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Changes in auditory cortex and the development of mismatch negativity between 2 and 6 months of age

Laurel Trainor*, Melissa McFadden, Lisa Hodgson, Lisa Darragh, Jennifer Barlow, Laura Matsos, Ranil Sonnadara

Department of Psychology, McMaster University, Hamilton, Canada ON L8S 4B2

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Abstract

Evoked responses to stimulus deviance were compared in infants between 2 and 6 months of age. A deviant stimulus containing a short silent gap occasionally replaced a repeating standard stimulus matched in duration, intensity and approximate spectral content. At two months, the standard stimuli evoked only a positive slow wave, and its amplitude was increased in response to the deviant stimuli. By 6 months, the deviant stimuli evoked an increased negativity at approximately 200 ms, similar to the mismatch negativity (MMN) response in adults. The results are considered with respect to layer-specific cortical maturation during this period.

Keywords: Infant; Human; Development; Auditory; Temporal; Gap detection; Mismatch negativity (MMN)

1. Introduction

A number of recent reports suggest that event-related potentials (ERPs) can be used to measure discriminative abilities in young infants. Occasional changes in the duration (Kushnerenko et al., 2001; Leppänen et al., 1999), pitch (Alho et al., 1990; Ceponiené et al., 2002; Leppänen et al., 1997; Morr et al., 2002) phonemic identity (Cheour et al., 1997, 1998, 2000; Dehaene-Lambertz and Baillet, 1998; Dehaene-Lambertz and Dehaene, 1994), or temporal gap size (Trainor et al., 2001) of a repeating sound stimulus give rise to changes in the evoked response. However, the nature of the reported changes varies considerably from study to study, with some reporting an increased positivity (Dehaene-Lambertz and Baillet, 1998; Dehaene-Lambertz and Dehaene, 1994; Leppänen et al., 1997, 1999; Morr et al., 2002) and others an increased negativity (Alho et al., 1990; Ceponiené et al., 2002; Cheour et al., 1997, 1998; Kushnerenko et al., 2001; Morr et al., 2002; Pang et al., 1998; Trainor et al., 2001). Two general differences across these studies are the age of the infants (between 0 and 8 months) and the nature of the occasional change in the stimulus. In the present paper we examine the development of evoked responses to the occasional insertion of a silent gap in a repeating tone pip stimulus across the first 6 months of life.

*Corresponding author. Tel.: +1-905-525-9140.
E-mail address: ljt@mcmaster.ca (L. Trainor).

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In adults, occasional changes in a repeating sound stimulus result in an increased negativity in the ERP between approximately 140 and 250 ms after stimulus onset in the infrequent deviant sounds compared to the frequent standard sounds (Näätänen, 1992; Näätänen and Winkler, 1999; Picton et al., 2000; Schröger, 1998). This mismatch negativity (MMN) has generators in auditory cortex, operates without conscious awareness, and represents the operation of a change detection mechanism rather than a change from the reduced firing of refractory neurons encoding the frequent stimulus to the normal firing of neurons representing the deviant stimulus. MMN is evoked not only to changes in the physical features of a sound stimulus such as frequency, location, intensity, and duration (Näätänen, 1992; Picton et al., 2000), but also in response to changes in patterns of sound (Näätänen et al., 2001; Picton et al., 2000) indicating, for example, automatic recognition of melodies transposed to different pitch ranges (Trainor et al., 2002). Thus, mismatch processes appear to be fundamental in keeping track of incoming auditory information and forming sensory memory traces, and similar mechanisms operate on various features at several different levels of analysis. As such, it is of considerable theoretical interest to know when young infants show MMN, both as an index of cortical maturation and as a measure of auditory function. In this paper, we examine the development of discriminative responses to small silent gaps in short tone pip stimuli in 2-, 3- and 4-month-olds, and compare them to our previous report of 6-month-olds (Trainor et al., 2001).

The human auditory cortex undergoes considerable development over the first 6 postnatal months. Synaptic development reaches a peak at approximately 3 months of age (Huttenlocher and Dabholkar, 1997) and auditory cortex changes from having mature functional neural activity restricted largely to layer I before 4 months of age to the beginnings of such activity in layers IV, V and VI after 4 months of age (Moore, 2002; Moore and Guan, 2001). Thus, significant changes in ERPs should be expected across this age range. In particular, the synaptic activity prior to 4 months of age is likely to be slow and unsynchronized. Indeed, responses evoked by a repeating stimulus tend to be dominated by a positive slow wave during the early months after birth (Alho et al., 1990; Leppänen et al., 1999; Kurtzberg et al., 1986; Morr et al., 2002), whereas those of older infants show a more complex series of faster positive and negative deflections (Pihko et al., 1999; Kurtzberg et al., 1986; Kushnerenko et al., 2002a; Pang et al., 1998; Trainor et al., 2001).

