Impact of Amyloid and Tau on the Aging Brain: The Harvard Aging Brain Study

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Country

USA

Title of project or programme

Impact of Amyloid and Tau on the Aging Brain: The Harvard Aging Brain Study

Source of funding information

NIH (NIA)

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15/07/2016

Total duration of award in years

7

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... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Health Disparities for IC Use... Neurodegenerative... Neurosciences... Prevention

Research Abstract
? DESCRIPTION (provided by applicant): The Harvard Aging Brain Study (HABS) PPG was launched just over five years ago with the goal of elucidating the biological and clinical significance of amyloid ?-protein (A?) accumulation in clinically normal (CN) older humans. We have accomplished a great deal over the current funding cycle, including the successful recruitment of more than 300 older individuals (ages 60-90) who are diverse in ethnicity and socioeconomic status. We have published over 70 manuscripts, and contributed to international guidelines and prevention trial design. We have found consistent evidence that the nearly 1/3 of older CN with elevated A?, detectable on PiB-PET imaging, also demonstrate evidence of impaired synaptic function and neurodegeneration, as well as subtle but detectable changes in cognition. However, our findings thus far support the hypothesis that A? accumulation is necessary but not sufficient to predict imminent cognitive impairment. Thus it is imperative that we find additional markers to accurately predict cognitive decline along the Alzheimer's disease (AD) trajectory. Neuropathologic studies have long suggested that the other hallmark pathology of AD – neurofibrillary tangles (NFTs) and other tau aggregates (referred to as Tau) – correlate more strongly with synaptic and neuronal loss, and the cognitive symptoms of AD. Remarkable recent advances in PET imaging now allow us to image Tau pathology in vivo. Our preliminary Tau PET data using 18F-T807 suggest this new technology will prove extremely valuable in our quest to elucidate the link between A?, Tau, and cognitive decline. Our preliminary T807 data confirm previous autopsy reports that MTL Tau accumulation is very common after age 60, but it remains unknown how this pathology contributes to ""age-related"" memory change, with or without A?. Based on our preliminary work, we postulate that A? accelerates the spread of Tau both within and beyond the MTL, disrupting function and initiating neurodegeneration in distributed brain networks, resulting in cognitive decline. To investigate this further, we propose 4 integrated Projects, supported by 4 Cores. Project 1: Investigate the relationship of PET A? and Tau measures to glucose metabolism, synaptic dysfunction, and cortical thinning. Project 2: Investigate the neuropathologic correlates of T807, and neuronal, glial and synaptic alterations associated with Tau in brain specimens from cohorts similar to the HABS population. Project 3: Implement advanced MRI techniques to detect A?- and Tau-related alterations in intrinsic brain networks at the individual subject level. Project 4: Detect early alterations in cognitive function through novel iPad tests and task-fMRI, and investigate the interactions between A? and Tau in the prediction of longitudinal cognitive decline. This PPG renewal will leverage an outstanding group of multidisciplinary investigators, access to cutting-edge imaging and laboratory technology, and an extremely well-characterized cohort with longitudinal multi-modality imaging and sensitive cognitive assessments to determine the factors that best predict resilience vs. progression along the trajectory of preclinical AD.

Lay Summary
PUBLIC HEALTH RELEVANCE: The Harvard Aging Brain Study Program Project Grant seeks to understand the earliest brain changes that will predict whether an older individual will develop memory loss and eventual cognitive decline associated with Alzheimer's disease or whether

they will demonstrate resilient brain aging. Our study utilizes special imaging tests to detect evidence of the abnormal accumulation of proteins associated with Alzheimer’s disease, such as amyloid plaques and tau tangles, in the brains of older people who do not yet show any symptoms of the disease. Our study has tremendous potential public health impact; if we can accurately identify people at high risk for cognitive decline, we can begin treatments aimed at these early brain changes and perhaps ultimately prevent Alzheimer’s disease dementia.

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

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