehead as ground. During cortical testing, infants were awake and seated on their mother's lap, distracted by another adult if required. Individual sweeps of the electroencephalic (EEG) activity were amplified and analogue filtered on-line at 0.1 Hz– to 100 Hz using a 24 dB/octave slope, and subsequently filtered off-line at 1 Hz to 30 Hz using a zero-phase filter (obtained by filtering the signal, time-reversing the output signal, refiltering it, and time-reversing it again). The recording window consisted of a 100 ms prestimulus baseline and a further 500 ms poststimulus onset, and artefact reject was set at -150 to +150 μV online and –100 to +100 μV offline.

Each stimulus, which was delivered using alternating onset polarity, was presented in blocks until 100 artefact-free EEG samples were acquired. Each block of stimuli was presented on two occasions and the stimulus

TABLE 1
P1 Amplitudes (Amp — Measured in μV) and latencies (Lat — Measured in ms) for /t/ by Duration and Electrode Site

	32 ms stimulus duration						79 ms stimulus duration					
	Cz		C3		C4		Cz		C3		C4	
	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat
	9.61	223	10.39	225	6.08	223	2.13	263	3.24	275	3.89	277
	7.04	174	11.08	211	6.27	227	10.71	207	12.23	224	8.03	196
	12.30	216	13.54	215	12.68	208	17.59	198	18.18	200	18.92	200
	9.63	176	9.28	174	10.49	175	13.13	179	12.16	177	12.94	179
/t /	5.60	229	9.61	240	8.31	223	9.75	218	8.58	240	11.73	209
	4.19	272	4.74	239	3.79	224	10.16	159	10.51	164	8.01	165
	4.32	242	4.12	209	9.79	250	7.68	205	11.82	238	10.16	235
	5.30	192	8.37	175	6.87	184	7.81	218	7.41	190	7.67	208
	7.23	201	7.15	225	11.20	201	4.54	249	6.77	243	7.14	271
	4.85	198	3.30	186	4.30	185	8.59	216	10.00	218	8.90	176
Mean	7.0	212.4	7.8	209.9	8.0	210.0	9.2	211.3	10.1	217.0	9.7	211.5
SD	2.7	30.5	3.4	24.4	3.0	23.7	4.3	30.2	4.0	34.1	4.1	38.3

order was randomised. The two replicated waveforms were averaged and two observers independently identified and marked the latency and amplitude of the first positive wave occurring after 100 ms, referred to as P1. The amplitude of this wave was measured from the mean prestimulus baseline level, which had zero amplitude following baseline correction, to the peak. For the purposes of this study the latency of the positive wave, which had one or two maxima, was marked at the intersection of visual lines of 'best-fit' applied to the slopes on either side of the positive wave. The component amplitude was always measured at the highest point of the positive wave. There was little disagreement between the examiners using this criterion, which was strictly applied irrespective of the test condition, but on the rare occasion where they did disagree, the two examiners consulted with each other to mark the peak. A visual inspection of the responses from the three recording sites was used as a cross-check for peak identification.

RESULTS

Table 1 and Table 2 show the amplitude and latency data for all participants in response to the stimulus /t/ (Table 1) and /m/ (Table 2). There is notable variability in both amplitude and latency measures across participants and across stimuli. Only the most robust latency and amplitude differences with changes to duration are likely to be found.

Figures 2 and 3 show the grand average waveforms recorded at the three sites (i.e., C3, Cz and C4) in response to variable durations for /m/ and /t/ respectively. There appears to be no consistent differences in amplitude or latency with duration that applies across both stimuli, although there appears to be an amplitude difference of 2 μV approximately when responses to the short and medium duration /t/ stimuli are compared. There are also differences in wave morphology for /m/ versus /t/. There is the notable addition of a biphasic response with a first peak latency of approximately 25 ms that is clearly evident for /t/ but not /m/. This is consistent with a postauricular muscle response (PAMR) which occurs with an approximate latency of 13 ms to 20 ms in adults and is known to be longer in young infants (O'Beirne & Patuzzi, 1999). The PAMR is a brainstem reflex that is sensitive to abrupt

TABLE 2
P1 Amplitudes (Amp — Measured in μV) and Latencies (Lat — Measured in ms) for /m/ by Duration and Electrode

