Rachel Johnson

BIOS 6623

11 December 2017

**Project 4 Final Report**

**Analysis Plan**

To evaluate the longitudinal associations between markers of peripheral inflammation, cognition, and brain structure for Aim 1A, separate multiple linear regressions will be fit including all individuals, with the respective outcomes of yearly change in CVLT memory score and yearly change in cortical thickness and one of the following cytokines as the primary predictor: baseline IL-6, TNF-alpha, MCP-1, Eotaxin-1, Beta-2 microglobulin, or ACT. These individual models will also adjust for age and sex. If supplementary cytokines or chemokines (TNF-alpha, MCP-1, Beta-2 microglobulin, ACT) are strong predictors, as defined by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, it will be included in the final model for each outcome, along with MCP-1, Eotaxin-1, age, sex, and a group of potential covariates including BMI, hypercholesterolemia, NSAID use, and immune related health conditions. These potential covariates will only be included in the model if they contribute to model fit, as determined by AIC, so as not to reduce power.

Identical methods will be used to test the hypothesis for Aim 1B, except for the models will include yearly change in cytokines/chemokines rather than baseline values.

To how markers of peripheral inflammation impact the relationship between AD pathology and clinical progression of aMCI in Aim 2, amyloid deposition will first be dichotomized based on whether a value is below or above the median. Then, separate multiple linear regressions will be run with change in CVLT memory score and change in cortical thickness as the respective outcomes. For each outcome, a separate model will be run for each cytokine/chemokine that includes the baseline level of the biomarker, dichotomized amyloid deposition, and interaction between the biomarker and amyloid deposition, as well as sex and age as precision variables. Then, for each cytokine/chemokine for which \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, a comprehensive multiple linear regression will be run for each outcome that includes the baseline biomarker levels, amyloid deposition categorization, interaction between amyloid deposition and biomarker values, age, sex, and the potential covariates listed in Aim 1. Similarly to Aim 1, the potential covariates will only be included if they improve model fit as determined by AIC.

**Power Analysis**

For Aim 1, a correlation of 0.2 was desired for detection between either of the two outcomes with any of the cytokines/chemokines. For a desired power of 80%, an alpha level of 0.01 to account for multiple testing corrections, and a two-tailed test, 287 individuals would be required to be analyzed. Assuming a dropout rate of 10%, 319 individuals would need to be recruited into the study.

Based on the 287 individuals in the analytic cohort, one would assume approximately 205 individuals with aMCI and 82 health individuals based on the recruiting proportions. Then, for a power of 80%, an alpha level of 0.01 to account for multiple testing corrects, and a two-tailed test, we would have the power to detect a difference of correlations between the healthy individuals and individuals with aMCI of 0.453.