

Gut Microbiome Dysregulation and Reward Circuitry in Youth Exposed to Early Adversity



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Introduction

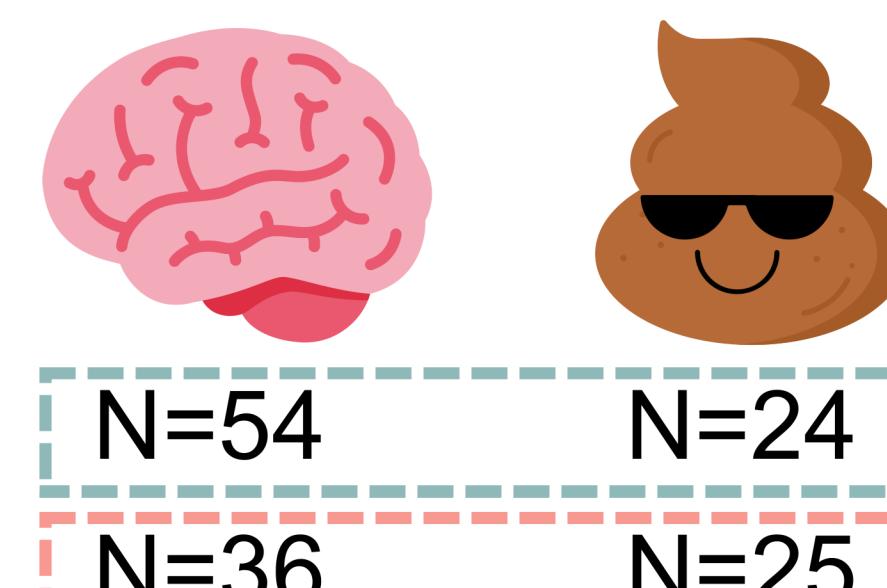
- Early adversity increases risk for health outcomes, such as depression or substance use disorders, that are linked to differences in corticostriatal reward circuitry¹
- Adversity-induced dysregulation of the gut microbiome may contribute to altered reward circuitry²
- Improved understanding of the relationship between the gut microbiome and neural reward networks will not only elucidate mechanisms underlying increased health risk following adversity exposure, but will also yield insight into potential microbiome-based treatments

Aims

- **Aim 1:** Examine effect of early adversity on resting-state functional connectivity rs-FC between the nucleus accumbens (NAcc) and the ventromedial prefrontal cortex (vmPFC)
- **Aim 2:** Test association between rs-FC and gut microbiome composition