	31 ms stimulus duration						79 ms stimulus duration						141 ms stimulus duration					
	Cz		C3		C4		Cz		C3		C4		Cz		C3		C4	
	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat
/m/	2.36	293	2.66	290	3.00	316	9.61	221	10.39	222	6.08	223	7.34	279	7.89	282	6.99	282
	4.46	170	7.02	178	4.07	171	5.86	253	5.22	233	4.44	251	5.00	292	7.27	287	4.19	297
	7.47	184	8.32	201	10.12	182	6.65	264	9.47	272	8.24	257	11.88	280	14.20	282	10.94	279
	5.55	240	9.82	229	7.42	248	2.40	233	6.02	236	4.54	252	0.58	267	3.37	253	3.01	297
	7.01	303	8.14	299	7.02	302	5.83	264	8.25	274	6.71	252	7.89	267	8.52	270	9.84	265
	3.32	210	2.35	210	3.74	214	0.44	204	2.58	200	3.52	200	5.83	248	2.71	250	3.46	244
	4.25	229	5.99	233	4.08	234	5.41	228	7.28	222	5.46	235	7.24	233	9.55	235	7.94	230
	3.94	258	4.99	262	2.81	275	3.60	242	5.24	215	4.96	230	5.29	204	7.61	192	1.92	199
	1.69	225	1.92	243	2.75	223	2.22	239	5.54	247	3.65	245	1.58	299	6.39	300	6.28	299
	4.26	237	4.51	238	2.91	238	0.51	196	3.94	198	2.95	196	2.15	279	4.42	270	3.32	263
Mean	4.4	234.9	5.6	238.4	4.8	240.3	4.3	234.5	6.4	231.7	5.1	234.1	5.5	265.0	7.2	262.0	5.8	265.5
SD	1.8	42.5	2.8	37.8	2.5	47.3	2.9	23.1	2.4	26.3	1.6	22.0	3.4	29.0	3.3	31.2	3.1	32.7

onset stimuli such as /t/ (Agung, Purdy, Patuzzi, O'Beirne, & Newall, 2005; Hall, 1992).

Four repeated measures factorial ANOVAs were performed to examine the effect of stimulus duration on the latency and the amplitude of the positive wave for the /t/ and /m/ stimuli. The factors were electrode site (i.e., C3, Cz and C4, all referenced to the right mastoid and entered as 3 levels), and stimulus duration with either two durations (i.e., /t/ with duration of 32 ms and 79 ms) or three durations (i.e., /m/ with durations of 31 ms, 79 ms, 141 ms). Results showed no effect of duration on the latency of P1 to the stimulus /t/, $F(1,9) = .05$; $p = 0.83$, or /m/, $F(2,18) = 2.46$; $p = .11$. Similarly, there was no effect of duration on the amplitude of P1 to the stimulus /t/, $F(1,9) = 3.40$; $p = .10$, or /m/, $F(2,18) = 1.42$; $p = .27$.

Although of secondary interest to this study, there was a main effect of electrode site on the amplitude of P1 to the stimulus /m/, $F(2,18) = 10.95$; $p = .0008$, but not to the stimulus /t/, $F(2,18) = 1.24$; $p = .31$. Bonferroni pair-wise comparisons showed that there was a significant difference in amplitude at C3 (mean = 6.38 μV, *SD* = 2.85) compared with Cz (mean = 4.72 μV, *SD* = 2.76) and C4 (mean = 5.21 μV, *SD* = 2.44), but there was no significant difference between Cz and C4. There were no factorial interactions involving electrode site.

A further two repeated measures factorial ANOVAs were performed where data from /m/ with duration of 141 ms were ignored and stimulus was examined as an additional factor. When the latency data was combined across all electrode sites and two durations, there was a significant stimulus effect where the latency of P1 in response to /t/ (mean = 212.00 ms, *SD* = 29.41) was significantly shorter than that of /m/ (mean = 235.64 ms, *SD* = 33.24), $F(1,9) = 9.48$; $p = .01$, but there was no main effect of duration on the latency data, $F(1,9) = 0.01$; $p = .91$. When the amplitude data was similarly combined across electrode sites and durations, the peak amplitude of P1 in response to stimulus /m/ (mean = 5.08 μV, *SD* = 2.41) was significantly less than that of /t/ (mean = 8.63 μV, *SD* = 3.65), $F(1,9) = 31.51$; $p = .0003$] and a main effect of

