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**Processing acoustic change and novelty in newborn infants**

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## **Abstract**

Research on event-related potential (ERP) correlates of auditory deviance-detection in newborns provided inconsistent results: temporal and topographic ERP characteristics differed widely across studies and individual infants. Robust and reliable ERPs responses were, however, obtained to sounds (termed ‘novel’ sounds) which cover a wide range of frequencies and widely differ from the context provided by a repeating sound (Kushnerenko et al., 2002, NeuroReport, 13, 1843-1848). The question we investigated here is whether this effect can be attributed to novelty *per se* or to acoustic characteristics of the ‘novel’ sounds, such as their wide frequency spectrum and high signal energy compared with the repeated tones. We also asked how sensitivity to these stimulus aspects changes with development. Twelve newborns and 11 adults were tested in four different oddball conditions, each including a ‘standard’ sound presented with the probability of 0.8 and two types of infrequent “deviant” sounds (0.1 probability, each). Deviants were a) ‘novel’ sounds (diverse environmental noises), b) white-noise segments, or harmonic tones of c) a higher pitch, or d) higher intensity. In newborns, white-noise deviants elicited the largest response in all latency ranges, whereas in adults, this phenomenon was not found. Thus, newborns appear to be especially sensitive to sounds having a wide frequency spectrum. On the other hand, the pattern of results found for the late discriminative ERP response indicates that newborns may also be able to detect novelty in acoustic stimulation, although with a longer latency than adults, as shown by the ERP response. Results are discussed in terms of developmental refinement of the initially broadly tuned neonate auditory system.

## Introduction

Auditory cortical responses to acoustic change may serve as early risk markers for language and cognitive development in children (Goswami, 2005). Change-related cortical responses are usually studied by recording event-related potentials (ERPs) in the auditory ‘oddball’ paradigm, in which a repetitive sound (standard) is occasionally exchanged for an acoustically different one (deviant). In adults, deviants elicit a negative component called the mismatch negativity (MMN) peaking at about 150 ms after change onset (Näätänen *et al.*, 1978); for a review, see Picton *et al.*, 2000). MMN is often followed by the P3a response peaking between 250 and 300 ms after change onset (Friedman *et al.*, 2001). In infants, the change-related ERP responses showed low consistency across studies, and the polarity of response was reported to be either negative (Alho *et al.*, 1990; Kurtzberg *et al.*, 1995; Leppänen *et al.*, 1997; Cheour *et al.*, 1998; Čeponienė *et al.*, 2002; Cheour *et al.*, 2002; Kushnerenko *et al.*, 2002; Morr *et al.*, 2002, Trainor *et al.*, 2003) or positive (Dehaene-Lambertz & Dehaene, 1994; Dehaene-Lambertz & Pena, 2001; Friederici *et al.*, 2002; Trainor *et al.*, 2003; Winkler *et al.*, 2003; Ruusuvirta *et al.*, 2004; Carral *et al.*, 2005), for reviews, see Kushnerenko, 2003; Leppänen *et al.*, 2004; Csibra *et al.*, in press). Moreover, response amplitudes are usually small and display high variability both in waveform and latency between individual infants (Cheour *et al.*, 1998; Kushnerenko *et al.*, 2002). These features of the change detection-related ERP responses in infants pose serious problems for the interpretation of the results as well as hindering possible clinical applications.

elicited in neonates using environmental sounds embedded in a repetitive tone sequence (Kushnerenko *et al.*, 2002). Similar to the responses in adults, neonate ERPs were characterized by an early negative, a medium-latency positive, and a later negative wave. Environmental sounds are commonly used as deviants amongst repetitive tonal stimuli in studying involuntary attention switching and ‘novelty’ processing in adults (Escera *et al.*, 2000). These environmental sounds are termed ‘novel’ sounds in ERP research, because, within the context of a repeating tone they represent qualitative (categorical) change; also they are usually presented only once or twice during the experiment. However, categorical change is not the only feature of such deviants, because they are usually also acoustically widely different from the repeating standard sound. That is, these ‘novel’ sounds typically cover a wider range of frequencies and thus carry more stimulus energy than the frequent tones. Therefore, the brain responses elicited by such ‘novel’ sounds confound the effects of ‘novelty detection’ with those caused by large acoustic change. In the present study, we investigated whether the ERP effects observed in neonates to the above described ‘novel’ deviants can be fully explained by changes in spectral width and loudness or the ERP effects of novelty, defined as a categorical change from an established stimulus context can also be observed under these experimental conditions. Because behavioural studies suggested that unlike adults, infants primarily respond to the ‘energy’ of stimulation (Lewkowicz & Turkewitz, 1980; Turkewitz *et al.*, 1983) we hypothesized that the acoustic characteristics of ‘novel’ sounds will have a larger effect on the pattern of ERP responses in infants than in adults. Therefore, in order to test whether the sensitivity of ERPs ‘quantitative’ contrasts (loudness, spectral change) changes during development we presented similar stimulus conditions to infants and

adult subjects.

In order to disentangle the different effects of environmental sounds on the ERP responses in neonates and adults we compared the ERPs elicited by infrequent environmental sounds embedded in a repetitive tone sequence with those elicited by louder deviants (loudness change) and with ERPs elicited by white noise segments (large spectral change) in the same acoustic context. The effects of spectral change on the ERP components were further assessed by comparing responses elicited by infrequent environmental sounds in three different contexts: among repetitive complex tones, white noise segments, and when presented alone.

## **Materials and methods**

### *Subjects*

Twelve newborn infants (4 female) were investigated at the age 1-4 days. Their gestation age was 38-41 weeks and birth weight 3000-4190 g. All newborns were recruited from the post-delivery wards of the Women's Hospital of the Helsinki University Central Hospital, with the written consent of their parents. The Ethics Committee for Pediatrics, Adolescent Medicine, and Psychiatry (Hospital District of Helsinki and Uusimaa) approved the study protocol. All neonates, declared healthy by a neonatologist, passed a hearing screening using evoked otoacoustic emissions (ILO88 Dpi system from Otodynamics Ltd.). They were tested in a silent room in the Hospital for Children and

Adolescents (HUCH). The mean noise level for the hospital recordings was 35 dB SPL. Newborn infants were sleeping in an infant cot with loudspeakers located at about 20-cm distance on both sides of the infant's head. Responses recorded in quiet and active sleep were averaged together, since no differences between these sleep stages has been revealed previously in newborn ERP research (Hirasawa et al., 2002; Kushnerenko, 2003; Martynova et al., 2003).

