

Memory network dysfunction as an early marker of preclinical Alzheimers Disease

<https://neurodegenerationresearch.eu/survey/memory-network-dysfunction-as-an-early-marker-of-preclinical-alzheimers-disease/>

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Country

USA

Title of project or programme

Memory network dysfunction as an early marker of preclinical Alzheimers Disease

Source of funding information

NIH (NIA)

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19/09/2014

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

network dysfunction, presenilin-1, Alzheimer's Disease, Memory, tau Proteins

Research Abstract

DESCRIPTION (provided by applicant): Finding a disease-modifying treatment for Alzheimer's disease (AD) is one of the greatest challenges of our generation. There is a consensus in the

scientific community that the key to success in treating AD is to begin therapies as early as possible before significant brain damage occurs. Thus characterizing preclinical biomarkers and early detection paradigms, which is the focus of my work, is paramount. A distributed network of brain regions, including the hippocampus, adjacent cortical regions in the medial temporal lobe, and other brain regions sub-serve memory function. Paired associative memory tasks that rely on this network have been shown to be sensitive to subtle deficits in the preclinical stages of AD. I propose to build upon my previous research with autosomal dominant AD to establish conceptual frameworks and comparisons with late-onset sporadic AD with an emphasis on the analysis of memory network disruption as an early marker of preclinical AD. To this end, I will leverage my access to two extraordinarily rich preclinical AD groups, 1) the Colombian kindred with Presenilin 1 E280A (Glu280Ala) mutation, estimated to have 1,500 mutation carriers, and 2) a group of asymptomatic older individuals who are participants in the Harvard Aging Brain Study (HABS) at MGH and are considered at high risk (by molecular pathology imaging) to develop late- onset sporadic AD. The primary goals of this application are to: (i) investigate abnormalities of associative-memory processes as a possible cognitive marker of preclinical AD; (ii) investigate brain hyper-activity/hyper- connectivity as a marker of early AD pathology; and, (iii) examine the role of tau and amyloid aggregation in memory network dysfunction. The research proposed in this application will use cognitive measures, fMRI and PET imaging to examine the hypothesis that memory network dysfunction occurs in early preclinical stages of Alzheimer's disease. This research will provide insight into the interaction of cognitive and brain function biomarkers in preclinical AD. In particular, this work will provide new understanding of how amyloid and tau pathology impact memory function very early in the disease process, and their role in subsequent neuronal death and cognitive decline.

Lay Summary

PUBLIC HEALTH RELEVANCE: Functional alterations in memory networks will be study in presymptomatic individuals with familial Alzheimer's disease (AD) caused by the mutation E280A in the Presenilin-1, and cognitively-normal older individuals at high risk (by molecular pathology imaging) to develop AD. This research will provide new understanding of how amyloid and tau pathology impact memory function in preclinical stages of the disease, and their role in subsequent neuronal death and cognitive decline.

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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