Differences between human auditory event-related potentials (AERP) measured at 2 and 4 months after birth

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Abstract

Infant auditory event-related potentials (AERP) show a series of marked changes during the first year of life. These AERP changes indicate important advances in early development. The current study examined AERP differences between 2- and 4-month-old infants. An auditory oddball paradigm was delivered to infants with a frequent repetitive tone and three rare auditory events. The three rare events included a shorter than the regular inter-stimulus interval (ISI-deviant), white noise segments, and environmental sounds. The results suggest that the N250 infantile AERP component emerges during this period in response to white noise but not to environmental sounds, possibly indicating a developmental step towards separating acoustic deviance from contextual novelty. The scalp distribution of the AERP response to both the white noise and the environmental sounds shifted towards frontal areas and AERP peak latencies were overall lower in infants at 4 compared to at 2 months of age. These observations indicate improvements in the speed of sound processing and maturation of the frontal attentional network in infants during this period.

Keywords: auditory event-related potential; infancy; auditory attention; cognitive development; oddball paradigm

1. Introduction

Infant auditory event-related potentials (AERPs) are often used to index the early development of information processing (for reviews, see Csibra et al., 2008;Kushnerenko et al., 2013; Leppänen et al., 2004). AERPs are based on non-invasive recording of brain activity and they are elicited even in the absence of conscious attention making them a useful tool for infant research. Because they do not require behavioral responses, AERPs elicited by identical stimulation can be compared across age groups irrespective of the rapidly changing behavioral capabilities of young infants. The functionality of processing rapidly presented sound sequences, sound discrimination, and categorization are important prerequisites of auditory perception including speech and language acquisition (e.g., Benasich et al., 2002; Leppänen et al., 2002).

The morphology of AERP responses undergoes large changes with learning and maturation of the infantile nervous system during the first year of life (Fellman and Huotilainen, 2006; Kushnerenko et al., 2002a; Kushnerenko et al., 2002b; Leppänen et al., 2004; Morr et al., 2002). The infant brain undergoes profound structural and functional maturation, such as synaptogenesis (Huttenlocher, 1984) and increases in myelination in the temporal lobe (Deoni et al., 2011). These, as well as the effects of early learning are reflected in morphological and functional changes in the infantile AERP responses. Mapping typical and atypical developmental trajectories of information processing requires the characterization of AERP changes occurring within relatively short periods of time. In our review of developmental AERP changes during the first year of life (Kushnerenko et al., 2013), we noticed a dip in the number of electrophysiologal studies targeting auditory processes during the first few months of infancy. Whereas much effort has been invested into characterizing AERPs at birth and at ca. 6 month, little is known about the typical AERP development between these two time points. He et al. (2009) suggested that the ability to detect pitch change similarly to adults probably emerges between 2 and 4 months of age. Moreover, previously Gomes et al. (2000) have shown that between 2 and 4 months of age, infants orient more to novel visual stimuli. However, it is yet unknown whether or not this also applies to the auditory modality. Thus, this short time period seems to be critical in the development of sound processing. The current study has been aimed at characterizing the development of AERPs during this period.

The auditory oddball paradigm allows assessing AERPs for both frequent repetitive and rare deviant sounds. Although by tradition, many previous studies focused on the differential response to rare and frequent sounds [the mismatch response (MMR); Alho et al., 1990; Dehaene-Lambertz and Gliga, 2004; Morr et al., 2002], it can be misleading in a developmental comparison, because this approach assumes that the developmental AERP changes for the frequent and infrequent sound *per se* (often of quite different acoustic makeup) have been identical, and thus the development of the difference response can be separately assessed. It is possible that a part of the previously observed dramatic developmental MMR changes during the first year of life (see Kushnerenko et al., 2002b; Leppänen et al., 2004; Morr et al., 2002) could have originated from separate developmental alterations of the AERPs elicited by the frequent and infrequent sounds employed. Because we aimed to assess AERP differences between two age groups for acoustically widely different sounds (white noise segments and environmental sounds), the frequent standard and some of the rare deviant sounds were qualitatively different. Therefore, we took the approach of separately assessing the responses to these sounds, testing the elicitation of MMR only when the standard and the deviant were identical sounds.

Large spectral changes (such as white noise and novel sounds appearing within a sequence of a repeating complex tone) have been found to reduce inter-individual variability and to improve the replicability of AERP responses in infants (Kushnerenko et al., 2002b; Kushnerenko et al., 2007), and might therefore provide a reasonably reliable assessment of typical AERP development. However, to date, only a few studies focused on the maturation of the processing of rare white noise and novel sounds. In newborn infants, Kusnherenko and collagues (2007) obtained similar responses for these two types of sounds in the context of a frequent tone stimulus. Háden and colleagues (2013) showed in neonates that whereas the morphology of the AERPs elicited by environmental sounds depended on the context (environmental sounds presented alone vs. amongst repeating complex tones), only the amplitude of the AERPs elicited by white noise segments was affected by the same manipulation. Otte and colleagues (2013) then obtained different AERP responses to white noise and novel sounds presented in the context of a repeating complex tone at 2 months of age. Using the same stimulus paradigm in the current study as Otte and colleagues (2013), we will look for further developmental steps in separating acoustic deviance from contextual novelty.

The present study explores the maturation of AERPs elicited in the context of the auditory oddball paradigm, comparing infants of 2 and 4 months of age. We expected that the separation of contextual novelty and acoustic deviance widens from 2 to 4 month of age and thus the difference between the AERPs elicited by white noise and environmental sounds to become larger during this period. Using Otte and colleagues' (2013) stimulus paradigm also allowed an investigation of the processing violations of a temporal regularity by recording responses to infrequent shortenings of the otherwise constant inter-stimulus interval (ISI). Auditory temporal features carry important information relevant to speech perception, such as stress and prosody. Recent evidence suggests that impairments in temporal processing skills are associated with developmental dyslexia (e.g., Flaugnacco et al., 2014). Thus, mapping the typical development of AERPs elicited by violating a temporal regularity may be useful as an early indicator of development in language acquisition.

