Mother's voice and heartbeat sounds elicit auditory plasticity in the human brain before full gestation

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Brain development is largely shaped by early sensory experience. However, it is currently unknown whether, how early, and to what extent the newborn's brain is shaped by exposure to maternal sounds when the brain is most sensitive to early life programming. The present study examined this question in 40 infants born extremely prematurely (between 25- and 32-wk gestation) in the first month of life. Newborns were randomized to receive auditory enrichment in the form of audio recordings of maternal sounds (including their mother's voice and heartbeat) or routine exposure to hospital environmental noise. The groups were otherwise medically and demographically comparable. Cranial ultrasonography measurements were obtained at 30 ± 3 d of life. Results show that newborns exposed to maternal sounds had a significantly larger auditory cortex (AC) bilaterally compared with control newborns receiving standard care. The magnitude of the right and left AC thickness was significantly correlated with gestational age but not with the duration of sound exposure. Measurements of head circumference and the widths of the frontal horn (FH) and the corpus callosum (CC) were not significantly different between the two groups. This study provides evidence for experience-dependent plasticity in the primary AC before the brain has reached full-term maturation. Our results demonstrate that despite the immaturity of the auditory pathways, the AC is more adaptive to maternal sounds than environmental noise. Further studies are needed to better understand the neural processes underlying this early brain plasticity and its functional implications for future hearing and language development.

auditory | brain | mother's voice | heartbeat | preterm newborns

One of the first acoustic stimuli we are exposed to before birth is the voice of the mother and the sounds of her heartbeat. As fetuses, we have substantial capacity for auditory learning and memory already in utero (1–5), and we are particularly tuned to acoustic cues from our mother (6–9). Previous research suggests that the innate preference for mother's voice shapes the developmental trajectory of the brain (10, 11). Prenatal exposure to mother's voice may therefore provide the brain with the auditory fitness necessary to process and store speech information immediately after birth (12, 13).

There is evidence to suggest that prenatal exposure to the maternal voice and heartbeat sounds can pave the neural pathways in the brain for subsequent development of hearing and language skills (14). For example, the periodic perception of the low-frequency maternal heartbeat in the womb provides the fetus with an important rhythmic experience (15, 16) that likely establishes the neural basis for auditory entrainment and synchrony skills necessary for vocal, gestural, and gaze communication during mother–infant interactions (17, 18).

Studies examining the neural response to the maternal voice soon after birth have found activation in posterior temporal regions, preferentially on the left side, as well as brain areas involved in emotional processing including the amygdala and orbito-frontal cortex (19). Similarly, Beauchemin et al. have found activation in language-related cortical regions when newborns listened to their mother's voice, whereas a stranger's voice seemed to activate more generic regions of the brain (20). In addition, Partanen et al. have shown that the neural response to maternal sounds depends on experience as full-term newborns react differentially to familiar vs. unfamiliar sounds they were exposed to as fetuses, suggesting correlation between the amount of prenatal exposure and brain activity (21). Taken together, the above studies suggest that the mother's voice plays a special role in the early shaping of auditory and language areas of the brain.

Numerous animal studies have shown that brain development relies on developmentally appropriate acoustic stimulation early in life (22–32). Auditory deprivation during critical periods can adversely affect brain maturation and lead to long-lasting neural despecialization in the auditory cortex (AC), whereas auditory enrichment in the early postnatal period can enhance neural sensitivity in the primary AC, as well as improve auditory recognition and discrimination abilities.

Preterm infants are born during a critical period for auditory brain development. However, the maternal auditory nursery provided by the womb vanishes after a premature birth as the preterm newborn enters the neonatal intensive care unit (NICU). The abrupt transition of the fetus from the protected environment of the womb to the exposed environment of the hospital imposes significant challenges on the developing brain (33). These challenges have been associated with neuropathologic consequences, including reduction in regional brain volumes, white matter microstructural abnormalities, and poor cognitive and language outcomes in preterm compared with full-term newborns (34–41).

