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Neuropsychologia



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Maturation of cortical mismatch responses to occasional pitch change in early infancy: Effects of presentation rate and magnitude of change

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A R T I C L E I N F O

Article history: Received 14 November 2007 Received in revised form 28 July 2008 Accepted 30 July 2008 Available online 3 August 2008

Keywords: Mismatch negativity (MMN) Infant Pitch Development Tempo Presentation rate Magnitude of stimulus change

ABSTRACT

Previous studies have reported two types of event-related potential (ERP) mismatch responses in infants to infrequent auditory changes: a broad discriminative positivity in younger infants and a negativity resembling adult mismatch negativity (MMN) in older infants. In the present study, we investigated whether the positive discriminative slow wave and the adult-like MMN are functionally distinct by examining how they are affected by presentation rate and magnitude of change. We measured ERPs from adults, 2-month-olds, and 4-month-olds to a repeating piano tone (standard) that occasionally changed in pitch (deviant). The pitch changes between standards and deviants were either small (1/12 octave) or large (1/2 octave)octave) in magnitude, and the stimulus presentation rate was either slow (800 ms SOA) or fast (400 ms SOA). As the presentation rate increased, both adults and 4-month-olds showed an MMN response that decreased in latency, but was unaffected in amplitude. As the magnitude of the pitch change increased, MMN increased in amplitude. On the other hand, only a broad positive mismatch response was seen in 2-month-olds. As the presentation rate increased, 2-month-olds' responses to standard tones decreased in amplitude while their responses to deviant tones were unaffected. The magnitude of the pitch change did not affect 2-month-olds' responses. These results suggest that pitch is processed differently in auditory cortex by 2-month-olds and 4-month-olds, and that a cortical change-detection mechanism for pitch discrimination similar to that of adults emerges between 2 and 4 months of age.

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1. Introduction

Thirty years of extensive research in adults indicates that the mismatch negativity (MMN) component of the event-related potential (ERP) is a reliable physiological representation of cortical auditory discrimination processes in adults (Näätänen & Winker, 1999). MMN is a frontocentrally negative component (with polarity reversal below the Sylvian fissure) elicited by occasional changes (deviants) in a sequence of identical sounds or sounds from the same category (standards). MMN occurs in response to occasional deviations in pitch, duration, loudness, phonemic category, rhythmic pattern, and other abstract features, with the peak latency (between 120 and 230 ms from the onset of deviant stimulus) depending on the stimulus rate, magnitude of change, and type of change (for a review, see Picton, Alain, Otten, Ritter, & Achim, 2000). MMN is often followed by a frontal-positive P3a component around 280 ms that reflects involuntary capture of attention

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by perceptually novel stimuli (Czigler, Csibra, & Csontos, 1992; Gaeta, Friedman, Ritter, & Cheng, 2001; Polich, 1988; Sams et al., 1985). However, MMN itself can be elicited automatically without attention or an overt response, suggesting that it is related to the detection of deviant events at a pre-attentive level (e.g., Oades & Dittmann-Balcar, 1995; Sussman, Ritter, & Vaughan, 1998). Thus, it is of interest to use MMN in developmental research with prelinguistic infants who have limited repertoires of behavioural responses.

Eighteen years have passed since the first study on the infant mismatch response was conducted (Alho, Sainio, Sajaniemi, Reinikainen, & Näätänen, 1990). Although ERPs potentially provide an objective measure of the relation between brain and behaviour in the early years of life, ERP responses in infants and young children differ substantially from those of adults (for a review, see Trainor, 2007). For example, the N1b component generated in auditory cortex is not seen robustly in children until about five years of age, and does not reach adult levels of maturity until the late teenage years (Ponton et al., 2000; Shahin, Roberts, & Trainor, 2004). Mismatch responses are also different in young infants compared to adults. In fact, two different responses to stimulus change have been reported in infants: (1) a negative response similar in morphology to adult MMN (e.g. Alho et al., 1990; Čeponiené et al., 2000, 2002; Hirasawa,



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^{0028-3932/\$ -} see front matter © 2008 Elsevier Ltd. All rights reserved. doi:10.1016/j.neuropsychologia.2008.07.019

Kurihara, & Konishi, 2003; He, Hotson, & Trainor, 2007; Trainor, Samuel, Desjardins, & Sonnadara, 2001; Trainor et al., 2003) and (2) an increase in the slow positive wave that dominates young infants' ERP responses (e.g. Cheour et al., 1999; He et al., 2007; Leppänen, Eklund, & Lyytinen, 1997; Leppänen, Guttorm, Pihko, Takkinen, & Lyytinen, 2004; Morr, Shafer, Kreuzer, & Kurtzberg, 2002; Trainor et al., 2001, 2003). He et al. (2007) summarized these studies in a table, and discussed the merits of various hypotheses concerning the conditions required for their elicitation. As explanations for when negative and when positive mismatch responses will be observed in infants, they ruled out infant state, physiological conditions such as risk for dyslexia, use of different stimuli, and methodological differences such as choice of reference electrode(s) and rate of stimulus presentation. On the other hand, Trainor et al. (2001, 2003), examining responses to the occasional insertion of a 16 ms silent gap in a repeated sequence of tone pips, found that younger infants showed only an increase in the slow positive wave whereas by 6 months, infants showed a negative response resembling the adult MMN. They proposed that the two responses represent different processes, and that the adult-like MMN response develops with cortical maturation (Moore & Guan, 2001). He et al. (2007) further demonstrated that a similar shift from the discriminative positive slow wave to the adult-like MMN occurs for pitch changes of half an octave, although the shift occurred slightly earlier, between 2 and 4 months of age. The presence of both components at 3 months of age suggested further that they represent different processes. In the present study, we investigated whether the positive discriminative slow wave and the adult-like MMN are functionally distinct by examining how they are affected by presentation rate and magnitude of change.

