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Lateralization of activation within the superior temporal gyrus during speech perception in sleeping infants is prospectively associated with language skills in kindergarten: a longitudinal passive listening task-fMRI study.

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Abstract

Brain asymmetries are hypothesized to reduce functional duplication and thus have evolutionary advantages. The goal of this study was to examine whether early brain lateralization contributes to skill development within the speech-language domain. To achieve this goal, 25 infants (2-13 months old) underwent behavioral language examination as well as fMRI during sleep while listening to forward and backward speech and then were assessed on various language skills at 55-69 months old. We observed that infant functional lateralization of the superior temporal gyrus (STG) for forward > backward speech was associated with phonological, vocabulary, and expressive language skills 4 to 5 years later. However, we failed to observe that infant language skills or the anatomical lateralization of STG were related to subsequent language skills. Overall, our findings suggest that infant functional lateralization of STG for speech perception may scaffold subsequent language acquisition, supporting the hypothesis that functional hemisphere asymmetries are advantageous.

Key words: infant; language development; longitudinal; speech processing; task-fMRI.

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1. Introduction

Comparative studies have suggested evolutionary advantages of hemisphere asymmetries. One assumption is that lateralized brains can avoid functional duplication and thus increase cognitive capacity (Güntürkün, et al., 2020; Rogers, 2021). Previous research has consistently shown that speech-related functions (i.e., the perception of sound, voice, rhythm, and various language information such as phonology, semantics, and syntax during auditory sentence processing) are left-hemisphere dominant for most adults (Knecht et al., 2000; Carey and Johnstone, 2014) and typically developing children as young as age four (e.g., Wood et al., 2004; Szaflarski et al., 2006; Holland et al., 2007; Olulade et al., 2020). However, there are still open questions about when the lateralization of speech perception emerges and whether individual differences in brain lateralization are related to concurrent or future individual differences in language skills. Research has shown that structural and functional brain development in the first two years of life is foundational for long-term development (Gilmore, et al., 2018). Consistent with this, previous studies have observed that speech-related white matter tracts, resting-state functional connectivity, and electrophysiological responses in infancy is predictive of subsequent language skills (e.g., Zuk et al., 2021; Yu, et al., 2021; Lohvansuu et al., 2021). However, whether brain lateralization subserving speech perception in infancy is prospectively associated with long-term language skills remains largely unknown. Exploring this question allows us to examine the hypothesis of hemisphere asymmetries in the speech-language domain and may provide preliminary evidence for an early neural marker of long-term language development if a robust effect is observed.

Several studies have examined brain lateralization of anatomical structure or functional connectivity as early as infancy or even during the fetal stage (e.g., cortical folds in Glasel et al., 2011; Dubois et al., 2008; Hill et al., 2010; surface area in Li et al., 2014; cortical thickness in Li et al., 2015; brain volume in Lehtola et al. 2019; white matter tracts in Dubois et al., 2009; 2016; Liu et al., 2010; Dean et al., 2017; Liu et al., 2010; Liu et al., 2021; and Ford et al., 2023; brain volume in Dean et al., 2018; Lehtolaetal et al., 2019; resting state functional connectivity in Liu et al., 2022; surface area, cortical thickness, and resting-state functional connectivity in William et al., 2023). Although findings were mixed due to small sample sizes, different age groups, and varied methodological approaches related to the rapid development of infant brains (see Ford et al., 2023 and William et al., 2023), there is some consistency at the population level. For example, regarding sulcal depth, infants tend to show rightward asymmetry for the superior temporal sulcus and leftward asymmetry for the lateral fissure. Concerning surface area, there is leftward asymmetry for the temporal pole and rightward asymmetry for the inferior parietal and posterior temporal areas. Additionally, infants tend to exhibit a rightward asymmetry of cortical thickness in the superior and middle temporal gyrus. Only two studies have focused on the relationship between individual differences in infant brain lateralization and language skills, and they both observed a predictive effect of infant/fetal brain lateralization on later language skills (i.e., resting-state functional connectivity in Emerson et al., 2016; sulcal depth in Bartha-Doering et al., 2023). Their findings support the hypothesis of a hemispheric asymmetrical advantage in the speech-language domain. However, since the measurements of brain structure and resting-state functional connectivity are independent of stimulus input, those studies cannot address whether infants exhibit adult-like left lateralization for speech perception. Moreover, it remains unknown whether such functional lateralization in infancy is related to subsequent language development.

Using task functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS) and employing sentence stimuli, previous cross-sectional studies have investigated infant brain activity during speech perception to examine the earliest functional lateralization. The literature suggests a clear left lateralization that emerges early in infancy during processing of auditory sentences compared to processing non-speech sounds (e.g., Dehaene-Lambertz et al., 2010; Shultz et al., 2014; Minagawa-Kawai et al., 2011). For example, using fMRI, Dehaene-Lambertz et al. (2010) showed that auditory sentences elicited greater activation in the left temporal region compared to music, whereas music induced greater activation than auditory sentences in the right planum temporale in 2-month-old infants. However, when tasks involved manipulated auditory sentences or auditory sentences from an unfamiliar language, observations of hemispheric dominance in infants have been inconsistent (e.g., Dehaene-Lambertz et al., 2002; Pena et al., 2003; Vannasing et al., 2016; May et al., 2011; 2018; Perani et al., 2011; Zhang et al., 2022). For example, some studies continued to observe left-lateralized brain activity in temporal areas in infants (e.g., forward + backward > rest in Dehaene-Lambertz et al., 2002; forward > rest in Pena et al., 2003; forward > rest in Vannasing et al., 2016). Others, however, observed no hemispheric dominance (e.g., forward speech > rest in May et al., 2011), right hemisphere dominance (e.g., forward speech > rest in Perani et al., 2011), or mixed findings of hemispheric dominance (e.g., forward > backward speech in May, et al., 2018; and Zhang et al., 2022).

Although speech perception is left-hemisphere dominant in many people, and this lateralization may emerge as early as infancy, it remains unclear whether the degree of this hemispheric dominance is linked to the development of typical and/or atypical language skills. In children five years and older, previous fMRI and functional transcranial Doppler ultrasound (fTCD) studies have reported mixed findings for the relationship between language skills and brain lateralization for speech perception, both when examining individual differences of typically developing children and when comparing children with and without developmental language disorders (DLD). For example, in the literature examining individual differences of typically developing children, some studies have observed a positive relationship between functional lateralization of speech perception and language skills (e.g., Everts et al., 2009; Greon et al., 2012; Younger et al., 2019). Others, however, have shown negative correlations between brain lateralization and language skills (e.g., Bartha-Doering et al., 2018), or have observed a range of correlations (i.e., from positive to negative to no correlations) depending on the task used (e.g., Lidzba et al., 2011) or the brain region examined (e.g., Berl et al., 2014). In research investigating children with versus without developmental language disorders (DLD), some studies have reported decreased left-lateralization in children with DLD (e.g., De Guibert et al., 2011; Badcock et al., 2012), whereas other studies with larger sample sizes have reported no differences in hemisphere dominance between children with and without DLD (e.g., Vansteensel et al., 2021; Krishnan et al., 2021; Wilson & Bishop, 2018).

While the first five years in a child's life are an important period for language development, studies examining the relationship between functional lateralization for speech perception and language skills in children younger than 5 years old are rare. Among the limited studies on younger children (e.g., 4-year-olds in Bishop et al., 2014 and 1- to 5-year-olds in Kohler et al., 2015 using fTCD; 6-month-olds in Cantiani et al., 2019 using EEG), studies by Bishop et al. (2014) and Cantiani et al. (2019) consistently showed atypical lateralization for speech perception or rapid auditory processing in children with DLD (or a familial risk of DLD) as compared to children without DLD (or a familial risk of DLD). This finding suggests an association between brain lateralization and atypical language skills. However, the fTCD studies by Bishop et al. (2014) and Kohler et al. (2015) did not report significant correlations between individual differences in language skills and individual differences of brain lateralization during an active language task to which children were asked to respond.

To better address whether the lateralization of speech perception contributes to language skills in early childhood, it is important to examine infant brain responses during passive-listening language tasks, which allows us to examine the earliest functional lateralization with few confounds of strategic processes. It is also important to use fMRI because it offers better spatial resolution to capture individual differences in functional lateralization for speech perception as compared to using fTCD and EEG. Furthermore, to the best of our knowledge, despite a few passive-listening fMRI studies suggesting an early emergence of functional lateralization for speech perception in infant brains (Dehaene-Lambertz et al., 2010; Shultz et al., 2014; Dehaene-Lambertz et al., 2002), no passive-listening fMRI study has examined whether infant functional lateralization for speech perception is related to their concurrent and/or future language skills.