Considering the acoustic gap between the NICU environment and the womb, it is not surprising that auditory brain development is compromised in preterm compared with full-term infants (42, 43). Numerous studies have suggested that the auditory environment available for preterm infants in the NICU may not be conducive for their neurodevelopment (44–47). These concerns are

Significance

Newborns can hear their mother's voice and heartbeat sounds before birth. However, it is unknown whether, how early, and to what extent the newborn's brain is shaped by exposure to such maternal sounds. This study provides evidence for experience-dependent plasticity in the auditory cortex in preterm newborns exposed to authentic recordings of maternal sounds before full-term brain maturation. We demonstrate that the auditory cortex is more adaptive to womb-like maternal sounds than to environmental noise. Results are supported by the biological fact that maternal sounds would otherwise be present in utero had the baby not been born prematurely. We theorize that exposure to maternal sounds may provide newborns with the auditory fitness necessary to shape the brain for hearing and language development.

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Table 1. Newborn characteristics

Parameters	Maternal sounds	Control	*P* value
Subjects, *n*	21	19	NA
Female, *n* (%)	9 (43)	4 (21)	0.141
Birth GA (wk)	28.9 ± 1.9	29.6 ± 2.1	0.262
Birth weight (g)	1,310 ± 344	1,397 ± 369	0.441
1-min Apgar	5.48 ± 2.50	5.26 ± 1.91	0.766
5-min Apgar	7.29 ± 1.52	7.68 ± 1.00	0.537
HC at 1-mo cUS (cm)	29.3 ± 2.6	29.9 ± 2.8	0.481
PMA at 1-mo cUS (wk)	33.06 ± 1.92	33.87 ± 2.12	0.211
Mechanical ventilation (d)	2.52 ± 2.87	3.47 ± 8.08	0.616
Antenatal corticosteroids, *n* (%)	13 (62)	11 (58)	0.796

cUS, cranial ultrasound; GA, gestational age; HC, head circumference; NA, not applicable; PMA, postmenstrual age.

derived from the frequent reality that hospitalized preterm newborns are overexposed to loud, toxic, and unpredictable environmental noise generated by ventilators, infusion pumps, fans, telephones, pagers, monitors, and alarms (48–51), whereas at the same time they are also deprived of the low-frequency, patterned, and biologically familiar sounds of their mother's voice and heartbeat, which they would otherwise be hearing in utero (33, 45). In addition, the hospital environment contains a significant amount of high-frequency electronic sounds (52, 53) that are less likely to be heard in the womb because of the sound attenuation provided by maternal tissues and fluid within the intrauterine cavity (54–56). Efforts to improve the hospital environment for preterm neonates have primarily focused on reducing hospital noise and maintaining a quiet environment. However, exposing medically fragile preterm newborns to low-frequency audio recordings of their mothers on a daily basis has been less acknowledged to be of necessity, and the extent to which such maternal sound exposure can influence brain maturation after an extremely premature birth has been a matter of much debate.

The present study aimed to determine whether enriching the auditory environment for preterm newborns with authentic recordings of their mother's voice and heartbeat sounds in the first month of life would result in structural alterations in the AC. The rationale driving this question lies in the fact that such enriched maternal sound stimulation would otherwise be present had the baby not been born prematurely.

Results

As shown in Table 1, the maternal sounds and control groups did not significantly differ in the following characteristics: sex, birth gestational age, birth weight, 1-min Apgar, 5-min Apgar, head circumference and postmenstrual age at 1-mo cranial ultrasound, days on mechanical ventilation, and administration of antenatal corticosteroids.

Results were based on structural measurements of the AC, the frontal horn (FH), and the corpus callosum (CC) obtained by cranial ultrasonography (Fig. 1). AC thickness was significantly different between the groups [$F(2, 37) = 10.10$, $P < 0.001$] (Fig. 2). Infants in the maternal sounds group had a significantly larger right and left AC compared with infants in the control group [$F(1, 38) = 20.45$, $P < 0.001$ and $F(1, 38) = 6.55$, $P = 0.015$, respectively]. The width of the FH and the CC were not significantly different between the two groups [$F(2, 37) = 0.90$, $P = 0.413$ and $t(38) = 0.56$, $P = 0.578$, respectively] (Fig. 2 and Table 2).

Spearman correlational analysis revealed that, in both groups, the magnitude of the right and left AC thickness was significantly correlated with gestational age (for right AC and gestational age: maternal sounds: $\rho = -0.55$, $P = 0.01$; controls: $\rho = -0.60$, $P = 0.007$; and for left AC and gestational age: maternal sounds: $\rho = -0.56$, $P = 0.008$; controls: $\rho = -0.51$, $P = 0.02$). The measurements of the control brain regions (FH and CC) were not significantly correlated with gestational in either group.