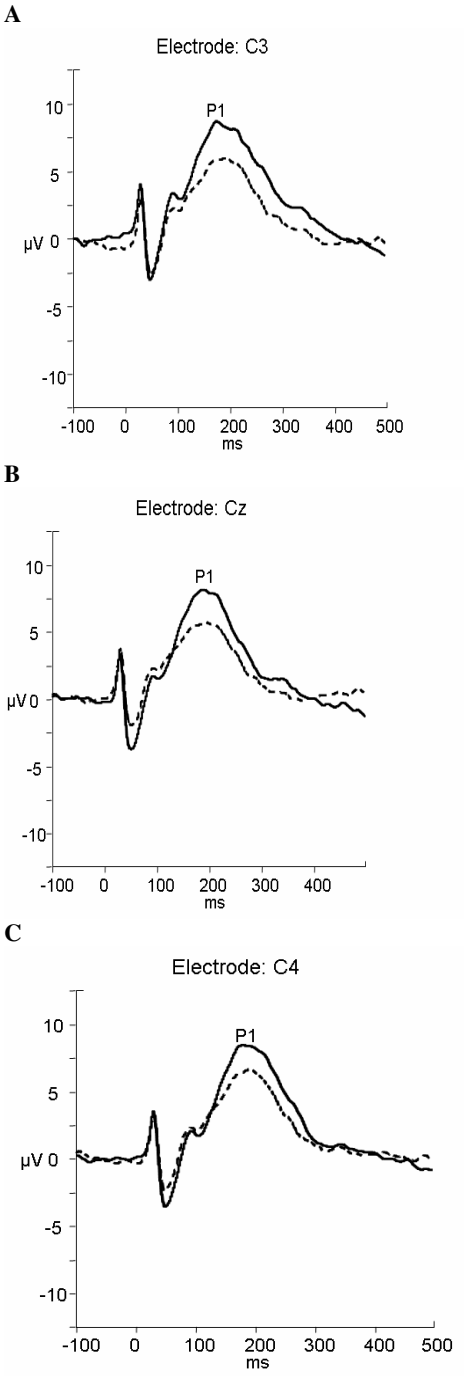

FIGURE 3

The grand average waveforms for 10 infants in response to the stimulus /t/ with a short duration of 31 ms (— – -) and medium duration of 79 ms (———) recorded at (A) C3, (B) Cz, and (C) C4.

TABLE 3
P1 amplitudes (Amp — Measured in μV) and Latencies (Lat — Measured in ms) for /t/ and /m/ for the Three Inter-Stimulus Intervals and Electrodes

	ISI = 750 ms						ISI = 1125 ms						ISI = 1500 ms					
	Cz		C3		C4		Cz		C3		C4		Cz		C3		C4	
	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat	Amp	Lat
	5.10	294	8.54	294	7.27	294	9.11	173	13.78	193	10.98	192	9.11	173	13.78	193	10.98	192
	11.12	163	10.20	185	8.72	185	16.57	204	18.08	206	16.76	203	18.48	197	20.35	197	18.73	201
	9.33	181	10.10	166	10.25	167	16.57	191	18.44	188	13.09	199	11.07	264	19.27	266	16.65	262
	11.13	200	8.06	190	9.77	185	10.90	236	10.14	233	5.09	193	16.99	222	16.84	223	14.98	237
/t/	9.38	173	14.82	186	12.96	172	16.21	173	21.38	172	14.61	187	6.17	146	10.25	147	8.33	167
	4.76	200	7.91	202	4.96	171	4.76	200	7.91	202	4.96	171	1.33	168	8.63	176	5.27	181
	8.81	157	9.13	156	9.18	157	11.95	151	9.34	150	12.40	153	20.21	255	19.00	225	17.06	257
	13.84	204	15.31	200	14.02	204	14.98	177	19.57	178	16.91	180	28.54	189	30.32	187	32.33	188
	11.70	229	16.44	229	13.56	230	19.37	259	21.56	208	21.17	210	28.53	179	29.19	229	32.33	179
	8.72	280	12.47	253	12.74	201	17.07	200	21.21	201	15.12	200	20.84	170	21.42	172	19.20	170
Mean	9.4	208.0	11.3	206.0	10.3	196.5	13.8	196.4	16.1	193.1	13.1	188.8	16.1	196.3	18.9	201.5	17.6	203.5
SD	2.8	46.8	3.2	41.8	3.0	40.3	4.5	31.7	5.4	22.6	5.1	16.9	9.1	38.8	7.1	34.4	9.0	35.4
	1.02	318	3.13	339	1.08	319	3.26	237	4.44	248	3.54	279	4.47	265	6.49	253	4.46	267
	6.02	241	8.28	256	3.71	256	5.36	288	5.29	290	5.12	299	7.97	172	6.98	184	7.92	179
	12.10	253	15.78	233	12.32	254	17.96	213	21.3	237	15.55	213	7.44	280	8.18	273	7.10	302
	3.38	218	5.80	175	2.82	218	8.90	207	10.12	208	8.74	218	7.83	294	9.32	282	9.59	222
	7.60	260	8.53	256	7.64	254	7.56	260	8.70	220	7.13	278	6.65	235	6.36	252	5.79	259
/m/	8.10	254	5.38	242	3.79	255	8.07	218	11.6	219	7.23	219	5.70	290	7.82	291	2.66	290
	5.50	277	7.58	270	6.80	229	6.21	248	3.01	291	3.25	242	7.10	176	5.58	177	5.94	160
	8.17	246	5.23	268	5.94	251	10.25	255	13.16	257	12.38	248	6.84	271	7.91	260	7.42	219
	8.04	200	11.72	201	8.85	199	11.62	267	16.97	265	16.06	268	7.66	228	14.05	213	11.17	223
	7.30	259	10.53	258	5.88	258	7.83	251	12.42	271	8.09	224	12.94	231	18.68	229	13.29	215
Mean	6.72	252.5	8.2	249.8	5.9	249.2	8.7	244.3	10.7	250.5	8.7	248.7	7.5	244.1	9.1	241.3	7.5	233.5
SD	3.0	32.0	3.7	43.6	3.3	31.7	4.0	25.8	5.7	29.5	4.6	30.6	2.2	43.9	4.1	39.5	3.2	45.8

