Preterm infants voice processing is mediated by voice familiarity

Manuela Filippa[1,2]*, Damien Benis[2,]*, Alexandra Adam-Darque[3], Petra S. Hüppi[1], Didier Grandjean[2]

[1] Division of Development and Growth, Child and Adolescent Department, University of Geneva, Geneva, Switzerland

[2] Swiss Center for Affective Sciences, Department of Psychology and Educational Sciences, University of Geneva, Geneva, Switzerland

[3] Laboratory of Cognitive Neurorehabilitation, Department of Clinical Neuroscience, Division of Neurorehabilitation, University Hospital of Geneva and University of Geneva, Geneva, Switzerland

Abstract

Understanding how prematurity and language or voice familiarity impact on language perception at birth becomes crucial to determine which brain regions support language processing at this age, and how an atypical early sensory experience affects language-related brain areas. However, the time-frequency correlates of maternal voice processing remain to date unknown.

Ten preterm and ten full-term newborns underwent EEG recordings during the presentation of their mother's or a stranger's speech. The speech could be naturalistic (presented in the forward order) or non-naturalistic (in the backward order). Time-frequency decomposition was performed and task-related responses were analyzed following a topographical data driven clustering using General Linear Mixed model approaches.

Differential responses were observed in left and right temporal areas. In the left-temporal areas, a specific processing of the naturalistic mother compared to stranger speech was observed in low-frequency bands (theta and alpha bands), but taking antagonistic forms in the two groups i.e. a power increase for full-term and a power decrease (theta) or maintenance (alpha) in preterm babies. Left-temporal low-beta activity presents, in full-term babies, in the forward condition, a power increase for the maternal voice and a power decrease for the stranger voice, which were not observed in preterm babies. In the right-temporal scalp area, we observed in the low-beta and low-gamma bands a mother forward specific power-decrease in the preterm population specifically, with higher values for the mother backward, while terms were mostly activated by the most unfamiliar stimulus, the stranger backward voice.

The current study shows, through complex time-frequency patterns, that the naturalistic mother voice elicits expected brain responses in the full-term newborns, which were different from the preterm's ones, both in the left and right temporal areas.

Introduction

Preterm newborns, at term equivalent age, show atypical auditory processing when compared to full-terms (Therien, Worwa, Mattia, & Raye-Ann, 2004). They use additional cortical regions involved in voice processing in fMRI when compared to their pair at term, and show a late mismatch response for maternal voice (Adam-Darque et al., 2020). In particular, they tend to process mother and stranger's voices more similarly, than their pairs at term do (Adam-Darque et al., 2020; Therien et al., 2004).

In the long-term preterm children are much more at risk of developing language problems than their term peers and about one third of them have a significant delay in language acquisition by the age of 3 (Sansavini et al., 2010). Which are the key altered components in auditory development, constituting early markers of long-term atypical auditory development, is still under debate.

As preterm newborns showed also differential responses to vocal emotional stimuli when compared to their peers born at term (Kostilainen et al., 2020), we hypothesize that an altered prosody perception, together with an altered perception of a salient and familiar voice, are potential key markers for assessing early auditory atypical development in the preterm infant's population.

To investigate the role of prosody perception in newborns, an efficient paradigm is the comparison between FW (FW) and BW (BW) speech. FW and BW speech share multiple acoustic characteristics. Firstly, they have the same average in intensity, pitch and spectral characteristics. This homogeneity between the two stimuli guarantees that the differential perception in newborns is not an effect of the arousal and it is not due to the acoustical parameters *di per se*, but to their dynamic organization changes in time, thus to their prosodic structure.

Several studies presented newborns with the paradigm FW versus BW speech with the aim of evaluating the differential brain and behavioral responses to linguistic (FW) or non-linguistic (BW) vocal stimuli. It is known that infants can discriminate between two languages, only if they are presented FW (Mehler et al.). Peña and colleagues (Pena et al., 2003) found greater activation to FW than to BW speech in newborns, only in the left hemisphere, in particular in the left ventral-anterior temporal cortex. Sato and colleagues (Sato et al., 2012) found a predominance of the left hemisphere for the FW versus BW speech, but only in the newborn's native language, being language familiarity a key element for FW versus BW discrimination. The same lateralization has been found in 3-month-old infants, with a dominant activation in the left angular gyrus for FW speech (Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2002).

Brain mechanisms related to the role of the language familiarity in speech processing have been systematically investigated at early stages of development using EEG. Peña and colleagues (Peña, Pittaluga, & Mehler, 2010) showed that young infants' exposure to familiar language induced an increase in gamma response (55-75 Hz) compared to non-familiar language. They also showed that the latency of an anterior central ERP positive component, at 200ms after the onset of stimuli, was shorter for full terms at 6 compared to 3 months of age, and shorter for preterms for the 9 compared to 6 months. Authors conclude that brain maturation constrains the impact of experience on language acquisition during the firstmonths of life.

How preterm born infants process linguistic, FW speech, versus non-naturalistic vocal stimuli, BW speech, and whether this processing is modulated by voice familiarity (mother vs stranger) has still not been investigated.

In the present study we aim, thus, to investigate the temporal dynamics in different frequency bands of the newborn's perception of naturalistic (FW) and non-naturalistic (BW) speech stimuli when presented by familiar (mother) and unfamiliar voices, and to assess the influence of prematurity on these spectral modulations.

