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Early asymmetric inter-hemispheric transfer in the auditory network: insights from infants with corpus callosum agenesis

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Abstract

The left hemisphere specialization for language is a well-established asymmetry in the human brain. Structural and functional asymmetries are observed as early as the prenatal period suggesting genetically determined differences between both hemispheres. The corpus callosum is a large tract connecting mostly homologous areas; some have proposed that it might participate in an enhancement of the left-hemispheric advantage to process speech. To investigate its role in early development, we compared 13 3–4-month-old infants with an agenesis of the corpus callosum ("AgCC") with 18 typical infants using high-density electroencephalography in an auditory task. We recorded event-related potentials for speech stimuli (syllables and babbling noise), presented binaurally (same syllable in both ears), monaurally (babbling noise in one ear) and dichotically (syllable in one ear and babbling noise in the other ear). In response to these stimuli, both groups developed an anterior positivity synchronous with a posterior negativity, yet the topography significantly differed between groups likely due to the atypical gyration of the medial surface in AgCC. In particular, the anterior positivity was lateral in AgCC infants while it covered the midline in typical infants. We then measured the latencies of the main auditory response (P2 at this age) for the different conditions on the symmetrical left and right clusters. The main difference between groups was a ~60 ms delay in typical infants relative to AgCC, for the ipsilateral response (i.e. left hemisphere) to babbling noise presented in the left ear, whereas no difference was observed in the case of right-ear stimulation. We suggest that our results highlight an asymmetrical callosal connectivity favoring the right-to-left hemisphere direction in typical infants. This asymmetry, similar to recent descriptions in adults, might contribute to an enhancement of left lateralization for language processing beyond the initial cortical left-hemisphere advantage.

Keywords Corpus callosum · Corpus callosum agenesis · Brain development · Electroencephalography EEG · Auditory network · Asymmetry · Inter-hemispheric transfer · Language · Brain specialization

Introduction

The left-hemisphere specialization for language processing is a well-established example of hemispheric lateralization in the human brain consistently demonstrated in adult

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studies over the years both at the structural and functional levels (Toga and Thompson 2003; Van Essen 2005). In fetuses and preterm neonates, hemispheric asymmetries are already clearly visible, especially in perisylvian areas. At the macrostructural level, the Yakovlean torque that raises and pushes the right hemisphere forward relative to the left is observed before term age featuring the common characteristic of the human brain: right frontal and left occipital petalia, a more ventral and horizontal left than right Sylvian fissure, a larger left than right planum temporale, and a deeper right than left superior temporal sulcus (Dubois et al. 2010; Glasel et al. 2011; Habas et al. 2012; Leroy et al. 2011). Inter-hemispheric differences are also observed at the microstructural level and in the maturational calendar of the superior temporal and inferior frontal regions (Leroy et al. 2011), and of the arcuate fasciculus (Dubois et al. 2009,

2016). Finally, several functional magnetic resonance imaging (fMRI) and near-infrared spectroscopy (NIRS) studies have reported larger activations to speech in the left than the right planum temporale, and more generally in the left than right hemisphere during the first post-natal months (Dehaene-Lambertz et al. 2002; Mahmoudzadeh et al. 2013; Pena et al. 2003; Shultz et al. 2014).

Thus, the left-hemispheric functional advantage for speech processing described in adults appears to be rooted in the first stages of development, suggesting a strong genetic component. It is difficult to compare the strength of this left-lateralization for speech between infants and adults. Nevertheless, the functional reorganization after a lesion of the left hemisphere suggests a better plasticity at an early age: linguistic functions may move to the contralateral right hemisphere with less subsequent deficits in infants than later on, suggesting a strengthening of the hemispheric specialization for speech with age (Bates et al. 1999; Dehaene-Lambertz et al. 2004). Thus, other factors beyond the initial left-hemispheric bias might contribute to speech lateralization. The corpus callosum, which gathers most of the white matter fibers connecting both hemispheres (Aboitiz et al. 1992), has been suggested as a candidate factor (Jeeves and Temple 1987; Karbe et al. 1998; Selnes 1974). Caminiti et al. (2009) reported a relative stability of the corpus callosum's structure over the course of evolution between chimps and humans despite the increase in brain size and thus distances between brain areas. They hypothesized that the "relative" slowdown of the inter-hemispheric transfer between humans and chimps incites each hemisphere to specialize. Other authors have postulated a more active role of callosal fibers either through inhibition from one hemisphere to the other (Cook 1984; Dennis 1981; Karbe et al. 1998), or excitation (Yazgan et al. 1995).

The growth of fibers constituting the corpus callosum starts during the second trimester of pregnancy, and all callosal connections are in place toward the end of gestation. This tract is heterogenous, constituted of different types of fibers connecting mostly, but not always, homologous areas (Innocenti 1986). During infancy, pruning of irrelevant and useless fibers occurs most intensly in the first postnatal year (Kostović and Jovanov-Milošević 2006), and myelination progresses until the end of adolescence, accelerating the inter-hemispheric transfer time (IHTT) (Brody et al. 1987; Yakovlev and Lecours 1967). This IHTT is variable along the tract, depending on the diameter of the fibers, on their state of maturation, and on the distance the signal travels between two connected areas (Ringo et al. 1994). In adults, the visual IHTT is the slowest (Caminiti et al. 2009), but given the fast maturation of visual areas during the first post-natal trimester, myelination might compensate for the longer distance between visual areas at this age relative to the closer but less mature auditory areas. The question of

when these fibers are sufficiently mature to be functionally efficient is still unknown. Neonates are able to transfer tactile and haptic information from one hand to the other (Sann and Streri 2007), suggesting that somatosensory inter-hemispheric connections are rapidly efficient. By contrast, in the visual domain, de Schonen and Mathievet (1990) did not find any signature of visual inter-hemispheric transfer at 10 months due to infants' difficulties in generalizing learning from one visual hemifield to the other (de Schonen and Mathivet 1990). They further postulated that visual integration between both hemifields does not emerge before 24 months (Liégeois et al. 2000). However, in a recent study using event-related potentials (ERPs) during the first post-natal semester, we were able to measure the IHTT of the visual P1 for faces presented in the left and right hemifields (Adibpour et al. 2018). The IHTT decreased from ~315 to ~80 ms. While we related the IHT speed with the maturation of visual fibers from the corpus callosum splenium, we also showed that the transfer of face-specific responses was far from being complete in the first post-natal semester. Regarding the auditory domain, whether inter-hemispheric connectivity is efficient enough to convey speech information during early infancy remains an open question so far.

One way to investigate the role of callosal fibers in the development of inter-hemispheric transfer is to compare typical infants and infants with impaired growth of the corpus callosum. In fact, early development of callosal fibers can be disrupted due to a genetic disease (Bedeschi et al. 2006; Bonneau et al. 2002), environmental factors (Evrard et al. 2003), or no identified causes (Paul et al. 2007), and a partial or complete absence (agenesis) of the corpus callosum (AgCC) might occur with no other brain malformations (isolated agenesis). With a prevalence of at least 1/4000 births (Guillem et al. 2003), this pathology often has little impact on general cognitive abilities (Chiarello 1980) but may sometimes coincide with a range of specific cognitive impairments. Particularly in the language domain, AgCC subjects may have difficulties in phonological and rhyming processing, syntax and linguistic pragmatics (Sanders 1989; Temple and Ilsleya 1993; Temple et al. 1989).

So far, studies in adults with AgCC have favored a weak modulation of the linguistic left-hemispheric advantage by the corpus callosum. Using fMRI, Pelletier et al. (2011) found similar lateralization indices in six AgCC adults relative to controls in expressive and receptive tasks once controlled for IQ. On the other hand, Hinkley et al. (2016) observed a reduced language lateralization in AgCC subjects compared to controls during expressive linguistic tasks using magnetoencephalography (MEG), as Komaba et al. (1998) reported in one patient studied with positron emission tomography (PET) and a Wada test, and Riecker et al. (2007) in another case studied with fMRI.

