



Home language and literacy environment and its relationship to socioeconomic status and white matter structure in infancy

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Abstract

The home language and literacy environment (HLLE) in infancy has been associated with subsequent pre-literacy skill development and HLLE at preschool-age has been shown to correlate with white matter organization in tracts that subserve pre-reading and reading skills. Furthermore, childhood socioeconomic status (SES) has been linked with both HLLE and white matter organization. It is important to understand whether the relationships between environmental factors such as HLLE and SES and white matter organization can be detected as early as infancy, as this period is characterized by rapid brain development that may make white matter pathways particularly susceptible to these early experiences. Here, we hypothesized that HLLE (1) relates to white matter organization in pre-reading and reading-related tracts in infants, and (2) mediates a link between SES and white matter organization. To test these hypotheses, infants (mean age: 8.6 ± 2.3 months, $N = 38$) underwent diffusion-weighted imaging MRI during natural sleep. Image processing was performed with an infant-specific pipeline and fractional anisotropy (FA) was estimated from the arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF) bilaterally using the baby automated fiber quantification method. HLLE was measured with the Reading subscale of the StimQ (StimQ-Reading) and SES was measured with years of maternal education. Self-reported maternal reading ability was also quantified and applied to our statistical models as a proxy for confounding genetic effects. StimQ-Reading positively correlated with FA in left AF and to maternal education, but did not mediate the relationship between them. Taken together, these findings underscore the importance of considering HLLE from the start of life and may inform novel prevention and intervention strategies to support developing infants during a period of heightened brain plasticity.

Keywords Brain · Development · Diffusion-weighted imaging · Language · Literacy · Infants · MRI · Reading · Socioeconomic status · White matter

Introduction

Learning to read is a primary goal of elementary education, and is associated with subsequent academic achievement, vocational success, and even health outcomes (Sanfilippo

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et al. 2020). However, before a child begins formal reading instruction, they develop pre-literacy skills that serve as a foundation for learning to read (de Jong and van der Leij 1999; Georgiou et al. 2008; Scarborough 1998; Schatschneider et al. 2004). There is now considerable evidence that pre-literacy skill development is shaped by the child's home language and literacy environment (HLE), which may comprise oral language input, parent–child shared reading experiences, and reading resources in the home. For instance, the richness of HLE has been shown to aid in children's pre-literacy skill development, including phonological awareness (Frijters et al. 2000), print knowledge (Levy et al. 2006), and oral language skills (Burgess et al. 2002; National Early Literacy Panel 2008; Storch and Whitehurst 2002). However, links between HLE and literacy have predominantly been examined in children closer to the time of formal reading instruction (Scarborough and Dobrich 1994).

Although studies examining HLE in infancy and toddlerhood are rarer, these too have reported that HLE contributes to the prediction of pre-literacy and language outcomes. For instance, infants' HLE, as measured by parent-informed reports, has been associated with receptive vocabulary during infancy and has been shown to be prospectively associated with expressive vocabulary during toddlerhood (Schmitt et al. 2011). Parent–child shared book reading experience at 8 months also predicted subsequent expressive language abilities at 12 as well as 16 months (Karrass and Braungart-Rieker 2005). Similarly, receptive and expressive language outcomes at 18 months have been predicted by aspects of shared reading experience (e.g., time spent reading together, children's interest in reading, and maternal questions during shared reading) at 10 months (Muhinyi and Rowe 2019) and 14 months (Laakso et al. 1999). In children aged 14–30 months, parent–child book reading interactions (specifically quantity of parent utterances) were associated with subsequent receptive vocabulary during 2nd grade and reading comprehension at the end of 3rd grade (Demir-Lira et al. 2019). Also, qualitative aspects of parent–child reading interactions (i.e., caregiver conversational input that elaborates on the text in the book) at 24 months was associated with child receptive vocabulary at roughly 5 years (Malin et al. 2014). The evidence supporting the relationship between HLE during infancy and pre-literacy and language skills later in childhood underscores the importance of considering HLE from the earliest stages of life. However, it is important to note that these observed links between HLE and literacy skill have historically been of modest effect sizes (Bus et al. 1995; Scarborough and Dobrich 1994) and others have suggested that literacy development may be attributed largely to genetic heritability (Hart et al. 2021; van Bergen et al. 2016). Nevertheless, links between HLE and subsequent reading outcomes are

consistent, which warrants careful investigation of underlying brain mechanisms.