There is debate in the adult literature as to the nature of the MMN response. For example, it has been proposed that MMN is simply an augmentation of the N1 response (Jääskeläinen et al., 2004). N1 is a vertex-negative component that can be evoked in adults by virtually any transient sound, with typical latency around 100 ms. N1 is thought to be generated by the afferent transient detecting neurons in the auditory cortex (for a review, see Hyde, 1997). Like MMN. N1 increases in amplitude when occasional deviant stimuli are inserted in a repeating pattern. This is thought to occur because the neural circuits representing the standard stimuli become somewhat refractory/adapted whereas those encoding the occasional deviant stimuli do not, resulting in larger responses to the deviant than standard stimuli. However, a number of lines of evidence suggest that MMN and N1 are distinct (for a review, see Näätänen, Jacobsen, & Winkler, 2005). One line involves manipulation of stimulus presentation rate. The N1 response diminishes in amplitude with increases in presentation rate, indicative of a refractory process (Czigler et al., 1992; Mäntysalo & Näätänen, 1987), whereas the MMN amplitude remains the same or increases with increases in presentation rate (Friedman, Cycowicz, & Gaeta, 2001; Roeber, Berti, & Schröger, 2003; Sabri & Campbell, 2001), indicative of a change-detection mechanism. A second line involves manipulation of the magnitude of stimulus change. With smaller differences between standards and deviants, the difference in N1 elicited by standards and deviants becomes very small, again suggesting a refractory process because the representations of standards and deviants increasingly overlap as they become more similar (Näätänen et al., 2005). With decreasing magnitude of stimulus change, the amplitude of the MMN also decreases (Näätänen & Alho, 1997). However, it remains relatively robust with very small differences between standard and deviant stimuli, again suggesting a change-detection mechanism at work (Sams et al., 1985; Scherg, Vajsar, & Picton, 1989).

In the present study, we examined whether the adult-like MMN seen in older infants and the discriminative slow positive wave seen in younger infants behave like the MMN seen in adults. We used the piano tone stimuli of He et al. (2007), but manipulated the stimulus presentation rate and the magnitude of the pitch change between standard and deviant stimuli. Regarding the stimulus presentation rate, if changes in the presentation rate have little effect on the amplitude of the infant mismatch response, this would be consistent with a change-detection mechanism. If, on the other hand, the infant mismatch response diminishes with faster presentation rates, this would be consistent with an N1-like refractory response. A few previous studies found no effect of presentation rate on the adult-like MMN in infants (Pihko et al., 1999; Kushnerenko et al., 2002; Hirasawa et al., 2003), suggesting that this component behaves as if reflecting a change-detection mechanism rather than a refractory N1 mechanism, but there are no studies examining the effect of presentation rate on the infant discriminative slow positive mismatch response. As far as the magnitude of the pitch change, one study (Morr et al., 2002) suggested that the discriminative positive slow wave might only occur in response to large stimulus changes. Here we test whether the infant MMN and discriminative slow positive wave responses are different for pitch changes near threshold compared to those well above threshold.

2. Methods

2.1. Participants

Three different age groups (2-month-olds, 4-month-olds, adults) were tested in two conditions involving a small pitch change (semitone), one at a fast presentation rate and one at a slow presentation rate. Ten (seven female) healthy university students (aged 18-20 years, mean age 18.7 years) with no hearing deficits participated (two were tested in the slow SOA condition only, two in the fast presentation rate condition only, and six in both). Informed written consent was obtained from all the participants prior to the experiment and course credits were assigned to compensate their participation. A total of 67 healthy, full term infants with no known hearing deficits were included in the final sample. The slow presentation rate condition included fifteen 2-month-olds (10 female) and fifteen 4-month-olds (9 female). The fast presentation rate condition included twenty-two 2-month-olds (14 female) and fifteen 4-month-olds (10 female). All the infants were awake during testing. An additional 23 infants (fifteen 2-month-olds and eight 4-month-olds) were excluded from the final sample either because they fell sleep during testing (eight 2-montholds and four 4-month-olds) or because they became fussy during testing and failed to produce the minimum of 100 artifact-free deviant trials for averaging (seven 2month-olds and four 4-month-olds). Informed written consent was obtained from all the parents prior to the experiment. After the experiment, a certificate and a bath toy were provided as thanks for their participation.

In order to examine the effect of the magnitude of the pitch change, the data from the fourteen 4-month-olds (9 female) and fourteen 2-month-olds (11 female) in the large (tritone) pitch change (slow presentation rate) condition of He et al. (2007) were compared to the present data in the small (semitone) pitch change (slow presentation rate). In addition, 8 (5 female) university students (18–23 years, mean age 20.2 years) were tested in the large (tritone) condition (slow presentation rate), as the previous study did not include data from adult participants.

