Behavioral/Cognitive

Language Experience during Infancy Predicts White Matter Myelination at Age 2 Years

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Parental input is considered a key predictor of language achievement during the first years of life, yet relatively few studies have assessed the effects of parental language input and parent–infant interactions on early brain development. We examined the relationship between measures of parent and child language, obtained from naturalistic home recordings at child ages 6, 10, 14, 18, and 24 months, and estimates of white matter myelination, derived from quantitative MRI at age 2 years (mean = 26.30 months, SD = 1.62, N = 22). Analysis of the white matter focused on dorsal pathways associated with expressive language development and long-term language ability, namely, the left arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF). Frequency of parent–infant conversational turns (CT) uniquely predicted myelin density estimates in both the AF and SLF. Moreover, the effect of CT remained significant while controlling for total adult speech and child speech-related utterances, suggesting a specific role for interactive language experience, rather than simply speech exposure or production. An exploratory analysis of 18 additional tracts, including the right AF and SLF, indicated a high degree of anatomic specificity. Longitudinal analyses of parent and child language variables indicated an effect of CT as early as 6 months of age, as well as an ongoing effect over infancy. Together, these results link parent–infant conversational turns to white matter myelination at age 2 years, and suggest that early, interactive experiences with language uniquely contribute to the development of white matter associated with long-term language ability.

Key words: conversational turns; development; early childhood; infancy; language environment; white matter

Significance Statement

Children's earliest experiences with language are thought to have profound and lasting developmental effects. Recent studies suggest that intervention can increase the quality of parental language input and improve children's learning outcomes. However, important questions remain about the optimal timing of intervention, and the relationship between specific aspects of language experience and brain development. We report that parent–infant turn-taking during home language interactions correlates with myelination of language related white matter pathways through age 2 years. Effects were independent of total speech exposure and infant vocalizations and evident starting at 6 months of age, suggesting that structured language interactions throughout infancy may uniquely support the ongoing development of brain systems critical to long-term language ability.

Introduction

Early language exposure varies widely in quantity, content, and interactional style, and this variation has been linked to multiple aspects of children's linguistic and cognitive development. Beyond the quantity and linguistic quality of home language input (for recent review, see Rowe and Snow, 2020; Rowe and Weisleder, 2020), social-interactional variables are increasingly viewed as important predictors of early and longer-term language achievement (Tamis-LeMonda and Bornstein, 2002; Hirsh-Pasek et al., 2015; Gilkerson et al., 2017, 2018; Tamis-LeMonda et al., 2019), as well as language-related brain structure and function in childhood (Romeo et al., 2018a, b, 2021).

A hallmark of supportive social interaction is the presence of conversational contingency, meaning that speech is on-topic and

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contextually relevant, with limited response delay across speakers (Bornstein et al., 2008; Tamis-LeMonda et al., 2014; Masek et al., 2021). Contingency encourages shared and sustained attention (Masek et al., 2021), and has been shown to provoke higher-quality output from learners, including vocalizations that are more consistent with native phonology during adult–infant interactions (Goldstein et al., 2003; Goldstein and Schwade, 2008; Warlaumont et al., 2014). Moreover, speakers adjust and coordinate their output during contingent interactions (Smith and Trainor, 2008; Huttenlocher et al., 2010; Warlaumont et al., 2014; Abney et al., 2017; Albert et al., 2018; Elmlinger et al., 2019), which provides a more effective language stimulus, optimized to the learner's needs and ability level, in real time.

Conversational turn counts are often used to characterize the quality of verbal interactions based on the number of temporally contingent, back-and-forth exchanges between speakers (Hirsh-Pasek et al., 2015; Gilkerson et al., 2018). Conversational turns recorded during naturalistic parent–child interactions have been found to correlate with vocabulary learning in early childhood (Zimmerman et al., 2009; Gilkerson et al., 2017; Donnelly and Kidd, 2021), and to predict measures of cognitive and linguistic ability into adolescence (Gilkerson et al., 2018). Moreover, conversational turn counts have been shown to correlate with structural and functional measures of language-related brain development in childhood, from 4 to 6 years (Romeo et al., 2018a, b, 2021).

Despite a wealth of behavioral research, studies relating parental input and parent–child interactions to brain development before age 3 are still relatively scarce. Given that the first 2 years of life are marked by considerable growth in language-related abilities, as well as ongoing white matter maturation and extensive refinement of local cortical architecture (Kostović et al., 2019), research targeting this period is especially needed. To help fill this gap, the current study examines the relationship between white matter myelination at 2 years of age and longitudinal measures of parental input, child output, and parent–child interactions from 6 to 24 months of age. Naturalistic home recordings were used to estimate to total speech exposure, or adult word counts (AWC), child-directed speech (CDS), child speech output (CS), and parent child conversational turns (CT) when children were 6, 10, 14, 18, and 24 months old. Macro-molecular proton fraction (MPF) mapping (Yarnykh, 2012, 2016) was used to obtain quantitative estimates of myelin density in the same participants at 2 years of age.