duration was also observed, $F(1,9) = 12.68$; $p = .006$. The amplitude of P1 was significantly less for shorter durations (i.e., /m/ at 31 ms and /t/ at 32 ms) (mean = 6.26 μV, *SD* = 2.97) than medium durations (i.e., /m/ and /t/ at 79 ms; mean = 7.46 μV, *SD* = 3.99) by 1 μV approximately.

A main effect of electrode site was also found when amplitude data for both stimuli and two durations were combined, $F(2,18) = 6.92$; $p = .006$. Bonferroni pairwise comparisons showed that the amplitude at C3 (mean = 7.45 μV, *SD* = 3.53) was significantly different to Cz (mean = 6.23 μV, *SD* = 3.60) but C3 was not significantly different to C4 (mean = 6.89 μV, *SD* = 3.52) and there was no significant difference between Cz and C4. There were no factorial interactions for latency or amplitude data.

EXPERIMENT 2 (ISI)

Method

Participants. Infants were screened for normal outer hair cell function and middle ear pathology using transient evoked otoacoustic emissions prior to cortical testing. There were 4 female and 6 male infants aged 3–6 months (mean = 4.4 months, *SD* = 0.9 months) in this experiment.

Stimuli. The test stimuli of /m/ and /t/, which were described for experiment one, were presented in this second experiment with a fixed duration of 79 ms following the outcome of Experiment 1 where a slight increase in amplitude was observed for medium duration stimuli. The ISI (i.e., the period between stimulus offset and the following stimulus onset) in this second experiment was systematically varied such that /m/ and /t/ were presented with an ISI of 750 ms, 1125 ms and 1500 ms.

