Processing of horizontal sound localization cues in newborn infants

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Abstract

Objectives: By measuring event-related brain potentials (ERP) we tested the sensitivity of the newborn auditory cortex to sound lateralization and to the most common cues of horizontal sound localization.

Design: Sixty-eight healthy full-term newborn infants were presented with auditory oddball sequences composed of frequent and rare noise segments in four experimental conditions. We tested in them the detection of deviations in the primary cues of sound lateralization (interaural time and level difference) and in actual sound source location (free-field and monaural sound presentation). ERP correlates of deviance detection were measured in two time windows.

Results: Deviations in both primary sound localization cues as well as in the ear of stimulation elicited a significant ERP difference in the early (90-140 ms) time window. Deviance in actual sound source location (the free-field condition) elicited a significant response in the late (290-340 ms) time window.

Conclusions: The early differential response may indicate the detection of a change in the respective auditory features. We suggest that the late differential response, which was only elicited by actual sound source location deviation, reflects the detection of location deviance integrating the various cues of sound source location. Although the results suggest that all of the tested binaural cues are processed by the neonatal auditory cortex, utilizing the cues for locating sound sources of these cues may require maturation and learning.

1. Introduction

Locating the source of a sound is a fundamental ability of the auditory system. It requires the accurate and rapid evaluation of the direction-dependent cues generated by the head, the torso and external ears (King et al. 2001). Horizontal sound localization primarily depends upon two cues that stem from having two ears separated in space by the head with other monaural and binaural cues supplementing the main ones (Palmer and Grothe 2005). The interaural time difference (ITD) results from a longer sound path to the far ear when the sound is located off the midline, and is mostly useful at lower frequencies (below 1500 Hz), for which the wavelength is longer than the head width. Interaural level difference (ILD) results from the shadowing effect of the head causing an attenuation of the intensity with which the sound reaches the far ear. This cue is especially efficient at high frequencies (above 3000 Hz) for which the shadowing effect of the head is larger. Intensity difference between the two ears can be as high as 20 dB in adults (Bundy 1980; Clifton et al. 1988).

Adults use these binaural cues effectively, but young infants cannot perform precise localization based on these cues. Electrophysiological studies using auditory brainstem response (ABR) and middle latency response (MLR) techniques have revealed that although the neural mechanisms responsible for binaural processing are established at birth, they are immature (especially at higher stations of the brainstem) and require activity-based sensory experience for improved localization accuracy (Jiang and Tierney, 1996; Cone-Wesson, Ma and Fowler, 1997; King et al, 2001; for a review, see Fowler, 2004). Further, during the first months following birth, rapid change in head size takes place, which requires continuous recalibration of the auditory spatial

map of infants (Clifton et al. 1988; King et al. 2001). For instance, regarding the ITD value, a completely lateralized sound source causes a delay of about 411 µsec in neonates, which increases to 660 µsec by adulthood (Clifton et al. 1988). Although young infants' localization abilities have been shown to be imprecise (Clifton et al. 1988; Litovsky and Ashmead 1997), there exist some findings demonstrating that they are sensitive to the cues required for horizontal sound localization. Measured with a visual fixation paradigm, Bundy (1980) demonstrated that 16 week old infants could detect reversals in a 6-dB intensity difference between the two ears, although they were unable to accurately localize the leader sound. He also showed that 8 week old infants could detect the reversals of a 300-µsec time difference between the two ears, but they did not respond to the intensity cue, supporting observations that young infants appear to be more sensitive to interaural time than interaural level difference (Litovsky and Ashmead 1997).

Even newborn infants orient their heads toward the hemifield of a sound source (Muir and Field 1979; Clifton et al. 1981). However it is estimated that they can only detect an azimuth change of the sound source position exceeding 30° (Morrongiello et al. 1994). The minimum detectable angle (Mills, 1958) decreases to about 14° by 7 months (Litovsky and Ashmead 1997), reaching the adult level of 1° by 5 years of age (Litovsky 1997), showing a prolonged developmental trajectory for sound localization acuity during childhood.

One caveat of the behavioral measures is that it is difficult to study young infants' sound localization abilities before ~ 4 months of age, because, due to the maturation of higher cortical mechanisms that take place during the first three months, the head-orienting response cannot be reliably elicited before that age (Muir and Clifton 1985; Litovsky and Ashmead 1997). By measuring short-latency electrophysiological responses, such as ABR and MLR, previous results have indicated that the auditory pathways responsible for sound localization are functional at

birth (Jiang and Tierney, 1996; Cone-Wesson, Ma and Fowler, 1997; Furst et al., 2004). However, these responses do not provide information about later, higher-level processes.