Eleven healthy volunteers (5 females; 19 to 24 years of age, the average age 20.8 years) with normal hearing (assessed with audiometry) were recruited for the adult version of the experiment. Written informed consent was obtained from all subjects after the procedures of the study were explained to them. The study was approved by the Review Board of the Institute for Psychology, Budapest. During the experiment, subjects were sitting in a sound-attenuated chamber watching a self-selected silent movie with subtitles. They were instructed to ignore all sounds presented to them through Sennheiser HD-430 headphones.

### *Stimuli*

The duration of the sounds was 100 ms, including 5-ms rise and 5-ms fall times. The inter-stimulus (offset-to-onset) interval was 700 ms. Novel sounds (101 different ones) consisted of clicks, chirps, simulations of bird vocalizations, vowels, and syllables and they appeared only twice in each condition. The intensity of the novel sounds ranged from 57.7 to 81.9 dB sound-pressure level (SPL), with the mean being 68.8 dB SPL. Harmonic tones of 500 and 750 Hz fundamental frequency were constructed from the 3

lowest partials, with the second and third partials having a lower intensity than the first one by 3 and 6 dB, respectively. For newborns, the intensity of the tone and white-noise sounds was 70 dB SPL similarly to our previous studies (Čeponienė *et al.*, 2002; Kushnerenko *et al.*, 2002; Fellman *et al.*, 2004; Ruusuvirta *et al.*, 2004). In order to improve signal to noise ratio, for the adult subjects, these intensity levels were individually adjusted to 60 dB above the hearing threshold level of the 500-Hz harmonic tone. This cannot be done in newborns, because they would be disturbed and awakened by louder sounds. Because of the widespread differences between newborn and adult ERP response patterns, direct comparison between them is not possible. Therefore, this difference between the stimulation for neonates and adults will not affect the conclusions that can be drawn from the results.

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Place Table 1 at about here

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Four different auditory oddball conditions were administered (see Table 1). In all oddball conditions, 80% of the stimuli were identical (standards). Two different types of infrequent sounds (10% probability, each) occurred at random positions of the sequences, with the restriction that these sounds were always followed by at least two standard sounds. This design follows that of many experiments testing the ERP effects of novel sounds (Alho *et al.*, 1998; Escera *et al.*, 2001, Čeponienė *et al.*, 2004). In addition to the oddball conditions, novel sounds were also presented alone (Condition 5) using the same timing as in the Condition 1 oddball sequences but with the standard and

frequency-deviant sounds replaced by silence.

Newborns received 1 block of 800 stimuli for each condition. The experiment lasted about 1 hour. Longer experiments lead to the infant waking up, which usually prevents further recording. In the adult experiment, each condition received 3 blocks of 400 stimuli (ca. 1.5 hours altogether). The order of the stimulus blocks was separately randomized for each subject. More stimuli were presented to adults than to infants to improve the signal to noise ratio, which resulted in slightly higher number of accepted trials for deviant and novel sounds after artifact detection in adults (between 93 and 100) than for infants (and between 76 and to 80). Again, because infant and adult responses will not be directly compared, this difference does not affect the conclusions.

#### *Data acquisition and analysis*

Individual (in newborns, single-use) electrodes were attached to the F3, F4, C3, Cz, C4, P3, and P4 scalp locations (also Fz and Pz for adults; the international 10-20 system) and to the right (RM) and left mastoids (LM), respectively. The common reference electrode was attached to the tip of the nose and the ground electrode to the forehead. Eye movements were monitored with two electrodes, one placed below the right eye, the other lateral to the right outer canthus.

The electroencephalogram (EEG) was recorded (sampling rate 250 Hz; bandpass 0.1-30 Hz for infants, DC-40 Hz for adults) using NeuroScan Synamp amplifiers. The signals were filtered off-line with a bandpass of 1.0-15 Hz (1.0-16 Hz for adults). Epochs of 900

ms duration, including 100-ms pre-stimulus interval, were extracted for each stimulus and separately averaged for the different conditions and stimulus types. In newborns, standard-stimulus responses were estimated by the average response elicited by standards immediately preceding a deviant or a novel sound. Further, the first three epochs of each block and those exceeding 150  $\mu$ V at any signal channel were excluded from averaging. In adults, standards were represented by the average response to all standards except for the two tones immediately following each deviant and novel sound. Because it has been shown that estimating the standard-stimulus responses in the above-described ways does not affect the results (Csépe et al., 1992), no group difference can be expected to result from this analysis difference. Epochs within which the signal difference exceeded 10  $\mu$ V between any two temporally adjacent sampling points and those with the signal range exceeding 75  $\mu$ V during the epoch were excluded from averaging.

Amplitude measurements were averaged separately for the three major observable ERP waves and referred to the average voltage in the 100-ms long pre-stimulus baseline. Time windows for amplitude measurement were selected on the basis of the grand averaged waveforms for the regions of interest. Since the ERP peaks were generally wider in infants, 100-ms long measurement windows were used in newborns as opposed to the 50-ms long windows used in adults. Measurements were then analyzed with two-way repeated-measures ANOVAs [Stimulus type (Standard vs. Infrequent 1 vs. Infrequent 2)  $\times$  Electrode (F3 vs. F4 vs. C3 vs. Cz vs. C4)], separately for each time interval. ANOVA comparisons across the conditions had the structure of Condition  $\times$  Electrode. Tukey HSD post-hoc tests were conducted to specify the significant effects. Huyn-Feldt

correction of the degrees of freedom was applied where appropriate. All significant effects are discussed.

