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# Fiber pathways supporting early literacy development in 5–8-year-old children

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ABSTRACT

The development of fluent reading is an extended process that requires the recruitment of a comprehensive system of perisylvian brain regions connected by an extensive network of fiber pathways. In the present cross-sectional study, we focused on fiber pathways—the arcuate fasciculus (AF), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), and vertical occipital fasciculus (VOF)—proposed to support early literacy in typical 5–8-year-old children. We related quantitative metrics of fiber pathway microstructure in these pathways to early literacy measures of phonological awareness and decoding. We found that diffusion properties of the AF, ILF, and VOF not only show age-related differences, but also are predictive of early literacy skills after controlling for the effects of age, general white matter development, sex, IQ, and phonological skill. Perhaps most novel, we provide evidence supporting the involvement of the recently re-identified VOF in early literacy, and further, we provide evidence that a bilateral network of fiber pathways supports early literacy development.

## 1. Introduction

The ability to read and write is a cultural invention that emerges from, and is intimately tied to, the human capacity for language (Dehaene, 2009; Dehaene, Cohen, Morais, & Kolinsky, 2015). Reading requires several brain regions specialized for processing visual, phonological and linguistic information, and effective communication between these regions is supported by various white matter pathways (Vandermosten et al., 2012; Wandell & Yeatman, 2013; Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012). It is only within the last decade that advances in neuroimaging techniques, such as diffusion tensor imaging (DTI), have enabled us to examine the microstructural properties of white matter pathways *in vivo* and examine the association between white matter microstructure, age, and behavior. Neuroimaging research has shown that learning to read results in functional changes in the cortical networks for vision and language (Dehaene et al., 2010). More recently, efforts have aimed to investigate the concomitant structural changes in microstructure of candidate fiber pathways supporting reading development. Despite these efforts, knowledge about which fiber pathways support early reading skills, particularly in elementary school-aged children, who have minimal experience reading, remains sparse.

The most prominent contemporary brain model supporting reading is a dual-route model analogous to that of the language and visual system (Dick & Tremblay, 2012; Ungerleider & Haxby, 1994; Vandermosten et al., 2012; see Fig. 1). The model proposes 1) a dorsal, indirect phonological route for mapping visual letter representations (i.e., graphemes) to speech sound representations (i.e., phonemes), and 2) an "expert" ventral, direct lexical route for linking printed words directly to meaning (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Dejerine & Thomas, 1891; Schurz et al., 2010; Wimmer et al., 2010). In novice readers, reliance on the indirect phonological route is considerable because they rely on grapheme-phoneme conversion and segmentation of phonological constituents of words to "sound out" most words they encounter. This ability to manipulate individual sounds in words is called phonemic awareness, and constitutes a sub-

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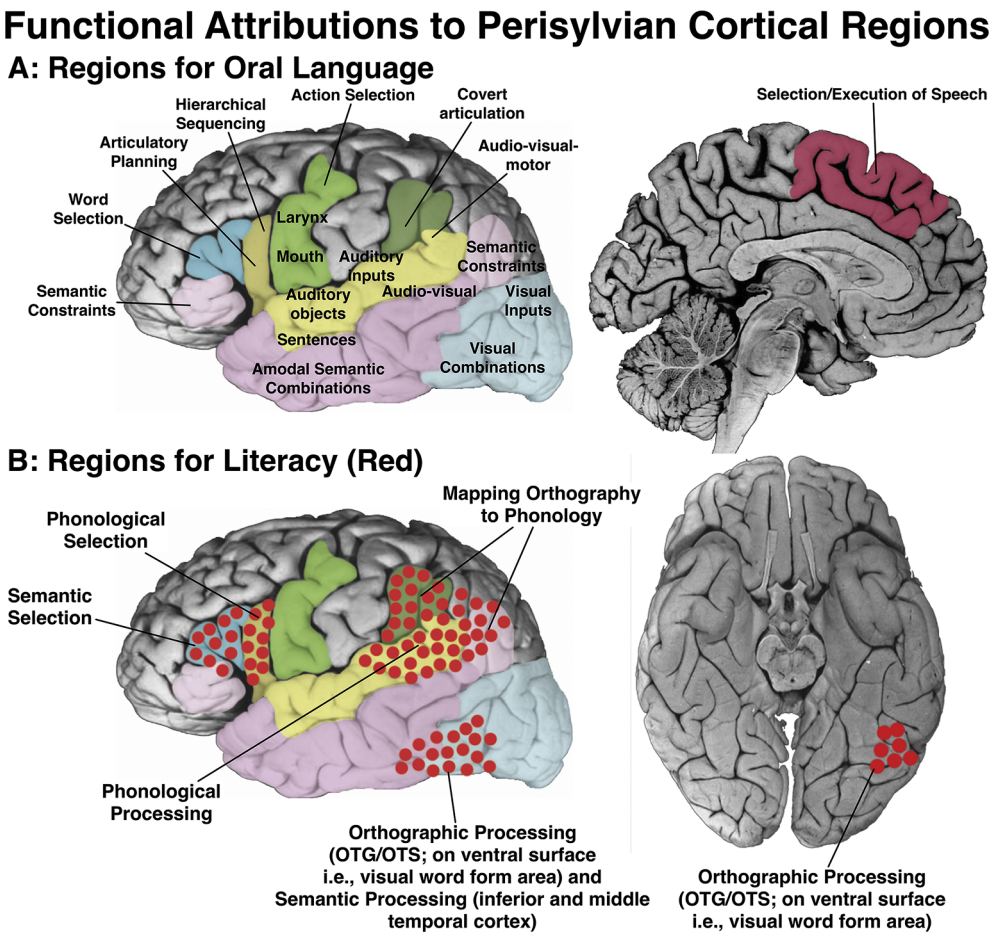


**Fig. 1.** Functional attributions to perisylvian cortical regions associated with speech, language, and literacy. Top: This figure is modified from Price (2010). The anatomy of language: A review of 100 fMRI studies published in 2009. *Annals of the New York Academy of Sciences, 1191,* 62–88. The figure shows a summary of broad functions attributed to perisylvian cortical regions associated with speech and language. Bottom: In red, we have highlighted the central nodes and associated functions of the reading network that overlap with speech and language, and the visual word form area of the ventral visual stream.

category of the broader ability, phonological awareness, which describes the general recognition that words are made up of individual sound units including phonemes and syllables (Anthony & Francis, 2005). Early phonological skills include judging whether two words rhyme or identifying syllables, and blending and segmenting words into their phonological constituents. It is these early reading skills that are linked to later reading development (Anthony, Williams, McDonald, & Francis, 2007; Bryant, MacLean, Bradley, & Crossland, 1990; Byrne & Fielding-Barnsley, 1993; Lonigan, 2015).