Recording long-latency auditory event-related brain potentials (LAERPs) may allow one to bridge the gap between the two types of information. This non-invasive procedure allows one to investigate perceptual/cognitive abilities, such as auditory discrimination, right from birth. Auditory sensory discrimination can be studied in the so-called oddball paradigm in which acoustically or temporally deviant stimuli are embedded in a sequence of a repetitive sound (termed the "standard"). ERP responses elicited by the rare deviants can tell about whether they have been processed differently from the standards. That is, whether they triggered at least partially different neural activity than the standard sound. This method has been widely used to characterize auditory discrimination in infants and adults. When compared to the responses elicited by standards, deviant stimuli elicit a differential ERP component termed the mismatch negativity (MMN; Näätänen at al. 1978; for a recent review, see Näätänen et al. 2011), peaking over fronto-central scalp locations between 100 and 200 ms from stimulus onset in adults. Several studies showed that the amplitude of the MMN measure closely follows performance in behavioral discrimination both within and across individuals (for a review, see Näätänen and Alho 1997). In infants, including newborns, deviant stimuli elicit a morphologically different mismatch response (MMR), which however possesses the main characteristics of the adult MMN component (Alho et al. 1990; Kushnerenko et al. 2002; for a review, see Kushnerenko et al. 2013), including those necessary for assessing sensory discrimination (see, e.g., Novitsky et al. 2007). As newborns have been shown to be more sensitive to sounds with rich spectral contents as opposed to pure tones (Kushnerenko et al. 2007; Háden et al. 2013), in the current study, white-noise segments were delivered to them.

We addressed the question of whether newborn infants encode sound horizontal source localization related deviations by delivering to them two sounds in auditory oddball sequences and separately measuring the ERP responses to the rare and frequent sounds of the sequences. Assessing sensitivity to the primary cues of sound localization in the horizontal plane, we presented neonates with noise segments having ITD (Condition 1) or ILD (Condition 2) values corresponding to fully lateralized sound sources at the two sides. In each stimulus block, one ITD or ILD value appeared frequently and the other infrequently. Irrespective of the observed sensitivity to these primary cues, we also wished to assess, whether the newborn auditory cortex distinguishes widely different sound source locations in the azimuth. Therefore, we delivered two more conditions with more ecologically-valid stimulation. In the free-field (FF) condition, we presented noise segments to neonates with two loudspeakers located at 45 degrees on each side in front of the infant (Condition 3). Finally, we also presented neonates with noise segments monaurally (MA) through earphones (Condition 4). In each stimulus block, sounds appeared frequently at one side and infrequently at the other side. Starting from the results of the short-latency electrophysiological measures on sound localization in young infants (Jiang and Tierney, 1996; Cone-Wesson, Ma and Fowler, 1997; Furst et al., 2004), we hypothesize that both the individual binaural cues of sound location as well as actual source location is further processed in the neonatal auditory cortex. This innate cortical sensitivity to sound source location would be reflected in significant differences between the ERP responses elicited by the rare and the frequent sounds (MMR elicitation) in all four stimulus conditions. In adults, lateralized sounds elicit higher-amplitude responses over the contralateral hemisphere because of the higher proportion of crossed than uncrossed afferent pathways in the human auditory system (Adams 1979). Further, the MMR typically peaks over fronto-central scalp locations (Kushnerenko et al.,

2013). Therefore, we hypothesized that the scalp distributions of the responses elicited in the current experiment would show these characteristics.

2. Materials and methods

2. 1. Participants

The demographic and birth statistics of participant groups are listed in Table 1. Only healthy infants born to term with an Apgar score of at least 9 were admitted to the study. The recordings were carried out in a dedicated experimental room at the Department of Obstetrics-Gynaecology and Perinatal Intensive Care Unit of the Military Hospital, Budapest after informed consent was obtained from one or both parents. The mother of the infant could opt to be present during the recording. The study was conducted in full accordance with the Helsinki Declaration and it was approved by the relevant ethics committees: ETT-TUKEB, Hungary.

The measurement was done during day 1 to 3 postpartum. During the auditory stimulation the infant was lying on her or his back in an infant cot with a shaped pillow holding her head in position. The experiment was terminated if the infant became fussy or cried for several minutes or the mother decided to stop the measurement. Some infants' data were discarded due to excessive number of artefacts – see Table 1 and the "Data analysis" section for details of artefact rejection.

2. 2. Stimuli

In all Conditions, sleeping newborns were presented with frozen white-noise segments (200-ms duration with 5-ms rise and fall times, 80 dB sound pressure level [SPL]) in an auditory oddball paradigm (750 ms stimulus onset asynchrony [SOA]). The paradigm consisted of one stimulus block in which one of the two sounds occurred infrequently (12.5%) and the other frequently