Our first aim was to test effects of parent and child language on dorsal language pathways associated with language comprehension and production, namely, the left arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF). The dorsal language system has long been associated with speech production and sensory-motor integration (Hickok and Poeppel, 2007; Hickok, 2012; Skeide and Friederici, 2016), receptive and expressive language skills in infants and toddlers (Salvan et al., 2017; Girault et al., 2019; Sket et al., 2019), and phonological awareness and linguistic processing in childhood (Lebel and Beaulieu, 2009; Saygin et al., 2013; Skeide et al., 2016; Romeo et al., 2018b; Su et al., 2018). Moreover, the organization of these white matter pathways has been found to correlate with conversational turn counts in older children, and to mediate the association between conversational turns and language skills at 4-6 years of age (Romeo et al., 2018b). After examining these pathways, we conducted an exploratory analysis that included the right hemisphere AF and SLF, as well as 16 additional projection, association, and commissural tracts (Mori et al., 2006).

The studies cited above used diffusion imaging to obtain metrics, such as fractional anisotropy (FA), which are sensitive to multiple aspects of the underlying tissue organization (Le Bihan, 1991; Beaulieu, 2002; Alexander et al., 2007, 2019). Validation studies suggest that diffusion-based metrics are often only modestly or moderately correlated with myelin content (Mancini et al., 2020; Lazari and Lipp, 2021). The current study therefore combines diffusion imaging with quantitative MPF mapping, to more specifically probe myelin-related tissue properties. MPF is sensitive to changes in myelin content within both gray and white matter (Khodanovich et al., 2017, 2019; Corrigan et al., 2021; Kisel et al., 2022), and validation studies have demonstrated a strong linear relationship between MPF and myelin density estimates obtained from histologic staining (Underhill et al., 2011).

The current sample was drawn from a larger intervention study (Ferjan Ramírez et al., 2019, 2020), which manipulated parental language input from 6 to 18 months. In that study, the quantity of parent–child conversational turns, but not total adult words in the environment, increased during the intervention period, and predicted language outcomes in the second year of life (Ferjan Ramírez et al., 2019, 2020). Language input variables and child language abilities are frequently interrelated over development (Rowe, 2012; Rowe et al., 2012; Bornstein et al., 2016; Tamis-LeMonda et al., 2019; Donnelly and Kidd, 2021), and so the current sample provides a unique opportunity to assess the relative effects of specific language variables over the first 2 years of life.

Materials and Methods

Participants. Seventy-nine families were recruited through the University of Washington Subject Pool as part of a previously published home language intervention study (Ferjan Ramírez et al., 2019, 2020). Criteria for inclusion were full-term birth and normal birth weight (6-10 lb), no birth or postnatal complications, and English as the sole language spoken at home. The Hollingshead Index (Hollingshead, 1975) was used to create a socio-economic status (SES) score based on parental occupation and formal education level. SES ranged from 30 to 66 (mean = 47.82, SD = 10.84) in the current sample (i.e., working- to upper-middle class).

All families provided informed consent during an orientation session when children were 6 months old. After completing the intervention study, families in both the intervention and control groups were invited to return for a follow-up MRI session when children were ~2 years old (mean = 26.30 months, SD = 1.62). Fifty-one families returned and completed at least a partial MRI scan (MRI sessions were ended if children became restless before completing the full set of scans). Nineteen children completed all structural scans with usable data, and 3 additional children completed all but the diffusion MRI scan with usable data (details on MRI data quality assurance and subject exclusions are given below). In total, 22 children (14 female) were included in the current analysis. Five were members of the control group, while the rest had participated in the home language intervention. Since the goal of the current study was to examine the correlation between home language experience and markers of white matter myelination at 2 years of age, data were analyzed for the whole available sample as a single group. Behavioral analysis of the larger dataset is reported in a separate set of publications (Ferjan Ramírez et al., 2019, 2020).

Language environment and child language measures. The home Language Environment Analysis System (LENA Pro version 3.4.0, LENA 2015) was used to collect naturalistic first-person recordings from all families over 2 weekend days when children were 6, 10, 14, 18, and 24 months old. Parent and child language variables were manually coded from the LENA recordings by trained research assistants, following procedures outlined previously (Ramírez-Esparza et al., 2014, 2017a,b;

Ferjan Ramírez et al., 2019, 2020, 2021), and summarized below. Although the LENA software package can be used to obtain automated counts of child vocalizations and parent-child conversational turns, prior studies suggest that these estimates are susceptible to error and bias because of factors such as overlapping speech and noise in the recordings (Gilkerson and Richards, 2008; Gilkerson et al., 2017; Bulgarelli and Bergelson, 2020; Cristia et al., 2020, 2021; Ferjan Ramírez et al., 2021). We therefore opted to use manually coded measures. LENA's automatic AWC measure was used for the purposes of coding interval selection and to control for ambient speech exposure in statistical models, as described below.

Each family's two daily recordings were first preprocessed using the LENA Advanced Data Extractor Tool, and custom software was written to identify 50 unique 30 s intervals per day containing the highest daily AWC, spaced at least 3 min apart. This step ensured that all selected intervals contained enough language data for analysis and excluded uninformative periods, such as infant naps. In total, 100 30 s intervals were identified per participant at each age. Coders then tabulated the percentage of intervals containing child speech or speech-like vocalizations (CS) and/or child-directed speech (CDS) from adults, and the total number of parent–child conversational turns (CT) across all intervals. Intraclass correlations were calculated using a training file from Ramírez-Esparza et al. (2014) to assess intercoder reliability (see also Shrout and Fleiss, 1979; Ramírez-Esparza et al., 2017a,b). Mean intraclass correlation coefficients ranged from 0.93 and 0.98. Exact variable definitions used by the coders are given in Table 1. All participants had usable LENA recordings at all time points, from 6 to 24 months.

