African Ancestry and the Genomic Architecture of AD and Other Common Neurodegenerative Disease Neuropathologies

https://neurodegenerationresearch.eu/survey/african-ancestry-and-the-genomic-architecture-of-ad-and-other-common-neurodegenerative-disease-neuropathologies/

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Country

USA

Title of project or programme

African Ancestry and the Genomic Architecture of AD and Other Common Neurodegenerative Disease Neuropathologies

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 10,278,138.53

Start date of award

15/09/2016

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)... Biotechnology... Brain Disorders... Cerebrovascular... Dementia... Epidemiology And Longitudinal Studies... Genetics... Human Genome... Lewy Body Dementia... Minority Health for IC Use... Neurodegenerative... Neurosciences

Research Abstract

ABSTRACT The proposed study, African Ancestry and the Genomic Architecture of AD and Other Common Neurodegenerative Disease Neuropathologies, is in response to PAR-15-356. To be called the Study of Ancestry and Neurodegenerative Diseases (SAND), the proposal is highly responsive to the RFA whose funding purpose is to support projects in cognitive epidemiology and genetics/genomics relevant to AD, especially projects enhancing the power of multiethnic cohort studies, exploring trends in the risk of AD and their explanation via putative risk and protective factors, and by collecting and sequencing DNA samples from well characterized cases and controls. The overall goal of SAND is to identify genomic variants of African and European Ancestry associated with AD and other common neurodegenerative disease pathologies, including: cerebrovascular disease, Lewy body disease, TDP-43, and hippocampal sclerosis. We will leverage a unique resource to procure post-mortem data on brain pathologies, and genomic data, from 10,000 admixed Brazilian brains. In an innovative series of admixture analyses applying cutting edge genomic approaches, we will characterize the entire genome for African, European, and Native Brazilian Ancestry. Aim 1 will use 6000 brains in a discovery GWAS, followed by replication in Aim 2 with 4000 additional brains, and a joint analyses of all 10,000. Additional analyses will determine the relevance of the variants that emerge to clinical dementia among the same 10,000 persons. Translational Aims 3 and 4 will extend the findings to North Americans by examining the relation of the genomic variants to AD in African Americans and non-Latino Whites from the USA. Additional analyses will leverage available neuropathologic and neuroimaging data from the USA for further extension of the findings. The proposed study brings together a unique team of neurologists, epidemiologists, neuropathologists, geneticists, statisticians, and geriatricians from the USA and Faculty of Medicine at the University of São Paulo to conduct a study that is simply not possible in the USA. The study will deliver novel genomic variants associated with the pathologies of the five most common causes of dementia. By leveraging neuropathologic traits, the approach can target the full spectrum of each disease from asymptomatic to clinically demented. Finding additional genomic variants related to neuropathologic traits of African and European ancestry will greatly facilitate our understanding of the complex processes that lead to dementia and have a strong and sustained effect on the field.

Lay Summary

PUBLIC HEALTH IMPACT The proposed study will identify genomic variants in loci of African and European ancestry associated with the pathologic indices of AD, LBD, CVD, HS and TDP-43, and will determine the clinical relevance of these loci by examining their association with dementia in older African and European Americans in the USA. Finding genomic variants related to neuropathologic traits of African and European ancestry will facilitate our understanding of the processes that lead to dementia and have a strong and sustained impact on the field of Aging and AD, especially with under-represented minorities.

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