1H and 31P MR Spectroscopy of Hippocampal Hyperactivity in Aging and MCI

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Country

USA

Title of project or programme

1H and 31P MR Spectroscopy of Hippocampal Hyperactivity in Aging and MCI

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

389793.578

Start date of award

15/05/2016

Total duration of award in years

1

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Basic Behavioral and Social Science... Behavioral and Social Science... Bioengineering... Brain Disorders... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Mental Health... Neurodegenerative... Neurosciences... Vascular Cognitive Impairment/Dementia

Research Abstract

? DESCRIPTION (provided by applicant): Our memory changes as we age. Age-related

memory decline in and of itself represents a significant public health impact, but cognitive decline – and in particular memory decline – has been shown to be an important risk factor for Alzheimer's Disease (AD). Examining neurocognitive aging will help us better characterize pathological and non--pathological changes in the brain throughout the lifespan and identify preclinical markers for cognitive decline. The goal of this proposal is to test key predictions of neurocognitive model of aging and amnestic Mild Cognitive Impairment (aMCI) that suggests changes in connectivity and activity within structures in the MTL underlie behavioral deficits in memory. In particular, in both rodent and human studies, the hippocampus exhibits ""hyperactivity"" – a potentially dysfunctional state that has been tied to behavioral shifts away from successful mnemonic discrimination (derived from pattern separation and leading to accurate memory for details) and towards over--generalization (derived from pattern completion). To this end, reduction of this hyperactivity in aMCI using a low--dose antiepileptic s associated with improved performance in a mnemonic discrimination task that we have used many times to index hippocampal function and age-- and aMCI--related changes. Without the direct recording of hyperactivity possible in rodents, human studies have often relied on the indirect and relative measures provided by BOLD fMRI. Here, we propose a directed, novel, metabolic investigation into the neuronal pathways responsible for this hyperactivity to determine the applicability of the rodent model. Using magnetic resonance imaging spectroscopy (MRS) and metabolite imaging methods, we aim to measure the metabolic signatures for excitatory and inhibitory activity (e.g. GABA, glutamate, choline, etc.), testing th hypothesis that hippocampal hyperactivity arises from the release of inhibition on the CA3 recurrent collaterals within the hippocampus, leading to an increase in excitatory activity and a decrease in inhibitory activity when the hippocampus is actively processing new information. We propose utilizing two MRS scans, 1H--MRS and 31P--MRS to determine which scan is more sensitive to this hyperactivity. Finally, we will evaluate if these MRS measures of hyperactivity have an inverse relationship with performance on several hippocampal--dependent memory tasks, known to be sensitive to aging and MCI.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A