2.2. Stimuli

In both the slow and fast presentation rate conditions, piano tones C₅ and C#₅, with fundamental frequencies of 523.25 and 554.37 Hz were used as standard and deviant stimuli, respectively, representing a pitch change of 1/12 octave (semitone). In the large pitch change (slow presentation rate) condition, the standard was again C₅ but the deviant was F#₅ (f_0 = 698.46), representing a pitch change of half an octave (tritone). For the slow presentation rate, the duration of the stimuli was 600 ms and the stimulus onset asynchrony (SOA) was 800 ms to enable direct comparison with the previous dataset of He et al. (2007). For the fast presentation rate, the duration of the stimuli was 300 ms and the SOA was 400 ms. Stimuli were shorter in this condition to accomodate the short SOA. For such piano tones, with abrupt onsets and where the amplitude subsequently fades gradually to zero, the ERP response to the tone offset is negligible.

2.3. Apparatus

All of the piano tones were synthesized with Reason 2.0 software (Propellerhead Software) and recorded with Adobe audition 1.0 software (Adobe Software). Stimuli were played using E-prime 1.1 software (Psychology Software Tools, Inc.) on a Dell OptiPlex280 computer with an Audigy 2 platinum sound card (Creative Labs) through a WestSun loudspeaker (WestSun Jason Sound, JSIP63) located one meter directly in front of the participant. The stimuli were presented at a level of 70 dB (A) at the location of the head of the participant, over a background noise level of 29 dB (A).

2.4. Procedure

Participants sat on a comfortable chair (infants sat on their parents' laps) in a sound-treated room containing floor-to-ceiling double velvet curtains and acoustic ceiling panels. Participants watched a silent movie (adult participants) or an animated video (infants) in a passive protocol while the piano tone stimuli were played. An oddball paradigm was used with 80% standard trials and 20% deviant trials. Stimulus order was randomized with the constraint that at least two standards occurred between successive deviants. The complete experiment consisted of 1600 trials (320 deviant trials) but testing was stopped early if infants became fussy. For adult participants who completed both the slow semitone and fast semitone conditions, the order of conditions was randomized. All study procedures were approved by the McMaster University Research Ethics Board.

2.5. Recording and analysis

EEG was recoded from 124 locations on the scalp for infants and 128 locations for adults with a Geodesic Sensor net (Electrical Geodesics, Inc). All electrode impedances were maintained below 50 k Ω . The electrical potential was digitized at 1000 Hz. The online recording was referenced to the vertex with a band-pass filter of 0.1–400 Hz.

EEG responses were filtered between 0.5 and 20 Hz for adults. In order to isolate the infant slow discriminative mismatch response and the adult MMN-like fast negative mismatch response, band-pass filters of 0.5-3 and 3-20 Hz were used, respectively. In all cases, filters had a roll-off of 24 dB/oct. (For more detail of this method, see He et al., 2007.) The filtered continuous data were then segmented into 700-ms epochs, including a 100-ms prestimulus-onset baseline (50-ms baseline for the fast presentation rate condition, as stimuli were separated only by a 100-ms inter-stimulus interval in this condition). EEG epochs from adult participants were then subject to fixed threshold $(\pm 120 \,\mu V)$ epoch rejection to omit the artifact due to eye blinks. The number of accepted deviant epochs across all nine adult participants ranged from 233 to 308 (M=282). For infants, channel-independent epoch rejection with a threshold of $\pm 120\,\mu V$ was conducted to remove the epochs contaminated by blinks, eye, head, or body movement. The number of accepted deviant epochs across the 67 infants ranged between 114 and 271 (M = 206). The accepted standard and deviant epochs were averaged separately, excluding the standard epochs immediately following deviant epochs, baseline corrected, and referenced to an average reference. Difference waves were obtained by subtracting the standard from the deviant waveforms.

76 of 124 selected channels were divided into four groups for each hemisphere to represent the average response from frontal (20 channels), central (20 channels), parietal (20 channels), and occipital (16 channels) scalp regions. (See He et al., 2007, for details of the grouping scheme.)Two-tailed paired *t*-tests were calculated at each time point between standard and deviant waveforms to reveal the time periods of significant difference separately for adults and infants at all eight scalp regions (see figures).

For the MMN in adults and the MMN-like negativity in 4-month-olds, the peak latency and absolute amplitude of the MMN-like negativity and the following P3alike positivity were measured in the difference waveforms of each participant. The MMN-like negativity was defined as the largest frontally negative peak between 100 and 300 ms, and the P3a-like positivity as the largest frontally positive peak between 200 and 400 ms. When a peak could not be measured, it was treated as missing data. Separate ANOVAs were calculated on peak latencies and amplitudes for the MMN-like negativity and the P3a-like positivity in order to examine whether they varied significantly across hemisphere and scalp region. For the broad discriminative slow wave mismatch responses in 2- and 4-month-olds, slow wave deflections rendered peak picking difficult, so the absolute average amplitudes of the difference wave (deviant-standard) in successive 50-ms time bins between 0 and 400 ms after stimulus onset were measured for each scalp region. Repeated-measures ANOVAs were performed to test whether the slow discriminative positivity varied significantly across presentation rate, magnitude of pitch change, time bin, hemisphere, and scalp region.

In all of the above ANOVAs, the Greenhouse-Geisser correction was applied to all within-subjects measures with more than two levels. The Tukey HSD test was used for post hoc comparisons. The Bonferroni correction was used for multiple within-subject comparisons.