To identify the underlying mechanisms that could explain the link between HLE and subsequent reading outcomes, several studies have examined brain characteristics related to HLE. Among preschool-age children, HLE was associated not only with better language and pre-literacy skills, but also with white matter organization in pathways thought to be important for reading, including the arcuate fasciculus (AF), superior longitudinal fasciculus (SLF), and corpus callosum (Hutton et al. 2020). Also, shared book reading between parent and child has been shown to positively relate to fractional anisotropy (FA) in the left AF among kindergarten-age children (Davison et al. 2022). Similarly, parent–child conversational interactions, which have been subsumed under HLE (Schmitt et al., 2011), were related to FA in left AF and left SLF in preschool- and kindergarten-age children (Romeo et al. 2018) and to functional connectivity among posterior temporal brain regions in infants (King et al. 2021). Importantly, findings in the AF and SLF in particular consistently overlap with tracts involved in typical and atypical reading development in children prior to reading onset (Wang et al. 2017; Zuk et al. 2021a) and infants specifically (Langer et al. 2017; Zuk et al. 2021b). Overall, emerging evidence suggests that some of the key characteristics of high-quality HLE are associated with alterations in left hemisphere white matter tracts at preschool age. However, the relationship between HLE and white matter structure has not been investigated in children younger than preschool-age. This represents a critical gap as the first 2 years of life are marked by rapid changes in FA (Geng et al. 2012), potentially making neural circuitry particularly amenable to experiential input during this period (Tau and Peterson 2010).

It is important to note that the relationship between HLE and brain structure can also be contextualized as part of a larger model relating SES to language and literacy outcomes. Such a model has behavioral support in that SES is associated with features of HLE, such as shared book reading (Hamilton et al. 2016) and child-directed speech (Hoff 2003; Kuntay and Ahtam 2004). In turn, this association mediates the relation between SES and pre-literacy outcomes, including phonemic awareness and vocabulary knowledge (Foster et al. 2005), as well as literacy outcomes, including word-level literacy and reading comprehension (Hamilton et al., 2016). However, this certainly does not imply that low HLE and low academic outcomes always accompany low SES (e.g., Christian et al. 1998). More recent work integrating brain measures has postulated, and subsequently shown in older children (5–9 years), that the linguistic environment mediates the relationship between SES and language-supporting brain regions, and these brain regions in turn mediate relationships between the linguistic environment

and subsequent language abilities (Merz et al. 2020; Noble et al. 2012).

We propose that an analogous model could apply to infants (Fig. 1). In such a model, HLE would mediate the association between SES and brain areas or pathways subserving pre-literacy skills such as the AF and SLF. In older children, the white matter tracts associated with childhood SES include those thought to subserve reading, such as the left AF (Vanderauwera et al. 2019), left SLF (Gullick et al. 2016), and left inferior longitudinal fasciculus (Ozernov-Palchik et al. 2018). It is possible that SES relates to white matter organization in additional tracts. However, our focus in the current study was foremost to examine the relationship between HLE and white matter organization in infancy. Taken together, these considerations motivated limiting our examination of possible mediation pathways to tracts previously related to HLE in older children (Davison et al. 2022; Hutton et al. 2020; Romeo et al. 2018) and language and literacy in infants (Langer et al. 2017; Zuk et al. 2021b).

The aim of the present study was to examine the relationship between HLE and white matter organization in infancy. Accordingly, diffusion-weighted imaging was performed to examine white matter tracts previously associated with HLE in preschool-age children (Davison et al. 2022; Hutton et al. 2020; Romeo et al. 2018) and shown to be involved in language and literacy in early development (Langer et al., 2017; Wang et al. 2017; Zuk et al. 2021a, 2021b), namely, AF and SLF. HLE was measured with the StimQ, a validated questionnaire that asks caregivers about parent–child shared reading and the extent of reading-related resources in the home. Importantly, as parent–child shared reading includes rich vocabulary, complex sentences, and conversational turns (Scheele et al. 2010), StimQ serves as a viable indicator for HLE.

Furthermore, to test the model by Noble et al. (2012), we also investigated whether HLE mediated an association between a prominent aspect of reported SES (i.e., maternal education) and FA in AF and SLF. Importantly, parental reading ability can contribute to children’s reading ability directly through genes and indirectly through HLE (Friend et al. 2008, 2009). To control for potential genetic confounds in the present study, we incorporated self-reported maternal reading ability into all statistical models to serve as a proxy for genetic transmission (Hart et al. 2021). Ultimately, these inquiries have implications for literacy interventions for developing infants.

Methods

Participants and study design

Infants examined in this study were part of a larger NIH-funded longitudinal investigation of brain, language, and pre-literacy development among children from infancy to school age (NIH–NICHD R01 HD065762). While the larger study tracks over 150 infants, only 70 of these had diffusion data, and of these, only 38 had HLE and SES datasets. Notably, the cohort in the present study does not overlap with the infant cohort presented in previous studies by our group (Langer et al. 2017; Zuk et al. 2021b).

Families were recruited from the Greater Boston Area through the Research Participant Registry within the Division of Developmental Medicine at Boston Children’s Hospital, as well as through ads and flyers disseminated in local newspapers, schools, community events, and social media. Families were invited for participation at the time of their child’s infancy with anticipation of continued participation at future developmental time points. Infants completed brain MRI scan sessions and their attending parent(s) completed questionnaires pertaining to the children’s medical history, home environment, and socioeconomic context (please see Table 1 for full demographic details).

