Project 2

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Introduction

The purpose of this analysis is to develop an analysis plan and perform sample size calculations for a research grant involving Alzheimer's disease (AD). The goal of the grant is to examine the relationship between inflammation, AD pathology, and cognitive decline over time. The research team would like to have an analysis plan and sample size justification for two particular aims. The aims are as follows:

1. Evaluate longitudinal associations between markers of peripheral inflammation, cognition, and brain structure in Amnestic Mild Cognitive Impairment (aMCI).

2. Examine how markers of peripheral inflammation impact the relationship between AD pathology and clinical progression of aMCI.

The investigative team is interested in a longitudinal evaluation (from baseline to one year follow-up) of innate immune system-associated mechanisms of cognitive decline in aMCI.

Analysis Plan

We will develop two models, one for each aim. The first, addressing aim one, will be a linear model to predict change in memory measured by the California Verbal Learning Test II (CVLT) and cortical thickness from baseline to one year based on six cytokines and chemokines (, whilst adjusting for age and sex, and including baseline cytokine and chemokine level as a covariate. Additionally, for aim 1 part b, we are interested in the same linear model, but rather, adjusting for the change in chemokine and cytokine level as a covariate instead or baseline value. And the second, addressing aim two part a, will be a linear model to predict change in memory from baseline to one year based on the interaction of amyloid deposition and cytokine and chemokine level, while adjusting for inflammatory markers, age, and sex. Multiple cytokines and chemokines will be tested. To adjust for multiple comparisons, we will use the Benjamin-Hochberg False Discovery Rate (FDR). And addressing aim two part b, will be a linear model to predict change in clinical progression (change in

memory) and interactions of amyloid deposition and chemokines and cytokines, or the interactions of cortical thickness and chemokines and cytokines.

Sample Size Justification

This study was powered initially using the association described in Aim 1., the association between basiline cytokine and chemokine levels, and change in memory from baseline. To detect a correlation of 0.25, using a Bonferroni correction [1] to correct for six chemokines and cytokines, and adequate power of 80%. This sample-size calculation yielded a sample size of 186.

Using a sample size of 186 for Aim 2, where there are 93 in each of the low and high amyloid deposition groups (low and high), and a correlation of 0 for the low amyloid group and a correlation of 0.4 for the high amyloid group, yielded a power of only 58%. In order to account for 80% power in Aim 2, the sample size was recalculated. For each of the low- and high-amyloid deposition groups, we now need 138 subjects.

After recalculation, and accounting for 10% attrition, the final necessary sample size is 304 subjects, where 121 will be HC and 183 will be aMCI. All sample size and power calculations were done using G * Power. [2]

Budget Justification

The final aspect of this consult is to develop a budget justification for each of the necessary job functions, including: Data Manager, Senior Biostatistician, Junior Biostatistician and Research Assistant. The total estimate 5-year statistical support budget is $389000, with larger amounts allocated for the first and last years (Table 1.). The job of the Senior Biostatistician is to be the statistical support team supervisor. In the first year the senior on the team will be attending meetings, and advising the junior and Research Assistant, as well as any potential supervision of the Data Manager. The Junior Biostatistician will be the primary analyst on all analyses, with support from the Research Assistant, and supervision from the Senior Biostatiscian. The Data Manager will require little supervision, and may require some support from the Research Assistant. The data manager is only need for the first two and final years.

Please note that each member of the statistical support team expects to be supported both financially, and academically by inclusion as co-authors in any manuscripts where contributions were made. Manuscript writing will be done primarily by the Junior and Research Assistant, with editorial supervision from the Senior Biostatistician.

	Year 1	Year2	Year 3	Year 4	Year 5
Senior Biostatistician					
Salary ($)	115000	115000	115000	115000	115000
Benefits	32200	32200	32200	32200	32200
Effort (%)	15	5	5	5	15
Cost	22080	7360	7360	7360	22080
Junior Biostatistician					
Salary ($)	80000	80000	80000	80000	80000
Benefits	22400	22400	22400	22400	22400
Effort (%)	50	25	25	25	50
Cost	51200	25600	25600	25600	51200
Data Manager					
Salary ($)	65000	65000	NA	NA	65000
Benefits	18200	18200	NA	NA	18200
Effort (%)	50	25	NA	NA	5
Cost	41600	20800	NA	NA	4160
Research Assistant					
Salary ($)	31000	31000	31000	31000	31000
Benefits	13000	13000	13000	13000	13000
Effort (%)	50	25	25	25	50
Cost	22000	11000	11000	11000	22000
Total	136880	64760	43960	43960	99440

Table 1. Five year statistical support budget justification.

References

1. Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyzes using G * Power 3.1: Tests for correlation and regression analyzes. Behavior Research Methods , 41 , 1149-1160
2. Bonferroni, C. E. (1935). Il calcolo delle assicurazioni su gruppi di teste. Studi in onore del professore salvatore ortu carboni, 13-60.