White Matter Hyperintentisities in Aging and Dementia

https://neurodegenerationresearch.eu/survey/white-matter-hyperintentisities-in-aging-and-dementia/

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Country

USA

Title of project or programme

White Matter Hyperintentisities in Aging and Dementia

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 727,972.48

Start date of award

01/07/2009

Total duration of award in years

6

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)... Brain Disorders... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Health Disparities for IC Use... Minority Health for IC Use... Neurodegenerative... Neurosciences... Translational Research... Vascular Cognitive Impairment/Dementia

Research Abstract
As the older segment of our population increases, Alzheimer’s disease (AD) has emerged as one of the most devastating international public health epidemics. There are currently no effective disease-modifying treatment or preventative strategies available. Current pathogenic models and newly implemented diagnostic criteria for AD emphasize a single pathway of disease pathogenesis, but underestimate the important contribution of vascular risk factors and of small vessel cerebrovascular disease, which manifests primarily as white matter hyperintensities (WMH) on T2-weighted magnetic resonance imaging (MRI). During the previous four years of this project (R01 AG034189), we confirmed our hypotheses that accumulation of WMH predicts incident AD, particularly when distributed in parietal regions, and is associated with the presence of cerebral microbleeds, an indicator of cerebral amyloid angiopathy (CAA) in a large multi-ethnic cohort of older adults. Accordingly, we extended our research to examine mechanistic interactions between cerebrovascular disease and AD. Our new preliminary data suggest that individuals with evidence of fibrillar amyloidosis have increased parietal lobe WMH and that hemodynamic markers of autoregulatory dysfunction are associated with both WMH and amyloid deposition, which in turn interact to promote the clinical expression of AD. This proposed competitive renewal will continue our systematic evaluation of the intersection between regional WMH and AD, and ask innovative and novel questions about the role of cerebral autoregulation and bloodbased lipid biomarkers. The aims of the project are: 1. To examine whether regional WMH and amyloid pathology confer independent or interactive risk for cognitive decline, clinical AD, mild cognitive impairment (MCI), and neurodegeneration, indexed by regional atrophy, across racial and ethnic groups; 2. To examine the relationship of autoregulation with WMH severity, amyloid pathology, and cognition and diagnosis; and 3. To explore established and newly-modeled blood-based lipidomic profiles and their association with WMH and amyloid pathology. Importantly, we will examine the extent to which small vessel cerebrovascular disease accounts for racial and ethnic disparities in cognitive decline, and diagnosis of MCI or AD. Beginning in 2012, 500 individuals from a newly-established ethnically and racially diverse older adult cohort received clinical evaluation, high-resolution structural MRI, and a subset (n=100) received positron emission tomography (PET) to quantify fibrillar forms of beta amyloid. The current study seeks to conduct longitudinal analysis on these individuals by repeating these procedures, in addition to collecting transcranial Doppler-derived measures of cerebral autoregulation and analyzing stored blood samples for lipid profiles. The study will provide novel mechanistic insight into the pathogenesis of AD and identify new targets for intervention.

Lay Summary
The prevalence of Alzheimer’s disease (AD) and associated societal and economic burden is rising as the size of the elderly population continues to increase, yet the causes of this devastating disease are poorly understood. This project will examine the degree to which small vessel cerebrovascular contributes independently or interactively to the development and

clinical expression of AD across racial and ethnic groups. It will also examine the roles of cerebral autoregulation and lipid biomarkers to provide novel mechanistic insight into the disease and help identify new targets for intervention.

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