Research Use Statement for Application for Genomic Data from NIAGADS

Please limit to 2,200 characters max. The statement should include the following components:

- Objectives of the proposed research;
- Study design;
- Analysis plan, including the phenotypic characteristics that will be evaluated in association with genetic variants

Title: Integrative modeling and dynamic prediction of Alzheimer's disease

Research Use Statement:

Objective: To develop an integrative modeling framework to incorporate relevant clinical data and genetic markers from genome-wide association studies.

Study design: We propose a novel integrative modeling framework to provide statistically-principled inference, accurate personalized prediction of disease progression, and dynamic prediction update, based on new subject-specific data. This novel model development is important to identify risk and protective factors for AD and target high risk individuals, as well as to personalize the management, prognosis, and treatment selections. The model development and validation will be based on the clinical data from National Alzheimer's Coordinating Center (NACC) and the genetic data (ADC 1-7) from National Institute on Aging Genetics of Alzheimer's Disease Data Storage (NIAGADS). In Aim 1, we will use the clinical data to develop and validate novel AD prediction models which provide more accurate personalized predictions of disease progression and dynamically updates the predictions based on new subject-specific data. In Aim 2, we generalize the prediction models to incorporate relevant genetic markers from genome-wide association studies.

Analysis plan: In Aim 1, we will develop a novel prognostic joint model, based on nonparametric functional data analysis (FDA) to comprehensively evaluate the combined prognostic value of multiple longitudinal clinical variables. The model will provide several critically important personalized measures: a prognostic index, the risk of AD diagnosis, and predictions of health outcome trajectories which can all be dynamically updated over time as new measurements become available. In Aim 2, we aggregate these risk alleles into a polygenic risk score (PRS, or genetic risk score) and include it as a covariate in our prognostic joint model developed in Aim 1.

Non-Technical Summary for Application for Genomic Data from NIAGADS

Non-Technical Summary

This project uses rich multi-modal (clinical and genetic) data to develop a novel integrative modeling framework to provide statistically-principled inference, accurate personalized prediction of disease progression, and dynamic prediction update, based on new subject-specific data. This project not only facilitates the discovery and evaluation of Alzheimer's disease (AD) variables for disease progression, but also is highly relevant for optimizing AD clinical trial design.