Participating infants were screened for neurological and sensory impairments, contraindications for MRI evaluation (e.g., metal implants), and premature birth; infants screening positive for any of these criteria were excluded from the study. All children included were from English-speaking families and were born at gestational week 37 or later. Anatomical T1-weighted MRI scans (please see parameters below) were reviewed for clinical abnormalities by a

Table 1 Demographic and behavioral data

<i>N</i>	38
Sex (F/M)	15/23
Age (months)	8.6 ± 2.3
Age range (months)	4.6–12.5
StimQ Reading subscale	14 ± 3.7
Maternal education ^a	6.5 ± 1.7
Adult Reading History Questionnaire	29 ± 13

^aRescaled with “1” indicating less than 12 years of formal education and “8” indicating 20 or more years of formal education

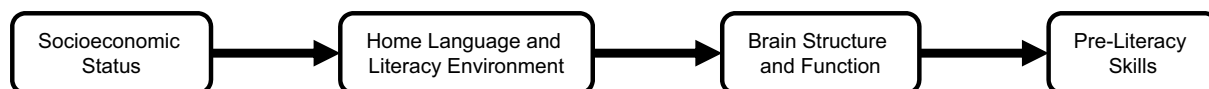


Fig. 1 Hypothesized model for pre-literacy skill development

pediatric neuroradiologist at Boston Children's Hospital, and no participating infants exhibited any malignant brain features. This study was approved by the Institutional Review Board of Boston Children's Hospital (IRB-P00023182). Informed written consent was provided by each participating infant's parent(s).

Environmental characteristics

An inventory of each infant's home language and literacy environment (HLE) was gathered from their parents using the StimQ Cognitive Home Environment (infant version), a validated parent report measure that includes four subscales: availability of learning materials, reading, parental involvement in developmental advance, and parental verbal responsivity (<https://med.nyu.edu/departments-institutes/pediatrics/divisions/developmental-behavioral-pediatrics/research>). The Reading subscale of the StimQ (StimQ-Reading), which was the only subscale used in subsequent analyses, instructs caregivers to respond to 15 questions about parent–child shared reading-related activities and the reading materials used. The response scale ranges from 0 to 19 (Table 1).

Socioeconomic status (SES) was measured using maternal education, consistent with previous neuroimaging studies on SES (Betancourt et al. 2016; Brito et al. 2016; Lawson et al. 2013; Merz et al. 2018; Noble et al. 2015; Ozernov-Palchik et al. 2018). Maternal education was coded on an 8-point ordinal scale, with “1” indicating less than 12 years of formal education (less than high school or equivalent), and “8” indicating 20 or more years of formal education (graduate or professional degree; Table 1).

Self-reported maternal reading ability

Each mother completed the Adult Reading History Questionnaire (ARHQ), which is designed to measure the risk of reading disability in adults by asking questions about the individual's reading history and current reading habits. Biological mothers answered questions assessing their past and current reading frequency, reading speed, and difficulty reading and spelling, as well as about having to repeat grades or courses, attitudes toward school, and whether they received extra help with learning to read. This questionnaire has demonstrated validity in predicting reading skill (Lefly and Pennington 2000), making it suitable to use in this study as a measure to control for genetic transmission of reading abilities from mother to child (please see Introduction). All responses were given on a Likert scale and summed for each mother. Lower values indicate greater reading ability (Table 1).

Neuroimaging data acquisition

Neuroimaging data were acquired, while all the infants were naturally sleeping, without sedation, using an established infant neuroimaging protocol (Raschle et al. 2012; Turesky et al. 2021b). Diffusion-weighted and structural T1-weighted images were acquired on a 3.0 Tesla Siemens MRI scanner with a standard Siemens 32-channel radio frequency head coil. One parent remained in the MRI room with the infant for the duration of the scan, in addition to a researcher who stood by the bore to monitor changes in the infant's sleeping state and potential motion. Structural T1-weighted whole-brain multi-echo magnetization-prepared rapid gradient-echo sequences with prospective motion correction (mocoMEMPRAGE) were acquired for each participant with the following parameters: repetition time (TR) = 2270 ms; echo time (TE) = 1450 ms; acquisition time (TA) = 4.51 min; flip angle = 7°; field of view = 220 mm × 220 mm; voxel size = 1 × 1 × 1 mm³; 176 slices; in-plane GRAPPA acceleration factor of 2. Diffusion echo planar images were acquired using the following parameters: TR = 4600 ms; TE = 89 ms; TA = 5.36 min; flip angle = 90°; field of view = 256 mm × 256 mm; voxel size: 2 × 2 × 2 mm³; 64 slices; in-plane GRAPPA acceleration factor = 2; slice-acceleration (SMS/MB) factor = 2; partial Fourier encoding = 6/8, 30 gradient directions of $b = 1000$ s/mm², 10 non-diffusion-weighted volumes of $b = 0$ s/mm² acquisitions, 1 phase-encoding anterior-to-posterior volume, 1 phase-encoding posterior-to-anterior volume.