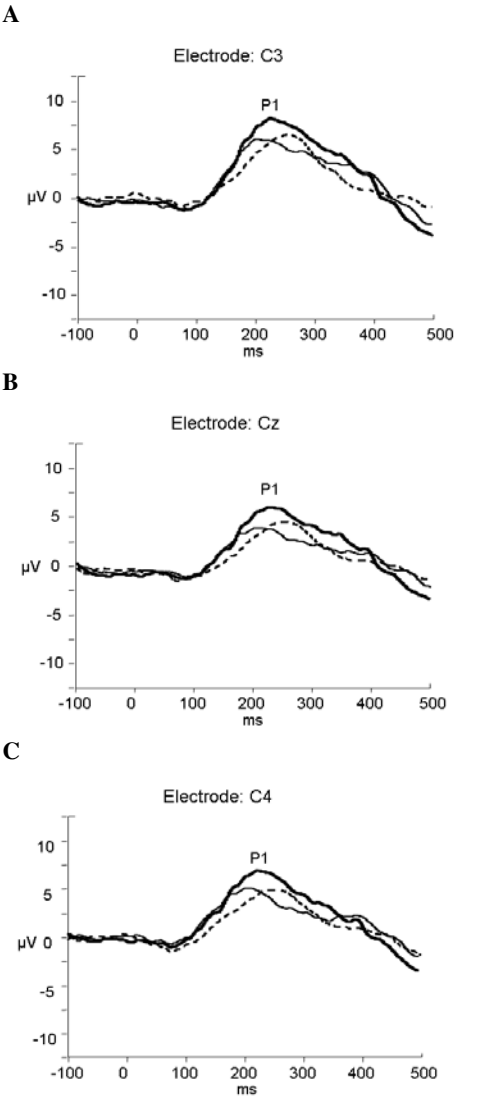

FIGURE 4
The grand average waveforms for 10 infants in response to the stimulus /m/ with an ISI of 750 ms (— – -), an ISI of 1125 ms (———) and an ISI of 1500 ms (———) recorded at (A) C3, (B) Cz, and (C) C4.

Procedure

The procedure used in experiment one was followed in this second experiment.

RESULTS

Table 3 shows the amplitude and latency data for all participants in response to the stimulus /t/ and /m/ with variable ISI. Again, there is notable variability in both amplitude and latency data across participants and across stimuli. Only the most robust latency and amplitude differences with changes to the ISI are likely to be found.

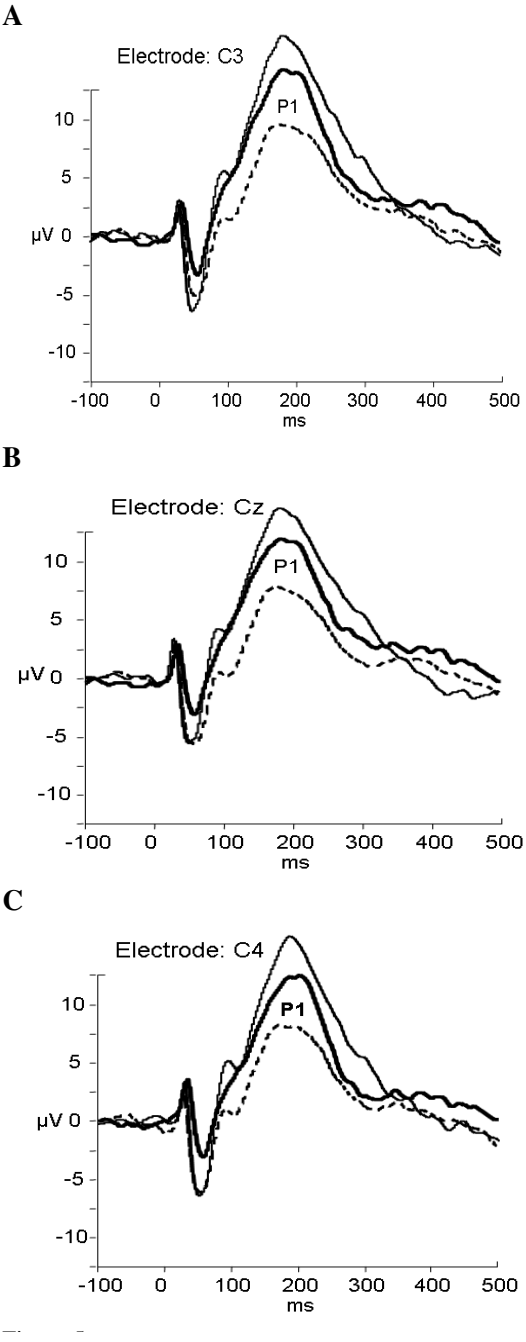

FIGURE 5

The grand average waveforms for 10 infants in response to the stimulus /t/ with an ISI of 750 ms (— – -), an ISI of 1125 ms (———) and an ISI of 1500 ms (———) recorded at (A) C3, (B) Cz, and (C) C4.

Figures 4 and 5 show the grand average waveforms recorded at the three sites (i.e., C3, Cz and C4) in response to variable ISI for /m/ and /t/ respectively. There appears to be no consistent differences in amplitude or latency with ISI changes that applies across both stimuli, although there appears to be an amplitude increase of 7 μV approximately when responses to the ISI of 750 ms are compared with those of 1500 ms for /t/ stimuli only. The addition of an early response in the first 100 ms of the response to /t/ is again evident.

Two repeated measures factorial ANOVA were performed to examine the effect of ISI on the latency and peak amplitude for the positive wave. The factors were ISI (i.e., 750 ms, 1125 ms, 1500 ms), electrode site (i.e., C3, Cz, C4, all referenced to the right mastoid) and stimulus (i.e., /t/, /m/).

