Measuring temporal resolution in infants using mismatch negativity

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We show that the mismatch negativity (MMN) component of the event-related potential can be used to measure auditory temporal resolution in human infants. Infrequent stimuli with silent gaps of 4, 8, or 12 ms modulated the P2 component, generated MMN, and produced a P3a-like positivity. The data indicate that within-channel gap detection thresholds at 6 months are essentially at adult levels under conditions of little adaptation. Since MMN is elicited without attention and does not require a behavioural response, it can be measured similarly across the lifespan. We are now in a position to study the development of cross-channel temporal resolution and adaptation effects in infancy, and to examine how these abilities in infancy relate to later language acquisition. *NeuroReport* 12:2443–2448 © 2001 Lippincott Williams & Wilkins.

Key words: Auditory system; Development; Event-related potential (ERP); Gap detection; Infancy; Language; Mismatch negativity (MMN); Perception; Speech perception; Temporal processing

INTRODUCTION

Many of the features distinguishing speech sounds rely on timing differences of a few milliseconds, and poor temporal resolution is one of several basic auditory processing deficits that has been linked to language-learning problems [1–3]. Children with language-learning problems are typically not diagnosed until they are at least 3 years of age because of the large variability in the age at which children acquire various aspects of language (e.g. 10% of children understand 100 words at 8 months and produce >350 words at 18 months, whereas 10% of children do not understand 100 words until 16 months and do not produce 350 words until 30 months) [4]. Thus, the development of a reliable method for measuring temporal resolution in infancy could potentially allow the identification of children at risk for language impairment in early infancy, at a time when brain plasticity might be optimal for successful intervention. However, little is known about the normal development of temporal resolution. In this paper, we investigate the feasibility of using electrophysiological methods to assess temporal resolution in infancy.

One of the most common ways of assessing temporal resolution in the auditory system is to measure gap detection thresholds, in which the smallest silent gap that can be detected between initial and final sound markers is determined [5,6]. However, gap detection thresholds vary greatly as a function of several parameters such as the duration and spectral content of the markers [6–9], and are higher if the initial and final markers are processed in different frequency channels [10,11]. There are two published behavioural studies of gap detection in infants. Werner *et al*. [12] found that infants' thresholds for detecting gaps in continuous broadband noise were around 10 times higher than those of adults. On the other hand, Trehub *et al.* [13] found that infants' thresholds for detecting gaps bounded by short Gaussian-modulated sine-wave tones were roughly double those of adults. This difference across studies may reflect larger adaptation effects in infants than in adults, as continuous noise would be expected to produce greater adaptation than the short tone markers [13]. Indeed, there is evidence that forward masking may be particularly immature in infants [14].

In our initial study of gap detection in infants, we attempted to obtain the most pure measure of temporal processing possible by using short Gaussian-modulated sine-wave tone pip markers [15,16] that minimize adaptation and masking effects. These stimuli are identical to those used in previous studies of adults, and thus allow direct comparisons across age groups [16].

Previous studies of gap detection in infants have used behavioural methodologies in which a motor response, such as a head turn, is elicited in response to a change in the auditory stimulus. With such methods, however, it can be difficult to separate attentional abilities, motivational factors, and motor skills from perceptual abilities. This is a particular problem when examining perceptual development across age because there are huge advances in attentional, cognitive, and motor skills with increasing age. Furthermore, developing cognitive, attentional, and motor capabilities often dictate the use of different behavioural methodologies at different ages, which makes comparisons across age even more difficult.

The mismatch negativity (MMN) component of the event-related potential (ERP), on the other hand, is well

suited to examine temporal processing development across the first year of life. MMN is generated primarily in auditory cortex [17–19]. It is measured at the scalp between about 150 and 250 ms after stimulus onset as a greater negativity at frontal sites, and a greater positivity at mastoid sites, to infrequent deviant stimuli in comparison with frequent standard stimuli. In our gap detection task, the infrequent deviant stimulus contained a silent gap (bounded by Gaussian-modulated tone pip markers) whereas the frequent standard 'no-gap' stimulus did not (Fig. 1). In adults, MMN measures are correlated with behavioural discrimination [19]. Importantly for work with infants, MMN is elicited without attention or a behavioural response [19], and hence can be measured in a similar manner across the lifespan. Furthermore, several studies show that MMN can be reliably elicited in young infants [20]. We have shown previously that MMN can be used to measure gap detection in adults [16] and that thresholds obtained with MMN (~4 ms) agree well with previous behavioural measures of adult gap detection thresholds [13,15]. In the present study, we used the identical stimuli to measure temporal resolution thresholds in 6-month-old infants.