2. Methods

The study was approved by the ‘Central Committee on Research involving Subjects’ and was conducted in full compliance with the Helsinki declaration. All mothers and fathers signed an informed consent form after the goals and procedures of the study had been explained to them. The experiment was conducted within the framework of a prospective study assessing the long-term effects of prenatal exposure to maternal anxiety, i.e. the Prenatal Early Life Stress (PELS)-study. Here we focus on comparing AERPs between the full 2- and 4-month-old groups of awake infants. Data obtained at 2 months of age have been previously reported by Otte et al. (2013), who compared the ERP responses between sleeping and awake infants.

2.1. Participants

Participants from a typical (i.e., non-clinical) population had been recruited from a general hospital and four midwives' practices: 178 women had been recruited before their 15th week of pregnancy and 12 women between the 15th and the 22nd week of their pregnancy. The women were followed up during their pregnancies and were invited for postnatal observations either 2 or 4 months after the birth of their baby. From the 91 2-month-olds and the 43 4-month-olds who participated in the ERP measurements, we included a total of 36 2-month-olds (19 girls) and 26 4-month-olds (12 girls) in the current study. These 2-month-olds had a mean age of 9.59 weeks (SD = .87), a mean birth weight of 3470 g (SD = 508) and a mean gestational age of

39.78 weeks (SD = 1.36). The 4-month-olds had a mean age of 17.96 weeks (SD = 3.48), a mean birth weight of 3443 g (SD = 354) and a mean gestational age of 39.73 (SD = 1.19).

The data obtained from infants who fell asleep during the experiment (40 2-month-olds and 9 4-month-olds) were excluded from the analysis because previous results suggested that the infants' state of alertness affects the AERP responses (e.g. Friederici, Friedrich, & Weber, 2002; Otte, et al., 2013) and we did not have sufficient number of sleeping 4-month olds to assess the state of alertness effects. In addition, from the 2-month-old group, nine infants were excluded because of too few (< 40) acceptable EEG epochs (due to excessive movements/artefacts), two because of excessive crying, and another four due to technical problems. From the 4-month-old group, four infants were excluded because of too few acceptable EEG epochs, three due to excessive crying, and one because the infant had been born prematurely. There were no significant differences among the excluded and included infants in gestational age or birth weight. All infants were healthy and had passed an otoacoustic emission-based screening test for hearing impairments, performed by a nurse from the infant health care clinic between the 4th and the 7th day after birth.

2.2. Stimuli and procedure

The infants were presented with an auditory oddball sequence composed of four types of sound events: A complex tone of 500 Hz base frequency presented with .7 probability followingan ISI (offset-to-onset interval) of 300 ms (the “standard” tone); the same tone following an ISI of 100 ms (.1 probability; the “ISI-deviant”); a white noise segment (.1 probability; 300 ms ISI); and various environmental sounds (.1 probability; 300 ms ISI; “novel sounds”). Standard and ISI-deviant tones were constructed from the 3 lowest partials, with the intensity of the second and third partials set 6 and 12 dB lower, respectively, than that of the base harmonic. The novel sounds were 150 unique environmental sounds (e.g., door slamming, dog barking, etc.) and they were presented only once during the experiment to maintain their novelty throughout. The short ISI was chosen because larger MMR amplitudes were reported with faster rather than slower presentation rates for 2-month and 4-month-old infants (He, Hotson, & Trainor, 2009). The common stimulus duration was 200 ms including 10 ms rise and 10 ms fall times, resulting in an onset-to-onset interval of 500 ms preceding the standard tones, white noise and novel sounds, and 300 ms preceding the ISI-deviant tones; the common intensity was 75 dB (SPL). Sequences consisted of 1500 stimuli presented in a pseudorandom order with the restriction that novel/white noise stimuli were always preceded by two or more standard tones or a combination of a standard tone and an ISI-deviant. Further, consecutive ISI-deviants were always separated from each other by at least two standards or by a standard tone combined with either a white noise or a novel sound. The sequences were divided into 5 blocks of 300 stimuli, each, which were presented to the infants in a counterbalanced order. The duration of each stimulus block was approximately 2.5 minutes resulting in a total of 12.5 minutes for the whole recording.

The experiment took place in a dimly lit and sound-attenuated room at the Developmental Psychology Laboratory of the university. The complete procedure including electrode placement and removal, EEG recording, and necessary breaks lasted for approximately 60 minutes. During the EEG recording, infants sat or lay on their parent's lap between two loudspeakers placed at a distance of 80 cm from each side of the infant’s head. The whole experimental procedure was recorded with two cameras: One placed behind and the other in front of the infant and the parent. The camera recordings were used to determine whether the baby was crying or moving.

2.3. ERP measurement and data processing

EEG was recorded with Biosemi Active Two amplifiers (www.biosemi.com) with a sampling rate of 512 Hz and filtered by a 5th order sinc filter with the -3 dB point at 1/5th of the sample rate (~102 Hz). Sixty-four Ag/AgCl electrodes were placed on the infant's scalp according to the International 10-20 system. Two reference electrodes were placed on the left and right mastoids; these were later mathematically combined to produce an average mastoids reference derivation (Luck, 2005).