We hypothesize that FW maternal voice would activate brain areas engaged in the voice recognition of native language more than BW unfamiliar speech in term infants. We further hypothesize that these discrimination abilities are not equally evident in the preterm newborn's brain at term equivalent age.

Material and methods

Population

A total of 20 infants, 10 preterm (mean gestational age at birth = 29.1 weeks, 12 preterm), and 10 at term (mean gestational age=39.9 weeks, SD=1.2 weeks) were included in the study. Full-term infants were tested between the second and fifth days of life, whereas preterm infants at term-equivalent age (mean age at test = 41weeks, SD=0.9 weeks). All infants were born to French-speaking mothers at the University Hospital of Geneva. Infants with severe neurological complications such as brain injury including periventricular leukomalacia and intraventricular hemorrhage and those with hearing or other developmental problems were excluded from the study. From birth to the stabilization phase (up to 32-34 weeks of gestation), premature infants were hospitalised in a private, then semi-private room.

The study was approved by the institutional ethics review board of the University Hospital of Geneva. All informed consents for participation in the study were obtained from the parents.

Procedure

The maternal voices were recorded in a soundproof room, with a noise floor <25 dBA, with the following fixed parameters: signed 16-bit PCM wave, 44 100 Hz, 705 kbps, mono. Voices were normalized to ensure homogeneity of intensities through the Goldwave Inc. software program. Notice that in each vocal track the dynamic envelopes of amplitudes and intensities were kept unchanged. For the BW condition phrases were reversed using the software program MATLAB (MathWorks Inc.).

Term and preterm newborns were exposed to the French words "pleure pas" ("do not cry" in English), in FW and BW forms, pronouced by the mother or a stranger. All audio files had the same length of 1250 ms and the voice presentation began after 17 ms of silence. The mean word duration was 716 ms (SD=136 ms). Sounds were presented in a pseudocasual order for 100 trials in each EEG condition. The interval between stimuli varied randomly from 1500 to 2500 ms. Data were collected while the newborns were in a state of sleep or quiet rest without any sedation, and they were fed prior to testing to facilitate falling asleep before and during data collection. The voice of the unfamiliar mother varied for each infant, and was the voice of the previousely included mother.

The present study is a part of a larger research involving both EEG and fMRI techniques (Adam-Darque et al., 2020).

EEG data acquisition and pre-processing

A 128-channel Hydrocel Geodesic Sensor Net® sensor (Electrical Geodesics Inc., Eugene, OR, USA), was used for EEG data acquisition, with a sampling rate of 1000 Hz and a recording reference at the vertex (Cz electrode). Impedances were kept below 30 kΩ during recording. Data were filtered between 1 and 30 Hz and redirected to the common mean reference. Signals that had ocular and motion artifacts were discarded by visual inspection. For each subject and condition, data were then averaged from -100 ms before sound onset to 1000 ms after. A baseline correction from -100 to 0 ms was performed. In subsequent danalysis steps, peripheral channels located on the infant's cheeks and in the nape of the neck were excluded, thus bringing the channels from 128 to 109. Finally, a 3D-spline manipulation process allowed interpolation of the bad signals.

EEG preprocessing

Preprocessing of EEG data was performed on Brainvision Analyzer (Brain Products GmbH). After data filtering (0.5Hz high-pass filter) and resampling (256Hz), bad channels were interpolated (using spline interpolation), and an average reference was applied to the data. Data was then imported to the Fieldtrip MATLAB toolbox and epoched using a 4 second window centered on the voice onset. Strongly artifacted epochs were rejected (peak to peak amplitude above 400µv). Eye -movement and heart-rate artifacts were removed using an infomax Independent Component Analysis. A standard time-frequency decomposition procedure was then performed separately for high (60–100 Hz, multitaper) and low-frequency responses (2–40 Hz, hanning single taper) in steps of 50ms using the Fieldtrip toolbox. For low frequency response (2–40 Hz), we used a single hanning taper decomposition with an adaptative time window (6 cycles) at frequencies for 2 to 40 Hz with a 1Hz step. For high frequency responses (60–100 Hz), time-frequency decomposition in a 400 ms time window using seven discrete slepian tapers at frequencies for 60 to 100 Hz with a 5Hz step. The decomposition was performed on the whole 8s epoch length to decrease the influence of border effects, however in the analyses, only the time period from -0.5 pre-voice onset to 1s post-voice onset was statistically analyzed. Baseline correction was performed for each trial by subtracting the average power obtained in a 500ms period prior to sound onset. An additional artifact rejection was then performed, using for each channel a threshold of the mean + 1.96std of the mean power along trial-length on the whole trial pool in the 2-20Hz, 20-40Hz and 60-100Hz bands (around 13% of trials rejected).