MRI image processing

Raw T1-weighted images were submitted to Infant FreeSurfer for tissue segmentation (<https://surfer.nmr.mgh.harvard.edu/fswiki/infantFS>; Zöllei et al. 2020), and then ACPC-aligned using *acpcdetect* (<https://www.nitrc.org/projects/art/>); ACPC transformation matrices generated in the latter step were applied to the tissue segmentations. This order of steps was chosen to avoid running Infant FreeSurfer on resampled, interpolated T1-weighted images.

Subsequently, ACPC-aligned tissue segmentations were submitted to MRtrix3 (<https://www.mrtrix.org/>; Tournier et al. 2019) to generate 5tt (i.e., five-tissue-type) images, each containing separate volumes for cortical gray matter, subcortical gray matter, white matter, cerebrospinal fluid, and other tissue (Smith et al. 2012). In turn, 5tt images served as inputs to generate gray/white matter interface masks (Smith et al. 2012).

DWI preprocessing and tractography were performed according to the pipeline established for the Developing Human Connectome Project (Bastiani et al. 2019; Pietsch et al. 2019), which mainly relies on MRtrix3 software. As such, DWI data were denoised using Marchenko–Pastur

principal component analysis (Cordero-Grande et al. 2019; Veraart et al. 2016b, 2016a), and corrected for susceptibility distortions, eddy currents, motion, and intensity inhomogeneity using the MRtrix3 wrappers for (i) FSL's topup and eddy (with slice-to-volume correction) functions (Andersson et al. 2017, 2003; Andersson and Sotiropoulos 2016; Skare and Bammer 2010; Smith et al. 2004), and (ii) ANT's N4 bias correction tool (Tustison et al. 2010). Preprocessed DWI datasets were then registered to their corresponding ACPC-aligned T1-weighted images with gradient directions rotated accordingly using the VISTALab diffusion MRI software suite (<https://vistalab.stanford.edu/>).

Three tissue response functions for spherical deconvolution were then estimated from ACPC-aligned DWI images using the Dhollander algorithm, a 0.1 fractional anisotropy threshold, and 8 maximum harmonic degrees (Dhollander et al. 2016). Fiber orientation densities (FODs) were calculated with multi-shell, multi-tissue constrained spherical deconvolution (Jeurissen et al. 2014; Tournier et al. 2004) and then normalized using multi-tissue informed log-domain intensity normalization. Normalized FOD maps were then used as source data for whole-brain tractography, wherein 2 million streamlines were generated by seeding the gray/white matter interface and then tracking with the iFOD1 probabilistic algorithm and Anatomically Constrained Tractography framework. Additional tractography parameters, such as step size, minimum and maximum length, and maximum step angle, were set to default (Smith et al. 2012; Tournier et al. 2012).

Automated fiber quantification

Resulting connectomes were submitted for fiber segmentation to babyAFQ (Grotheer et al. 2022), a new toolkit within the Automated Fiber Quantification (AFQ) suite (<https://github.com/yeatmanlab/AFQ>; Yeatman et al. 2012a). Similar to AFQ, babyAFQ uses regions-of-interest (ROIs) defined in template space and mapped to native space as waypoints to classify fibers according to tract. Then, these classified fibers are compared to fiber-tract probability maps to ensure that reconstructed tracts contain only fibers that conform to the expected shape. Tract cleaning was performed using a statistical outlier rejection algorithm. Unlike the standard AFQ, babyAFQ uses ROIs and probabilistic atlases defined using the UNC Neonate template, as opposed to an adult template, to accommodate the smaller infant brain. Next, tracts were resampled to 100 equidistant nodes and diffusion properties, including fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD), were computed at each node.

Finally, arcuate fasciculus (AF) and superior longitudinal fasciculus (SLF) were inspected visually by two separate raters to verify successful reconstruction (Supplementary

Fig. 1). For context, the AF constitutes the long segment of the dorsal language pathway (Catani and Dawson 2017). It connects superior temporal gyrus and inferior frontal gyrus, and is important for naming abilities (Ivanova et al. 2021), word repetition (Sierpowska et al. 2017), and reading (Gullick and Booth 2015; Thiebaut De Schotten et al. 2014). The SLF is a tripartite tract and mainly connects parietal to frontal areas (Yagmurlu et al. 2016). As constrained spherical deconvolution signal modeling and probabilistic tractography were used, all segments were captured as a single tract (Schurr et al. 2020). Relevant to the inquiries posed in this study, one segment (SLF III) constitutes the anterior segment of the dorsal language pathway (Catani and Dawson 2017), which has a role in fluency and naming (Ivanova et al. 2021). It connects supramarginal gyrus to inferior frontal gyrus (Yagmurlu et al. 2016), two regions involved in reading and reading-related processes (Eden et al. 2016). Ultimately, reconstruction success rates were as follows: 34/38 for left AF, 33/38 for right AF, 34/38 for left SLF, and 37/38 for right SLF. Tract profiles are depicted in Supplementary Fig. 2.