Finally, within the maternal sound group, the average duration of sound exposure was 23.6 d with a narrow distribution (SD = 3.4), which was insufficient to significantly correlate with any of the AC measures (right AC: $\rho = -0.12$, $P = 0.59$; left AC: $\rho = +0.09$, $P = 0.68$).

Discussion

This study examined the effect of sound exposure on brain development in hospitalized preterm newborns. We compared the exposure effects between unfiltered hospital noise (currently the standard of care) vs. a modified care practice, which includes daily auditory enrichment in the form of low-pass filtered recordings of mother's voice and heartbeat sounds. Our results demonstrate auditory brain plasticity induced by exposure to womb-like maternal sounds in preterm newborns. Newborns receiving added exposure to mother's voice and heartbeat sounds in the early postnatal period showed significantly larger AC at 1 mo of age compared with control newborns receiving routine care. The magnitude of the right and left AC thickness was significantly correlated with gestational age at birth. The negative direction of the correlations indicates that younger babies had larger AC measurements relative to the transtemporal diameter (TTD) of their brain, suggesting that the relative size of AC is more pronounced earlier in gestation. As we discuss below, this study illustrates a highly specific modifiability within the AC in response to maternal sounds and highlights the importance of the newborn's sensory experience during postnatal hospitalization.

Our findings of auditory brain plasticity before full gestation are in keeping with several studies, primarily by Merzenich and colleagues, showing that early auditory experience, either in the form of enrichment or impoverishment, can have a substantial impact on both the structural and functional development of the AC in rat pups (26, 27, 29, 31, 57, 58). Similarly, an established body of work by Lickliter and colleagues has shown that

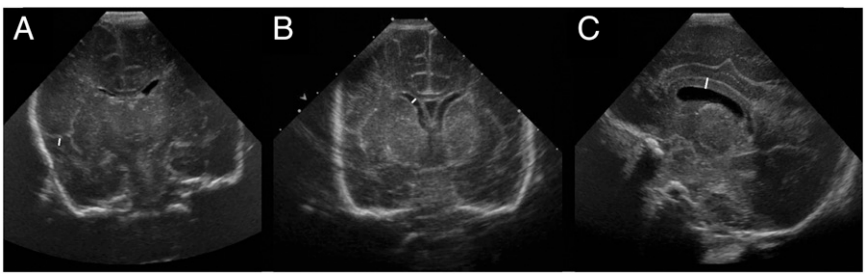

Fig. 1. Shown are measurements (white lines) of the (*A*) thickness of the AC in the coronal plane, (*B*) width of the FH of the lateral ventricle in the coronal plane, and (*C*) width of the body of the CC in the midsagittal plane.

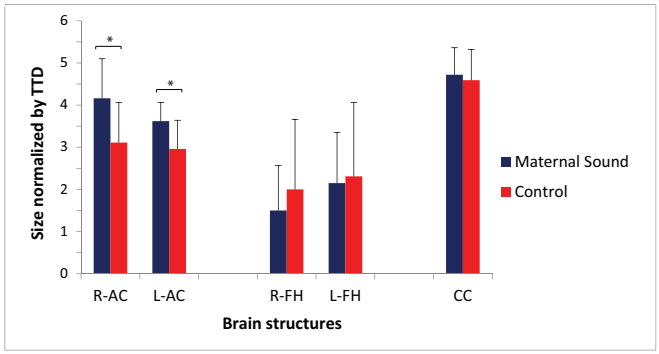

Fig. 2. Mean brain measurements are shown for the maternal sounds (blue) and control (red) groups in normalized arbitrary units, including the right and left AC thickness (R-AC and L-AC), right and left FH width (R-FH and L-FH), and width of the body of the CC. All measurements were individually normalized by the transtemporal diameter (TTD) of the newborn. Error bars represent SD. Asterisks denote statistically significant results ($P < 0.05$); values are given in Table 2.

bobwhite quail chicks receiving auditory stimulation early in embryogenesis demonstrated improved auditory learning and memory when tested postnatally (59–61). The collective impression of the above studies indicates that the early postnatal period provides a critical window of opportunity wherein sensory enrichment or sensory deprivation can play a major role in the development of the auditory brain system.

It is important to highlight that newborns in the maternal sound group were exposed to premixed audio recordings that included both the maternal voice and the maternal heartbeat played at the same time, much like they would have otherwise experienced had they not been born prematurely and were still in the womb. The concurrent inclusion of both the maternal heartbeat and the maternal voice on a single audio track was necessary to simulate the in utero experience, consistent with previous protocols used in recent studies from our laboratory (62, 63). Therefore, the present study cannot determine the relative contribution of mother's voice vs. the maternal heartbeat to the observed effects on auditory brain development.