Latency did not vary significantly with changes in the ISI, $F(2,18) = 0.21$; $p = 0.82$. When latency data was combined across all electrode sites and ISIs, however, the overall latency for stimulus /m/ (mean = 245.97 ms, $SD = 35.26$) was significantly longer than that for stimulus /t/ (mean = 198.89 ms, $SD = 34.34$), $F(1,9) = 43.94$; $p = < .0001$.

Peak amplitude varied significantly with changes in ISI, $F(2,18) = 8.01$; $p = .003$. Bonferroni pair-wise comparisons showed a significant difference in P1 amplitude for ISIs of 750 ms (mean = 8.64 μV, $SD = 3.60$) and ISIs of 1125 ms (mean = 11.85 μV, $SD = 5.44$), and for ISIs of 750 ms and 1500 ms (mean = 12.79 μV, $SD = 7.84$) but not between ISIs of 1125 ms and 1500 ms. A significant interaction between stimulus and ISI for peak amplitude, $F(2,18) = 4.83$; $p = .02$)] was also found and illustrated in Figure 6. Bonferroni pair-wise comparisons showed no significant difference in peak amplitude with changes to the ISI for stimulus /m/. For stimulus /t/ however, the response amplitude for an ISI of 750 ms (mean = 10.34 μV, $SD = 3.01$) was significantly different to the response amplitude for an ISI of 1500 ms (mean = 17.54 μV, $SD = 8.24$), but not between ISIs of 750 ms

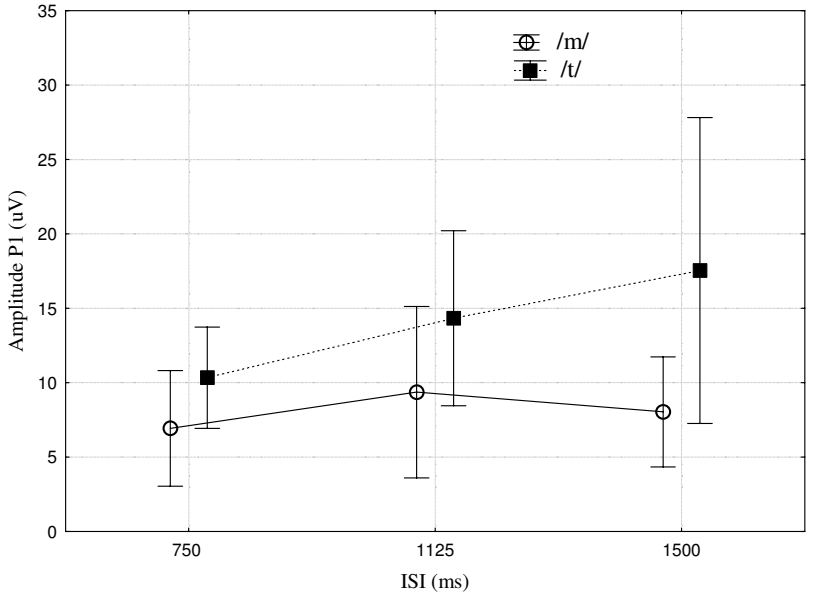

FIGURE 6

The mean amplitudes of cortical responses to /m/ and /t/ are shown as a function of the ISI. The error bars indicate 95% confidence intervals.

and 1125 ms (mean = 14.33 μV, *SD* = 5.0) or ISIs of 1125 ms and 1500 ms.

A main effect of electrode site on the amplitude of P1, $F(2,18) = 13.39$; $p = .0003$, was also found which was of secondary interest to this study. Bonferroni pair-wise comparisons showed a significant difference in peak amplitude between C3 (mean = 12.40 μV, *SD* = 6.19) and Cz (mean = 10.36 μV, *SD* = 5.78) and between C3 and C4 (mean = 10.53 μV, *SD* = 6.27), but not between Cz and C4. Finally, there was a main effect of stimulus on the amplitude of P1 when the amplitude data was combined across all electrode sites and ISIs. The amplitude for stimulus /m/ (mean = 8.12 μV, *SD* = 3.93) was significantly less than that for stimulus /t/ (mean = 14.07 μV, *SD* = 6.48), $F(1,9) = 22.16$; $p = .001$.