All families also completed the MacArthur–Bates Communicative Development Inventory, Words and Sentences form (Fenson et al., 1994). Measures of child productive vocabulary and the mean length of a child's three longest utterances (M3L) at 24 months were derived from the inventory and used to assess child language skill.

MRI acquisition protocol. All data were acquired using a 3.0 T Philips Ingenia MRI system with a 32-channel head coil while children were in natural sleep. High resolution T1-weighted images were acquired using a multiecho MPRAGE sequence with FOV = 230 × 230 × 180, acquisition voxel size 1.0 × 1.0 × 1.0 mm^3, reconstructed voxel size 0.5 × 0.5 × 0.5 mm^3, TR/TI/TE1/TE2 = 13/1200/3.7/9.7 ms, shot interval 2250 ms, and flip angle = 8°. T1-weighted images were used as a common reference space for later anatomically guided analysis of MPF maps and of diffusion-weighted images, as described below.

A fast 3D protocol was implemented for MPF mapping, according to the single-point synthetic reference method (Yarnykh, 2012, 2016), including three spoiled gradient-echo sequences with magnetization transfer (TR = 31 ms, flip angle = 8°), proton-density (TR = 21 ms, flip angle = 4°), and T1 (TR = 21 ms, flip angle = 25°) contrast weightings. Off-resonance saturation in the magnetization transfer-weighted sequence was applied at the offset frequency 4 kHz with effective flip angle = 430° and pulse duration 7 ms. All images were obtained in the sagittal plane with dual-echo readout (TE1/TE2 = 4.9 ms/10.0 ms), FOV = 240 × 240 × 200 mm^3, and actual voxel size of 1.25 × 1.25 × 1.24 mm^3 interpolated to 0.625 × 0.625 × 0.620 mm^3. Actual flip-angle imaging B1 maps (Yarnykh, 2007) (TR1/TR2/TE= 60/240/4.8 ms, flip angle = 60°, voxel size 2.5 × 5.0 × 5.0 mm^3) were acquired in the same geometry and reconstructed with 0.625 × 0.625 × 0.620 mm^3 voxel size.

Diffusion-weighted data were acquired using a single-shot DWI-EPI sequence with FOV = 230 × 230 × 146, acquisition voxel size 1.8 × 1.8 × 1.9 mm^3, reconstructed voxel size 1.4 × 1.4 × 1.9 mm^3, TR/TE = 11 926/97 ms, flip angle = 90°. Each diffusion scan included 6 non–diffusion-weighted (b = 0) volumes and 64 diffusion-weighted volumes acquired with a b-value of 2000 s/mm^2 (50 noncollinear gradient directions) or 800 s/mm^2 (12 additional noncollinear gradient directions). An additional set of 6 non–diffusion-weighted volumes were acquired using the same parameters but a reversed phase encoding direction (posterior-anterior), for use in correcting EPI distortions (Andersson et al., 2003), as described below.

MPF mapping. MPF maps were reconstructed according to a single-point synthetic reference algorithm (Yarnykh, 2016) with correction of B1 field nonuniformity using custom-written C-language software and previously determined constraints for the nonadjustable two-pool model parameters (Yarnykh, 2012); software for reconstruction of MPF maps is available at https://www.macromolecularmri.org. Before map reconstruction, individual echo images in each dataset were averaged to increase SNR (Helms and Dechent, 2009). Rigid-body registration of the component image volumes was performed using the FLIRT toolbox of the FSL software package (Smith, 2002). Resulting MPF maps were then aligned to each subject's own T1-weighted anatomic image, again using rigid body registration. For visualization purposes, a study-specific template was constructed using the "buildtemplateparallel" function of the Advanced Normalization Tools software package (version 2.2.0).

Table 1. Parent and child language variables measured from 6 to 24 months[a]

Variable name	Variable definition
CDS	Total number of intervals (of 100) in which an adult spoke directly to the child
CS	Total number of intervals (of 100) in which children either repeated or independently produced one or more of the following: fully resonant vowels, consonant–vowel syllables, syllable strings, speech utterances intermixed with nonspeech, word-like strings, single words, or word strings
CT	Total number of adult utterances directed to the child followed within 5 s by a child utterance directed to the adult, or vice versa; counted in discrete pairs (child-to-parent = 1 turn; parent-to-child-to-parent = 1 turn; child-to-parent-to-child-to-parent = 2 turns)

[a]Variable definitions used in manual coding of the Language Environment Analysis System (LENA) recordings at each age.