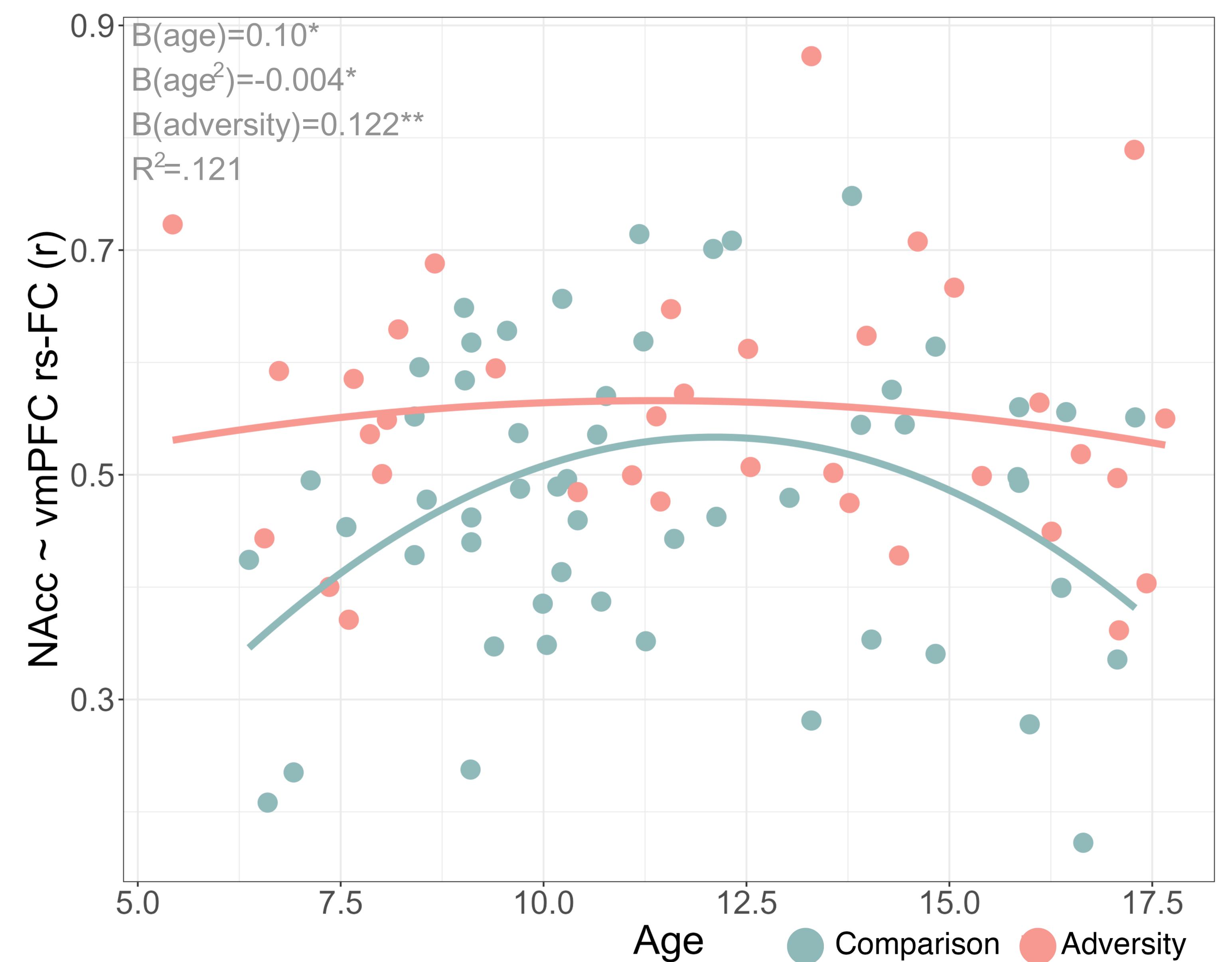
Methods

- Early adversity group: history of adoption/foster care
- Comparison group: low adversity
- Ages 6-18
- 5-minute resting-state fMRI
- 16S stool sequencing
- Amplicon sequence variants (ASVs) formed with DADA2³
- Distance & abundance-based analyses

