MILD TRAUMATIC BRAIN INJURIES IN CHILDHOOD ARE ASSOCIATED WITH ALTERATIONS IN MYELIN SENSITIVE MRI MEASURES IN FEMALES

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BACKGROUND

- As maturation of the brain continues throughout development, there is risk of interference from mild traumatic brain injury (mTBI).
- An mTBI can cause shearing of axons and may alter developmental myelination.
- Altered white matter maturation could impact cognitive processes that are under development.

OBJECTIVE

1. Investigate differences in white matter and cortical myelin development between children with a history of mTBI and a population sample using myelin sensitive imaging in: **Cortical Gray Matter**, **Superficial White Matter**, **Deep White Matter**
2. Investigate the relationship between neurite density and cognitive outcomes

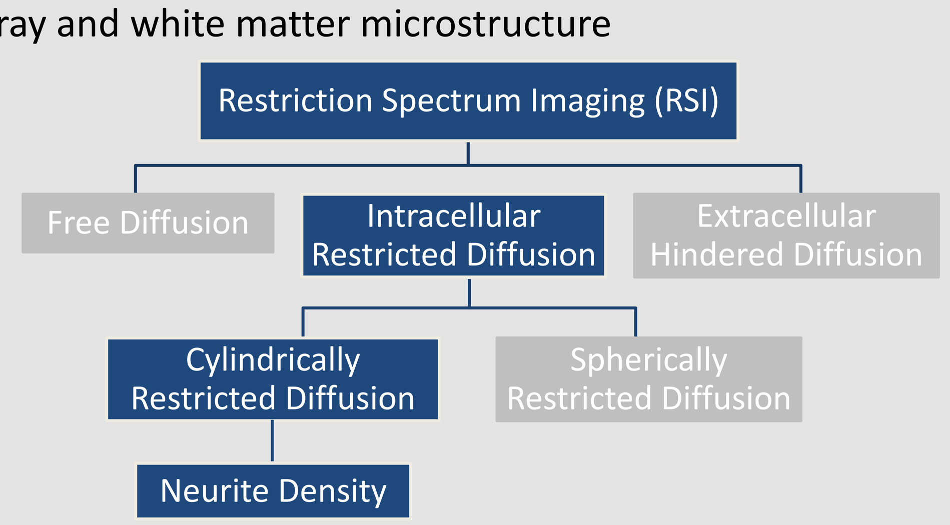
METHODS

ADOLESCENT BRAIN COGNITIVE DEVELOPMENT STUDY

- Publicly available dataset of children ages 9 to 10 years old, including children with a history of mTBI, who had diffusion weighted images.

RESTRICTION SPECTRUM IMAGING

- Multi-shell diffusion weighted imaging technique, sensitive to gray and white matter microstructure



- Neurite density is sensitive to myelinated axons

STATISTICAL ANALYSES

Objective 1

- Group-wise analyses to investigate relationship between group, sex, age and their interactions
- Race/ethnicity, total combined family income, and pubertal status included as covariates

Objective 2

- Principal component analysis (PCA) was performed on neurite density values in ROI to extract a collection of ROI (PCs) that explain the largest variance in the data
- PCs with $\lambda > 1$ were used to investigate the relationship with cognitive outcomes (Flanker Inhibitory Control and Attention Test & Pattern Comparison Processing Speed Test)

RESULTS

OBJECTIVE 1: GROUP COMPARISONS

Table 1. Sex and age of sample

	mTBI	Controls
Sex F/M	133 (39.6%)/203 (60.4%)	3524 (47.8%)/3843 (52.2%)
Mean Age in Months (SD)	120 (7.47)	119 (7.40)