MATERIALS AND METHODS

Participants: The final sample consisted of 28 infants between 6 and 7 months of age (15 male, 13 female) whose parents gave informed consent for participation. All infants were born within 2 weeks of term, weighed $\geqslant$2500 g at birth, had no known abnormalities, and all were healthy at the time of testing. The data from a further 22 infants were unusable, eight because of equipment failure and 14 because too few artifact-free trials were collected due to infant fussing and movement.

Stimuli: In each of three conditions, gap stimuli were constructed with two 200 Hz Gaussian-enveloped tone pip markers (s.d. 0.05 ms) whose peak amplitudes were separated by 4, 8, or 12 ms. The matching no-gap stimuli were created as in Schneider *et al.* [15] and Desjardins *et al.* [16] to match the gap stimuli in duration and energy, and roughly in spectral content (Fig. 1).

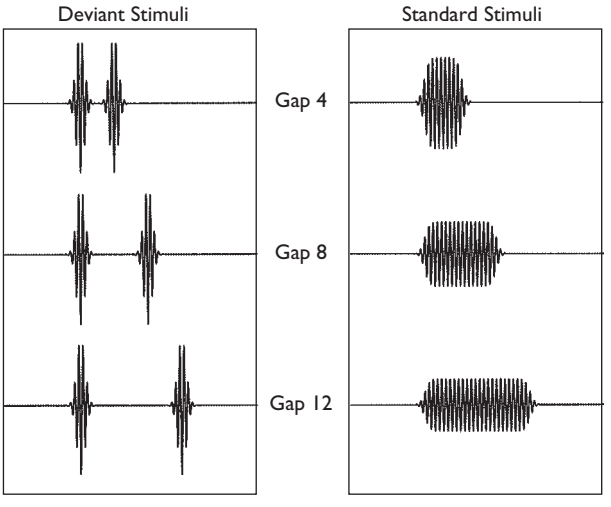

Fig. 1. Deviant gap (left panels) and standard no-gap (right panels) stimuli matched in duration and energy. Gap sizes are 4 ms (upper panel), 8 ms (middle panel), and 12 ms (lower panel) peak to peak.

We chose to use the short Gaussian-modulated sine-wave markers for the following reasons. First, we used short markers in order to minimize adaptation and masking effects. Second, we used sine-wave tones rather than broad-band noise because we are interested in comparing gap detection in different frequency regions in future studies. We chose not to use band-limited noise because, although band-limited noise is better than sine-wave tone pips at masking the spectral splatter that occurs when a sound is turned on or off (spectral splatter could be used as a cue to the presence of a gap), the random amplitude fluctuations in band-limited noise can be confused with the gaps [5,6]. Third, we used Gaussian envelopes to modulate the sine wave tones because this envelope minimizes the spectral splatter, and the degree of spectral splatter is independent of the size of the gap [15]. Fourth, we did not present the stimuli in noise, as is commonly done to minimize spectral splatter cues, because infants are particularly impaired by noise [21]. We are further justified in this because, for adults, gap thresholds for these stimuli in the absence of masking noise are not affected by lower stimulus intensity levels in which there is less information from spectral splatter (no difference in gap thresholds between 20 and 60 dB above hearing threshold) [15].

Apparatus: The sounds were presented with a SoundBlaster AWE32 Gold card (Creative Technology) running on a Comptech pentium computer, a Denon PMA 480R amplifier, and a Grason Stadler speaker at a level of 65 dB(B) SPL. The EEG was recorded with NeuroScan software using Synamps and electrocaps in a shielded room.

Procedure: An oddball paradigm was used. In each of the three conditions (gap 4, gap 8, gap 12) 80% of the trials consisted of the no-gap standard stimulus and 20% of the trials the deviant gap stimulus, with trial onset-to-onset of 800 ms. Infant movement was controlled by having them watch a screen saver program or watch an experimenter play with a toy, whichever kept the infants most still. If the infant became fussy, the procedure was halted until the infant was comforted and became calm. If it was not possible to calm the infant, testing ended. We attempted to obtain 1600 trials from each infant, but the actual number of trials obtained varied between 400 and 1600.