Therefore, to fill the literature gap, the current study investigated the lateralization of brain function underlying speech perception in infants during natural sleep. Next, we examined the relationship between such functional lateralization and children's language skills in infancy and subsequent language skills during preschool/kindergarten. We employed a passive-listening fMRI speech task, including both forward and backward speech blocks to assess neural activity for speech perception in sleeping infants. Our focus was on the lateralization of activation in the superior temporal gyrus (STG), a region consistently associated with speech perception and phonological processing in adults and older children (Hickok & Poeppel, 2000; Leonard & Chang, 2014; Wang et al., 2020; 2021) and commonly observed in sleeping infants during speech tasks (Dehaene-Lambertz et al., 2010; Shultz et al., 2014; Dehaene-Lambertz et al., 2002). Language skills were evaluated during the preschool/kindergarten period because major milestones of language, such as phonological, semantic, and syntactic skills, have typically been acquired by this age (Gervain, 2021). Additionally, we measured children's language skills in infancy not only to evaluate brain-behavioral correlations concurrently but also to utilize these early language skills as a control variable to examine if infant brain lateralization predicted language growth over time. This control approach, widely used in previous longitudinal studies (e.g., behavioral: Wagner et al., 1997; Oakhill & Cain, 2012; Adachi & Willoughby, 2015; neural: Cousijin et al., 2014; Suárez-Pellicioni, & Booth, 2018), could allow a somewhat stronger causal inference by accounting for baseline individual differences. If not controlled for, differences in the dependent measurement could be attributed to variations in the baseline rather than the effect of our predictor of interest. Following the hypothesis that brain lateralization is advantageous for cognitive development (Güntürkün, et al., 2020; Rogers, 2021), we expected that the lateralization of brain activation for speech perception in STG at the infant timepoint would predict later language skills in preschool/kindergarten, even after controlling for the autoregressive effect of language skills at the infant timepoint.

2. **Methods**

2.1. Participants

This study was part of a larger longitudinal project from the National Institute of Health (R01 HD065762). Families were recruited from the Greater Boston Area through the Research Participant Registry within the Division of Developmental Medicine at Boston Children's Hospital and through community outreach. Families were first invited when children were infants and agreed to the longitudinal study design. Infants underwent behavioral assessments and brain MRI scans, and parents completed questionnaires pertaining to their child's medical history, home environment, and socioeconomic context. All children who participated in the study met the following criteria: (1) from monolingual, American English-speaking families, (2) born at or after 37 weeks gestational age, (3) with no neurological illness or sensory impairments, (4) with no contraindications for MRI scanning, and (5) with a typical hearing screening.

At the infant timepoint, a cohort of 113 children were invited to participate in the MRI scan and to perform the fMRI speech task. Among them, no data were collected for 28 infants as they did not fall asleep after arrival. Due to awakening and/or movement, 17 children did not start the fMRI speech task after the anatomical scans (i.e., MRI and/or DTI), and 8 children did not finish the fMRI speech task. Among the 60 children who completed the fMRI speech task, 55 of them were assessed with language skills using the Preschool Language Scale Fifth Edition. Later at the preschool/kindergarten timepoint, 26 children were re-evaluated on language skills using the Woodcock-Johnson IV Tests of Oral Language, a language test that includes three composite language scores. Among these, we obtained oral expressive composite scores from 26 children, listening comprehension scores from 11 children, and phonetic coding from 21 children. Of the 26 children with fMRI speech task data collected during infancy and oral expressive composite scores collected at the preschool or kindergarten age, one child had an oral expressive standard score 2.56 standard deviations (corresponding to a probability of 1%) below the mean and was excluded from the final analysis.

As a result, 25 children (13 males, 12 females) were included in the final analysis. Figure 1 shows the details of the inclusion procedure. Participants were 3 to 13 months old at the infant timepoint and 55 to 69 months old at the preschool/kindergarten timepoint. Among the 25 participants, 11 participants had a familial risk of dyslexia as determined by parent questionnaires reporting at least 1 first-degree relative with a dyslexia diagnosis or history of reading difficulty. All experimental procedures were approved by the institutional review boards at Boston Children's Hospital and Harvard University. Before participation, informed written consent was obtained from each child's parent or legal guardian.

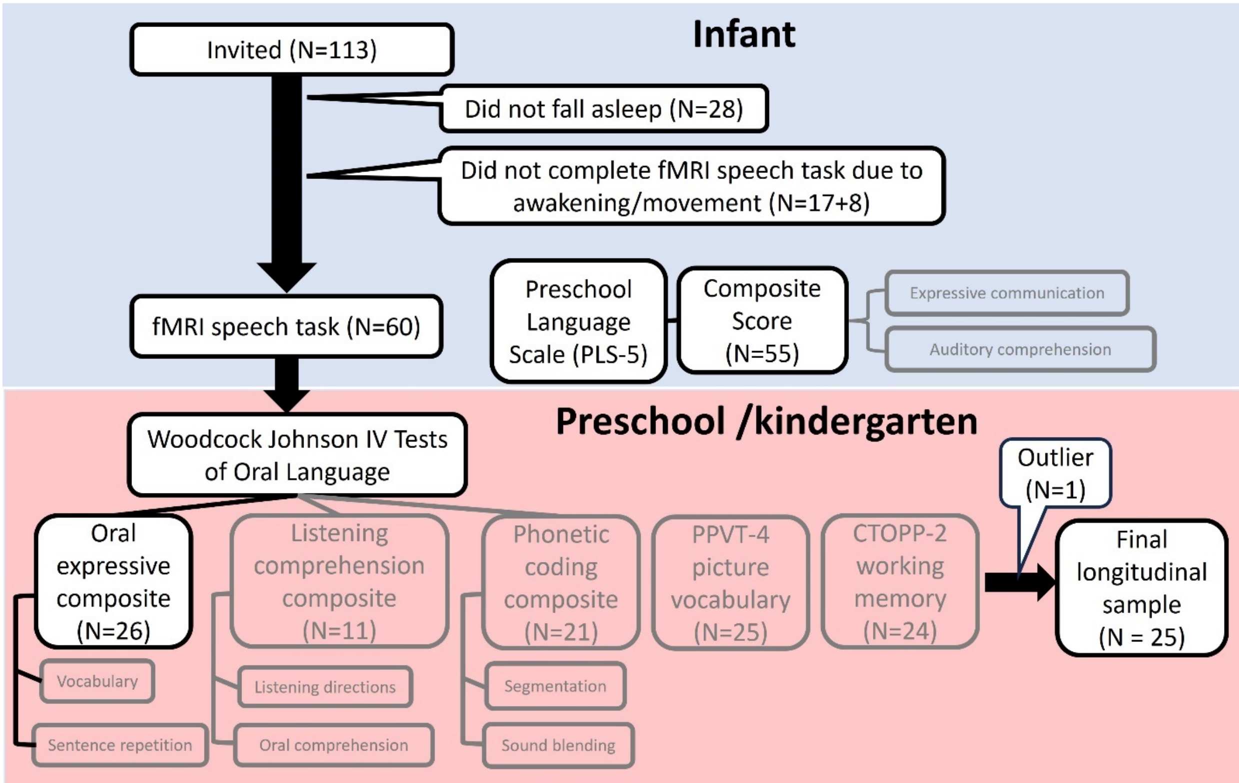


Figure 1. The inclusion procedure for the current study. At the infant time point, brain activity was measured using an fMRI speech task, and language skills were assessed using the Preschool Language Scale (PLS-5). At the time of analysis, 26 of the 60 children who performed the fMRI speech task in infancy had been re-evaluated during preschool or kindergarten using oral expressive, listening comprehension, and phonetic coding scores from the Woodcock-Johnson IV Tests of Oral Language, picture vocabulary scores from the PPVT-4, and working memory scores from the CTOPP-2. The primary variables of interest in this study are highlighted in white. All 25 participants included in the final longitudinal sample had PLS-5 language composite scores assessed during infancy. N represents the number of participants and the subtests included in each composite are displayed in the bubbles below or beside the composites.

2.2. Procedure

2.2.1. Language measures and fMRI task during infancy

After arriving at Boston Children's Hospital, infants underwent a standardized behavioral testing session to fatigue them and prepare them for the f/MRI scanning. The Preschool Language Scale Fifth Edition (PLS-5, Zimmerman, Steiner, & Pond, 2011) was used to assess the infant's language skills. This test yields a composite language score with two subtests. In the expressive communication subtest, infants were evaluated on vocal development and social communication, including babbling or gestures. In the auditory comprehension subtest, infants were tested on target skills that are considered important precursors for language development such as attention to speakers or appropriate object play. Standard scores for the language composite were calculated by adding the standard scores of expressive communication and auditory comprehension and then converting them into new standard scores based on a norm table for the appropriate age range.

All scanning was performed during natural sleep without sedation. Once the infant fell asleep, earplugs, earmuffs ("Minimuffs", Natus Medical Inc., San Carlos, CA), and MRI-compatible headphones were placed on the infant. Then, the infant was slowly and gently placed on the prepared scanner bed. The infant's head was positioned in the coil and the researcher carefully adjusted the restraint straps in place to secure the infant and limit their movements. The scan began once the infant was snuggled into the space with a soft warm blanket and confirmed to be soundly asleep (for details, see infant scan procedures in Raschle et al., 2012). A block-design speech task fMRI was utilized. In this passive speech task, a female-voice recording of an excerpt of Dr. Seuss's “One Fish, Two Fish” was played through headphones while the infant was asleep. The audio stimuli were presented in alternating forward and backward speech blocks that lasted about 18 seconds each. Rest blocks of 18 seconds were inserted randomly. Overall, there were 6 blocks of forward speech, 6 blocks of backward speech and 4 blocks of rest. An extra 7.2s fixation screen was included at the beginning of the task to achieve scanning stability. Throughout the scan, the caregiver and a team member stayed in the scanner room. If the infant began to wake, the MRI acquisition was paused, and the caregiver would attempt to soothe the infant back to sleep. If the infant cried or became distressed at any time during the scan, the research team immediately stopped the scanning and removed the baby from the scanner.

