Alzheimer neuroimaging-biomarkers in pre-clinical cognitive decline from a population-based study

https://neurodegenerationresearch.eu/survey/alzheimer-neuroimaging-biomarkers-in-pre-clinical-cognitive-decline-from-a-population-based-study/

Principal Investigators

SNITZ, BETH ELLEN

Institution

UNIVERSITY OF PITTSBURGH AT PITTSBURGH

Contact information of lead PI
Country

USA

Title of project or programme

Alzheimer neuroimaging-biomarkers in pre-clinical cognitive decline from a population-based study

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,073,246.79

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 including Alzheimer's Disease Related Dementias (AD/ADRD)... Basic Behavioral and Social Science...

Behavioral and Social Science... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Epidemiology And Longitudinal Studies... Health Disparities for IC Use... Neurodegenerative... Neurosciences... Prevention

Research Abstract

? DESCRIPTION (provided by applicant): We propose here a novel investigation that directly addresses two of the most vexing questions in Alzheimer Disease (AD) research: (1) How does early AD start to diverge from normal cognitive aging? (2) Are biomarker studies in clinical research settings generalizable to the general population? This Project will investigate in vivo brain imaging of the two neuropathological hallmarks of AD in older adults evidencing pre-clinical cognitive decline. Specifically, we will use Pittsburgh Compound-B (PiB)-PET to image amyloid-beta (A?) plaque deposition, and [F-18]AV-1451 to image aggregated tau pathology. We will apply these imaging tools to a carefully selected and characterized group of recruited participants, leveraging 4-8 years of serial, annual cognitive data from a population-based study to define pre-clinical cognitive decline. The result will be a unique nested case-control design of `decliners' and `non-decliners' within the constraints of clinically normal cognitive status. This individual-difference characterization from the parent study allows us to probe the divergence between early-stage AD trajectories and normal-aging trajectories, with baseline and 30-month follow-up PET imaging, and continued, annual clinical-cognitive monitoring for incident MCI. We will test three competing models of early-AD vs. normal-aging-variant pathways with specific hypotheses about associations and temporal order among: 1) pre-clinical decline, 2) A? deposition, 3) mesial and neocortical tau deposition, and 4) progression to MCI. Further, using known epidemiologic dementia risk factors for AD measured 8 years earlier in the parent study (lifestyle, health-history, cognitive reserve, and vascular), we will build predictive models for presence of preclinical A? and tau pathology at baseline, as well as their dynamic rate of change over 2.5 years. Finally, we will evaluate generalizability and external validity of study results (i.e., risk-protective associations with PET-imaging outcomes) back to the original larger population cohort (N=1982), using propensity-weighted modeling. This Project will advance knowledge of how the processes of age-related cognitive decline intersect with the development of AD. Findings will help elucidate the sequence of pathologic events early in AD and thereby inform prevention strategies regarding the timing of interventions. Inferences from study results will generalize beyond highly selected clinic or convenience samples typical of neuroimaging studies, to date, to a more socioeconomically inclusive representation of older adults.

Lay Summary

PUBLIC HEALTH RELEVANCE This Project will study whether subtle changes in memory and thinking in older age may (or may not) be the starting point for early Alzheimer Disease. The Project will do this by examining brain imaging of the abnormal proteins of Alzheimer Disease in older adults without frank memory problems. The results will lead to better understanding of when and how the disease process starts and therefore help determine when is the optimal time to intervene and eventually prevent the full disease syndrome.

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