To add an additional layer of biological authenticity to our maternal sound stimulation, newborns in the maternal sound group were intentionally exposed to a low-pass filtered version of the maternal sounds recordings, which naturally eliminated most segmental speech information. Low-pass filtering usually disrupts the intelligibility of individual syllables and speech rate in the utterances, and the resulting muffledness makes prosody the primary acoustic element contributing to auditory perception (64, 65). It is therefore tempting to speculate that the sole prosodic information of the maternal sounds stimulus was sufficient to yield the observed increase in cortical thickness of the AC among our preterm newborn listeners. Prosodic features, such as melody, intensity, and rhythm, are known to be essential for language acquisition, and there is compelling evidence to suggest that newborns are strongly influenced by prosodic features of their native language long before first words are even produced (66–69). The question of whether daily exposure to unfiltered maternal sounds would result in different structural patterns of brain maturation is still unclear and needs to be investigated in future studies.

Our results suggest that daily exposure to biologically meaningful acoustic stimulation in the form of mother's voice and heartbeat sounds, even for a relatively short duration of time (i.e., 3 h/d), was yet sufficient to yield structural changes in the developing auditory cortex. One should bear in mind that for the vast majority of the time, newborns in the maternal sounds group were exposed to routine noises in the hospital environment, much like infants in the control group. The exposure difference between the groups comes down to only 3 h of recorded maternal sound exposure per day. It is therefore striking that newborns exposed to recorded maternal sounds demonstrated significant microstructural plasticity in the AC with minimal dosage and within less than 1 mo of exposure. These rapid changes are particularly interesting given that the rate of microstructural brain maturation in preterm newborns has been previously correlated with cortical growth, and predicted higher developmental test scores at 2 y of age (70). Although the auditory brain system undergoes experience-dependent plasticity across the lifespan (71), it is theorized that the probability of such plasticity may be higher and much needed during critical periods when the underlying developmental processes are still in flux, such as following a premature birth. In future studies, it would be interesting to test whether added exposure to maternal sounds in the early postnatal period can better facilitate synaptic pruning and neural migration in the AC than exposure to hospital environmental noise, a question that was beyond the scope of the present study and is yet to be determined.

Notably, exposure to maternal sounds in our study did not seem to influence overall brain growth, but instead led to a rather region-specific structural plasticity in the AC, a brain area that is most intuitively expected to be affected by the auditory stimulation. The fact that both newborns' head circumference (Table 1) and the width of the lateral ventricular horns (Table 2)—measures that have been previously correlated with total brain tissue volume (72)—did not significantly differ between the groups may be taken as evidence that the neuroplasticity induced by maternal sounds did not appear to increase overall brain matter, consistent with the specialized nature of experience-dependent plasticity (73, 74).

The possibility that newborns in the control group had smaller AC to begin with has been ruled out by our method of analysis, by which we normalized the size of the AC for each infant based on the TTD of the brain. This normalized measure represents the cortical thickness of the AC compared with the size of the brain, accounting for any possible differences between the groups in AC size before the study onset. Future ultrasonography studies, using a volume probe and a repeated-measure design over a longer period are needed to determine the effects of exposure to maternal sounds on total brain volume at term-equivalent age and beyond.

The bilateral plasticity in the AC is noteworthy. Given the linguistic nature of the stimulus the newborns were exposed to (i.e., maternal speech sounds), one might expect the effect to be primarily on the left side of the brain because of the functional lateralization typically seen in the adult brain when processing speech (75–78). However, it is possible that because the preterm newborns in our study were at a very early stage of development, essentially at an age equivalent to the last trimester of pregnancy and before full gestation, their brains had not yet begun to exhibit hemispheric specialization for speech, and thereby auditory neuroplasticity occurred more globally on both sides of the AC.

Table 2. Anatomical size of brain structures

Brain structure (width)	Maternal sounds	Control	*P* value
Auditory cortex			
R-AC	4.16 ± 0.94	3.11 ± 0.44	0.000
L-AC	3.62 ± 0.95	2.96 ± 0.68	0.015
Frontal horn			
R-FH	1.50 ± 1.07	2.00 ± 1.66	0.270
L-FH	2.15 ± 1.20	2.31 ± 1.75	0.723
Corpus callosum	4.72 ± 0.64	4.59 ± 0.73	0.578

Measurements normalized for each infant by the TTD.