Topographical clustering

For dimension reduction purposes, we opted, in the current analysis, for a canonical frequency bands approach already used in infants around the age-period of the babies recorded in the current study (Attaheri et al., 2022). It should be noted that the boundaries of frequency bands in babies are not currently well-defined and significant differences are present between studies (Saby & Marshall, 2012). The relevance of the frequency bands boundaries used in the current study were then confirmed by visual inspection of the actual time-frequency patterns obtained in the current study which seem to organize around the canonical frequency bands observed in adults (Delta: 2-4Hz, Theta: 4-8Hz; Alpha: 8-12Hz; Low-Beta: 12-20Hz; High-Beta: 20-30Hz; Low-Gamma: 30-40Hz; Gamma60: 60-80Hz and high-Gamma: 80-100Hz). To extract the topographical organization of oscillatory responses to the maternal voice in the FW or BW conditions in preterm and full-term babies, we used a data-driven topographical clustering approach. First, dimension reduction was performed using a principal component

analysis (PCA) with electrodes as cases and, as columns, the mean power of the electrode for each frequency band in 100ms timebins starting at voice onset. Eight separate PCAs were performed (one for each condition, mother and stranger, FW and BW in the preterm and full-term population). The cutoff was determined using the following criteria: eigenvalues above 1 and a clear dissociation in the cumulative eigenvalue distribution. Resulted 7.6 ± 1.21 factors per condition accounting for 43.38 ±4.79% of the variance. Then, the resulting factors were entered in a clustering algorithm (hcut R function from the factoextra R package) using a Euclidean distance metric and a complete linkage (highest cophenetic coefficient among available options, Cophenetic coefficient= 0.61), and a cutoff at 19 clusters was chosen as it yielded the highest average silhouette value. Visual inspection showed that clusters were indeed mainly topographically consistent (with the exception of 5 clusters organizing which had to be divided into two (4 out of 5) or three clusters (1 cluster) based on spatial location). Thus, after this final division, 27 topographical clusters were obtained. After exclusion of non-topographically replicable patterns (clusters containing less than 3 electrodes), 21 topographical clusters were obtained.

Statistical analysis

For all the undermentioned analyses, a false discovery rate correction was applied to all p-values, and significance level was chosen at 0.05 (Benjamini & Hochberg, 1995).

First, on each topographical cluster, for each group, was considered a significant deviation of a given condition relative to the baseline if the deviation exceeded a threshold defined as 3 time the average baseline (-0.5-0s before sound onset) standard deviation of the 4 conditions considered (mother vs stranger FW versus BW).

In each topographical cluster, the average power for each trial in each frequency bands were averaged in 100ms bins from voice onset to 1s post-voice onset. From this database, the time course in each cluster for each frequency bands was analyzed as follows: at each timepoint, the frequency-band's mean power for all trials was entered into a general linear mixed model (R lme4 package) with the baby ID as random factor testing the three-way interaction between factors Group (2 levels; preterm versus full-term babies) X Voice Familiarity (2 levels, mother versus stranger) X FW-BW (2 levels, FW versus BW). Upon confirmation of the significance of the three-way interaction, contrast analysis was performed to determine significant differences in voice familiarity (mother versus stranger for each group in the FW and BW condition), and natural versus non-natural speech perception (FW versus BW for each group in the mother and stranger condition), or group differences (preterm versus full-

term in each condition). To avoid spurious effects, a difference was considered if the duration of a significant three-way interaction persisted over at least two consecutive 100ms timebins and the average power for one condition of interest during the trial exceeded the 3 std threshold of average baseline power for at least 50ms.

Results

Data-driven clustering yielded 21 topographically defined functional clusters presenting differential time-frequency patterns including all participants, trials, and experimental conditions. Among them, 13 presented a significant three-way interaction Group X Voice Familiarity X FW-BW response (after FDR correction) to the task for in least one frequency band, see Supplementary Figure 1 in SI.

In this paper we specifically focus the analysis of the results observed in the temporal-left (Figure 1, C9 in SI Fig.1), and right (Figure 2, C1,C19 and C14 in SI Fig.1) clusters. Frontal, central and occipital clusters presented less-well defined significant responses to the task (significant results are reported in full in SI).

Low-frequency responses to the maternal voice in the FW condition in the temporal left-hemisphere for full-term versus preterm babies

The left-temporal cluster presented a significant sustained Group X Voice familiarity X FW-BW three-way interaction in the theta (100-600ms, 4-8 Hz, $p<0.05$ FDR corrected), alpha (200-600ms, 8-12Hz), low-beta (300-600ms, 12-20Hz).

In the theta band (4-8 Hz), a significant power increase relative to baseline was observed for mother FW speech in full-term babies (around 100ms post-voice onset, Figure 1). In full-term babies, theta-power was also significantly higher for the mother FW compared to the stranger FW speech (100-400ms post-voice onset, contrast analysis, $p<0.05$ FDR, Table 2) and to the BW mother speech (0-300ms). Conversely, in preterm babies, a significant decrease in theta power relative to baseline was observed for mother FW speech (~400ms), and lower power in the theta band was observed for the mother FW compared to the stranger FW speech (100-700ms post-voice onset, contrast analysis, $p<0.05$ FDR) and to the mother BW speech (200-1000ms). This translated into a significant group effect (full-term > preterm) for the mother FW speech, from 300-700ms post-sound onset (Figure 1), with an increase for full-term and an opposite decrease in preterms. Note that a significant increase in theta power relative to baseline was also observed in preterm babies for mother BW speech as well as stranger FW and BW speech (~100ms) and this translated for the stranger FW condition into a significant group effect (full-term < preterm) from 200-300ms post-sound onset (Figure 1), with a decrease for full-term and an opposite increase in preterms.

