Epidemiology of Familial Late-Onset Alzheimers Disease

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Country

USA

Title of project or programme

Epidemiology of Familial Late-Onset Alzheimers Disease

Source of funding information

NIH (NIA)

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15/04/2012

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5

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Epidemiology And Longitudinal Studies... Genetics... Human Genome... Neurodegenerative... Neurosciences... Prevention

Research Abstract

DESCRIPTION (provided by applicant): A current theme underlying research for genetic influences in complex diseases such as late onset Alzheimer's disease (LOAD) is the ""common disease, common variant"" hypotheses. This theory posits that multiple common variants underlie the cause of LOAD. The goals of this project is to validate and quantify the clinical impact of these newly identified genetic risk factors, namely SNPs in PICALM, CLU, BIN1, MS4A gene clusters, CD33, CD2AP, ABCA7 and EPHA1 using the multiplex families recruited through the National Institute on Aging-Late Onset Alzheimer's Disease Family Study (NIA-LOAD). The availability of rich phenotypic and molecular genetic information in these families places us in a unique position to estimate the genotype relative risks for these variants and others identified in the recent GWA meta-analyses and the exome sequencing projects currently underway. The proposed longitudinal follow-up, the characterization of additional relatives with ascertainment of antecedent risk factors, and recruitment for autopsy will also greatly benefit the field by expanding the scientific value of the NIA-LOAD Family Study. This resource of families provides distinct advantages for characterizing the impact of genetic variants on disease risk. First, multiplex families are likely to be enriched for genetic variants associated with increased risk, providing increased statistical power to estimate the effects. Second, analysis of these families provides insight into the remaining unknown genetic influences (i.e., the ""residual heritability) as well as antecedent modifying factors that interact with identified genetic variant to influence disease risk. Third, family members at risk are followed at regular intervals, facilitating prospective investigation of the effects of the genetic variants on age-at-onset as wel as the modifying effects of antecedent risk and protective factors. Finally, family data can provide information regarding the influence of known variants on the rate of disease progression and the residual heritability of disease progression. We will address two overall hypotheses: 1) the risk of late onset Alzheimer's disease differs among families and is related to the inheritance of specific genetic variants. The impact of these variants on disease risk is greater in multiplex families than in sporadic cases. Phenocopies and incomplete penetrance in families are related to modifying risk factors. 2) The rate of disease progression is genetically influenced, and related to the same genetic variants that influence disease susceptibility.

Lay Summary

Although the identification of genetic associated with risk of late onset Alzheimer's disease is extremely exciting and vitally important, the clinical impact remains unknown. Families containing multiple affected individuals provides an opportunity to improve understanding of this clinical impact and estimating of the effects of carrying one or more specific genetic variants. Estimation of the risk (or penetrance of genetic variants) for LOAD associated with specific genotypes is critical for determining the clinical validity of geneti testing and screening for these SNPs. Clarifying the ways in which risk or protective factors modify the effects of the variants on disease risk could also point to the development of public health recommendations targeted to specific subgroups.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A