An alternative hypothesis to explain the bilateral plasticity in the AC in the present study can be supported by a growing body of research, suggesting that the apparent left-sided lateralization for speech and language processing, specifically in the AC, is not an absolute dominance but rather a shared expertise by the two hemispheres (79–81). The above hypotheses must be made with caution because at this premature age, cortical folding is still in flux and the majority of neurons are still migrating and have not yet reached their final cortical destination. Thus, brain imaging at this age can only provide a snapshot in time of the current developmental course and no firm conclusions regarding permanent hemispheric dominancy can be drawn based on the present study. In addition, the early onset of left hemispheric differentiation in newborns is primarily based on functional rather than structural evidence. Previous studies in preterm neonates have found left-hemispheric functional advantage for speech processing in the posterior temporal region, as indicated by faster and more sustained responses to speech sounds over the left than over the right hemisphere (82). These findings are consistent with similar results suggesting that infants are born with a left hemisphere functional specialization for speech processing (83–85). The ultrasound data obtained in our study are solely based on structural measurements, and thus our findings cannot dispute or support the above-mentioned studies. However, our results indicate that newborns in the maternal sounds group had larger AC on the right compared with the left side of the brain (Fig. 2). Although this difference was not statistically significant, it is congruent with previous evidence showing that many sulci appear 1–2 wk earlier on the right than on the left side of the brain, with larger temporal sulci on the right hemisphere (86, 87).

Interestingly, we found no differences in CC size between the two groups of newborns in our study. The CC was chosen as a control region because of its central location and global role in interhemispheric communication, connecting the auditory areas between the two hemispheres (88). In addition, because the size of the CC is known to correlate with overall brain volume, we assumed that the CC may have a good predictive value for experience-dependent changes of global brain growth (89). Previous studies have found increased CC size in musicians (90, 91), although it is unclear whether this effect was solely caused by enhanced auditory stimulation or a more integrated influence of the multisensory experience (visual, auditory, motor, and tactile) associated with intense musical training (92). The fact that exposure to maternal sounds in our study did not elicit significant structural changes in the CC does not rule out the possibility that these changes would eventually occur at a later gestational age or with longer exposure periods. Further studies are needed to determine the degree of neural specificity and experience-dependent plasticity induced by maternal sounds exposure in preterm infants undergoing intensive care.

In considering the clinical relevance of our results, the limitations of cranial ultrasonography should be discussed. Although cranial ultrasound is the diagnostic imaging of choice for ruling out the appearance of brain pathology in the population of high-risk preterm neonates (93–96), and clearly an acoustically quieter examination than an MRI, some consider MRI to be more accurate. Linear measurements from cranial ultrasound have been strongly correlated with major neonatal cerebral sites seen on MRI (72, 93, 97–99), although several regions, including the posterior horn depth of the lateral ventricle and the cortex of the cingulate gyrus, may appear to be slightly narrower than when measured sonographically (97). For that reason, in the present study we intentionally chose not to focus on absolute values of brain measurements, but rather report normalized values based on the TTD of each infant. In the absence of MRI data available for our cohort of newborns, this approach allowed us to reliably examine the difference in brain structures between the groups regardless of whether or not the measurements correlate with MRI.

To summarize, this study provides evidence for auditory cortex plasticity in preterm newborns receiving daily exposure to maternal sounds in the first month of life. The functional implication of this early brain plasticity is still unclear and warrants further investigation. We theorize that exposing preterm newborns to mother's voice and heartbeat sounds provides them with a biologically familiar sensory experience that may play an important role in negating the effects of the noxious hospital environment on brain development. In addition, the use of recorded maternal sounds in the first month of life may be especially helpful in this high-acuity population of newborns whose exposure to live maternal stimulation is often limited because of infrequent parental visits. Despite the prospects of these results, the clinical benefits of maternal sound exposure are still a matter of speculations and no firm conclusions can be drawn based on the present study. Clearly, preterm newborns have more working against them than can be fully compensated for by added exposure to maternal sounds. However, the present study begins to show the effect that maternal sounds could have on very early brain development. Further studies are needed to determine the functional implications of these results and their predictive value of long-term hearing and language outcomes.

