Amyloid Pathology and Cognition in Normal Elderly

https://neurodegenerationresearch.eu/survey/amyloid-pathology-and-cognition-in-normal-elderly/

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Country

USA

Title of project or programme

Amyloid Pathology and Cognition in Normal Elderly

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NIH (NIA)

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01/03/2005

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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)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): The goal of this revision application (competing supplement) is to integrate the assessment of brain tau deposition as a unique marker of “”neurodegeneration”” (ND). Our guiding concept is that isolated medial temporal tau (MT-tau) in the hippocampus and entorhinal cortex (i.e., Braak stages I-III) is more a factor of aging than Alzheimer’s disease (AD) pathology, but neocortical tau (NC-tau; Braak IV-VI) is typically amyloid-beta (A?)-dependent and part of the AD pathophysiological process and is thus a marker of ND. The central goal of the project as a whole remains further understanding the association of asymptomatic A? deposition and ND markers (NC-tau, hippocampal volume and cerebral metabolism) with progression to clinical cognitive impairment – as A? deposition alone cannot fully explain cognitive variability. In addition to the A? and ND markers we currently collect using Pittsburgh Compound-B (PiB) positron emission tomography (PET), structural MRI and [F-18]fluorodeoxyglucose (FDG) PET, in this revision, we now propose to collect [F-18]AV-1451 (formerly T807) PET data on tau deposition to more fully understand the biomarker correlates of cognitive decline. Our cohort has now matured to the point that the occurrence of incident MCI and incident A?-positivity [incident-A?(+)] is sufficient to address other hypothese that could not be properly addressed until sufficient follow-up was in place – as is the case now. One critical hypothesis that we can now test is that A?(+) cognitively normal older adults are at high risk to develop clinically-significant cognitive impairment (i.e., MCI) (Aim 1). In addition, ur growing cohort of incident-A?(+) subjects allows us to observe the transition from being A?-negative to the earliest A?-positive [A?(+)] state (Aim 2.2). Also, our longitudinal fMRI data in incident-A?(+) individuals will allow us to test for the first time the assumption that higher functional activity/connectivity in A?(+) individuals reflects a true increase from baseline, and ot a maintenance of lifelong high activity/connectivity and will aid us in predicting when A?(+) individuals will develop cognitive decline (Aim 3). Finally, we propose to enhance our cohort to more effectively address the relationship between A? deposition and cognition by broadening the cognitive range of our cohort (Aim 2.1). We will interpret all of these data in the context of neurodegeneration markers (tau PET, atrophy and hypometabolism) as well as A? PET. The overall impact and significance of this study will be to further our understanding of: 1) the incidence of asymptomatic A?and tau deposition; 2) the relationships between early A? and tau deposition and other neurodegeneration markers, functional activity/connectivity and cognition; and ultimately, 3) the relationship of asymptomatic A? and tau deposition and clinical MCI (and the timing of that association). Innovative aspects of this project include: 1) the study of incidet MCI in A?(+) individuals; 2) the study of incident-A?(+) cases; 3) the longitudinal study of the natural history of functional activity/connectivity in incident-A?(+) individuals and its relationhip to progression to MCI; and 4) the integration of tau PET.

Lay Summary

PUBLIC HEALTH RELEVANCE: Our field has recently initiated four NIH-funded trials aimed at the prevention of Alzheimer’s disease (AD) by targeting the amyloid-beta protein that is believed to start building up in the brains of many older adults as much as 10-15 years before any memory problems occur. However, we have no firm understanding of the time frame or risk of progression from this asymptomatic “”amyloid-positive”” state to the onset of memory problems and Alzheimer’s disease or the role of tau deposition in the transition. We propose to use state-of-the-art brain imaging to continue the study of a group of older adults who have already been studied by us for up to 10 years to assess how the amyloid and tau deposition lead to the development of memory problems and Alzheimer’s disease, thus facilitating the interpretation of the ongoing prevention trials.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

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Alzheimer's disease & other dementias

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2016

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