## **Results**

ERP responses are separately described for each stimulus condition (see Table 1), focusing on the components elicited only by the infrequent sounds as compared with the response elicited by the frequently presented sound. This is followed by comparisons across the conditions and a description of the inter-individual variance in newborns.

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Place Figure 1 at about here

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Although, in general, the morphology of neonate ERP responses substantially differs from that observed in adults, the overall structure of the neonate ERP response to novel sounds is amazingly similar to that found in adults (compare panels A and E on Figure 1): novel sounds elicit an early negative response, followed by a large positive wave and by a late negativity.

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Place Table 2 at about here

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*Condition 1.* In this condition, the repetitive sequence of a harmonic tone (standard) was occasionally broken either by a similar tone of higher frequency (deviant), or by an environmental (novel) sound (Table 1, 1<sup>st</sup> line). In newborns, standard tones only elicited a wide positive deflection between ca. 100 and 400 ms from stimulus onset. ERP responses to novel sounds showed three main components (see Figure 1A and Table 2): an early negativity (significantly different from the standard-stimulus response; for the ANOVA Stimulus-type main effect, see Table 2; Tukey HSD post-hoc comparison was significant at  $p < .05$ ), a central positivity, and a late negativity, both with higher amplitudes than those for standards or deviants (all comparisons significant by at least  $p < .05$ ). Frequency deviants only elicited a significant central positivity ( $p < .05$  compared with the standard-stimulus responses). In the adults, the response to standard tones showed a more detailed component structure than that in newborns (Figure 1E). The early negativity showed an approximately equal amplitude for deviants and novels, both having a higher amplitude than that elicited by the standard stimulus ( $p < .001$ , each). Only the novel sounds elicited a central positivity that significantly differed from the standard-stimulus response ( $p < .01$ ). This was followed by a late negativity with a centrally (Cz) higher amplitude than that for deviants and standards (Stimulus-type  $\times$  Electrode interaction:  $F(8,80)=3.07$ ,  $p < .01$ ).

*Condition 2.* In this condition, the repetitive sequence of a harmonic tone was occasionally broken either by a similar tone of higher frequency (frequency deviant) or by one of higher intensity (intensity deviant; Table 1, 2<sup>nd</sup> line). In newborns, intensity deviants elicited a central positivity, which was of a higher amplitude than that elicited by either frequency deviants or standards ( $p < .001$ , each; Figure 1B, Table 2). In adults,

lower-amplitude early negativities were elicited by intensity than by frequency deviants ( $p < .01$ ; Figure 1F, Table 2). In contrast to newborns, in adults, intensity deviants did not elicit a significant central positivity, but rather an early and wide second negative wave, which was higher in amplitude than either the standard or the frequency-deviant response ( $p < .001$ , each). In both groups of subjects, frequency deviants elicited a response, which was not significantly different from that found in the Condition 1.

*Condition 3.* In this condition, the repetitive sequence of a harmonic tone was occasionally broken either by a white-noise segment (white-noise deviant), or by an environmental (novel) sound (Table 1, 3<sup>rd</sup> line). In newborns, novel sounds elicited a significant central positivity and a late negativity ( $p < .01$ , for each comparison with the standard-stimulus response). White-noise deviants elicited a similar response pattern as that found for novel sound, however with higher amplitudes for all three components (at least  $p < .01$ , for all three comparisons; Figure 1C, Table 2). In contrast, in adults, white-noise deviants elicited a lower-amplitude early negativity ( $p < .05$ ) and a higher-amplitude central positivity compared with the response elicited by novel sounds ( $p < .01$ ; Figure 1G, Table 2). Novel sounds elicited a higher-amplitude early negativity, a central positivity and a central late negativity compared with the response to standards ( $p < .01$ , for the early negativity and central positivity; for the late negativity, Stimulus-type  $\times$  Electrode interaction:  $F(8,80)=3.07$ ,  $p < .01$ ).

*Condition 4.* In this condition, the repetitive sequence of a white-noise segment (white-noise standard) was occasionally broken either by a harmonic tone (tone deviant), or by an environmental (novel) sound (Table 1, 4<sup>th</sup> line). In newborns, no significant difference was found between the responses elicited by the white-noise standards and

novels in any of the latency ranges, whereas frequency deviants did not elicit the central positive response and thus significantly differed from the standard response ( $p < .05$ ; Figure 1D, Table 2). In adults, both novels and frequency deviants elicited significant early negative responses (compared with that elicited by white-noise standards;  $p < .001$ , each) and further, the late negativity was of centrally (Cz) higher amplitude in response to novels than to standards or deviants (Stimulus-type  $\times$  Electrode interaction:  $F(8,80)=6.72$ ,  $p < .001$ ; Figure 1H).

*Comparisons across conditions.* Two types of comparisons were made between ERPs elicited by rare stimuli: 1) between ERPs elicited by different sounds delivered within the same sound-sequence context, testing the effects of stimulus quality and 2) between ERPs elicited by novel sounds in different sequence contexts, testing the effect of the acoustic context on the processing of the novel sounds.

Comparing the responses to intensity deviants (Condition 2) with those elicited by novels in the same context (Condition 1), in newborns, novels elicited a higher-amplitude early negativity than the intensity deviants (Condition effect:  $F(1,11)=7.68$ ;  $p < .05$ ). In adults, novels elicited a higher-amplitude central positivity than the intensity deviants ( $F(1,10)=10.95$ ;  $p < .01$ ).

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Place Figures 2 a and b at about here  
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Figures 2a and 2b compare the ERPs elicited by novel sounds across the different experimental conditions (Condition 1, Condition 3, Condition 4, and Condition 5). In newborns, the early negativity was largest in the Condition 1, although this effect was only marginally significant ( $F(3,33)= 2.72$ ;  $p<.06$ , Figure 2a). The amplitude of the central positivity was significantly lower in the Condition 4 than in the Condition 1 ( $F(3,33)=4.30$ ;  $p<.05$ ), whereas the amplitude of the late negativity was significantly higher in the Condition 1 and Condition 3 than in the other two conditions ( $F(3,33)=6.06$ ;  $p<.01$ ). In adults (Figure 2b), novels presented alone elicited the highest-amplitude early negative and central positive responses (Condition  $\times$  Electrode interaction:  $F(12,120)=19.26$  and  $13.20$ ,  $p<.001$ , each), with the latter having a lower amplitude in the Condition 4 than in any other condition ( $p<.01$ ).