3. Results

3.1. Effect of presentation rate

Infant mismatch responses and adult MMN in slow (800 ms SOA) and fast (400 ms) stimulus conditions with the small magnitude of



Fig. 1. The effect of presentation rate on adult mismatch responses. Difference waves (deviant–standard) show an MMN around 130 ms followed by an early P3a around 250 ms, with earlier MMN peaks for the slow compared to fast rate, but similar peak amplitudes. Portions of the waveforms where MMN and P3a are significant are shown in the bars above and below these components, respectively.

pitch change were compared in order to investigate the influence of presentation rate on infant mismatch responses at different stages of maturation. Figs. 1–3 show the difference waves of 2-montholds, 4-month-olds, and adults in the slow and fast conditions. Adults showed MMN to the pitch changes in both fast and slow presentation rate conditions (Fig. 1), with earlier responses to the slow rate. For infants, clear differences in amplitude between fast and slow presentation rates can be observed in the slow discriminative positive mismatch responses of both 2- and 4-month-olds (Fig. 2) under the 0.5–3 Hz band-pass filter. As for the MMN-like negative mismatch responses in infants (Fig. 3), under 3–20 Hz band-pass filter 2-month-olds showed only hints of a negative response at both presentation rates. However, 4-month-olds displayed a response



Fig. 2. The effect of presentation rate on the infant broad discriminative positive mismatch responses. Difference waves (deviant-standard) illustrate that both 2- and 4-month-olds showed a broad discriminative positivity centered around 300 ms, with larger peak amplitude for the fast than slow presentation rate. Portions of the waveforms where the discriminative positivity is significant are shown in the bars above and below the waveforms.

pattern that parallels the adult MMN, with earlier peaks for the slower presentation rate. Statistical analyses were conducted to compare fast and slow presentations rates at each age.

3.1.1. The discriminative positive slow wave (0.5–3 Hz band-pass filtered)

Adults showed no evidence of slow wave activity, but standard and deviant waves in both 2- and 4-month-olds showed a prominent slow wave with similar topography (anterior positivity and posterior negativity; Fig. 4). However, the positivity was larger for deviants than standards. The differences between the two resulted in a broad discriminative positivity. To compare the broad discriminative positivity between the fast and slow conditions the absolute averaged amplitude of the difference waves in each successive 50 ms time bin from 0 to 400 ms was calculated and then subjected to a repeated-measures ANOVA, with presentation rate and age as between-subjects factors and time bin (8 bins in total), brain region (frontal, central, parietal, occipital), and hemisphere (left, right) as within-subject factors. The main effect of presentation rate was significant ($F_{(1,63)} = 6.78$, p = 0.01, η^2 = 0.097), with larger amplitude in the fast (1.12 ± 0.049 µV; S.E. are reported with all means) than in the slow (0.93 \pm 0.053 $\mu V)$ condition. The presentation rate by time bin interaction was significant, $F_{(7,441)} = 2.82$, p = 0.03, $\eta^2 = 0.043$, indicating that the amplitudes in the fast condition were particularly stronger than in the slow condition at certain time periods. Post hoc comparisons found significant differences between 150–200 ms (*p* = 0.01), 250–300 ms (*p* = 0.02), 300-350 ms (p=0.02), and 350-400 ms (p=0.001). Not surprisingly, the main effect of time bin was also significant, $F_{(7,441)}$ = 39.40, p < 0.001, $\eta^2 = 0.385$, reflecting a stronger amplitude between 150 and 400 ms than between 0 and 150 ms (all ps < .05), indicating the presence of the broad discriminative positivity between 150 and 400 ms. Although the main effect of age was not significant, the time bin by age interaction was, $F_{(7,441)} = 3.77$, p = 0.008, $\eta^2 = 0.056$, with larger absolute amplitude in 2-month-olds than in 4-montholds only between 150 and 200 ms (p = 0.05). This result can be



Fig. 3. The effect of presentation rate on infant MMN-like mismatch responses. For 4-month-olds, difference waves (deviant-standard) show an adult-like MMN centered around 200 ms followed by a P3a-like positivity around 300 ms, with earlier peaks for the slow compared to fast presentation rate, but no clear difference in peak amplitude. For 2-month-olds, there were trends for a similar MMN-like response pattern as in 4-month-olds, but only the P3a-like component achieved significance, and in only a few regions. Portions of the waveforms where MMN and P3a are significant are shown in the bars above and below these components, respectively.

seen in Fig. 2 in the delayed slow positive wave in 4-month-olds in comparison to 2-month-olds, which was possibly due to left over unfiltered fast MMN-like activity. The main effect of region achieved significance ($F_{3,189} = 4.90$, p = 0.004, $\eta^2 = 0.072$) with larger amplitudes (p = .02) at occipital ($1.14 \pm 0.054 \mu$ V) region than at parietal regions ($0.943 \pm 0.051 \mu$ V), consistent with previous studies (He et al., 2007).

