The Macrovascular and Microvascular Contributions to Alzheimers Disease: MESA VASCAD

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Country

USA

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The Macrovascular and Microvascular Contributions to Alzheimers Disease: MESA VASCAD

Source of funding information

NIH (NIA)

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01/09/2016

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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)... Atherosclerosis... Brain Disorders... Cardiovascular... Cerebrovascular... Clinical

Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention... Vascular Cognitive Impairment/Dementia

Research Abstract
Project Summary Improving vascular health for delaying the onset of Alzheimer's disease (AD) is identified as a critical goal by the Alzheimer's Disease and Related Dementias Conference, the 2015 NIA AD Summit and PAR-15-356 (to which this application is responding). Yet, critical barriers exist to implementing vascular prevention strategies for AD, and elucidating the role of midlife metabolic, macro- and micro- vascular factors in AD is essential to addressing these barriers. Each type of factor may manifest different pathologies in the brain that contribute to dementia sub-types, making a new and sufficiently comprehensive clinical trial a costly and time-consuming undertaking. To address this essential gap, we propose to leverage the rich longitudinal cohort data from the Multi-Ethnic Study of Atherosclerosis (MESA) study with the addition of detailed cognitive testing and multimodal brain neuroimaging – the MESA VASCAD study. MESA participants at the Wake Forest site (46% African-American, 54% non-Hispanic Caucasian) have already undergone extensive metabolic and vascular phenotyping, repeated retinal imaging and a brief cognitive assessment in 2010-2012. The MESA VASCAD study will add clinical and cognitive assessments (Uniform Data Set and supplemental cognitive tests); neuroimaging (MRI, amyloid PET); and reanalysis of retinal images. We propose to enroll 540 MESA participants in 2 years and repeat assessments 3 years later to more fully characterize targeted, modifiable vascular risk factors for AD. Through our Specific Aims, we will (1) test the hypothesis that baseline macrovascular and microvascular biomarkers in middle-age predict both standard AD neuroimaging outcomes (e.g. hippocampal volume and amyloid deposition assessed with PET) and more novel cerebrovascular biomarkers (e.g. microinfarcts, lacunar infarcts, neurite density and cerebral microbleeds); (2) determine if changes in metabolic and vascular biomarkers over 15 years predict cognitive and AD biomarker trajectory; and (3) using high-dimensional machine learning approaches, determine common, differential and interactive metabolic and vascular risk factor profiles among racial and APOE genotype groups. This proposed ancillary study, approved by the MESA Steering Committee, is led by a New Investigator with an experienced, multi- disciplinary team of collaborators. The MESA study is an ideal cohort for interrogating the questions in this proposal: it has highly detailed longitudinal risk factor data collected over 15+ years in a diverse cohort, which we can leverage and augment with cerebrovascular biomarkers, AD biomarkers, and cognitive reassessments – thereby creating a comprehensive brain phenotype dataset for vascular and AD risk factors. These new data will enable us to examine the timing and impact of vascular biomarkers on dementia biomarkers and cognitive trajectories before a diagnosis of pre-clinical and clinical AD-related disorders, meeting a critical gap in information that will help guide the development of novel therapeutic or prevention strategies for various forms of AD-related dementias.

Lay Summary

Project Narrative Vascular and metabolic disorders are proposed as potent modifiable risk factors for Alzheimer’s disease (AD) and related dementias, and may provide key routes for therapeutic and preventive interventions. We propose to leverage the vast resources of the NIH-sponsored Multi-Ethnic Study of Atherosclerosis (MESA) study to examine the potential contributions of macrovascular and microvascular subclinical disease to AD-related pathology. At the Wake Forest MESA site, we will add neuroimaging, repeated cognitive testing, and reprocessing of existing digital retinal scans with novel measures of retinal microvascular architecture.

Further information available at:

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Investments > €500k

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United States of America

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