Genetic Epidemiology of Cerebrovascular Factors in Alzheimers Disease

https://neurodegenerationresearch.eu/survey/genetic-epidemiology-of-cerebrovascular-factors-in-alzheimers-disease/

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Country

USA

Title of project or programme

Genetic Epidemiology of Cerebrovascular Factors in Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 8,074,140.37

Start date of award

01/08/2016

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Cardiovascular... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Epidemiology And Longitudinal Studies... Genetics... Human Genome... Minority Health for IC Use... Neurodegenerative...

Neurosciences... Prevention... Vascular Cognitive Impairment/Dementia

Research Abstract

PROJECT SUMMARY Clinical criteria for late-onset Alzheimer's disease (LOAD) excludes individuals with "substantial cerebrovascular disease" but as many as up 70% of patients with LOAD have cerebrovascular pathology in addition to amyloid plaques and neurofibrillary tangles at postmortem examination. Whether cerebrovascular damage represents a cause of LOAD, an additional brain insult or whether cerebrovascular pathology interacts with genetic factors remains unknown. The Washington Heights and Inwood, Columbia Aging Project is a large, epidemiological investigation of dementia in a multi-ethnic community in northern Manhattan, New York. The investigators have estimated the ethnic and sex-specific rates of late onset Alzheimer's disease and mild cognitive impairment, conducted longitudinal assessments of cognitive performance, health and lifestyle factors, mood, ADLs, blood pressure, anthropometry, several blood-based biomarkers, genome wide association studies (GWAS), structural MRI and is in the process of completing whole exome sequencing (WES) in 4100 individuals. We intend to take advantage of this multi-ethnic, longitudinal cohort to test hypotheses concerning how genetic variants, cardiovascular and cerebrovascular risk factors and cerebrovascular disease predispose to LOAD and whether these relationships differ by ethnic group. We intend to address three critical questions: 1) Do genetic variants influence both LOAD and cardio-cerebrovascular risk factors independently or do they interact? 2) Do cardio- cerebrovascular risk factors lead to cerebrovascular pathology, present on brain MRI, which in turn simply lowers the threshold for clinical onset of dementia? 3) Are genetic variants unrelated to cardio-cerebrovascular risk factors and simply exacerbate the effects of cerebrovascular pathology leading to LOAD? Or could the reverse be true, that silent cerebrovascular disease exacerbates the effects of genetic variants on LOAD risk? LOAD and cerebrovascular disease are likely to be part of a continuum in which the onset and clinical manifestations of dementia are jointly determined. Thus, investigating the relationship between genes harboring variants, vascular risk factors, cerebrovascular disease and LOAD would advance our understanding of this complex disease process and will help develop potential targets for treatments or preventive measures that are more precise for the individual patient.

Lay Summary

PROJECT NARRATIVE (RELEVANCE) Despite the fact that criteria for late-onset Alzheimer's disease (LOAD) excludes individuals with "substantial" cerebrovascular disease, postmortem studies indicate that up to 70% of patients will have cerebrovascular pathology in addition to amyloid plaques and neurofibrillary tangles. Whether cerebrovascular damage represents a cause of LOAD, an additional brain insult or whether cerebrovascular disease interacts with LOAD-related genetic factors remains unknown. Cardiovascular and cerebrovascular risk factors (e.g. smoking, hypertension, hyperlipidemia) are associated with an increased risk of LOAD as well as cardiovascular and cerebrovascular diseases. LOAD related genetic influences such as APOE-e4 and loci from genome wide association studies implicate pathways also relevant to both LOAD and vascular disease: inflammation, immune function and lipids. In this proposal we will investigate whether cardio- cerebrovascular risk factors, cerebrovascular disease and LOAD share genetic influences.

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