DISCUSSION

The temporal cue of stimulus duration is considered crucial in distinguishing phonetically similar stimuli (Simos & Molfese, 1997) but it has not been examined systematically as a factor in infant cortical responses. Results from our duration experiment showed no significant difference in peak amplitude or latency with changes in duration over the constrained range of durations used in this experiment for either the /m/ or /t/ stimulus. When duration was re-examined by combining response data from short duration stimuli and comparing it with data from medium duration stimuli only, there was still no significant difference in latency. By contrast, a significant difference in amplitude was found where responses to medium duration stimuli had higher amplitude than responses to short duration stimuli but this amplitude difference was minimal at 1 μV, on average, and therefore likely to be of little consequence clinically.

Previous studies, albeit with adult participants and tonal stimuli, showed that durational increases in tonal stimuli of up to 70 ms increased the amplitude of the adult N1 response and decreased the latency (Alain, Woods, & Covarrubias, 1997). In more recent reports using magnetoencephalographic

(MEG) techniques, the N1 equivalent response — known as the N100m — also showed increased amplitude with increased duration up to 40 ms for 1k Hz stimuli (Gage & Roberts, 2000). An increase in latency but no change in amplitude was, however, reported for 1k Hz stimuli that varied from 50 ms to 100 ms and to 200 ms (Rosburg, Haueisen, & Sauer, 2002). These apparent contradictions of increased or decreased latency, and increased or unchanged amplitude, with increasing stimulus duration may arise either because of inconsistencies in the rise/fall of the stimuli across studies, or because of differences in CAEP elicited using electric versus magnetic recording techniques. Scalp-recorded evoked potentials are known to arise from diverse cortical sources, while multiple-coil magnetic responses appear to localise cortical activity with higher precision and so differences between the outcomes from the two techniques are likely (Cheour, Imada, Taulu, et al., 2004; Hari, 1990).

In the present study, the lack of expected latency change and the limited evidence for amplitude increase as stimulus duration increased may have arisen from two possibilities or a combination of them. First, predicting CAEP outcomes in infants based on the outcomes of adult studies is highly problematic given the substantial differences in the components of the response (Ceponiene, Rinne, & Naatanen, 2002), and the likely differences in the encoding processes of temporal cues within the auditory system of adults and the maturing pathways of infants (Musiek, Verkest, & Gollegly, 1988; Pasman, Rotteveel, Maassen, et al., 1999). Second, amplitude and latency differences for cortical responses to tonal stimuli versus more complex speech stimuli are expected, because the processing of speech sounds is likely to take place, at least partly, in different regions of the auditory cortex to that of tonal stimuli (Pang & Taylor, 2000). Eulitz and colleagues (Eulitz, Diesch, Pantev, Hampson, & Elbert, 1995; Eulitz, Obleser, & Lahiri, 2004) reported that the peak latency of the adult N1 and N100m response was found to be earlier for tonal than speech stimuli and the generator for the tonal stimulus of 1000 Hz, which is frequently used in adult studies, was located more posterior, inferior and medial relative to the generators for vowels. It is therefore unreasonable to assume that findings generated with tonal stimuli may be applied when speech stimuli are used. Irrespective of the reasons for our findings, our results suggested that there was a minor increase in amplitude when a medium duration (i.e., 79 ms) for the vowel-free speech stimuli was selected.

In our second experiment the stimulus duration was therefore fixed at 79 ms, but the ISI was varied. As the ISI was increased from 750 ms to 1500 ms, the amplitude of P1 increased significantly for /t/ but not for /m/. This effect was not, however, linear as there was no change in amplitude as the ISI increased from 1125 ms to 1500 ms. Latency did not, however, vary at all with ISI changes using either /t/ or /m/ stimuli. Adult studies, where the N1 or the magnetic equivalent response have been recorded, also reported increasing amplitude but no change in latency as the ISI between tone burst stimuli increased (Budd, Barry, Gordon, Rennie, & Michie, 1998; Hari, Kaila, Katila, et al., 1982; Imada, Watanabe, Mashiko, Kawakatsu, & Kotani, 1997). Nelson and Lasserman (1968) reported that dramatic increases in amplitude could be observed as ISI increased from 500 ms to 2 or 3 seconds, with more gradual increases in amplitude observed between 3 seconds and 10 seconds. This increased amplitude with increased ISI is consistent with neural refractory periods (Budd, Barry, Gordon, et al., 1998), which are up to 10 seconds long for some neurons associated with late responses (Picton, 1990).