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Place Figure 3 at about here  
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*Individual responses.* Figure 3 shows the individual variability of the ERPs recorded in newborn babies. In contrast to the usually substantial variability of newborn ERPs, responses to white-noise deviants showed a high degree of morphological similarity across the infants. Responses to ‘novels’ too, were rather consistent, but those elicited by frequency deviants showed considerable variability: The responses obtained in some infants mainly disclosed a single positive response, whereas in other infants, early and the late negative peaks can also be discerned. It is important to note that there were no

differences in number of accepted responses between frequency and white-noise deviants or ‘novels’.

## **Discussion**

‘Novel’ (environmental) sounds embedded in the repetitive sequence of a simple tone are commonly used to study the orienting of attention in adults (Alho *et al.*, 1998; Escera *et al.*, 2001) and school-age children (Gumenyuk *et al.*, 2001; Rääkkönen *et al.*, 2003; Čeponienė *et al.*, 2004). Since in most studies, each novel sound is presented no more than twice during the experiments, it is suggested that the response to such sounds reflects the electrophysiological signature of novelty processing. In our previous study (Kushnerenko *et al.*, 2002), we obtained a similar pattern of results in sleeping newborn infants as is commonly found in adults and school-age children. The question in the current study was whether the pattern observable in neonates could be attributed to genuine processing of novelty or to the acoustic characteristics of the novel sounds. Our results suggest that newborns are most sensitive to the spectral width of sounds, because the largest and most stable ERP was elicited by white-noise sounds, which covered a wide range of the frequency spectrum but were not unique and thus could not be regarded as ‘novel’. Although spectral width also affected the adult ERPs, the responses indicated that finer aspects of acoustic change and contextual aspects of the sounds were processed as well.

In the adults, “novel” sounds elicited a high-amplitude early negative response peaking at 100-150 ms from stimulus onset, followed by a large positive response in the 250-350 ms latency range and by a late negativity peaking at 350-450 ms (Alho *et al.*, 1998; Escera *et*

al., 1998; Friedman et al., 2001) see Figure 1, panel E). The first negative wave sums together the auditory N1 response (Näätänen & Picton, 1987), which is sensitive to abrupt stimulus onsets and, if the novel sounds are embedded in an otherwise repetitive sound sequence, the mismatch negativity response (MMN; (Näätänen *et al.*, 1978)), which is elicited by deviations from some regular auditory stimulation (Näätänen & Winkler, 1999; Picton *et al.*, 2000). The central positivity (termed the P3a; see (Squires et al., 1975) is associated with a crucial precursor of the orienting reflex (OR): involuntary switching of attention to an incoming stimulus, for reviews, see Escera et al., 2000; Friedman et al., 2001). The late negativity (termed the reorienting negativity: RON; see (Schröger & Wolff, 1998), which is usually elicited in adults when a task-irrelevant deviant or novel stimulus causes distraction from some primary task, is assumed to reflect processes directing attention back to the task.

Although we obtained morphologically similar responses in neonates, different generators may underlie the observed components. For example, the adult-like N1 wave was not shown to emerge before the age of 3 years (Paetau *et al.*, 1995; Sharma *et al.*, 1997; Pang & Taylor, 2000; Ponton *et al.*, 2000; Shahin *et al.*, 2004). Although it is possible that the infantile early negativity may represent a precursor of one of the subcomponents of the adult N1 wave,, currently there is no widely accepted functional interpretation of this ERP response. Also, the late negative component elicited by auditory deviance in infants and children (sometimes termed the Nc or LDN; see (Kurtzberg *et al.*, 1986; Courchesne, 1990; Dehaene-Lambertz & Dehaene, 1994; Nelson, 1994; Friederici *et al.*, 2002; Čeponienė *et al.*, 2004) may not reflect reorientation to the primary task, as is assumed of the similar-latency RON response in adults.

The most intriguing finding of the present study is that newborns exhibited strikingly larger response to infrequent white-noise segments than to any other stimulus. Figure 1 also shows that the response to white-noise segments was quite large even when this sound was presented frequently and there was no difference between the response to the frequently presented white-noise sound and that to rare ‘novel’ sounds in any latency window. Thus, the stable morphology of the newborn ERP responses to ‘novel’ sounds and their relatively high amplitude can be most likely attributed to spectral richness and not to novelty *per se*. In contrast, in the adult subjects, only the central positivity (probably P2) appeared to be sensitive to spectral width as it has relatively high amplitude in response to frequently presented white-noise segments (Figure 1H).

In adults, the early negative wave was elicited when rare stimuli included no new frequencies compared to the standard (the White-noise standard condition; see Figure 1H). This finding indicates the presence of the adult MMN component, which is elicited irrespective of whether or not a rare deviant stimulus contains additional frequencies compared to those present in the regular stimulus sequence (cf., Näätänen *et al.*, 2005). In the neonates, the early negativity was largest with large magnitudes of frequency deviation (i.e., in response to white-noise deviants and novel sounds presented amongst tone standards, and frequency-deviants presented amongst white-noise standards), while it was absent in response to intensity deviants, despite their substantial deviation from the standard. These results suggest that large spectral changes are required for the elicitation of the early negativity in newborns (for compatible evidence in young infants, see (Kushnerenko *et al.*, 2002; Morr *et al.*, 2002).