Various white matter pathways are proposed to support these dual routes of reading, including the arcuate fasciculus (AF), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), and recently re-identified vertical occipital fasciculus (VOF; Hoeft et al., 2011; Yeatman et al., 2012; Saygin et al., 2013; Myers et al., 2014). The AF is proposed to comprise the indirect route (Vandermosten et al., 2012; Wandell & Yeatman, 2013), the ILF and IFOF proposed to comprise the direct route (Vandermosten et al., 2012), and the VOF proposed to facilitate processing between the two routes (Wandell & Yeatman, 2013) (see Fig. 2).

The AF is a complex system of fronto-parieto-temporal connections. Diffusion-weighted investigations have revealed that the AF can be parsed into three separate segments (1) an anterior segment, connecting supramarginal gyrus to the inferior frontal gyrus, (2) a long segment, connecting posterior superior and middle temporal cortex to the inferior frontal gyrus and ventral premotor cortex, and (3) a posterior segment connecting posterior superior and middle temporal regions to the angular gyrus (Catani, Jones, & Ffytche, 2005). The anterior segment has been related to phonological awareness (Travis, Adams, Kovachy, Ben-Shachar, & Feldman, 2016), the long segment has been related to both phonological awareness and reading fluency (Gullick & Booth, 2015; Saygin et al., 2013; Yeatman et al., 2011, 2012), and the

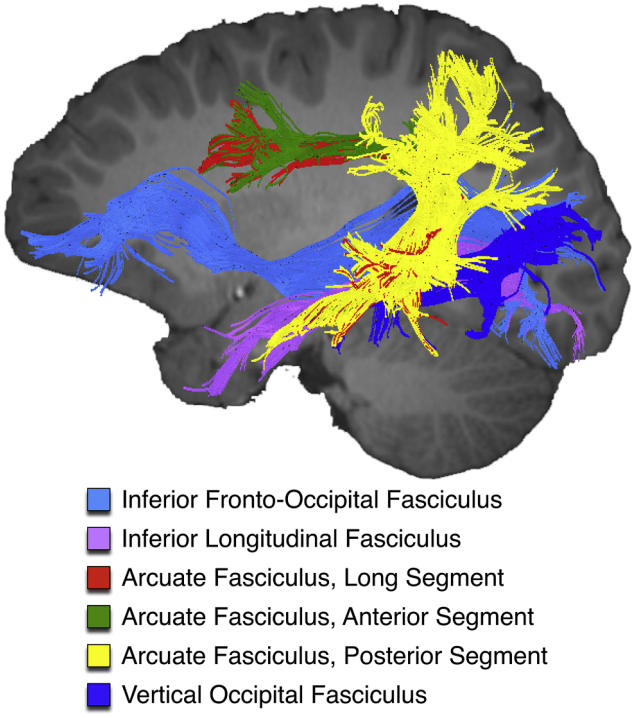


**Fig. 2.** Intrahemispheric fiber pathways supporting literacy. Temporo-parieto-frontal pathways of the arcuate fasciculus (AF), occipito-temporo-frontal pathways of the inferior fronto-occipital fasciculus (IFOF), occipito-temporal pathways of the inferior longitudinal fasciculus (ILF), and temporo-parieto-occipital fibers of the vertical occipital fasciculus (VOF) are proposed to support literacy in the developing and adult brain.

posterior segment has been related to whole-word reading (Gullick & Booth, 2015; Thiebaut de Schotten, Cohen, Amemiya, Braga, & Dehaene, 2014). The AF is also associated with phonological awareness skill in typical children and in children at risk for dyslexia (Christodoulou et al., 2016; Myers et al., 2014; Vanderauwera, Vandermosten, Dell'Acqua, Wouters, & Ghesquière, 2015; Yeatman et al., 2011, 2012).

Less is known about the relation between ILF and IFOF and beginning reading skills of phonological awareness and decoding. The ILF is a long association fiber pathway connecting occipital and posterior inferior temporal gyrus to anterior and medial temporal cortex (Catani, Jones, & Donato, 2003; Dick & Tremblay, 2012; Dick, Bernal, & Tremblay, 2014; Yeatman, Rauschecker, & Wandell, 2013), and based on its connectivity, is proposed to support mapping visual information about words to their lexical meaning (Yeatman et al., 2012; Yeatman, Rauschecker, et al., 2012; Wandell & Yeatman, 2013; Cummine et al., 2015; Qi, Han, Garel, Chen, & Gabrieli, 2015). While some studies suggest that the ILF plays a role in reading (Epelbaum et al., 2008; Steinbrink et al., 2008; Yeatman et al., 2012), others do not (Saygin et al., 2013; Thiebaut de Schotten et al., 2014). For example, organization of the ILF predicts word and decoding abilities in children 7–12 years old (Yeatman et al., 2012). However, these findings have not been reported in younger children (Christodoulou et al., 2016; Saygin et al., 2013; Vandermosten et al., 2015). The IFOF is located medial to the ILF and projects from inferior and medial occipital lobe and in some accounts the medial parietal lobe, to the inferior frontal gyrus, the medial and orbital frontal cortex, and the frontal pole through the external capsule (Catani & Thiebaut de Schotten, 2008; Dick & Tremblay, 2012; Dick et al., 2014). The IFOF has been associated with semantic processing during auditory language and orthographic processing in adults, and disruption to it by electrostimulation elicits semantic disturbances (Duffau et al., 2005; Mandonnet, Nouet, Gatignol, Capelle, & Duffau, 2007; Moritz-Gasser, Herbet, & Duffau, 2013). With respect to reading, Vandermosten et al. (2015) have found that microstructural properties of the bilateral IFOF are associated with phonological awareness in 5-year-old children, but others find no relationship, specifically as it relates to adults learning new words (López-Barroso et al., 2013) and illiterate adults learning to read (Thiebaut de Schotten et al., 2014).