Auditory behavior also changes qualitatively from before compared to after approximately 4 months of age. For example, newborns orient slowly left or right to the location of broadband auditory signals, probably on the basis of subcortical processing (Muir et al., 1989). This response disappears at approximately 2 months of age, but returns at 3 or 4 months in a form that is fast, accompanied by visual search, and accurate within a hemifield, suggesting cortical control. Hearing thresholds for speech noise also improve dramatically over the first months of life, asymptoting at approximately 6 months of age (Tharpe and Ashmead, 2001). Qualitative changes in phonemic processing are also seen. Newborns can discriminate different speech sounds, perhaps on the basis of subcortical processing, but language-specific categorization does not begin to emerge until after 4 months of age (Polka and Werker, 1994)

In this paper, we examine infant ERPs generated in an oddball paradigm in which the occasional deviant stimulus contained a short silent gap in the middle, while the frequent standard stimulus (matched in duration and intensity) did not. We chose this stimulus for a number of reasons. First, we already have ERP data on gap detection in 6-month-olds (Trainor et al., 2001). Second, this previous study indicated that these stimuli give rise to robust responses in 6-month-olds resembling MMN in adults. Third, we are interested in the development of temporal resolution because poor processing in this domain has been linked with both language-learning problems and reading problems (Farmer and Klein, 1995; Tallal et al., 1998). We are investigating whether ERPs can be used to measure temporal resolution in adults (Desjardins et al., 1999) and to track the development of temporal processing with the hope of being able to identify children at risk for language

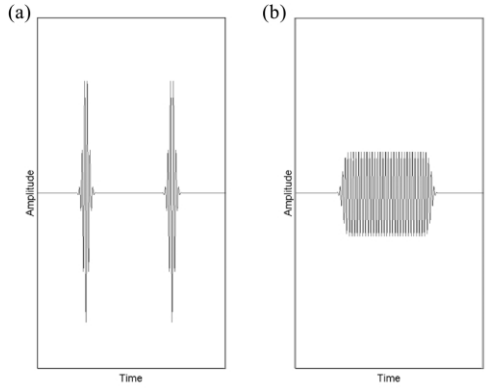

Fig. 1. (a). The deviant stimulus, consisting of two Gaussian-enveloped (S.D.=0.5 ms) 2000 Hz sine wave tone markers, whose peaks are separated by 16 ms. (b) The standard stimulus, generated by the addition of a series of the sine wave markers of the deviant stimulus delayed over time (see Schneider et al., 1994). The standard stimulus matches the deviant stimulus in duration, amplitude, and approximate spectral content.

and/or reading problems in early infancy (Trainor et al., 2001).

2. Materials and method

2.1. Participants

The final sample consisted of 11 2-month-old infants (mean age=80 days, S.D.=7 days; 6 male, 5 female), 13 3-month-old infants (mean age=110 days, S.D.=12 days; 8 male, 5 female), and 19 4-month-old infants (mean age=138 days, S.D.=9 days; 9 male, 10 female). The data from an additional 43 infants could not be used because the infant fussed or moved too much to produce at least 20 artifact-free deviant trials. All infants were healthy at the time of testing, were born within 2 weeks of term weighing at least 2500 g, and had no family history of hearing impairments.

2.2. Stimuli

The deviant gap stimulus consisted of two 2000 Hz Gaussian-enveloped tone pip markers (S.D.=0.5 ms) whose peak amplitudes were separated by a 16 ms gap (Fig. 1). The standard no-gap stimulus was created as in Schneider et al. (1994), Desjardins et al. (1999) and Trainor et al. (2001) to match the gap stimulus in duration, energy, and approximate spectral content (Fig. 1). Short markers were chosen in order to minimize adaptation effects (see Trehub et al., 1995), sine wave tones in order to compare gap detection across different frequencies in the future and to avoid the random amplitude modulations in band-limited noise (see Moore, 1997; Philips, 1999), and Gaussian envelopes in order to minimize spectral splatter (Schneider et al., 1994).