It was found recently that neurons both in auditory cortex (Ulanovsky *et al.*, 2003) and in the midbrain of mammals (Perez-Gonzalez *et al.*, 2005) showed stimulus-specific adaptation and selectively responded to spectral sound change with a relatively short delay. It is quite possible that these primitive mechanisms of novelty detection function in human newborns and thus may contribute to the observable early negative response. Alternatively, our finding that the early negative response was not elicited by all deviant sounds in the present study (but only by novel sounds and white-noise segments) may indicate immature frequency tuning in newborns (Werner, 1996), resulting in higher auditory thresholds for tones compared with broadband sounds (Werner & Boike, 2001). This interpretation of the results is in line with the finding showing that, at least in the rat, the receptive fields in the neonate primary auditory cortex are broadly tuned in frequency and tonotopic maps develop later through maturation and exposure to appropriate auditory stimulation (Zhang *et al.*, 2001). Furthermore, unlike in newborns, novel sounds elicited a larger early negative response than that elicited by white-noise deviants in adults (see Figure 1G). A possible explanation of this difference is that the receptive fields of the afferent neuronal circuits become narrower during development and, as a result, a fewer number of neurons respond to any given specific stimulus. Thus in adults, the contribution to the ERP waveform by lower-level adaptive circuits detecting raw spectral change (reflected by the supratemporal N1) is relatively low; the early negative response receives a substantial contribution from higher-level aspects of change detection, those that are reflected by the MMN component.

Figure 3 shows that the spectral richness of sound plays an important role also in the morphological stability of the infantile ERP responses (for a similar conclusion in 6-year

old children, see, (Räikkönen *et al.*, 2003). Furthermore, unlike in the adults, white-noise segments elicited ERP responses of much higher amplitudes in newborns (both as standards and as deviants) than did any other stimulus. This effect cannot be explained by differences in skull conductivity between newborns and adults, because the ERP amplitudes elicited by frequency deviants and standards were comparable in two groups. Presumably, because of their spectral richness, noise sounds activate a wider range of afferent neuronal populations and induce a larger synchrony in the stimulus-elicited neural activity, thus increasing both the amplitude and stability of the ERP responses. This result is of particular importance to clinical applications of the ERP method, which were hampered by high inter-individual variability of the responses elicited by the commonly used tonal sounds (Kurtzberg *et al.*, 1986; Kushnerenko *et al.*, 2002; Kushnerenko, 2003).

The current results are also consistent with behavioral findings, which have shown that young infants exhibit broadly tuned response systems in multiple modalities and that as development progresses these response systems become more differentiated (Turkewitz *et al.*, 1983). Unlike adults, infants match stimuli across modalities (visual and auditory) according to their intensity (Lewkowicz & Turkewitz, 1981), thus responding to the overall energy of stimulation, rather than to its specific modal characteristics. Because broadband noise carries more acoustic energy compared to harmonic tones, newborns respond better to white-noise segments than to tones (Turkewitz *et al.*, 1972). Here we observed differences between newborns and adults in responding to the high-intensity deviant: the same intensity deviants, which elicited an enhanced central positivity in newborns (Figure 1B), altogether failed to elicit a P3a in adults (Figure 1F), although in

the majority of the conditions, we found close correspondence between the neonate central positive component and the adult P3a. Loud sounds, which carry more acoustic energy just as broadband signals, may represent stronger cues for orienting in newborns than in adults.

Finally, we observed that the late negative component showed an effect of contextual deviation. Novel sounds elicited the late negativity with the highest amplitude when they were presented amongst frequent repetitions of a harmonic tone (Figure 2a), significantly higher amplitude than when they were presented alone. The latter finding cannot be explained by refractoriness or adaptation of frequency-specific neuronal circuits. Refractoriness should be minimal, when no tones intervene between two novel sounds and in the absence of a repeated tone, no adaptation occurs to a “standard”. Therefore, if the late negativity was governed by these mechanisms, novels delivered alone should have elicited the largest late negative component. Furthermore, no or very small late negativity was elicited by tone deviants presented amongst tone standards (Figure 1A-C) and by novels presented amongst white-noise standards (Figure 1D). These findings can be explained by assuming that the newborn brain uses very simple “perceptual categories” in describing stimuli, such as harmonic vs. non-harmonic sounds. These features of the newborn response pattern suggest that the infantile late negativity reflects the activation of neural circuits sensitive to contextual novelty. Unlike the newborns, the adults showed approximately equal-amplitude late negativities to novel Condition 5 (novel stimuli presented alone; Figure 2b) and the late negativity was also elicited by novels presented amongst white-noise deviants and by tone deviants presented amongst tone standards (Figure 1). These results suggest that adults form representations of finer

sound categories than newborns and, therefore, all of the current contrasts fell across some category boundary. Furthermore, in adults earlier ERP responses (MMN and P3a) are affected by categorical change (novelty; for reviews, see Friedman *et al.*, 2001; Näätänen *et al.*, 2001). Thus it is likely that adults process faster the contextual aspects of stimuli than neonates.

The current findings of differences between the infant and adult patterns of responses suggest that maturation and learning lead to decreased sensitivity to primary surface stimulus features (such as stimulus energy and raw spectral change) but faster and more elaborate processing of contextual attributes. A prime example of this developmental change is that starting in early infancy, discrimination sensitivity decreases for phonetic features within the phoneme categories of one's native tongue, whereas the speed and precision of detecting even small changes dramatically improves at the boundary between two phoneme categories (Kuhl, 1991; Werker & Tees, 2005). In short, a primary facet of development is that we learn to rapidly extract higher-level relationships and regularities from the ever-changing sensory environment while becoming less sensitive to gross changes in primary sensory features.

## Conclusions

The results of the present study show that spectral width plays the most crucial role for newborn infants. Unlike newborns, adults detected 'novel' sounds even against spectrally rich white-noise standard background, which resulted in significant MMN response, thus suggesting a major difference in what aspects of the stimulation newborns and adults are sensitive to. However, P3a was affected by large spectral change in adults as well, showing that such changes do not lose their relevance in capturing attention. We also

found that broadband stimuli and large spectral changes elicit electric brain responses, which are highly invariant across individual neonates. Finally, the current results support the notion that neonates form simple perceptual categories and detect when the stimulation changes from one to another.