Similarly, in the alpha band (8-12Hz), a significant power increase relative to baseline was also observed for mother FW speech in full-term babies (around 100ms post-voice onset,

Figure 1) with alpha-power in this group being significantly higher for the mother FW compared to the stranger FW speech (300-500ms post-voice onset, contrast analysis, $p<0.05$ FDR) and to the BW mother speech (0-300ms). No significant mother FW modulation was observed relative to baseline for this condition in preterm newborns. However, a significant alpha power increase relative to baseline was observed in preterm babies for stranger FW (~100ms) and BW voices (~0ms) and mother BW voices(~100ms), leading to a significant group effect (full-term < preterm) for the mother BW speech, starting 300ms post voice onset (Figure 1). This alpha power increase observed for stranger FW and mother BW translated into a significantly higher alpha power for both these conditions (at 300-400ms and 200-600ms respectively) compared to mother FW voices.

In the low-beta band (12-20Hz), a significant power increase relative to baseline was observed for mother FW and BW speech in full-term babies (around 100ms post-voice onset, Figure 1), while the significant power increase for stranger speech occurs much later (~400ms for stranger BW and 600ms for stranger FW). Low-beta-power in this group is significantly higher for the mother compared to stranger voices in the FW condition only (300-600ms post-voice onset, contrast analysis, $p<0.05$ FDR). Furthermore, low-beta-power in this group is significantly lower for stranger FW compared to stranger BW voices (400-600ms post voice onset). Interestingly, no significant low-beta power increase relative to baseline is observed for the mother FW condition, translating into a significant group-effect for this condition (full-term > preterm) from 300-400ms post-sound onset (Figure 1) while low-beta power in the mother BW condition displays a similar increase as observed in the full-term group relative to baseline (~100ms). A significant increase of low-beta power is observed for the stranger FW condition relative to baseline (~300ms) translating to a significantly higher power for stranger FW voices compared to mother FW voices (300-400ms), and a significant group effect for the stranger FW condition (full-term < preterm, 400-500ms). Stranger BW voices elicited no significant low-beta power modulation.

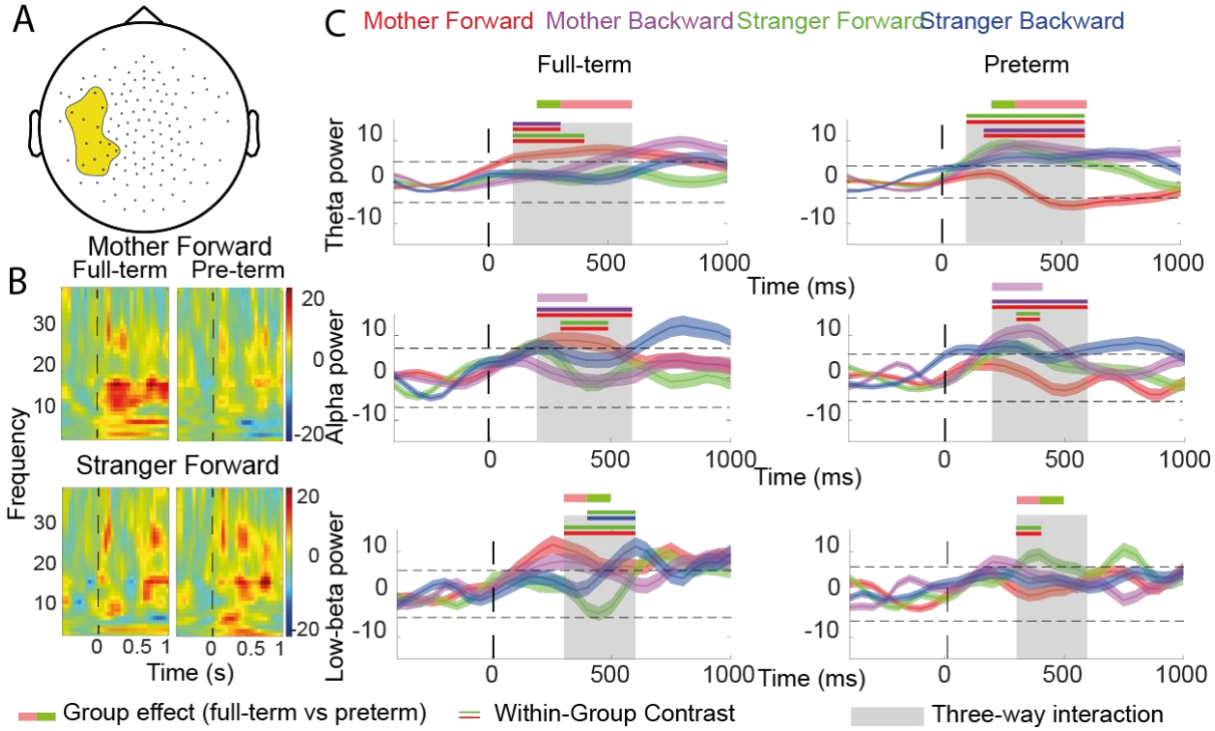

Figure 1: Left-temporal responses to the maternal and stranger voice in the FW and BW order. *A- Topographical location of the analyzed cluster. B- Time-frequency map of preterm and full-term babies' temporal response to the mother and stranger voice in the FW condition. C- Timecourse of theta (4-8Hz), alpha (8-12Hz) and low-beta (12-20Hz) power in response to mother FW (red), mother BW (magenta), stranger FW (green) and stranger BW (blue) voices. 0 is the onset of the voice. Grey areas represent timepoints for this frequency band where a significant FDR corrected Group X Voice Familiarity X FW-BW three-way interaction was detected. Dual horizontal thin lines represent significant contrasts (contrast analysis, p<0.05 FDR corrected), colors of the horizontal lines represent the conditions contrasted (a green and red line represent a significant mother FW vs stranger FW contrast for example). Horizontal thick lines represent group contrast (preterm versus full-term) in the condition expressed by the color code. B-C For display purposes, the absolute baseline corrected power is frequency-wise z-normalized using the average baseline power for all conditions, statistics and analyses are performed on absolute baseline corrected data (see methods).*