Statistical analyses

Correlation analyses were conducted among HLLE, diffusion, and SES variables, and where HLLE variables correlated with both diffusion and SES measures, subsequent mediation analyses were performed. All correlation analyses were conducted in MATLAB. Because StimQ-Reading was not normally distributed according to D'Agostino & Pearson omnibus normality tests ($K2 = 10.4$, $p < 0.01$), non-parametric statistics (i.e., Spearman) were used. Significance testing was done using non-parametric bootstrapping to simulate the sampling distribution in the general population to ensure proper evaluation of effect sizes (Zuk et al. 2021b). This approach involved simulating the population distribution based on semipartial correlations using 5000 replicated samples with replacement from the original sample (Nichols and Holmes 2002).

First, to examine whether HLLE and maternal education were related, correlations between StimQ-Reading and maternal education were computed. Second, relations to FA for nodes along each tract of interest were done according to semipartial correlations (adjusting FA for infant age at the time of scan, sex, and self-reported maternal reading ability) for StimQ-Reading and for maternal education. To correct for multiple tests of correlation within each tract (100 tests), a cluster-based non-parametric permutation method was applied using an adapted version of the AFQ_MultiCompCorrection function in the AFQ suite adjusted to include covariates and Spearman testing. This function estimated the number of contiguous nodes significant at an uncorrected $p < 0.05$ that were needed for a family-wise

error correction (FWE) $p < 0.05$, which differed according to tract and behavior estimate. FA estimates of contiguous nodes passing correction for multiple comparison were then averaged for visualization purposes. To determine whether other white matter properties were related to the observed associations between FA and StimQ, post-hoc correlations were also computed between the three diffusivity measures (mean, radial, and axial) and StimQ.

Finally, a 10,000-repetition bootstrapped, non-parametric mediation analysis was run using R statistical analysis software (<https://www.rdocumentation.org/packages/mediation/versions/4.5.0/topics/mediate>; Tingley et al. 2014), with maternal education as the independent variable, FA as the dependent variable, StimQ-Reading as the mediator, and infant age at time of MRI, sex, and self-reported maternal reading ability as confounding variables. The FA values used in the mediation were taken from the contiguous nodes that were significant (after FWE correction) in correlations with StimQ and maternal education. Indirect effects were deemed significant when 95% confidence intervals did not include 0. Code used for data processing and analyses may be found at <https://github.com/TeddyTuresky/diffusionHLLE2021>.

Results

The Reading subscale of the StimQ (StimQ -Reading) correlated with maternal education ($r = 0.32$, $p < 0.05$). StimQ-Reading also correlated with FA in the mid-portion of the left AF between nodes 14 and 28 (out of 100), inclusive, controlling for age at time of scan, sex, and self-reported maternal reading ability ($r_{\text{average}} = 0.39$, $p_{\text{FWE}} < 0.05$, Fig. 2). No other segment of the left AF or any segment of the left

SLF, right AF, or right SLF, or any other diffusivity measure (MD, RD, or AD) exhibited a significant correlation with StimQ-Reading after FWE correction.

Maternal education within this group was also strongly correlated with left AF FA between nodes 14 and 27, inclusive, controlling for age of the infant and self-reported maternal reading ability ($r_{\text{average}} = 0.43$, $p_{\text{FWE}} < 0.05$, Fig. 3). No other segment of the left SLF, right AF, or right SLF or diffusivity measure showed any significant correlation with maternal education after FWE correction.

Given that StimQ-Reading correlated with maternal education and FA in left AF, a mediation model was constructed to test for an indirect effect of StimQ-Reading (mediator) on the relationship between maternal education (independent variable) and FA of the left AF in the cluster of nodes that overlapped in the FA-StimQ and FA-maternal education associations above (dependent variable). However, indirect effects were not significant after controlling for infant age, sex, and self-reported maternal reading ability.

Discussion

In the present study, we show that the home language and literacy environment (HLLE), as measured with the Reading subscale of the StimQ, correlates with maternal education and white matter structure in the left arcuate fasciculus. Along with previous work showing that white matter in infancy relates to later language outcomes (Zuk et al. 2021b), these findings offer a neurobiological mechanism to the corpus of behavioral literature linking HLLE during infancy and toddlerhood to pre-literacy and language development (Karrass and Braungart-Rieker 2005; Laakso