A larger discriminative positivity for fast compared to slow presentation rates was not expected. To examine this effect further, the standard and deviant waves in infants (as shown in Fig. 4) were analyzed by conducting an five-way ANOVA analysis on the absolute mean peak amplitude between standard and deviant waves among the time bins where the slow wave was present (150–400 ms). The between-subject factors were presentation rate and age and the within-subject factors were stimulus type (deviant, standard), scalp region, and hemisphere. The ANOVA showed a significant main effect of stimulus type ($F_{(163)}$ =51.60, p < 0.001, η^2 = 0.45), with a larger absolute mean amplitude in the deviant $(1.48\pm0.063\,\mu V)$ than in the standard $(0.84 \pm 0.062 \,\mu\text{V})$ waves, which again confirmed that the broad positive mismatch response in the difference waves was significant. The main effect of presentation rate was also significant, $F_{(1,63)}$ = 41.80, p < 0.001, η^2 = 0.40, indicating a larger amplitude in the slow $(1.45\pm0.064\,\mu\text{V})$ than in the fast $(0.89\pm059\,\mu V)$ condition. A stimulus type by presentation rate interaction was significant as well ($F_{(1,63)} = 7.48, p = 0.008, \eta^2 = 0.11$), further indicating that, although both deviant and standard waves have smaller amplitude in the fast presentation rate condition than in the slow presentation rate condition, the amplitude difference between the two conditions in the standard waves (0.81 µV, p < 0.001) is much larger than the difference between the two conditions in the deviant waves ($0.32 \mu V$, p = 0.01). The comparison of the mean amplitude between the slow and fast presentation rate conditions is shown in Fig. 5. Because the larger responses in the slow compared to the fast condition were much larger for standards than



Fig. 4. Standard and deviant waves at fast and slow presentation rates for 2- and 4-month-olds. There is a trend for the slow wave to be larger in amplitude for slow compared to fast presentations rates for both standard and deviant waves, but this trend is larger and only reaches significance for standard waves.

for deviants, the standard rather than deviant waves contribute most to the difference waves, resulting in the larger discriminative positivity for the fast compared to the slow presentation rate. Other significant effects were age ($F_{(1,63)} = 38.50$, p < 0.001, $\eta^2 = 0.237$),

with a larger mean amplitude in 4-month-olds $(1.36 \pm 0.065 \,\mu\text{V})$ than in 2-month-olds $(0.97 \pm 0.058 \,\mu\text{V})$, and a main effect of region $(F_{(3,189)} = 16.7, \, p < 0.001, \, \eta^2 = 0.21)$. The effect of region was similar as in the analyses of the difference waves, above.



Fig. 5. The mean amplitude of the slow positive wave in deviants and standards for fast and slow presentation rates in 2- and 4-month-olds infants. With increases in presentation rate, standards decrease in amplitude much more than do deviants. As standards are more frequent, and therefore closer in time on average compared to deviants, these results are consistent with the interpretation that the slow positive wave is subject to refractory processes.

In sum, the slow wave response in standards decreased with increased presentation rate, consistent with a refractory or inhibitory process. There was less decrement with deviants, which were more spread out in time at both the fast and slow presentation rate because they occur relatively rarely.

3.1.2. The adult MMN-like negativity

3.1.2.1. 2-Month-olds. Although there were hints of the MMN-like negativity in the difference wave for 2-month-olds, no significant response peaks were found between deviant and standard waves by pair-wise *t*-test (indicated by significance bars in Fig. 3) at either the slow or fast presentation rates. This result is consistent with a previous study by He et al. (2007) using a similar paradigm and stimulus, which indicates that the adult MMN-like negativity is only beginning to emerge at this age. A P3a-like component was also marginally present, with short regions of significance at a couple of regions.

3.1.2.2. 4-Month-olds. Because both an MMN-like negativity and a P3a-like positivity were prominent in the difference waves of 4-month-olds, separate analyses were conducted to compare the latency and amplitude differences between the fast and the slow conditions for each peak.

For the MMN-like negativity, the peak latencies were measured from each infant and subjected to an ANOVA with presentation rate as a between-subjects factor and hemisphere and scalp region as within-subject factors. The main effect of presentation rate was significant, $F_{(1,28)} = 7.60$, p = 0.01, $\eta^2 = 0.21$, reflecting earlier peak latency for the slow ($221 \pm 3 \text{ ms}$) than for the fast ($232 \pm 3 \text{ ms}$) presentation rates. The peak amplitude of the MMN-like negativity was subjected to an ANOVA with the identical factors as for the latency analysis, above. No significant main effect or interactions involving presentation rate were found. The only significant effect was region, $F_{(3,84)} = 10.05$, p < 0.001, $\eta^2 = 0.264$, with amplitudes at frontal sites ($1.08 \pm 0.11 \mu$ V) greater than at occipital sites ($1.05 \pm 0.099 \mu$ V), which were greater than at central sites ($0.89 \pm 0.074 \mu$ V), which were greater than at parietal sites ($0.74 \pm 0.064 \mu$ V).

The results for the P3a-like positivity echoed those of the MMN-like negativity. For latency, there was a significant main effect of presentation rate, $F_{(1,28)} = 6.00$, p = 0.02, $\eta^2 = 0.18$, with earlier peaks in the slow $(320 \pm 3 \text{ ms})$ than in the fast $(329 \pm 3 \text{ ms})$ condition. For amplitude, only the region effect was significant, $F_{(3,84)} = 9.45$, p < 0.001, $\eta^2 = 0.25$, with amplitudes at occipital sites

 $(1.10 \pm 0.12 \,\mu\text{V})$ greater than at frontal sites $(0.96 \pm 0.11 \,\mu\text{V})$, which were greater than at central sites $(0.81 \pm 0.081 \,\mu\text{V})$, which were greater than at parietal sites $(0.73 \pm 0.074 \,\mu\text{V})$.

In sum, the presentation rate did not affect the peak amplitude of either the MMN-like negativity or the P3a-like positivity, but latencies were earlier for the slow compared to the fast presentation rate for both peaks.