Here we explored the role of auditory callosal fibers during the first stages of language acquisition using high-density electroencephalography (EEG, 128 channels) in 3–4-month-old infants with a corpus callosum agenesis compared with typical infants. We studied auditory-evoked potentials for speech stimuli presented binaurally (in both ears), monaurally (in one ear) or dichotically (different stimuli in both ears) in 13 AgCC and 18 typically developing infants. We compared the ERP topography but mainly the ERP latencies in both groups. Due to the crossing of the projection pathways in all sensory modalities, the hemisphere contralateral to stimulation is reached first, and information is transferred to the ipsilateral hemisphere via callosal fibers. For the visual modality, the efficiency and maturation of the corpus callosum can be estimated by the delay between contra- and ipsilateral responses since the neural pathways clearly direct each visual hemifield to the contralateral hemisphere (Adibpour et al. 2018). However, for the auditory modality, numerous crossings occur at the subcortical level, and the ipsilateral pathway has a strong cortical projection, which makes it difficult to separate the direct ipsilateral response from the response transferred from the contra- to the ipsilateral hemisphere through callosal fibers.

We thus reasoned that ERP components depending on the direct ipsilateral and contralateral pathways would have a similar latency in both AgCC and typical infants, but that any response depending on a callosal transfer would be significantly different between the two groups. Two findings could be considered: (1) because of the transfer delay, ipsilateral responses are slower than contralateral responses in typical infants but not in AgCC infants; (2) ipsilateral latencies are similar in both groups, in which case we may conclude that there is no inter-hemispheric transfer in typical infants at the processing stage we analyzed (P2 component of infant's auditory evoked potentials) due to the immaturity of the corpus callosum. We also studied whether left-to-right and right-to-left transfers were equivalent in AgCC and typical infants, since in adults, an asymmetric inter-hemispheric transfer of neural information is described between auditory cortices at rest (Andoh et al. 2015) and during auditory motion processing (Krumbholz et al. 2007).

Materials and methods

Subjects

We studied 13 infants with an agenesis of corpus callosum aged between 10.9 and 18.4 weeks (mean age: 16.3 ± 2.2 weeks, 4 girls and 9 boys). Agenesis was detected during gestation by ultrasonography monitoring followed by an anatomical MRI to detect other brain anomalies. Three out of the 13 infants had a partial agenesis with at least no splenium, where auditory callosal fibers cross, and the remaining 10 infants had a complete agenesis of the tract. At 2 years of age, developmental quotient was in the normal range (87–112), except for one girl who was also dysmorphic and had a dysplasia of the aortic valve. At 8–10 years of age, 9 out of 13 children followed a normal academic curriculum with special help for three of them due to reading difficulties. Therefore, 6/13 had some cognitive difficulties in following a normal school curriculum. By contrast, one of them was particularly gifted at school, being one year ahead in his curriculum. We also studied 18 typical infants (healthy and born full-term) aged between 9.6 and 17 weeks (mean age: 13.9 ± 2 weeks, 8 girls and 10 boys). We had no follow-up for these infants but they should represent the normal population as no difficulties were noted during pregnancy, birth, or the first post-natal months. The study was approved by the regional ethical committee for biomedical research. All parents were informed about its content and goals and gave written informed consent.

EEG data acquisition

EEG was recorded by a 64-electrode-net (net amp 200 system EGI, Eugene, USA) referenced to the vertex. The net was placed on the infants' heads relative to anatomical markers, and earphones were placed over the ears to present the auditory stimuli. The infants sat on their parents' laps. To keep them calm, distracting visual stimuli unsynchronized with the auditory stimuli were presented on a screen in front of them. EEG was continuously digitized at a sampling rate of 250 Hz during the whole experiment. The experiment was stopped as soon as infants became restless.

Stimuli

Two consonant–vowel syllables (/ba/ and /ga/) were produced by a female speaker with the same flat intonation and matched for intensity, total duration (285 ms), pre-voicing, and voiced formant transition duration (40 and 45 ms, respectively). We further created a 'babble'-like sound (referred to as babbling noise) covering the same range of frequencies, dynamics, and timbre as the syllables by superposing several sentences produced by the same speaker (duration 3 s), asynchronously in order to avoid any word recognition.

Experimental paradigm

As in our usual design (Dehaene-Lambertz and Dehaene 1994), each trial comprised four syllables, spaced by an interval of 600 ms. The last syllable was either similar or different from the first three syllables in order to constitute a standard or a deviant condition, and the repeated syllable

(/ba/ or /ga/) was randomly chosen for each trial. Syllables were presented either bilaterally or monaurally in the left or right ear. Following a monaural stimulation, both contralateral and ipsilateral pathways contribute to the measured responses, so we aimed to saturate the ipsilateral pathway by simultaneously presenting a complex and continuous stimulation in the opposite ear (Kouider and Dupoux 2005). We thus played the babbling noise starting at 600 ms before the first monaural syllable, which lasted for 3 s, thus during the presentation of the syllables train.

The experiment consisted of 360 trials separated by 2 s of silence, corresponding to 30 repetitions×2 conditions (4th syllable to be standard or deviant)×2 syllables (/ba/ /ga/)×3 sides of presentation (both ears, left ear, right ear). The trial order was randomized. Stimulus presentation and synchronization with the recording system were carried out using the EXPE software (Pallier et al. 1997) on a PC compatible with a Pro-audio Spectrum 16 D/A Board. Syllables were played through earphones at a comfortable hearing level.

EEG pre-processing

EEG recordings were band-pass filtered between 0.5 and 20 Hz using zero-phase lag filter from EEGLAB (Delorme and Makeig 2004), and further processed using MATLAB toolboxes: EEGLAB and Brainstorm (Tadel et al. 2011). Two of our initial goals were to compare the ERPs when the syllables were presented bilaterally and monaurally, as well as to study discrimination responses depending on the presented side. However, while the response amplitude is large for the first syllable in this paradigm, it decreases with repetition (Dehaene-Lambertz and Dehaene 1994), and here the response to the last syllable was weak, likely attenuated by the superimposed babbling noise. The insufficient signal-to-noise ratio associated with the relatively small number of AgCC infants prevented robust analyses of the change of syllable. Thus, we focused our comparisons between the AgCC and typical groups on the first syllable of the bilateral and monaural trials, and also on the response to the babbling noise. Therefore, the signal was segmented into epochs of 1400 ms: [−200, +1200] ms relative to the onset of the first stimulus in the trial (i.e. the first binaural syllable or the babbling noise).

Channels contaminated by movement or eye artifacts were automatically rejected on a trial-by-trial basis based on amplitude variations inside an epoch: each channel epoch was rejected when the fast average amplitude exceeded 250 µV, or when deviation between fast and slow running averages exceeded 150 µV. Electrodes were rejected for the entire recording if they were marked as bad in more than 70% of the epochs, and trials were rejected if more than 50% of electrodes were marked bad. Recordings were then re-referenced by subtracting the average activity of all channels

over the brain to obtain average-reference recordings then baseline-corrected over the first 200 ms of the segment (i.e. before the onset of babbling noise presentation).

Signals for comparable trials were then averaged together to measure auditory-evoked potentials. In order to increase the signal-to-noise ratio and because we focused on the first syllable, we merged standard and deviant trials, and trials with /ba/ or /ga/ as repeated syllable. It led to 120 trials per side of syllable presentation [left/right/both ear(s)], and after the pre-processing stage, we kept on average 60/60/60 correct trials in the typical group, and 74/74/75 trials in the AgCC group for the left/right/binaural trials.