Quality assurance for the T1-weighted anatomic images and the source images used to construct the MPF maps was performed as follows: One operator first rated all of the images using a 3 point scale (0 = severe artifacts precluding further usage; 1 = minor artifacts present but further processing can be performed; and 2 = no problems with image quality). Datasets containing any image with a quality grade of 0 were excluded from further analysis. After MPF map reconstruction, two operators performed consensus reviews of MPF maps for the presence of residual artifacts. In total, 4 participants were excluded based on quality review. Three additional participants were found to have minor artifacts in one or more images that did not preclude further analysis. The final MPF sample size (N = 22) reflects the participants who passed quality assessment.

Diffusion MRI analysis. Diffusion data preprocessing was conducted using the FSL tools (version 6.0.1) for motion and eddy current correction (FSL eddy) (Andersson and Sotiropoulos, 2016) and brain extraction (FSL BET) (Smith, 2002). Quality assurance of the raw diffusion-weighted and B0 images was first performed by an operator using the same 3 point scale that was used to assess the T1-weighted images and the MPF source images (0 = severe artifacts precluding further usage; 1 = minor artifacts present but further processing can be performed; and 2 = no problems with image quality). Datasets containing any image with a quality grade of 0 were excluded from further preprocessing and analysis. The final diffusion MRI sample size (N = 19) reflects the participants who passed quality assessment.

After quality assurance, diffusion-weighted volumes were first aligned to an average of the non–diffusion-weighted volumes in each scan using rigid body registration (SPM version 12) (Ashburner and Friston, 1997). Volumes were next aligned to the subject's own T1-weighted anatomical image, again using rigid body registration. Diffusion gradients were adjusted to account for transformations applied during image registration and motion correction (Leemans and Jones, 2009).

Additional processing was performed using the MRtrix3 software package (Tournier et al., 2019). Single-tissue constrained spherical deconvolution (Tournier et al., 2004) was used to estimate the single-fiber response function within white matter using the b = 0 and 2000 s/mm^2 volumes (FA cutoff: 0.8, lmax = 4). Probabilistic fiber tracking was then conducted using the iFOD2 algorithm (Tournier et al., 2010), with 500,000 initial streamlines. The resulting whole-brain fiber estimates were segmented using the Automated Fiber Quantification software package (AFQ, https://github.com/yeatmanlab/AFQ) (Yeatman et al., 2012b) to identify specific white matter fiber tracts in subject native space.

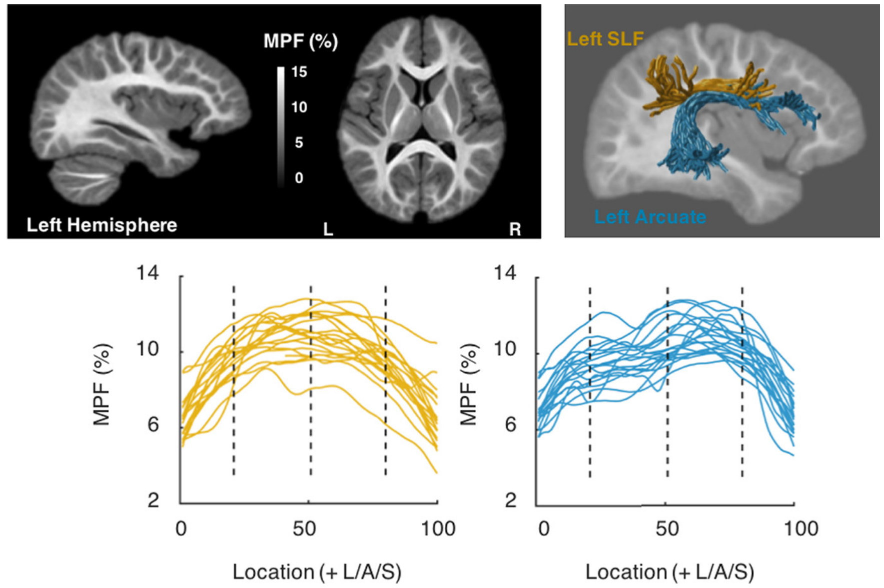

Figure 1. Anatomical ROIs and MPF estimates. Top left, Average macro-molecular proton fraction (MPF) values throughout the gray and white matter, visualized in group template space. Top right, Example tractography-based reconstructions of the left superior longitudinal fasciculus (SLF) and left arcuate fasciculus (AF). Bottom, Individual MPF estimates are plotted at each sampled location along the SLF and arcuate, for all participants. Dashed lines indicate the boundaries of the posterior (left) and anterior (right) ROIs for each tract. Tract profiles are visualized with left/anterior/superior (L/A/S) coordinates increasing from left-to-right in the plots.

Analysis of MPF profiles. For all participants who completed the diffusion MRI scans ($N = 19$), MPF values were extracted for each fiber tract and summarized as a weighted-mean across fiber nodes at the tract core (Yeatman et al., 2012b). For participants who did not complete the diffusion MRI scans ($N = 3$), tracts were identified as follows: MPF maps were first aligned to a standard-space template brain and probabilistic white matter labels were used to define initial candidate tracts (Mori et al., 2006). Tract locations were then visually confirmed relative to the same waypoint ROIs used in AFQ, after transformation into subject native space. Finally, the core of each tract was defined in 3D coordinates using the MATLAB Image Processing Toolbox (using the bwmorph3 and bwconncomp functions). All analyses were replicated with and without these 3 participants.

