NeAim 1: evaluate longitudinal associations (baseline and 1 year?) between markers of peripheral inflammation, cognition, and brain structure in amnestic mild cognitive impairment (aMCI).

Aim 2: Examine how markers of peripheral inflammation impact the relationship between Alzheimer’s Disease (AD) pathology and clinical progression of aMCI.

Variables:

Aim 1:

* Hypothesis:
  + Higher baseline cytokine and chemokine levels in plasma will predict declines in memory and decrease cortical thickness.
    - Like project 0
  + Bigger increases in cytokines and chemokines will be associated with greater declines in memory and cortical thickness.
    - Differences in cytokines as covariates-change/baseline?
    - Like project 0
* Explanatory Variables
  + cytokine and chemokine levels (blood inflammation): IL-6, TNF-alpha, MCP-1, Eotaxin-1, Beta-2 microglobulin and Alpha 1-antichymotrypsin (ACT)
    - All continuous
  + Age and Sex and Status
  + Other things?
    - Will want to control for other variables that may affect inflammation.
    - BMI, NSAID use, genotype, health history
    - Need to clarify this!
      * Have all of these in model, and backward select out.
* Outcomes:
  + Change in Cognitive Test Measures in 1 year-all continuous?
    - CVLT
    - Benson Figure
    - MST
    - Story Recall
  + Change in Cortical Thickness in 1 year
    - Measure brain structure changes
    - Via a MRI

Aim 2:

* Hypothesis:
  + Identify the relationship between blood inflammation and memory (same as above) over two time points and how it relates to amyloid deposition (PET imaging at baseline).
  + There is an interaction between inflammation and amyloid deposition: elevated peripheral inflammatory markers will be strongest predictors of memory decline and cortical thickness.
    - More intense in AD than non AD
* Explanatory Variables:
  + Aim 2a:
    - Inflammatory markers
    - Age, Sex, Status, confounders?
  + Aim 2b:
    - Amyloid deposition
    - Status, Age, Sex
    - Cortical thickness
    - Inflammatory markers
    - Interaction between inflammatory and amyloid deposition or cortical thickness
* Outcomes:
  + Aim 2a:
    - Amyloid deposition (PET imaging)
      * Average SUVR value
      * Dichotomous if needed
    - Cortical thickness
  + Aim 2b:
    - Change in Memory
      * Test in Aim 1

Sample Size

* Expecting 125 aMCI and 50 HC
* Will enroll 137 amCI and 55 HC to all for 10% dropout
* Can get more if needed, if low power.

Questions

* Multiple comparisons: want different models for each cytokine or all in one?
* Is the PET imaging only done at beginning?
* Is aim 2a only done for baseline data-change?
* Power for all covariates?

For Aim 1:

What covariate to power for (which cytokine-values in paper in C2?)

Estimate of slope, sd of cytokine (and sd of change in cytokine), sd of change in cognitive test, sd of change in cortical thickness, correlation

For Aim 2a:

What covariate to power for (which cytokine-values in paper in C2?)

Estimate of slope, sd of cytokine (and sd of change in cytokine), sd of change in amyloid, sd of change in cortical thickness, correlation

For Aim 2b:

What covariate to power for (amyloid, cortical?)

Estimate of slope, sd of x, sd of change in amyloid, sd of change in cortical thickness, correlation