Analyses of auditory-evoked responses in typical and AgCC infants

We analyzed the ERPs to three types of sound presentation: (1) binaural stimulation (bilateral presentation of a syllable), (2) monaural babbling noise (focusing on the time period between the noise onset and the presentation of a monaural syllable at 600 ms), and (3) dichotic stimulation (babbling noise in one ear, a syllable in the other ear, for a time period of 600 ms after the trial onset).

Comparison of ERPs topographies in typical and AgCC infants

We first aimed to compare the voltage topographies between the two groups. To avoid topography differences being explained by a difference in voltage amplitude rather than a genuine difference over the scalp, we "scaled" the EEG signal in each infant: the signal recorded at each electrode and at each time point was converted to a z-score based on the mean and standard deviation of the time series for all electrodes obtained after averaging all trials over the time-window [−200, 1200] ms. For each type of sound presentation (binaural syllables, monaural babbling noise, dichotic stimulation), we performed unpaired t tests between the two groups on rescaled amplitudes, for each channel, and each time sample during a time-window of 600 ms from the stimulus onset (either syllables or babbling noise). We first identified clusters showing group differences by clustering neighboring channels and time-samples with a probability below 0.1 and computed their significance probability (noted p_{cor}) using nonparametric statistics (Maris and Oostenveld 2007). This was done by performing similar t test comparisons and cluster extractions for 5000 random permutations of the group labels on the original data and computing p_{cor} based on the number of times the real data produced clusters with higher t values than the shuffled data. For each of the identified clusters and time windows, we also reported the effect size of amplitude differences between groups using Cohen's d coefficient.

Using the same approach, we also compared the topographical differences between the left and right stimuli within each group. To do so, we compared the response topography to left stimuli with flipped response topography to the right stimuli, i.e., left noise–right noise (flipped) or left syllable–right syllable (flipped).

Comparison of P2 characteristics in typical and AgCC infants

We secondly compared the two groups based on the P2 component, since it is the most robust auditory response at this age and it can be identified in each infant contrarily to earlier weaker responses (Wunderlich and Cone-Wesson 2006). This component peaks around 150–350 ms and corresponds to a bilateral positive response over the anterior electrodes synchronous with a bilateral negativity over the posterior electrodes (Dehaene-Lambertz and Dehaene 1994). To reliably identify the component in both hemispheres, we considered the best set of electrodes for each group, which differed across groups given the topography differences highlighted by the previous analysis. Based on the topography of the grand average computed over all trials and all infants in each group, these sets were determined to cover the positive pole of the P2 component and consisted of nine left and right symmetrical electrodes. In typical infants, the two sets comprised nine electrodes around F3–F7 and F4–F8 in the left and right hemispheres, respectively. In AgCC infants, the sets were more lateral, around T7 and T8 extending up to F3 and F4 anteriorly and to P7 and P8 posteriorly.

In each infant and for each type of sound presentation (binaural syllables, monaural babbling noise, dichotic stimulation), P2 was identified as the first distinguishable positive peak on ERPs averaged over the left and right sets independently. We then measured individual P2 latency as well as P2 amplitude from the average amplitude over a 50-ms time window centered on the peak latency of the original, unscaled data.

To compare the typical and AgCC infants, we performed the following analyses of variance (ANOVAs) for each characteristic latency/amplitude as the dependent variable. In the ANOVA for the binaural condition, we considered the group (typical/AgCC) as a between-subject factor, the cerebral hemisphere (left/right) as a within-subject factor, and the interaction between factors. In the ANOVAs for the monaural and dichotic conditions, we considered the brain response side (contralateral/ipsilateral relative to the stimulated ear) as an additional within-subject factor as well as interactions between the different factors. For significant effects or interactions, we further performed post-hoc analyses using t-tests to detect the significant differences between conditions (p values were corrected for multiple comparisons using the false discovery rate (FDR) approach). We also reported the effect sizes of differences between groups using Cohen's d coefficient.

Comparison of P2 responses to different stimulations

We finally investigated whether P2 characteristics were modulated by the type of sound presentation in our paradigm. We thus performed an ANOVA on each characteristic latency/amplitude as the dependent variable with the stimulation type (binaural syllables/monaural babbling noise/dichotic stimulation) and cerebral hemisphere (left/right) as within-subject factors, and group as a between-subject factor (typical/AgCC). For the response to monaural and dichotic stimulations, we averaged the characteristics across the two response sides (contralateral and ipsilateral) in order to keep the same sample size as for the response to binaural stimulation.

Results

Comparison of ERPs topographies in typical and AgCC infants

We first compared the topographical maps of the left and right stimuli within each group using cluster-based analyses and did not observe any significant difference between the response topographies in any of the infant groups. We then compared the topography of auditory ERPs between typical and AgCC infants for the three types of auditory stimulation (binaural presentation of syllables, monaural presentation of babbling noise, dichotic presentation of opposite-side babbling noise and syllables).

As can be seen in Fig. 1 and also in Fig. 2a, the anterior positivity synchronous with a posterior negativity typical of an auditory response at this age was observed in both groups, but the anterior positivity fused at the midline in typical infants. This was not the case in AgCC infants in whom the positivity appeared much more lateral than in controls. These topographical differences were objectivized by the statistical analyses for each type of stimulation.

Binaural stimulation (response to syllables)

The difference in topography between both groups was statistically significant over a fronto-medial cluster of 12 electrodes during the time window (396–556) ms post syllable onset ($p_{cor} = 0.031$, Cohen's d on rescaled amplitudes over the cluster = 1.1, Fig. 1a) in which a weaker activity was recorded in AgCC relative to typical infants.
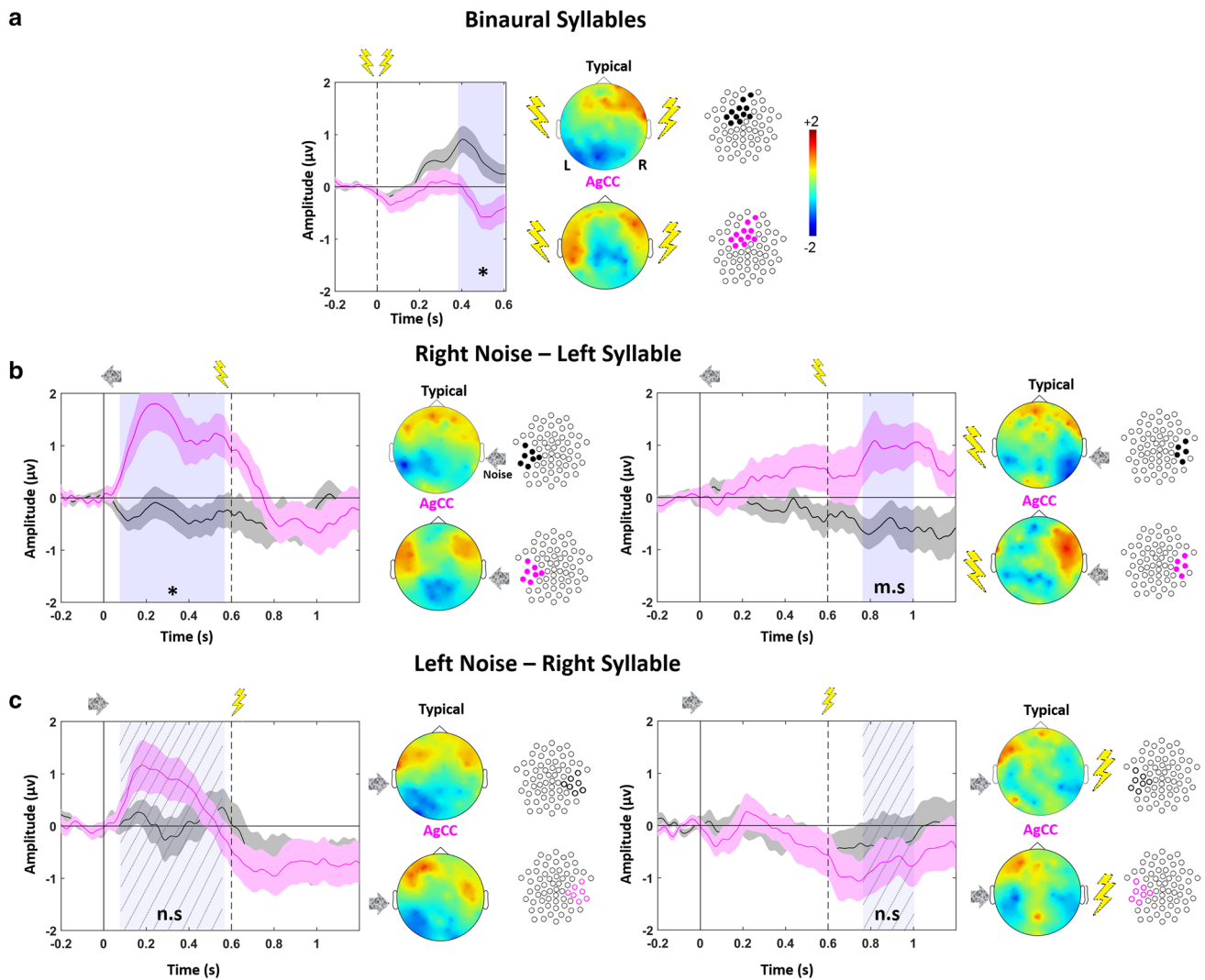
Fig. 1 Topographical differences between typical and AgCC infants: ERP time courses of the grand average responses in typical (black) and AgCC (magenta) infants for **a** binaural trials; **b** dichotic trials: right-ear babbling noise/left-ear syllable trials; **c** dichotic trials: left-ear babbling noise/right-ear syllable. In **a, b** significant differences between both groups are observed for the highlighted clusters and over the time-windows shaded in light blue (asterisk correspond to $p < 0.05$, *m.s* marginally significant trends $p < 0.1$). In **c** no group difference was observed; thus we outlined comparable clusters and time-windows to that of **b** and highlighted them with shaded light blue filled with diagonal stripes (*n.s.* non-significant). 2D voltage topographies correspond to the shaded time-windows