3.1.2.3. Adults. MMN and P3a components in adults were analyzed in the same way as in 4-month-olds. For the MMN, the ANOVA on latency found a significant effect of presentation rate, $F_{(1,14)} = 5.14$, p = 0.04, with earlier peaks in the slow $(111 \pm 6 \text{ ms})$ than in the fast $(130 \pm 6 \text{ ms})$ condition. The ANOVA on amplitude found only a significant effect of region, $F_{(3,42)} = 9.45$, p < 0.001, with amplitudes at occipital sites $(0.76 \pm 0.051 \,\mu\text{V})$ greater than at frontal sites $(0.70 \pm 0.049 \,\mu\text{V})$, which were greater than at central sites $(0.68 \pm 0.045 \,\mu\text{V})$, which were greater than at parietal sites $(0.49 \pm 0.032 \,\mu\text{V})$.

The ANOVA on peak P3a latency showed no significant main effects or interactions. For P3a amplitude the only significant main effect was region $F_{(3,42)} = 64.50$, p < 0.001, with the amplitudes at occipital sites $(0.95 \pm 0.037 \,\mu\text{V})$ greater that at central sites $(0.85 \pm 0.041 \,\mu\text{V})$, which were greater than at frontal sites $(0.74 \pm 0.032 \,\mu\text{V})$, which were greater than at parietal sites $(0.46 \pm 0.031 \,\mu\text{V})$.

In sum, for adults, the presentation rate had no effect on MMN or P3a amplitude. However, MMN (although not P3a) was significantly later for the fast compared to the slow presentation rate. The latencies of MMN in adults were about 100 ms earlier than latencies of MMN-like negativity in 4-month-olds.

3.2. Effect of magnitude of pitch change

Difference waves for small (6% of f_0) and large (33% of f_0) pitch change conditions from 2-month-olds, 4-month-olds, and adults are shown in Figs. 6–8. Adults showed an increased MMN for large compared to small pitch changes (Fig. 6). Under the 0.5–3 Hz bandpass filters (Fig. 7) a discriminative slow wave for both magnitudes of pitch change can be seen for 2- and 4-month-olds, but discriminative slow waves were similar in amplitude for both small and large pitch changes. Under the 3–20 Hz band-pass filter (Fig. 8), 4month-olds showed clear MMN and P3a responses, again parallel with adult MMN, while 2-month-olds showed hints of a MMN-like response. ANOVAs were conducted with the same factors as those in the analyses of presentation rate, above.

3.2.1. The discriminative positive slow wave (0.5–3 Hz band-pass filtered)

Adults showed no evidence of slow wave activity. For 2- and 4-month-olds, the ANOVA on the amplitude of the discriminative positivity between small and large pitch change conditions revealed no significant main effect of age, no significant main effect of the magnitude of pitch change and no significant interaction between magnitude of pitch change and time bin. The only significant factors were time bin $(F_{(7,378)} = 32.5, p < 0.001,$ η^2 = 0.40), with larger amplitudes between 150 and 400 ms than between 0 and 150 ms (all ps < .05), indicating that the slow wave occurred between 150 and 400 ms, time bin by age interaction $(F_{(7.378)} = 3.924, p = 0.01, \eta^2 = 0.069)$, indicating that the slow wave started later for 4-month-olds as with the analyses of presentation rate above, and region ($F_{3.162} = 4.21$, p = 0.01, $\eta^2 = 0.075$), again with similar details as for the analyses of presentation rate. Thus, both age groups showed a discriminative positive slow wave, but it was not affected by the magnitude of the pitch change.



Fig. 6. The effect of magnitude of pitch change on adult mismatch responses. Difference waves (deviant-standard) show clear MMN and P3a components. The MMN was larger for the large pitch change compared to the small pitch change, with no significant difference in latency. Portions of the waveforms where MMN and P3a are significant are shown in the bars above and below these components, respectively.

These results indicate that there was no evidence that the magnitude of pitch change affected this discrimination process.

3.2.2. The adult MMN-like negativity

3.2.2.1. 2-Month-olds. The 2-month-olds showed hints of an MMNlike response pattern with the 3–20 Hz filter, with two of eight regions showing short periods of significance (Fig. 8). There were also hints of a P3a-like response, with short periods of significance at two of eight regions.

3.2.2.2. 4-Month-olds. The ANOVA on the latency of the MMN-like negativity revealed a significant main effect of magnitude of pitch

change, $F_{(1,27)} = 25.82$, p < 0.001, $\eta^2 = 0.49$, with an earlier latency for the large (199 ± 3 ms) than for the small (221 ± 3 ms) pitch difference. The main effect of region was also significant, $F_{(3,81)} = 5.83$, p = 0.002, $\eta^2 = 0.18$, with a later latency in parietal (216 ± 2 ms) than in frontal (206 ± 2 ms, p = 0.02) and central (205 ± .003 ms, p = 0.008) regions. The ANOVA on MMN-like amplitude only found a significant main effect of region, $F_{(3,81)} = 7.67$, p < 0.001, $\eta^2 = 0.22$, with amplitudes at frontal sites ($1.22 \pm 0.099 \,\mu$ V) greater than at occipital sites ($1.16 \pm 0.12 \,\mu$ V), which were greater than at central sites ($1.073 \pm 0.088 \,\mu$ V), which were greater than at parietal sites ($0.87 \pm 0.083 \,\mu$ V). The main effect of magnitude of pitch change was not significant, but there was a trend for larger peak amplitude with the larger ($1.22 \pm 0.12 \,\mu$ V) than with the smaller ($0.95 \pm 0.12 \,\mu$ V) pitch change, $F_{(1,27)} = 2.63$, p = 0.12, $\eta^2 = 0.089$.