Lastly, the VOF is known in the classical neurology literature (for a review see Yeatman et al., 2014) and has received renewed attention only recently in diffusion-weighted imaging studies of reading (Ben-Shachar, Dougherty, & Wandell, 2007; Takemura et al., 2015; Yeatman et al., 2014). The fibers of the VOF are located posterior to the AF and lateral to the ILF and the IFOF (Weiner, Yeatman, & Wandell, 2016; Yeatman et al., 2014). They project from the occipital temporal cortex and inferior temporal gyri to lateral occipital regions, particularly the transverse occipital sulcus, posterior intraparietal sulcus, middle occipital gyrus, lateral occipital sulcus, and in some cases to the angular gyrus (Takemura et al., 2015; Yeatman et al., 2013; Yeatman et al., 2014). Some suggest that the VOF may support word-reading abilities because of its putative connectivity with the angular gyrus (Yeatman et al., 2013) which is important for reading development (Houston et al., 2014). While the reading-related functions of this tract are supported by postmortem studies of patients with lesions (Greenblatt, 1973, 1976), which report that disruption of the fibers of the VOF by tumor or lesion is specifically associated with pure alexia, no diffusion-imaging studies have directly related the microstructure of the VOF to behavior. In addition, no studies have addressed whether this pathway shows age-related changes or reading-related changes in young children. Therefore, a principal motivation for the present study is to determine whether the VOF plays a role in early reading skills, particularly in young children with minimal exposure to reading.

In the present study, we thus examine associations between microstructural properties of white matter pathways and early reading skills (i.e., phonological awareness or decoding) that go beyond the effects of age, sex, and IQ. We focus on children 5–8-years-old with varying levels of reading experience. Furthermore, while the recently re-identified VOF has been proposed to support reading development based on its putative connectivity, the present study is the first, to our knowledge, to empirically test this hypothesis in children. In fact, the VOF has never been tracked at all in children, and thus this study represents the first attempt to do so.

## 2. Materials and methods

### 2.1. Participants

Twenty typically developing children (10 females, 10 males; age range = 5–8 years, M age = 6.9 years, SD = 1.1 years) comprised the final sample. All participants were screened by phone for contraindication to MRI, were right-handed according to the Edinburgh Handedness Inventory, bilingual English/Spanish speakers with normal hearing (self-reported), and had normal (or corrected to normal) vision, and were not seeking services for reading/language delay, or any other developmental disability or delay. An additional 3 children completed the diffusion-weighted scan but were not analyzed because of image artifacts indicated after the scan (one was due to an error of the technician; two were removed due to obvious motion artifact). An additional 11 children were consented but did not complete the diffusion-weighted scan because of their refusal to assent, or to significant movement during the T1-weighted structural scan before the diffusion-weighted scan was initiated. Thus, a total of 34 children were tested to arrive at the final usable sample. Written informed consent/assent was obtained from all parents and children. All participants provided informed consent and assent, and the Western Institutional Review Board and the Florida International University Institutional Review Board approved the study.

### 2.2. General procedure

Data were collected during two visits. The first included an MRI scan at Nicklaus Children's Hospital, Miami, FL. The second visit was scheduled within two weeks of the first visit and took place at Florida International University, Miami, FL during which we administered a battery of speech, language, and early literacy measures.

### 2.3. Battery of speech, language, and literacy measures

In a session lasting about 90 min, the following assessments were administered to obtain a comprehensive understanding of each child's speech and early literacy ability: (1) Speech was assessed using the articulation and phonology subtests of the Diagnostic Evaluation of Articulation and Phonology (DEAP; Dodd, Hua, Crosbie, Holm, & Ozanne, 2010) and (2) early literacy was assessed using Word Attack (Test 3), Sound Awareness (Test 7), and Sound Blending (Test 8) subtests of the Woodcock-Johnson III Diagnostic Reading Battery (W-JIII; Woodcock, Mather, & Schrank, 2004). Word Attack is a measure of decoding, or the ability to read nonsense words, which requires application of the knowledge of letter-sound relations. The Sound Awareness and Sound Blending components combined provide a measure of phonological awareness (i.e., the understanding of the phonological or sound structure of words). We also measured non-verbal intelligence using the Block Design subtest of the Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI – III; Wechsler, 2002) and Receptive Language (Concepts and Following Directions, Word Classes, and Sentence Structure) and Language Content Indices (Concepts and Following Directions, Word Classes, and Expressive Vocabulary) using the Clinical Evaluation of Language Fundamentals-4 (CELF-4; Semel, Wiig, & Secord, 2003). In this analysis, we focus on literacy (W-JIII and a related measure of DEAP phonology), and included the non-verbal intelligence measure as a covariate. Standardized scores were used in

the analysis for all subtests.

### 2.4. Data acquisition

Participants were scanned on a 3 Tesla Philips MRI scanner with a SENSE coil housed at Nicklaus Children's Hospital. Prior to the actual scanning session, participants underwent a simulated scan in a mock scanner to familiarize them to the MRI scanner environment. In addition, vitamin E capsules were placed on participants' fronto-temporal left forehead to verify orientation of images during post-processing. Diffusion-weighted images were collected to measure age-related differences in white matter microstructure and relate the white matter microstructure with measures of early literacy (behavioral testing) in individual children (age 5–8 years old). Images were acquired using single-shot spin-echo echo-planar imaging sequence (15 gradient directions, $b$ value = 900 s/mm$^2$ and $b$ = 0 s/mm$^2$ (single reference scan), matrix size = 112 × 112, time echo [TE] = 60, time repetition [TR] = 6157, NEX = 3, FOV = 240 × 240 mm$^2$, slice thickness = 2 mm, number of axial slices = 55 (no gap), and voxel size = 0.938 mm × 0.938 mm × 2 mm). We also collected a whole brain T1 anatomical image for each participant using an 8-min sagittal 3-D spoiled gradient recall (SPGR) sequence (120 axial slices, voxel size = 1.5 × 0.938 × 0.938 mm resolution). To minimize head motion, we placed cushions around the participants' head and secured a strap across their forehead. The duration of scanning time was less than 25 min per participant.