Monaural stimulation (response to babbling noise)

As can be seen in Fig. 1b, c, the response was more lateral in AgCC than in typically developing infants, yielding a significant difference between groups on a contralateral left temporal cluster when babbling noise was presented in the right ear [7 electrodes in the time window (76–568) ms post babbling noise onset, $p_{cor} = 0.034$, Cohen's $d = 1.4$, Fig. 1b]. By contrast, no significant difference was observed for babbling noise presented in the left ear, although visual inspection of the ERP shows a similar pattern (Fig. 1.c).

Dichotic stimulation (response to the syllable in the presence of contralateral babbling noise)

A difference between groups was also observed following dichotic stimulation, but only for one side of presentation, i.e., a trend when the syllable was presented in the left ear (babbling noise in the right ear) over a contralateral right temporal cluster [5 electrodes during the time window (164–404) ms post-dichotic onset, $p_{cor} = 0.093$, Cohen's $d = 1.0$, Fig. 1b), whereas no significant cluster was identified for syllables in the right ear (babbling noise in the left ear) (Fig. 1c).
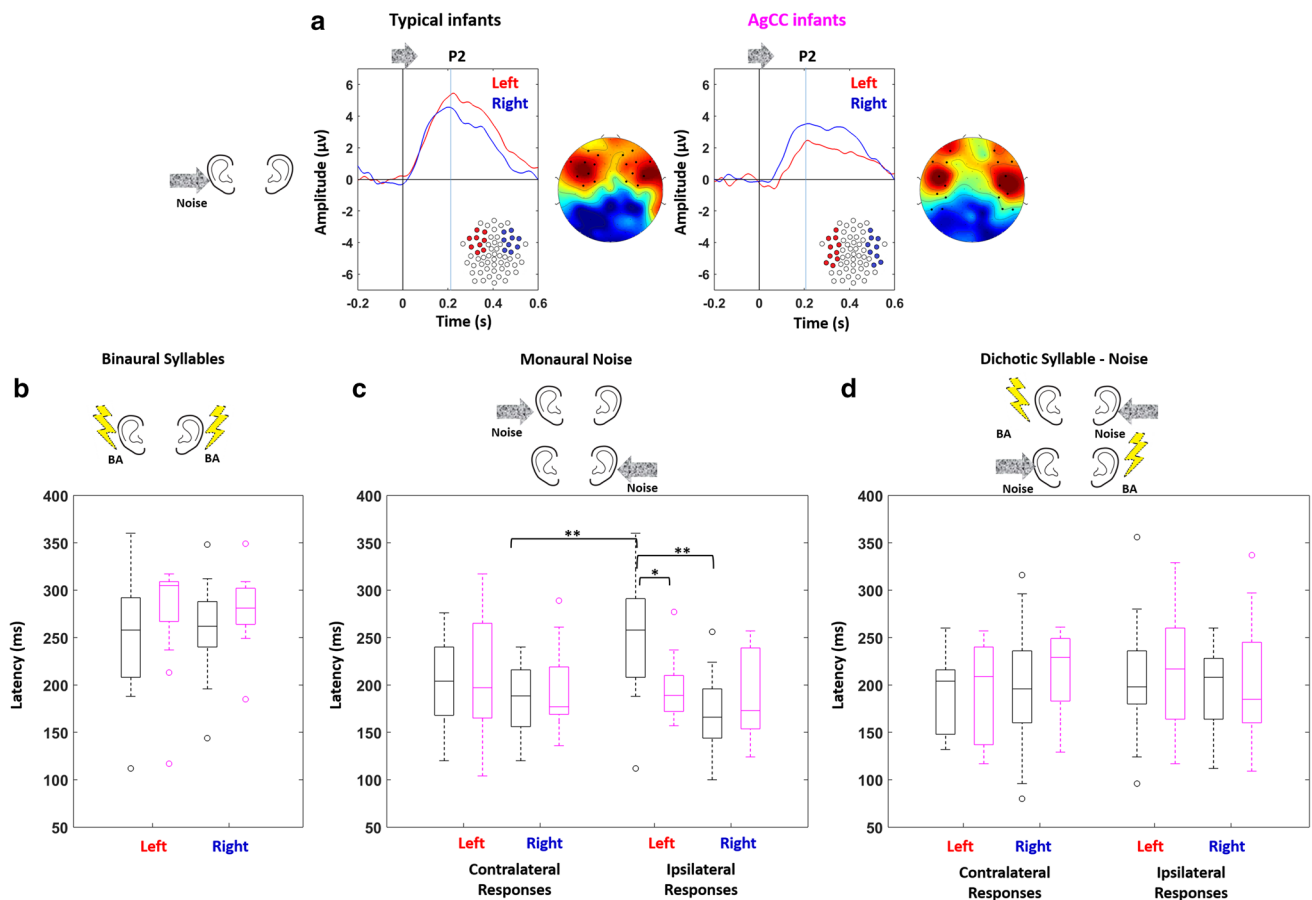
Fig. 2 Comparison of P2 response latency between typical and AgCC infants: **a** grand average ERP time courses in response to monaural babbling noise presented to the left ear, averaged over left (red) and right (blue) sets of electrodes optimized for typical (left panel) and AgCC (right panel) infants (averaged ERP time courses for other stimuli are shown in supplementary Fig. 1). P2 latency was measured as the delay between the stimulus onset and the first positive peak.