Data were analysed using Brain Vision Analyzer 2.0.2 using the ActiView software (Brain Products GmbH). The signals were filtered (phase shift-free Butterworth filters) off-line with a bandpass of 1.0 – 30 Hz (slope 24 dB). These filter settings were chosen to make the results comparable with the study by Otte et al. (2013) and to add compatible evidence to the maturational database created by previous studies (e.g., Brannon et al., 2004; He et al., 2007; Kushnerenko et al., 2007).

Subsequently the data were segmented into epochs of 600 ms duration including a 100 ms pre-stimulus period. Epochs with a voltage change exceeding 150 µV within a sliding window of 200 ms duration as well as those including changes that exceeded the rate of 100 µV/ms at any electrode were rejected from further analysis. On average, the number of remaining trials included for analysis for the four stimulus types were as follows: standard: 600 (2-month-olds) vs. 601 (4-month-olds); ISI-deviant: 86 (2-month-olds) vs. 87 (4-month-olds); white noise: 85 (2-month-olds) vs. 86 (4-month-olds); novel sounds: 86 (2-month-olds) vs. 88 (4-month-olds).

Infants with less than 40 trials for any of the four stimulus categories were rejected from further analysis (see the *Participants* section above). Next, ERPs for each infant were averaged separately for the four different stimulus types and baseline-corrected to the average voltage in the 100 ms pre-stimulus period.

The time windows for peak detection were selected on the basis of visual inspection of the group-average ERPs from the electrodes F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4, separately for the standard and the three oddball stimuli. The following time windows were used for peak latency measurements in individual infants: for the standard (see Figure 1), a time window of 180-250 ms was set for the positive peak corresponding to P2; for the ISI-deviant (see Figure 2) a time window of 175-275 ms was set for the negative and another of 350-500 ms for the positive peak corresponding to the N250 and P350, respectively; for the white noise sound (see Figure 3), a window was set at 100-200 ms for the first positive peak corresponding to the early part of the bifurcated infantile P2 (P150), another one at 175-275 ms for the negative-going peak corresponding to the N250, and a third one at 300-450 ms for the second positive peak (P350); for the novel sound (see Figure 4), a time window of 250-450 ms was set for the positive peak corresponding to the infant P3a waveform. Peaks were termed in accordance with the nomenclature set up by Kushnerenko et al. (2002a,b; 2007). Note that the time windows of the white-noise P350 and novelty P3a extend over the onset of a possible following ISI-deviant tone. However, because the average amplitude of the ISI-deviant response in the overlap period is low (below 1 μV) and the overlap occurs only for ca. 10% of the white-noise and novel sounds, the bias caused by the overlap is below 3% of the measured amplitudes and it is approximately equal between the two age groups. Peaks were detected automatically as the highest/lowest point within the respective time windows. Average amplitudes were measured as the mean voltage in

60 ms long intervals centred on the peaks of the group-averaged response, separately for the two age groups.

In addition, for illustration purposes, topographical maps were created for the components showing significant ERP scalp distribution differences between 2- and 4-month-olds for the white noise and novel sounds. From the 64 electrodes, P9, P10, O1, Oz, O2, and Iz had to be excluded, because almost all infants showed a large number of artefacts on these electrodes (this was probably caused by the round shape of the EEG cap not matching well with the infants' typical shape at the back of the head). When necessary, the signals recorded from the included electrodes were interpolated by spherical spline interpolation (order = 4, degree = 10, and lambda = 1E-05; Perrin et al., 1989).

2.4. Statistical analysis

For comparing the two age groups on peak latency and amplitude measures at the nine electrode sites, mixed model repeated-measures ANOVAs with 'Anterior vs. Posterior' (frontal, central, parietal) x 'Laterality' (left, medial, right) as within-subjects factors, and 'Age-Group' (2 months and 4 months) as a between-subject factor were carried out for each stimulus type (standard, ISI-deviant, noise, and novel sound) and component. All analyses were controlled for gestational age at birth (GA) and birth weight (BW) of the infants by including these variables into the analysis as covariates. These covariates were included because previous studies, especially those of prematurely born infants, showed effects of gestational age at birth and birth weight on auditory ERPs (e.g., Hövel et al., 2014) and brain development (Ment and Vohr, 2008). Only effects including the Age-Group factor are interpreted. For the significant Age-Group × Anterior vs. Posterior interactions post-hoc tests were conducted by separate ANOVAs of Age-Group for the frontal (F3, Fz, F4), central (C3, Cz, C4), and parietal arrays of electrodes

(P3, Pz, P4). For the significant Age-Group by Laterality interactions, ANOVAs of Age-Group were separately conducted for the left (F3, C3, P3), middle (Fz, Cz, Pz), and right array of electrodes (F4, C4, P4). GA and BW were always corrected for in post-hoc tests, too.

For assessing whether the brain of 2-month and 4-month-old infants distinguished the ISI-deviant from the standard stimulus, we subtracted the response to the standard from that of the ISI-deviant and then compared the difference against zero by repeated-measure ANOVAs with 'electrodes' (all nine electrodes) as a within-subject factor, separately for each age group and peak.

All statistical analyses were performed using SPSS 19.0 for Windows. Greenhouse-Geisser correction was applied where appropriate (ε correction factors reported). All significant ($\alpha = .05$) results involving the age-group factor are reported, together with the partial η^2 effect size values.

3. Results

Table 1 shows the group-mean peak latencies and mean amplitudes measured from 60-ms long windows centered at the mean peak latency (μV) averaged over all nine electrodes for all stimuli, separately for the 2- and 4-month-olds.