2.3. Apparatus

The sounds were presented from a custom-built flat-response speaker (Jason Sound P63) in an acoustically treated room (acoustic panels hanging from the ceiling, double row of sound-absorbing velour drapes around the walls) and generated by a SoundBlaster AWE32 Gold card (Creative Technology) running on a Comptech pentium computer via a Hafler P1000 amplifier located outside the room. The sounds were presented at a level of 69 dB(C) over a noise floor of 29 dB(A). The EEG was recorded with NeuroScan software using Synamps and sintered Ag/AgCl electrocaps.

2.4. Procedure

Infants were tested in an oddball paradigm in which 20% of the trials consisted of the deviant gap stimulus and 80% consisted of the standard matched no-gap stimulus. Trial onset-to-onsets were 800 ms. The infant sat on his or her parent's lap, and the parent was instructed to remain as still as possible. We attempted to control infant movement by a number of means, including watching a silent video, watching soap bubbles, or watching the experimenter manipulate a toy. We attempted to obtain 1600 trials from each infant, but included infants with fewer trials if they met the criterion outlined in the data analysis section below.

2.5. Recordings

Recordings were made from 20 sites, 7 frontal sites (FP1, FP2, F7, F8, F3, F4, Fz), 5 central

sites (T7, T8, C3, C4, Cz), 4 parietal sites (P7, P8, P3, P4), two occipital sites (O1, O2), and the mastoids (M1, M2), and were referenced to Pz. Because infants sometimes scrunched their necks and sometimes tried to lean the back of their head against their parent, we were not always able to obtain clean recordings from the parietal, occipital and mastoid sites, making it inappropriate to use an averaged reference or a mastoid reference. Pz is a reasonable reference point as the MMN looks negative at frontal sites and positive at occipital and mastoid sites with respect to Pz (see Trainor et al., 2001). The sampling rate was 500 Hz, and impedance levels were maintained below 4 kΩ.

2.6. Data analysis

The recordings were bandpass filtered between 0.5 and 20 Hz. The continuous EEG data was segmented into 650 ms epochs including a baseline defined as the 100 ms before stimulus onset. Epochs were rejected on which the measured activity exceeded ±120 μV during the epoch or ±30 μV during the baseline. Standard (no-gap) and deviant (gap) trials were averaged separately, with standard trials immediately following deviant trials excluded. Data from infants who failed to produce at least 20 acceptable deviant trials were excluded from the analysis. The mean number of acceptable deviants was 84.2 (range = 41–155) in the 2-month-old group, 58.6 (range = 39–146) in the 3-month-old group, 59.5 (range = 24–90) in the 4-month-old group, and 126 (range = 59–126) in the 6-month-olds from Trainor et al. (2001). To form difference waves, standard waveforms were subtracted from deviant waveforms, and two-tailed *t*-tests were employed to determine the regions of the waveform that were significantly different from 0 across participants.

3. Results

Group average standard and deviant waves for 2-month-olds across the 20 electrodes are shown in Fig. 2a. No MMN is evident. The only clear component is a large frontal positive slow wave. Interestingly, however, this slow wave was increased in amplitude for the deviant compared to the standard waveforms, indicating that the 2-month-olds discriminated the gap from the no-gap stimuli (see difference waves, Fig. 2b, left panel). In order to compare these results to those previously published for 6-month-olds (Trainor et al., 2001) the data were filtered between 3 and 18 Hz and reanalyzed. The resulting waveforms were flat, and there were no significant differences between standard and deviant waves (Fig. 2b, right panel). Thus, no MMN-like component was found at 2 months of age, although discrimination of the stimuli was demonstrated by the positive modulation of the slow wave.

