**Second-year Project**

* RQ1: Can stress-sensitivity PRS predict psychopathology-related symptoms?
  + Sub-aim: How does this stress-sensitivity PRS compare to previously established PRS for PTSD, MDD, and antisocial behavior?
    - How to do this? Cross-lagged panel (type of SEM, can do multiple factors?), MLM with family as random factor, something else?
    - Need to identify which PRS to use as comparison. Could also use ADHD or PRS for broader disorders eg anxiety disorders. Need to check ancestry for each PRS. Tweak script from Jinhan when trying to calculate.
* RQ2: How does exposure to environmental factors as captured with an exposome score affect the relationship between stress-related PRS and psychopathology-related symptoms?
  + Sub-aim: Which components of environmental exposure explain the most variance in psychopathology-related symptoms?
  + If prs doesn’t matte for 1 then what if its only bc it works in stressful environment
* RQ3: Can stress-based PRS and environmental exposures predict psychopathology-related changes in brain structure and/or function?
  + Sub-aim 1: structure - dec cortical thickness and volume in mPFC and dlPFC; dec volume in amygdala and hippocampus [use centiles, use pubertal status as covariate]
  + Sub-aim 2: function - dec amygdala-mPFC, amygdala-dACC, hippocampus-sgACC connectivity; inc amygdala-insula, hippocampus-insula connectivity [cortical network to subcortical regions not individual cortex]
* Exploratory:
  + Urbanome
  + Longitudinal
  + [threat v dep]

Allof these for nrsa, longitudinal as exploratory. No prediction

Methods: use S3, keep only SNPs that are sig for dex and not sig for vehicle (should be 79). Note that were only 78 (see paper) and 11 not in ABCD data set so final count is 66.

Can use logFC as ES. If have to, could use S9

Okay that started with SNPs from eQTL even though based on 160 white males (just need to be careful in interpretation)

DNA methylation: could potentially use, need to find from brain tissue though (ie not blood)

RSID should be same for ABCD and S3 but check two alleles are same

Outcome: minimum plan = CBCL, add-ons are structural and functional (need to be more concrete), potentially multiple time points (baseline vs latest version), compare this PRS against others eg PTSD, MDD, GAD or maybe even latent PRS for psychopathology

Exposome as moderator: SEM? Use cross-lagged panel model? Can put in model overall and then if sig later figure out which parts are most important

For NRSA, try to have PRS created and some descriptive stats; take CITI course sent by Sam in slack

**Methods**

* Imaging (baseline and year 2, no quality control available for year 4 yet)
  + Structural MRI
    - Cortical thickness
    - Cortical volume
    - Subcortical volume
    - To get estimates of how relates developmentally to other kids, use Centilebrain (regional) or Brainchart (global) [but remember to delete ABCD from comparison data set]
    - Need to batch harmonize data to account for site / scanner differences with COMBAT and/or GAMLESS (can do in Brainchart and maybe in Centilebrain)
  + Resting-state functional MRI
* Behavioral outcomes: parent-reported CBCL subscale scores (baseline, year 1, year 2, year 3, year 4)
* MLM
  + Levels: family, school, district, site
  + Account for: scanner type, average brain volume, sex, age

**Project B: Research Questions**

Exposome + neuroimaging transcriptomics ( corr w map between regions of brain, weight of ES, how are these weights corr w diff exp genes, need to look brainwide)