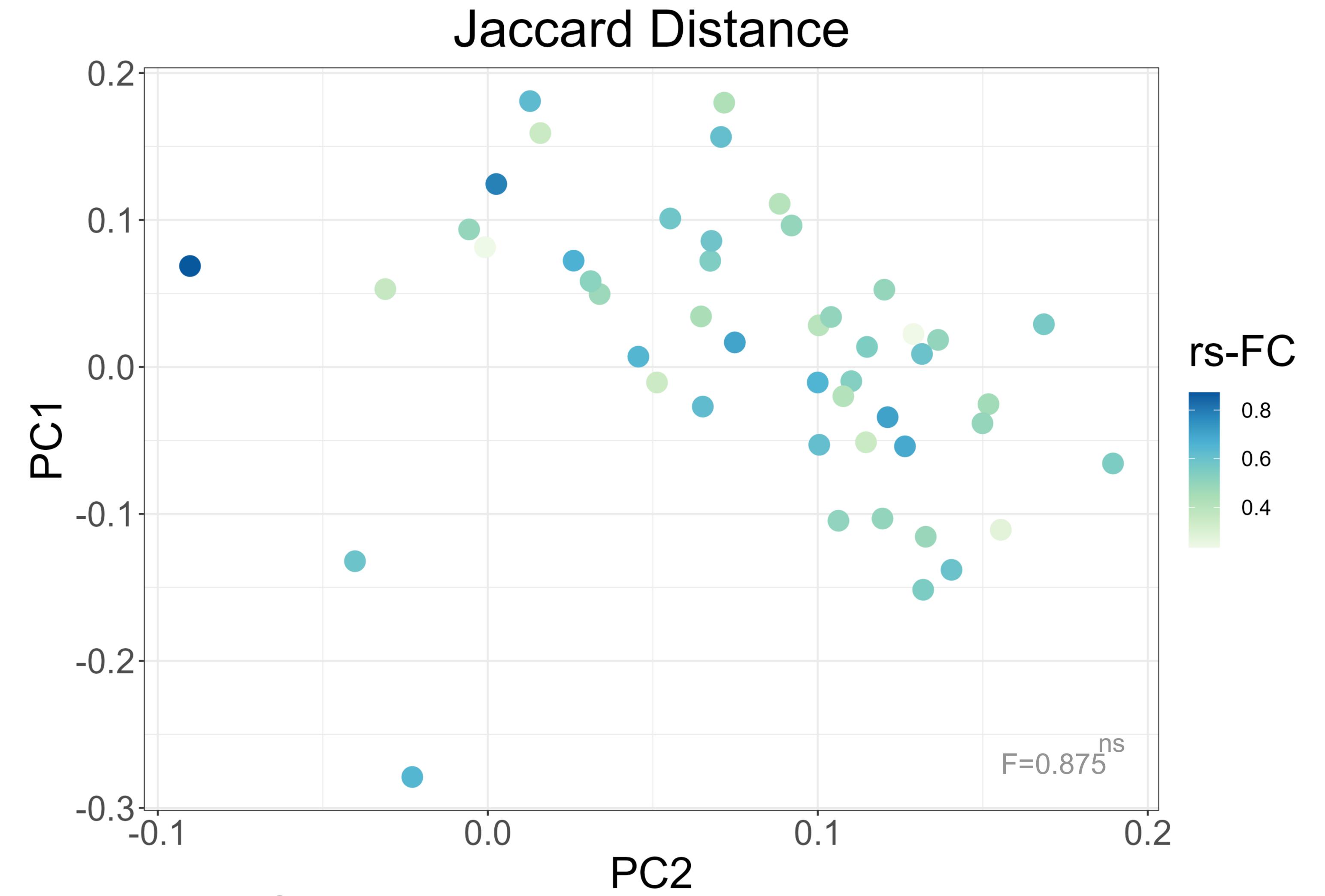


Aim 1 Results: Adversity is associated with higher rs-FC between the NAcc and vmPFC^a

