NIAGADS

RESEARCH USE STATEMENT AND NON-TECHNICAL SUMMARY

Research Use Statement:

Previously our group has used the GWAS approach to map genes for a range of complex diseases. We have shown that loci overlap between a wide variety of complex traits. We will use the Alzheimer's disease GWAS result summary statistics (Kunkle et al 2019) to assess genetic correlation between AD and disease related traits in the healthy population. Where an interaction effect of *APOE* genotype is apparent we will also use *APOE*-Stratified summary statistics (Jun et al 2015). We will investigate the effect of genetic risk for AD on dementia-related endophenotypes to identify prodromal disease markers. In addition we will use Mendelian randomization approaches to provide evidence about putative causal relations between modifiable risk factors and disease.

We will use the AD GWAS summary statistics together with both summary GWAS data, and individual level data from our extensive in-house GWAS cohorts and publically available datasets including UK biobank. Phenotypic characteristics that will be investigated include neurophysiological and neuroimaging measures, and modifiable lifestyle risk factors.

Non-Technical Summary:

We will investigate overlapping genetic risk variants between Alzheimer's disease (AD) and other traits. We will also test for an association of AD genetic risk variants with brain related changes in individuals who are free from dementia to see early dementia related changes before diagnosis.

The investigation of both risk factors and early changes in the AD process is vital in the fight against dementia. This information will allow us to make lifestyle changes to reduce risk, and enable us to identify people who are at the beginning of the disease process for early intervention.