Box plots represent the latency of P2 responses measured in typical (black) and AgCC (magenta) infants, in each hemisphere, following stimulation by **b** binaural syllables, **c** monaural babbling noise and **d** dichotic babbling noise-syllable. Bilateral responses are considered in **b**, while both contralateral and ipsilateral responses are shown in **c, d**. Differences between response latencies are highlighted with asterisks (*$p < 0.05$; **$p < 0.005$)

Comparison of P2 latencies in typical and AgCC infants and across brain hemispheres

The P2 characteristics were reliably measured in each infant over the left and right sets of electrodes, covering the positive peaks in each group (see Fig. 2 for an example of P2 topography, and supplementary Fig. 1 for the identification of P2 peaks based on ERP time courses for each type of auditory stimulation). ANOVA results for the P2 latency are summarized below and detailed in Table 1 and Fig. 2 (the complete ANOVA results for the P2 amplitude are presented in Supplementary Information 1 and 2).

Overall, the difference between the two groups was more visible for the trials in which babbling noise was presented in the right ear and syllables in the left ear. The comparison of effect sizes suggested that group differences were larger for babbling noise than for syllables.

Binaural stimulation

We detected no main effect of group (AgCC: 278 ms, 95% CI [259, 297] vs. typical: 256 ms, 95% CI [238, 274], nor hemisphere [left: 264 ms, 95% CI [242, 286] vs. right: 267 ms, 95% CI [251, 283]), nor any interaction between group and hemisphere (Fig. 2a; Table 1).

Monaural stimulation (response to babbling noise)

We observed a main effect of hemisphere but no main effect of group or response side (see Table 1 for complete results). The interactions group×hemisphere, response side×hemisphere, and group×response side×hemisphere were also significant, while the interaction group×response side was only marginally significant. Post-hoc t tests of the three-way interactions demonstrated different points. In typical infants, the contralateral response was faster than the ipsilateral response for

Table 1 ANOVAs of P2 response latency in the binaural, monaural and dichotic trials

Binaural	Monaural	Dichotic
Group: F (1,29) = 1.8, p = 0.191	Group: F (1,29) = 0.1, p = 0.703	Group: F (1,29) = 0.5, p = 0.481
Hemisphere: F (1,29) = 0. 1, p = 0.719	Hemisphere: F (1,29) = 21.9, p < 0.001**	Hemisphere: F (1,29) < 0.1, p = 0.993
	Response side: F (1,29) = 0.6, p = 0.459	Response side: F (1,29) = 0.6, p = 0.424
Group × hemisphere: F (1,29) < 0.1, p = 0.86	Group × hemisphere: F (1,29) = 5.7, p = 0.023*	Group × hemisphere: F (1,29) = 0.2, p = 0.626
	Group × response side: F(1,29) = 3.7, p = 0.065	Group × response side: F (1,29) < 0.1, p = 0.928
	Hemisphere × response side: F (1,29) = 4.4, p = 0.045*	Hemisphere × response side: F (1,29) = 1.7, p = 0.200
	Group × hemisphere × response side: F (1,29) = 5.3, p = 0.029*	Group × hemisphere × response side: F (1,29) = 0.2, p = 0.689
	Typical L ipsi > AgCC L ipsi: t = 3.3, p = 0.01*	
	d: 1.1, 95% CI [21.6, 91.7]	
	Typical L ipsi > R ipsi: t = 5.0, p = 0.002**	
	d: 1.2, 95% CI [49.3, 120.5]	
	Typical L ipsi > R contra: t = 4.5, p = 0.003**	
	d: 1.0, 95% CI [36.2, 100.7]	
	Typical L contra > R ipsi: t = 2.4, p = 0.097	
	d: 0.5, 95% CI [3.5, 61.4]	
	Typical L ipsi > L contra: t = 2.4, p = 0.097	
	d: 0.6, 95% CI [7.4, 97.4]	
	AgCC L ipsi vs. R ipsi: t = 0.6, p = 0.568	
	d: 0.2, 95% CI [−24.0, 41.7]	
	AgCC L ipsi vs. R contra: t = 0.2, p = 0.843	
	d: 0.05, 95% CI [−0.7, 0.9]	
	AgCC L contra vs. R ipsi: t = 1.4, p = 0.406	
	d: 0.4, 95% CI [−13.2, 64.0]	
	AgCC L ipsi vs. L contra: t = −1.1, p = 0.431	
	d: −0.3, 95% CI [−15.1, 48.0]	

For each ANOVA, the main effects and their interactions are first reported, followed by post-hoc analyses using t tests when interactions were significant. Effect sizes (Cohen's d) and 95% confidence intervals (CI) on the averaged differences are indicated. Significant p values, corrected for multiple comparisons are highlighted by asterisks: **$p < 0.005$; *$p < 0.5$

AgCC agenesis of corpus callosum, *ipsi* ipsilateral, *contra* contralateral, *L* left hemisphere, *R* right hemisphere

left ear babbling noise (contralateral: 186 ms, 95% CI [168, 203] vs. ipsilateral: 254 ms, 95% CI [224, 284], p = 0.003), whereas for right ear babbling noise, a weak trend suggested faster ipsilateral than the contralateral response [ipsilateral: 169 ms, 95% CI [148, 190] vs. 202 ms, 95% CI [178, 225], p = 0.097). The within-hemisphere latency difference for the ipsi- and contralateral babbling noise was significantly larger in the left hemisphere (left: 52 ms, 95% CI [7, 97] vs. right: −16 ms, 95% CI [−40, −7], p = 0.045) due to the significantly slower ipsilateral response in the left than the right hemisphere (left: 254 ms, 95% CI [224, 284] vs. right 202 ms, 95% CI [178, 225], p = 0.002). This slow left ipsilateral response in typical infants was also significantly different from the latency in the same condition in AgCC infants (typical: 254 ms, 95% CI [224, 284] vs. AgCC: 197 ms, 95% CI [177, 218], p = 0.01) suggesting that in typical infants, the left ipsilateral response comprised a transferred component through the corpus callosum but not the right ipsilateral response (Fig. 2b). For the AgCC infants, there was no significant difference between the latencies of the ipsi- and contralateral responses (Table 1).

Dichotic stimulation (response to syllables in the presence of contralateral babbling noise)

None of the main effects of group, hemisphere, response side, or interactions were significant (Fig. 2c; Table 1).

To summarize, differences between groups were observed only for a monaural stimulation (i.e. babbling noise), characterized by a slower left ipsilateral response in typical infants relative to AgCC.

Different P2 latencies depending on the paradigm of auditory stimulation

When comparing P2 latencies for the three types of auditory stimulation, we observed a main effect of the stimuli type

(respectively 266/201/199 ms, 95% CI [252, 279]/[192, 210]/[190, 209] for binaural syllables/monaural babbling noise/dichotic syllables) and a main effect of hemisphere (respectively 220/207 ms, 95% CI [210, 229]/[198, 216] for left/right stimuli), but no effect of group (see complete results in Fig. 3; Table 2). We also observed a significant interaction stimuli type × hemisphere. Post-hoc *t* tests analyses revealed a longer latency in both hemispheres for binaural syllables relative to the other two types of stimuli (monaural babbling noise and dichotic babbling noise-syllable trials) whereas the difference between these two latter stimuli was weak (Table 2). (The complete ANOVA results for the dependency of the P2 amplitude on the paradigm of auditory stimulation are presented in Supplementary Information 3).

