Vascular Pathology in Early and Asymptomatic Cerebral Amyloid Angiopathy

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Country

USA

Title of project or programme

Vascular Pathology in Early and Asymptomatic Cerebral Amyloid Angiopathy

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NIH (NIA)

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30/09/2014

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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... 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... Neurodegenerative... Neurosciences... Rare Diseases... Vascular Cognitive Impairment/Dementia

Research Abstract
DESCRIPTION (provided by applicant): Cerebral amyloid angiopathy(CAA) is an age-related cerebral small vessel disease that is a common cause of lobar intracerebral hemorrhage (ICH) and vascular cognitive impairment in the elderly. It is characterized by progressive deposition of ß-amyloid (Aß) in the walls of cortical and leptomeningeal arteries. Although CAA is a widely recognized cause of lobar ICH, neuropathological studies suggest that milder forms of CAA are far more common in the elderly. In non-demented individuals without ICH, nearly 14% have moderate to severe CAA and greater than 50% have at least mild degrees of CAA that independently contributes to cognitive impairment. Based on these data, it is conceivable that CAA may play an important role in a large percentage of individuals with subtle cognitive symptoms or mild cognitive impairment (MCI). As our preliminary data suggest that strictly lobar MB have high specificity for CAA even in the absence of ICH, individuals with early CAA may be now readily identified. However, an important unanswered question is what additional vascular lesions predispose these individuals to develop cognitive symptoms and what role Alzheimer's disease (AD) pathology plays in cognitive impairment. Indeed, beyond MB, other neuroimaging and laboratory biomarkers appear be associated with vascular Aß accumulation. Dilated perivascular spaces (DPVS) in the white matter (a recently identified important marker of cerebral small vessel disease), chronic bleeding in the subarachnoid space (known as superficial siderosis) and posterior distribution of white matter hyperintensities (a marker of chronic cerebral ischemia) have all been associated with advanced CAA. This is likely related to increased vascular amyloid deposition in posterior brain regions-supported by evidence showing elevated relative occipital burden of Pittsburgh Compound B (PiB) in patients with CAA, the PET ligand that detects fibrillar and vascular amyloid deposition in vivo. Patients with CAA have also been shown to have depletion of the Aß40 species of amyloid protein in cerebrospinal fluid (CSF). Finally, cerebral microinfarctions on pathology appear to be very common in CAA. The current application aims to examine the role of Aß-mediated vascular pathology in cognitive symptoms in the elderly. The key questions motivating this proposal are: 1) Is there a signature of neuroimaging and laboratory biomarkers that can reliably identify patients with early CAA? 2) Do patients early CAA have a particular neuropsychological profile distinct from patients with mild cognitive symptoms due to early AD? and 3) What are the predisposing risk factors that lead to cognitive decline in patients with early CAA?

Lay Summary
PUBLIC HEALTH RELEVANCE: This project aims to achieve a more detailed understanding of early (even “”prodromal””) stages of CAA prior to the development of dementia or hemorrhagic stroke. Identifying individuals with early and asymptomatic CAA will be critically important in the design of future therapeutic trials to prevent the devastating consequences of this disease. The results from this study could yield important insights for better understanding vascular cognitive impairment in the elderly.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

Years:
2016

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