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**Abbreviations:** ERP, event-related potentials, OR, orienting reflex, MMN, mismatch negativity

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**Table 1. Stimulus make-up of the different conditions.**

Condition	Standard (80%)	Infrequent 1 (10%)	Infrequent 2 (10%)
Condition 1	500-Hz tone	750-Hz tone	Novel
Condition 2	500-Hz tone	750-Hz tone	500-Hz tone/+10dB
Condition 3	500-Hz tone	White-noise segment	Novel
Condition 4	White-noise segment	500-Hz tone	Novel

Each sound sequence contained three types of sounds: one, which was delivered frequently (standard) and the two with equally low probabilities. The order of the tones was randomized with the constraint that the infrequent sounds were always followed by at least two standard sounds. 101 different environmental sounds were used for “novel” sounds.

**Table 2. Group-average central (Cz) ERP amplitudes (in  $\mu\text{V}$ ; standard deviations in parentheses).**

Condition		Newborns				Adults	
	Lat. (ms)	50-150*	250-350***	450-550**	90-140***	200-250*	400-450
Condition 1	Tone-std.	0.27 (2.90)	0.54 (2.02)	-1.06 (1.45)	-0,86 (0,82)	-0,83 (1,51)	-0,48 (1,03)
	Freq.-dev.	-0.43 (2.91)	2.53 (2.52)	0.55 (2.36)	-3,09 (1,85)	0,11 (2,14)	-0,65 (1,16)
	Novel	-1.94 (3.17)	7.12 (4.62)	-3.49 (3.73)	-3,03 (1,67)	3,02 (2,72)	-1,40 (1,29)
	Lat. (ms)	50-150	250-350***	450-550	90-140***	150-200*	200-250***
Condition 2	Tone-std.	-0.39 (2.02)	0.05 (2.83)	-1.30 (2.64)	-0,80 (1,10)	0,52 (1,64)	-1,01 (1,37)
	Freq.-dev.	-0.33 (2.04)	1.92 (2.78)	0.79 (1.88)	-3,36 (1,89)	0,62 (2,20)	0,19 (2,52)
	Int.-dev.	1.30 (2.07)	7.04 (4.88)	-1.69 (2.54)	-1,90 (1,87)	-0,53 (1,88)	-2,22 (2,02)
	Lat. (ms)	100-200**	250-350***	450-550***	90-140*	200-250***	400-450
Condition 3	Tone-std.	0.29 (2.97)	0.03 (2.27)	-0.56 (1.42)	-0,78 (0,90)	-0,92 (1,67)	-0,41 (1,00)
	Noise-dev.	-3.27 (3.38)	14.98 (9.27)	-12.11 (9.66)	-1,39 (1,80)	5,79 (2,64)	-0,59 (1,65)
	Novel	0.16 (2.18)	5.48 (4.78)	-5.83 (4.76)	-2,70 (1,66)	2,79 (2,72)	-1,04 (1,53)
	Lat. (ms)	100-200	250-350*	450-550	90-140***	200-250	400-450
Condition 4	Noise-std.	-0.77 (2.47)	4.17 (3.03)	-1.63 (1.48)	0,89 (1,12)	0,71 (1,40)	-0,07 (1,33)
	Tone-dev.	-1.49 (3.42)	-0.68 (3.06)	1.11 (1.76)	-3,09 (2,12)	0,85 (1,99)	-0,85 (1,91)
	Novel	0.18 (2.51)	1.61 (3.94)	0.12 (2.56)	-1,87 (1,60)	1,40 (2,44)	-1,62 (1,61)
	Lat. (ms)	50-150	250-350	450-550	90-140	200-250	400-450
Condition 5	Novel	-0.11 (2.41)	4.67 (2.47)	-1.38 (2.76)	-5,46 (2,51)	6,78 (3,75)	-0,24 (1,16)

For each condition, responses to different stimuli are presented in separate rows. Within each age group, the amplitude measurements for the different latency ranges are given in

separate columns, with the header showing the latency range of the measurement, which was separately adapted for each condition and age group. Significant ANOVA Stimulus Type main effects differentiating between the three types of sound presented together in a stimulus sequence are marked at the latency headers, separately for each condition, subject group, and latency range; with \*, \*\*, and \*\*\* denoting significance at  $p < .05$ ,  $.01$ , and  $.001$ , respectively. (Interactions and the results of the post-hoc paired comparisons are described in the text.)

### Figure legends

**Figure 1.** Group-averaged central (Cz) ERP responses elicited in the four oddball conditions. ERP responses elicited by frequent (standard) and two types of infrequent sounds are shown separately for newborn infants (left side) and adults (right side). Observe the similar patterns of response to novel sounds in newborns and adults by comparing the waveforms depicted by thick continuous lines on panels A and E with each other: The early negative peak is first followed by a central positive wave and then by a broad negativity. Corresponding conditions are shown in the same row for the two subject groups. Standard responses are marked with thin continuous lines, frequency/white-noise deviant responses with dashed lines, and novel or intensity-deviant responses with thick continuous lines. Stimulus onset is at 0 on the  $x$  axis.

**Figure 2 (a and b).** Group-averaged ERP responses elicited by novel sounds. ERP responses are shown separately for newborn infants (Figure 2a) and adults (Figure 2b) in three oddball and the Condition 5 at all scalp locations recorded. Different line types

denote the responses elicited by the same novel sounds in the different experimental conditions. The electrode locations are marked by their name defined in the international 10-20 system, except LM and RM, which denote the left and right mastoids, respectively. The insert panels (within frames) show the diagrams of the group-averaged central (Cz) novel-sound response amplitudes measured for the early negativity, central positivity, and late negativity, separately in the four experimental conditions (marked by the shading of the rectangles) and subject groups (top vs. bottom). The standard deviation is marked on the top of each rectangle.