3.1. Standard tone

The standard tone elicited a fronto-centrally distributed P2 in both age groups (Figure 1). Although a significant Age-Group x Anterior vs. Posterior interaction was found for the peak latency [$F(2;120)=4.61$, $p<.05$, $\eta^2=.071$, $\varepsilon=.764$], this interaction was no longer significant after controlling for gestational age at birth and birth weight. The ANOVA of the mean amplitudes yielded a significant Age-Group × Anterior vs. Posterior interaction [$F(2;108)=5.00$, $p<.05$, $\eta^2=.085$, $\varepsilon=.838$]. Post hoc tests showed a trend for a difference between 2- and 4-month-olds at the central electrodes, with a larger amplitude for 4-month-olds [$F(1;54)=3.72$, $p=.06$, $\eta^2=.064$], but no significant difference at the frontal and parietal electrodes. Controlling for gestational age and birth weight did not change this result.

3.2. ISI-deviant

Figure 2 shows that in both age groups, ISI-deviants elicited a fronto-centrally distributed negative-going wave (N250) followed by a similarly distributed positive-going wave (P350). Age had a significant effect on the peak latency of the P350, with a shorter peak latency for the 4- than the 2-month-olds [$F(1;60)=8.05$, $p<.01$, $\eta^2=.118$]. Controlling for gestational age and birth weight did not alter this effect. Because the ISI-deviant sound is identical to the standard sound, for this rare sound we also tested whether the violation of the temporal regularity elicited a significant MMR response. The response to the ISI-deviant significantly differed from the standard-stimulus response for both age groups and latency ranges: N250 [$F(1;35)=29.13$, $p<.001$ and $F(1;25)=13.53$, $p<01$, in the 2- and the 4-month-old group, respectively] and P350 [$F(1;35)=-3.263$, $p<.01$ and $F(1;25)=7.74$, $p<.01$, respectively]. Thus, violating a temporal regularity elicited significant MMR responses in both age groups.

3.3. White noise

White noise sounds elicited a waveform with the following peaks: the P2 dissociated into P150 and P350 separated by the emerging N250 (Figure 3A). Figure 3A shows that in the 4-month-olds, the presence of an N250 component is more apparent than in the 2-month-olds. Thus the N250 appears to become prominent between 2 and 4 month of age. This interpretation is supported by the finding of a significant interaction between 'Age Group' and 'Laterality' for the N250 peak amplitude [$F(2;108)=3.25$, $p<.05$, $\eta^2=.057$, $\varepsilon=.970$]. Post-hoc test indicated that the amplitude differs between 2- and 4-month-olds mainly over the right hemisphere [$F(1;54)=4.29$, $p<.05$, $\eta^2=.074$], with a positive mean value for the 2-month-olds and a negative one for the 4-month-olds [1.4 vs. -.7 µV].

Figure 3A shows that the P150 and the P350 responses to white noise peaked significantly earlier in the 4- than in the 2-month-olds: for P150 [148 vs. 168 ms, respectively; $F(1;60)=7.39$, $p<.01$, $\eta^2=.120$] and for P350 [362 vs. 383 ms, respectively; $F(1;54)=6.00$, $p<.05$, $\eta^2=.100$]. For the P350 amplitude, a significant Age group by Anterior vs. Posterior interaction was obtained [$F(2;108)=5.31$, $p<.05$, $\eta^2=.089$, $\varepsilon=.675$]. Post-hoc tests revealed larger amplitudes in the 2- compared with the 4-month-olds at the parietal electrodes [$F(1;54)=7.57$, $p<.01$, $\eta^2=.123$], but not at the frontal or central electrodes. Figure 3B shows that in 2-month-olds, P350 peaks over parietal areas; in contrast, in 4-month-olds, this response appears to have shifted more towards frontal areas with very low amplitudes over parietal areas.

To examine whether the P350 amplitude difference between 2- and 4-month-olds was due to the emergence of the negative N250 peak, we performed correlation analysis (Pearson correlation) between the N250 and P350 amplitudes averaged over all electrodes and pooling the two age groups. The analysis revealed a significant positive correlation between the amplitudes measured from the N250 and P350 latency ranges [$r(1;62)=.65$, $p<.001$]. This result shows that when the N250 is not prominent (i.e., the voltage in the N250 range is positive), the P350 amplitude is large. When the N250 emerges (smaller positive or negative values) reducing or even eliminating the positivity in its range, the P350 amplitude is reduced.

3.4. Novel sounds

Novel sounds elicited a slow positive-going waveform (the P3a; Figure 4A). A significant Age-Group × Anterior vs. Posterior interaction was found for the P3a amplitude [$F(2;108)=12.84$, $p<.001$, $\eta^2=.192$, $\varepsilon=.766$]. Post-hoc tests revealed a significant parietal difference between the two age groups with lower P3a amplitudes at 4 than at 2 month of age [$F(1;60)=7.58$, $p<.01$, $\eta^2=.123$]. This pattern of results suggests that the P3a response to novel sounds has shifted towards frontal areas in 4- compared to 2-month-olds (see Figure 4B).

4. Discussion

The current study showed AERP differences between typically developing 2- and 4-months-olds for a repetitive complex tone and three rare sound events. We found that by 4 month of age morphological differences appeared between the responses elicited by white noise and novel sounds compared to the responses obtained at 2 months. This result supports the hypothesis that the processing of contextual novelty and wide acoustic deviance becomes increasingly separated within this period.

The findings suggest that the N250 displays marked development between 2 and 4 months after birth. As shown in Figure 4, novel sounds elicited a P3a-like prolonged positive response (cf., Kushnerenko et al., 2002a,b; 2007). In contrast, white noise sounds elicited the P150-N250-P350 response complex (Kushnerenko et al., 2013; Figure 3), which became more prominent by 4 months compared to the response pattern at 2 months: Significantly more negative N250 amplitude was found over the right hemisphere in the 4- as compared to the 2-month-olds with no corresponding difference in the preceding P150 peak. The emergence of the N250 between these two ages in response to spectrally rich, widely deviant sounds (white noise segments) but not in response to unique novel sounds is consistent with the hypothesis of increased separation between processing acoustic deviance and contextual novelty (Kushnerenko et al., 2013). The fact that one should take into account, however, is that the infant brain might distinguish these two sets of sounds by differences in the spectral contents (environmental sounds have typically narrower bandwidth than white noise segments) and/or by difference in temporal structure (environmental sounds typically showed spectral changes over time, whereas the white noise segments did not). Differential processing of environmental sounds and white-noise segments (but not the emergence of the N250) has also been observed in neonates (Háden et al., 2013).