2.2.2. Language measures at preschool or kindergarten age

All infants with fMRI data were invited back between preschool and kindergarten for a longitudinal follow-up. The Woodcock-Johnson IV Tests of Oral Language (Schrank, Mather, & McGrew, 2014) were used to re-evaluate their language skills. This set of tests produces three composite language scores. The oral expressive composite score comprises a picture vocabulary subtest, where the child names stimulus items presented by the examiner, and a sentence repetition subtest, where the examiner speaks a sentence, and the child repeats it exactly, with sentence complexity and length increasing as the child progresses. The listening comprehension composite score includes an oral comprehension subtest, where the child provides an omitted word through syntactical and semantic cues after listening to a brief audio-recorded passage, and a listening direction subtest, where the child points to items on a page of testing material in a specific order after listening to a brief audio-recorded instruction. The phonetic processing composite score contains a segmentation subtest, where the child identifies parts of words, and a sound blending subtest, where the child listens to a sequence of syllables from an audio recording and combines the sounds into a word. Raw scores from these tests were entered into an online scoring system, producing the standard score of their composite scores. In addition to using the Woodcock-Johnson IV Test of Language, the Peabody Picture Vocabulary Test (PPVT-4, Dunn and Dunn, 2007) was used to assess children's picture vocabulary skills. In this test, the examiner reads a single word, and children are asked to select the picture (out of four possible choices) that represents the target word. Furthermore, children's working memory was measured by the Memory for Digits subtest of the Comprehensive Test of Phonological Processing (CTOPP-2; Wagner et al., 2013), in which children are asked to repeat strings of numbers, which vary in length from two to eight digits. As the number of children with oral expressive composite scores (n = 26) exceeded those for other language and cognitive measures (n = 11 for listening comprehension and n = 21 for phonetic coding, n = 25 for PPVT-4 picture vocabulary, n = 24 for CTOPP-2 working memory), and a larger sample size enhances the power of correlational analyses, our main longitudinal analyses utilized the oral expressive composite scores. However, statistics on other language scores (i.e., listening comprehension, phonetic processing, PPVT-4 picture vocabulary) and working memory (i.e., from CTOPP-2 memory for digits) are also reported for the current sample.

2.3. Scanning parameters

All infant brain images were acquired at Boston Children’s Hospital between 2016 and 2019 utilizing a Siemens scanner with a 32-channel head coil. T1-weighted images were acquired using a sequence of Magnetization-Prepared Rapid Acquisition Gradient Echo (MPRAGE) with the following parameters: TR = 2520 ms, TE = 1.74 ms, flip angle =7, field of view = 192 mm, slice thickness = 1 mm, voxel size = 1 mm x 1 mm x 1 mm, matrix size = 192 x 192, number of slices = 144. Functional images were acquired using a sequence of echo planar imaging (EPI) with the following parameters: TR = 720 ms, TE = 30 ms, flip angle = 60, multiband acceleration factor = 3, field of view = 192 mm, slice thickness = 4 mm, voxel size = 3 mm x 3 mm x 4.8 mm, matrix size = 64 x 64, number of slices = 33, acquisition sequence = interleaved from foot-to-head.

2.4. Data analyses

sMRI preprocessing.

Infant FreeSurfer image analysis suite (Zollei et al., 2020) was used to extract the brain from the skull, correct for intensity inhomogeneity, and segment T1 images into different tissue classes (gray matter, white matter, cerebrospinal fluid) and brain regions. To improve tissue classification accuracy, T1 images were submitted in parallel to iBEATv2.0 Docker (Wang et al., 2018; Li et al., 2014; 2015; 2018). Resulting segmentations from each software package were then combined and resubmitted to a modified FreeSurfer "recon" pipeline to generate white matter and pial surfaces and then regional estimates of gray matter volume, surface area, and cortical thickness.

fMRI analysis in a 7.5-month-old template space.

Preprocessing. Before conducting any fMRI preprocessing, the first 10 functional volumes were discarded. All functional images were then realigned to the mean functional image using Statistical Parametric Mapping (SPM12). Co-registration of functional images to their corresponding skull-striped T1-weighted image was estimated using the Advanced Normalization Tools (ANTs) with a rigid transformation, but functional images were not resampled at this step. After that, the skull-stripped T1-weighted image was warped to the standard space of the 7.5-month-old pediatric anatomical template developed by Richards et al. (2016) using ANTs with both affine and syn deformable transformations. We then applied the transformations (rigid co-registration + affine and syn deformable transformations) to the functional images such that they were normalized to the 7.5-month-old pediatric template using one interpolation. Finally, smoothing was applied to all normalized functional images using a 4-mm Gaussian kernel. Artifact Detection Tools (ART) was used to identify outlier volumes with greater than 1.5-mm scan-to-scan displacement or 4% global signal change from the mean. All participants had no more than 20% outlier volumes.

First-level modeling and lateralization calculation. A general linear model (GLM) was generated using SPM12 by entering the onsets and durations for the forward speech, backward speech, and rest conditions as covariates of interest. Motion parameters, artifact regressors, and global mean signal generated by ART were entered into the GLM as covariates of no interest. The hemodynamic response function (HRF) in SPM12 was replaced with an infant HRF, which had a protracted and attenuated positive peak with an increased undershoot-to-peak ratio compared with adults (Arichi, et al., 2012). The contrast of forward > backward speech was generated to evaluate speech perception in the brain. Because no Automated Anatomical Labeling (AAL) atlas is developed for the 7.5-month-old pediatric anatomical template in Richards et al.(2016), we warped the widely used UNC 1-year-old AAL atlas (Shi et al., 2011) to the 7.5-month-old MRI template space using ANTS. Then, the left and right STG masks were generated based on this warped AAL atlas using the AFNI 3dcalc function. To calculate the lateralization of brain activation in the superior temporal gyrus (STG), brain activation for the contrast of forward > backward speech was then extracted from the most activated 100 voxels in the left and right STG respectively. The lateralization index of brain activation in STG was calculated using (left – right)/(left + right) for each participant. This individualized top-100 voxel approach has been used several times in previous studies to examine (1) brain-behavioral correlations across language, reading, and math domains (e.g., Bitan, et al., 2009; Younger et al., 2019; Gullick, & Booth, 2014; Suarez-Pellicioni, et al., 2020; Yamasaki, et al., 2021; Wang et al., 2020; 2021) and (2) subtle functional specialization in infants (e.g., Deen et al., 2017; Kosakowski et al., 2023; Yates, Ellis, & Turk-Browne, 2023). Additionally, we used the most activated 50 and 150 voxels to assess the robustness of our findings using the top 100 voxels. To ensure engagement of bilateral STG during natural sleep, we conducted a one-sample t-test for the contrasts of forward speech > rest, backward speech > rest, and forward > backward speech within the bilateral STG mask using a lenient threshold of voxel-wise $p < 0.05$, cluster size > 50. Whole brain activation maps are also displayed as supplementary material (see **Figure S1**).

fMRI analysis in each individual's native space.

Because our infants were aged between 2 and 13 months, a period of rapid brain growth, normalizing infant fMRI data to a 7.5-month-old infant template may introduce confounds and distortions. Therefore, we re-analyzed children's functional lateralization in their native space to assess the robustness of our findings.

Preprocessing. The first 10 functional volumes were discarded, and all functional images were realigned to the mean functional image using Statistical Parametric Mapping (SPM12). After this, smoothing using a 4-mm Gaussian kernel was applied. The software Artifact Detection Tools (ART) was used to identify outlier volumes with greater than 1.5-mm scan-to-scan displacement or 4% global signal change from the mean.

First-level modeling and lateralization calculation. A general linear model (GLM) was generated using SPM12 by entering the onsets and durations for the forward speech, backward speech, and rest conditions as covariates of interest. Motion parameters, artifact regressors, and global mean signal generated by ART were entered into the GLM as covariates of no interest. The hemodynamic response function (HRF) in SPM12 was replaced with an infant HRF, which had a protracted and attenuated positive peak with an increased undershoot-to-peak ratio compared with adults (Arichi, et al., 2012). The contrast of forward > backward speech was generated to evaluate speech perception in the brain. Because individual's brain activation maps were in native space, we conducted several steps to generate individualized bilateral STG masks by warping the UNC 1-year-old AAL atlas (Shi et al., 2011). First, we co-registered the infant's skull-striped T1-weighted images to their functional images using the Advanced Normalization Tools (ANTs) with a rigid transformation. Then, we warped the UNC 1-year-old template to the infant's skull-striped T1-weighted image using ANTs with both affine and syn deformable transformations. After that, we applied the transformations (rigid co-registration + affine and syn deformable transformations) to the UNC 1-year-old AAL atlas such that this atlas was aligned with the infant's T1-weighted image and functional images.

Finally, the bilateral STG masks for each individual were generated based on this warped UNC 1-year-old AAL atlas using the AFNI 3dcalc function. To calculate the lateralization of brain activation in the superior temporal gyrus (STG), brain activation for the contrast of forward > backward speech was then extracted from the most activated 100 voxels in the individualized left and right STG masks, respectively. The lateralization index of brain activation in STG was calculated using (left – right)/ (left + right) for each participant.

Correlational analyses with functional lateralization in STG.

All language scores were first tested for normality using Shapiro-Wilk tests. Pearson correlations were used to evaluate intercorrelations among all normally distributed variables, and Spearman correlations were conducted to assess intercorrelations among variables violating normal distributions. The significance of concurrent correlations between functional lateralization in STG and PLS-5 language scores (i.e., total, expressive communication, auditory comprehension) during infancy were determined using a Bonferroni correction for 3 tests ($p < 0.05/3 = 0.017$). The significance of longitudinal correlations between functional lateralization in STG during infancy and five language or cognitive scores at the preschool/kindergarten age (i.e., Woodcock-Johnson IV oral expressive, listening comprehension, and phonetic coding scores, PPVT-4 picture vocabulary, and CTOPP-2 working memory scores) were determined by using a Bonferroni correction for 5 tests ($p < 0.05/5 = 0.01$). To examine a potential causal influence of infant functional lateralization on subsequent language skill development, a hierarchical regression analysis controlling for infant language composite scores was further conducted, with infant functional lateralization entered as the predictor, and language or cognitive scores in preschool/kindergarten entered as the dependent variable.

