Cerebral Microbleeds in Young Adults: risk factors, biomarkers and genetics

https://neurodegenerationresearch.eu/survey/cerebral-microbleeds-in-young-adults-risk-factors-biomarkers-and-genetics/

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Country

USA

Title of project or programme

Cerebral Microbleeds in Young Adults: risk factors, biomarkers and genetics

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01/06/2015

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2

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... Cardiovascular... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Genetic Testing... Genetics... Human Genome... Neurodegenerative... Neurosciences... Prevention... Stroke... Vascular Cognitive Impairment/Dementia

Research Abstract

? DESCRIPTION (provided by applicant): Subclinical cerebrovascular disease detected using

brain MRI, of which cerebral microhemorrhages (CMB) is an important understudied component, is more frequent, precedes and predicts clinically evident cerebrovascular disease and dementia. CMB are attributed mainly to two major forms of hemorrhage prone cerebral small vessel disease: hypertensive vasculopathy and cerebral amyloid angiopathy. CMB are predictors of increased risk of stroke (ischemic and hemorrhage), cognitive impairment and dementia. Their presence complicates prevention, treatment and research efforts (immunotherapy) for ischemic stroke and Alzheimer's disease. However the underlying pathophysiology, prevalence in young to middle age and genetic risk factors of CMB are unclear. The Framingham Heart Study (FHS) has a wealth of longitudinal data on cardiovascular risk factors, genetic, biomarker and subclinical cardiovascular disease measures readily available. FHS third generation (Gen 3) participants (N=1621; mean age 45±8 years) had brain MRI with gradient echo sequences, and simultaneous assessment of cognitive performance. In the proposed grant we hypothesize that CMB will be detected as early as the 4th decade, prevalence will increase with age, and be related to cardiovascular risk factors and select cardiovascular medication use. We will investigate the relation of CMB to subclinical measures of vascular dysfunction (tonometry), and to novel circulating biomarkers of inflammation, vascular dysfunction and neurodegeneration (LpPLA2, VEGF, clusterin, beta-amyloid). We will also relate CMB to novel MRI measures of brain injury and aging (diffusion tensor imaging, gray matter volumes), traditional MRI measures of aging and vascular injury (white matter hyperintensity volume, total brain and hippocampal volumes) and cognitive performance. Finally, we will use {the dense familial relationships across the 3 generations to assess heritability of CMB, and perform linkage and association analyses using single variants and gene/region based tests, bioinformatics to search for genetic variants associated with CMB using available exome chip and whole exome sequencing data}. The present project will be an adjunct to a K23 award “”AG038444: Risk Factors, Genetics and Cognition in Cerebral Microbleeds: Framingham Study (PI: Romero)””, that is investigating CMB in the 1st and 2nd generation of FHS participants. In the present proposal we request modest funds to create and analyze a new dataset of CMB data in Gen 3. In addition to expanding our current knowledge of CMB prevalence and risk factors to a younger sample than has previously been studied, the present application will study 3 major novel aspects: the relation of biomarkers of neurodegeneration (plasma clusterin and beta-amyloid) to CMB, the relation of CMB to novel MRI measures of brain integrity and aging (DTI and gray matter volumes), and the existence of {common and} rare genetic variants associated with CMB. The proposed research project will advance our understanding of the pathophysiology of CMB in young adults, and improve effective prevention of stroke and dementia.

Further information available at:

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United States of America

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Years:
2016

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