The Longitudinal Course OF Imaging Biomarkers in People At RISK of AD

https://neurodegenerationresearch.eu/survey/the-longitudinal-course-of-imaging-biomarkers-in-people-at-risk-of-ad/

Principal Investigators

JOHNSON, STERLING C

Institution

UNIVERSITY OF WISCONSIN-MADISON

Contact information of lead PI
Country

USA

Title of project or programme

The Longitudinal Course OF Imaging Biomarkers in People At RISK of AD

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 6,572,844.95

Start date of award

15/08/2004

Total duration of award in years

11

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... Diagnostic Radiology... Epidemiology And Longitudinal Studies... Neurodegenerative... Neurosciences... Prevention

Research Abstract

The goal of this ongoing R01 is to chart the progression of pathobiologic markers of presymptomatic Alzheimer's Disease (AD) and their effect on neural function and cognition in a late-middle-aged cohort enriched with risk for AD. There is an appreciable gap in knowledge about the temporal disease course in this age range that this ongoing project has been directly addressing with serial multimodal imaging including amyloid, cerebrospinal fluid (CSF) collection, and serial cognitive measurement. In the next funding cycle we will add a new positron emission tomography (PET) imaging technique sensitive to fibrillar tau [F-18]THK5351 indexing neurofibrillary pathology. In the prior funding period we recruited 179 individuals from a registry of 1,545 people at risk for AD known as WRAP (Wisconsin Registry for Alzheimer's Prevention). We found that [C-11]PIB amyloid burden is detectable in 20% of people with parental history of AD at a mean age of 60. Baseline amyloid is more extensive in the presence of higher CSF total tau levels, and 2-year increases in PiB amyloid are significantly predicted by higher baseline CSF tau. The hypothesis for this renewal is that tau- related neurofibrillar pathology begins early (in accord with the neuropathology literature) in people at AD risk and its strategic spatial burden explains changes in amyloid, neural function and cognitive decline. Aim 1: To test the premise that amyloid burden is necessary but not sufficient to evoke preclinical cognitive change. We will examine effects of longitudinal amyloid and tau change on episodic memory trajectories over time in 235 at risk individuals including all subjects we previously enrolled and follow them over 2 years with advanced multimodal imaging and CSF. Aim 2: To assess the effects of tau and amyloid imaging on MRI and CSF indicators of neural injury and function. Aim 3: To develop a multimodal disease marker to maximize efficiency of clinical trials in preclinical AD. Following our work in creating tools for efficient clinical trials in MCI, we will extend these concepts to the pre-MCI phase of disease utilizing deep learning architectures with tau, amyloid and structural imaging inputs. We will also examine change over time in tau, amyloid and cognition as outcomes. As any of these features considered singularly may be affected by age, and as amyloid and tau may be `necessary but not sufficient' by themselves, a derived multimodal marker may have eventual clinical utility in enriching prevention trials with those most likely to progress, and increasing power to detect change attributable to preclinical interventions. Significance: Relative tau and amyloid imaging profiles have not been empirically established in the presymptomatic time frame and this information is urgently needed to identify incipient disease. No comparable studies exist regarding the evolution of tau and amyloid signal in the critical late-middle-age time frame of preclinical AD. This ongoing project represents a unique opportunity to examine the earliest determinants of AD progression, when treatments may be most meaningful.

Lay Summary

PUBLIC HEALTH RELEVANCE/ NARRATIVE Identifying the earliest neuropathological features of AD including tau and amyloid pathology will improve early detection and inform clinical trials in the presymptomatic time frame. This project will examine these features with advanced imaging methods in a cohort at risk for AD who are largely asymptomatic. An outgrowth of the project will be information about the rate of change in AD pathology which can help us plan clinical trials in this population using derived outcomes about the brain itself, thereby reducing the number of subjects needed in a trial and increasing sensitivity to detecting change.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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N/A

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