Analyses of the P3a-like positivity echoed the above results of the MMN-like negativity. The ANOVA on latency showed a significant main effect of presentation rate, $F_{(1,27)} = 25.30$, p < 0.001, $\eta^2 = 0.49$, with much earlier peak latency for the large $(294\pm4\,ms)$ than for the small $(321\pm4\,ms)$ pitch differences. The main effect of region was also significant, $F_{(3,81)} = 4.51$, p = 0.01, $\eta^2 = 0.13$, with a trend for later latency in parietal $(313 \pm 3 \text{ ms})$ than in frontal $(304 \pm 3 \text{ ms}, p = 0.02)$ and central $(303 \pm .003 \text{ ms})$ regions. The ANOVA on amplitude found a significant main effect of magnitude of pitch change, $F_{(1,27)} = 5.35$, p = 0.03, $\eta^2 = 0.17$, reflecting larger peak amplitude for the large $(1.29 \pm 0.13 \,\mu\text{V})$ than for the small $(0.87 \pm 0.13 \,\mu\text{V})$ pitch changes. The main effect of region was also significant ($F_{(3,81)} = 4.48$, p = 0.02), with amplitudes at occipital sites $(1.24 \pm 0.11 \,\mu\text{V})$ greater than at frontal sites $(1.09 \pm 0.12 \,\mu\text{V})$, which were greater than at central sites $(1.06 \pm 0.10 \,\mu\text{V})$, which were greater than at parietal $(0.94 \pm 0.071 \,\mu V)$ sites.

In sum, the above analyses showed that, for 4-month-olds, the larger pitch change led to larger peak amplitudes and earlier peak latencies for both the MMN-like negativity and the P3a-like positivity.

3.2.2.3. Adults. The ANOVA on MMN latency found no significant main effects or interactions. The ANOVA on MMN amplitude found a significant effect of magnitude of pitch change, $F_{(1,13)}$ = 36.58, p < 0.001, $\eta^2 = 0.74$, with larger peaks for the large ($0.86 \pm 0.019 \mu$ V) than for the small ($0.70 \pm 0.018 \mu$ V) pitch changes. The main effect of region was also significant ($F_{(3,39)}$ = 17.13, p < 0.001, η^2 = 0.57), with larger amplitudes at occipital sites ($0.87 \pm 0.031 \mu$ V) than at frontal sites ($0.83 \pm 0.022 \mu$ V), which were larger than at central sites ($0.76 \pm 0.019 \mu$ V), which were larger than at parietal sites ($0.66 \pm 0.021 \mu$ V).

The ANOVA on peak P3a latency showed no significant main effects or interactions. For P3a amplitude, the main effect of magnitude of pitch change was significant, $F_{(1,13)} = 5.34$, p = 0.04, η^2 = 0.29, with smaller amplitude for the large (0.62 ± 0.035 µV) than for the small $(0.73 \pm 0.032 \,\mu\text{V})$ pitch changes. The main effect of region was also significant, $(F_{(3,39)} = 60.99, p < 0.001, \eta^2 = 0.82)$, with amplitudes at occipital sites $(0.87\pm0.035\,\mu V)$ greater than at central sites ($0.75 \pm 0.035 \,\mu$ V), which were greater than at frontal sites $(0.64 \pm 0.019 \,\mu\text{V})$, which were greater than at parietal sites $(0.45 \pm 0.031 \,\mu\text{V})$. P3a amplitude was actually smaller for the large pitch changes. However, the literature suggests that the P3a following the MMN is normally parallel to the MMN, with peak amplitudes correlating to the magnitude of stimulus change (Gaeta et al., 2001). One possibility is that the P3a result in the above analysis occurred because the strong MMN we observed partially overlapped the P3a component, decreasing its apparent amplitude. Indeed, a reanalysis with either Cz or the average of the mastoids as the reference showed no significant difference in P3a amplitude between the



Fig. 7. The effect of magnitude of pitch change on the infant broad discriminative positive mismatch responses. Difference waves (deviant-standard) illustrate that both 2and 4-month-olds show a broad discriminative positivity centered around 300 ms for both large and small pitch changes. There was no significant difference in the broad discriminative positivity between large and small pitch changes in either 2- or 4-month-olds. Portions of the waveforms where the discriminative positivity is significant are shown in the bars above and below the waveforms.

small and large pitch changes. To get around this, instead of measuring the absolute peak voltage from baseline, we measured the amplitude of the MMN-P3a complex from the peak of the MMN to the peak of the P3a, and then carried out the same ANOVA as above. In this case, the MMN-P3a complex amplitude was significantly larger in the large (mean = $1.22 \pm 0.036 \,\mu$ V) than in the small (mean = $0.97 \pm 0.026 \,\mu$ V, *p* = 0.04) pitch change condition. Thus, we conclude that the magnitude of the MMN-P3a complex actually changed similarly to that of the MMN, and in the same manner as with 4-month-olds.

In sum, the amplitudes of MMN and the P3a (as measured in the MMN-P3a complex analysis) in adults were sensitive to the magnitude of pitch change, with larger amplitude for the large than for small pitch change. These results for amplitude parallel those of 4-month-olds. Unlike 4-month-olds, however, the magnitude of pitch change did not affect the latency of these peaks in adults.

