Neural and Biochemical Mechanisms of Cognitive Aging

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Country

USA

Title of project or programme

Neural and Biochemical Mechanisms of Cognitive Aging

Source of funding information

NIH (NIA)

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€ 3,877,536.70

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15/09/2009

Total duration of award in years

6

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... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Mental Health... Neurodegenerative... Neurosciences

Research Abstract

PROJECT SUMMARY/ABSTRACT This project is focused on the basis of altered memory function at the boundary between normal aging and what has recently been described as preclinical Alzheimer's disease (AD). Both aging and AD are characterized by the aggregated proteins tau and ?-amyloid (A?). In the model that underlies the project, tau in the medial temporal lobe (MTL) is hypothesized as a major factor associated with mild age-related decline in episodic memory and disruption of hippocampal function. In preclinical AD, however, early A? accumulation occurs in the posterior cingulate (PCC) and retrosplenial cortex (RSC); as this A? accumulation occurs, tau accumulation is found outside the MTL and connectivity of the hippocampus to neocortex (PCC/RSC) is disrupted. These effects severely disrupt memory function and also affect other cognitive processes. We plan to test this model by recruiting a lifespan cohort of healthy people ranging in age from 20 to 90. The previous phase of this study recruited 157 older subjects, all of whom will have approximately 6 years of longitudinal follow up. All participants will undergo tau imaging using the novel ligand [18F]AV-1451, amyloid imaging using [11C]PIB, structural MRI scanning, and resting state MRI scanning. Recruitment of those over 60 will be balanced by PIB status (PIB+/PIB-). All subjects will also be studied using task-based functional MRI (fMRI) while they perform an episodic memory task using a pattern separation paradigm. In this task subjects must discriminate between visual stimuli that are similar, but not identical, to previously viewed stimuli. Identification of these similar stimuli as "old" is evidence of pattern completion and failure of memory processing; this has characteristically been associated with hippocampal hyperactivation which is likely detrimental. We anticipate that increasing MTL tau will bias subjects towards pattern completion, and that tau accumulation, and A?- related hippocampal disconnection will be related to hippocampal hyperactivation. Other key hypotheses are that (1) age will be associated with increased MTL tau, while A? will be associated with tau in neocortex and (2) episodic memory function will be related to MTL tau while global cognition will be related to both A? and neocortical tau. The ultimate goal of the project is to define relationships between age, tau, and A? and to show that the mechanisms underlying memory failure in aging and preclinical AD involve qualitatively different effects of A? and tau on behavior, hippocampal connectivity and hippocampal function. Differentiating normal cognitive aging from AD by studying these effects will be important for early detection of AD, selection of subjects for clinical trials, and developing diagnostic and therapeutic approaches to non-AD age-related cognitive decline.

Lay Summary

PROJECT NARRATIVE As we age, numerous alterations in brain function occur, some of which are benign and others more malignant. This project focuses on the borderland between normal brain aging, associated with mild memory loss, and the early stages of Alzheimer's disease (AD), associated with more severe and progressive memory loss. By using PET scanning with agents that permit detection of two abnormally accumulating proteins in the brain – ?- amyloid and tau – we will define the mechanisms underlying these different types of memory loss and thereby help to understand differences between normal aging and early AD.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
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