Evolution of memory related fMRI activation over the course of MCI and AD

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Country

USA

Title of project or programme

Evolution of memory related fMRI activation over the course of MCI and AD

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,136,088.99

Start date of award

01/05/2006

Total duration of award in years

10

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... Clinical Trials and Supportive Activities... Dementia... Diagnostic Radiology... Mental Health... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): This is a competing renewal application of R01-AG02745 to characterize memory related changes in functional magnetic resonance imaging (fMRI) activity over the course of mild cognitive impairment (MCI) due to Alzheimer's disease (AD). We have been very successful in accomplishing our Aims over the first funding cycle of this grant, recruiting over 140 older subjects and publishing over 40 scientific manuscripts in high impact journals. We have demonstrated a characteristic pattern of functional disruption in a distributed memory network that: 1) has good test-retest reproducibility; 2) is associated with amyloid-¿ deposition as estimated with PiB-PET imaging; 3) predicts rapid cognitive decline, and 4) remains dynamic over the course of MCI. The next phase of this R01 will build on our previous discoveries, and leverage our strong group of multi- disciplinary investigators, to translate our findings into measures that are feasible to track progression of MCI and detect an early signal of efficacy in ""Proof of Concept"" clinical trials for early symptomatic stages of AD. n addition, we propose to probe the mechanistic underpinnings of aberrant fMRI activity, utilizing a novel combination of multi-modality imaging techniques. Aim 1 will build on our fMRI work with face-name paradigms to develop and validate short clinical versions of the face-name associative memory exam (FNAME) that are sensitive to the effects of early AD pathology and will track progression over the continuum of MCI. Aim 2 will investigate the relationship between memory task fMRI and resting state functional connectivity that will be more feasible in multi-center clinical trials. We predict that early task-related hyperactivity will precede and predict progression of functional disconnection during the resting state. Aim 3 will test the hypothesis that the observed hyperactivity is an indicator of early excitotoxicity that will predict synaptic failure, neuronal loss and rapid clinical decline. We will employ a novel PET ligand (18-F-PEB) for the metabotropic glutamate receptor, mGluR5, which has been implicated in both learning and in excitotoxicity, in combination with 11-C-PiB amyloid imaging, 18-F-FDG glucose metabolism, with longitudinal functional and structural imaging to elucidate the neural mechanisms underlying progressive memory impairment over the course of early AD.

Lay Summary

This project will develop and optimize cognitive and imaging biomarkers to track progression through the early symptomatic stages of Alzheimer's disease. Building on our discoveries in the first funding cycle of this R01, we will develop sensitive face-name associative memory tests and functional MRI paradigms that are feasible for use in ""Proof of Concept"" clinical trials. We will also utilize a unique combination of PET and MR imaging measures to probe the mechanistic underpinnings of the functional changes we have observed over the course of mild cognitive impairment (MCI).

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