### 2.5. Diffusion tensor imaging post-processing

We used FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/), DSI Studio (http://dsi-studio.labsolver.org/) and Matlab (http://www.mathworks.com) software packages for all analyses. Diffusion-weighted images were visually inspected for artifacts, including "striping" and susceptibility artifact (as noted, three children were removed at this stage). Images were denoised using the Non-Local Means Filter adapted to Rician noise distribution (NLMr; Coupe, Manjón, Robles, & Collins, 2012; Descoteaux, Wiest-Daesslé, Prima, Barillot, & Deriche, 2008). Data were also preprocessed for eddy currents and subject motion, using affine registration to a single non-weighted diffusion reference image ($b$ = 0). Using DSI Studio, we determined the tensors in each voxel using an over-determined linear equation system with least squares fitting (Jiang, van Zijl, Kim, Pearlson, & Mori, 2006). The gradient table, which is necessary to extract the diffusion tensor, was computed using an open source PARtoNRRD toolbox in Matlab (Farrell et al., 2007). The diffusion tensor was used to calculate the eigenvalues reflecting diffusion parallel and perpendicular to each of the fibers along 3 axes (x, y, z). The resulting eigenvalues were then used to compute indices of fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD; Basser, Mattiello, & LeBihan, 1994; Hasan & Narayana, 2006). FA is an index for the amount of diffusion asymmetry within a voxel, normalized to take values from zero (isotropic diffusion) to one (anisotropic diffusion). FA is sensitive to microstructural changes in white matter, with higher FA values indicating more directional diffusion of water. This value can be decomposed into AD, measuring the parallel eigenvalue ($\lambda_1$), and RD, measuring the average of the secondary and tertiary perpendicular eigenvalues ($[\lambda_2 + \lambda_3]/2$). AD and RD quantifications are sensitive to axon integrity and myelin integrity, respectively (Winston, 2012). In addition to FA associations, we evaluated RD and AD associations which facilitate interpretation of the underlying biological basis (e.g., axonal or myelin) influencing behavior.

#### 2.5.1. Fiber tract identification

All fiber tracking identification procedures were based on anatomical landmarks and defined on the FA map in DSI Studio, with a FA threshold of 0.20 and fiber angles of less than 45° between connecting pixels (Catani & de Schotten, 2012). As recommended by Côté et al. (2013) deterministic fiber tracking was used to track the fiber pathways. In order to maintain the anatomical integrity of the child brain, fiber tracking was conducted in the native MRI space. The following tracts were reconstructed: the three segments of the arcuate fasciculus (AF), the inferior longitudinal fasciculus (ILF), the inferior fronto-occipital fasciculus (IFOF), and the vertical occipital fasciculus (VOF).

*2.5.1.1. Arcuate fasciculus (AF).* The AF was defined as the green bundle of fibers running in the anterior-posterior direction located above the body of the corpus callosum and the posterior temporal stem, medial to the corona radiata, posterior to the precentral sulcus and anterior to the intraparietal sulcus (Catani & Thiebaut de Schotten, 2008; Catani et al., 2005). We segmented the AF into three segments, namely the long (fronto-temporal), anterior (fronto-parietal) and posterior (temporo-parietal) segments. To track the long segment of the AF, we drew two ROIs on coronal slices, corresponding to the anterior and posterior boundaries, and a single ROI on an axial slice where the fronto-temporal connections project to temporal regions (Broce, Bernal, Altman, Tremblay, & Dick, 2015; Eluvathingal, Hasan, Kramer, Fletcher, & Ewing-Cobbs, 2007). Identical ROIs were used to track the anterior segment, with the exception that the axial ROI was loaded as a region of avoidance (ROA). To track the posterior segment, we used a five ROI approach identified on axial slices (Thiebaut de Schotten et al., 2014).

*2.5.1.2. Inferior longitudinal fasciculus (ILF).* Tract segmentation of the ILF was implemented using a two-ROI approach (Catani et al., 2003). First we drew a temporal ROI on five axial slices posterior to the anterior portion of the external capsule. Second, we drew an occipital ROI on approximately 12–15 axial slices, with the parieto-occipital fissure serving as the superior border and the posterior end of the cingulum serving as the anterior border.

*2.5.1.3. Inferior fronto-occipital fasciculus (IFOF).* Tract segmentation of the IFOF was implemented using a two-ROI approach (Forkel et al., 2014). We drew an occipital ROI on the white matter of the occipital lobe, posterior to the parieto-occipital sulcus and the temporooccipital notch, and a ventral ROI on the white matter of the external/extreme capsule.

*2.5.1.4. Vertical occipital fasciculus (VOF).* The VOF was identified on the color map on approximately 4 sagittal slices as running superior–inferior, posterior to the AF and lateral to the ILF and IFOF (Pajevic & Pierpaoli, 1999; Takemura et al., 2015; Yeatman et al., 2013; see Supplemental Fig. 1). The ventral part of the VOF is proposed to include the fusiform, inferior occipital, or inferior temporal gyri. The dorsal part is proposed to include lateral occipital gyri and sulci and, in some accounts, angular gyrus. Investigating the fiber pathways associated with early literacy is the focus of the study. Thus, in this analysis we focused on projections from temporal (fusiform gyrus, lateral occipitotemporal sulcus, inferior temporal gyrus) to dorsal regions. To do this, we imported fusiform, lateral occipitotemporal sulcus, and inferior temporal ROIs provided by FreeSurfer's Desikan-Killiany parcellation available in DSI Studio (Desikan et al., 2006). These gray-matter ROIs were mapped to the participant's native space using nonlinear registration between the anisotropy map and the atlas, also included in the DSI Studio package. This mapping was verified visually with reference to a published atlas (Duvernoy, 1999). Fibers that projected to adjacent regions, including the inferior occipital gyrus, were excluded from the analysis. Thus, it would be more accurate to state that we tracked the subset of fibers of the VOF that emanate from the fusiform gyrus, lateral occipitotemporal sulcus, and inferior temporal gyrus, and connect to middle and superior occipital gyri and

sulci, posterior inferior parietal (angular gyrus), and superior parietal regions (although these parietal projections were not found in all subjects).

### 2.6. Data analysis

Within the R statistical package (v. 3.2.4; http://www.R-project.org) we related our measures of white matter microstructure and laterality to age and to behavioral measures using robust estimates of correlation ($r_{rob}$; using the R function relplot; Wilcox, 2005) and robust regression (R function *rlm*; Wright & London, 2009). The American Psychological Association (APA; Wilkinson, 1999) recommends these procedures over traditional least-squares methods, which are heavily influenced by outlying values (Wilcox, 1998).