Recordings: Recordings were made from frontal sites FP1, FP2, F3, F4, and mastoid sites TP9 and TP10, and referenced to Pz. We had planned to use the mastoids (TP9, TP10) as the reference; however, with infant movement, these electrodes tended to fall off. We also found it difficult to record from other potential reference sites: recordings from occipital sites were poor because the infants often scrunched their necks, and the infants would not tolerate a nose electrode. Pz makes a reasonable reference for MMN because, relative to this site, the MMN should be negative at frontal sites and positive at mastoid sites. Impedance levels were maintained below 5 kΩ.

Data analysis: Because of the presence of prominent slow waves, the recordings were band-pass filtered between 3 and 18 Hz. Baseline was defined as the mean amplitude for the 100 ms preceding the onset of the stimulus. Epochs were defined as the 550 ms beginning from the onset of the stimulus. All trials on which the measured activity at any electrode exceeded $\pm 100\,\mu V$ were rejected as containing movement artifact. Across infants, the number of usable deviant trials varied between 48 and 176 (mean 133 trials, s.d. 75). The waveforms on the standard trials and deviant trials were averaged separately for each infant, and the amplitude and latency of the P2 component determined for each infant. Standard waveforms were also subtracted from deviant waveforms to create difference waves. Two-tailed *t*-tests were employed to determine the portions of the differences waves that were significantly different from 0 across the participants in each condition.

RESULTS

Both standard and deviant waveforms showed an early negativity followed by a positivity (P2; Fig. 2). The deviant waves were more negative than the standards around 220 ms after stimulus onset (MMN) and showed an additional late positive component.