Discussion

In this study, we compared infants with corpus callosum agenesis to typical infants in order to understand the role of the callosal fibers in auditory responses during early development, in terms of topography, latency, amplitude, and lateralization. Note that we are studying a late response, the auditory P2, which is a high-level component originating from associative cortices, mainly because this component can be robustly identified in each individual at this age contrary to earlier components (Wunderlich and Cone-Wesson 2006). First, we observed a different P2 topography between groups. The anterior positivity extended more toward the lateral temporal regions in AgCC and over the midline in typical infants. Second, we found no difference in amplitudes
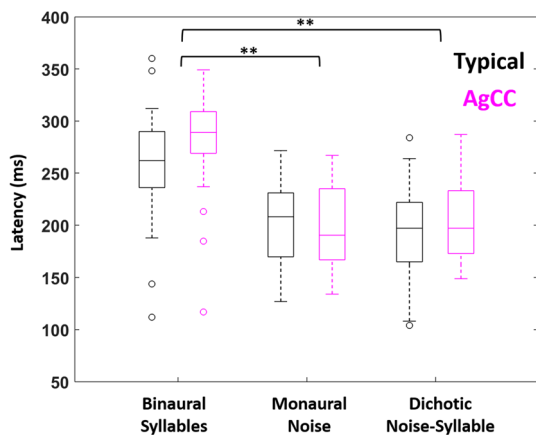

Fig. 3 Influence of the type of stimulation on P2 response latency: box plots represent the P2 latencies averaged over both hemispheres (left and right sets of electrodes, corresponding to both contralateral and ipsilateral responses) in response to binaural syllables, monaural noise and dichotic babbling noise-syllables in typical (black) and AgCC (magenta) infants. Differences between response latencies are highlighted with asterisks (**p < 0.005; *p < 0.5), showing that responses for binaural syllables are slower than for other stimuli

Table 2 Summary of ANOVA analyses on P2 latencies in function of the type of auditory stimulation

Dependency of P2 latencies on auditory stimulation
Stimuli type: $F_{(1,58)} = 50.1$, $p < 0.001$**
Group: $F_{(1,29)} = 0.8$, $p = 0.385$
Hemisphere: $F_{(1,58)} = 4.5$, $p = 0.042$*
Stimuli type × group: $F_{(2,58)} = 1.4$, $p = 0.255$
Stimuli type × hemisphere: $F_{(2,58)} = 7.1$, $p = 0.002$**
Group × hemisphere: $F_{(2,58)} = 1.8$, $p = 0.190$
Stimuli type × group × hemisphere: $F_{(2,58)} = 1.6$, $p = 0.210$
Bin syllable left > mon babbling left: $t_{(1,30)} = 4.5$, $p < 0.001$**; *d*: 0.8, 95% CI [24.9, 65.8]
Bin syllable right > mon babbling right: $t_{(1,30)} = 9.4$, $p < 0.001$**; *d*: 1.7, 95% CI [65.7, 102.3]
Bin syllable left > dichotic syllable left: $t_{(1,30)} = 5.8$, $p < 0.001$**; *d*: 1.0, 95% CI [41.6, 86.9]
Bin syllable right > dichotic syllable right: $t_{(1,30)} = 8.0$, $p < 0.001$**; *d*: 1.4, 95% CI [50.5, 84.9]
Mon babbling left vs. dichotic syllable left: $t_{(1,30)} = 2.1$, $p = 0.059$; *d*: 0.4, 95% CI [0.4, 37.4]
Mon babbling right vs. dichotic syllable right: $t_{(1,30)} = -1.7$, $p = 0.088$; *d*: 0.3, 95% CI [−35.2, 2.6]

The main effects and their interactions are first reported, followed by post-hoc analyses using *t* tests. Effect sizes (Cohen's *d*) and 95% confidence interval (CI) on averaged differences are indicated. Significant *p* values, corrected for multiple comparisons are highlighted by asterisks: **p < 0.005; *p < 0.5

bin binaural, *mon* monaural

between ipsi- and contralateral responses nor between typical and AgCC infants, suggesting an efficient and robust ipsilateral auditory pathway at this age. Third, the ipsilateral P2 was slower in typical infants compared to AgCC infants for left-ear but not for right-ear babbling noise. As the ipsilateral response corresponds to both the direct pathway and to the trans-hemispheric transfer, this difference in responses to a lateralized sound indicates an asymmetric transfer of the auditory responses between hemispheres. Our AgCC group included three children with partial agenesis. Our rational was that it should not affect our analyses given that auditory callosal fibers were inexistent in these infants since they cross at the level of the missing part of the corpus callosum, i.e., its posterior portion. Nevertheless, analyses conducted without these infants provided similar results (see Supplementary Information 4), although with a drop in the significance due to the reduced number of subjects.

Altered topography of auditory responses in AgCC infants

The corpus callosum is a large tract connecting both hemispheres. In the case of agenesis, the would-be callosal fibers, which no longer cross the midline, become oriented along the anterior-posterior direction, constituting an aberrant

tract, the Probst fibers. A recent tractography study in 12 children with corpus callosum dysgenesis revealed the complex connectivity of these fibers, which is not limited to frontal-occipital regions (Bénézit et al. 2015). Numerous fibers along the Probst main tract connect temporal and parietal areas. The fact that the Probst fibers do not degenerate and furthermore have similar DTI characteristics as remnants of the corpus callosum in the case of partial callosal agenesis (Bénézit et al. 2015) prove that they are functional and may propagate activity within the hemisphere to unexpected areas altering the voltage topography on the scalp.

Additionally, the absence of crossing callosal fibers affects the gyration of the cortex, the most obvious difference from a typical brain gyration being the orientation of the sulci on the medial surface of the brain which is vertical instead of wrapped around the corpus callosum. At a microstructural level, the lack of callosal fibers might also change the vector orientation of the electric field within the cortical columns. All these factors might affect the surface topography in AgCC subjects. Unfortunately, without an MRI in each infant, a correct reconstruction of the active sources of the auditory P2 was not possible. However, the group difference for the frontal positivity is congruent with the proposal of a source in the anterior cingulate cortex in complement of those in the superior temporal cortices at the origin of the P2 (Ortiz-Mantilla et al. 2012). Indeed, it is at this level that the difference of gyration is maximal between groups and thus might affect the surface topography most strongly.

A strong contribution of the ipsilateral pathway to auditory processing in the developing brain

The input to each ear travels to both hemispheres through ipsi- and contralateral pathways. The responses are subsequently transferred from one hemisphere to the other through the callosal fibers. Subjects lacking callosal splenial fibers are thus the only adequate model to evaluate the respective contribution of contra- and ipsilateral pathways to auditory ERPs. In human adults and animals, contralateral pathways are generally predominant relative to ipsilateral pathways (Majkowski et al. 1971; Rosenzweig 1951) until the auditory cortices; however, depending on the task (e.g. attention oriented toward on ear) and on the stimulus (e.g. speech vs. music), the predominance of one hemisphere over the other might vary at the cortical level. Here, in AgCC infants, the P2 following monaural babbling noise was simultaneously recorded over both hemispheres, revealing that both pathways were equally efficient at 3 months of age. The lack of differences in amplitude on the clusters ipsi- and contralateral to the stimulated ears further emphasizes the strength of the ipsilateral response at this age. As there was also no difference in ERP amplitude between AgCC and typical infants (see Supplementary Information 1), we may hypothesize that

it is the common rule at this age. Our stimulus presentation was passive, and all stimuli were speech, limiting the generalization of our results, yet we show here that a robust ipsilateral pathway ensures that both hemispheres are a-priori similarly reachable by the auditory stimulation without inter-hemispheric connectivity. It may explain why linguistic left-lateralization, especially in receptive tasks, is similar in AgCC adults and in controls (Pelletier et al. 2011).