(87.5%), and a reversed block in which the roles of the two sounds were exchanged. 1500 sounds were presented in each stimulus block. The order of the blocks was randomized across newborns. The oddball sound sequences were played by the E-Prime software (Psychology Software Tools, Inc., Pittsburgh, PA). In Conditions 1, 2, and 4, the noise segments were presented binaurally through ER-1 earphones (Etymotic Research Inc., Elk Grove Village, IL, USA) connected via sound tubes to self-adhesive ear-couplers (Natus Medical Inc., San Carlos, CA, USA) placed over the infants' ears. Sound pressure levels were calibrated by a Head Acoustics HSU III.2 HEAD-Shoulder Unit, while sounds were delivered by the same equipment as in the experiment. In Condition 1 (ITD), the sounds were presented with a 385-microsecond delay in one ear compared to the other ear (and vice versa). In Condition 2 (ILD), the sounds were presented with the intensity at one ear being 8 dB greater than at the other ear (80 and 88 dB SPL) and vice versa. In Condition 4 (MA), the sounds were presented to one or the other ear. In Condition 3 (FF), the noise segments were delivered by one or the other loudspeaker (SBS A40 USB Speakers, Creative Labs Ltd., Dublin, Ireland). The two loudspeakers were located in front of the infant at a 45-degree angle at each side at a distance of 80 cm from the infant's head on the same horizontal plane.

2. 3. Procedure and EEG recording

EEG was recorded with Ag/AgCl electrodes attached to the scalp at the F3, Fz, F4, C3, Cz, C4, P3, Pz and P4 locations according to the International 10-20 System (Jasper 1958). The common reference electrode was placed on the tip of the nose and the ground electrode on the forehead. Eye movements were monitored bipolarly between an electrode placed lateral to the outer canthus of left eye and Fp1. EEG was recorded with 24 bit resolution at a sampling rate of

1000 Hz by a direct-coupled amplifier (V-Amp, Brain Products, Munich, Germany). The signals were on-line low-pass filtered at 110 Hz.

2. 4. Data analysis

EEG was filtered off-line between 1 and 30 Hz. For each stimulus, an epoch of 600 ms duration including a 100 ms pre-stimulus interval was extracted from the continuous EEG record. Epochs with a voltage change exceeding100 µV on any EEG or EOG channel were rejected from further analysis. The remaining epochs were baseline-corrected by the average voltage in the 100 ms pre-stimulus period and averaged separately for each stimulus type and block (2 x 2 bins). Only data from infants with at least 85 artifact-free trials in each bin were included in the statistical analysis. Electrodes located at corresponding left and right scalp locations were exchanged as necessary to produce an ipsilaterally- vs. contralaterally-lateralized electrode montage with respect to the laterality (for the ITD/ILD condition, cue-based laterality) of each sound. Standard and deviant ERP responses were then separately merged from the two stimulus blocks with reversed roles for the two sounds. This resulted in both the averaged standard and the deviant ERP response being composed of responses to both left- and right-lateralized sounds. The mean number of artifact-free trials per infant was then 1901 and 271 for standards and deviants, respectively in Condition 1, 1783 and 253 in Condition 2, 1700 and 238 in Condition 3, and 1894 and 270 in Condition 4.

For amplitude measurements in all four stimulus conditions, two 50-ms-long time windows were selected based on the grand-averaged waveforms obtained at the Cz electrode. One window was centered on the negative peak in the 90-140 ms latency range and the other on the positive peak in the 290-340 ms latency range. The effects of Condition and Stimulus type and their possible

interactions with the scalp locations were analyzed with four-way mixed-design analyses of variance with Condition as the grouping variable (ANOVA: Condition [ITD vs. ILD vs. FF vs. MA] × Stimulus type [Standard vs. Deviant] × Frontality [Frontal vs. Central vs. Parietal] × Laterality [Ipsilateral vs. Middle vs. Contralateral]). Greenhouse-Geisser correction of the degrees of freedom was applied where appropriate, and the ε correction factors as well as the η_p^2 effect sizes are given in the text. ANOVA results were further specified by Tukey's HSD post hoc tests. All significant results are described.

3. Results

Figure 1 shows the group-averaged ERP responses, while Figure 2 shows the response from one representative infant elicited by the deviant and standard stimuli at nine different electrode sites in the four experimental conditions. The first ANOVA was aimed at analyzing the differences between the mean amplitudes of the ERP responses elicited by the standard and deviant stimuli measured from the 90-140 ms latency range in all four stimulus conditions. Scalp distribution related results were analyzed for assessing possible contralaterality of the responses and conformity to the typical MMR response. The ANOVA yielded a significant main effect of Frontality ($F(2, 128)=7.44$, $p<0.01$, $\eta_p^2=0.1$, $\varepsilon =0.68$), and Laterality ($F(2, 128)=17.43$, $p<0.001$, $\eta_p^2=0.21$), as well as significant Condition × Stimulus type ($F(3, 64)=2.88$, $p=0.04$, $\eta_p^2=0.12$), Condition × Laterality ($F(6, 128)=2.4$, $p=0.03$, $\eta_p^2=0.1$), Frontality × Laterality ($F(4, 256)=3.84$, $p=0.01$, $\eta_p^2=0.06$, $\varepsilon=0.8$), and Condition × Stimulus type × Frontality ($F(6, 128)=2.86$, $p=0.01$, $\eta_p^2=0.12$) interactions. Post-hoc tests showed that responses measured at middle electrode sites were more negative than those measured from lateral electrodes at both sides ($p<0.001$) in Condition 3 (FF) and from ipsilateral electrodes ($p=0.03$) in Condition 4 (MA). The deviants of

