Metabolic Signatures Underlying Vascular Risk Factors for Alzheimer-type Dementias

https://neurodegenerationresearch.eu/survey/metabolic-signatures-underlying-vascular-risk-factors-for-alzheimer-type-dementias/

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Country

USA

Title of project or programme

Metabolic Signatures Underlying Vascular Risk Factors for Alzheimer-type Dementias

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 5,780,198.17

Start date of award

30/09/2015

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

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)... Behavioral and Social Science... Brain Disorders... Cardiovascular... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Heart Disease... Neurodegenerative... Neurosciences... Nutrition... Prevention... Vascular Cognitive

Impairment/Dementia

Research Abstract

? DESCRIPTION (provided by applicant): Metabolomics, the global science of biochemistry, provides enabling tools for a more detailed understanding of the biochemical mechanisms by which vascular factors contribute to the complex etiology of Alzheimer's disease. An extensive literature documents a relationship between altered lipid metabolism and not only vascular disease (VD) but also amyloidogenesis, neurotransmission, oxidative stress, and apoptosis. In particular, the apolipoprotein E ?4 (APOE ?4) allele, a major risk factor for AD, has important functional roles in lipid metabolism/transport as well as synaptic repair and amyloidogenesis. These previous studies suggest that disturbances in lipid metabolism and transport are common mechanisms underlying both VD and AD pathogenesis. However, research in this area has focused primarily on measuring a small number of plasma lipids such as cholesterol, triglycerides, and oxidized phospholipids that are largely carried on circulating lipoproteins. Thi provides only a limited view of lipid metabolism and cannot provide detailed mechanistic insights into cardiovascular risk factors contributing to AD. ""Lipidomics,"" a branch of metabolomics, is a new discipline that brings together biochemistry with quantitative systems biology and high-throughput techniques, providing powerful tools for mapping global lipid changes in disease including failures within biochemical pathways and metabolic networks. Over four years we have assembled an interdisciplinary team of experts in metabolomics, lipidomics, genetics, biochemistry, bioinformatics, neuropsychology, biomarker discovery and clinical trials, and have begun to define perturbations in interlinked biochemical pathways across the AD trajectory. Our own work as well as work by other groups using lipidomics and metabolomics approaches in the study of AD (Han, PLOS ONE 2011; Mapstone, Nature Medicine 2012) has highlighted major changes in phosphatidylcholines (PC), phophatidylethanolamines (PE) and ethanolamine plasmalogens (PlsEtn), and the sphingolipidome (SL) in patients with early disease. Similar work by others in the study of cardiovascular disease (CVD) has implicated species within these same lipid classes in CVD pathogenesis. These early findings with lipid metabolism suggest some common metabolic defects between AD and CVD and point to the promise of lipidomics in providing deeper mechanistic insights about a VD contribution to AD pathology. In this application we leverage our interdisciplinary team of experts and our partnerships with the national AD Neuroimaging Initiative (ADNI) study and the community-based MURDOCK Memory and Cognitive Health Study (MHS) to test hypotheses that alterations in specific lipid classes and networks mediate the links between vascular disease and AD pathogenesis. We will connect central and peripheral metabolic defects in AD pathways to test hypotheses about systemic vascular and metabolic factors affecting the disease process.

Lay Summary

PUBLIC HEALTH RELEVANCE: We propose to use state of the art metabolomics/lipidomics and bioinformatics tools to define metabolic signatures and biochemical changes that are mechanistically related to vascular and metabolic conditions associated with Alzheimer's disease risk. We will leverage extensive biochemical and longitudinal clinical data being generated through our Alzheimer's Disease Metabolomics Consortium using ADNI samples and those from a large community health study in North Carolina, the ""MURDOCK Study"".

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

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