Studies of ISI and its impact on the components of a child's CAEP have shown that an increased number of response components can be reliably observed as the ISI increases. Ceponiene and colleagues (Ceponiene, Cheour, & Naatanen, 1998; Ceponiene, Kushnerenko, Fellman, et al., 2002) demonstrated that with short ISIs (i.e., 350 ms–600 ms) only a P1 and N2 response

was evident in young children of 4 to 9 years but, as the ISI was widened, N1 or its childhood equivalent (i.e., N160) may be observed with increased amplitude. Gilley and colleagues (Gilley, Sharma, Dorman, et al., 2005) also found age-related response patterns in 3 to 12 year olds, using the speech segment /uh/, as the ISI was sequentially reduced from 2 sec to 360 ms. The authors reported that 3 to 4 year olds had a robust P1 with increased latency and decreased amplitude as the ISI reduced but N1/P2 was only observed in 40% of these children and only when a slow stimulation rate (i.e., 2 sec ISI) was used.

In our study of infant cortical responses the amplitude of P1 increased, albeit in a nonlinear manner, in response to /t/ as the ISI increased from 750 ms to 1500 ms, which is consistent with these reports. The effect was not, however, evident for /m/ and no increase in latency was observed as the ISI was reduced for either stimulus. This irregularity across stimuli in amplitude change and the lack of latency change as ISI varied was surprising in the light of earlier findings in young children (Gilley, Sharma, Dorman, et al., 2005). Age-related increases in synaptic density and myelination are expected from a conceptual age of 27 weeks (Huttenlocher & Dabholkar, 1997), but in the highly immature central auditory system, lower cortical excitability is also expected (Surwillo, 1981) and therefore, perhaps, imperfect sensitivity to rate change should be expected in infants. As there was some increase in response amplitude to /t/ but not for /m/ with increasing ISI, a compromise of 1125 ms ISI was selected for our ongoing research on CAEPs in infants with normal hearing and hearing impairment.

Finally, there were two outcomes from our studies that were of secondary interest but worthy of note. First, the stimuli used in our studies were /t/, an unvoiced stop consonant and /m/, a voiced nasal consonant and there were significant latency and amplitude differences between the responses generated to each stimulus. These differences became apparent when data from the short/mid duration and electrode sites were combined in the first study, and again when all ISIs' and electrode sites' data were combined in the second study. The responses generated using an unvoiced stop consonant had a greater amplitude and shorter latency than those generated using a voiced nasal consonant. This is inconsistent with earlier studies where CAEPs in response to voiced CVs produced greater amplitudes and shorter latency responses than unvoiced CVs (Kurtzberg, 1989; Tremblay, Friesen, Martin, et al., 2003) but it is consistent with a MEG study that investigated the response to sounds with different onset characteristics (Gage, Poeppel, Roberts, & Hickok, 1998). These authors reported that larger amplitude and shorter latency responses were observed to monosyllabic words with initial stop consonants of /b/ or /t/ compared with responses associated with /m/ and /f/. It was suggested that stops contain more energy at onset than no-stop stimuli (Gage, Peoppel, Roberts, et al., 1998) and that the rate of change in sound pressure at sound onset determines the strength and latency of neural responses (Philips, Hall, & Boehnke, 2002). This might explain why the stop consonant /t/ that is characterised by a very fast onset of peak energy produced an earlier and stronger response in our study than the nasal /m/ with its slower rise in energy. Second, the amplitude of P1 was consistently greater at C3 (left temporal electrode) than at the other two sites by 1 to 2 μV approximately in both our studies. This may reflect a test ear effect (recall that our test speaker was positioned to the right side in both studies) which is consistent with other studies where amplitude advantages for CAEPs have been found over the hemisphere contralateral to the test ear (Paavilainen, Alho, Reinikainen, et al., 1991; Ponton, Eggermont, Khosla, et al., 2002).

Research to date suggests that the complexity of the evoked potential to an acoustic stimulus is quite remarkable and our knowledge of how these measures reflect specific aspects of auditory function and perception is still rudimentary (Kraus & Cheour, 2000; McGee,

Kraus, King, & Nicol, 1996; Wunderlich & Cone-Wesson, 2006). A number of studies have examined important acoustic features such as duration and ISI, but the majority of these have been conducted using adult populations and tonal stimuli. Results from the present study, using infant participants, can confirm that the application of adult findings to infant populations is highly problematic. If these objective techniques are to assist our understanding of the speech perception capacity of infants and young children, it is apparent that more studies into the effect of acoustic change on the infant CAEP is needed.

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