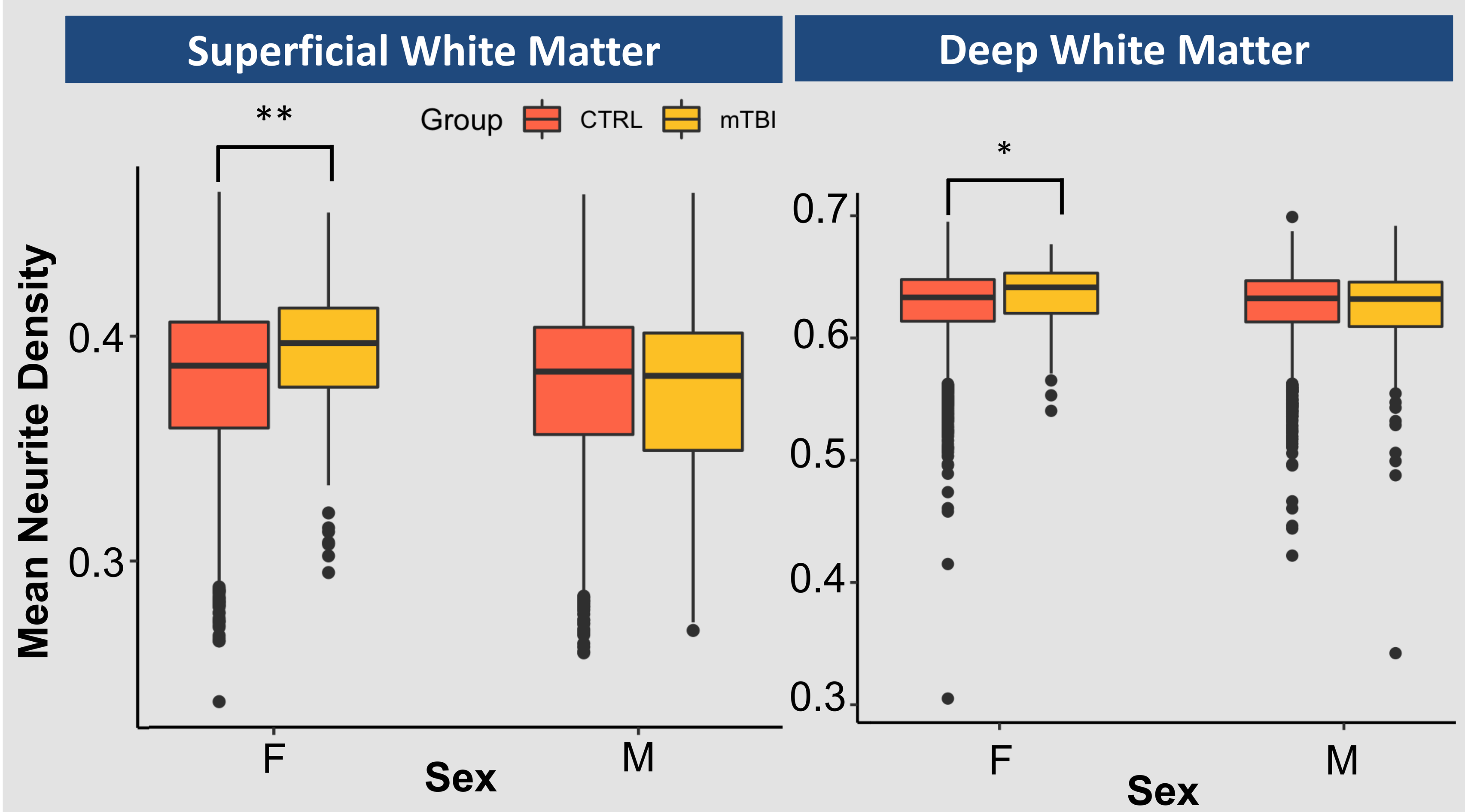


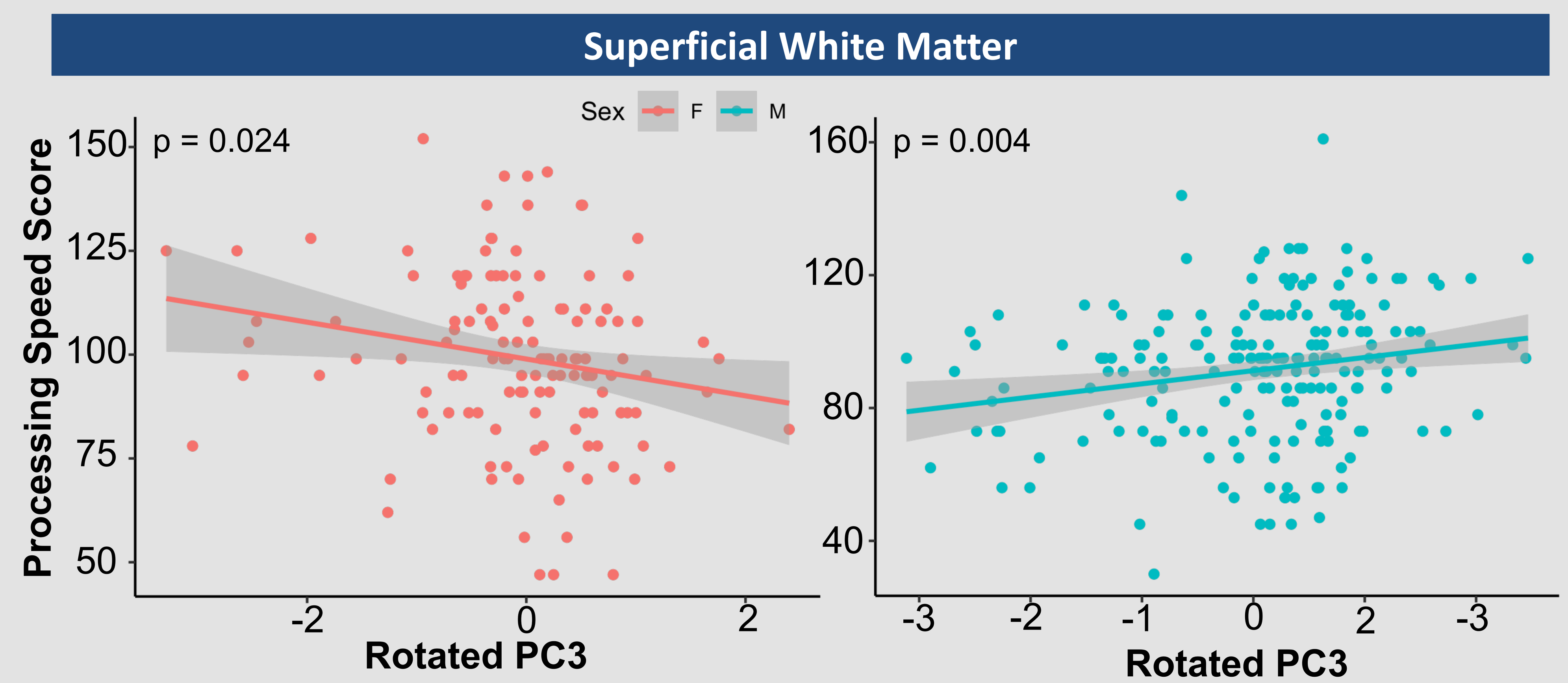
Table 2. *P* values for the interaction between group and sex and for female mTBI compared to female control.