Exploratory correlational analyses with structural lateralization in STG.

Several previous cross-sectional studies observed that children with developmental language disorder show typical left hemisphere structural asymmetry within the temporal language regions, providing little support for the link between gray matter asymmetry in STG and language skills (see review by Mayes, Reilly, & Morgan, 2015). However, one recent longitudinal study (Bartha-Doering et al., 2023) observed that the fetal temporal sulcus depth asymmetry was prospectively related to later language skills. Therefore, as part of exploratory analyses, the current study also conducted correlational analyses to examine if the lateralization of STG using brain structural indices (i.e., surface area, cortical thickness, gray matter volume) in infancy was related to language skills (i.e., total, expressive communication, and auditory comprehension scores) in infancy. The significance of the concurrent correlational effects was determined by using Bonferroni correction for 9 tests ($p < .05/9 = .0056$). In addition, we examined longitudinal correlations between the lateralization of STG using brain structural indices and language and cognitive skills (i.e., the oral expressive, listening comprehension, and phonetic coding scores from the Woodcock-Johnson IV Test of Oral Language, picture vocabulary score from the PPVT-4, and working memory from the CTOPP-2). Bonferroni correction for 15 tests ($p < .05/15 = .0033$) was applied to determine the significance of the longitudinal relationships.

3. Results

3.1. Description of Age, Language skills, and Brain Functional and Anatomical Lateralization in STG.

The mean, standard deviation, and range for children's age, cognitive, and language skills at both the infant and preschool/kindergarten timepoints are displayed in **Table 1**. Independent sample t-tests between children with a familial history of dyslexia and those without a familial history of dyslexia showed no significant differences in any language or cognitive scores (*p*s > .125).

Table 1. *Description of children's age in months and language skills at both timepoints.*

Timepoints	*Variables*	*Number of participants*	*Mean*	*Standard Deviation*	*Range*
Infant	*Age (months)*	*25*	*7.5*	*3.4*	*2.5 – 12.9*
	Language composite	*25*	*95.3*	*9.1*	*73 – 112*
	Expressive communication	*25*	*94.8*	*10.4*	*69-114*
	Auditory comprehension	*25*	*101.5*	*11.4*	*79-130*
Preschool/ Kindergarten	*Age (months)*	*25*	*60.9*	*4.0*	*55.0 – 69.1*
	Oral expressive	*25*	*114.2*	*10.4*	*96 – 133*
	Listening comprehension	*11*	*108.4*	*13.7*	*81-124*
	Phonetic coding	*21*	*122.1*	*16.9*	*80-150*
	PPVT-4 picture vocabulary	*25*	*121.1*	*11.6*	*97-143*
	CTOPP-2 working memory	*24*	*102.3*	*13.8*	*80-135*

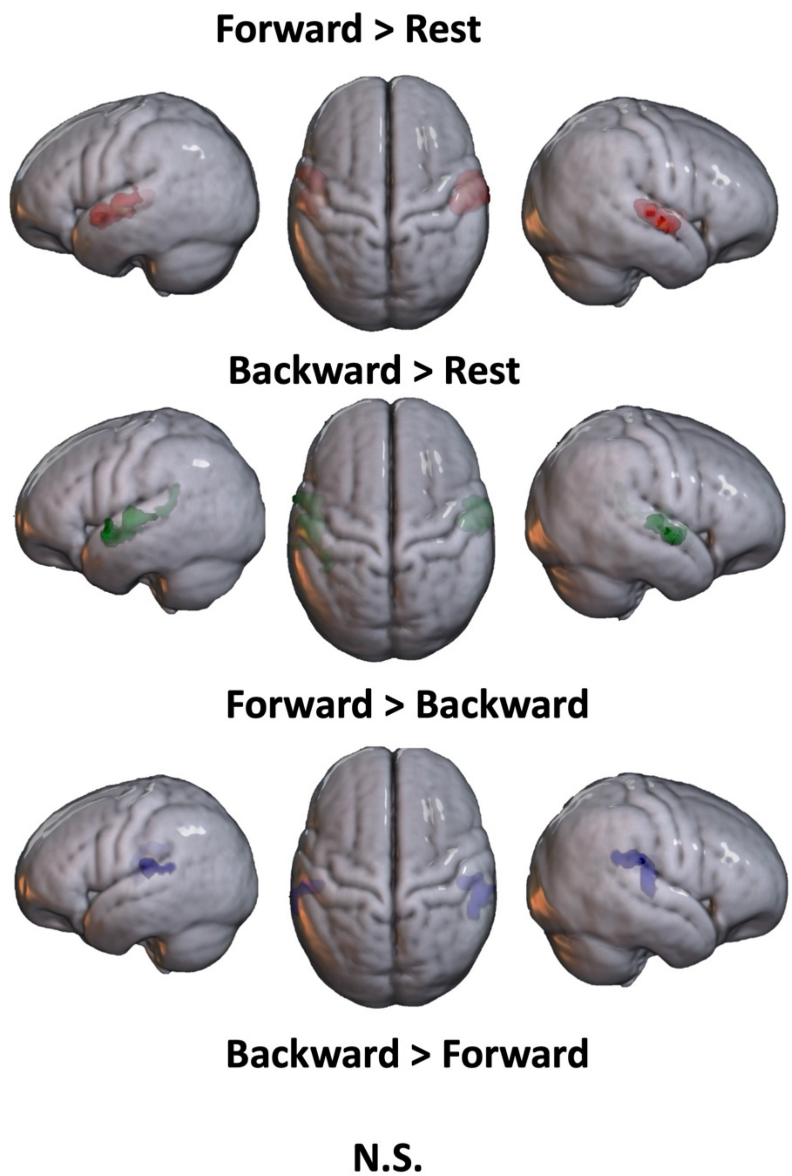
Note: The language composite score at the infant timepoint is the composite score of both expressive comprehension and auditory comprehension from the Preschool Language Scale (PLS-5). The oral expressive, listening comprehension, and phonetic coding scores at the preschool/kindergarten timepoint are three composite scores from the Woodcock Johnson IV Tests of Oral language. Ages are displayed in months and all language scores are reported with standard scores.

Regarding brain activation, when analyzing fMRI data in a 7.5-month-old template space, both the left and right STG were activated at the group level for the contrasts of forward speech > rest, backward speech > rest, and forward > backward speech, indicating bilateral STG engagement during the speech fMRI task, even when infants were asleep (**Table 2** and **Figure 2**). After confirming bilateral STG engagement during speech perception, we estimated lateralization of brain activation within the most activated 100 voxels. **Figure 3** shows the extent to which the top 100 voxels within the STG mask overlap across participants and in subgroups of children based on their lateralization of brain activation in STG for forward > backward speech in infancy or their oral expressive composite scores at the preschool/kindergarten timepoint. We observed low overlap among participants' top 100 voxels. In addition, there were no systematic pattern differences in the location of the top 100 voxels for different sub-groups of participants (i.e., left-lateralized vs. right-lateralized infants; high-language vs. average-language children). The lateralization of brain activation in STG for forward > backward speech had a mean value of -0.05, a standard deviation of 0.21, and a range from -0.43 to 0.22. Positive values indicate left lateralization, whereas negative values mean right lateralization. When re-calculating infant functional lateralization in each individual's native space, the lateralization of brain activation in STG for forward > backward speech had a mean value of -0.05, a standard deviation of 0.22, and a range from -0.46 to 0.32. Independent sample t-tests showed no significant differences in the functional lateralization of STG for speech perception in children with a familial history of dyslexia versus those without a familial history of dyslexia [lateralization in a 7.5-month-old template space: $t(22) = 0.77$, $p = .449$, uncorrected; lateralization in each individual's native space: $t(22) = 0.68$, $p = .500$, uncorrected]. In addition, age was not related to infant functional lateralization or standard language and cognitive skills scores measured at either infant or preschool/kindergarten timepoint (ps > .324, uncorrected).