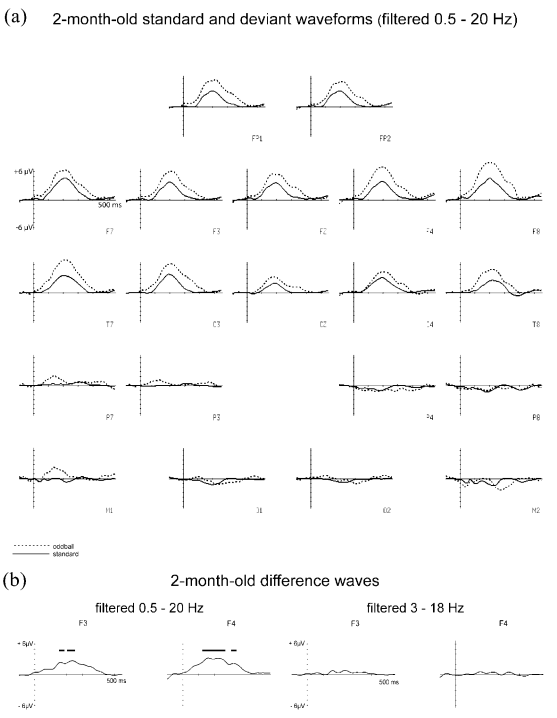

Fig. 2. (a) Two-month-old infants' evoked responses to the standard and deviant stimuli across the scalp. The waveforms were filtered between 0.5 and 20 Hz. Note the prominent frontal positivity and its modulation by stimulus deviance. (b) Difference waves (deviants–standards) at left and right frontal sites. The 0.5–20 Hz. filter condition shows the modulation of the positive wave. The 3–18 Hz filter condition shows that there are no fast difference components present. Gray bars above the waveforms indicate the portions of the waveform that are significantly different from zero.

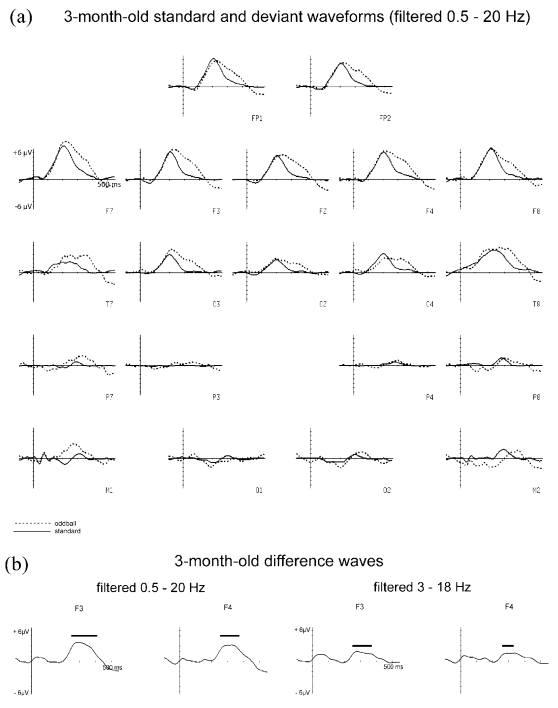

Fig. 3. (a) Three-month-old infants' evoked responses to the standard and deviant stimuli across the scalp. The waveforms were filtered between 0.5 and 20 Hz. Note the prominent frontal positivity and its modulation by stimulus deviance. (b) Difference waves (deviants—standards) at left and right frontal sites. The 0.5–20 Hz filter condition shows the modulation of the positive wave. The 3–18 Hz filter condition shows the reduction in the slow wave modulation when only faster components are considered. Gray bars above the waveforms indicate the portions of the waveform that are significantly different from zero.

Group average standard and deviant waves for the 3-month-olds across the 20 electrodes are shown in Fig. 3a. Again, the only clear component is a large positive slow wave. Difference waves show that it was significantly more positive for the deviant than for the standard stimuli at F3 and F4 (Fig. 3b). Nine of the 3-month-olds showed only a positivity, similar to the 2-month-olds, which was increased in response to the deviant stimuli (Fig. 4a). However, unlike in the 2-month-old group where all infants showed a positive difference wave, the difference waves of 4 of the 13 3-month-olds (31%) showed a negativity approximately 200 ms followed by a positivity (Fig. 4b), similar to the difference waves of 6-month-old infants from Trainor et al. (2001) (Fig. 6c). Furthermore, these difference waves were relatively unaffected by refiltering between 3 and 18 Hz (Fig. 4b, right panel), whereas the positivity was significantly reduced in the group showing no negativity when the waveforms were filtered between 3 and 18 Hz (Fig. 4a, right panel).

