Atypical white matter mechanisms underlying reading development in adolescents with fetal alcohol spectrum disorders

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Introduction

- Prenatal alcohol exposure (PAE) affects brain development *in utero*, resulting in deficits in a broad range of cognitive domains[1,2,3], including reading[4,5].
- Compared to controls, alterations in white matter (WM) development have been observed in children and adolescents with fetal alcohol syndrome (FAS), which has been linked to their atypical cognitive abilities[6,7].
- However, to date, few studies have systematically investigated the neurobiological mechanisms underlying reading impairments associated with FAS.

Methods

Participants:
93 adolescents, 26 full/partial FAS (FAS/PFAS; age = 16.9 ± 0.7 years), 28 heavily exposed (HE) nonsyndromal (16.4 ± 1.2 years), and 39 controls (16.3 ± 1.0 years) recruited from Cape Town, South Africa. Groups balanced on age and gender.

PAE Assessment/FAS Screening:
Mothers interviewed about drinking during and after pregnancy. Measures constructed from volume of absolute alcohol (AA) consumed. Participants examined for growth and FAS anomalies using standard protocol[8].

Behavioral Assessment:
Reading skill was assessed using the Gray Oral Reading Test (GORT, 5th edition)[9].

MRI Acquisition:
MPRAGE and DTI acquired on a 3T Siemens Trio scanner at Cape Universities Brain Imaging Centre (CUBIC).

DTI Data Processing:
DTIPrep for detection and removal of artifactual volumes[10], FSL/topup function for head motion and eddy current correction[11], AFQ for tractography[12]. FA estimated for eight reading-relate WM tracts - bilateral AF, SLF, ILF, and IFOF.

Lateralization:
Lateralization index calculated as prior research suggests reduced lateralization may contribute to reading impairment[13].
LI = 100 x [left measure – right measure]/[right measure + left measure].

Statistical Analyses:
Potential group differences in WM mechanisms underlying reading examined using:
1. One-way ANOVAs with group as between-subject variables
2. Linear regression models incorporating group, GORT scores and their interaction term

Results

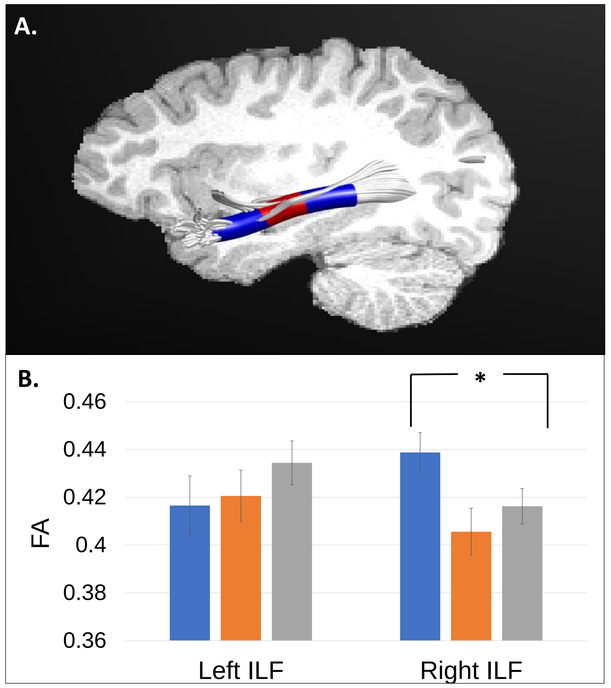

Figure 1. Significant group effect in left LI of the inferior longitudinal fasciculus (ILF). A. Sagittal view of ILF (left hemisphere shown). Segment with a significant group effect in red. B. Fractional anisotropy (FA) of each group for left and right ILF. Post-hoc analyses revealed significant FA differences among the three groups in right ILF ($F_{2,92}$ = 3.5, p = 0.035), but not in left ILF ($F_{2,91}$ = 0.85, p = 0.43).

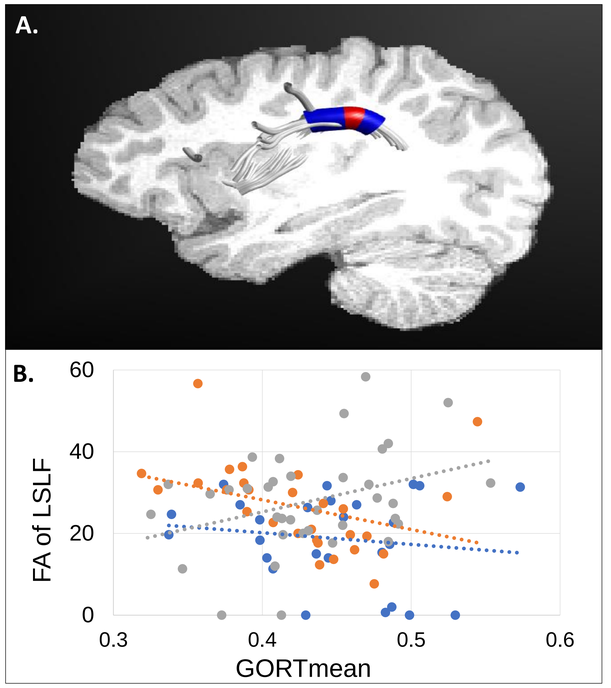

Figure 2. Significant interaction effect between group by reading performance in left superior longitudinal fasciculus (LSLF). A. Sagittal view of LSLF. Segment with significant interaction effect in red. B. Scatter plot for association between FA of LSLF and reading performance. Post-hoc correlation analyses revealed a positive correlation only in the control group (r = 0.34, p = 0.041) but not in the HE (r =-0.36, p = 0.059) or FAS/PFAS groups (r =-0.15, p = 0.47).

Discussion

- A significant GORT*group interaction effect was observed in LSLF, driven by a significant association between GORT scores and FA of the LSLF in the control group but not in either alcohol-exposed group. This indicates atypical left-hemispheric WM tract development associated with PAE, which may underlie reading impairments in individuals with FAS.
- Compared to a typical leftward asymmetry in controls, adolescents with FAS/PFAS showed a right-lateralization of the ILF, a WM tract previously linked to reading abilities[14]. This result may suggest an increased right hemispheric reliance in the FAS/PFAS group.

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