The robust correlation $r_{rob}$ is similar to the Pearson *r*, but is less influenced by outlying values, a property that is desirable when dealing with smaller samples. Rather than removing outliers, the statistical procedure reduces their influence, and also produces a robust elliptical plot indicating outliers by placing them outside the outer ellipse of the plot (Goldberg & Iglewicz, 1992). The $r_{rob}$ can be interpreted the same as the Pearson *r*. The robust regression also reduces the influence of outliers, in this case using a Huber loss function to apply different weights to each observation. The regression results can be interpreted in the same way as in least square regression. In fact, in cases where there are no outliers, robust methods will give identical results to least squares methods. We also improved the estimation of the reliability of the parameter estimate by using the bootstrap method (Efron, 1981, 1987) to calculate the standard errors and 95% confidence intervals. Laterality was assessed using the formula (left − right)/(left + right) for FA (Thiebaut de Schotten et al., 2011). Thus, positive values indicate left laterality.

## 3. Results

### 3.1. Identification of the fiber tracts

We were able to reliably track the bilateral ILF and right VOF in all children, the bilateral anterior, long, and posterior AF segments, the left and right IFOF in 18 children, and the left VOF in 17 children. FA for these tracts fell within the normal range for children in this age range (Krogsrud et al., 2016; Morriss, Zimmerman, Bilaniuk, Hunter, & Haselgrove, 1999; Vandermosten et al., 2015), which serves as a validation of our tractography approach with respect to the available literature.

### 3.2. Age-related differences, sex differences and laterality in the perisylvian white matter

To characterize age-related differences in white matter microstructure of the AF, ILF, IFOF, and VOF, we first conducted robust correlations. We found significant positive correlations with age and FA in the AF long segment and right VOF (Table 1). In follow-up analyses evaluating RD or AD in these two tracts, we found a significant negative RD correlation between age and the VOF ($r_{rob} = -0.52$; $p < .05$). Neither AD or RD was significantly related to the AF long segment, suggesting that the diffusion signal was largely driven by directional anisotropy. We further investigated the association between age and laterality across all four tracts. We found a significant positive correlation between age and laterality of the ILF, suggesting greater left lateralization with age. The opposite pattern was revealed for the VOF, suggesting greater right lateralization with age. For the AF long segment, increasing left lateralization with age was found only for the AD measure (see Fig. 3).

We then assessed whether the observed associations between FA, laterality, and age were confounded by various nuisance variables, including sex, whole brain white matter microstructural properties

**Table 1**
Summary of white matter microstructure measures and correlation with age in months for each tract.

| Measures | Hemisphere | ILF | IFOF | AF: Anterior Segment | AF: Long Segment | AF: Posterior Segment | VOF |
|---|---|---|---|---|---|---|---|
| FA | Left | 0.50 (0.03) [0.08] | 0.51 (0.02) [0.37] | 0.46 (0.02) [0.31] | 0.48 (0.03) [0.50]* | 0.47 (0.02) [−0.25] | 0.41 (0.03) [0.1] |
| | Right | 0.49 (0.03) [−0.53] | 0.50 (0.03) [0.20] | 0.46 (0.02) [0.22] | 0.46 (0.03) [−0.04] | 0.45 (0.02) [0.17] | 0.41 (0.05) [0.46]* |
| | Laterality | 0.005 (0.03) [0.49]* | 0.01 (0.02) [0.22] | 0.00 (0.02) [0.16] | 0.02 (0.40) [0.44] | 0.02 (0.03)* [−0.32] | 0.00 (0.07) [−0.45]* |
| AD ($\lambda_1$), $10^{-3}$mm$^2$/s | Left | 1.4 (0.005) [−0.02] | 1.4 (0.04) [0.04] | 1.2 (0.03) [−0.14] | 1.3 (0.04) [−0.08] | 1.3 (0.03) [−0.62]* | 1.2 (0.04) [−0.11] |
| | Right | 1.4 (0.007) [−0.56]** | 1.4 (0.05) [−0.06] | 1.2 (0.03) [−0.02] | 1.3 (0.05) [−0.36] | 1.3 (0.03) [−0.25] | 1.2 (0.05) [0.29] |
| | Laterality | 0.00 (0.02) [0.65]** | 0.00 (0.01) [0.35] | 0.00 (0.01) [0.01] | 0.01 (0.02) [0.49]* | 0.01 (0.01)** [−0.28] | 0.01 (0.03) [−0.22] |
| RD ($\lambda_2 + \lambda_3$)/2, $10^{-3}$mm$^2$/s | Left | 0.60 (0.04) [−0.05] | 0.6 (0.03) [−0.21] | 0.61 (0.03) [−0.36] | 0.59 (0.03) [−0.44] | 0.60 (0.03) [−0.02] | 0.63 (0.03) [−0.21] |
| | Right | 0.61 (0.04) [0.3] | 0.6 (0.03) [−0.29] | 0.60 (0.03) [−0.29] | 0.59 (0.03) [−0.23] | 0.60 (0.03) [−0.21] | 0.63 (0.05) [−0.52]* |
| | Laterality | −0.01 (0.01) [−0.22] | 0.01 (0.01)* [0.01] | 0.01 (0.03) [−0.14] | 0.01 (0.02) [−0.33] | 0.01 (0.02) [0.25] | 0.01 (0.03) [0.57]** |

*Note.* Means, standard deviations (in parentheses), and correlations with age in months (in brackets) are presented for each measure. FA = Fractional Anisotropy. AD = Axial Diffusivity. RD = Radial Diffusivity. Laterality is calculated as (Left − Right)/(Left + Right). Corrected and uncorrected significance tests are reported for laterality and age. * $p < .05$; ** $p < .01$ (False Discovery Rate [FDR] Corrected).