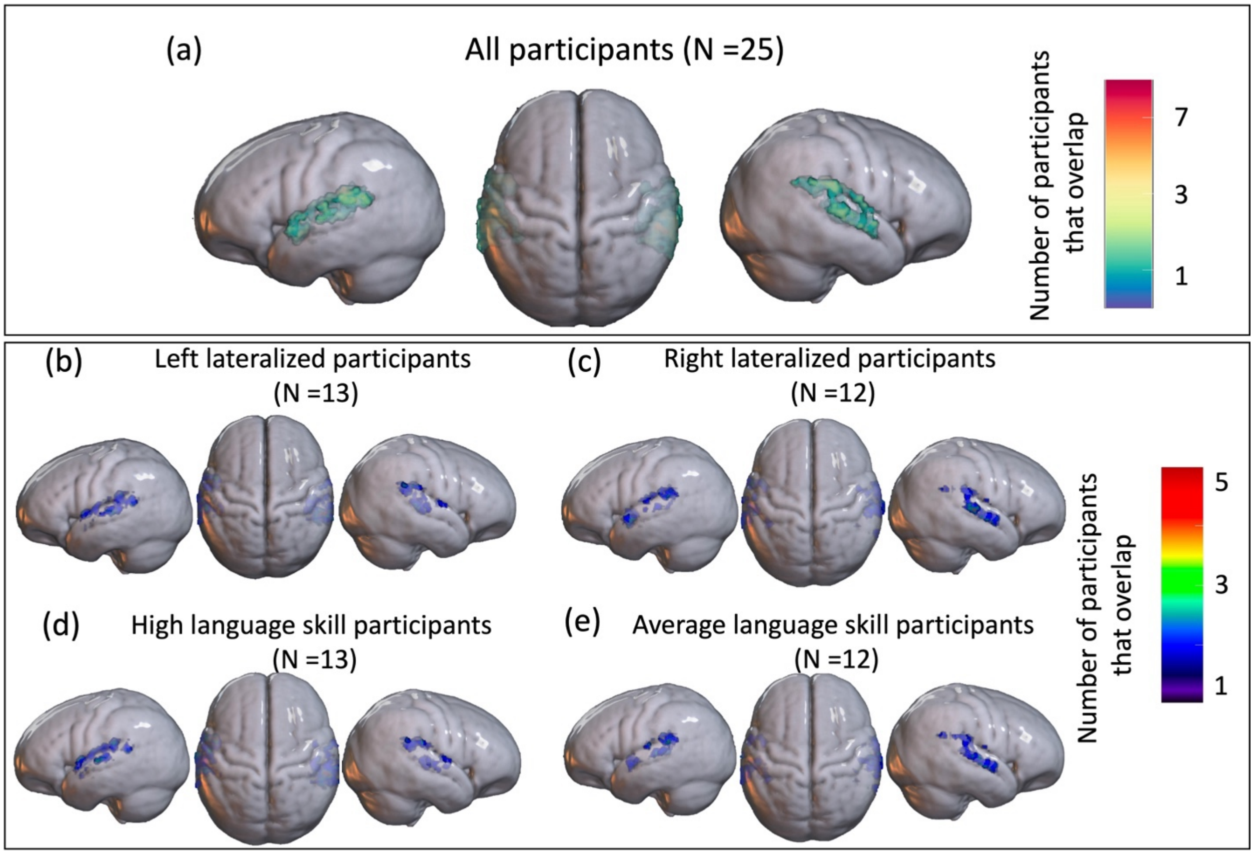
Table 2. *Group-level brain activation in the left and right STG for the contrasts of forward speech > rest, backward speech > rest, and forward > backward speech.*

Contrasts	*Left Superior Temporal Gyrus*		*Right Superior Temporal Gyrus*	
	T value of peak	*Cluster size (Num. of voxels)*	*T value of peak*	*Cluster size (Num. of voxels)*
Forward speech > Rest	*4.91*	*244*	*3.23*	*314*
Backward speech > Rest	*5.10*	*311*	*2.68*	*192*
Forward > Backward speech	*2.45*	*86*	*3.23*	*181*

Note: the MNI coordinates are not reported due to the use of an infant-specific space (i.e., a 7.5-month-old template).



<u>Figure 2.</u> *Group-level brain activation maps on a 7.5-month-old template for the contrasts of forward speech > rest (red), backward speech > rest (green), and forward > backward speech (blue) within the left and right STG masks at a threshold of voxel-wise $p < 0.05$, cluster size > 50, uncorrected.*



<u>Figure 3</u>. The overlap of individualized top 100 voxels within the STG masks among participants on a 7.5-month-old template. (a) The overlap across all participants. (b) The overlap among participants who showed left lateralized brain activation in STG (i.e., positive values) for forward > backward speech in infancy. (c) The overlap among participants who exhibited right-lateralized brain activation in STG (i.e., negative values) for forward > backward speech in infancy. (d) The overlap among participants (High language skill participants, Mean = 122, SD = 6.0) who had oral expressive composite scores above the median in preschool/kindergarten. Among these 13 high language skill participants, 10 had left-lateralized brain activation in STG for forward > backward speech in infancy. (e) The overlap among participants (Average language skill participants, Mean = 105, SD = 5.8) who had oral expressive composite scores below the median in preschool/kindergarten. Among these 12 average language skill participants, 9 had a right-lateralized brain activation in STG for forward > backward speech in infancy. N indicates the total number of participants in each brain map. Color bar represents the number of participants overlapped at the same voxel location.

Regarding infant anatomical lateralization in STG, the lateralization of surface area had a mean value of 0.04, a standard deviation of 0.04, and a range from -0.07 to 0.1. The lateralization of volume had a mean value of 0.02, a standard deviation of 0.04, and a range from -0.07 to 0.11. In addition, the lateralization of cortical thickness had a mean value of -0.01, a standard deviation of 0.02, and a range from -0.05 to 0.03. Again, positive values indicate left lateralization, whereas negative values mean right lateralization. There were no significant differences between infants with a familial history of dyslexia and those without a familial history of dyslexia in the lateralization of STG using volume [$t(22) = -1.60$, $p = .124$, uncorrected], cortical thickness [$t(22) = 0.86$, $p = .400$, uncorrected], or surface area [$t(22) = -2.59$, $p = .018$, uncorrected] when a Bonferroni correction for 3 independent sample t-tests ($p < .05/3 = .017$) was applied. In addition, age was not associated with structural lateralization of STG in our study (*p*s > .148, uncorrected).

3.2. Brain-Behavioral Correlations for Infant Functional Lateralization in STG.

Based on Shapiro-Wilk tests, all language scores were normally distributed (*p*s > .153) except for the listening comprehension composite score from the Woodcock-Johnson Tests of Oral Language ($p = .035$), which has the smallest sample size (N = 11). We observed that the lateralization of brain activation in STG (calculated either using a 7.5-month-old template or each individual's native space) during infancy was prospectively correlated with the oral expressive, phonetic coding, and PPVT-4 picture vocabulary scores at preschool/kindergarten age (**Table 3**). The scatterplots show that the more left-lateralized brain activation for speech perception infants had, the higher their subsequent oral expressive, phonetic coding, and PPVT-4 picture vocabulary scores in preschool/kindergarten (**Figure 4**). Although there also appeared to be a correlation between the lateralization of brain activation in STG and the expressive communication score during infancy, this effect reached significance only when using functional lateralization calculated with a 7.5-month-old template. Moreover, we observed that none of the language scores during infancy were significantly correlated with language or cognitive scores measured at the preschool/kindergarten timepoint.

***Table 3**. The relations of functional lateralization during infancy to language and cognitive skills at infant and preschool/kindergarten timepoints.*

Variables	*2.INF-language composite (N=25)*	*3.INF-expressive comm. (N=25)*	*4. INF-auditory comp. (N=25)*	*5.PRE-oral expressive (N=25)*	*6.PRE-listening comp. (N=11)*	*7.PRE-phonetic coding (N=21)*	*8. PRE-PPVT-4 vocabulary (N=25)*	*9. PRE-working memory (N=24)*
1.INF-functional lateralization (template space)	*.411 (.041)*	***.527 (.007)***	*.340 (.096)*	***.556 (.004)***	*.494 (.123)*	***.604 (.004)***	***.624 (<.001)***	*.285 (.176)*
1. INF-	*.265 (.200)*	*.397 (.049)*	*.109 (.602)*	***.544 (.005)***	*.367 (.267)*	***.602 (.004)***	***.616 (.001)***	*.292 (.165)*

functional lateralization (native space)							
2.INF-language composite	*.660 (<.001)*	*.767 (<.001)*	*.370 (.069)*	*.354 (.285)*	*.428 (.053)*	*.334 (.102)*	*.043 (.840)*
3.INF-expressive communication		*.693 (<.001)*	*.005 (.980)*	*.408 (.213)*	*.227 (.322)*	*.064 (.761)*	*-.020 (.926)*
4.INF-auditory comprehension			*.378 (.063)*	*.576 (.064)*	*.424 (.056)*	*.356 (.081)*	*.352 (.092)*
5.PRE-oral expressive				*.835 (.001)*	*.581 (.006)*	*.699 (<.001)*	*.329 (.117)*
6.PRE-listening comprehension					*.660 (.037)*	*.643 (.033)*	*.560 (.073)*
7.PRE-phonetic coding						*.700 (<.001)*	*.397 (.083)*
8. PRE-PPVT-4 vocabulary							*.337 (.108)*

Note: INF = the infant timepoint. PRE = the preschool/kindergarten timepoint. Outside the parenthesis are r values, whereas inside the parenthesis are p values, uncorrected. ***Bolded values*** *indicate significant brain-behavioral correlations after Bonferroni correction for 3 concurrent correlational tests during infancy (p < 0.05/3=0.017), and for 5 longitudinal correlational tests (p < 0.05/5=0.01). Infant functional lateralization for forward > backward speech in the superior temporal gyrus (STG) was calculated using either a 7.5-month-old template or each individual's native space.*