Group average standard and deviant waves for the 4-month-olds across the 20 electrodes are shown in Fig. 5a. As with the 3-month-olds, the only significant component in the differences waves at F3 and F4 is a positive component (Fig. 5b). Eight of the 19 4-month-olds (42%) showed only a positivity, similar to the 2-month-olds, which was significantly increased in response to the deviant stimuli (Fig. 6a, left panel) and greatly

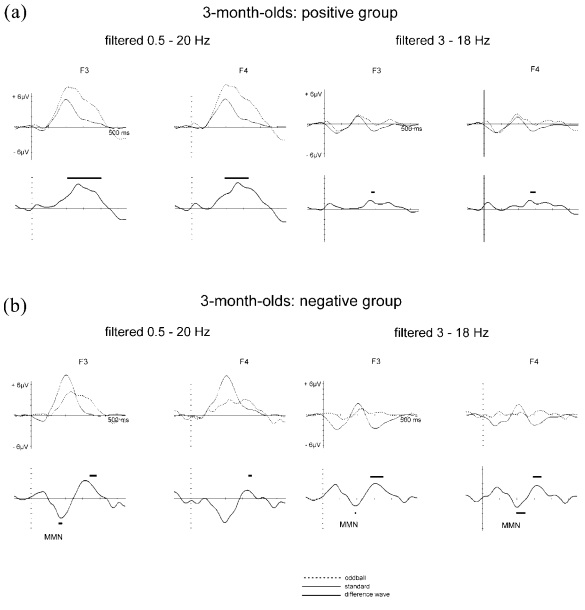

Fig. 4. (a) Standard, oddball, and differences waves at left and right frontal sites for the 9 3-month-olds showing the 2-month-old pattern of frontal positive slow wave modulation. The modulation is prominent when the low frequencies are included (0.5–20 Hz filter condition) but is reduced when the low frequencies are not included (3–18 Hz filter condition). (b) Standard, oddball, and difference waves for the 4 3-month-olds showing an adult-like MMN. The negativity is present for both filter conditions. Gray bars above the waveforms indicate the portions of the waveform that are significantly different from zero.

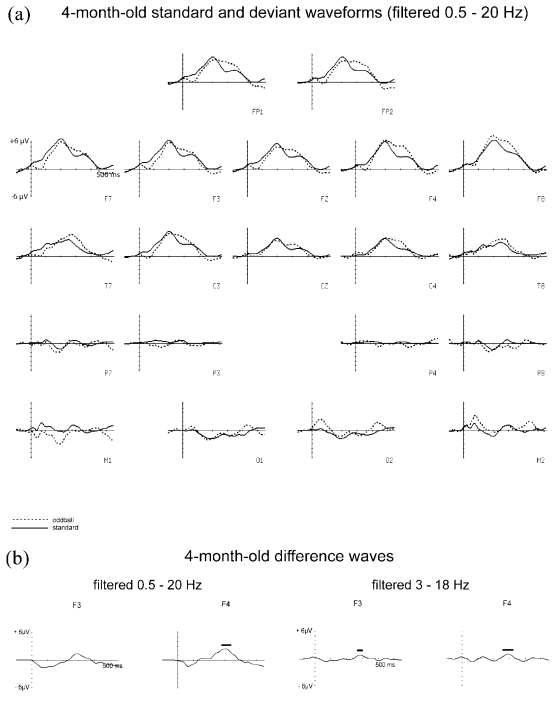

Fig. 5. (a) Four-month-old infants' evoked responses to the standard and deviant stimuli across the scalp. The waveforms were filtered between 0.5 and 20 Hz. As with the younger infants, there is a prominent frontal positivity which is modulated by stimulus deviance. (b) Difference waves (deviants—standards) at left and right frontal sites. The 0.5–20 Hz filter condition shows the modulation of the positive wave. The 3–18 Hz filter condition shows the reduction in the slow wave modulation when only faster components are considered. Gray bars above the waveforms indicate the portions of the waveform that are significantly different from zero.

reduced in the 3–18 filter condition (Fig. 6a, right panel). However, 11 of the 19 4-month-olds (58%) showed a negativity approximately 200 ms followed by a positivity (Fig. 6b), similar to the difference waves of 6-month-old infants from Trainor et al. (2001) (Fig. 6c). Furthermore, this negativity is more clearly seen when the slow components are removed in the 3–18 Hz filter condition (Fig. 6b, right panel).