Right-temporal and frontal mother-FW-voice specific beta and low gamma responses in for full-term versus preterm babies

In the two right-frontal-temporal clusters, the Group X Voice Familiarity X FW-BW three-way interaction did not reach significance for any timings in the theta nor in the alpha band (Figure 2). However, a significant interaction was observed in the anterior temporal cluster in the low-beta band (12-20 HZ, 0-400ms, Figure 2), and in the right fronto-temporal cluster in the gamma80 band (80-100 HZ, 200-400ms, Figure 2).

In the anterior-right-temporal cluster, a low-beta band (12-20 Hz) significant power decrease for mother FW and increase for mother BW relative to baseline was observed in preterm

babies (around 100ms post-voice onset, Figure 1) followed by a late power increase for stranger FW voices (~500ms). Consequently, a significant low-beta power dissociation is observed between mother FW and BW conditions in this population from 0-400ms post-voice onset. Conversely, in the full-term population, no significant low-beta power deviation from baseline was observed for mother FW and BW conditions, translating into a significant group effect for the mother BW condition (full-term < preterm, 100-200ms). In this population, the only deviation from baseline observed is a low-beta increase for stranger BW voices ~200ms post-voice onset translating into a significant stranger vs mother BW low-beta power significant dissociation (200-400ms).

In the right-fronto-temporal cluster, a gamma80 band (80-100 Hz) significant power decrease for stranger FW (~300ms) and stranger BW (~500ms) speech was observed relative to baseline in preterm babies only. Consequently, the maintenance of a higher gamma80 power was observed during mother FW voices presentation compared to stranger FW voices (200-400ms, Figure 2, contrast analysis, $p<0.05$ FDR corrected), and mother BW voices (300-400ms). No such dissociations or deviation from baselines were observed in the full-term group, hence a significant group-effect was observed (full-term>preterm, 200-400ms) for the stranger FW condition.