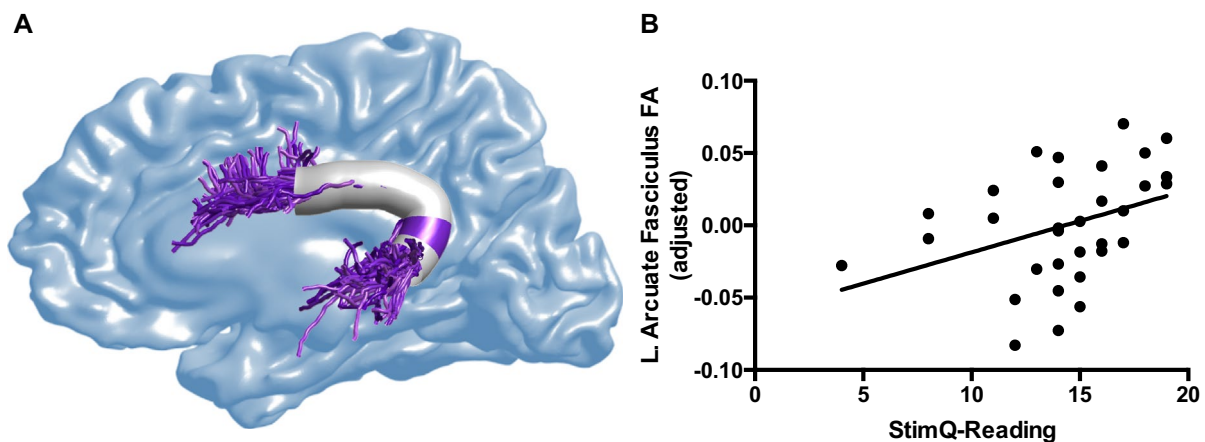


Fig. 2 Association between StimQ-Reading and white matter organization in the left AF. **A** Nodes exhibiting significant associations between StimQ-Reading and FA (after FWE correction for multiple comparisons), superimposed on a midsagittal slice of one infant (pur-

ple). **B** Scatterplot depicting average FA from nodes represented in A in relation to StimQ-Reading. FA was adjusted for infant age, sex, and self-reported maternal reading ability

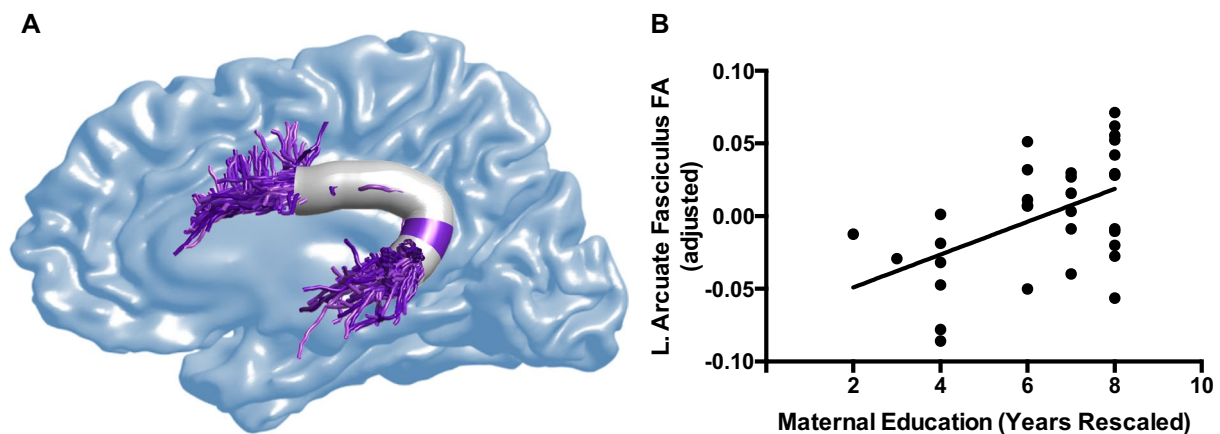


Fig. 3 Association between maternal education and white matter organization in left AF. **A** Nodes exhibiting significant associations between maternal education and FA (after FWE correction for multiple comparisons), superimposed on a midsagittal slice of one infant

et al. 1999; Malin et al. 2014; Muhinyi and Rowe 2019; Schmitt et al. 2011). Furthermore, the finding of an environmental factor relating literacy to white matter organization (independent of familial transmission as measured by self-reported maternal reading ability) complements previous reports, showing that familial risk of reading difficulty (which did not relate to HLLE in their cohort) was related to white matter organization in infancy (Langer et al. 2017). Taken together, our findings indicate that HLLE is associated with white matter organization early in development, prior to prolonged exposure to literacy input.

Our main findings were localized to a segment in the posterior (temporoparietal) portion of the left AF, a tract that connects inferior frontal and superior temporoparietal brain regions and, together with the SLF, forms the dorsal perisylvian language pathway known to be associated with language and early reading development (Catani et al. 2005; Wandell et al. 2012; Yeatman et al. 2012b). Further illustrating the importance of the left AF in literacy, FA in this tract has been shown to correlate with reading outcomes in typically developing children (Hoeft et al. 2011; please note that this study defined left SLF as including left arcuate fasciculus). Moreover, children with a family history of dyslexia have lower FA in the temporoparietal segment of the left AF compared with children without a family history of dyslexia at beginning and fluent reading stages, and in fact, this discrepancy has been noted even prior to the onset of reading onset (Wang et al. 2017). The combination of our results linking HLLE to left AF anatomy in infancy and past findings relating infant left AF anatomy to literacy outcomes (Zuk et al. 2021b) supports behavioral literature linking HLLE in infancy to language outcomes (Duff et al. 2015; Laakso et al. 1999; Muhinyi and Rowe 2019; Schmitt et al. 2011). However, follow-up work examining reading

(purple). **B** Scatterplot depicting average FA from nodes represented in A in relation to maternal education. FA was adjusted for infant age, sex, and self-reported maternal reading ability

outcomes in the children in this study and causal mediation testing will be needed to confirm the hypothesis that HLLE impacts subsequent reading ability via left AF structure.