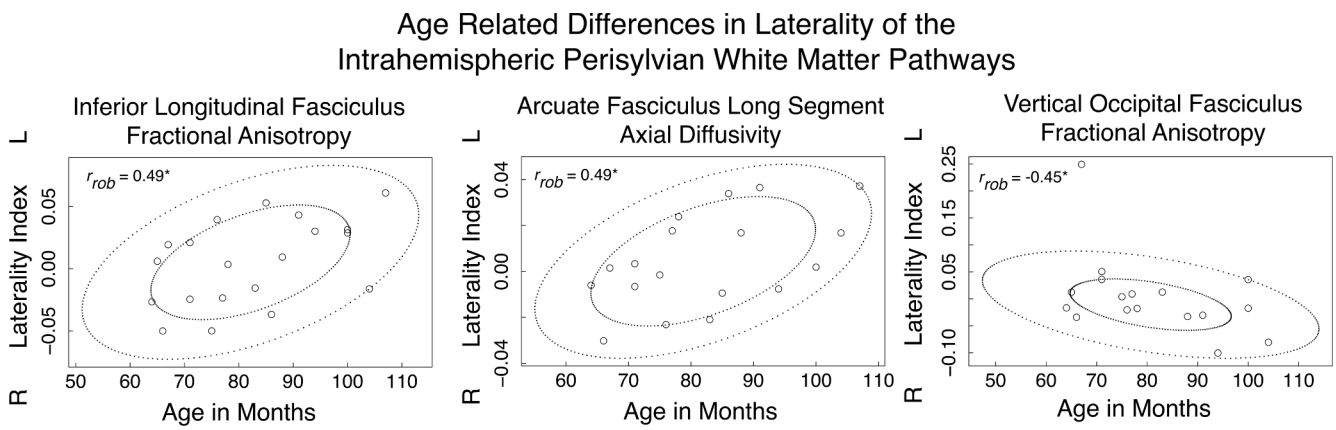


**Fig. 3.** Age-related differences in laterality of the intrahemispheric perisylvian white matter pathways. The graphs show robust elliptical plots of the relation between age and laterality of the inferior longitudinal fasciculus (ILF), arcuate fasciculus (AF) long segment, and vertical occipital fasciculus. Robust correlation measures ($r_{rob}$) are provided in each graph. * $p < .05$. ** $p < .01$.

(calculated for each parameter of interest), non-verbal ability (as measured by block design). Results from the robust linear regressions revealed that all except one of the age effects survived after controlling for the nuisance variables. The association between age and the right VOF FA was no longer significant.

### 3.3. Relation of perisylvian white matter pathways to early literacy measures

To relate the white matter microstructure of the examined perisylvian fiber pathways to early literacy, we constructed robust linear models for FA, RD, AD, and laterality white matter indices. Our early literacy measures included phonological awareness and decoding. Table 2 reports the effect of white matter microstructure on early literacy skill, after controlling for age in months, non-verbal ability (as measured by block design), sex, whole brain white matter microstructural properties (calculated for FA, AD, and RD for each respective regressor of interest), and phonemic ability (as measured by the DEAP phonology subtest). We controlled for phonemic ability, defined as children's ability to manipulate individual sounds of spoken words, because doing so allowed us to better assess children's ability to manipulate larger components of spoken language (i.e., words, syllables), which are associated with early literacy (Fowler, Brady, & Shankweiler, 1991; Webster & Plante, 1995; Webster, Plante, & Couvillion, 1997). For these analyses, we report results in which the 95% CI did not cover zero.

As Table 2 and Fig. 4 show, differences in ILF, VOF, and AF white matter microstructure were related to early literacy skill. The left ILF FA positively predicted phonological awareness. Children with better phonological awareness skills had lower RD and greater AD. Also, children with greater leftward asymmetry of the ILF had better early literacy skills. In contrast to the ILF, the left and right VOF FA negatively predicted phonological awareness. More specifically, children with greater phonological awareness skill had lower AD in the left VOF. Neither AD or RD in the right VOF significantly predicted phonological awareness. Further, we show bilateral involvement of the AF associated with early literacy. The left AF long and posterior segments predicted decoding and phonological awareness, respectively, and the right AF anterior and posterior segments predicted phonological awareness. These associations were negative, such that children with better early

**Table 2**
Relation of early literacy skills to diffusion indices of the perisylvian fiber pathways.

| Predictor → Outcome | B (SE) | ß | 95% CI |
|---|---|---|---|
| *Fractional Anisotropy (FA)* | | | |
| Left ILF → Phonological Awareness | 10.0 (4.9) | 0.35 | 0.6–19.7 |
| Left VOF → Phonological Awareness | −16.0 (5.2) | −0.47 | −26.0 to −5.6 |
| Right VOF → Phonological Awareness | −10.0 (3.7) | −0.53 | −17.3 to −2.9 |
| *Axial Diffusivity (AD)* | | | |
| Left ILF → Phonological Awareness | 9.0 (2.9) | 0.46 | 3.1–14.7 |
| Left VOF → Phonological Awareness | −18.3 (4.01) | −0.64 | −26.1 to −10.4 |
| Left AF Long Segment → Decoding | −67.8 (30.7) | −0.25 | −127.2 to −70.1 |
| Left AF Posterior Segment → Phonological Awareness | −24.6 (6.7) | −0.69 | −37.6 to −11.1 |
| Right AF Anterior Segment → Phonological Awareness | −17.4 (7.2) | −0.49 | −31.2 to −3.0 |
| Right AF Posterior Segment → Phonological Awareness | −14.3 (6.1) | −0.44 | −26.1 to −19.6 |
| Laterality ILF → Decoding | 143.6 (63.3) | 0.36 | 20.46–268.6 |
| *Radial Diffusivity (RD)* | | | |
| Left ILF → Phonological Awareness | −8.8 (4.0) | −0.35 | −16.5 to −1.0 |
| Right IFOF → Decoding | −122.5 (54.8) | −0.34 | −227.9 to −13.2 |

*Note.* Effects reported for robust linear models after controlling for age in months, sex, DEAP phonology, whole brain microstructure quantities (FA, AD, RD, for each respective regression), and block design. Only results in which the 95% confidence interval did not cover zero are reported. ILF = Inferior Longitudinal Fasciculus. IFOF = Inferior Fronto-Occipital Fasciculus. VOF = Vertical Occipital Fasciculus. AF = Arcuate Fasciculus. DEAP = Diagnostic Evaluation of Articulation and Phonology. To reduce digits, AD, and RD values were divided by a constant (1000).