ISI deviants elicited significant MMR responses in both age groups, but no age-related difference was obtained between the responses to the deviant events in the MMR latency range. The peak latency of the P350 was lower in 4 months compared to 2 months old infants. Although the AERP responses look visually different, with more pronounced peaks in 4- compared to 2-month-olds, these differences did not reach statistical significance. This could be due to high between subject variability of AERP responses for this stimulus type. This suggests that the development of processing shortening of the inter-stimulus interval progresses less uniformly during this period than the processing of spectrally rich sounds.

The significant latency decrease found for several AERP responses from 2 to 4 month of age is in line with the previous reports (e.g., Cheour et al., 1998; Jing and Benasich, 2006) and it suggests faster processing in 4- than in 2-month-olds. Faster processing is assumed to be due to processes such as increasing myelination in the developing nervous system (see Dehaene-Lambertz et al., 2010).

We also found topographical differences between some of the ERPs elicited in the two age groups. Firstly, we found a difference in the scalp topography between 2- and 4-month-olds for the standard tones with a larger ERP response over central electrode sites for 4- compared to 2-month-olds. For the novel and the white noise sound, a difference in scalp topography was found for the P350/P3a with larger positive voltage on parietal electrode sites for 2- compared to 4-month-olds. The topographical maps of these components (Figures 3B and 4B) seem to indicate a developmental shift from 2 to 4 months of age towards frontal areas with a corresponding decrease of the positive voltage over parietal areas. The latter result is compatible with those of Kushnerenko et al. (2002a) demonstrating a developmental decrease of the P350 from 3 to 6 months of age (for a review, see Kushnerenko et al., 2013). These authors suggested that the decrease of the P350 was due to its overlap with the growing N250 component. Our post-hoc correlation analysis confirmed this suggestion: Higher (more negative) N250 amplitudes coincided with lower (less positive) P350 amplitudes. The interpretation of the assumed adult equivalents of these components (e.g., Escera et al., 2000) suggests that the mature version of these responses index the involvement of the frontal attention network.

Controlling for gestational age at birth and birth weight resulted in the elimination of a few of the initially statistically significant effects, suggesting that some differences in the variance of the AERPs of these two age groups are partly explained by the level of the infants' maturity at birth. While controlling for these covariates is often done in ERP-studies on prematurely born infants (Fellman et al., 2004; Hövel et al., 2014), many ERP-studies on infants born to term do not control for them. Our results, obtained in full-term infants, indicate that even in typically developing infants one should add these covariates to the statistical analyses when comparing between two groups of infants (such as between two age groups).

5. Conclusion

We found significant differences in AERPs within the short time period between 2 and 4 month after birth. This finding suggests that during this period, substantial maturation and learning takes place in the infant auditory information processing system. Data are consistent with the notion of early developmental improvements of infantile abilities in specifying their responses to novel auditory events, representing the temporal structure of sound sequences, and increasing the speed of sound processing. The emergence of the N250 AERP component was the most prominent AERP difference between the two tested age groups. This AERP development helps in understanding the developmental trajectory of auditory information processing in early infancy.

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List of abbreviations

ERP	Event-related potential
AERP	Auditory event-related potential
ISI	inter-stimulus-interval
MMR	mismatch response

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Figure 1: Group-average ERP responses elicited by the standard tones in the 2- (solid line) and 4-month-old infants (dashed line) over frontal, central and parietal electrodes. The grey box at Cz indicates the time window within which the “P2” amplitudes were measured.

Figure 2: Group-average ERP responses elicited by the ISI-deviant in the 2- (solid line) and 4-month-old infants (dashed line) over frontal, central and parietal electrodes. The grey boxes at Cz indicate the time windows within which the “N250/MMR” and “P350” amplitudes were measured.

Figure 3: (**A**) Group-average ERP responses elicited by the Noise sounds in the 2- (solid line) and 4-month-old infants (dashed line) over frontal, central and parietal electrodes. The grey boxes at Cz indicate the time windows within which the “P2”, “N250”, and “P350” amplitudes were measured. And (**B**) topographical maps for the P350 amplitude elicited by white noise segments in 2- (left) and 4-month-old infants (right), measured over 300-450 ms time period. The common color scale is below the left panel.

Figure 4: (**A**) Group-average ERP responses in elicited by the Novel sounds in the 2- (solid line) and 4-month-old infants (dashed line) over frontal, central and parietal electrodes. The grey box at Cz indicates the time window within which the“P3a” amplitudes were measured. And (**B**) topographical maps for the P3a amplitude elicited by novel sounds in 2- (left) and 4-month-old infants (right), measured over 250-450 ms time period The common color scale is below the left panel.

Table 1: Group-average peak latencies (ms) and mean amplitudes measured from 60-ms long windows centered on the mean peak latency (μV) averaged over the nine analyzed electrodes, separately for the 4 stimulus types, the ERP peaks (rows) and for the 2- and 4-month-old infants (columns).

