USING QUANTITATIVE TRAITS TO IDENTIFY NOVEL GENES FOR ALZHEIMERS DISEASE AND OTHER COMPLEX TRAITS

https://neurodegenerationresearch.eu/survey/using-quantitative-traits-to-identify-novel-genes-for-alzheimers-disease-and-other-complex-traits/

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Country

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Title of project or programme

USING QUANTITATIVE TRAITS TO IDENTIFY NOVEL GENES FOR ALZHEIMERS DISEASE AND OTHER COMPLEX TRAITS

Source of funding information

NIH (NIA)

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15/09/2016

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1

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... Genetics... Neurodegenerative... Neurosciences... Prevention

Research Abstract
Recent genetic studies of complex traits and diseases have focused on the identification of common variants associated with risk through genome-wide association studies (GWAS). Other aspects such as rate of progression, age at onset and the effect of rare variants are generally not investigated. These studies have been very successful in identifying novel loci associated with many complex diseases. The current proposal focuses on these understudied aspects of disease etiology, namely the role of common and rare genetic variation on quantitative diagnostic and prognostic endophenotypes of Alzheimer’s disease (AD). We will use GWAS and exome-chip data to identify single variants, genes and pathways associated with cerebrospinal fluid (CSF) levels of known AD biomarkers (tau, ptau, A?, YKL40, VILIP1) and other AD-related proteins (CLU, APOE, TREM2). The integration of these endophenotypes will enable us to disentangle the genetic architecture of AD. With this insight, we will then determine whether those SNPs, genes or pathways are also associated with other AD phenotypes (risk, age at onset or progression), and whether we can use genetic information to increase the diagnostic or prognostic ability of these CSF biomarkers. Further, we will utilize Mendelian Randomization and a novel network-based approach to identify causal plasma and CSF proteins involved in AD and other complex traits. We will have access to a unique resource – a large number of CSF and plasma protein levels – allowing us to leverage unbiased approaches to reveal novel biomarkers and endophenotypes associated with AD and complex traits.

Lay Summary
Alzheimer’s disease (AD) is a common neurodegenerative disease with devastating personal, familial, and societal burdens, and there is currently no effective means of prevention or treatment. We will use cerebrospinal fluid levels of known AD biomarkers (tau, ptau, A?, YKL40, VILIP1) and other AD-related proteins (CLU, APOE, TREM2), as endophenotypes for genetic studies to disentangle the genetic architecture of AD. If successful, our research will reveal novel intermediate traits and genetic variants involved in AD and other complex traits, potentially leading to prospective therapeutic targets, and will also provide guidelines for accurate and practical assessments of AD status, which will be invaluable for evaluations of effectiveness of experimental treatments in clinical trials.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

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