Brain Imaging, APOE & the Preclinical Course of Alzheimers Disease

https://neurodegenerationresearch.eu/survey/brain-imaging-apoe-the-preclinical-course-of-alzheimers-disease/

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Country

USA

Title of project or programme

Brain Imaging, APOE & the Preclinical Course of Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 9,279,898.17

Start date of award

01/05/2008

Total duration of award in years

17

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)... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Genetics... Minority Health for IC Use... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): We request five years of continued support for the longitudinal study of cognitively normal persons with two, one, or no copies of the apolipoprotein E (APOE) ¿4 allele, the major late-onset Alzheimer's disease (AD) susceptibility gene. This study utilizes an extensive battery of brain imaging, fluid biomarker, cognitive, and other measurements. Our program includes a cohort of 35 ¿4 homozygotes, 50 ¿4 heterozygotes, and 75 ¿4 non-carriers to permit detection, tracking, and scientific study of preclinical AD in persons at three levels of risk and set the stage for the accelerated evaluation of preclinical AD treatments. It also includes a cohort of 15 ¿4 carriers and 30 ¿4 non-carriers from the Latino community to help establish the extent to which our findings are relevant to this understudied minority group. Persons in each genetic group were demographically matched and initially late middle-aged; their current age is 67 years (range 49-81). And, all participants have had genome-wide single nucleotide polymorphism (SNP) genotyping. During the proposed funding period participants will have PET measurements of regional cerebral metabolic rates of glucose (CMRgl) and fibrillar amyloid-¿ (A¿) deposition, an expanded magnetic resonance imaging (MRI) battery, serum and plasma samples drawn and stored, and an extensive battery of clinical, neuropsychological, functional, and behavioral tests every two years. At least half will have longitudinal cerebrospinal fluid (CSF) samples drawn, stored, and assayed every two years. For nearly two decades our overriding goals have been to characterize the biomarker and cognitive measurements associated with preclinical AD and provide a foundation for the accelerated evaluation of promising prevention therapies. With the growing number of participants progressing to mild cognitive impairment (MCI) and dementia due to AD, we will begin to characterize the extent to which different biomarker and cognitive measurements predict subsequent rates of clinical progression. With an expanded arsenal of biomarkers and data analysis tools, we will further characterize the biological processes involved in the predisposition to AD. With our preclinical endophenotypes and complementary datasets, we will help clarify relationships between genetic risk factors and potentially dissociable elements of AD. With an expanded data and sample sharing program, we will provide an accessible worldwide resource to advance the study of preclinical AD. With this foundation of participants, samples, and longitudinal data, we will prepare for the evaluation of an A¿-modifying agent in cognitively normal APOE ¿4 carriers and help to advance a new era in AD prevention research.

Lay Summary

PUBLIC HEALTH RELEVANCE: Our longitudinal research program is designed to characterize the biological and cognitive changes that precede the onset of memory and thinking problems in people at three levels of genetic risk for Alzheimer's disease (AD), develop faster ways to test prevention therapies, and make it possible to find treatments that work without losing another generation. It will use an expanded battery of brain imaging techniques, spinal fluid and blood samples, and memory and thinking tests every two years for the continued study of 160 people with 2, 1 or no copies of the APOE4 gene every two years. It will continue to detect and track AD before the onset of symptoms and determine the extent to which different measurements predict the onset of memory and thinking problems; it will investigate the extent to which the growing number of confirmed genetic risk factors contribute to different elements of the disease; it will help us prepare for the Alzheimer's Prevention Initiative (API's) next prevention trial and help to advance a new era in AD prevention research.

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