Stimulus type and ERP peak	***Peak latency (SD)***		***Mean amplitude (SD)***	
	2-month-olds (N=36)	*4-month-olds (N=26)*	*2-month-olds (N=36)*	*4-month-olds (N=26)*
Standard tone				
P2	214 (3)	206 (4)	.2 (.3)	.5 (.3)
ISI-deviant				
N250	216 (7)	210 (8)	-2.1 (.4)	-2.2 (.5)
P350	435 (6)	411 (7)	.7 (.5)	1.6 (.6)
White noise				
P150	167 (4)	148 (5)	2.5 (.5)	2.2 (.6)
N250	221 (4)	224 (5)	1.2(.6)	-.4 (.7)
P350	383 (5)	365 (6)	4.3 (.6)	3.5 (.7)
Novel				
P3a	308 (7)	325 (8)	5.2 (.6)	5.1 (.7)

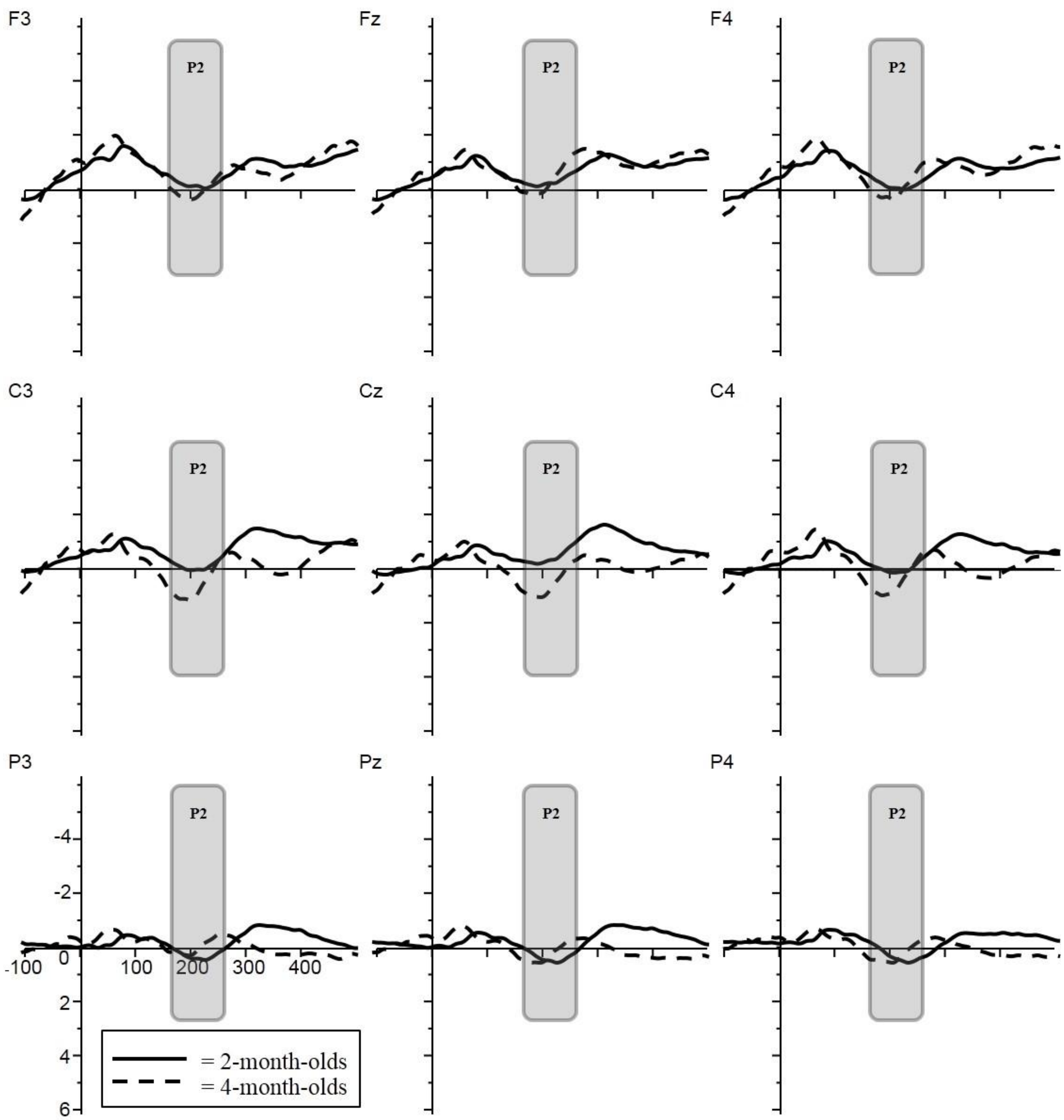
F3
Fz
F4
C3
Cz
C4
P3
Pz
P4
P2
-4
-2
0
2
4
6
-100
100
200
300
400
= 2-month-olds
= 4-month-olds

