

Role of lipid droplets in neurovascular inflammation

<https://neurodegenerationresearch.eu/survey/role-of-lipid-droplets-in-neurovascular-inflammation/>

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Country

USA

Title of project or programme

Role of lipid droplets in neurovascular inflammation

Source of funding information

NIH (NIA)

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15/09/2014

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3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Neurodegenerative... Neurosciences... Prevention... Vascular Cognitive Impairment/Dementia

Research Abstract

DESCRIPTION (provided by applicant): Previous studies have strongly linked lipids and lipoproteins with neurovascular inflammation and dementia. However, the mechanisms and impact of lipid-induced or lipotoxic injury on neurovascular inflammation, microvascular cell death, blood-brain barrier permeability, and cognitive function is not known. This proposal aims to address two important questions about lipotoxic neurovascular injury: 1) What are the cell signaling pathways induced by lipotoxic injury in the brain microvasculature? 2) What are the pathophysiological outcomes of lipotoxic injury to the brain? We will examine cell signaling pathways using brain microvascular endothelial cells and mouse and human brain microvessels. Pathophysiological outcomes will be assessed by measuring brain microvascular cell death, blood brain permeability, and cognitive function. Answering these questions will enable us to develop a better understanding of the development of neurovascular inflammation and point the way to potential therapies for prevention and treatment of vascular dementia. This proposal is innovative because it will investigate the microvascular determinates of neuroinflammation, rather than concentrating only on the neuropathological causes. Also, we plan to use state-of-the-art and novel techniques in this project to examine neurovascular pathophysiology at a level not previously possible. This proposal has a strong translational component in that we will test the concepts developed in cell culture in mouse and human brain microvessels, and mouse models of cognitive impairment. The results of this project could result in a reassessment of blood lipids and lipoproteins in terms of their potential to induce microvascular neuroinflammation and determine if diets that modulate blood fatty acids, rather than lipoproteins, reduce vascular dementia.

Lay Summary

PUBLIC HEALTH RELEVANCE: Lipotoxicity is a metabolic disorder that results from accumulation of lipids, particularly fatty acids, in non- adipose tissue leading to cellular dysfunction, lipid droplet formation, and cell death. Our studies indicate for the first time that he neurovascular circulation also can manifest lipotoxicity, which is the major focus of this proposal. Previous studies have shown that therapies aimed at attenuation and prevention of macrovascular diseases are not necessarily beneficial in microvascular disease. Further, brain microvascular pathologies are a difficult area of investigation to explore at both the cellular level and clinically. This proposal offers the opportunity to not only investigate basic mechanisms of microvascular injury, but also to identify and test potential therapies for brain microvascular disease.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Alzheimer's disease & other dementias

Years:

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Database Categories:

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