White matter damage in age-related cognitive decline

https://neurodegenerationresearch.eu/survey/white-matter-damage-in-age-related-cognitive-decline/

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Country

USA

Title of project or programme

White matter damage in age-related cognitive decline

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,265,661.47

Start date of award

15/08/2009

Total duration of award in years

7

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)... Brain Disorders... Cerebrovascular... Dementia... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): Vascular brain injury from small (micro) vessel

dysfunction (?VBI) and Alzheimer’s disease (AD) are highly prevalent in older adults, are commonly co-morbid, are major contributors to the dementia syndrome in the elderly, and are present in over 85% of cognitively normal individuals 75 years of age or older where these diseases presumably contribute to age-related cognitive decline. Enigmatically, while tremendous effort has been invested in understanding mechanisms of gray matter damage and neuron death in neurodegenerative diseases, carefully executed studies in humans and non-human primates have shown that neuron loss is not a feature of advancing age. In contrast, numerous studies, mostly neuroimaging-based, have associated white matter (WM) changes with advancing age; however, the molecular and cellular bases of this WM injury (WMI) with advancing age remain unclear. In this renewal, we hypothesize that ?VBI and AD cause WMI through direct and indirect mechanisms that converge on deleterious responses that impede myelin repair. Indeed, our observations from the current cycle indicate that ?VBI and AD conspire in the adult human brain to produce WMI and perturb response and repair of WMI through cellular and molecular mechanisms that are very similar to what we and others have demonstrated previously in pediatric WMI and adult demyelinating diseases. Our highly integrated multi-component R01 will continue to pursue the following Specific Aims: (1) Developing a unique and highly complementary resource of brain tissue from a human population-based study of brain aging and incident MCI. Tissue is prepared to maximize investigation of white matter. Using tissue from this unique resource, we will continue our work determining associations magnetic resonance imaging (MRI), histological, and immunohistochemical measures of white matter damage, (3) free radical damage to myelin or axons, (4) specific subpopulations of oliogodendrocyte precursor cells (OPCs), and (5) biochemical factors that suppress appropriate maturation and function of OPCs in aged brain. This project not only will continue to develop a unique resource for the community of scientists investigating white matter injury, but also employs this resource to answer key questions about the structural, cellular, and biochemical bases of WMI associated with cognitive decline in the elderly.

Lay Summary

Age-related cognitive decline and prodromal dementia are of paramount public health import given the projected demographics of the US population. While numerous studies have associated white matter changes with advancing age, the structural and cellular bases of this white matter damage remain enigmatic. Continuation of our research project not only will continue to develop a unique resource for the community of scientists investigating white matter injury, but also will employ this resource to answer key questions about the structural, cellular, and biochemical bases of white matter damage associated with cognitive decline in the elderly.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
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