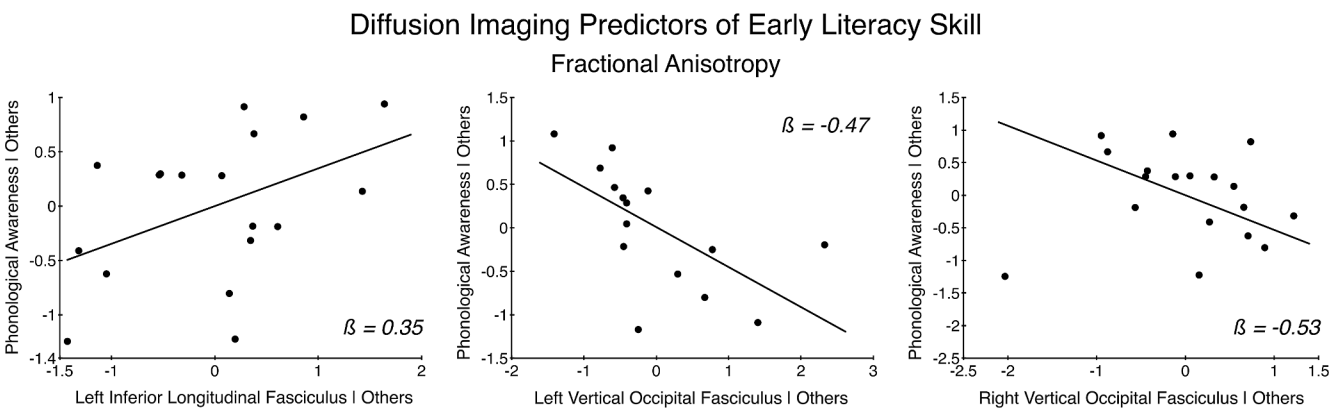


**Fig. 4.** Diffusion imaging measures associated with phonological awareness and decoding. The results of robust regressions from Table 2, predicting Woodcock-Johnson Phonological Awareness and Decoding, are graphically shown here. These graphs depict partial regressions controlling for variables of age, sex, whole brain diffusion measures, block design, and Diagnostic Evaluation of Articulation and Phonology (DEAP) phonology subtest scores. Only findings in which the 95% confidence interval (CI) did not cover zero are reported.

literacy scores had lower AD values.

## 4. Discussion

The present study reports several novel findings that contribute to the growing understanding of the white matter connections supporting early literacy in young typically developing children, 5–8-years-old. Broadly, we found that microstructural properties (as measured by diffusion imaging) of the AF, ILF, and VOF not only show age-related differences, but also are predictive of early reading skills (i.e., phonological awareness or decoding). Further, these effects are evident after controlling for the effects of general white matter development, age, sex, IQ, and phonological skill. Perhaps most novel, we provide evidence supporting the involvement of the recently re-identified VOF in early literacy, and further, suggest that a bilateral network of fiber pathways supports early literacy development. In the following sections, we summarize these findings for each track—the AF, ILF, IFOF, and VOF—and relate them to the broader literature.

### *4.1. Vertical occipital fasciculus (VOF)*

For the first time in children, we report the identification of the VOF using diffusion-weighted imaging and relate diffusion metrics to behavioral measures of literacy. It is thus important to emphasize that, even in young children, it is possible to identify this pathway. In all children, we were able to track the right VOF, and in 17 out of 20 children we tracked the left VOF. Even in children, this pathway is dissociable from the posterior AF (here using our deterministic method, and using probabilistic methods; Weiner et al., 2016). The majority of VOF fibers project from the lateral occipitotemporal regions (including VWFA) to the lateral superior and middle occipital extrastriate regions, and to the angular gyrus (Yeatman et al., 2013). The functional role of the VOF is still being investigated, but in addition to its connectivity, which by itself suggests an important role for reading development (Yeatman et al., 2014), tumors or lesions disrupting the fibers of the VOF are specifically associated with pure alexia (Greenblatt, 1973, 1976). Our study is the first, to our knowledge, to establish an association between this particular fiber pathway and early literacy skill in developing readers, although the possibility of this was suspected a decade ago (Ben-Shachar et al., 2007). The data suggest that diffusion correlates of white matter microstructure of the VOF become less associated with phonological awareness as this literacy skill improves.

It is notable that the association between phonological awareness and the VOF was significant for both the left and the right VOF. The right hemisphere's contribution to reading has been investigated in a number of studies (Horowitz-Kraus, Wang, Plante, & Holland, 2014; Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003; Yamada et al., 2011). However, most available evidence suggests progressive disengagement of the right hemisphere as literacy development proceeds. For example, Turkeltaub et al. (2003) used fMRI to show that, in children aged 6–22 years, learning to read was associated with increased left hemisphere middle temporal and inferior frontal activity accompanied by progressive decrease in activity of the right inferior temporal cortex. Additional compelling data were presented by Yamada et al. (2011). In that study of 5-year-old beginning readers, children who were on track in acquiring early literacy skills showed left lateralized activation in a letter-reading task, whereas children who were at-risk for reading delay (based on behavioral measures) showed bilateral activation during the task. Our data suggest some involvement of the right hemisphere in early literacy skills that may shift to left lateralization with age. However, this is just suggestive evidence, and a larger study with a longitudinal design would be necessary to establish this claim.

### *4.2. Inferior longitudinal fasciculus (ILF) and Inferior Fronto-Occipital fasciculus (IFOF)*

We found that diffusion measures of ILF microstructure were correlated with phonological awareness. The direction and significance of the effects—i.e., increasing FA and AD, and decreasing RD are associated with better performance on the measures of phonological awareness—is broadly consistent with some prior work in older children. For example, in a longitudinal DWI study of 55 7–12-year-old children Yeatman et al. (2012) showed that the rate of change in FA in the left ILF was predictive of total reading scores. In another study, rate of FA change of the left ILF was also found to correlate with silent word reading efficiency in 5–12-year-old pre-readers assessed longitudinally (Wang et al., 2016). It does not replicate, however, the null finding reported by Saygin et al. (2013), who tested for, but did not find, a relation between ILF microstructure and phonological awareness in young children (pre-K and kindergarten aged children 4–5-years). Notably though, in conducting simple correlations between diffusion measures and the outcome measure, their analysis did not control for potential nuisance variables (e.g., age, sex, non-verbal ability and whole brain white matter values) that might hide or diminish the effects of interest. Furthermore, and potentially more importantly, in contrast to the children in our study, all of the children in that study were pre-readers. The ILF may become more important to literacy acquisition as the child acquires greater skill in reading.

