

# Sex-specific associations between early-life exposure to manganese and white matter microstructure in adolescents and young adults

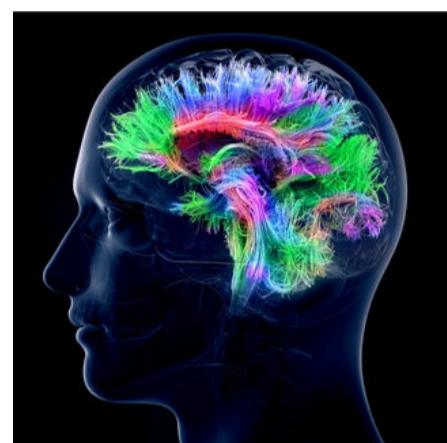
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## Conclusions

- Early-life Mn exposure to manganese is associated with white matter microstructure alterations within regions involved in widespread functions
- The effect of Mn exposure on the brain differs by sex.

## Background

- The brain white matter (WM) connects gray matter regions into functional networks
- WM is critical for human cognition and behavior.
- Early-life metal exposure can disrupt WM maturation and lead to long-lasting changes in neuronal circuitry.
- Despite evidences suggesting associations between Manganese (Mn) and neurodevelopmental effects, the underlying brain mechanisms of these associations are poorly understood.
- **Objective:** To examine associations between early-life exposure to manganese (Mn) and WM microstructure in young adults.

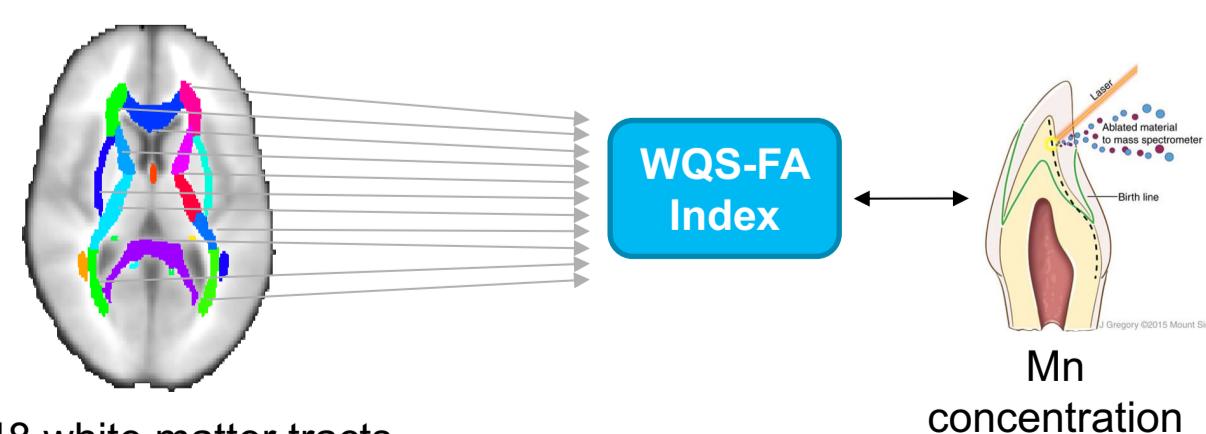


## Methods



**Participants:** 73 adolescents and young adults from the **PHIME cohort** (Age 16 - 23 years; 39 females)

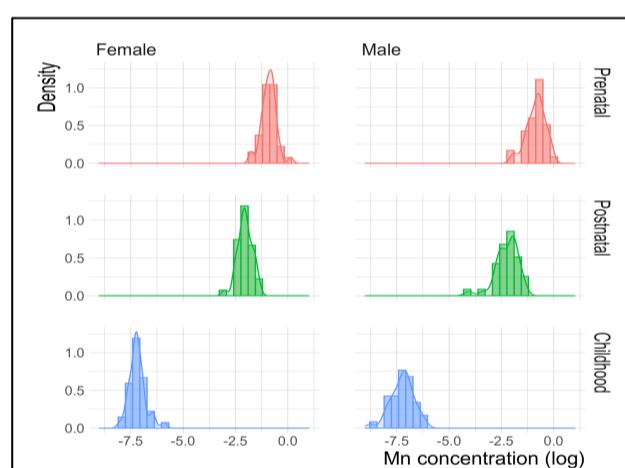
- Prenatal, early postnatal and childhood Mn concentrations were measured in deciduous teeth using laser ablation-inductively coupled plasma-mass spectrometry.
- White matter integrity measured using fractional anisotropy (FA) metric from diffusion tensor imaging (DTI)
- **Statistical analysis:** weighted quantile sum (WQS) regression.