Fig. 1

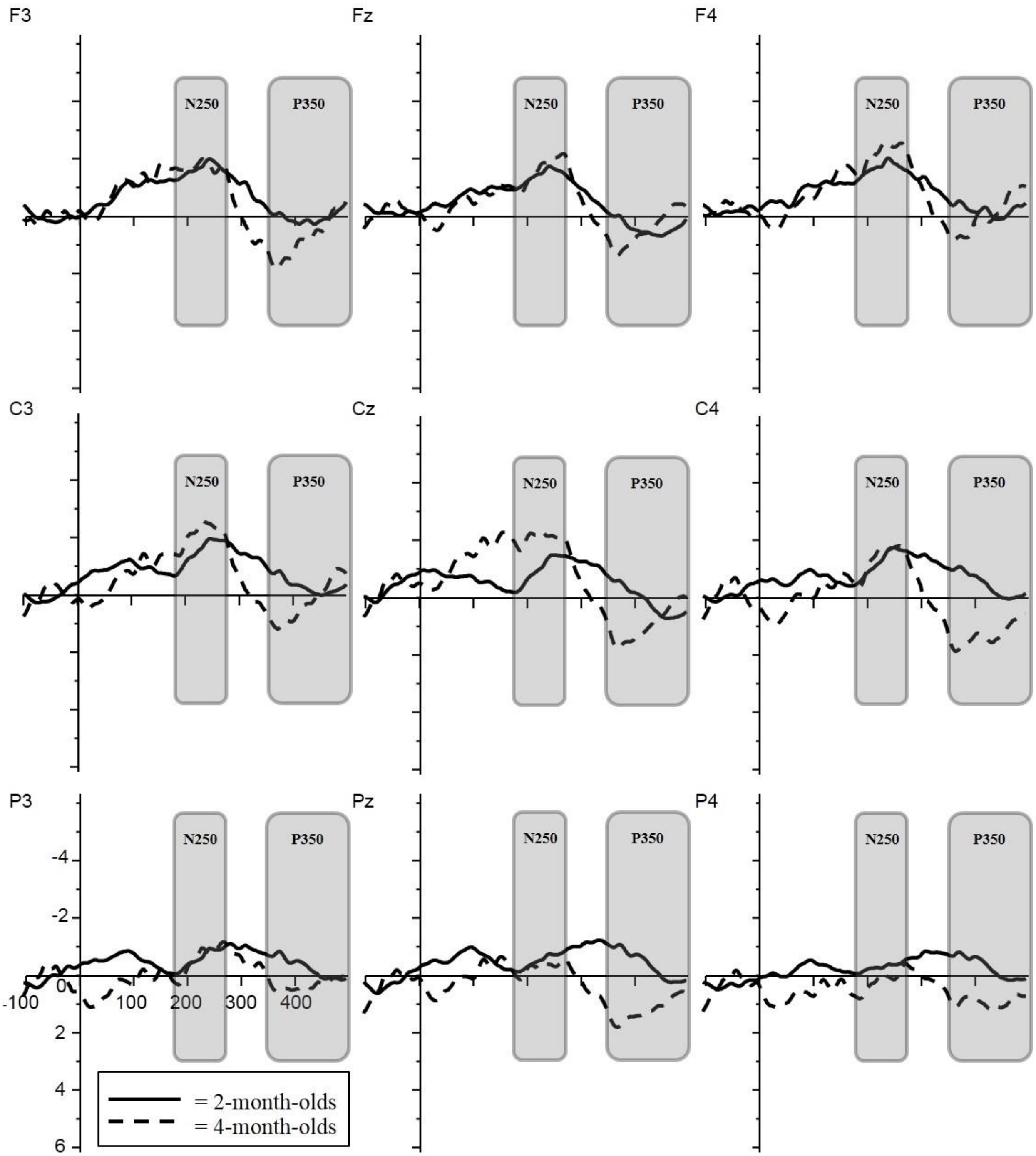
F3
Fz
F4
C3
Cz
C4
P3
Pz
P4
N250
P350
-4
-2
0
2
4
6
-100
100
200
300
400
= 2-month-olds
= 4-month-olds

Fig. 2

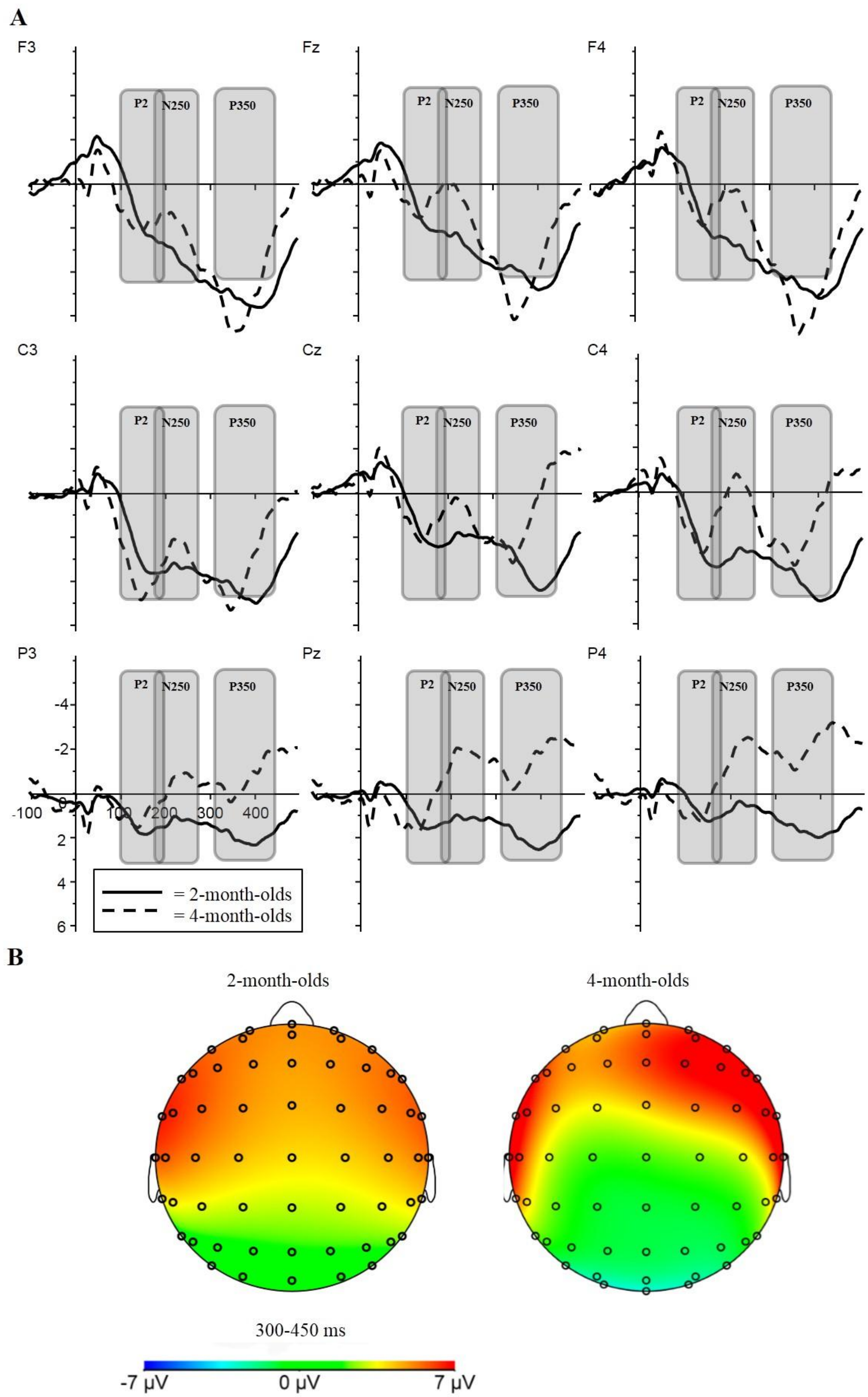
A
F3
Fz
F4
C3
Cz
C4
P3
Pz
P4
P2
N250
P350
-4
-2
0
2
4
6
-100
100
200
300
400
= 2-month-olds
= 4-month-olds
B
2-month-olds
4-month-olds
300-450 ms
-7 µV
0 µV
7 µV