Asymmetry of inter-hemispheric connections

To grasp the role of the corpus callosum, we compared AgCC and typical infants listening to monaural babbling noise. The two groups notably differed in the latency of the ipsilateral left response when babbling noise was presented in the left ear. We interpreted the delay in the peak of the ipsilateral left P2 as resulting from a superposition of the ipsilateral direct response and the inter-hemispheric transfer of the contralateral response. Taking either the lag between the contra- and ipsilateral responses in typical infants (69 ms) or the difference between AgCC and typical infants (57 ms) for the ipsilateral left response provides a similar estimation of the inter-hemispheric transfer time of auditory information at this age. Although slow relative to adult IHTT values, which are estimated to be a few ms (from 3 ms for tactile stimuli (Tame and Longo 2015) to ~12 ms for auditory stimuli (Krumbholz et al. 2007), and 10–30 ms for visual stimuli (Saron and Davidson 1989; Whitford et al. 2011) depending on their complexity), a value of ~ 60 ms is in agreement with the values we previously reported for the visual P1 transfer around the same age, the distance being longer for a visual transfer than for an auditory transfer. Using visual hemifield presentation of faces, we measured a decrease in the IHTT during the first post-natal semester from around 315 ms at 6 weeks to 84 ms 4 months later (Adibpour et al. 2018). By contrast, it was surprising to record no difference between groups for right-side babbling noise, suggesting that there was little left-to-right inter-hemispheric transfer at this age for this type of auditory information that could be recovered at the level of the P2 response. In the experiment cited above (Adibpour et al. 2018), there was no asymmetry in the transfer time for the visual P1 responses. However in adults, a similar asymmetry in the auditory inter-hemispheric connectivity was previously described: TMS applied over the right but not the left auditory cortex changed the functional connectivity between auditory cortices during resting-state in proportion to the volume of auditory callosal fibers (Andoh et al. 2015). Similarly, Gotts et al. (2013) reported stronger functional connectivity within the left hemisphere, especially for regions located within the language network, compared to the right hemisphere counterparts that interacted more widely with both hemispheres (Gotts et al. 2013). This asymmetrical

pattern of inter-hemispheric interactions may, therefore, find its roots during early development.

How this asymmetry in inter-hemispheric communications affects language lateralization is not yet clear. It might facilitate language learning by integrating all information in the same areas instead of distributing resources in both hemispheres. Although brain plasticity is sufficient to allow linguistic reorganization in the right hemisphere in the case of an early left-sided lesion (Bates et al. 1999), competing hemispheres might be deleterious when attentional resources are limited as is the case in young children. It may explain why AgCC children may have learning difficulties as pointed out by Sander (1989), Temple et al. (1989) and Temple and Ilsleya (1993) and as seen in our cohort in which 6 out of 13 required extra help to follow their primary school cursus. However, corpus callosum agenesis might also be the visible symptom of more diffuse neural anomalies not seen with currently available MRI, which alleviates the hypothesis of a unique role of corpus callosum transfer in these difficulties.

We might have expected a similar effect for the subsequent syllable presented in the other ear than the babbling noise, but there was no difference between groups nor delays of the ipsilateral left response for a left-ear syllable. However, in this case, the left hemisphere was saturated by the continuous babbling noise in the right ear projecting to the left hemisphere and blocking the right-to-left transfer. Still, no evidence of a left-to-right transfer was observed. Although the amplitude was much weaker for the dichotic syllables relative to the same syllables presented binaurally likely due to the masking babbling noise, the P2 latency was shorter (~ 66 ms). We interpret this acceleration of the P2 peak as the attention trigger that preceded the babbling noise in 2/3 of the trials.

Conclusions

Our study on the developing auditory network reveals an asymmetry between left-to-right and right-to-left effective connections, whereas the current structural approaches (e.g. diffusion imaging combined with tractography) cannot dissociate them. Our conclusions rely on the simple hypothesis that infants with corpus callosum agenesis have a similar auditory network except the missing corpus callosum. While our conclusions may be oversimplified, our interpretation is sensible, given the relative similarity in latencies and amplitudes of the auditory responses between both groups aside the notable exception of the left ipsilateral response for monaural stimulation we have discussed above. This result enters in the now large amount of evidence showing that the human brain architecture is lateralized very early on and differently depending on the cognitive domain and brain areas. Why evolution has selected this asymmetric architecture and how it contributes to the development of complex cognitive functions remains to be understood.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from all infants' parents included in the study.

References

Aboitiz F, Scheibel AB, Fisher RS, Zaidel E (1992) Fiber composition of the human corpus callosum. Brain Res 598(1):143–153

Adibpour P, Dubois J, Dehaene-Lambertz G (2018) Right but not left hemispheric discrimination of faces in infancy. Nat Hum Behav 2:67–79

Andoh J, Matsushita R, Zatorre RJ (2015) Asymmetric inter-hemispheric transfer in the auditory network: evidence from TMS, resting-state fMRI, and diffusion imaging. J Neurosci 35(43):14602–14611

Bates E, Vicari S, Trauner D (1999) Neural mediation of language development: perspectives from lesion studies of infants and children. In: Tager-Flusberg H (ed) Developmental cognitive neuroscience. Neurodevelopmental disorders. The MIT Press, Cambridge, MA, US, pp 533–581

Bedeschi MF, Bonaglia MC, Grasso R, Pellegri A, Garghentino RR, Battaglia MA, Bresolin N (2006) Agenesis of the corpus callosum: clinical and genetic study in 63 young patients. Pediatric Neurol 34(3):186–193

Bénézit A, Hertz-Pannier L, Dehaene-Lambertz G, Monzalvo K, Germanaud D, Duclap D, Moutard M-L (2015) Organising white matter in a brain without corpus callosum fibres. Cortex 63:155–171

Bonneau D, Toutain A, Laquerriere A, Marret S, Saugier-Veber P, Barthez MA, Gélot A (2002) X-linked lissencephaly with absent corpus callosum and ambiguous genitalia (XLAG): clinical, magnetic resonance imaging, and neuropathological findings. Ann Neurol 51(3):340–349

Brody BA, Kinney HC, Kloman AS, Gilles FH (1987) Sequence of central nervous system myelination in human infancy. I. An autopsy study of myelination. J Neuropathol Exp Neurol 46(3):283–301

Caminiti R, Ghaziri H, Galuske R, Hof PR, Innocenti GM (2009) Evolution amplified processing with temporally dispersed slow neuronal connectivity in primates. Proc Natl Acad Sci USA 106(46):19551–19556. https://doi.org/10.1073/pnas.0907655106

Chiarello C (1980) A house divided? Cognitive functioning with callosal agenesis. Brain Lang 11(1):128–158

Cook ND (1984) Homotopic callosal inhibition. Brain Lang 23(1):116–125

de Schonen, Mathivet E (1990) Hemispheric asymmetry in a face discrimination task in infants. Child Dev 61(4):1192–1205

Dehaene-Lambertz G, Dehaene S (1994) Speed and cerebral correlates of syllable discrimination in infants. Nature 370(6487):292

Dehaene-Lambertz G, Dehaene S, Hertz-Pannier L (2002) Functional neuroimaging of speech perception in infants. Science 298(5600):2013–2015

Dehaene-Lambertz G, Pena M, Christophe A, Landrieu P (2004) Phoneme perception in a neonate with a left sylvian infarct. Brain Lang 88(1):26–38

Delorme A, Makeig S (2004) EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J Neurosci Methods 134(1):9–21

Dennis M (1981) Language in a congenitally acallosal brain. Brain Lang 12(1):33–53

Dubois J, Hertz-Pannier L, Cachia A, Mangin J, Le Bihan D, Dehaene-Lambertz G (2009) Structural asymmetries in the infant language and sensori-motor networks. Cereb Cortex 19(2):414–423

Dubois J, Benders M, Lazeyras F, Borradori-Tolsa C, Leuchter RH-V, Mangin J-F, Hüppi PS (2010) Structural asymmetries of perisylvian regions in the preterm newborn. Neuroimage 52(1):32–42