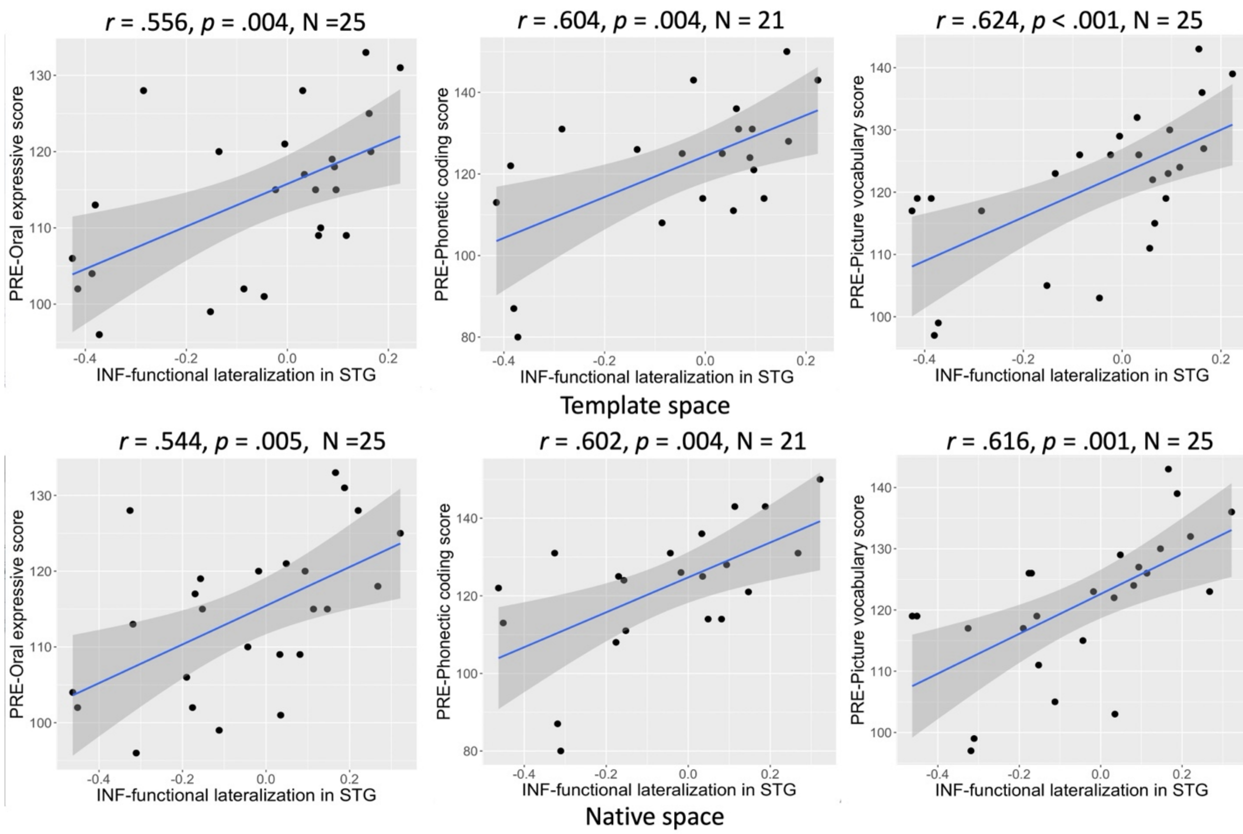


Figure 4. *The scatterplots of the relations between infant functional lateralization for forward > backward speech in STG (calculated using either a 7.5-month-old template or each individual's native space) and various language skills (i.e., the oral expressive, phonetic coding, and PPVT-4 picture vocabulary scores) in preschool/kindergarten. N represents the number of participants. INF = the infant timepoint, and PRE = the preschool/kindergarten timepoint. STG = superior temporal gyrus. For INF-functional lateralization in STG, a positive value indicates left lateralization, whereas a negative value means right lateralization.*

In addition to correlational analyses, three follow-up hierarchical regression analyses were conducted to examine the predictive effects of infant functional lateralization in STG, calculated using a 7.5-month-old template (**Table 4**) and each individual's native space (**Table 5**). For functional lateralization calculated using a 7.5-month-old template (as shown in **Table 4**), we observed that after controlling for the language composite score in infancy, the lateralization of brain activation in STG for speech perception at the infant timepoint still significantly predicted later oral expressive, phonetic coding, and picture vocabulary scores at the preschool/kindergarten timepoint. These predictions explained an additional 19.7%, 27.0%, and 28.4% variances, respectively, beyond infant language skills. Additional analyses revealed that even when controlling for expressive communication and auditory comprehension scores in infancy separately, infant functional lateralization continued to be a significant predictor for subsequent oral expressive scores (i.e., controlling for infant expressive communication skill: beta = 24.80, p = .026, ΔR^2 = 14.8%; controlling for infant auditory comprehension skill: beta = 31.44, p = .002, ΔR^2 = 34.8%), phonetic coding scores (i.e., controlling for infant expressive communication skill: beta = 42.98, p = .020, ΔR^2 = 22.0%; controlling for infant auditory comprehension skill: beta = 48.34, p = .007, ΔR^2 = 32.5%), and picture vocabulary scores (i.e., controlling for infant expressive communication skill: beta = 33.98, p = .005, ΔR^2 = 26.3%; controlling for infant auditory comprehension skill: beta = 38.32, p < .001, ΔR^2 = 41.0%). Those longitudinal effects remained consistent when calculating infant functional lateralization in STG using each individual's native space (see **Table 5**). Moreover, all of the longitudinal effects remained significant when using the top activated 50 or 150 voxels instead of the top activated 100 voxels.

Table 4. *Hierarchical regression analyses for the longitudinal effects of infant functional lateralization in STG calculated within a 7.5-month-old template space.*

Models	*Predictors*	*Dependent variable*			
		Beta	*p*	*R^2*	*R^2 change*
		PRE-Oral expressive score (N = 25)			
1	*INF-language composite*	*0.42*	*.069*	*.137*	*-*
2	*INF-language composite*	*0.19*	*.384*		
	INF-functional lateralization in STG (Template)	***24.39***	***.018***	*.334*	*.197*
		PRE-Phonetic coding score (N = 21)			
1	*INF-language composite*	*0.90*	*.053*	*.183*	*-*
2	*INF-language composite*	*0.64*	*.107*		
	INF-functional lateralization in STG (Template)	***44.35***	***.008***	*.453*	*.270*
		PRE-Picture vocabulary score (N = 25)			
1	*INF-language composite*	*0.43*	*.102*	*.112*	*-*
2	*INF-language composite*	*0.12*	*.612*		
	INF-functional lateralization in STG (Template)	***32.94***	***.004***	*.396*	*.284*

Note: INF = the infant timepoint. PRE = the preschool/kindergarten timepoint. N indicates the number of participants. ***Bolded values*** *indicate significant effects.*

Table 5. *Hierarchical regression analyses for the longitudinal effects of infant functional lateralization in STG calculated within each individual's native space.*

Models	*Predictors*	*Dependent variable*

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		Beta	*p*	R^2	R^2 *change*
		PRE-Oral expressive score (N = 25)			
1	*INF-language composite*	*0.42*	*.069*	*.137*	*-*
2	*INF-language composite*	*0.28*	*.187*		
	INF-functional lateralization in STG (Native)	***22.52***	***.013***	*.351*	***.214***
		PRE-Phonetic coding score (N = 21)			
1	*INF-language composite*	*0.90*	*.053*	*.183*	*-*
2	*INF-language composite*	*0.71*	*.069*		
	INF-functional lateralization in STG (Native)	***40.75***	***.006***	***.472***	***.289***
		PRE-Picture vocabulary score (N = 25)			
1	*INF-language composite*	*0.43*	*.102*	*.112*	*-*
2	*INF-language composite*	*0.24*	*.290*		
	INF-functional lateralization in STG (Native)	***29.92***	***.003***	***.411***	***.299***

Note: INF = the infant timepoint. PRE = the preschool/kindergarten timepoint. N indicates the number of participants. ***Bolded values*** *indicate significant effects.*

3.3. Brain-Behavioral Correlations for Infant Anatomical Lateralization in STG.

Exploratory analyses did not reveal any significant longitudinal associations between the lateralization of brain structure (i.e., surface area, cortical thickness, gray matter volume) in STG at the infant timepoint and any of the three language composite scores at the preschool/kindergarten timepoint. In addition, there were no significant concurrent correlations between structural lateralization in STG and language scores at the infant timepoint (see **Table 6**).

Table 6*. The relations of structural lateralization during infancy to language and cognitive skills at both the infant and preschool/kindergarten timepoints.*

Variables	*2.INF-language composite (N=25)*	*3.INF-expressive comm. (N=25)*	*4. INF-auditory comp. (N=25)*	*5.PRE-oral expressive (N=25)*	*6.PRE-listening comp. (N=11)*	*7.PRE-phonetic coding (N=21)*	*8. PRE-PPVT-4 vocabulary (N=25)*	*9. PRE-working memory (N=24)*
1.INF-structural lateralization (surface area)	*.257 (.215)*	*.232 (.264)*	*.025 (.906)*	*-.015 (.943)*	*-.138 (.687)*	*-.262 (.252)*	*-.021 (.919)*	*-.120 (.578)*
1. INF-	*.248 (.232)*	*.268 (.195)*	*.035 (.869)*	*.127 (.545)*	*.207 (.542)*	*-.216 (.347)*	*.166 (.428)*	*.085 (.694)*

structural lateralization (volume)									
1.INF-structural lateralization (cortical thickness)	*-.007 (.973)*	*.037 (.859)*	*.077 (.716)*	*.019 (.928)*	*.189 (.577)*	*-.113 (.627)*	*.228 (.274)*	*.166 (.440)*	

Note: INF = the infant timepoint. PRE = the preschool/kindergarten timepoint. Outside the parenthesis are r values, whereas inside the parenthesis are p values, uncorrected.

4. Discussion

The current study utilized fMRI to examine the longitudinal relationship between functional and structural brain lateralization in infancy and subsequent language skills in preschool/kindergarten. We observed that early lateralization of brain activation in the superior temporal gyrus (STG) for forward versus backward speech in infancy significantly predicted oral expressive, phonetic coding, and picture vocabulary scores in preschool/kindergarten, even after controlling for the language composite score obtained in infancy. In contrast, neither the language scores nor the anatomical lateralization index of STG measured in infancy were correlated with subsequent language scores in preschool/kindergarten. These findings suggest a scaffolding role of early brain lateralization in subsequent language acquisition, supporting the hypothesis that functional brain lateralization is advantageous.