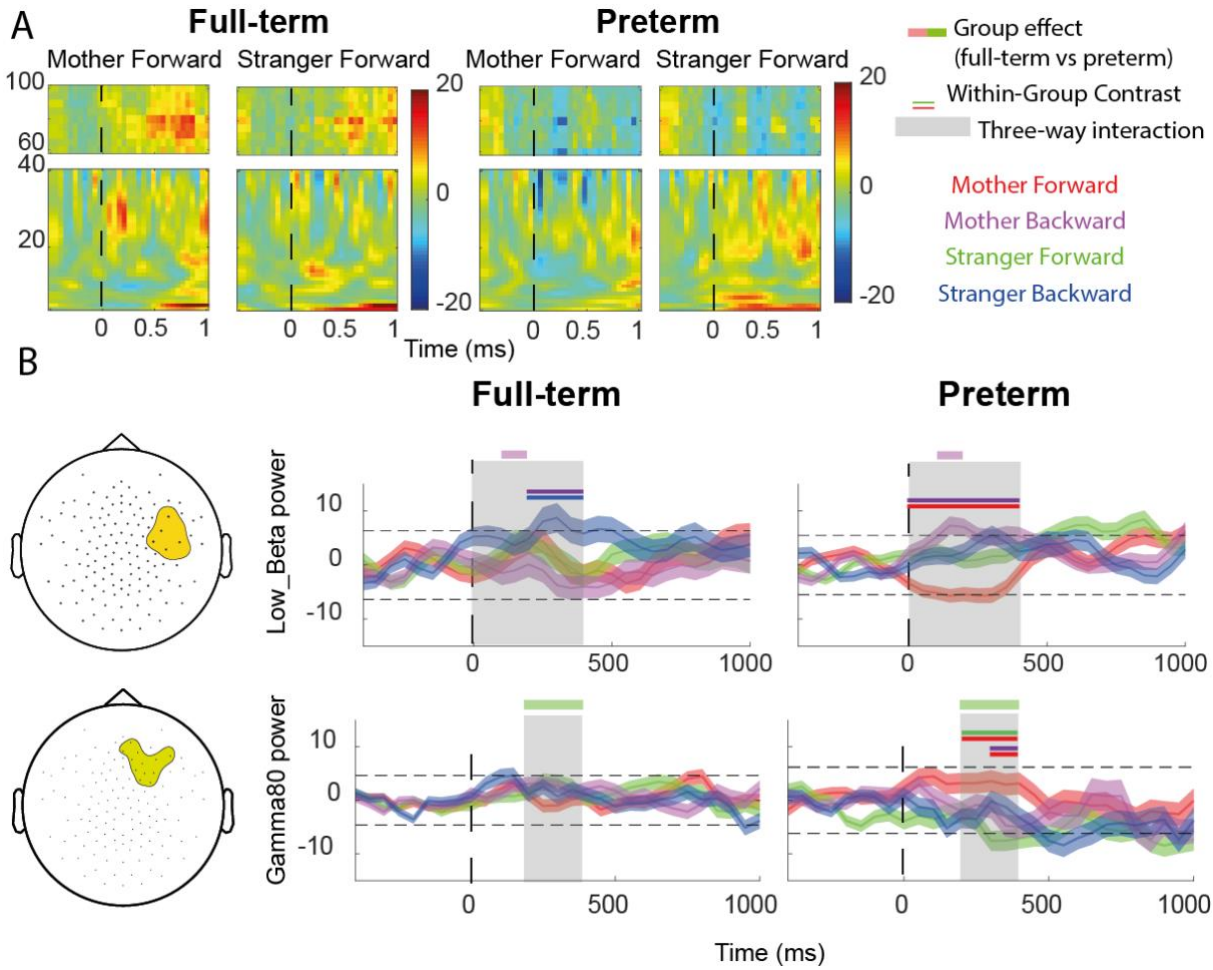

Figure 2: Right-temporal responses to the maternal and stranger voice in the FW and BW order. *A- Time-frequency map of preterm and full-term babies' temporal response to the mother and stranger voice in the FW condition. B- Timecourse of low-beta (12-20Hz), and gamma80 (80-100Hz) power in response to mother FW (red), mother BW (magenta), stranger FW (green) and stranger BW (blue) voices. 0 is the onset of the voice. On the left, the topographical cluster from which the timecourse on the right panel is extracted is presented. Grey areas represent timepoints for this frequency band where a significant FDR corrected Group X Voice Familiarity X FW-BW three-way interaction was detected. Dual horizontal thin lines represent significant contrasts (contrast analysis, p<0.05 FDR corrected), colors of the horizontal lines represent the conditions contrasted (a green and red line represent a significant mother FW vs stranger FW contrast for example). Horizontal thick lines represent group contrast (preterm versus full-term) in the condition materialized by the color code. A-B For display purposes, the absolute baseline corrected power is frequency-wise z-normalized using the average baseline power for all conditions, statistics and analyses are performed on absolute baseline corrected data (see methods).*

Discussion

In the present study we analyzed the perception of term and preterm infants of four types of vocal stimuli, from the most familiar – mother FW voice – to the less familiar – stranger BW voice. The current study shows that the mother voice is differently processed in preterm

compared to full-term babies, and that this differential treatment occurs in different frequency bands in the left and right temporal lobes, and is dependent upon the natural and non-natural presentation of speech (FW and BW).

Previous studies have indicated that the temporal lobes are functional in the newborn period for subtle discriminations, in a familiar native language (Dehaene-Lambertz & Baillet, 1998; Dehaene-Lambertz et al., 2002). Here we showed that in the left-temporal scalp area, a specific processing of the naturalistic mother voice (mother FW) compared to a stranger voice is observed in low-frequency bands (theta and alpha bands), but taking antagonistic forms in the two groups i.e. significant power increase for full-terms and a power decrease (theta) or maintenance (alpha) in preterms (not significant different from the baseline). Theta band involvement in speech tracking by newborns has already been suggested using multivariate temporal response function method on spectral whole-brain average EEG activity (Attaheri et al., 2022). Our study indicates that such low-frequency familiar speech (i.e. forward mother) tracking activity originates from the left-hemisphere for typical auditory development, as no significant task-specific low-frequency activation is observed in the right temporal scalp area. This left lateralization is coherent with previous literature. Indeed, neonates showed a significant activation in this left region only for FW speech but not for BW (Pena et al., 2003). Similarly, An ERP analysis previously performed on the same population showed significant left-hemisphere dissociations around ~530ms in full-term babies for the maternal speech (Adam-Darque et al., 2020). In 3-month-old infants, activation in response to FW and BW stimuli was significantly larger in the left than in the right planum temporal (Dehaene-Lambertz et al., 2002). More precisely, differences between the FW and BW stimuli were found in the left angular gyrus and the left mesial parietal lobe (precuneus). Furthermore, a left-frontal alpha increase was observed when 3-month old babies were exposed to human voices, which is coherent with the average pattern across conditions observed in the current study for both groups (Mai et al., 2014).

In our study, left-temporal low-beta activity in full-term babies presents, in the FW condition, a power increase for the maternal voice and a power decrease for the stranger voice leading to a significant mother-stranger dissociation. As opposite, in the preterm population, only the stranger FW induced a short increase of low-beta power. This result is in coherence with fMRI results pointing to a significantly different bilateral STG activation between the stranger and the mother's voice in full-term babies but not in the preterm group (Adam-Darque et al., 2020). In line with the observed significant theta power decrease for mother FW in preterms in our study, Scher and collaborators have also shown a power reduction in this frequency

band in the left central region (Scher, Steppe, Sclabassi, & Banks, 1997) when compared to term babies.

The significant difference between mother FW compared to mother BW in alpha band observed in the present study in the preterm group is in line with previous studies indicating that the unfamiliarity of the voice (BW and/or stranger) induced higher responses in preterms compared to terms (Peña et al., 2010).

To sum up, in light with the previously reported literature, our study shows that preterm infants at term equivalent age can discriminate between mother and stranger FW voices, in the left temporal lobe. However, if in full-terms, the mother's FW voice induces a theta, alpha and low beta bands increase, in the preterm population, this area is marked, - in the same frequencies by a power increase for the stranger FW voice. As opposite, in preterm infants, the mother BW voice induces a theta and alpha band increase, while in full-terms the same familiar but non-natural voice (BW) does not display similar activations in the left temporal lobe.