MA Condition elicited responses with positive amplitude which differed significantly from the negative amplitude responses elicited by the deviants of ITD Condition (p=0.04). Tukey's post-hoc tests for the three-way interaction revealed that as compared to standards, deviants elicited more positive responses over parietal scalp locations in the ITD Condition (all p<0.05), more negative responses over frontal and parietal sites in the ILD Condition (all p<0.05), and more negative responses over all scalp locations in the MA Condition (all p<0.05). These ANOVA results showed that in the early latency range the neonatal auditory system differently responded to the standard and deviant stimuli in the three of the four stimulus conditions. The three-way interaction is depicted on Figure 3.

The second ANOVA was aimed at analyzing the differences between the mean amplitudes of the ERP responses elicited by the standard and deviant stimuli measured from the 290-340 ms latency range in all four stimulus conditions. The possible interactions of the MMR and scalp distributions in each condition were also analyzed to assess the possible differences in the amplitude distribution of the MMR over the scalp. The ANOVA yielded significant main effects of Condition ($F(3, 64)=7.56$, $p<0.001$, $\eta_p^2=0.26$), Frontality ($F(2, 128)=42.34$, $p<0.001$, $\eta_p^2=0.4$, $\varepsilon=0.8$), and Laterality ($F(2, 128)=29.88$, $p<0.001$, $\eta_p^2=0.32$, $\varepsilon=0.82$), as well as significant Condition × Frontality ($F(6, 128)=5.05$, $p<0.001$, $\eta_p^2=0.19$), Condition × Laterality ($F(6, 128)=5.72$, $p<0.001$, $\eta_p^2=0.21$), Frontality × Laterality ($F(4, 256)=17.09$, $p<0.001$, $\eta_p^2=0.21$, $\varepsilon=0.61$), Condition × Frontality × Laterality ($F(12, 256)=7.46$, $p<0.001$, $\eta_p^2=0.26$), and Condition × Stimulus × Frontality ($F(6, 128)=4.19$, $p<0.001$, $\eta_p^2=0.16$) interactions. Post-hoc tests showed that noise segments elicited the highest-amplitude responses in the ITD Condition, which differed significantly from the responses measured in the ILD Condition (p=0.04). Further, ERP responses in the MA Condition had the lowest amplitude and they differed significantly from

those measured in the ITD (p<0.001) and the FF Conditions (p=0.02). Responses measured at middle electrode sites were more positive than those measured from lateral electrodes over either hemisphere (p<0.001) in Condition 1 (ITD) and Condition 2 (ILD). Compared to frontal scalp locations, all stimuli elicited more positive responses over central and parietal sites in ITD (p<0.001) and ILD Conditions (p<0.02); and more positive responses over parietal sites in FF Condition (p<0.001). Only the Condition × Stimulus × Frontality three-way interaction was investigated further, because we were primarily interested in assessing the effects of the laterality changes (represented by the Stimulus factor): in the FF, but not in any other Condition, deviants elicited more positive responses than standards at any electrode site (all p<0.05), except that responses elicited by deviants over frontal sites did not significantly differ from those elicited by standards over parietal sites. The ANOVA results showed that, in the late latency range, the neonatal auditory system differently responded to the standard and deviant stimuli in the FF condition, and that the distribution of the MMR was not lateralized. The Condition × Stimulus × Frontality three-way interaction is depicted on Figure 4.

4. Discussion

To the best of our knowledge, this is the first study investigating by ERPs whether the newborn auditory cortex encodes changes in binaural sound localization cues. We found that 1) deviations in both primary sound localization cues as well as deviance in the ear of stimulation elicited a significant response in the early (90-140 ms) latency range 2) only real sound location deviance elicited a significant response at the late (290-340 ms) latency range. These results suggest that all of the deviations tested were encoded by the neonatal brain.

ITD deviants elicited an early positive differential response over parietal sites. In contrast, ILD and ear of stimulation deviants elicited negative differential responses of more central scalp

distribution in the same latency range. The latter polarity and scalp distribution is similar to the early negativity observed by several previous ERP studies in neonates for spectrally rich deviant sounds (Kushnerenko et al. 2007, 2013). Therefore, although Bundy (1980) found no evidence for sensitivity to change in ILD until 16 weeks of age as measured with a visual fixation paradigm, we can conclude that the neonatal auditory cortex is sensitive to deviation in ILD and the ear of stimulation. Presenting the sounds monaurally (Condition 4) created a large acoustic difference between the standard and deviant sounds, thus making it easier for the auditory system to detect the deviations. This is reflected in the more robust negative deflection in the early time window. In contrast, no previous study has described an early positive parietally maximal differential response to auditory deviance. Therefore, replication of the current ITD-deviance related response is needed before accepting the conclusion that the neonatal brain is sensitive to ITD deviations.