4.1. Infant functional lateralization in STG for speech perception was associated with subsequent language skills in preschool/kindergarten.

The key finding of the current study is that infant functional lateralization of STG for speech perception was significantly associated with expressive language, phonological, and vocabulary skills 4-5 years later. Importantly, we observed that the longitudinal correlation between functional lateralization of STG and subsequent language skills remained significant even after controlling for language skills in infancy, providing stronger evidence for potential causal inference. Together, these findings suggest that earlier functional lateralization scaffolds later language development.

Compared to previous studies on children younger than age five, which suggested weak or no evidence for the association between brain lateralization for speech perception and language skills (Bishop et al., 2014; Kohler et al., 2015; Cantiani et al., 2019), the current study may have provided increased sensitivity for capturing the relationship between functional lateralization and language skills because of the following reasons. Firstly, we examined infant functional lateralization using a passive listening task during natural sleep. Previous literature suggests that the use of strategies can alter brain lateralization by engaging multiple brain areas (e.g., Tomasino & Ruimiati, 2004; Welsh & Elliott, 2001). The studies by Bishop et al. (2014) and Kohler et al. (2015) both used active language tasks that required children to respond. Active language tasks are more likely to induce strategic processes as children are trying to meet the requirements of the task. Therefore, our study, by focusing on infants and using a passive listening task, allowed us to more sensitively examine the earliest functional lateralization for speech perception with fewer confounds from strategic processes. Second, unlike previous studies using EEG or fTCD, which have low spatial resolution, the use of fMRI allowed the current study to localize the region of interest more precisely to better calculate brain lateralization. Moreover, we examined brain lateralization using brain activity from the top activated voxels (~ 5%) within STG for each infant, instead of considering the whole STG or group-activated STG. As compared to individualized ROIs, the use of anatomical masks or group-activated clusters often ignores subtle but important individual differences. Consistent with this argument, we observed that the overall overlap of the individualized top 100 voxels among participants was low. Additionally, we did not observe any systematic patterns of activation between left- and right-lateralized infants or between participants with high or average language skills at the group level. These visualizations of overlapped participants further confirmed that there were large variances among infants' brain activity for speech perception, highlighting the need to use individualized ROIs to better examine individual differences. This individualized top-voxel approach has also been shown to be more sensitive in finding brain-behavioral correlations across language, reading, and math domains (e.g., Bitan, et al., 2009; Younger et al., 2019; Gullick, & Booth, 2014; Suarez-Pellicioni, et al., 2020; Yamasaki, et al., 2021; Wang et al., 2020; 2021) and has successfully been employed in several recent infant fMRI studies for detecting subtle functional specialization (e.g., Deen et al., 2017; Kosakowski et al., 2023; Yates, Ellis, & Turk-Browne, 2023).

Although our results suggest a significant scaffolding effect of infant functional lateralization on later expressive language, vocabulary, and phonological skills, we did not observe significant longitudinal effects on receptive language skills, as measured by the listening comprehension composite, or on working memory skill, as measured by CTOPP-2 memory for digits. The lack of correlation with receptive language skills is likely due to the small sample size of only 11 participants. The absence of a correlation with working memory may be attributed to the fMRI speech task, which was designed to detect brain activity responsive to language processes such as phonological, semantic, and syntactic processing and does not specifically target working memory. Moreover, we failed to observe a correlation between language skills measured in infancy and language skills measured 4-5 years later. In addition, the correlation between infant language skills and infant functional lateralization was not significant. One reason could be the lack of power to find significant effects with a small sample size. Another potential reason is that infants acquire the ability to produce their first words at approximately 12 months of age (Kuhl, 2004), making it very challenging to examine early language skills behaviorally. Therefore, infant behavioral measures may be not as sensitive as brain measures in capturing and predicting individual differences in their language processing ability.

4.2. Infant functional lateralization in STG for forward > backward speech was overall right-lateralized.

Another critical observation of the current study is that although brain activity for both forward and backward speech as compared to rest is left-lateralized in STG, infants exhibited right-lateralized activation patterns in STG for forward versus backward speech at the group level. The observed left-lateralized activation in STG for both forward and backward speech compared to rest is consistent with the majority of previous research on infants (Dehaene-Lambertz et al., 2010; Shultz et al., 2014; Minagawa-Kawai et al., 2011; Dehaene-Lambertz et al., 2002; Pena et al., 2003; Vannasing et al., 2016), which suggests that processing speech sentences (i.e., both forward and backward speech) is likely already left-lateralized in infants. However, when simply using the contrast of forward or backward sentences versus rest, brain activity may be confounded by basic auditory processing. The forward and backward speech shared basic auditory information but only the former was intelligible, containing phonological, semantic, and syntactic information. Therefore, the current study employed the contrast of forward versus backward speech in order to target the lateralization of brain activation in STG for processing the linguistic information in speech perception. Contrary to the left-lateralized brain activation for speech perception commonly observed in children beyond age 4 (e.g., Olulade et al., 2020), we observed slightly right-lateralized activation in STG in infant brains. This observation is not surprising because in previous infant studies, when the task involved speech sentences that were manipulated (reversed or flattened) or from an unfamiliar language, the findings of brain lateralization for speech processing were also mixed (e.g., Dehaene-Lambertz et al., 2002; Pena et al., 2003; Vannasing et al., 2016; May et al., 2011; 2017; Perani et al., 2011; Zhang et al., 2022).

An explanation for the right-hemisphere dominance observed in the current study may involve the specific linguistic processes potentially employed by infants during speech perception. Previous literature has shown that phonological, lexico-semantic processing tends to be left-hemisphere dominant, whereas prosody is often right-hemisphere dominant in adults and infants (e.g., Price, 2012; Arimitsu et al., 2011). We suspect that in sleeping infants, the left-hemispheric sensitivity to fine-grained linguistic information constrained in their native language is not yet fully developed. When presented with speech versus non-speech stimuli (or rest), infants can consistently engage left-lateralized STG to process the acoustic and linguistic information. However, when presented with manipulated speech stimuli that require fine-grained linguistic processing, infants whose linguistic representation in the left STG is coarse may need to rely on prosody represented in the right STG to help increase the contrast between their native versus manipulated speech. Besides, previous literature suggests that when learning a new language, adults engage their right hemisphere during the initial learning stage but disengage it as they become more skilled (e.g., Qi et al., 2019; Qi & Legault, 2020). Therefore, another possibility for the overall right hemisphere dominance for speech perception in our infant study could be that these infants were still novice learners of their native language and needed to engage their right hemisphere to help process speech and language information. In the current study, despite infants showing overall right-lateralized activation, which may indicate reliance on prosody or being novice learners, individuals who showed stronger left-lateralization in infancy, likely indicating those who had more fine-grained linguistic representation or more advanced skills of their native language, had better subsequent language skills at preschool/kindergarten.

4.3. *Infant anatomical lateralization in STG using gray matter volume, surface area, and cortical thickness was not related to language skills either in infancy or preschool/kindergarten.*

In terms of infant anatomical lateralization in the STG, we observed leftward asymmetry for surface area (mean = 0.04) and volume (mean = 0.02), and rightward asymmetry for cortical thickness (mean = -0.01) at the group level. These findings of leftward asymmetry in surface area and rightward asymmetry in cortical thickness in the STG are consistent with previous research (William et al., 2023). Lehtola et al. (2019) examined brain volumes and observed a rightward asymmetry of the temporal lobe in 2-to-5-week-old infants. Our finding of a leftward asymmetry in the STG appears to contradict this study. However, Lehtola et al. (2019) did not specify different gyri of the temporal lobe and focused on younger children. Therefore, further investigation into brain lateralization of volume asymmetry, specifically focusing on sub-parts of the temporal lobe, is needed.

In terms of the longitudinal relationship with language skills, while our findings indicated that infant functional lateralization of the STG predicted subsequent language skills, exploratory analyses showed that anatomical lateralizations of the STG using gray matter volume, surface area, and cortical thickness were not predictive. Some previous studies examined the correlation between structural measurements and language skills. However, they either used different brain measurements (e.g., Aeby et al., 2013; Bartha-Doering et al., 2023) or observed an effect in other brain regions (e.g., Qi et al., 2019). Aeby et al. (2013) showed that the mean diffusivity (MD) of the left STG using diffusion tensor imaging in 41 pre-term infants at term equivalent age was associated with children's language skills at 2 years old. Bartha-Doering et al. (2023) reported that less right lateralization of fetal superior temporal sulcus depth was significantly associated with better verbal abilities 6 to 13 years later. Qi et al. (2019) observed that the left lateralization of cortical thickness in the inferior frontal lobe in 76 5- to 6-year-old children was correlated with language skills at 7 years old. In studies with atypical population, although several previous studies occasionally demonstrated atypical (more or less) grey matter volume in STG in children with DLD as compared to typically developing children (Asaridou & Watkins, 2022), among the studies that examined structural asymmetry, the majority reported that children with DLD do demonstrate typical hemisphere structural asymmetry within temporal language regions including the posterior STG, similar to that seen in typically developing children (Mayes, Reilly, & Morgan, 2015). Although brain structure is typically thought to underlie function, our study observed that structural lateralization of STG using surface area, volume, and cortical thickness in infancy was not associated with language skills either in infancy or 4 to 5 years later. This additional finding suggests that only functional, and not structural, lateralization of the STG is sensitive to predicting subsequent language skills. However, it could also be attributed to the small sample size, insensitivity of the chosen structural measurements, and/or incorrect brain regions selected, warranting further investigation in future studies.