Greater ILF involvement in reading as a function of reading experience is supported by models of reading development that emphasize the importance of the left ventral occipitotemporal regions

involved in phonological decoding of familiar and unfamiliar letter strings (Richlan, 2012). Our findings are consistent with suggestions that as children acquire better phonological awareness and decoding skills, there is less reliance on the indirect phonological route (i.e., dorsal route) connectivity between temporal-parietal-inferior frontal regions via the AF, less reliance on direct connections between the ventral occipital-temporal lobe and angular gyrus via the VOF, and less reliance on the homologous tracts of the right hemisphere. As such, there is a shift to more reliance for these skills on the direct lexical-route (i.e., ventral route) involved in supporting the orthographic lexicon and fast, automatic word recognition. This is consistent with the idea that there is a bidirectional relation between the acquisition of literacy and reading-related phonological processing skills such as phonological awareness (Suortti & Lipponen, 2016). Thus, as children gain more exposure to text, they rely less on non-lexical form recognition systems to process words (Lonigan et al., 2009; Turkeltaub et al., 2003). It is also consistent with the Interactive Account of reading, proposed by Price, Devlin and colleagues (Devlin, Jamison, Gonnerman, & Matthews, 2006; Price & Devlin, 2011; Price & Mechelli, 2005), in which, as children (and adults) learn to read, orthographic inputs come to more strongly trigger appropriate representations in phonological and semantic areas of the temporal lobes.

It is thus reasonable to expect that efficiency in lexical access and semantic processing would rely on fibers of the ILF, which by virtue of its putative connectivity links the VWFA with the rest of the temporal lobe, including the temporal pole, a proposed "semantic hub" (Binney, Embleton, Jefferies, Parker, & Ralph, 2010; Holland & Lambon Ralph, 2010), and the posterior middle temporal gyrus, a proposed site for long term storage of semantic and lexical information (Binder et al., 2003; Binder, Desai, Graves, & Conant, 2009; Price, 2010). Indeed, if the VWFA is an interface between visual representation and their phonological and semantic attributes, as Price, Devlin, and their colleagues have suggested (Devlin et al., 2006; Price & Devlin, 2011; Price & Mechelli, 2005), then the connectivity with other regions of the temporal lobe would be critical for mature reading. There is some direct suggestion that this is the case. For example, Gil-Robles et al. (2013) showed that electrostimulation of the ILF during awake surgery elicits reading disturbances, suggesting an important role played by this pathway in reading. Our results support this notion that the fiber pathways of the ventral temporal cortex, especially the ILF, are associated with early literacy skills (Vandermosten et al., 2015; Wang et al., 2016; Yeatman et al., 2013).

In addition to the ILF, other authors have found that microstructure of the IFOF is also associated with phonological awareness. For example, Vandermosten et al. (2015) found that, in pre-reading children, both left and right IFOF microstructure is associated with phonological awareness. We found this effect for the right IFOF (AD negatively predicted decoding), but our strongest findings were found for the ILF. Again, as with the study by Saygin and colleagues, the study by Vandermosten and colleagues exclusively assessed pre-readers. The results of our study, and of those we have reviewed above, suggest that the ventral pathways of the temporal lobe (namely ILF and IFOF) also participate in phonological aspects of reading (Brem et al., 2010; Yamada, 2009; also see Raschle, Zuk, & Gaab, 2012; Richlan, 2012 for relevant functional imaging findings).

### 4.3. Arcuate fasciculus (AF)

We also found a relation between microstructure of the AF and our early literacy outcomes. Specifically, the left AF long segment was associated with decoding, and the left AF posterior segment, and right AF anterior and posterior segments, were associated with phonological awareness. However, the association we found between these AF segments and literacy measures were negative. Although this is the opposite of what has been reported in a number of studies, not all studies show a positive association between the AF and phonological awareness/decoding. For example, in children 7–11-years, Yeatman et al. (2011) found a negative relation between phonological awareness and microstructure of the AF pathway. In a follow-up longitudinal study, Yeatman et al. (2012) showed that, for the AF, younger children who are good readers have FA that declines over time, and those who are poor readers have FA that increases over time. Thus, early on, lower FA of the AF is associated with better reading ability. More recently, Christodoulou et al. (2016) found the same negative association between AD and pseudoword reading in typical children. As in our study, this latter finding was specific to the AD measure (i.e., like Christodoulou et al., we found no significant association for the FA measure). This was interpreted by Christodoulou and colleagues as a pattern that changes as children learn to become expert readers.

### 4.4. Limitations

Despite the compelling findings of the present study, there are a few limitations that must be considered. The first is the sample size, which due to lower power might make it difficult to reveal associations with fiber pathways, such as the left IFOF, that have been found in previous studies. However, the fact that a number of statistical relations were revealed in the current sample, even after controlling for several potentially confounding variables, suggests that for large and consistent effects, the sample size is sufficient. A second limitation is the use of the DTI method, which makes it challenging to resolve crossing and/or kissing fibers in pathways that are dissociable, but overlapping. These crossing/kissing fibers can be resolved using more advanced diffusion-weighted imaging methods (for example, high angular resolution imaging (HARDI) or diffusion-spectrum imaging (DSI); Daducci et al., 2014; Descoteaux, Angelino, Fitzgibbons, & Deriche, 2006; Wedeen, Hagmann, Tseng, Reese, & Weisskoff, 2005), and with methodological advances these scans can be acquired with short scan times appropriate for children. Moreover, the physical and biological basis of parameters obtained from diffusion MRI are difficult to interpret. Diffusion indices are influenced by many microstructural components, including the cytoskeleton (neurofilaments and microtubules), axonal membranes, and the myelin sheath (Winston, 2012). However, there is not a one-to-one correspondence between these features and diffusion methods (Jones, Christiansen, Chapman, & Aggleton, 2013). Our results should be interpreted with these caveats in mind.

## 5. Conclusion

Examination of the development of fiber pathways supporting early literacy allows researchers to understand how a system for implementing literacy evolves from first exposure to written language as children enter formal schooling to emerging expertise over the early school years. Thus, we have a snapshot of the white matter pathways before children evolve into expert readers. Our data provide the first evidence that the VOF is associated with early literacy development. They also reinforce the associations reported in the literature between ventral stream pathways (ILF and IFOF) and dorsal stream pathways (AF) and literacy development. This study adds to a growing corpus of research investigating developing fiber pathways supporting early literacy in emerging readers.

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## Appendix A. Supplementary material

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