

Introduction

- Learning to read requires transformation from print to speech and print to meaning, which involves multiple functional brain regions connected through white matter pathways¹.
- Multiple white matter pathways have been linked to language or reading and atypical white matter diffusivity has been reported in children with developmental dyslexia (DD) or children with a family of history of DD^{2,3} before children received formal reading instruction.
- This study examined the characteristics of white matter fibers and its relationship to basic reading skills in 29 typically developing children (age range: 4.61 – 9.97).

Materials and Methods

- **Participants:** A total of 29 typically developing native-English speaking children participated in both visit 1 and visit 2. Two datasets were excluded due to poor quality. 27 children were divided into two age groups. 15 pre-readers (6.29 years old, 7M) and 12 decoding readers (8.11 years old, 6M).
- **Behavioral assessments (Visit 1):** Kaufman Brief Intelligence Test 2nd addition (KBIT2) and phonological awareness (PA), word identification (WID), word attack (WA) subtests of Woodcock Reading Mastery Tests (WRMT™-III) were administered. WA assess phonetic decoding skills.
- **Imaging scan (Visit 2):** Diffusion weighted imaging (DWI) data were collected using spin-echo echo planar imaging (EPI) sequence with these parameters: acquisition time=6:22 minutes, slices# = 60, voxel size = 2x2x2mm³, TR=2.7s, TE=95ms, FOV=220x220, six b=0 and two 1000 s/mm², diffusion weighting isotropically distributed along 64 directions.
- **Imaging Processing:** DWI quality control was done with DTIPrep and visual inspections. Then, Topup, Eddy Current correction, and diffusion tensor fitting using a linear least-squares fit⁴ were completed using FSL.

- **Automatic Fiber Quantification (AFQ)⁵:** (1) whole-brain tractography using a deterministic streamline tracking algorithm (STT)^{6,7} with an FA threshold of 0.2 and angle threshold of 30°, (2) region-of-interest (ROI)-based fiber tract segmentation, (3) fiber-tract cleaning using a statistical outlier rejection algorithm and (4) diffusion characteristics quantification at each node along the trajectory of the fiber. Initially 50 nodes were computed for each tract. AFQ generated FA for each node along each fiber tract at equal distance.
- **Statistical analyses:** All statistical analyses were executed using the R system (version 3.1.0 64 bit)⁸. Family Discovery Rate (FDR) correction was used for multiple comparison correction (q < 0.05). For brain-behavioral correlation, age and sex were controlled.

Results

Table [1]	age	Verbal IQ	Non Verbal IQ	WRMT PA	WRMT WID	WRMT WAT
pre-readers	6.29 ± 0.68	113.27 ± 9.25	107.40 ± 15.30	111.47 ± 18.38	109.20 ± 12.89	107.47 ± 15.52
decoding reader	8.11 ± 0.83	115.75 ± 11.7	108.67 ± 18.86	111.33 ± 6.93	114.00 ± 13.60	110.08 ± 13.43
p-value	0.000 *	0.555	0.823	0.980	0.361	0.643

* sig p < 0.05 mean ± standard deviation

Table 1 summarized the descriptive statistics by group. All the scores were standardized. For brain-behavior correlation, we decided to use standardized scores to minimize the collinearity.

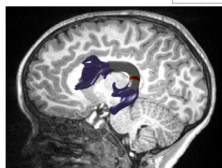
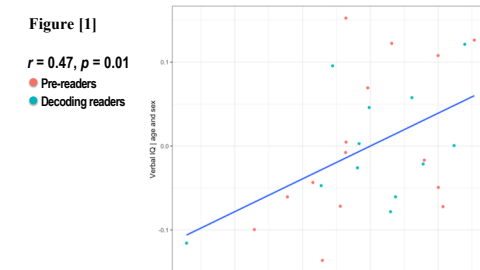


Figure 1 showed Fractional Anisotropy (FA) of the nodes 36-39 of the left Arcuate Fasciculus (AF)

(red portion of the AF fiber tract) significantly correlated with the KBIT verbal IQ, controlling for age and sex.

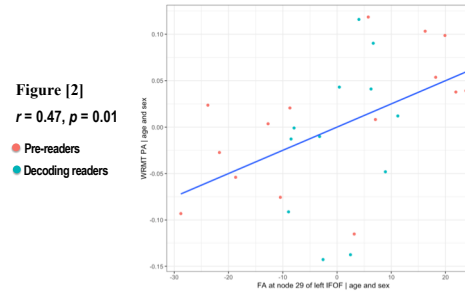
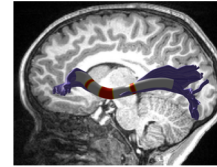


Figure [2]
r = 0.47, p = 0.01
● Pre-readers
● Decoding readers

Figure 2 demonstrated FA of the nodes 18-19, 28-33, 39-40 of the left inferior fronto-occipital fasciculus (IFOF) significantly correlated with the WRMT PA subtest standardized scores, controlling for age and sex.

Conclusion

Our results show the brain-behavior correlation between FA values and behavioral measures. FAs of the left posterior AF tract were significantly positively correlated with standardized scores of standardized Verbal IQ measured by KBIT, while FAs of the left IFOF were significantly positively correlated with standard scores of PA subtests of WRMT-III. During the verbal IQ task, children listen to spoken words and are asked to point the picture representing the words. Children's neural maturity in the left inferior frontal gyrus (Broca's area) predicts their performance on the KBIT verbal IQ test⁹, which indicated the connection between the KBIT verbal IQ scores and language processing in the brain region. Our results aligned with the functional results. The left AF, as the structural connection between the Broca's area and Wernicke's area, plays an important role in language production and relates to children's

verbal knowledge. The PA tests the phonological ability. The IFOF positively correlates with the PA standardized scores, which may suggest the role of IFOF on PA tasks. More investigations are needed to study the functional supports of these fiber tracts. Our findings indicate: (1) white matter fiber tracts are sensitive measures to examine brain-behavior relationship and experience-driven brain changes, (2) white matter pathways support language and literacy development in young children who have limited formal reading instructions, and (3) white matter fiber tracts may help our understanding of different theoretical models of reading development.

References

1. Wang Y et al. 2017 Cereb Cortex 27(4): 2469-2485.
2. Saygin Z et al. 2013 J. Neurosci. 33(33): 13251-13258
3. Yeatman J et al. 2012 PNAS 109(44): 17756-
4. Rohde GK et al. 2004 Magn Reson Med 51:103-114.
5. Yeatman J et al. 2012 PLoS ONE e49790.
6. Mori S et al. 1999 Annals of Neurology 45:265-269.
7. Basser PJ et al. 2000 Magn Reson Med 44:625-632.
8. Ihaka R and R Gentleman 1996 J Comput Graph Statist 5:299-314.
9. Cantlon J.F. and Li R. 2013 PLoS Biology 11(1): e1001462

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