**Figure 3.** Individual ERP responses for the 12 newborn infants measured. Central (Cz) ERP responses elicited by frequency deviants (thick continuous line; from the Condition 1), white-noise deviants (dashed line; from the Condition 3), and novel sounds (thin continuous line; from the Condition 3) are displayed.

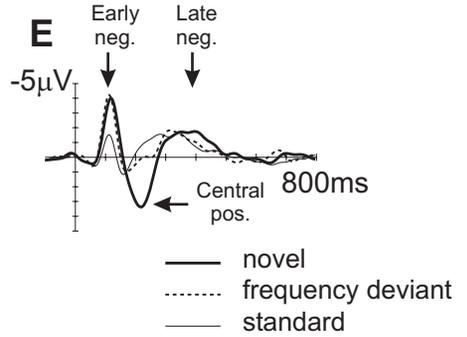
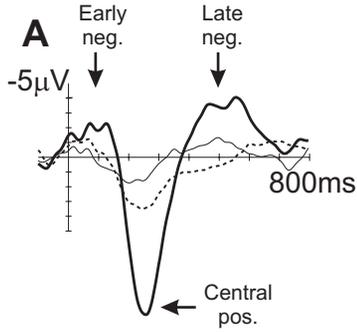
# Electric Brain Responses

## Infants

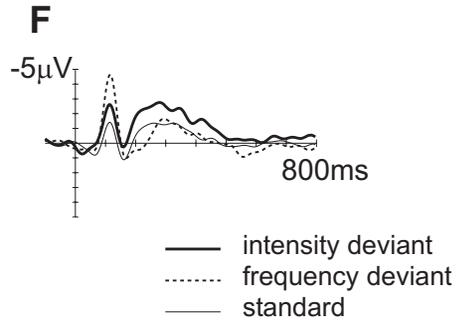
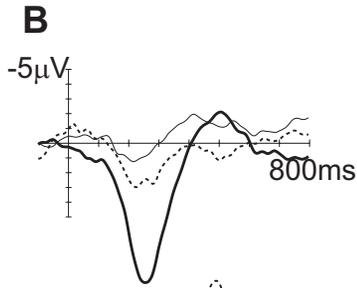
## Adults

CONDITION

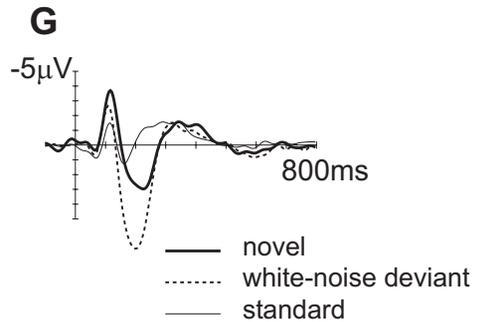
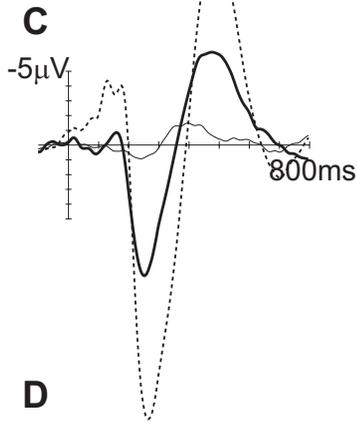
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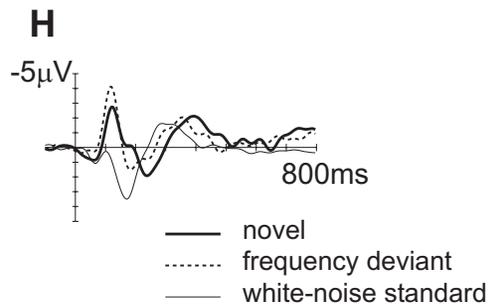
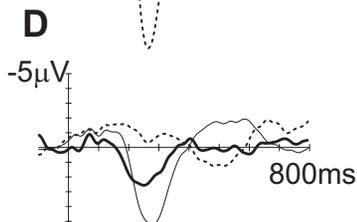
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3

