High-resolution imaging of hippocampal mechanisms in age-related memory decline.

https://neurodegenerationresearch.eu/survey/high-resolution-imaging-of-hippocampal-mechanisms-in-age-related-memory-decline/

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Country

USA

Title of project or programme

High-resolution imaging of hippocampal mechanisms in age-related memory decline.

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NIH (NIA)

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€ 1,772,690.83

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15/09/2014

Total duration of award in years

3

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)... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): Memory decline is a frequent symptom among aging adults. A substantial literature points to an age-related deterioration of episodic memory (the capacity to encode and subsequently retrieve memories for events). The hippocampus is critical for episodic memory, and comprises multiple subfields thought to contribute differentially to pattern separation and pattern completion – fundamental mechanisms of memory — and to exhibit differential vulnerability to age. In particular, selective changes in hippocampal subfield structure and function may drive age-related changes in memory performance, and these changes may relate, in part, to preclinical evidence of Alzheimer's disease (AD) pathology. Recent developments in high-resolution magnetic resonance imaging (MRI), including (a) high-resolution functional MRI (hr-fMRI) combined with powerful multivariate analysis methods and (b) ultra-high field 7T structural MRI, provide a means to study human hippocampal subfields in vivo and to examine hippocampal mechanisms of memory. Here, we propose to apply these innovative MRI techniques to a large, 200-person cross-sectional population of healthy older adults (e60 years) to test the following central hypothesis: In older adults, selective changes in hippocampal subfield function and structure drive mechanistic changes in pattern separation and pattern completion, which relate to age-related decline in associative recollection (a central form of episodic memory) and, in part, to preclinical AD pathology. In Aim 1, we will use hr-fMRI at 3T, along with representational similarity analysis and multivoxel pattern analysis, to quantitatively estimate hippocampal pattern separation at encoding and pattern completion at retrieval, with the latter indexed by cortical reinstatement; we further aim to relate these quantitative measures of hippocampal function to associative recollection and item recognition memory performance. In Aim 2, we will use high-resolution structural MRI at 7T to quantify hippocampal subfield structural atrophy, and we will relate these structural measures to our quantitative hr-fMRI indices of pattern separation and cortical reinstatement, as well as to memory behavior. In Aim 3, we will relate cerebrospinal fluid assays of AD biomarkers (Abeta42, tau, and phospho-tau proteins) to hr- fMRI functional metrics, 7T MRI hippocampal subfield structural metrics, and memory behavior. The novelty and power of the proposed research, which is grounded in strong preliminary data, derives from our ability to synthesize data across these Aims to discover how function, structure, and early pathology interact to affect episodic memory in aging. The project may ultimately inform diagnostic and intervention approaches for addressing age-related memory decline in unimpaired older adults, as well as those suffering from amnestic Mild Cognitive Impairment and AD.

Lay Summary

PUBLIC HEALTH RELEVANCE: Memory decline among older adults is not just a frequent annoyance, but also an impediment to daily function. The hippocampus a brain area responsible for the formation and retrieval of new memories demonstrates age-related (1) alterations in neural function, (2) atrophy, and (3) accumulation of disease- related pathology. Using innovative, high-resolution brain imaging technologies and biomarker analysis, the proposed work aims to discover how these age-related hippocampal changes converge to cause memory decline.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:
Alzheimer's disease & other dementias

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2016

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