In Conditions 1, 2 and 4, we did not observe a significant difference between the standard and deviant responses in the late time window. In contrast, in the free-field (FF) condition, we obtained the opposite pattern of results: in the earlier time window, the responses elicited by the deviants and standards did not significantly differ from each other. However, FF deviants elicited a robust positive difference response in the 290-340 ms latency range. This response is similar to the "central positivity" described in many previous ERP studies of neonatal sound discrimination (Kushnerenko et al. 2007, 2013). Thus we conclude that the newborn brain encodes changes in sound source location.

How can one explain the differences between the two patterns of results? Let us assume that the late difference represents the detection of change in sound source location. This suggests that although newborn infants process at least some of the binaural localization cues, subsets of these

cues are not necessarily sufficient yet for horizontal sound localization. One should note that although the ERP technique enables us to gain insights into auditory processing abilities at an age at which one cannot easily observe behavioral consequences of these processes, it cannot tell us whether newborns indeed perceived the sounds as lateralized. Thus sensitivity to some cues of sound lateralization does not necessarily mean that the presence of these cues evokes the perception of a lateralized auditory source. In contrast, when the sounds were presented via loudspeakers, the ITD and ILD cues might have been less saliently separated (i.e., the loudspeakers were not fully lateralized, the background noise in the room may have reduced the S/N ratio). Therefore, separately they might have been insufficient for the neonatal auditory system to detect deviations in them and thus to generate the early differential response. (Alternatively, the opposite-polarity differential responses observed for the two main cues may have resulted in a null result.) However, in the FF condition, all localization cues (ITD and ILD, as well as the other cues of sound localization (King et al. 2001)) were congruently aligned. This congruency may have been sufficient for at least an approximate localization of the sound source. The results obtained in the FF Condition then suggest that the neonatal auditory system may need redundant information from multiple cues to achieve sound source localization. This explanation is also compatible with observations suggesting that the early negative difference response probably reflects feature processing, whereas later responses probably index more holistic and categorical representations of the auditory input (Kushnerenko et al. 2007).

In adults, lateralized sounds elicit higher-amplitude responses over the contralateral hemisphere (e.g., the N1 response; Näätänen and Picton 1987). This is caused by the higher proportion of crossed than uncrossed afferent pathways in the adult auditory system (Adams 1979). No sign of contralateral dominance was apparent in the neonatal ERP responses. The laterality effects

observed in the present data were caused by higher ERP amplitudes at the midline that at lateral electrodes. It is possible that the contralateral dominance appears together with the ontogenetically later emergence of the P1-N1-P2 sequence of auditory components that characterizes the late exogenous auditory ERP response in adults. The lack of contralateral dominance in neonates may be a sign of immaturity of the neonatal auditory pathways (Moore et al. 1995). Results of animal studies have suggested that contralateral dominance is not an innate feature of the auditory system. For example, in rodents, contralateral dominance starts to emerge 49-51 days after birth (Mrsic-Flogel et al. 2006). However, there is no comparable evidence from infants and children. A recent magnetoencephalographic (MEG) study found contralateral dominance at 6 years of age, when the auditory system still produces immature cortical responses (Mäenpää 2013). Thus the developmental trajectory of contralateral dominance in the auditory system requires further research.

The fetus in utero receives sounds by bone conduction which means that there is no interaural sound difference until birth (Graven and Browne 2008). The mother's tissues and the amniotic fluid also establish a specific environment for the fetus filtering out most high-frequency sounds in the uterus (Graven and Browne 2008). Moreover, the small size of the head and external ear of the newborn may also bias their sound localization toward higher frequencies and reduce the effectiveness of the time difference cue (Clifton et al. 1988; Werner 2002). From birth onwards, a rapid growth of the head size occurs requiring a continuous recalibration between the interaural cue values and the actual location of sound sources. This implies that the development of the sound localization requires learning and adaptation during infancy (Clifton et al. 1988; Litovsky and Ashmead 1997; Werner 2002). Here we have shown that although sound localization accuracy may be poor within the first months (Morrongiello 1988; Litovsky 1997; Litovsky and

Ashmead 1997), the newborn auditory cortex shows sensitivity to different types of binaural sound localization cues.