Tract profiles were first visualized by extracting 100 evenly spaced nodes along each tract (Yeatman et al., 2012b). Mean MPF values were then calculated for each tract by averaging the middle 80% of locations between cortical endpoints. This approach helps to minimize the influence of bending/branching fibers near cortical termination points, and also helps to avoid errors related to partial volume effects near the white/gray matter border. A study in older children (Romeo et al., 2018b) previously reported effects that were specific to the anterior section of the left AF and SLF. Therefore, tracts were also subdivided into evenly sized "posterior" and "anterior" portions (nodes 11:50 and 51:90), and mean MPF values were tested within these subregions. Finally, a more fine-grained analysis was conducted along each tract by extracting 20 summary locations per subject and tract. Output from AFQ was transformed such that all tract profiles were oriented with nodes increasing from right to left, posterior to anterior, and inferior to superior, to simplify visualization of tract profiles.

Experimental design and statistical analysis. Statistical analyses were performed in MATLAB (R2020a) using custom software and the MathWorks Statistics and Machine Learning toolbox. Bivariate correlations (Pearson's r, two-tailed test of significance) with were first tested for each language variable (AWC, CDS, CS, and CT) and each white matter ROI (left posterior AF; left anterior AF; left posterior SLF; left anterior SLF). Simple effects of SES and sex were also tested, and found to be nonsignificant (all $p > 0.1$), so these variables were not included in further analyses. After testing the bivariate effects, MPF was regressed on CT while controlling for environment-level (CDS, AWC) and child-level (CS) variables, to test whether significant effects of CT might be explained more simply in terms of greater overall speech exposure (CDS, AWC) or greater child "talkativeness" (CS). Finally, longitudinal mixed models were used to estimate individual growth in CT from 6 to 24 months. Visualization of raw CT scores suggested a nonlinear effect of time, and model comparisons suggested that including both age and age^2 effects provided a better fit than including only a linear effect of age. Age was centered at 6 months, and restricted maximum likelihood estimation was used for the final model fits. Individual intercept, slope (age), and acceleration (age^2) terms were then used to predict 26-month MPF.

In older children (4-6 years) (Romeo et al., 2018b), correlations with child language and parent–child conversational turns have been found to colocalize, and white matter organization has been shown to account for the relationship between conversational experience and child language. Correlations were therefore tested for MPF and child language skill (child productive vocabulary and mean utterance length, M3L), to assess whether similar relationships might exist in the current sample.

Effects were first tested using mean MPF values calculated for the anterior and posterior subregions of each tract, and then at each of the more finely sampled node locations. For the node-wise analysis, results were corrected for multiple comparisons along each tract using a permutation-based approach (Nichols and Holmes, 2002) to account for spatial similarity within individual white matter tracts (Yeatman et al., 2012b). To evaluate anatomical specificity, effects were tested in the same manner within right hemisphere AF and SLF tracts, as well as within 16 additional projection, association, and commissural tracts identified as part of the automated tract segmentation in AFQ (Mori et al., 2006; Yeatman et al., 2012b).

For the full sample ($N = 22$), given $\alpha = 0.05$ and $1 - \beta = 0.8/0.7$, the current study was powered to detect an effect size of 0.39/0.31 in a regression with a single predictor, and an effect size of 0.617/0.497 in a multiple regression with three predictors. A prior study examining the effect of conversational turns in 4- to 6-year-old children reported effects sizes for the FA in the left AF and SLF that ranged from 0.42 to 0.51 (Romeo et al., 2018b). We therefore expected that the current study should be adequately powered to detect the hypothesized relationships.

Code accessibility. Software for white matter tract segmentation is available at https://github.com/yeatmanlab/AFQ. Software for reconstruction of MPF maps is available at https://www.macromolecularmri.org/. Custom software written for statistical analysis and figure creation is available at https://github.com/libbyhuber/JN2023. All additional software used for image reconstruction and analysis is available from the authors by request.

Results

Figure 1 shows example tractography-based reconstructions for the left AF and SLF, and sample mean MPF maps. Table 2 shows bivariate correlations for mean MPF in each white matter ROI versus AWC, CDS, CS, and CT at each age. Significant effects ($p < 0.05$) were observed for CDS and CT at all ages tested from 6 to 18 months, although no significant correlations were observed at 24 months, the age closest in time to the MRI scan (mean = 26.30 months, SD = 1.62 months, $N = 22$). After

