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Brain white matter structure and language ability in preschool-aged children

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ABSTRACT

Brain alterations are associated with reading and language difficulties in older children, but little research has investigated relationships between early language skills and brain white matter structure during the preschool period. We studied 68 children aged 3.0–5.6 years who underwent diffusion tensor imaging and participated in assessments of Phonological Processing and Speeded Naming. Tract-based spatial statistics and tractography revealed relationships between Phonological Processing and diffusion parameters in bilateral ventral white matter pathways and the corpus callosum. Phonological Processing was positively correlated with fractional anisotropy and negatively correlated with mean diffusivity. The relationships observed in left ventral pathways are consistent with studies in older children, and demonstrate that structural markers for language performance are apparent as young as 3 years of age. Our findings in right hemisphere areas that are not as commonly found in adult studies suggest that young children rely on a widespread network for language processing that becomes more specialized with age.

1. Introduction

One of the most important developmental gains seen in young children is the acquisition of language skills. Language ability in early childhood has been associated with future reading success, and can affect academic achievement, mental health, and future career prospects (Carroll, Maughan, Goodman, & Meltzer, 2005). Although most children develop fluent reading skills, 5–17% will be diagnosed with dyslexia, a disorder characterized by reading problems that may persist throughout life (Shaywitz, 1998). Interventions in kindergarten-aged children at risk for dyslexia have been shown to be effective at improving grade school reading ability (Elbro & Petersen, 2004); however, reading disabilities are typically not diagnosed and treated until the third grade, when reading delays are clearly measureable (Gabrieli, 2009). There is general consensus that the roots of dyslexia begin before initial reading instruction, and that assessment of phonological processing skills could assist in early identification of children at risk for dyslexia (Gabrieli, 2009).

Neuroimaging studies have helped develop a better understanding of the relationship between white matter brain architecture and language and reading (Smits, Jiskoot, & Papma, 2014), and contributed to a dual stream model of language that includes dorsal and ventral pathways (Hickok & Poeppel, 2004). The dorsal pathway, specifically the arcuate fasciculus (AF), connects left frontal and temporal-parietal regions (Dick & Tremblay, 2012), is related to sensory-motor mapping of sound to articulation (Saur et al., 2008), and sustains phonological aspects of reading (Vandermosten, Boets, Poelmans, et al., 2012; Vigneau et al., 2006). The ventral pathways, which include the uncinate fasciculus (UF), inferior longitudinal fasciculus (ILF), and inferior fronto-occipital fasciculus (IFOF), connect frontal, temporal, and occipital regions (Dick & Tremblay, 2012), are involved with linguistic processing of sound to meaning (Saur et al., 2008), and are thought to sustain orthographic aspects of reading, such as the ability to identify words by sight (Jobard, Crivello, & Tzourio-Mazoyer, 2003; Vandermosten, Boets, Poelmans, et al., 2012).

Diffusion tensor imaging (DTI) studies in school-aged children and adults demonstrate that language and reading abilities have positive relationships with fractional anisotropy (FA) and negative relationships with mean diffusivity (MD) in left temporal parietal and frontal areas (Vandermosten, Boets, Wouters, & Ghesquiere, 2012). Furthermore, longitudinal studies show that gains in language abilities are associated with changes in white matter structure over time (Keller & Just, 2009; Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012). While these studies convincingly demonstrate a relationship between reading/

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language and brain structure in older children and adults, it is unclear whether these relationships are identifiable before children begin to read. Two DTI studies investigated language abilities in children in Kindergarten, aged 5–6 years, and showed positive relationships between phonological processing and FA in the left AF (Saygin et al., 2013), or between phonological processing and FA in the bilateral AF and IFOF (Vandermosten et al., 2015). Another DTI study examined children as young as 5 years and found that pre-readers with a family history of dyslexia had lower FA in the temporal parietal segment of the AF, when compared to pre-readers with no family history of dyslexia (Wang et al., 2016). Similarly, Langer et al. (2015) found that infants aged 5–18 months with a family history of dyslexia had lower FA in the AF compared to infants with no family history, and that expressive language ability correlated with FA in the left AF across groups. Relationships between receptive and expressive language ability and myelin water fraction have also been observed in children 1–6 years of age (O'Muircheartaigh et al., 2013, 2014). The above mentioned studies show relationships between white matter structure and reading/language skills are apparent at a young age; however, no studies have yet examined the relationships between white matter structure and specific pre-reading skills such as phonological processing and speeded naming in children younger than 5 years. Understanding the relationships between brain structure and language abilities predictive of future reading skill is necessary to characterize the neurological basis of language disorders and the roots of reading difficulties. Therefore, the goal of this study was to investigate the relationship between white matter structure and pre-reading skills in a large group of typically developing preschool aged children.