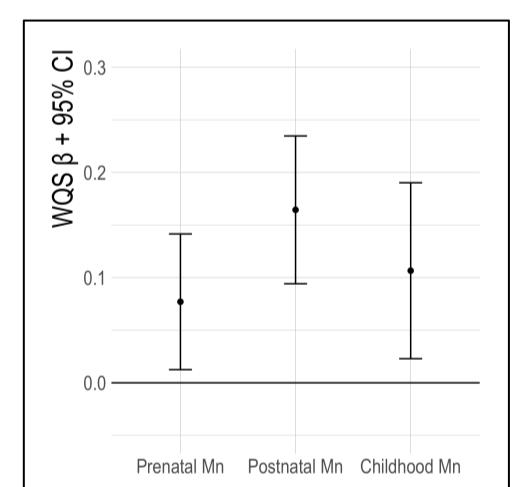
## Results

Table 1. Sex-stratified sociodemographic characteristics and exposure characteristics of 73 young adults participating in this study.

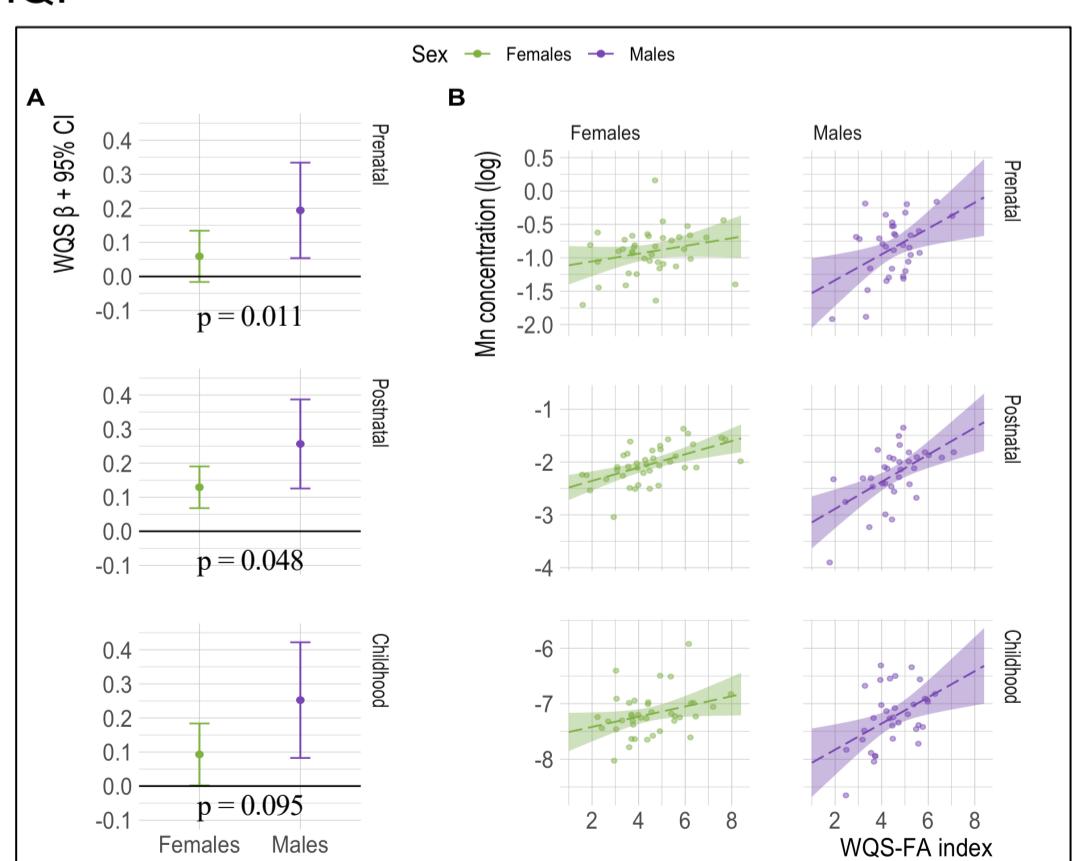
| Characteristic | All<br>Mean ± SD<br>or % | Females<br>Mean ± SD<br>or % | Males<br>Mean ± SD<br>or % | p <sup>a</sup> |
|----------------|--------------------------|------------------------------|----------------------------|----------------|
| Age (years)    | 19.5 ± 2.2               | 19.7 ± 2.1                   | 19.2 ± 2.4                 | 0.44           |
| SES            |                          |                              |                            |                |
| Low            | 11 %                     | 15 %                         | 6 %                        | ref            |
| Medium         | 66 %                     | 64 %                         | 68 %                       | 0.31           |
| High           | 23 %                     | 21 %                         | 26 %                       | 0.26           |
| IQ             | 104 ± 10                 | 102 ± 11                     | 106 ± 10                   |                |



**Figure 1.** Prenatal, postnatal, and early childhood manganese concentrations (log) measured in naturally shed deciduous teeth of 73 study participants, by sex.



**Figure 2.** Beta coefficients and 95% confidence intervals of the association between prenatal, postnatal, and early childhood manganese concentrations (log) and WQS-FA index. All models were adjusted for age, sex, SES and IQ.



**Figure 3.** (A) Beta coefficients and 95% confidence intervals of the association between Mn and WQS-FA index. Interaction p-values are provided for each timepoint. (B) Sex-stratified Regression lines and standard errors.