Cerebrovascular Contributions to Brain Aging and Dementia

https://neurodegenerationresearch.eu/survey/cerebrovascular-contributions-to-brain-aging-and-dementia/

Principal Investigators

SALAT, DAVID H

Institution

MASSACHUSETTS GENERAL HOSPITAL

Contact information of lead PI
Country

USA

Title of project or programme

Cerebrovascular Contributions to Brain Aging and Dementia

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,559,488.99

Start date of award

29/09/2007

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

cerebrovascular, aging brain, Alzheimer's disease risk, Dementia, white matter

Research Abstract

DESCRIPTION (provided by applicant): The proposed work aims to identify direct mechanisms by which vascular health influences neural integrity, and in turn, cognitive fitness in older adults as well as to determine how risk for Alzheimer’s disease (AD) contributes to a neural

environment in which degenerative processes are disproportionately facilitated due to enhanced vulnerability to limits in blood supply. We propose that age-associated decline in specific aspects of vascular health promotes progressive degenerative changes in white matter tissue structure and that this deterioration is a primary mechanism of cognitive decline. More advanced decline in vascular health compounded with risk for AD contributes to breakdown of the blood brain barrier, deterioration of the cerebral cortex and subcortical gray matter, and to a more generalized cognitive deficit. The Specific Aims of this continuation are: (1) to determine whether regions of reduced blood flow and altered flow regulation co-localize with white matter lesions and predict future lesion formation. We expect that white matter bordering the end zones of the long penetrating arteries and watershed areas will be most vulnerable to microstructural damage, and this damage will be directly associated with functional neuroimaging metrics of white matter perfusion and vascular autoregulation. (2) To characterize the regional profile of white matter damage and quantify the degree of tissue damage within white matter lesions. We hypothesize that taking quantitative information into account when characterizing white matter lesions will provide greater sensitivity to detect cognitive decline and other clinically relevant phenomena. (3) To determine whether breakdown of the blood brain barrier with risk for AD promotes white matter lesion formation. We hypothesize that individuals with risk for AD have a greater incidence of systemic inflammation and that this is associated with deterioration of the blood brain barrier, augmenting degenerative processes due to vascular risk. Taken together, these studies would demonstrate that regions of the cerebral white matter with spatial proximity to particular portions of the vascular tree are most susceptible to preclinical cerebral blood flow dysregulation and lesion formation. This initial pathway leads to the standard pattern of non-demented age-associated cognitive decline. Progressive decline in vascular function coupled with an AD-associated inflammatory response contributes to a breakdown of the blood brain barrier and additional degenerative changes predictive of subsequent cognitive decline. Data generated here could provide important and very practical insights for individualized clinical management and would identify mechanistic targets for future clinical intervention.

Lay Summary

PUBLIC HEALTH RELEVANCE: White matter lesions occur as a result of a decline in vascular health in older adults and contribute to cognitive impairment in this population. This damage is enhanced in individuals with Alzheimer’s disease. The proposed studies aim to determine mechanisms, patterns, and cognitive consequences of white matter deterioration in older adults and individuals at risk for Alzheimer’s disease through the detailed characterization of cerebrovascular structure and function and measurement of transvascular water exchange and blood brain barrier integrity.

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

Database Tags:
N/A