The Role of Intracranial Atherosclerosis in the Development of Alzheimers Disease

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USA

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The Role of Intracranial Atherosclerosis in the Development of Alzheimers Disease

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1

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Alzheimer's disease & other dementias

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Research Abstract

Rationale: Dementia is a growing problem in the US and worldwide. The lack of effective treatment or preventive strategies for Alzheimer's Disease (AD), the most common cause of dementia, has led to an increasing mortality rate and soaring medical costs. Intracranial atherosclerotic disease (ICAD) is also highly prevalent in older adults, and new evidence suggests it may be associated with AD and its precursor, mild cognitive impairment (MCI), but prospective validation is lacking. We propose to prospectively study the role of ICAD and its progression in the development of cognitive decline, MCI and dementia, in particular AD. Aims: We will determine if ICAD presence and measures by MRI, including its progression and a risk index based on baseline ICAD features, lead to cognitive decline, incident MCI and incident dementia. We will determine if ICAD adds to the predictive value of regional brain volume loss, a known predictor of AD. Finally, we will establish risk factors and plaque features that predict progression of ICAD. Design/Methods: We will conduct an ancillary study to the Atherosclerosis Risk in Communities (ARIC) Study, an NIH-funded cardiovascular cohort that began with about 16,000 participants, aged 45-64, who have been followed since 1987. The ARIC Neurocognitive Study (ARIC-NCS), conducted at the most recent ARIC visit in 2011-2013, acquired brain MRIs and cognitive evaluations to study cross-sectional associations of vascular risk factors and MRI brain changes with MCI and dementia. MRI also identified and measured stenosis and, for the first time, ICAD using a novel vessel wall imaging technique. This technique detects atherosclerotic plaques even if they do not result in stenosis and may be a better measure of atherosclerotic disease burden. We plan to acquire a repeat brain MRI in 1,000 participants at the next NIH-funded ARIC visit that begins in 2016 after a 5-8 year interval to measure ICAD progression, brain volume loss, and small vessel disease (SVD), another cause of blood flow impairment associated with AD. Repeat cognitive evaluations are also planned. We expect 335 and 266 incident cases of MCI and dementia, respectively, by the start of this exam. We will then evaluate the association of ICAD at baseline with incident cognitive outcomes. The MRI will allow us to make a specific diagnosis of AD (or AD-type in MCI), permitting analysis of its risk factors. In addition, we will use follow-up MRI data to measure changes in luminal stenosis and vessel wall thickness to identify ICAD progression. We will account for SVD and vascular risk factors when analyzing associations with ICAD. It is worth noting that large infarcts are an uncommon cause of dementia and not the primary focus of this study. Implications: Through our proposed study we will establish the role of ICAD in the development and progression of MCI and dementia, in particular AD. This will be the first study characterizing the natural history of ICAD progression and its ability to predict cognitive outcomes. This information could lead to preventive strategies and risk stratification for treatment protocols in an otherwise currently untreatable disease.

Lay Summary

Alzheimer's Disease is a common cause of dementia in the US and worldwide, and the reason for its development is complex and poorly understood. Atherosclerosis may contribute to Alzheimer's Disease development, and understanding its role could lead to preventive and therapeutic strategies in an otherwise untreatable major health problem.

Further information available at:

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