4. Discussion

The present study investigated how stimulus presentation rate and magnitude of pitch change influence the two types of infant mismatch responses. We found that the MMN/P3a components in adults and the MMN/P3a-like mismatch responses in 4-montholds showed very similar patterns of change across conditions, suggesting that the mismatch responses in 4-month-olds have similar functional characteristics as the adult MMN responses. The broad discriminative positivity in the infants at 2 and 4 months of age, on the other hand, showed a different response pattern across conditions, suggesting that the slow positivity reflects different underlying neuromechanisms than the mismatch responses in older infants and adults.

In adults, the effects of presentation rate and magnitude of stimulus change on the MMN and P3a responses were consistent with the literature. MMN and P3a remained robust in amplitude with fast



Fig. 8. The effect of magnitude of pitch change on infant MMN-like mismatch responses. Only a few regions in 2-month-olds showed a significant MMN-like response. For 4-month-olds, difference waves (deviant-standard) illustrate that the MMN-like negativity shows a larger amplitude for larger than for smaller pitch changes. Portions of the waveforms where MMN and P3a are significant are shown in the bars above and below these components, respectively.

presentation rates, and MMN latency was later for the faster than for the slower presentation rate (consistent with, e.g., Friedman et al., 2001; Gonsalvez et al., 1999; Roeber et al., 2003; Sabri & Campbell, 2001; Schröger & Winkler, 1995; Trainor, McDonald, & Alain, 2002). The magnitude of stimulus change affected the amplitude of the MMN and P3a such that both were correlated positively with the magnitude of stimulus change (consistent with Katayama & Polich, 1998; Lang et al., 1990; Näätänen & Alho, 1997; Sams et al., 1985).

In 4-month-olds, the presentation rate had no effect on the amplitude of MMN or P3a, but MMN and P3a were later at the faster presentation rate. This response pattern is very similar to that of adults, and suggests that the MMN-like component seen in 4-month-olds likely represents change-detection processes, as in adults, rather than refractory or habituation processes, because a decrease in amplitude would be expected with increased presentation rate in the latter case. As far as the magnitude of pitch change, MMN and P3a were larger and earlier for the larger pitch change, as in adults. However, adults did not show earlier peaks for

larger pitch change. This may be because the smaller pitch change is approaching behavioural thresholds of infants at 4 months of age (Olsho, Schoon, Sakai, Turpin, & Sperduto, 1982), but this pitch change is well above adults' thresholds. That the MMN and P3a responses in infants remain robust for a pitch change near threshold is once again consistent with the MMN representing an adult-like change-detection process.

The broad discriminative positivity seen in 2- and 4-month-olds behaved differently than the MMN/P3a components seen in 4month-olds and adults. Although the slow wave appeared to begin slightly later in 4-month-olds than in 2-month-olds, likely due to the presence of overlapping MMN-like activity in older infants, the effects of presentation rate and magnitude of pitch change were similar at both ages. The amplitude of the broad discriminative positivity was not affected by the magnitude of pitch change. For presentation rate, the amplitudes of the deviant waves were similar across fast and slow presentation rates, but the standard waves decreased substantially in amplitude with the faster compared to slower presentation rate. This is consistent with refractory processes, as suggested by Čeponiené et al. (2002), Trainor et al. (2003), and Trainor (2007), according to the following argument. At the fast presentation rate, the standard stimuli are sufficiently close in time that the neural circuit encoding the pitch in 2- and 4-month-olds is unable to fully recover between presentations of the standard stimulus, leading to reduced amplitude of the slow wave response. The deviant stimuli, on the other hand, occur more rarely, and are thus relatively far apart in time, even at the fast presentation rate, so less refractory reduction in amplitude is seen. This suggests that the standards and deviants had somewhat different generators as a result of their different spectral makeup, although we did not have sufficient resolution to see significant differences between them in our analyses of region.

Despite the functional and morphological similarities between the mismatch responses of 4-month-olds and adults, it is still possible that the underlying neuromechanisms might be different. In adults, the MMN appears to be generated in the deeper layers of auditory cortex (for a review, see Näätänen & Alho, 1997; Picton et al., 2000). However, the deeper layers of auditory cortex are still largely immature in terms of functional neural connections at the age of 4 months. (Moore & Guan, 2001). In fact, it has been suggested that the frontal and temporal components of the MMN have different maturational time-courses, with the temporal component still being immature in 5-year-olds (Gomot, Giard, Roux, Barthelemy, & Bruneau, 2000). As for the broad discriminative positivity in 2-month-olds, it remains for future research to determine the neural circuits that give rise to the slow positive responses. What is clear from the present results is that a cortical change-detection mechanism for pitch discrimination emerges around 3-4 months of age.

5. Conclusion

The present study investigated how the two types of infant mismatch response are affected by the presentation rate and the magnitude of pitch change. The MMN-like and P3a-like responses in 4-month-olds behaved similarly to the adult MMN and P3a, suggesting that the mismatch responses at 4 months reflect a change-detection mechanism, as in adults. The broad discriminative positivity in 2-month-olds, on the other hand, showed a different pattern. We conclude that cortical maturation between 2 and 4 months allows for the emergence of an adult-like change-detection mechanism for pitch.

Acknowledgements

This research was funded by a grant to LJT from the Canadian Institutes for Health Research. We thank Andrea Unrau for help in testing the infants.

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