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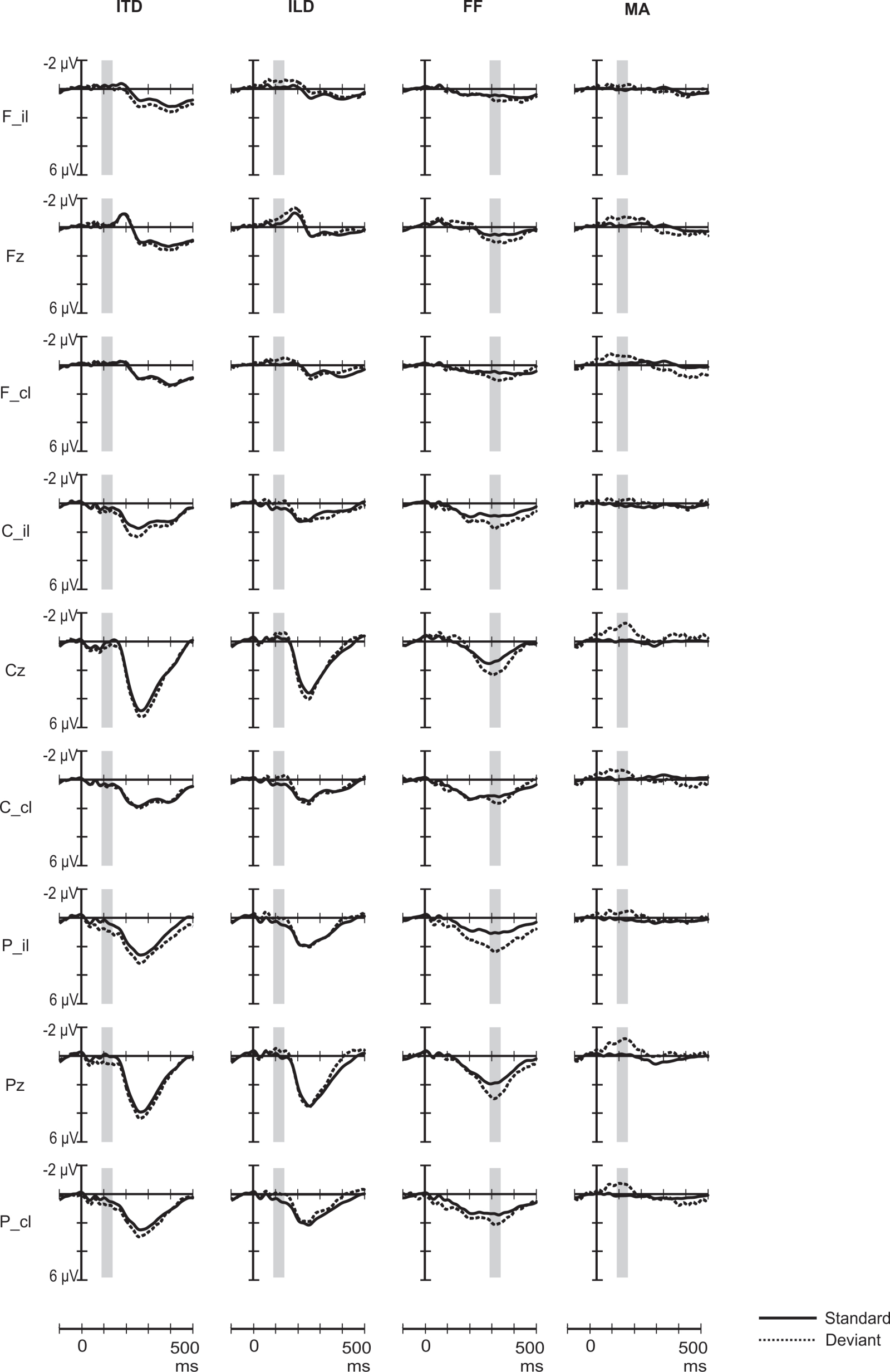
List of figures:

Figure 1. Group average AERP responses recorded from 9 different scalp locations (frontal ipsilateral [F_il], frontal midline [Fz], frontal contralateral [F_cl], central ipsilateral [C_il],
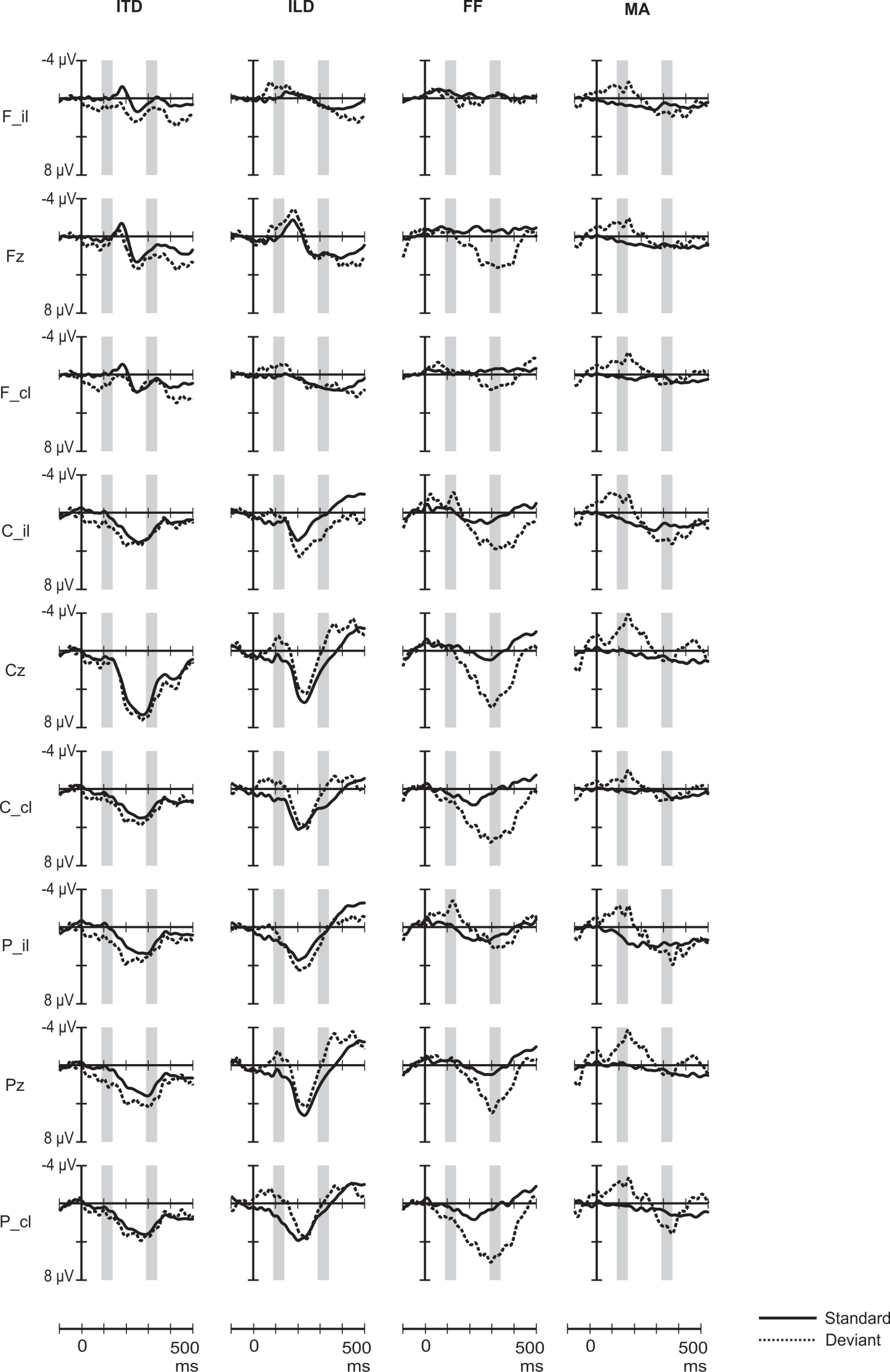
central midline [Cz], central contralateral [C_cl], parietal ipsilateral [P_il], parietal midline [Pz], and parietal contralateral [P_cl] in the four experimental conditions (Interaural time difference [ITD, first column], Interaural level difference [ILD, second column], Free-field [FF, third column], and Monaural [MA, fourth column]), elicited by the frequent (standard) sounds (solid line) and the deviant sounds (dashed line). Amplitude calibration is at the left column, time calibration below the bottom row. Sound onset is at the crossing of the two axes (time zero). The amplitude measurement windows (90-140 ms and/or 290-340 ms) with significant difference between the deviant and the standard ERP are indicated by grey bars.
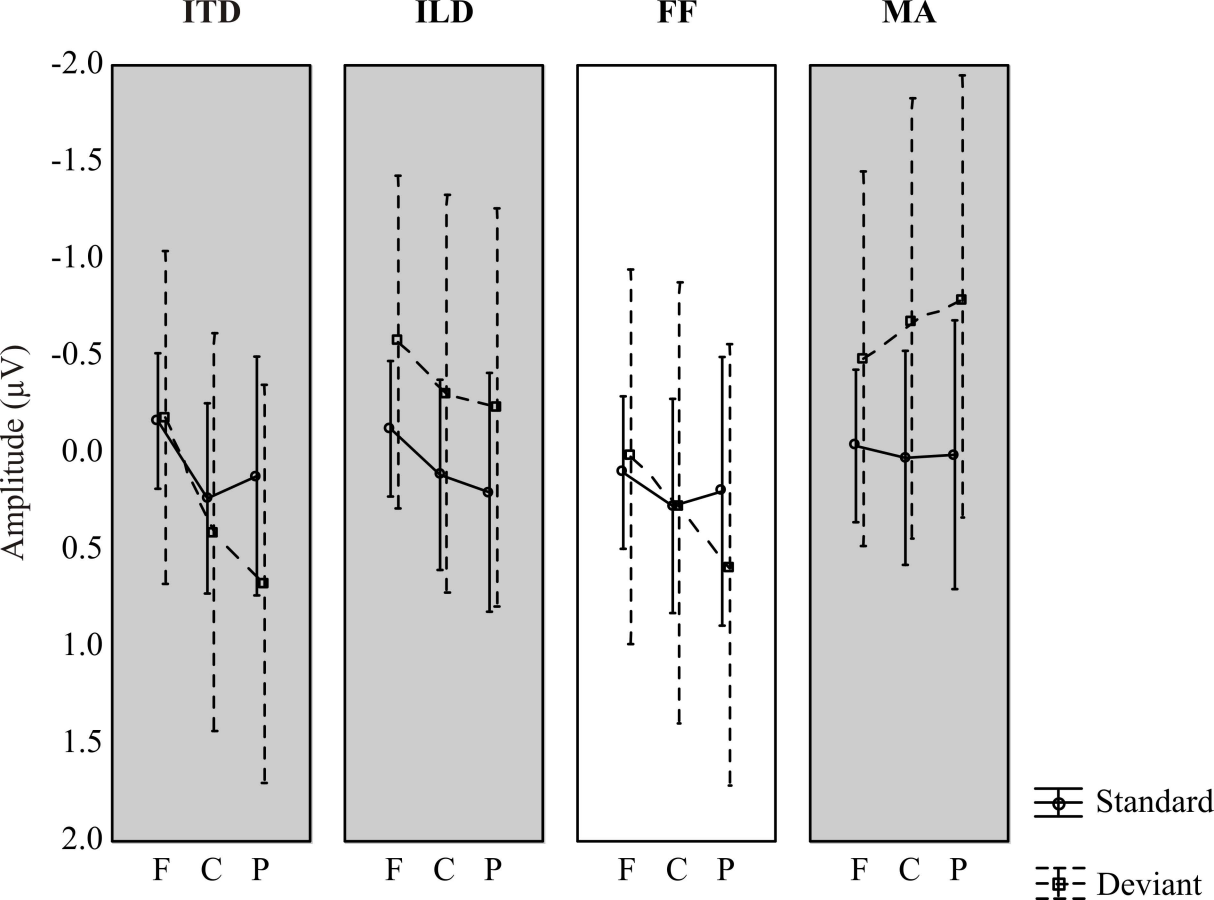
Figure 2. Mean AERP responses for one representative infant recorded from 9 different scalp locations (frontal ipsilateral [F_il], frontal midline [Fz], frontal contralateral [F_cl], central ipsilateral [C_il], central midline [Cz], central contralateral [C_cl], parietal ipsilateral [P_il], parietal midline [Pz], and parietal contralateral [P_cl] in the four experimental conditions (Interaural time difference [ITD, first column, infant code: 0402], Interaural level difference [ILD, second column, infant code: 0422], Free-field [FF, third column, infant code: 0634], and Monaural [MA, fourth column, infant code: 0549]), elicited by the frequent (standard) sounds (solid line) and the deviant sounds (dashed line). Amplitude calibration is in the left column, time calibration below the bottom row. Sound onset is at the crossing of the two axes (time zero). The amplitude measurement windows (90-140 ms and 290-340 ms) are indicated by grey bars. [Note that due to the somewhat higher voltage range of the individual responses, the amplitude calibration differs from Figure 1.]