Dubois J, Poupon C, Thirion B, Simonnet H, Kulikova S, Leroy F, Dehaene-Lambertz G (2016) Exploring the early organization and maturation of linguistic pathways in the human infant brain. Cereb Cortex 26(5):2283–2298

Evrard SG, Vega MD, Ramos AJ, Tagliaferro P, Brusco A (2003) Altered neuron–glia interactions in a low, chronic prenatal ethanol exposure. Dev Brain Res 147(1):119–133

Glasel H, Leroy F, Dubois J, Hertz-Pannier L, Mangin J-F, Dehaene-Lambertz G (2011) A robust cerebral asymmetry in the infant brain: the rightward superior temporal sulcus. Neuroimage 58(3):716–723

Gotts SJ, Jo HJ, Wallace GL, Saad ZS, Cox RW, Martin A (2013) Two distinct forms of functional lateralization in the human brain. Proc Natl Acad Sci USA 110(36):E3435–E3444. https://doi.org/10.1073/pnas.1302581110

Guillem P, Fabre B, Cans C, Robert-Gnansia E, Jouk P (2003) Trends in elective terminations of pregnancy between 1989 and 2000 in a French county (the Isere). Prenat Diagn 23(11):877–883

Habas PA, Scott JA, Roosta A, Rajagopalan V, Kim K, Rousseau F, Studholme C (2012) Early folding patterns and asymmetries of the normal human brain detected from in utero MRI. Cereb Cortex 22(1):13–25. https://doi.org/10.1093/cercor/bhr053

Hinkley LB, Marco EJ, Brown EG, Bukshpun P, Gold J, Hill S, Findlay AM, Jeremy RJ, Wakahiro ML, James Barkovich A, Mukherjee P, Sherr EH, Nagarajan SS (2016) The contribution of the corpus callosum to language lateralization. J Neurosci 36(16):4522–4533

Innocenti GM (1986) General organization of callosal connections in the cerebral cortex. In: Sensory-motor areas and aspects of cortical connectivity. Springer, Boston, MA, pp 291–353

Jeeves M, Temple C (1987) A further study of language function in callosal agenesis. Brain Lang 32(2):325–335

Karbe H, Herholz K, Halber M, Heiss WD (1998) Collateral inhibition of transcallosal activity facilitates functional brain asymmetry. J Cereb Blood Flow Metab 18(10):1157–1161. https://doi.org/10.1097/00004647-199810000-00012

Komaba Y, Senda M, Mori T, Ishii K, Mishina M, Kitamura S, Terashi A (1998) Bilateral representation of language function. J Neuroimaging 8(4):246–249

Kostović I, Jovanov-Milošević N (2006) The development of cerebral connections during the first 20–45 weeks' gestation. In: Paper presented at the seminars in fetal and neonatal medicine

Kouider S, Dupoux E (2005) Subliminal speech priming. Psychol Sci 16(8):617–625

Krumbholz K, Hewson-Stoate N, Schönwiesner M (2007) Cortical response to auditory motion suggests an asymmetry in the reliance on inter-hemispheric connections between the left and right auditory cortices. J Neurophysiol 97(2):1649–1655

Leroy F, Glasel H, Dubois J, Hertz-Pannier L, Thirion B, Mangin J-F, Dehaene-Lambertz G (2011) Early maturation of the linguistic dorsal pathway in human infants. J Neurosci 31(4):1500–1506

Liégeois F, Bentejac L, de Schonen S (2000) When does inter-hemispheric integration of visual events emerge in infancy? A developmental study on 19- to 28-month-old infants. Neuropsychologia 38(10):1382–1389

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. Proc Natl Acad Sci 110(12):4846–4851

Majkowski J, Bochenek Z, Bochenek W, Knapik-Fijałkowska D, Kopeć J (1971) Latency of averaged evoked potentials to contralateral and ipsilateral auditory stimulation in normal subjects. Brain Res 25(2):416–419

Maris E, Oostenveld R (2007) Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods 164(1):177–190

Ortiz-Mantilla S, Hämäläinen JA, Benasich AA (2012) Time course of ERP generators to syllables in infants: a source localization study using age-appropriate brain templates. Neuroimage 59(4):3275–3287

Pallier C, Dupoux E, Jeannin X (1997) EXPE: an expandable programming language for on-line psychological experiments. Behav Res Methods 29(3):322–327

Paul LK, Brown WS, Adolphs R, Tyszka JM, Richards LJ, Mukherjee P, Sherr EH (2007) Agenesis of the corpus callosum: genetic, developmental and functional aspects of connectivity. Nat Rev Neurosci 8(4):287–299

Pelletier I, Paquette N, Lepore F, Rouleau I, Sauerwein CH, Rosa C, Lassonde M (2011) Language lateralization in individuals with callosal agenesis: an fMRI study. Neuropsychologia 49(7):1987–1995. https://doi.org/10.1016/j.neuropsychologia.2011.03.028

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. Proc Natl Acad Sci 100(20):11702–11705

Riecker A, Ackermann H, Schmitz B, Kassubek J, Herrnberger B, Steinbrink C (2007) Bilateral language function in callosal agenesis. J Neurol 254(4):528–530

Ringo JL, Doty RW, Demeter S, Simard PY (1994) Time is of the essence: a conjecture that hemispheric specialization arises from interhemispheric conduction delay. Cereb Cortex 4(4):331–343

Rosenzweig MR (1951) Representations of the two ears at the auditory cortex. Am J Physiol Leg Content 167(1):147–158

Sann C, Streri A (2007) Perception of object shape and texture in human newborns: evidence from cross-modal transfer tasks. Dev Sci 10(3):399–410

Sanders RJ (1989) Sentence comprehension following agenesis of the corpus callosum. Brain Lang 37(1):59–72

Saron CD, Davidson RJ (1989) Visual evoked potential measures of interhemispheric transfer time in humans. Behav Neurosci 103(5):1115

Selnes OA (1974) The corpus callosum: Some anatomical and functional considerations with special reference to language. Brain Lang 1(2):111–139

Shultz S, Vouloumanos A, Bennett RH, Pelphrey K (2014) Neural specialization for speech in the first months of life. Dev Sci 17(5):766–774

Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM (2011). Brainstorm: a user-friendly application for MEG/EEG analysis. Comput Intell Neurosci 2011:8

Tamè L, Longo MR (2015) Inter-hemispheric integration of tactile-motor responses across body parts. Front Hum Neurosci 9:345

Temple C, Ilsleya J (1993) Phonemic discrimination in callosal agenesis. Cortex 29(2):341–348

Temple C, Jeeves M, Vilarroya O (1989) Ten pen men: rhyming skills in two children with callosal agenesis. Brain Lang 37(4):548–564

Toga AW, Thompson PM (2003) Mapping brain asymmetry. Nat Rev Neurosci 4(1):37–48

Van Essen DC (2005) A population-average, landmark-and surface-based (PALS) atlas of human cerebral cortex. Neuroimage 28(3):635–662

Whitford TJ, Kubicki M, Ghorashi S, Schneiderman JS, Hawley KJ, McCarley RW, Spencer KM (2011) Predicting inter-hemispheric transfer time from the diffusion properties of the corpus callosum in healthy individuals and schizophrenia patients: a combined ERP and DTI study. Neuroimage 54(3):2318–2329

Wunderlich JL, Cone-Wesson BK (2006) Maturation of CAEP in infants and children: a review. Hear Res 212(1):212–223

Yakovlev, Lecours (1967) The myelogenetic cycles of regional maturation in the brain. Blackwell, Oxford

Yazgan MY, Wexler BE, Kinsbourne M, Peterson B, Leckman JF (1995) Functional significance of individual variations in callosal area. Neuropsychologia 33(6):769–779