P2 peak amplitude and latency were determined at F3

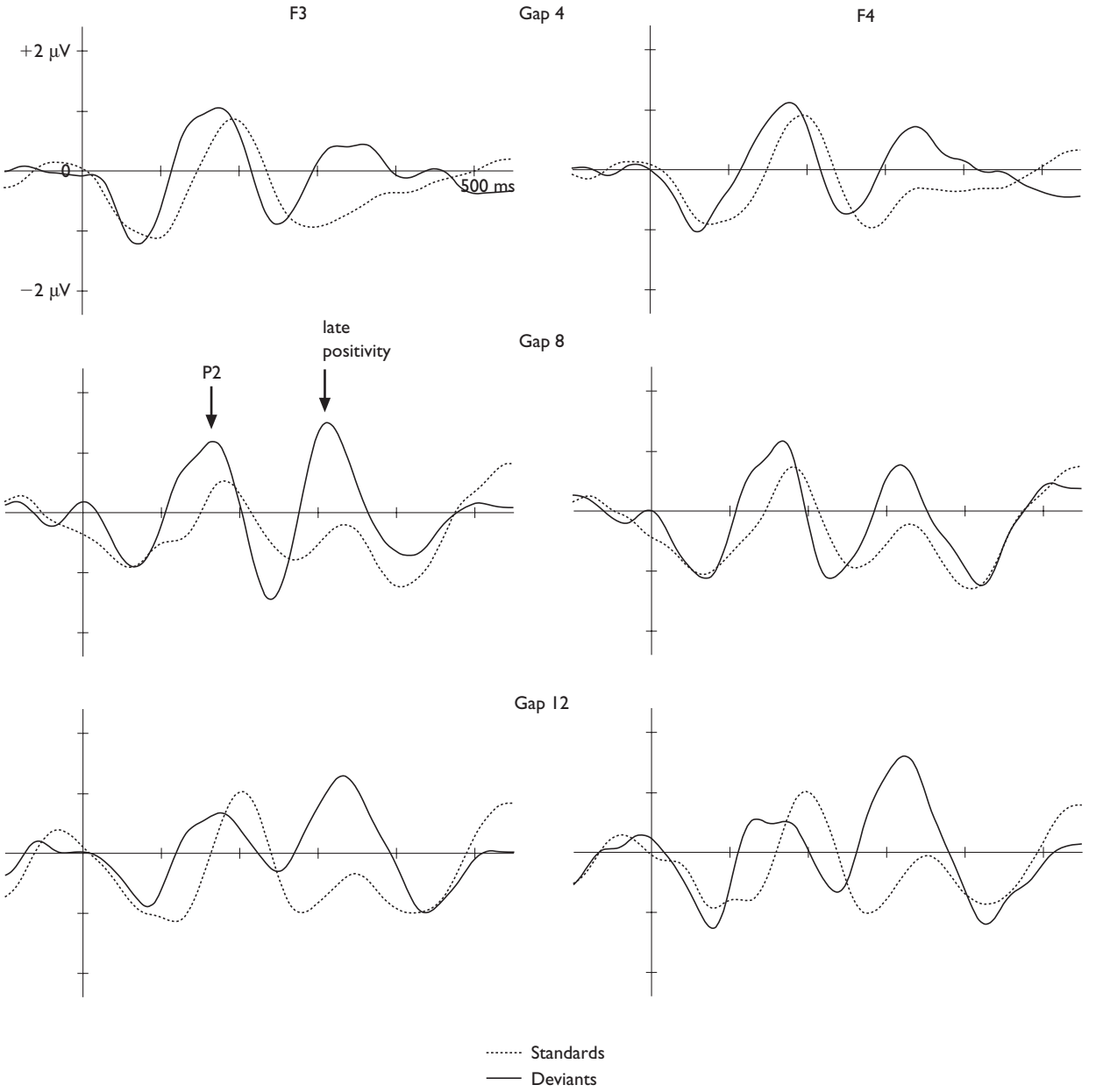

Fig. 2. Grand average standard and deviant waves for gap sizes 4, 8, and 12 ms at left frontal (F3) and right frontal (F4) sites. P2 peaks earlier in the deviants (average 162 ms) than in the standards (average 192 ms). A late positivity, peaking around 330 ms, is evident in the deviants only.

and F4 for each infant by finding the largest positive peak between 95 and 230 ms after stimulus onset. Four infants were excluded because there was no definable peak in this region. One infant in gap 4, one in gap 8, and 2 in gap 12 showed double P2 peaks. In these cases the average was used. There were no significant differences in P2 amplitude across sites or gap size. However, the P2 peaked significantly earlier for the deviants than the standards at both P3 and P4 for all gap sizes (all $ps < 0.05$, 2-tailed t-tests).

Difference waves (deviants−standards) are shown in Fig. 3. The time periods during which the difference wave was significantly different from zero ($p < 0.05$ by a 2-tailed test) for an extended number of adjacent time steps are shown in Table 1. Significant MMN was found for all three gap sizes (Table 1), and the MMN tended to peak later as the gap size diminished. The MMN peak amplitude and latency were determined for each infant in each condition, by choosing the largest negative peak in the difference wave between 175 and 290 ms after stimulus onset. The data from two infants were excluded from this analysis because there was no definable peak in the region. Using this measure, MMN for gap 12 was significantly earlier than MMN for gap 4 at F4 ($t(17) = 1.90$, $p < 0.04$), although the effect did not reach significance at F3. There were no significant effects of gap size on amplitude. The small number of electrodes used precluded topographical analysis. However, there were no significant left/right differences in either latency or amplitude.

Table 1. Periods (in ms after stimulus onset) where difference waves differed significantly from zero ($p < 0.05$), corresponding to the P2, MMN, and the late positivity.

	Gap 4	Gap 8	Gap 12
P2			
F3	116–158	144–178	*
F4	116–168	120–148	112–152
MMN			
F3	222–234	228–250	200–220
F4	230–238	208–222	196–234
Late positivity			
F3	290–346	280–344	272–332
F4	298–352	278–312	266–332

*At $p < 0.10$, the period of significance was 110–152.

It was not possible to analyze data from the mastoid electrodes for each group as a whole because we were not able to collect good data from these sites in most infants. However, Fig. 4 shows data from an individual infant in which there is good data at the mastoid sites. It can be seen

