Frontolimbic Resting-State Connectivity Mediates the Association Between Early Life Stress and Adolescent Psychopathology
Chase Antonacci 1, Lauren R. Borchers 1, Jessica L. Buthmann 1, Ian H. Gotlib 1
1 Department of Psychology, Stanford University, Stanford, CA

BACKGROUND
- Early environments exert profound and lasting effects on children’s development and well-being.1,2
- Youth growing up in adverse conditions often experience diverse forms of stress including poverty, neglect, air pollution, and maltreatment.3
- This multicitylinearity in early exposure has made it difficult to disentangle relations between specific stressors and outcomes, along with underlying psychobiological mechanisms.4
- Frontolimbic functional brain connectivity is one key pathway that may link early stress exposure and maladaptive developmental outcomes.5,6

Taxonomic Models of Early Stress:

METHODS
- Sample: n=186 youth (M_age=11.33, 59%F) recruited from the community
- Baseline (T1): Traumatic Events Screening Inventory (TESI), household SES, parenting behavior, caregiver psychopathology, environmental pollution, neighborhood characteristics, and resting state fMRI scan
- 2-year follow-up (T2): self- and parent-reported measures of psychopathology and behavioral difficulties

Analyses:
1. Exploratory factor analyses conducted on measures of stress exposure in childhood and measures of psychopathology in adolescence
2. Linear regression among obtained latent factors
3. Exploratory mediation analysis of frontolimbic functional connectivity

Regression analyses indicated that Parenting (b=20, p<0.003) and Household Threat/Unpredictability (b=18, p<0.007), but not Neighborhood Deprivation (b=0.003, p<0.647), significantly predicted Psychopathology.
- Across all predictor factors, there were no main effects of Age or Sex, or a significant interaction with the predictor.

RESULTS
Household Threat/Unpredictability, Hippocampus-dIPFC Connectivity, and Psychopathology
- Mediation analyses yielded a significant indirect effect for the association between Household Threat/Unpredictability and Psychopathology through functional connectivity between the right hippocampus and left dorsolateral prefrontal cortex (b=0.03, p<0.036).

DISCUSSION
- Factor analyses of diverse measures of early stress yielded three distinct factors. Of these, Parenting and Household Threat/Unpredictability significantly predicted adolescent psychopathology.
- Given the single Psychopathology factor that emerged in our analysis, our results offer mixed support for categorical models of adversity, which generally posit distinct relations between classes of stress exposure and domains of adverse outcomes.
- We did, however, find evidence of mechanistic specificity in the relation between Household Threat/Unpredictability exposure and frontolimbic functional connectivity.
- In the future, researchers might conduct data-driven analyses to identify changes in brain circuitry that are associated with stress exposure. In addition, they might also implement analytic strategies that are less dependent on co-occurrence between stressors.
- In sum, our results suggest broad dimensionality in the relation between stress exposure and psychopathology, warranting further investigation of such dimensions, especially with respect to individual differences and their implications for intervention targets.

REFERENCES & FUNDING