2. Methods

2.1. Participants

Sixty-eight children aged 3.0–5.6 years (4.0 ± 0.6 years, 31 females and 37 males) were recruited from an ongoing prospective study that recruited women during pregnancy (Kaplan et al., 2014). All children were healthy, free from neurological or developmental disorders, had no history of head trauma and had no contraindications to MRI scanning (e.g., metal implants). Gestational age at birth ranged from 36.7 to 41.9 weeks (39.5 ± 1.7 weeks). All children spoke English as a primary language, with 9 children identified as coming from a bilingual home. Family history of reading disability was collected from parental reports, which identified 7 children with a first or second degree relative that had been diagnosed with developmental dyslexia. Children's hand preference was assessed by parental questionnaire, of which 7 participants were identified as being predominately left handed, with the remaining 61 being predominately right handed (no participants were identified as ambidextrous). Number of years of maternal post-secondary education was collected as a proxy for socioeconomic status, and ranged from 1 to 12 years, with a mean of 5.0 ± 2.8 years. The institutional ethics review board approved this study, and informed consent was obtained from participant's legal guardian(s), and verbal assent was obtained from the children.

2.2. Language assessments

All participants completed the Phonological Processing and Speeded Naming subtests of the NEPSY-II (Korkman, Kirk, & Kemp, 2007). The Phonological Processing test assesses phonemic awareness, whereas the Speeded Naming subtest measures rapid semantic access to and production of names of colors and shapes. Phonological Processing Scaled Scores and Speeded Naming Combined Scaled Scores were used for the analysis. The Speeded Naming Combined Scaled Score takes into account both the speed and accuracy of the answers given by the child. These language assessments took approximately 10 min to complete, and were administered on the same day as MRI scanning.

2.3. MRI scanning

Imaging took place at the Alberta Children's Hospital on the same General Electric 3 T MR750w system using a 32-channel head coil (GE, Waukesha, WI). Children were scanned while awake and watching a movie, or while sleeping without sedation. Whole-brain diffusion weighted images were acquired using a single shot spin echo echo-planar imaging protocol, with 30 gradient encoding directions at $b = 750\,\mathrm{s/mm^2}$ and 5 images without gradient encoding ($b = 0\,\mathrm{s/mm^2}$). The DTI sequence was acquired with the following parameters: TR = 6750 ms, TE = 79 ms, 50 axial slices with a 2.2 mm thickness (no gap), $1.6 \times 1.6 \times 2.2\,\mathrm{mm^3}$ resolution, anterior-posterior phase encoding, scan time = 4:03 min.

2.4. Data processing

DTI data was quality checked and processed through in house, Matlab-based software designed to detect and remove motion-corrupted volumes. Motion in the DTI images was quantified based on the presence of black lines in the dataset. A Prewitt horizontal edge-enhancing filter was applied to sagittal and coronal views of the DTI data, then a Hough transform was used to detect and quantify black lines in these views. If the quantity of black lines exceeded a tested threshold, the volume was labeled as motion corrupted and removed from the data set. From an original sample of 74 children, 6 participants were excluded from the study because they had 15 or more diffusion weighted volumes removed for motion corruption. Of the 68 children included in the final sample, 97% of included participants had fewer than 5 volumes removed, and 76% of children had no motion-corrupted volumes. The number of motion-corrupted volumes was not significantly correlated with age ($p = .31$) or language scores (Phonological Processing $p = .70$; Speeded Naming $p = .37$).

Data was processed using FSL's diffusion pipeline (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012), including eddy current correction and simple head motion correction using an affine registration to a reference volume, fitting of a diffusion tensor model at each voxel, and calculation of fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). All processed images were visually inspected to ensure high quality.

2.5. Data analysis

Whole-brain voxel-wise analysis was performed using FSL's Tract Based Spatial Statistics (TBSS) (Smith et al., 2006). Using non-linear registration, each participant's FA image was aligned to that of every other participant. The most representative participant (i.e., the one that required the least warping for all other participants) was chosen as the target image. The target image was then aligned into MNI152 standard space using affine registration, and every image was transformed into 1 × 1 × 1 mm MNI152 space by combining the nonlinear transform to the target FA image with the affine transform from that target to MNI152 space. This method was selected because young children's brains would not necessarily align correctly to the adult template provided in TBSS.

A mean white matter skeleton was created using an FA threshold of 0.3, then participants' FA data was projected onto the skeleton and analyzed using voxel wise cross-subject statistics using non-parametric permutation testing (RANDOMISE). Significant clusters were identified at $p < .05$ using threshold free cluster enhancement and Gaussian random field based family wise error rate correction for multiple comparisons (Smith & Nichols, 2009). Clusters were labeled using the NatBrainLab white matter atlas (Thiebaut de Schotten et al., 2011). Projection onto the skeleton and statistics were repeated for MD, AD, and RD. Each DTI parameter was independently correlated with age-standardized Phonological Processing and Speeded Naming scores. Age, sex, hand preference, bilingualism, gestational age, family history of