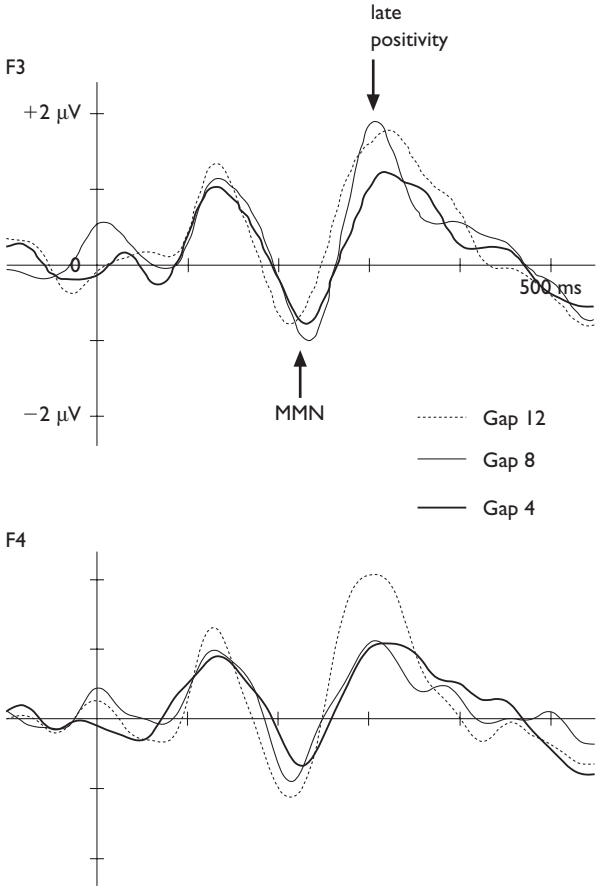

Fig. 3. Grand average difference waves (deviant minus standard) for gap sizes 4, 8, and 12 ms at left frontal (F3) and right frontal (F4) sites. The MMN peaks around 220 ms and is followed by a late positivity peaking around 330 ms after stimulus onset.

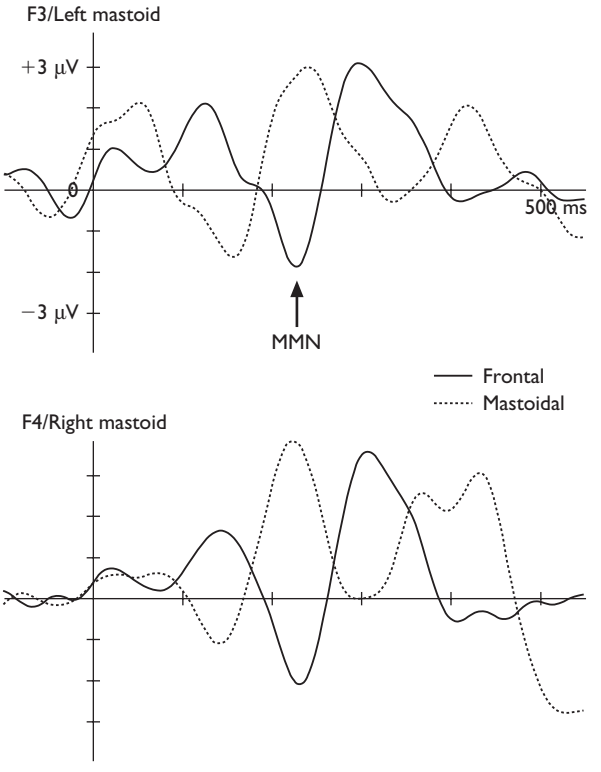

Fig. 4. Average difference waves (deviant minus standard) for an individual infant in gap 12. The MMN peaks around 220 ms at left and right frontal sites and reverses polarity at the mastoids.

that the waveforms show the expected polarity reversal. Furthermore, this figure demonstrates that clear MMN can often be seen in individual infants, suggesting its potential use as a clinical tool.

Interestingly, a clear late positivity followed the MMN at frontal sites, peaking around 300–350 ms after stimulus onset. This component was not seen in the adult data of Desjardins *et al*. [16], even when rereferenced to Pz to match the infant reference. The time intervals in the window 250–450 ms when the difference wave was significantly greater than zero ($p < 0.05$, a 2-tailed test) for an extended number of adjacent time steps are shown in Table 1. As with the MMN, the latency of the late positive peak increased with smaller gap sizes. The peak of the late positivity was significantly earlier for gap 12 than for gap 4 at both F3 ($t(17) = 2.64$, $p < 0.01$) and F4 ($t(17) = 2.54$, $p < 0.01$). As with the MMN analysis, there were no significant effects of gap size on the amplitude of the late positivity, nor were there significant left/right differences in either latency or amplitude. The component was also often clearly present in the waveforms from individual infants (see Fig. 3).

