

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

Research Use Statement:

Alzheimer's disease (AD) is a neurodegenerative disease in which genetic factors play an important role. Over the past decade, GWAS studies have discovered several genetic variants that are associated with development of AD, especially $\epsilon 4$ in APOE, which is considered the genetic variant with the greatest effect size so far. While substantial progress in advancing the understanding of AD's genetic underpinning has been made, the current findings suggest that many more variants are yet to discover. To complete the search, a large sample size of data and more powerful statistical tools are needed.

Our proposed research aims to develop a new statistical method for testing the association of gene variants with a time-to-event phenotype and to apply the developed method to Memory Aging Project (MAP) and Religious Orders Study (ROS) data to discover variants associated with age at AD onset. Our method accounts for possible gene-gene and gene-environment interactions to enhance the test's power. In the proposed application, our phenotype of interest is age to onset of AD. The genome-wide survival association analysis will be carried out at the SNP, gene or pathway level.

Carefully collected datasets of large sample sizes play a significant role in dissecting AD's genetic architecture due to its complexity. The dataset requested with this application is considerably large that our proposed statistical test is promising to replicate existing findings and identify novel variants when applied to the data.

The proposed uses of requested data sets are consistent with the NIAGADS data use limitations.

Non-Technical Summary for Application for Genomic Data from NIAGADS

The goal of this application is to discover genetic factors with ties to the age at AD onset through the application of our new genetic-survival association test to the data from MAP and ROS. The use of our new method to GWAS of AD may discover novel genetic factors having heterogeneous mechanism in AD development.