Aim 1 Secondary Finding: there is a quadratic relationship between rs-FC and age



Aim 2 Results: The gut microbiome is not significantly associated with rs-FC^b

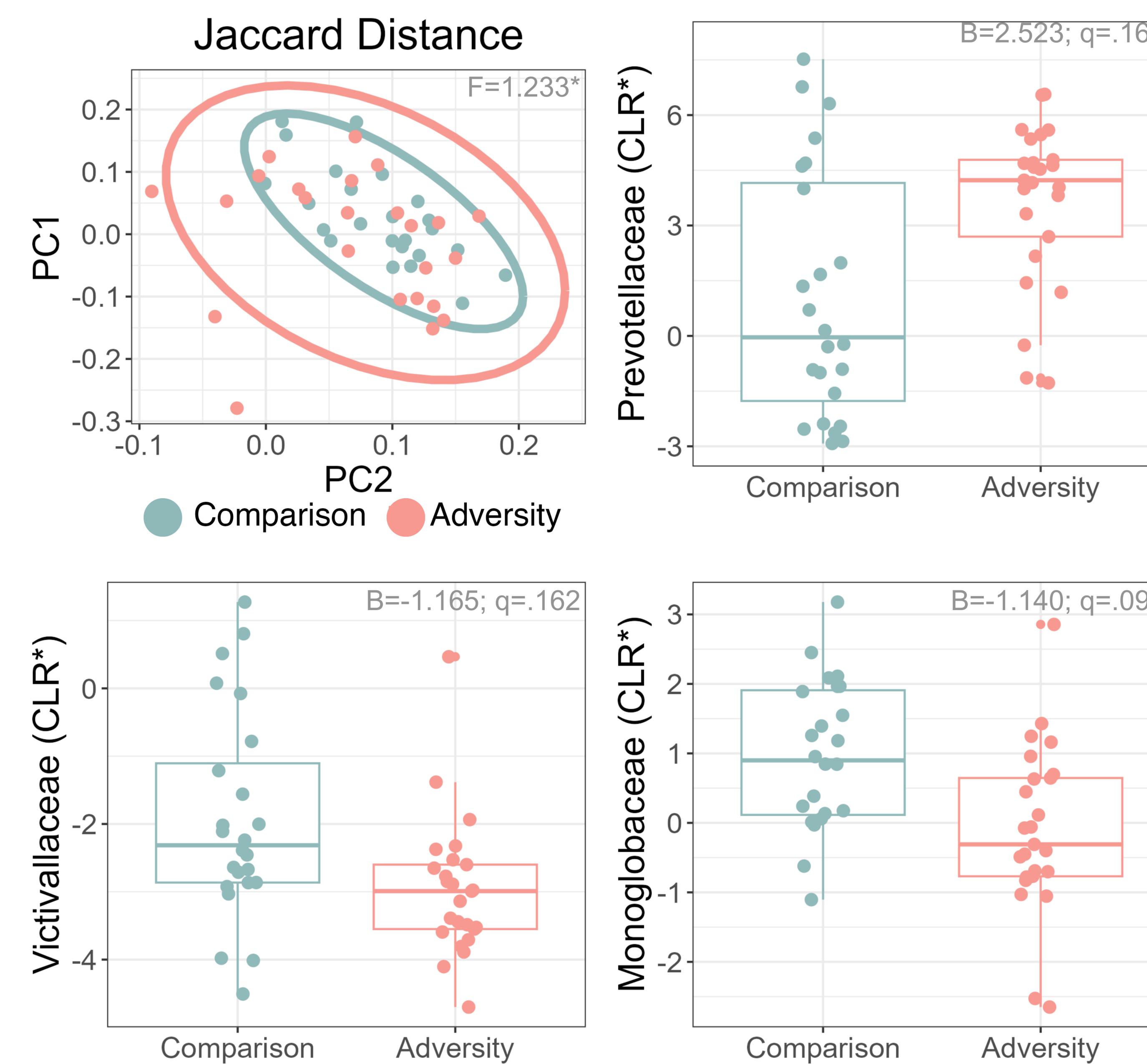


^aControlling for age and sex; r values are Fisher-transformed

^bControlling for age, sex, and adversity; r values are Fisher-transformed

*CLR: Center-Log Ratio

Aim 2 Secondary Finding: the gut microbiome is significantly associated with adversity



Conclusions

- Early adversity is associated with higher rs-FC between the NAcc and vmPFC. This suggests that reward circuitry may be altered in adversity-exposed youth, which is in line with prior literature¹.
- There is a quadratic relationship between rs-FC and age in our sample. Longitudinal study is needed in order to more accurately estimate the development of reward circuitry in this population.
- The gut microbiome is not significantly associated with rs-FC. However, more granular sequencing methods, such as metagenomic sequencing, may reveal microbiome-brain associations that are not apparent in 16S sequencing.
- The gut microbiome is significantly associated with adversity. This is in line with prior literature².

References

1. Hanson, J. L., Williams, A. V., Bangasser, D. A. & Peña, C. J. Impact of Early Life Stress on Reward Circuit Function and Regulation. *Front. Psychiatry* 12, 744690 (2021).
2. Coley, E. J. L. et al. Early life adversity predicts brain-gut alterations associated with increased stress and mood. *Neurobiol. Stress* 15, (2021).
3. Callahan, B. J. et al. DADA2: High-resolution sample inference from Illumina amplicon data. *Nat. Methods* 2016 13 13, 581–583 (2016).

ns: p>.05 | *: p<.05 | **: p<.01