Fig. 3

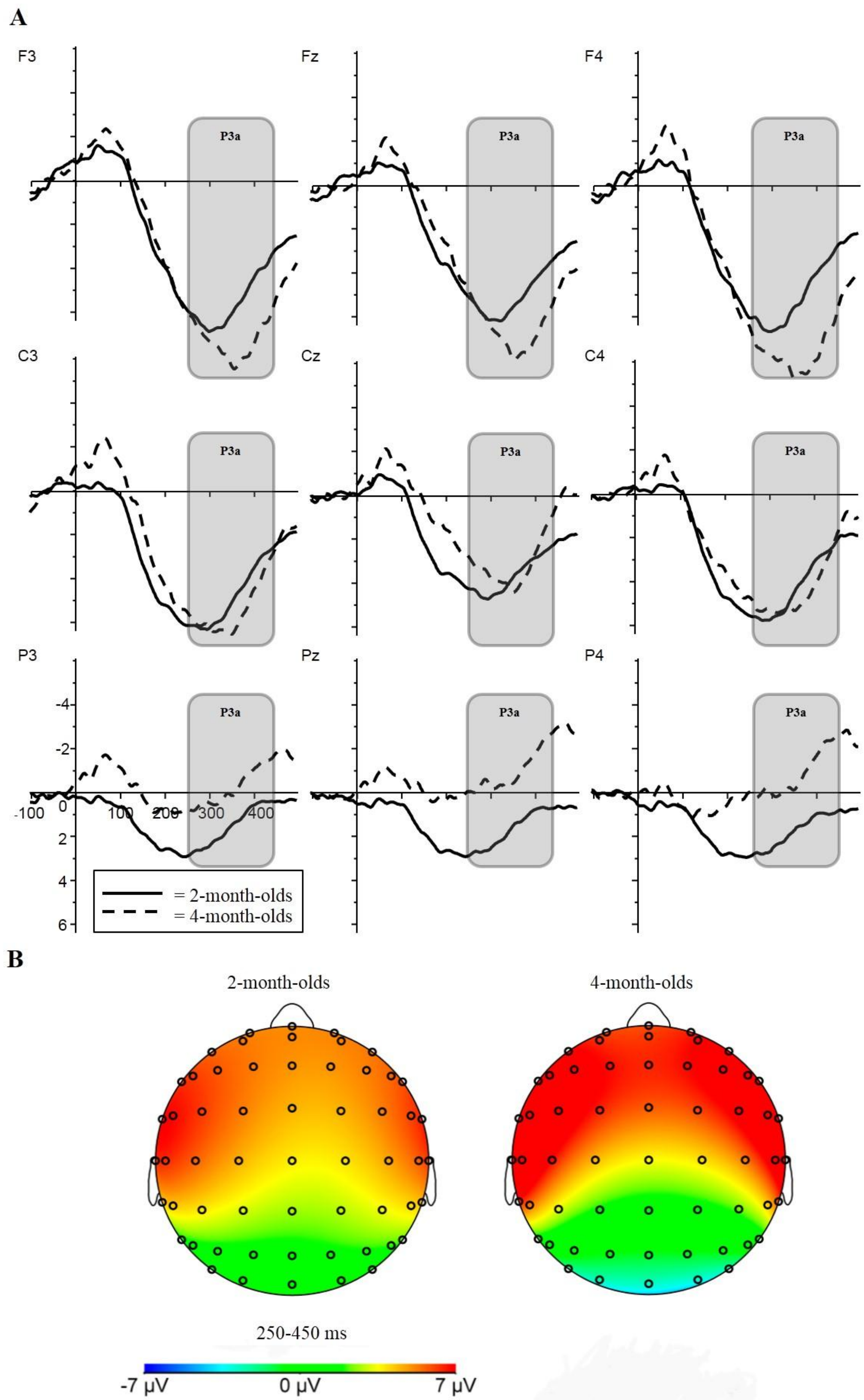
A
F3
Fz
F4
C3
Cz
C4
P3
Pz
P4
P3a
-4
-2
0
2
4
6
-100
100
200
300
400
= 2-month-olds
= 4-month-olds
B
2-month-olds
4-month-olds
250-450 ms
-7 µV
0 µV
7 µV

Fig. 4