Broadly, findings in infants of an association between HLLE and white matter structure are consistent with work previously done in preschool age children. Indeed, the present finding aligns with emerging work, showing that greater shared reading time is associated with greater FA in the left AF among kindergarten-age children (Davison et al. 2022). HLLE as measured with StimQ-Reading has also been associated with white matter organization in the left AF and other literacy-supporting white matter tracts as measured with whole-brain, tract-based spatial statistics (TBSS; Hutton et al. 2020), as well as with activation in left hemisphere brain regions in or near AF termini, such as inferior frontal gyrus (Hutton et al. 2017; Powers et al. 2016) and the parietal-temporal-occipital region on story listening and phonological processing tasks (Hutton et al. 2015). Also, HLLE was associated with white matter structure in other tracts supporting language and literacy (e.g., superior longitudinal fasciculus and inferior longitudinal fasciculus), in some cases bilaterally (Hutton et al. 2020). In the present study in infants, links were only observed for the left AF as estimated using a hypothesis-driven, tract-specific approach (with the SLF being the sole other tract examined). Such differences between the two developmental stages, though not directly tested here, would not be surprising, as white matter in all tracts undergoes substantial change between infancy and preschool (Lebel and Deoni 2018; Reynolds et al. 2019), and it is conceivable that variation in the developmental trajectories of these tracts would make them more or less amenable to environmental input at different developmental stages (Nelson and Gabard-Durnam 2020). Future longitudinal studies will be needed to determine whether

the associations between HLLE and white matter structure indeed become more widespread with age.

The present study also contributes to the literature on HLLE by partially controlling for genetic confounds using self-reported maternal (but not paternal) reading ability. Maternal reading history is important to consider, because genetic makeup shared by parent and child contributes to the child's reading ability directly via genetic inheritance and indirectly via parental reading ability and HLLE (Hart et al. 2021; van Bergen et al. 2016). Past studies using parental characteristics as a proxy for the direct/genetic pathway have largely reported diminished associations between HLLE variables and children's reading when controlling for parental reading ability (van Bergen et al. 2016) or reading-related skills (Puglisi et al. 2017). One study found associations between HLLE and child vocabulary after controlling for parental IQ/vocabulary, which the authors describe as a genetic variable; however, this study did not examine the relation between HLLE and child outcomes prior to controlling for parental IQ, making it difficult to determine the effect of the genetic confounding factor (Storch and Whitehurst 2001). As suggested by Hart et al. (2021), we have used a measure of parental reading ability (i.e., self-reported maternal reading ability) as a proxy for genetic transmission, and have found relations between HLLE and FA despite its inclusion, suggesting that HLLE relates to white matter organization independent of genetic influences.

Our results also speak to the association between SES and brain structure. Though consistently reported (Hanson et al. 2011; Jednorog et al. 2012; Luby et al. 2013; McDermott et al. 2019; Noble et al. 2015, 2012), including for white matter organization (Gullick et al. 2016; Ozernov-Palchik et al. 2018; Vanderauwera et al. 2019), the mechanism through which SES would influence brain structure is rarely examined empirically (for a discussion, please see (Farah 2017)). One exception is a report by Merz et al. (2020), which showed that linguistic input (measured as a composite of adult words and conversational turns) mediated the relation between parental education and left perisylvian surface area (Merz et al. 2020). In contrast, our results did not support an indirect pathway in which SES relates to white matter organization in left AF via HLLE. Possible explanations for these contrasting findings include differences in age, such that SES affects brain structure and function through different pathways at different developmental stages, as well as differences in brain measures examined (i.e., FA versus surface area). Ultimately, future studies will be needed to further clarify SES–brain relations.

The present findings also could have important implications for interventions, because compared with SES, HLLE is a modifiable environmental factor for which interventions can be designed to optimize language and literacy development (Powers et al. 2016). “Reach Out and Read” is one

such intervention, which distributes literacy materials to low-SES families in primary care medical clinics, and has demonstrated efficacy in improving language and pre-literacy skills in children (Zuckerman 2009). Concordantly, pediatricians and other child-facing clinicians may be aptly situated to educate families on HLLE, while the child is in their first year of life. Importantly, children with a familial risk for developing literacy or language difficulties may be especially vulnerable to the effects of rearing in low-SES backgrounds and/or with lower quality HLLE, since they would be incurring both genetic and environmental adversity (for discussions of gene–environment interactions related to reading and reading difficulty, please see Hart et al. (2021) and van Bergen et al. (2014)).