The 6-month-old data from Trainor et al. (2001) are shown replotted for comparison purposes in Fig. 6c. (Note that the 6-month-old data is in response to a gap size of 12 ms, the largest gap size used in that study, rather than the gap size of 16 ms in the case of the younger infants. This difference is not expected to change the morphology of the waveforms.) It can be seen that the MMN component is present whether the waveforms are filtered between 3 and 18 Hz as in Trainor et al. (2001) or between 0.5 and 20 Hz. The large positive slow wave seen at the younger

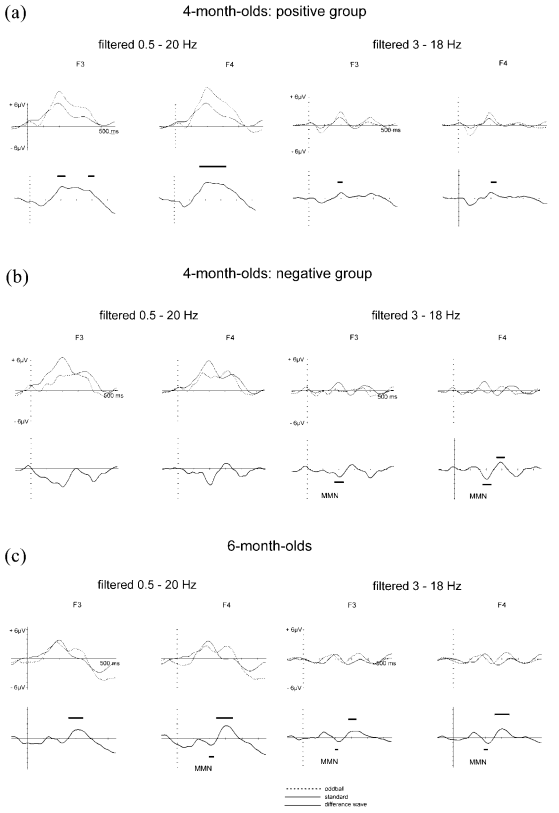

Fig. 6. (a) Standard, oddball, and differences waves at left and right frontal sites for the 8 4-month-olds showing the 2-month-old pattern of frontal positive slow wave modulation. The modulation is prominent when the low frequencies are included (0.5–20 Hz filter condition) but is reduced when the lower frequencies are not included (3–18 Hz filter condition). (b) Standard, oddball, and differences waves for the 11 4-month-olds showing an adult-like MMN. The negativity is most prominent when the slower components are removed in the 3–18 Hz filter condition. (c). Standard, oddball, and differences waves for the 6-month-olds from Trainor et al. (2001), showing adult-like MMN that is most clearly seen when the low frequencies are filtered out (3–18 Hz filter condition). Gray bars above the waveforms indicate the portions of the waveform that are significantly different from zero.

ages is greatly reduced in the 6-month-old data. It is possible that it exists but is not seen because it is also present at Pz, which was used as the reference. However, this is unlikely because it would imply that the slow wave is more widespread in the older than in the young infants, whereas it is known that the slow wave diminishes with increasing age and is not present in adults.

4. Discussion

Scalp-recorded evoked potentials change dramatically between 2 and 6 months of age in response to the occasional presence of a short silent gap in a tone pip stimulus. The data presented here indicate that scalp-recorded MMN responses to gaps resembling those of adults are seen in a few infants as young as 3 months of age (31%), in more infants by 4 months of age (58%), and in most infants by 6 months of age. Prior to this, a slow positivity dominates the evoked potential, a component that is not seen in adults. Although the 2-month-olds did not show any mismatch negativity, the amplitude of the positive slow wave increased in response to occasional deviant stimuli, suggesting that it may, like MMN, serve as an index of discrimination. This slow-wave activity is also present to some extent at 6 months, such that the faster MMN component is most clearly seen when the lower frequencies are filtered out (see Fig. 6).

The results presented here are consistent with studies reporting increases in positivity with stimulus deviance in younger infants (e.g. Dehaene-Lambertz and Baillet, 1998; Dehaene-Lambertz and Dehaene, 1994; Leppänen et al., 1997, 1999; Morr et al., 2002). The results are also consistent with reports of MMN in older infants (e.g. Cheour et al., 1998; Pang et al., 1998). However, the results are inconsistent with some reports of increased negativity to deviance in young infants (e.g. Alho et al., 1990; Alho and Cheour, 1997; Ceponiené et al., 2002; Cheour et al., 1998). The reason for these discrepancies is not yet clear. However, the type of stimulus deviance may play a role, with different maturational timetables for MMN development for different stimulus parameters. For example, timbre-based discriminations (e.g. phoneme, short gaps) may mature at a different rate than simple pitch or duration discriminations. It is also possible that MMN responses may be hidden by larger overlapping components, such as the positive slow wave, and that different signal processing methods may yield different conclusions. There is also evidence that MMN may not be very stable or reliable in young infants, opening the possibility that different criteria for accepting infant data may lead to different conclusions. A recent study by Kushnerenko et al. (2002b) indicates that MMN responses in young infants to frequency deviance may be inconsistent, with some infants showing a positive, and other infants a negative, component. Furthermore, infants showing a negative component at a young age may switch to a positive component a few months later, and vice versa. In sum, more study is clearly necessary in order to understand the developmental emergence of MMN responses.