Table 2. Correlations between 26-month MPF and 6- to 24-month language measures

Language Measure	White Matter ROI Left AF Posterior	Left AF Anterior	Left SLF Posterior	Left SLF Anterior
6-month				
AWC	−0.20 (.37)	0.046 (.84)	−0.096 (.67)	−0.060 (.79)
CDS	−0.198 (.39)	0.43* (.049)	0.24 (.29)	0.37 (.096)
CS	−0.18 (.42)	−0.27 (.22)	−0.42 (.052)	−0.042 (.85)
CT	−0.014 (.95)	0.56** (.0067)	0.46* (.031)	0.35 (.11)
10-month				
AWC	0.059 (.80)	−0.083 (.71)	−0.084 (.71)	−0.075 (.74)
CDS	−0.073 (.75)	0.58** (.0062)	0.25 (.27)	0.29 (.197)
CS	0.21 (.35)	0.23 (.31)	0.16 (.48)	−0.11 (.62)
CT	0.23 (.30)	0.52* (.012)	0.43* (.046)	0.22 (.32)
14-month				
AWC	−0.12 (.59)	0.11 (.64)	−0.11 (.62)	0.092 (.68)
CDS	−0.065 (.78)	0.52* (.016)	0.32 (.16)	0.297 (.19)
CS	−0.0055 (.98)	0.14 (.55)	0.19 (.39)	−0.045 (.84)
CT	0.13 (.56)	0.48* (.024)	0.45* (.034)	0.24 (.29)
18-month				
AWC	0.088 (.698)	0.11 (.62)	0.16 (.48)	0.042 (.85)
CDS	−0.17 (.46)	0.47* (.032)	0.31 (.17)	0.38 (.087)
CS	0.089 (.70)	0.20 (.38)	0.20 (.38)	0.16 (.48)
CT	−0.040 (.86)	0.62**+ (.0020)	0.38 (.08)	0.38 (.079)
24-month				
AWC	0.034 (.88)	0.298 (.18)	0.15 (.50)	0.32 (.15)
CDS	−0.43* (.0494)	0.065 (.78)	−0.026 (.91)	−0.093 (.69)
CS	0.064 (.78)	0.36 (.11)	0.398 (.07)	0.27 (.23)
CT	−0.24 (.27)	0.35 (.11)	0.20 (.37)	0.13 (.58)

*$p < .05$, **$p < .01$, +significant after Bonferroni correction for multiple comparisons (corrected $p < .05$).

Bivariate correlations (Pearson's r) were tested with macro-molecular proton fraction (MPF) in the left arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF) for each language measure obtained from the home Language Environment Analysis System (LENA) recordings: Adult-word count (AWC), child-directed speech (CDS), child speech or speech-like vocalizations (CS), and conversational turns (CT). Correlation values are given with exact p-values in parentheses.

correction for multiple comparisons across language variables and white matter ROIs, the effect of CT at 18 months remained significant for left anterior arcuate. Tract profiles for the left AF and SLF, and bivariate correlations with 18 month CT, are plotted in Figure 2. The effect of 18 month CT remained significant while controlling for concurrent (18 month) AWC (CT partial $r = 0.50$, $p = 0.0023$; AWC partial $r = 0.12$, $p = 0.40$), CDS (CT partial $r = 0.50$, $p = 0.025$; CDS partial $r = 0.0012$, $p = 0.996$), and CS (CT partial $r = 0.49$, $p = 0.0052$; CS partial $r = 0.034$, $p = 0.83$), consistent with a specific effect of CT, rather than overall speech exposure (AWC), directed speech input (CDS), or child output (CS).

An exploratory analysis of 18 additional white matter tracts identified as part of the AFQ pipeline (Mori et al., 2006; Yeatman et al., 2012b), including the right hemisphere AF and SLF, revealed no other significant correlations with 18 month CT. Examination of individual nodes showed small clusters of significant effects for 6 and 10 month CT within the left and right inferior longitudinal fasciculus (ILF) and inferior frontal occipital fasciculus (IFOF). Additionally, negative correlations in a small number of nodes were observed in the ILF and IFOF for CS at 6 and 18 months and AWC at 6 and 10 months. These effects were not significant after correcting for multiple comparisons across language measures, however.

As shown in Table 2, CT effects were strongest at 18 months, although comparable effects were observed in the left anterior arcuate across all ages. Individual growth estimates obtained from a linear mixed model showed a significant correlation between 26 month MPF and linear growth in CT from 6 to 24 months ($r_{(20)} = 0.70$, $p < 0.001$), as well as between 26 month MPF and change in CT growth over the same period (age^2; $r_{(20)} = -0.59$, $p = 0.0040$). In other words, greater initial growth in CT from 6 months predicted higher MPF at 26 months. To further examine the effect of growth in CT, individual growth estimates from 14 to 24 months (the middle through the final available time point) were obtained from a second model, with an intercept at 14 months and a linear effect of age. While the 14 month intercepts predicted 26 month MPF ($r_{(20)} = 0.59$, $p = 0.0037$), linear growth from 14 to 24 months was not a significant predictor ($r_{(20)} = 0.31$, $p = 0.16$).

Finally, correlations were tested between MPF and 24 month measures of productive vocabulary and mean utterance length (M3L). No significant correlations were observed for vocabulary in the left arcuate or SLF, and no significant correlations were observed in any white matter location for M3L. However, an exploratory analysis, including 18 additional tracts, showed significant correlations between vocabulary and MPF in the right ILF and the right IFOF, as shown in Figure 3. Average MPF within the posterior portion (nodes 11:50) of the right ILF and IFOF correlated with 24 month vocabulary ($p < 0.05$).

Discussion

The current study examines the relationship between home language interactions during infancy and white matter development, measured at 2 years of age. Parent–infant CT uniquely predicted MRI estimates of myelin density within the left AF, independent of total adult speech exposure, child-directed speech input, and children's speech-related utterances. Exploratory analyses in 18 additional white matter tracts indicated a high degree of anatomic specificity. Further, longitudinal analyses suggested a distinct contribution from CT at 6 and 14 months, and growth in CT over this period, within the left arcuate. Together, these findings suggest that white matter development is sensitive to interactional elements of language experience during first 2 years of life, and point to ongoing effects of language experience starting as early as 6 months of age.