It is important to notice also that recent NIRS and ERP studies in very premature infants, from 28 week of Gestational Age onward, have shown that their auditory discriminative abilities are much more mature than previously described (Edalati et al., 2021; Mahmoudzadeh et al., 2013; Mahmoudzadeh, Wallois, Kongolo, Goudjil, & Dehaene-Lambertz, 2017). However, it's also known that, at term postmenstrual age, the maternal voice does not elicit increase of activity in preterm infants compared to terms (Therien, 2004). As opposite, between 33 and 34 weeks of gestational age, fetuses show different brain activations in the left temporal area for mother and stranger (Jardri et al., 2012). We can argue, thus, that the extrauterine life sensory experience of preterm infants have a significant impact in their mother's voice processing characteristics.

Moreover, the overmentioned atypical mother-voice processing in preterm babies in the left hemisphere could also provide a potential rationale for the different trajectories observed in mother-babies early interactions (Salerni, Suttora, & D'Odorico, 2007) and in long-term children's social and communication abilities (Abrams et al., 2016).

In the right-temporal scalp area we observed in the low-beta and low-gamma bands a mother FW specific power-decrease and a mother BW increase, with a consequent dissociation, only in the preterm population, while in full-terms an increase in the activation was specifically observed for the most unfamiliar stimulus, the stranger BW voice.

To sum up, while terms dissociate mother FW versus BW only in the left temporal area, typically devoted to speech decoding, with an increased activation for the mother's voice, the

preterms dissociate the two stimuli also in the right temporal regions, but with a decreased activation for the mother's voice. We hypothesize that preterms babies' mother voice specific activation might provide a compensatory mechanism for the absence of left-temporal low-beta responses to the mother voice. Such compensatory mechanisms have indeed been described in the beta-band in the contralesional hemisphere of stroke patients (Barios et al., 2021) and in children suffering from agenesis of the corpus callosum (Koeda et al., 1995). Compensatory mechanisms have been outlined in the preterm infants' population, both at cellular and brain levels (Scafidi, Fagel, Ment, & Vaccarino, 2009). However, it is not always easy to understand whether these differences between terms and preterms during development are compensatory mechanisms for injuries or delays in the typical maturation process.

An alternative hypothesis might be that the naturalistic mother's voice might undergo a completely different treatment altogether in the preterm baby compared to the full-term: while the mother's voice may be processed mainly in the left temporal structures through low-frequency event-related synchronization in full-term babies, it may be processed bilaterally through an event-related desynchronization in a wider range of frequency bands. It has been suggested that these differential time-frequency pattern underly the mobilization of different functional networks (Whitman, Ward, & Woodward, 2013). An investigation at the source level and connectivity measures might provide further information allowing to partially disentangle these hypotheses. This could be also mainly due to the atypical sensory and interactional experience that preterms have with the mother's and stranger's voices during their hospital stay (Pineda et al., 2017; Santos, Pearce, & Stroustrup, 2015). The right temporal gamma80 modulations are interesting in this regard because the right frontotemporal cluster displays a significant mother-stranger FW gamma80 power dissociation in the preterm group compared to the full terms. A MEG study showed, in fact, that mother-child positive verbal interaction elicits an increase in gamma-band power in the right superior-temporal-sulcus (Levy, Goldstein, & Feldman, 2017), and infant-mother superior-temporal-sulcus phase-coupling in the gamma-band was observed during such positive interaction.

In conclusion, the current study allowed us to disentangle the oscillatory correlates of voice familiarity and naturalistic features processing in preterm and full-term babies, and a complex pattern of differences between the two groups in terms of topography, frequency bands and power differences emerged. As expected, a familiar naturalistic voice presentation seems to activate language-brain related areas in full-terms, which is not the case for preterms. This study might pave the way toward a better understanding of behavioral differences between

full-term and preterms and potential compensatory perceptual mechanisms put in place by the latter in the early stages of development.

References

Abrams, D. A., Chen, T., Odriozola, P., Cheng, K. M., Baker, A. E., Padmanabhan, A., . . . Menon, V. (2016). Neural circuits underlying mother's voice perception predict social communication abilities in children. *Proceedings of the National Academy of Sciences*, *113*(22), 6295-6300.

Adam-Darque, A., Pittet, M. P., Grouiller, F., Rihs, T. A., Leuchter, R. H.-V., Lazeyras, F., . . . Hüppi, P. S. (2020). Neural Correlates of Voice Perception in Newborns and the Influence of Preterm Birth. *Cerebral Cortex*.

Attaheri, A., Choisdealbha, Á. N., Di Liberto, G. M., Rocha, S., Brusini, P., Mead, N., . . . Williams, I. (2022). Delta-and theta-band cortical tracking and phase-amplitude coupling to sung speech by infants. *Neuroimage*, *247*, 118698.

Barios, J. A., Ezquerro, S., Bertomeu-Motos, A., Catalan, J. M., Sanchez-Aparicio, J. M., Donis-Barber, L., . . . Garcia-Aracil, N. (2021). Movement-Related EEG Oscillations of Contralesional Hemisphere Discloses Compensation Mechanisms of Severely Affected Motor Chronic Stroke Patients. *International journal of neural systems*, *31*(12), 2150053.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal statistical society: series B (Methodological)*, *57*(1), 289-300.

Dehaene-Lambertz, G., & Baillet, S. (1998). A phonological representation in the infant brain. *Neuroreport*, *9*(8), 1885-1888.

