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BIOS6623-Project 4

Analysis Plan

Aim 1

To test aim 1a, a separate univariate linear regression will be run on each outcome (change in cognitive test scores and cortical thickness from baseline to year 1) with each of six cytokine/chemokine (IL-6, TNF-alpha, MCP-1, Eotaxin-1, Beta-2 microglobulin, and Alpha 1-antichymotrypsin) baseline levels used as covariates. The results from the univariate analysis will be used in order to generate one multivariate linear regression for each outcome, now controlling for gender, sex, and other possible confounders (such as BMI, NSAID use, and cholesterol levels). Backward selection will then be performed, using AIC to assess model fit, in order to identify the best model of the data. The results of this model will used for interpretation.

To test aim 1b, the same analysis as above will be run, but the primary covariates will now be the change in cytokine/chemokine levels from baseline to year 1.

Aim 2

To test aim 2, a linear regression will be run for each cytokine/chemokine individually with each outcome (change in cognitive test scores and cortical thickness from baseline to year 1). Baseline cytokine/chemokine levels, baseline amyloid deposition and the interaction between the two will be the primary covariates of interest. The results from the univariate analysis will be used in order to generate one multivariate linear regression for each outcome, now controlling for gender, sex, and other possible confounders (such as BMI, NSAID use, and cholesterol levels). Backward selection will then be performed, using AIC to assess model fit, in order to identify the best model of the data. The results of this model will used for interpretation.

Power and Sample size estimations

Since aim 2 is exploratory, the study will be powered based on aim 1, and an estimate of the detectable difference for aim 2 will be calculated (based on a slightly simplified version of the model for computational purposes).

For aim 1, with 80% power and an alpha level of 0.01, a sample size of 287 in needed in order to detect a correlation of 0.2 between the outcomes and a cytokine. Assuming a 10% drop out rate, a total of 319 people should be recruited for the study.

For aim 2, individuals will be grouped into low or high amyloid deposition groups based on the median amyloid value, which would yield approximately 143 individuals in the low group and 144 individuals in the high group. Our hypothesis is now that the correlation between baseline cytokine/chemokine and the outcomes will differ between the two amyloid deposition groups. With 80% power and an alpha of 0.01, we would be able to detect a difference in correlations of 0.408.