Correlations with CT were localized to dorsal language pathways that are associated with the development of expressive and receptive language skills, as well as adult language performance. The left AF and SLF connect dorsal language regions within posterior/superior temporal and inferior frontal lobes, including classical Wernicke's (BA 22) and Broca's (BA 44/45) areas (Hickok and Poeppel, 2007; Rauschecker and Scott, 2009; Rauschecker, 2011). The dorsal language system has long been associated with speech production and sensory-motor integration (Wernicke, 1874; Saur et al., 2008; Hickok, 2012; Roelofs, 2014; Skeide and Friederici, 2016). Structural characteristics of the AF and SLF have also been shown to correlate with a variety of language-related measures over development, including phonological awareness, expressive vocabulary, syntactic processing, and emerging literacy skills (Dronkers and Ogar, 2004; Lebel and Beaulieu, 2009; Wilson et al., 2011; Yeatman et al., 2011, 2012a; Friederici and Gierhan, 2013; Lebel et al., 2013; Saygin et al., 2013; Skeide et al., 2016; Travis et al., 2017; Su et al., 2018; Vanderauwera et al., 2018). In addition, the arcuate has been implicated in general cognitive processes related to attention (de Diego-Balaguer et al., 2016) and working memory (Meyer et al., 2014).

Functional specialization for language has been reported within the first few months of life (Peña et al., 2003; Dehaene-

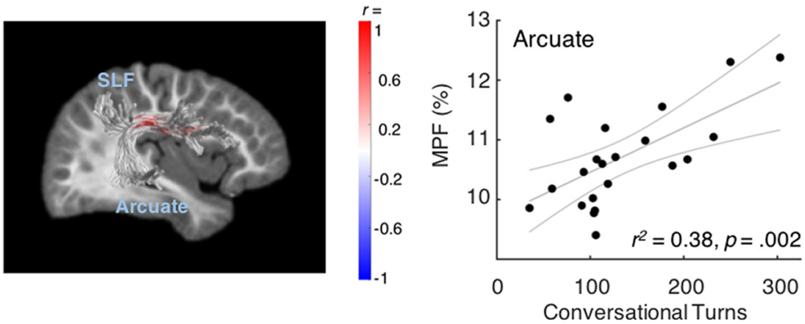

Figure 2. Correlations with conversational turns at 18 months. Left, Significant correlations ($p < 0.05$, corrected for multiple comparisons along each tract) between macro-molecular proton fraction (MPF) and 18-month conversational turns (CT) at each tested location along the left arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF). Color coding represents effect sizes at each anatomic location. Right, Scatterplot represents the correlation between 18-month CT and average MPF values within the left anterior AF (Bonferroni-corrected$p < 0.05$).

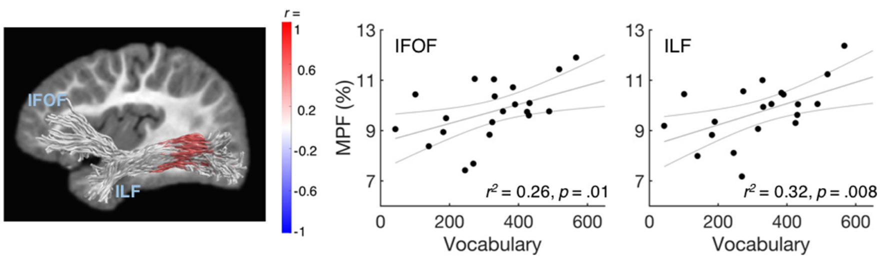

Figure 3. MPF correlations with child vocabulary at 24 months. Left, Significant correlations ($p < 0.05$, corrected for multiple comparisons along each tract) between macro-molecular proton fraction (MPF) and 24-month productive vocabulary at each tested location along the right inferior longitudinal fasciculus (ILF) and inferior fronto-occipital longitudinal fasciculus (IFOF) and IFOF. Color coding represents effect sizes at each anatomical location. Right, Scatterplots represent the correlation between 24-month productive vocabulary and average MPF values within the posterior portions of the right IFOF and ILF.

Lambertz et al., 2006; Homae et al., 2011; Sato et al., 2012; Shultz et al., 2014; Dehaene-Lambertz and Spelke, 2015; Dehaene-Lambertz, 2017), although the cortical language network is thought to undergo substantial development over the next 7-8 years (Skeide and Friederici, 2016). Similarly, white matter pathways associated with language are present at birth (Dubois et al., 2006; Perani et al., 2011; Skeide and Friederici, 2016), but they develop rapidly over the first 2 years of life (Geng et al., 2012; Dubois et al., 2014; Deoni et al., 2016; Gilmore et al., 2018; Lebel and Deoni, 2018), and show continued, but less dramatic, developmental myelination through adolescence (Lebel et al., 2012). In particular, frontal white matter is thought to be relatively immature through at least 7 years of age (Perani et al., 2011; Brauer et al., 2013; Skeide et al., 2016), with left lateralized frontal-temporal connectivity emerging toward the end of the first year (Emerson et al., 2016).