DISCUSSION

We have shown that a gap detection task elicits a clear MMN in 6-month-old infants. Furthermore, the MMN is robust, even at very small gap sizes. In fact, using this methodology and these stimuli (2000 Hz Gaussian-enveloped tone pip markers) there appears to be little difference in threshold between infants and adults, both of whom continue to show MMN to gaps as short as 4 ms. Future studies should therefore examine thresholds in younger infants, in order to determine when basic temporal resolution matures. In addition to MMN, two positive components were evident in the difference waves. Neither of these components were present in the adult data of Desjardins *et al*. [16], even when rereferenced to match the infant data. First, P2 was significantly earlier in deviants than in standards at all gap sizes. Prominent P2s have been reported previously in infants [22]. What is particularly interesting in the present context is that this component is modulated by rare events.

Second, a prominent late positivity to the deviant stimuli followed the MMN. This positivity is certainly not a P3b type of component related to conscious stimulus evaluation and working memory updating [17] because P3b is maximal at parietal sites when measured at the scalp, and we used Pz as the reference. It is possible that it is an early P3a type of component, however. In adults, the P3a appears to reflect the triggering of the attentional system to salient changes in an unattended channel and is maximal at frontal sites [17,23]. Interestingly, this component was not present in adults tested with the identical stimuli to those of the present study [16], even when rereferenced to Pz, perhaps indicating a more mature filtering out of irrelevant information to higher brain areas in adults than in infants.

The finding of similar thresholds for gap detection in infants and adults appears to be in contrast to the behaviourally determined thresholds of Trehub *et al*., [13] who found that infants' threshold were approximately double those of adults, and suggests that the MMN methodology might yield lower threshold estimates than traditional infant behavioural methods. However, a direct comparison between studies cannot be made because Trehub *et al.* used 500 Hz markers, while the present study used 2000 Hz markers. For adults, gap detection thresholds are higher at 500 Hz than at 2000 Hz [8]. There is also evidence that infants' processing matures first for higher than for lower frequencies, in terms of hearing thresholds [24]. Thus it is possible that gap detection thresholds mature first for higher- than for lower-frequency markers.

Our measure of temporal resolution contrasts more strongly with that of Werner *et al.* [12], who found that infants' gap detection thresholds in continuous noise were about 10 times higher that those of adults. Our results corroborate the proposal of Trehub *et al*. [13] that infants take much longer than adults to recover from adaptation effects. With the short tone pips of our study and those of Trehub *et al.* [13] there could be little adaptation, and we found little difference between infant and adult thresholds. However, with the continuous noise stimuli of Werner *et al*. [12], considerable adaptation would be expected, and they found large differences between infant and adult thresholds. In fact, adaptation effects may be important for identifying and understanding the underlying deficits in language-impaired children. Specifically, there is evidence that language-impaired children are particularly affected by backward masking [25]. Speech and music fall in between our stimuli and those of Werner *et al*. [12] in terms of the potential for adaptation effects, so the extent to which infants' slow recovery from adaptation affects their perception of speech and music remains an empirical question. However, given that infants' and adults' thresholds are similar under conditions of little adaptation, it can be concluded that temporal resolution itself is relatively mature in 6-month-old infants at 2000 Hz.

When the initial and final markers of a gap stimulate the same frequency channels, as in our stimuli, the task is said to be a within-channel gap detection task, and is likely performed relatively peripherally in the auditory system [5]. Adult thresholds for cross-channel gap detection are considerably higher than those for between-channel gap detection, suggesting that different mechanisms operate in the two domains [10,11]. There are no studies of cross-channel gap detection in infants. However, if cross-channel gap detection occurs at a more central level of the auditory system, it might be predicted to mature later than within-channel gap detection. Temporal processing in the speech domain involves, in part, the cross-channel mechanism, which may be particularly impaired in language-delayed and dyslexic populations [5]. Thus, in order to relate temporal processing deficits in the infancy period to risk for language impairment, it is important for future studies to examine cross-channel gap detection in infants.

CONCLUSION

We have shown that the temporal resolution of the auditory system can be measured with the MMN component of the event-related potential in infancy, and that by at least as young as 6 months, within-channel gap detection at 2000 Hz is essentially at adult levels under conditions of little adaptation. We have also shown that in infants rare events modulate the P2 component, and

produce a P3a-like positivity following the MMN response. Future studies will now be able to directly compare thresholds in younger and older infants, and to examine developmental changes in adaptation and cross-channel temporal processing as they relate to language acquisition.

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