In the discussion that follows, we consider the question of what physiological developments might underlie the emergence of the MMN response to gap deviance. In adults, an understanding of the layer-specific cortical events—sinks generated by depolarization of apical dendrites, sources representing passive current returns or hyperpolarization—that give rise to measured surface evoked potentials is emerging (e.g. Mitzdorf, 1985; Eggermont and Ponton, 2002; Kral et al., 2000; Javitt et al., 1994). In particular, depth recordings in monkeys suggest that MMN is generated in the supragranular layers of A1 by the depolarization of apical dendrites in superficial layer II, accompanied by a passive circuit-completing source in layer III (although an active source representing recurrent inhibition in layer III may also be involved) (Javitt et al., 1994). In adults, the MMN response appears to be associated with the extra-lemniscal pathway which projects from the caudomedical division of the thalamus to superficial layers of auditory cortex, and is therefore independent of the N1b response, which is associated with the tonotopically organized lemniscal pathway projecting from the ventral nucleus of the thalamic medial geniculate body to layer IV of auditory cortex (Kaas and Hackett, 2000; Kraus

et al., 1994; Näätänen and Picton, 1987; Ponton and Eggermont 2001; Winer, 1992).

Much less is known about the cortical events that give rise to the evoked potentials seen in infants. We will first consider what is known about the maturation of auditory cortex over the first months after birth, with particular emphasis on layer-specific maturation. We will then speculate about how this maturation may relate to the dramatic changes seen in the surface-recorded evoked potentials. A few caveats must be kept in mind during this exercise. First, our knowledge of detailed cortical anatomical development is limited. Second, while a coherent picture is emerging as to how the subcortical and cortical auditory areas are interconnected in adults, it remains largely unknown as to when in development the core, belt, and parabelt areas become functionally separate in human infants, and when the connections between these cortical areas and between these areas and subcortical areas mature. Indeed it is even possible that various pathways are differentially important at different stages of development, and that some pathways present in infancy may be largely lost by adulthood. Furthermore, different areas may serve different functions at different stages of development (Bates et al., 2000; Kolb et al., 1998).

It is clear that major physiological changes occur in auditory cortex over the first postnatal months. Huttenlocher and Dabholkar (1997) have documented that synaptic density reaches a maximum in auditory cortex at approximately 3 months of age, with more rapid development for deeper layers (IV, V, VI) than for superficial layers (II, III). Cerebral energy metabolism as measured in PET studies also increases in auditory cortex at approximately 3 months of age (Chugani and Phelps, 1986, 1990). Moore and colleagues (Moore, 2002; Moore and Guan, 2001) have examined the onset of function in human auditory cortex in a layer-specific manner by labeling axonal neurofilaments, the development of which is associated with increases in axonal diameter, development of myelin sheaths, and increases in conduction velocity. By this measure, only layer I is fully functional until the fourth postnatal month. After 4 months of age, vertical axons penetrating layers IV, V and VI from thalamic locations become fully functional, as do horizontal axons from cells in these deeper layers (Moore, 2002; Moore and Guan, 2001). Given the timing of this development, it may be associated with the emergence of an adult-like MMN response to gap deviance in infants between 3 and 6 months of age. Infant MMN is unlikely to involve layers II and III as axons in these layers do not fully mature until after 5 years of age (Moore, 2002; Moore and Guan, 2001), a time that corresponds to the emergence of the N1b response (Ponton and Eggermont, 2001).

The first question concerns how this anatomical data informs our interpretation of the slow positive potentials and their modulation by stimulus change. Given the relative immaturity of auditory cortex at 2 months, and the diffuse and extended nature of the slow positive wave, the possibility of a subcortical sink (depolarization), with a passive circuit-completing source in layer I needs to be considered. At least in adults, however, thalamic field potentials are not visible at the scalp as the dendrites involved are not all oriented in the same direction. As well, the major input to layer I in adults is non-specific, originating in the medial division of the medial geniculate body, and likely contributes only a widespread excitatory influence on deeper layers, making the modulation of the slow wave in infants by stimulus deviance difficult to explain. It is possible that more specific information reaches layer I in infants, as there are direct connections from the ventral division of the medial geniculate body to layer I in some mammals (see Moore, 2002 for a discussion), but on balance it appears unlikely that the slow wave activity seen in infant ERPs reflects subcortical depolarization. A more likely possibility is that, although layer IV neurons do not have mature neurofilaments, they do have functional synapses (Huttenlocher and Dabholkar, 1997), and are receiving input from thalamocortical neurons and depolarizing in response. Passive source returns might be located in layer I, where more mature neurons are found. Because layer IV neurons are immature, they cannot produce sharp synchronized responses, so scalp potentials resulting from their depolarization would be expect to be very broad. It remains to explain why the positive slow waves seen in young

