Aging Brain, Cognition, and Dopamine

https://neurodegenerationresearch.eu/survey/aging-brain-cognition-and-dopamine/

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Country

USA

Title of project or programme

Aging Brain, Cognition, and Dopamine

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NIH (NIA)

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4

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

Research Abstract

DESCRIPTION (provided by applicant): Brain aging is a complex, multifactorial process that can

involve aggregation of proteins such as b-amyloid (Ab) and tau, cerebrovascular disease, and alterations in neurochemical function. While many older people with cognitive decline may have Ab deposition related to presymptomatic Alzheimer's disease, in fact the majority of older people have little or no Ab in the brain. This project will specifically address a non-amyloid form of age- related cognitive decline that is associated with alterations in the brain's dopamine system. Dopamine is involved in frontal-striatal systems required for executive function. Executive dysfunction is a frequent hallmark of aging that is associated with fronto-striatal atrophy and which is manifest in tasks that require cognitive control, set-shifting, and attention. Our specific aims for this project are: (1) To recruit a sample of healthy individuals spanning ages 20-85; older subjects will have previously undergone PET scanning with [11C]PIB and will have no evidence of brain Ab. In these individuals we will characterize executive function with neuropsychological instruments and measure brain dopamine synthesis capacity using the PET tracer [18F]flurometatyrosine (2) To assess regional brain atrophy with structural MRI (3) To examine the interactions between large scale brain networks using MR measures of resting state functional connectivity and (4) To study brain activity using fMRI during a set-shifting task The overall framework guiding this study is that alterations in brain dopamine in aging produce adaptations that impair frontal-striatal executive function and produce cognitive inflexibility. We hypothesize that aging is associated with increased dopamine synthesis, resulting in ""overcompensation"" that disrupts cognition. We propose that older people will show regional atrophy in prefrontal cortex and striatum, and that greater atrophy will be associated with higher dopamine synthesis and poorer performance on neuropsychological tests reflecting executive function. Existing data in normal young people show that a frontoparietal control network (FPCN) is involved in directing attention to external or internal stimuli, and that it performs thi function by coupling to the default mode network (DMN) during internal processing or the dorsal attention network (DAN) during attention to external stimuli. We hypothesize that in aging, greater dopamine synthesis increases FPCN-DMN coupling, resulting in poorer performance on tests of executive function because of an inability to update or shift set in response to external stimuli. Finally, we propose that performance during a set-shifting task, requiring subjects to shift attention from internal to external stimuli, will be impaired in older subjects, and that thi will be associated with higher dopamine synthesis, reduced DMN deactivation during the task, greater FPCN-DMN coupling, and poorer performance on tests of executive function. These experiments will provide a new, neural systems approach to age-related cognitive decline that has major implications for underlying mechanisms and therapy.

Lay Summary
PUBLIC HEALTH RELEVANCE: Age related cognitive decline has many potential etiologies. Although such decline is frequently related to preclinical Alzheimer's disease, there are many other causes. This project will explore how changes in the brain dopamine system are related to aging. The study of these processes will lead to a better understanding of the neurochemistry of behavior, and also to potential therapies for non-Alzheimer age-related cognitive decline.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

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