4.4. Limitations of the current study.

The current study has several limitations. First, due to the extreme difficulties in collecting infant fMRI and retaining participants in a 5-year longitudinal study, the current study has a relatively small sample size. Future studies with larger sample sizes are needed to examine whether the findings of our study are replicable. Second, although most people develop left-lateralized language processing in the brain, studies have reported that people with right or no functional hemisphere dominance also show typical language skills (Knecht et al., 2000; Carey and Johnstone, 2014). This current study was conducted under the assumption that the participants included in our study followed a typical left hemisphere dominance trajectory for language processing, and thus, we observed, as expected, that the more left-lateralized the infant brains were for language processing, the better their subsequent language skills. However, we do not know whether cases of opposite or no hemisphere dominance were included in our study. Third, all the infants were sleeping during the fMRI scan. Previous research suggests that sleeping, as compared to an awake status, leads to reduced brain activity for linguistic information, especially in the higher-order frontal regions (e.g., Wilf et al., 2016). The use of the lateralization index, which scaled brain activity by using (left – right)/ (left + right), likely reduced the impact of the sleeping state on the individual differences in the amplitude of brain activation. However, we cannot rule out the potential impact of sleeping status on brain lateralization. Future studies scanning awake infants with task fMRI are needed to confirm the findings of our current study.

4.5. Conclusion.

Using task fMRI, the current study examined the longitudinal relationship between functional lateralization within STG for speech perception in sleeping infants and their subsequent language skills in preschool/kindergarten. We observed that infant functional lateralization in STG for forward > backward speech was significantly associated with later expressive language, vocabulary, and phonological skills in preschool/kindergarten, even after controlling for initial language skills. This finding provides preliminary evidence that infant functional lateralization of STG for speech perception scaffolds long-term language development, supporting the hypothesis that hemispheric lateralization is beneficial for skill development from a speech-language domain. However, before reaching a solid conclusion, more fMRI studies with larger sample sizes, awake infants, and longitudinal design are needed to examine the replicability of the current study.

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Data code availability statement

The data used in this study is accessible upon request. The code used for this study is shared on GitHub (https://github.com/wangjinvandy/infant_fMRI_lateralization_predicts_language_skil_at_preschool-kindergarten).

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Supplementary Materials

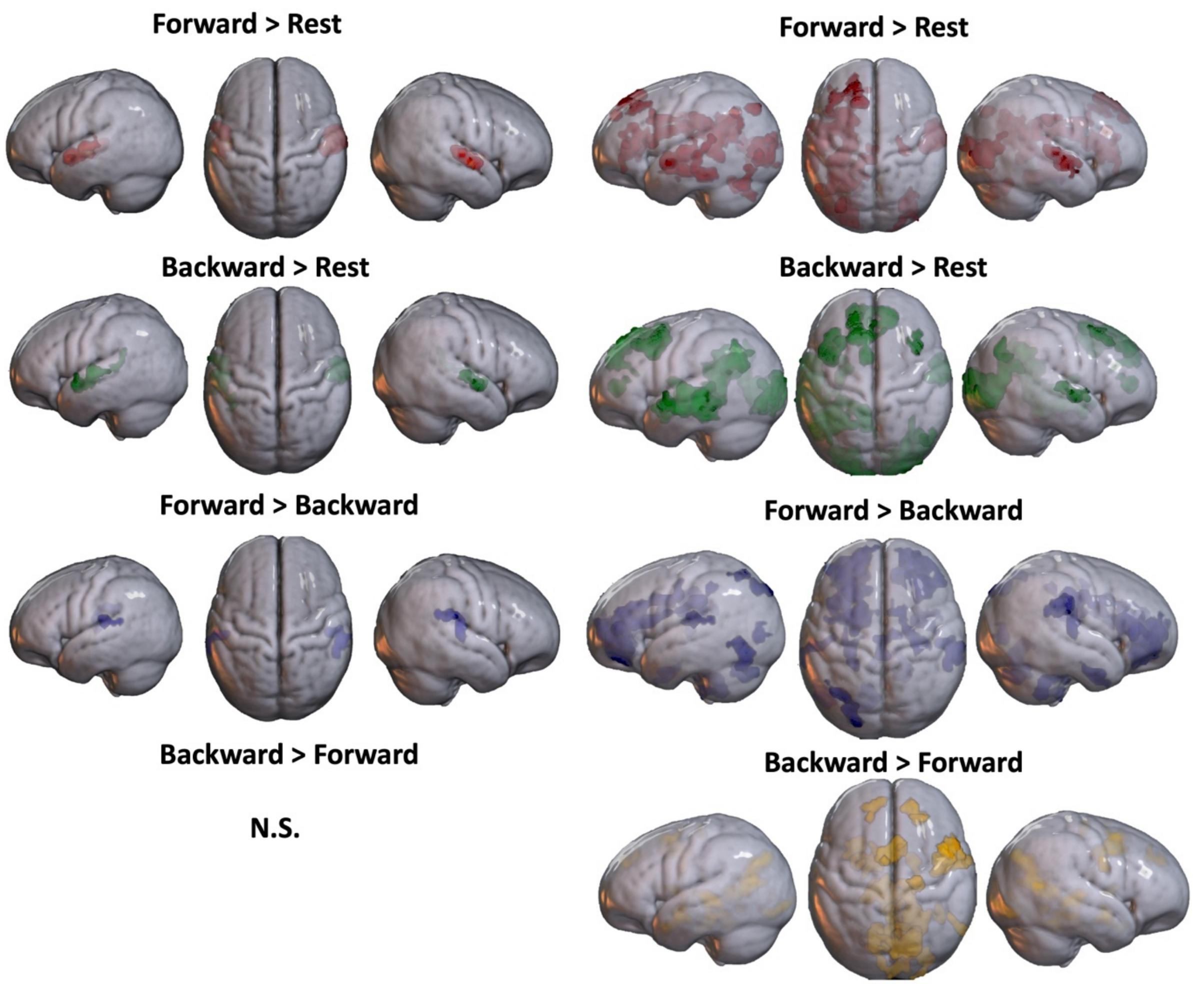

Figure S1. Brain activation maps within the STG masks (on the left) and whole brain activation maps (on the right) for the contrasts of forward speech > rest, backward speech > rest, and forward > backward speech at a threshold of voxel-wise $p < 0.05$, cluster size > 50, uncorrected.

Table S1. *Group-level whole brain activation for the contrasts of forward speech > rest, backward speech > rest, and forward > backward speech.*

Contrasts	*Brain Areas*	*Cluster size (Num. of voxels)*	*T value of peak*
Forward speech > Rest			
	Left Superior/Middle Temporal Gyrus	*652*	*4.91*

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	Left White Matter/ Supramarginal Gyrus	*2254*	*3.99*
	Left Occipital Cortex	*437*	*3.92*
	Right Occipital Cortex	*341*	*3.79*
	Left Lingual/fusiform Gyrus	*238*	*3.62*
	Right Superior Temporal Gryus	*368*	*3.23*
	Left Superior Frontal Gyrus	*258*	*3.04*
	Right White Matter	*59*	*2.48*
	Left Inferior Parietal Lobe	*60*	*2.50*
Backward speech > Rest			
	Right Occipital Cortex	*1101*	*5.53*
	Left Occipital Cortex	*626*	*5.14*
	Left Superior/Middle Temporal Gyrus	*2475*	*5.10*
	Left Medial Frontal Gyrus	*554*	*4.19*
	Left Superior/Middle Frontal Gyrus	*439*	*3.97*
	Right Superior Frontal Gyrus	*152*	*3.08*
	Left White Matter/Putamen	*99*	*3.02*
	Left Amygadala/White Matter	*57*	*2.97*
	Right Superior/Middle Frontal Gyrus	*75*	*2.74*
	Left Anterior Cingulum	*98*	*2.74*
		213	*2.68*
Forward > Backward speech			
	Right Frontal Gyrus Orbitalis	*1267*	*4.55*
	Right White Matter/Precentral	*239*	*4.08*
	Left Inferior Temporal Gryus	*174*	*3.76*
	Right Temporal Pole	*170*	*3.58*
	Left Frontal Gyrus Orbitalis	*1758*	*3.47*
	Left Cerebellum	*203*	*3.46*
	Right Middle Cingulum	*131*	*3.31*
	Right Superior Temporal Gyrus	*296*	*3.23*
	Left Inferior Parietal Lobe	*86*	*2.97*
	Left White Matter/Middle Occipital Lobe	*60*	*2.95*
	Right Cerebellum	*145*	*2.87*

	Left Superior Temporal Gyrus	*106*	*2.64*
	Right Cerebellum	*73*	*2.58*
	Left Superior Parietal Lobe	*52*	*2.24*
Backward > Forward speech			
	Right Precentral/Middle Frontal Gyrus	*517*	*4.04*
	Left Temporal Pole	*110*	*3.85*
	Right Precuneus	*2651*	*3.48*
	Right Occipital Cortex	*140*	*3.23*
	Medial Frontal Gyrus	*205*	*3.21*
	White Matter	*91*	*3.19*
	Right Hippocampus	*87*	*2.92*
	Right Fusiform Gyrus	*65*	*2.87*
	Left Hippocampus	*260*	*2.77*
	Right Middle Temporal Gyrus	*56*	*2.74*
	Right Superior Frontal Gyrus	*144*	*2.68*
	Right Precentral Gyrus	*97*	*2.41*
	Left Superior Frontal Gyrus	*84*	*2.29*

Note: the MNI coordinates are not reported due to the use of infant-specific space (i.e., a 7.5-month-old template). Whole brain activation was determined at a threshold of voxel-wise $p < 0.05$, cluster size > 50, uncorrected.