Dehaene-Lambertz, G., Dehaene, S., & Hertz-Pannier, L. (2002). Functional neuroimaging of speech perception in infants. *Science*, *298*(5600), 2013-2015. Retrieved from https://science.sciencemag.org/content/298/5600/2013.long

Edalati, M., Mahmoudzadeh, M., Kongolo, G., Ghostine, G., Safaie, J., Wallois, F., & Moghimi, S. (2021). Preterm neonates distinguish rhythm violation through a hierarchy of cortical processing. *arXiv preprint arXiv:2110.09336*.

Jardri, R., Houfflin-Debarge, V., Delion, P., Pruvo, J.-P., Thomas, P., & Pins, D. (2012). Assessing fetal response to maternal speech using a noninvasive functional brain imaging technique. *International Journal of Developmental Neuroscience*, *30*(2), 159-161.

Koeda, T., Knyazeva, M., Njiokiktjien, C., Jonkman, E., De Sonneville, L., & Vildavsky, V. (1995). The EEG in acallosal children. Coherence values in the resting state: left hemisphere compensatory mechanism? *Electroencephalography and clinical neurophysiology*, *95*(6), 397-407.

Kostilainen, K., Partanen, E., Mikkola, K., Wikström, V., Pakarinen, S., Fellman, V., & Huotilainen, M. (2020). Neural processing of changes in phonetic and emotional speech sounds and tones in preterm infants at term age. *International Journal of Psychophysiology*, *148*, 111-118.

Levy, J., Goldstein, A., & Feldman, R. (2017). Perception of social synchrony induces mother–child gamma coupling in the social brain. *Social cognitive and affective neuroscience*, *12*(7), 1036-1046.

Mahmoudzadeh, M., Dehaene-Lambertz, G., Fournier, M., Kongolo, G., Goudjil, S., Dubois, J., . . . Wallois, F. (2013). Syllabic discrimination in premature human infants prior to complete formation of cortical layers. *Proceedings of the National Academy of Sciences, 110*(12), 4846-4851.

Mahmoudzadeh, M., Wallois, F., Kongolo, G., Goudjil, S., & Dehaene-Lambertz, G. (2017). Functional maps at the onset of auditory inputs in very early preterm human neonates. *Cerebral Cortex, 27*(4), 2500-2512.

Mai, X., Xu, L., Li, M., Shao, J., Zhao, Z., Lamm, C., . . . Lozoff, B. (2014). Sounds elicit relative left frontal alpha activity in 2-month-old infants. *International Journal of Psychophysiology, 94*(3), 287-291.

Mehler, J., Jusczyk, P., Lambertz, G., Halsted, N., Bertoncini, J., & Amiel-Tison, C. (1988). A precursor of language acquisition in young infants. *Cognition, 29*(2), 143-178.

Pena, M., Maki, A., Kovačić, D., Dehaene-Lambertz, G., Koizumi, H., Bouquet, F., & Mehler, J. (2003). Sounds and silence: an optical topography study of language recognition at birth. *Proceedings of the National Academy of Sciences, 100*(20), 11702-11705.

Peña, M., Pittaluga, E., & Mehler, J. (2010). Language acquisition in premature and full-term infants. *Proceedings of the National Academy of Sciences, 107*(8), 3823-3828.

Pineda, R., Durant, P., Mathur, A., Inder, T., Wallendorf, M., & Schlaggar, B. L. (2017). Auditory exposure in the neonatal intensive care unit: room type and other predictors. *The Journal of pediatrics, 183*, 56-66. e53.

Saby, J. N., & Marshall, P. J. (2012). The utility of EEG band power analysis in the study of infancy and early childhood. *Developmental neuropsychology, 37*(3), 253-273.

Salerni, N., Suttora, C., & D'Odorico, L. (2007). A comparison of characteristics of early communication exchanges in mother-preterm and mother-full-term infant dyads. *First language, 27*(4), 329-346.

Sansavini, A., Guarini, A., Justice, L. M., Savini, S., Broccoli, S., Alessandroni, R., & Faldella, G. (2010). Does preterm birth increase a child's risk for language impairment? *Early human development, 86*(12), 765-772.

Santos, J., Pearce, S. E., & Stroustrup, A. (2015). Impact of hospital-based environmental exposures on neurodevelopmental outcomes of preterm infants. *Current opinion in pediatrics, 27*(2), 254.

Sato, H., Hirabayashi, Y., Tsubokura, H., Kanai, M., Ashida, T., Konishi, I., . . . Maki, A. (2012). Cerebral hemodynamics in newborn infants exposed to speech sounds: A whole-head optical topography study. *Hum Brain Mapp, 33*(9), 2092-2103.

Scafidi, J., Fagel, D. M., Ment, L. R., & Vaccarino, F. M. (2009). Modeling premature brain injury and recovery. *International Journal of Developmental Neuroscience, 27*(8), 863-871.

Scher, M. S., Steppe, D. A., Sclabassi, R. J., & Banks, D. L. (1997). Regional differences in spectral EEG measures between healthy term and preterm infants. *Pediatric neurology, 17*(3), 218-223.

Therien, J. M., Worwa, C. T., Mattia, F. R., & Raye-Ann, O. d. (2004). Altered pathways for auditory discrimination and recognition memory in preterm infants. *Developmental medicine and child neurology, 46*(12), 816-824.

Whitman, J. C., Ward, L. M., & Woodward, T. S. (2013). Patterns of cortical oscillations organize neural activity into whole-brain functional networks evident in the fMRI BOLD signal. *Frontiers in human neuroscience, 7*, 80.