Limitations

This study had several limitations. The first limitation has to do with our approach to controlling for genetic confounding, which was limited to self-reported maternal reading ability, rather than the reading abilities of both parents. Because children share 50% of genes with one parent, our approach only partially controlled for genetic confounding. Moreover, the Adult Reading History Questionnaire used here is not a direct measure of reading ability, but a reliable correlate (Lefly and Pennington 2000), and as with reading ability, is itself a proxy, rather than direct measure, of genetic transmission (Hart et al. 2021; van Bergen et al. 2016).

Second, our analyses focused on maternal, rather than paternal or parental, education and reading ability. One reason for this was that previous studies of brain development that examined both maternal and paternal variables found brain–behavior relations only for maternal education (Ozernov-Palchik et al. 2018) and maternal history of reading difficulty (Black et al. 2012). Another reason is that fewer paternal, compared with maternal, datasets were collected, as mothers accompanied their children more frequently to behavioral and MRI sessions; follow-up correspondences with families yielded few additional paternal datasets.

Third, we did not examine individual components of HLLE. While previous work has generally shown weaker associations between individual HLLE components and language outcomes than between composite HLLE measures and language outcomes (Burgess et al. 2002), additional other work has suggested that individual HLLE components may relate differently to outcomes (Muhinyi and Rowe 2019; Storch and Whitehurst 2001). Similarly, although the StimQ only asks caregivers about activities related to literacy, but not language, when considering that parent–child shared reading during infancy includes rich vocabulary, complex sentences, and other linguistic elements (Scheele et al. 2010), it becomes clear that the assessment measures the

combined language and literacy environment. Thus, parsing these domains was another limitation.

Fourth, the infants in this study comprise a relatively homogeneous sample in terms of SES, spoken language and dialect, and nuclear family structure, and it is not clear whether the associations we observed between HLLE and left AF white matter organization would persist in other populations. For instance, families in the present study were high SES and some have suggested that brain–behavior relations may depend on the degree of socioeconomic insufficiency (Brito and Noble 2014; Turesky et al. 2021a). While previous findings of HLLE–outcome relations in children from low-income families (Payne et al. 1994) suggest that HLLE–brain relations would indeed persist, empirical testing would be needed to confirm this. Similarly, parents were predominantly monolingual English-speaking and there is now mounting evidence and concern that many assessments validated for this population do not accurately measure language or reading-related abilities in bilingual and bidialectal populations (Odegard et al. 2022; Washington et al. 2018). Finally, our sample was limited to nuclear families in which infants were raised by two biological parents of opposite sex and it is not entirely clear whether our findings would generalize to families with non-biological or same-sex parents.

Fifth, the parameters used in the present study were selected to harmonize with infant datasets acquired previously by our group. While these sequences may have been optimized for the tools available at the time, they are considered suboptimal when compared with contemporary sequences for infants, which often rely on additional gradient and phase-encoding directions (Bastiani et al. 2019; Pietsch et al. 2019).

Sixth, our study relied on a relatively small sample size ($N=38$), which is problematic when considering that identifying reliable, replicable brain–behavior relationships with fMRI data can require sample sizes in the thousands (Marek et al. 2022) or within-subject approaches that maximize signal and minimize noise (Gratton et al. 2022). And although our study did not rely on fMRI data, it is thought that these experimental design standards persist when working with other brain measures (e.g., diffusion, as used in the present study; Gratton et al. 2022). Therefore, the brain–behavior relationships reported here should be viewed with caution.

Seventh, there are additional white matter tracts that have been shown to be associated with literacy development and HLLE in previous studies of older children, such as the inferior longitudinal fasciculus (ILF; e.g., Yeatman et al. 2012b). However, as this was the first examination of the relation between HLLE and white matter organization in infancy, analyses were restricted to tracts with consistently reported relations to HLLE in older children (Davison et al. 2022; Hutton et al. 2020; Romeo et al. 2018) and language and

literacy in infants (Langer et al. 2017; Zuk et al. 2021b). Overall, it might behoove future studies examining relations between HLLE and early white matter organization to examine individual HLLE components, a wider SES range, bilingual and bidialectal populations, larger sample sizes, additional tracts, and genetic, educational, and self-reported reading ability data from both parents to more accurately capture the genetic and environmental influences (Hart et al. 2021).

Conclusion

In conclusion, this study examines relationships among HLLE, SES, and white matter organization in infancy. Results show that HLLE is associated with maternal education and FA in the left AF. With these links to white matter organization, this study fills an important gap in behavioral literature linking HLLE and SES to neurocognitive outcomes and further evinces the importance of HLLE in child development.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00429-022-02560-4>.

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Data availability Due to Institutional Review Board regulations at Boston Children's Hospital at the time of consent, our data cannot presently be uploaded to a permanent third-party archive. However, data sharing can be initiated through a Data Usage Agreement upon request. Additionally, code used for analyzing the data may be found at <https://github.com/TeddyTuresky/diffusionHLLE2021>.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethics approval This study was approved by the Institutional Review Board of Boston Children's Hospital (IRB-P00023182).

Consent to participate and publish Informed written consent was provided by each participating infant's parent(s).

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