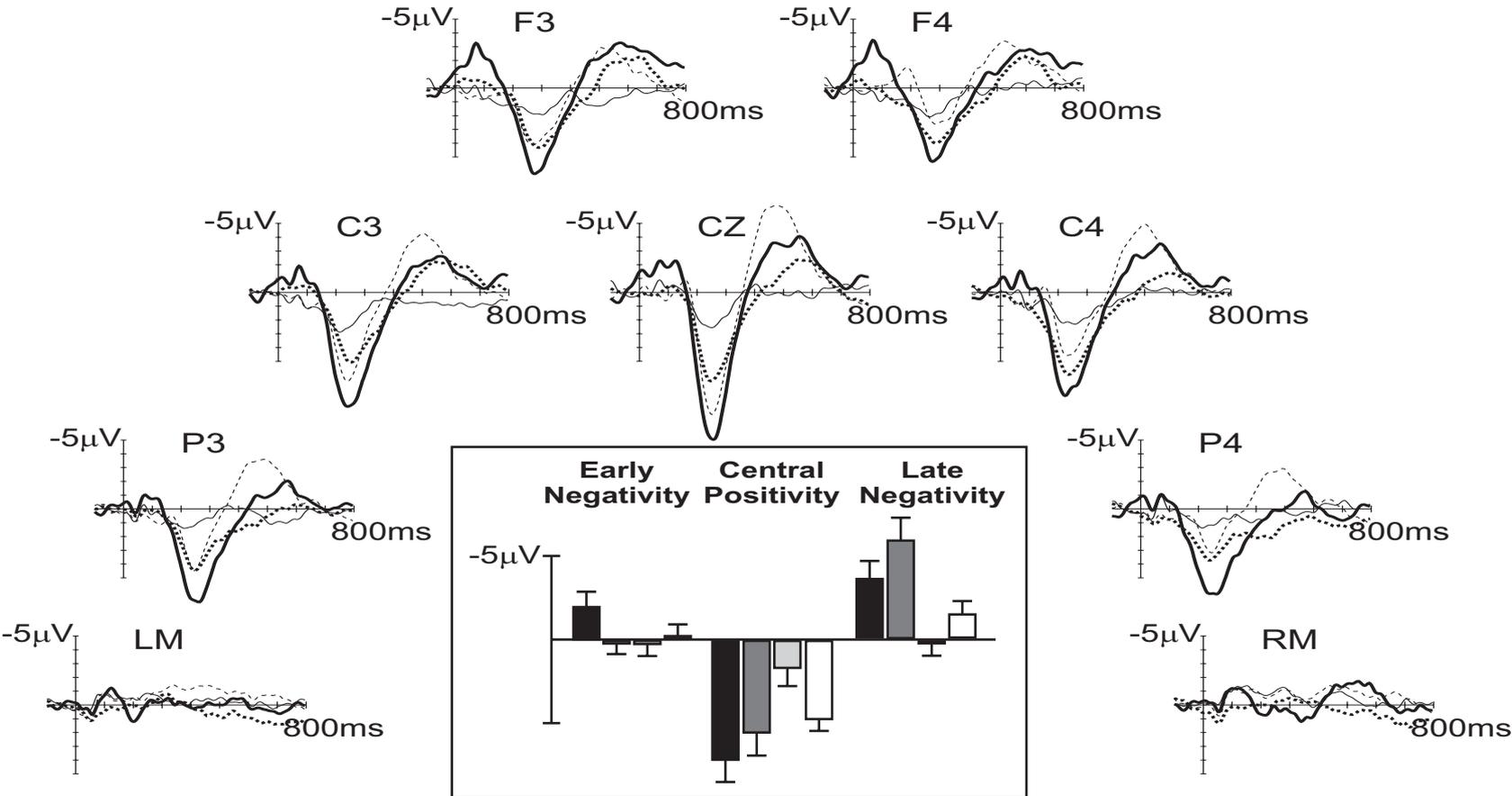


4



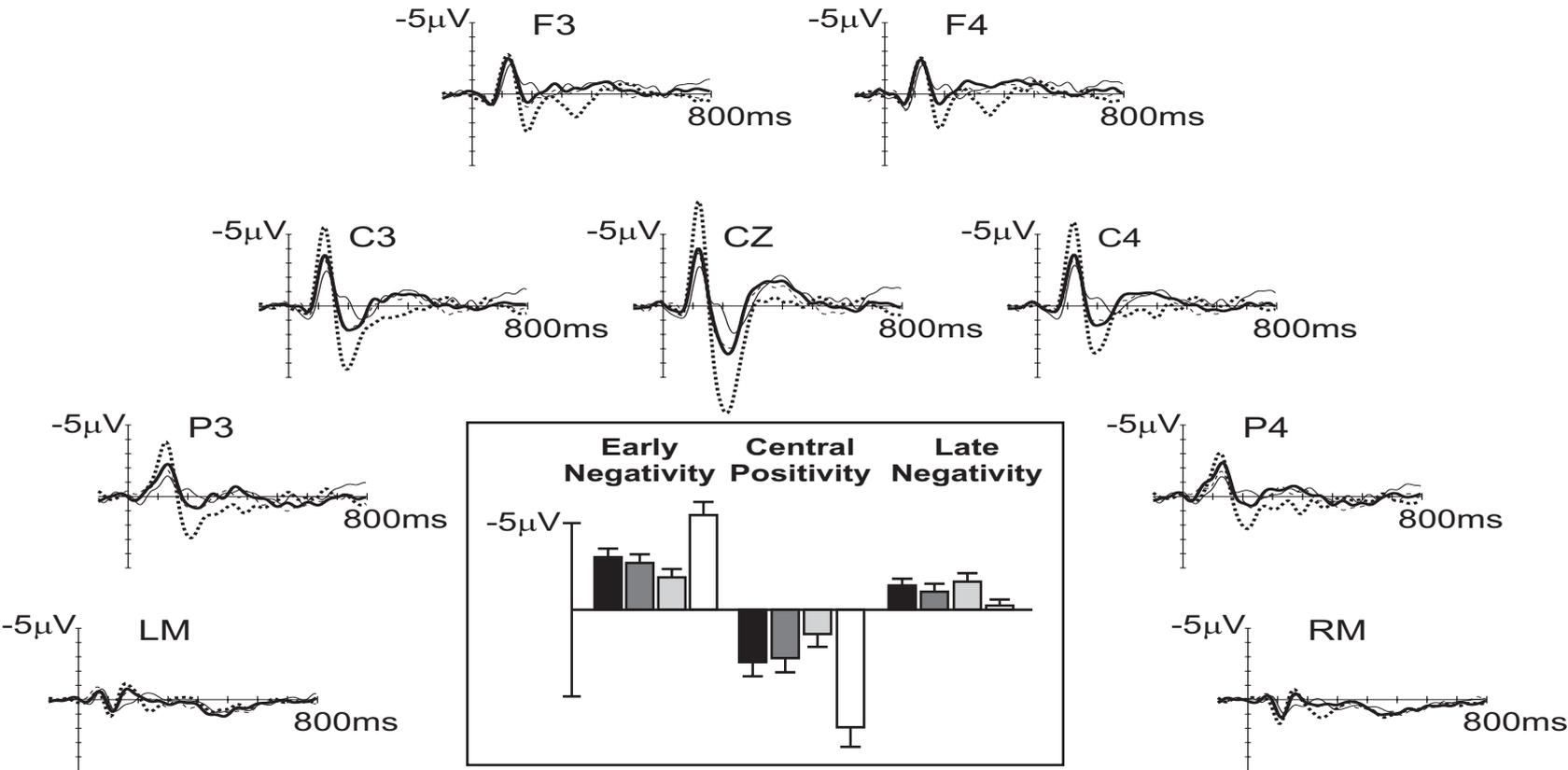
# Responses to Novel Sounds

## Infants



# Responses to Novel Sounds

## Adults



— Condition 1   
..... Condition 5 

..... Condition 3   
— Condition 4 

# Individual Brain Responses in Neonates