Figure 3. Three-way interaction between Condition (boxes from left to right: ITD, ILD, FF, MA), Stimulus type (Standard [solid line], Deviant [dashed line]), and Frontality (from left to right within each box: frontal [F], central [C], and parietal [P]) for mean amplitudes measured from the 90-140 ms time window. The standard deviation is shown for each measurement. Amplitude calibration is shown on the leftmost box. Those conditions for which post-hoc tests showed significant Stimulus type * Frontality effects are marked by shading the corresponding box.

Figure 4. Three-way interaction between Condition (boxes from left to right: ITD, ILD, FF, MA), Stimulus type (Standard [solid line], Deviant [dashed line]), and Frontality (from left to right within each box: frontal [F], central [C], and parietal [P]) for mean amplitudes measured from the 290-340 ms time window. The standard deviation is shown for each measurement. Amplitude calibration is shown in the left column. Those conditions for which post-hoc tests showed significant Stimulus type * Frontality effects are marked by shading the corresponding box.

	ITD	ILD	FF	MA
F_il				
Fz				
F_cl				
C_il				
Cz				
C_cl				
P_il				
Pz				
P_cl				

—— Standard

······ Deviant

	ITD	ILD	FF	MA
F_il	-4 µV / 8 µV			
Fz	-4 µV / 8 µV			
F_cl	-4 µV / 8 µV			
C_il	-4 µV / 8 µV			
Cz	-4 µV / 8 µV			
C_cl	-4 µV / 8 µV			
P_il	-4 µV / 8 µV			
Pz	-4 µV / 8 µV			
P_cl	-4 µV / 8 µV			

0   500 ms   0   500 ms   0   500 ms   0   500 ms

—— Standard
······ Deviant