Materials and Methods

Patient Population. Forty preterm newborns admitted to the NICU at Brigham and Women's Hospital participated in this study. Newborns were randomized to one of two groups. A description of the study population is given in Table 1. Inclusion criteria included gestational age at birth between 25 and 32 wk and available records of cranial ultrasounds at one month of age. Exclusion criteria included prenatal diagnosed brain lesions, intracranial hemorrhage, cystic periventricular leukomalacia, prominent extra-axial spaces, and dilated lateral ventricular atria. Additional restrictive exclusion criteria were included to ensure our results would not be skewed by common conditions known to alter brain anatomy, such as small for gestational age (100) and intrauterine growth restriction (101, 102). A written informed consent was obtained from parents.

Maternal Sound Group. Newborns in the maternal sounds group (n = 21) received daily exposure to audio recordings of their mother's voice and heartbeat sounds played inside their incubator for a total of 3 h/d (four times per day for a duration of 45 min each). Maternal sounds were not played between midnight and 5:00 AM and were avoided during parental visits or medical examinations.

Environmental Sound Group (Control). Control preterm newborns (n = 19) were exposed to unfiltered routine hospital noise as present in the NICU environment with no added exposure to audio recordings of their mother's voice and heartbeat sounds. The acoustic properties of the NICU environment were measured in a separate study. Noise measurements taken in our NICU revealed an average higher noise levels during daytime (Leq = 60.05 dBA) compared with night-time (Leq = 58.67 dBA). Spectral analysis of frequency bands (>50 dB) showed that infants were exposed to frequencies to high-fervency sounds >500 Hz 57% of the time (53).

Maternal Sound Exposure. Mother's voice was recorded individually for each infant. Voice recording was done in a standardized fashion via a large-diaphragm condenser microphone (KSM44, Shure), capturing three types of vocalizations (speaking, reading, and singing) from each mother. Voice recordings were attenuated using a low-pass filter with a cut-off of 400 Hz to mimic the low frequency womb-like experience. The maternal voice recording was overlaid with individualized recordings of the mother's heartbeat using a digital stethoscope (ds32a; Thinklabs Digital Stethoscopes). This was done in an attempt to simulate the auditory experience in utero wherein the fetus hears both the mother's voice and the sounds of her heartbeat simultaneously. The maternal recordings were loaded onto an MP3 player (Phillips Electronics, SA2RGA04KS) for playback inside the incubator via a micro audio system. Loud peaks >65 dBA (A-weighted) of the maternal sound recordings were attenuated to achieve a safe level of sound delivery as was measured by a sound level meter (Bruel & Kjaer, 2250), approximating the level of normal human conversation (Mean LAq = 58.6 dBA). The above protocol was administered individually for each infant randomized to the maternal sounds group as validated in a previous safety and feasibility study (103), as well as in several experimental reports from our group (63, 104, 105).

Neonatal Cranial Ultrasound Measurements. All neonatal cranial ultrasounds used in this study were conducted by a blinded radiology technician as part of routine screening for neonatal brain abnormalities on day of life 30 ± 3. Post hoc measurements were obtained with electronic calipers using Centricity Enterprise Web imaging software platform (v3.0.10, GE Healthcare). Measurements were obtained by a specially trained researcher and were additionally verified for accuracy and reliability by an experienced radiologist specialized in neonatal cranial ultrasound reading. The group placement of each infant remained deidentified.

The following measurements were obtained from each neonatal cranial ultrasound. In the coronal plane: (*i*) thickness of the right and left AC in the mid portion of the superior temporal gyrus, and (*ii*) width of the right and left FHs of the lateral ventricle in the short axis at the level of the foramen of Monro. In the midsagittal plane: width of the body of the CC. The above measurements were normalized for each infant based on the TTD (leading edge to leading edge at the roof of the temporal horns of the lateral ventricles). Sample measurements are shown in Fig. 1.

Data Analysis. SPSS 20 (IBM) was used for all data analyses. Analysis was focused on determining the effects of sound exposure (i.e., group) on cortical region of interest related to hearing and language. A multivariate analysis of variance (MANOVA) was conducted to test for possible differences in the thickness of the right and left AC (dependent variables) between the groups (independent variable). An additional MANOVA was used to compare the width of the right and left FH between the two groups. Group differences in the width of the CC were examined with a *t* test. Spearman correlation was used to assess the association between gestational age at birth and brain measures. Within the maternal sounds group, Spearman correlation was used to assess the association between days of maternal sound exposure and the brain measures.

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