infants are modulated by stimulus deviance. It is possible that either the thalamocortical input to cortex is increased for the deviant stimuli, and that the slow wave modulation is a reflection of this, or that the deviant thalamocortical input activates a somewhat different set of neurons that are not adapted and hence can fire at higher rates. In any case, it appears more plausible that the slow positive potentials seen at the scalp represent slow unsynchronized layer IV depolarizations than that they represent subcortical activity.

The second question concerns the cortical maturation related to the emergence of MMN-like responses between 3 and 6 months of age. As discussed above, according to one animal model (Javitt et al., 1994), MMN in adults appears to involve intra-cortical circuits with sinks in layer II and sources in lower layer III (Javitt et al., 1994). Given that layers II and III are extremely immature in infants (Moore, 2002; Moore and Guan, 2001), it would seem unlikely that the MMN-like component seen by 6 months could be generated in superficial layers. Rather, the timing of the emergence of MMN-like responses in infants is related to the onset of mature function of neurons in deeper cortical layers (Moore, 2002; Moore and Guan, 2001). In this case, either MMN-like responses are generated in different cortical layers in infants and adults, or the animal model does not apply to humans. It is also possible, however, that the MMN-like responses seen at 6 months of age do not reflect the activation of a true 'change detection' mechanism, but rather result from the deviant stimuli activating a new unadapted population of neurons which can fire at higher rates (see Näätänen, 1992; Picton et al., 2000 for a discussion of this issue in adults).

A related puzzle concerns why MMN responses develop so much earlier (by 6 months) than N1b responses (not mature until middle adolescence, Ponton et al., 2000b), although in adults both appear to involve layers II and III (Javitt et al., 1994). Interestingly, deaf children implanted with cochlear implants readily develop a MMN-like response, but do not develop N1b responses after a critical period of deprivation (Ponton et al., 2000a). Congenitally deaf cats implanted with cochlear implants also do not develop N1b responses (Kral et al., 2000). Although both MMN and N1b are thought to involve layers II and III in adults, MMN involves circuits within a cortical area whereas N1b involves communication between cortical areas, both within and across hemispheres (Eggermont and Ponton, 2002; Javitt et al., 1994; Ponton et al., 2000a). Thus it would appear that within-area sensory representation and comparison matures earlier than longer-range communication.

Change detection is a basic process in auditory cortex. Perhaps change detection circuits develop readily in different areas depending on the input that they receive. Indeed, the location of MMN generation depends on whether the change is for frequency, intensity, duration, location, or pattern (Alain et al., 1999; Alho et al., 1996; Csépe, 1995; Giard et al., 1995; Frodl-Bauch et al., 1997), suggesting that there are many change-detection circuits in adult auditory cortex. Infants and cochlear implant patients may not process stimulus changes in the same way as normal adults because they have immature superficial layers. However, they may be able to set up stimulus-change detection circuits in deeper layers of cortex. With the maturation of superficial layers, sensory representation and comparison may move to these layers, leaving the deeper layers available for other functions. However, much more developmental data is needed before this question can be answered definitively.

5. Conclusions

Occasional insertion of a silent gap in a repeating tone pip stimulus evokes an increase in the positive slow wave in 2-month-olds, whereas it evokes a shorter-duration negativity by 6 months. We hypothesize that the dramatic changes in scalp-recorded potentials between 2 and 6 months of age reflect layer-specific maturational processes in auditory cortex. Specifically, we speculate that the slow positivities seen at the youngest ages represent immature, slow, unsynchronized thalamic-driven depolarization (sinks) in layer IV with layer I passive returns, and that the emergence of MMN-like responses is associated with the maturation of deeper cortical layers. Further studies addressing

the maturation of cortical pathways and their functions in development are needed in order to further evaluate these speculations.

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