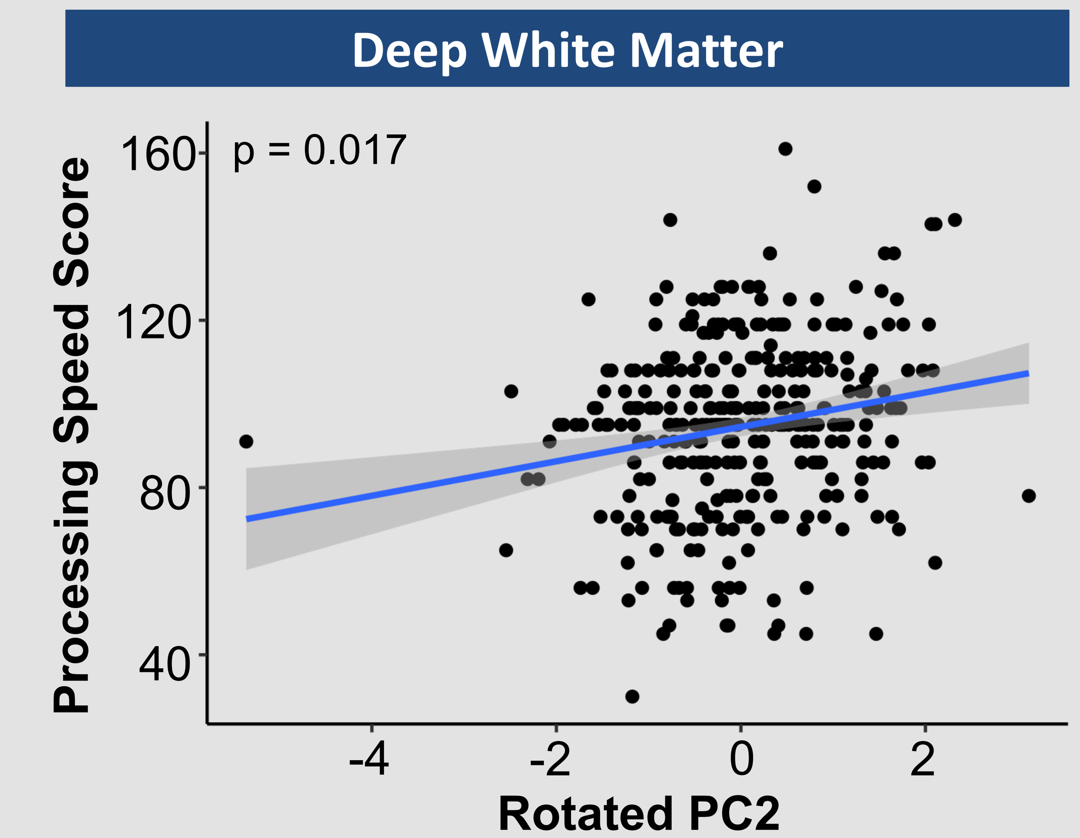
	Superficial White Matter	Deep White Matter
Group x Sex	0.004 **	0.017 *
F mTBI vs Control	0.001 **	0.027 *

- All imaging measures demonstrated robust relationships with age reflecting maturation of brain microstructure.
- Comparisons between children with and without a history of mTBI revealed significantly higher neurite density (more myelin) in deep and superficial white matter in females with mTBI.
- No group differences were observed in cortical neurite density.

OBJECTIVE 2: RELATIONSHIP WITH COGNITIVE OUTCOMES

- PCA of superficial white matter ROI revealed 9 PCs with $\lambda > 1$
- Variable loadings on PC3 included: Bilateral Orbital Frontal Cortex, L Parahippocampal Gyrus, L, Inferior Frontal Gyrus, Bilateral Temporal Gyrus, L Insula
- Higher neurite density in these regions is correlated with poorer processing speed in females





- PCA of deep white matter ROI revealed 5 PCs with $\lambda > 1$
- Variable loadings on PC2 included:
  Corticospinal/Pyramidal Tract
  Anterior Thalami Radiations
  Superior Corticostriate
- Higher neurite density in these regions is correlated with better performance on the processing speed test (no sex-specific effects)

CONCLUSION

- mTBI in childhood may accelerate white matter myelination in females but does not affect cortical myelin.
- This sex specific effect on the brain may be associated with enhanced vulnerability to persistent symptoms after concussion in females.
- Association between higher neurite density and lower scores on the Pattern Comparison Processing Speed Test suggests that altered myelin development after a childhood mTBI may influence cognitive development.

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