Studies with infants (3-12 months) and young children (1-5 years) suggest that developmental myelination coincides with the emergence of language-related skills. For example, MRI based estimates of myelin water fraction have been shown to correlate with early linguistic and cognitive performance, through 5 years of age (O'Muircheartaigh et al., 2014; Deoni et al., 2016). Changes in FA from 6 to 24 months have also been found to predict expressive language skills at 24 months (Swanson et al., 2017), suggesting that the rate of early white matter development has implications for subsequent language achievement. Within the left AF and SLF, correlations have been reported between neonatal FA and later receptive and expressive language skills, through age 2 years (Salvan et al., 2017; Girault et al., 2019; Sket et al., 2019). This latter set of findings suggests that language development may be constrained by stable differences in white matter organization, already present at birth. However, challenges related to participant motion and low signal-to-noise in the neonatal brain (Gilmore et al., 2018) have limited the availability of data in this age group.

In the current study, parent–infant CT was associated with myelin density estimates within the left AF and SLF at age 2 years, while controlling for total speech exposure and production. These findings suggest that direct, one-on-one interaction may specifically influence the development of these pathways. In line with this idea, findings from intervention and controlled experimental studies suggest that interactions with responsive adults may directly promote language learning (Kuhl et al., 2003; Goldstein and Schwade, 2008; Roseberry et al., 2009, 2014; Ferjan Ramírez et al., 2019, 2020; Leech and Rowe, 2021).

From a behavioral perspective, conversational interactions have several unique properties. For one, socially contingent interaction is thought to elicit higher quality output from children, including vocalizations that incorporate native phonology during infancy (Goldstein et al., 2003; Goldstein and Schwade, 2008). Prelexical "babbling" in infancy has, in turn, been shown to predict expressive language skills in the first 2 years of life (Oller et al., 1999; Lyakso et al., 2014; McGillion et al., 2017; Werwach et al., 2021), and to mediate the effects of parental language input (Ramírez-Esparza et al., 2014). Prior studies further suggest that both children and adults adjust and coordinate their output during conversational interactions (Smith and Trainor, 2008; Warlaumont et al., 2014; Abney et al., 2017; Albert et al., 2018; Elmlinger et al., 2019).

In addition, conversational interaction may enhance child uptake by supporting domain general processes, such as memory (Lugo-Gil and Tamis-LeMonda, 2008) and attention (Masek et al., 2021). Joint attention has long been linked to early lexical (Carpenter et al., 1998; Laakso et al., 1999; Brooks and Meltzoff, 2005, 2008; Mundy and Newell, 2007) and phonemic (Conboy et al., 2015) learning. Sustained (Ruff and Lawson, 1990; Lawson and Ruff, 2004; Kannass and Oakes, 2008) and selective (Francis and Nusbaum, 2002) attention has also been implicated in language acquisition, and social contingency may facilitate development of these abilities (Masek et al., 2021).

In contrast to prior findings for 4- to 6-year-old children (Romeo et al., 2018b), MPF correlations with child vocabulary and CT did not colocalize within the white matter. Instead, correlations between MPF and 24-month vocabulary were observed within the right posterior ILF and IFOF. Recent MEG findings suggest that neural activity within the right inferior frontal cortex may be especially relevant for vocabulary learning in the first years of life (Bosseler et al., 2021). Specifically, evoked responses at 14 months predicted later child vocabulary, through 30 months of age (Bosseler et al., 2021). In another recent study, MPF within right lateralized temporal-parietal white matter at 7 months was found to predict 24 month vocabulary (Corrigan et al., 2022). The current findings are therefore in line with recent evidence for a right-hemisphere contribution to early word learning.

The current results extend prior findings by demonstrating a relationship between parent-infant conversational turns and white matter development within the first 2 years of life, much sooner than previously observed. Longitudinal analyses suggest an effect of conversational experience occurring as early as 6 months of age. CT at 6 months may be especially relevant for the development of neural systems related to phonological analysis and phonemic learning, given that this age marks the onset of a critical period for native phoneme categorization (Werker and Tees, 1984; for review, see Kuhl, 2010; Maurer and Werker, 2014). By 12 months, most infants have exited the critical period for phonemic learning, but other windows of sensitivity may remain, or be newly open (Werker and Hensch, 2015). The current analysis suggests an additional effect of CT at 14 months, which might reflect distinct processes related to higher-level linguistic skills, such as lexical processing (Rowe and Weisleder, 2020), or ongoing development of general cognitive skills related to attention or working memory (Reynolds and Romano, 2016).

Limitations

The current study has important limitations, which need to be mentioned. First, the sample is limited to native English speakers and children without known environmental or genetic risk factors, such as lower SES or family history of dyslexia. Further, the sample size is relatively small, and most of the study participants received a home language intervention that increased parental language input and parent-infant interaction. Future work is therefore needed to clarify whether the current findings generalize to larger and more diverse samples, including samples participants who did not experience an enriched language environment as a result of intervention.

Interactions with caregivers play a vital role in early language learning. The current results suggest that parent-child interactions may also shape the development of language-related white matter pathways, starting during infancy. Future work is needed to examine how these early developmental differences contribute to longer-term language outcomes.

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