The role of cerebral small vessel disease in cognitive aging

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Sweden

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Research Abstract

The ultimate goal of this 5-year research project is to advance our understanding of the role of cerebral small vessel disease (SVD) in cognitive disorders in aging (e.g. problems in memory, language, thinking, attention, or judgement), taking into account genetic susceptibility and drug therapy. The proposal is based on the hypothesis that vascular risk factors (VRFs; e.g. smoking, obesity, hypertension, diabetes, and high cholesterol) contribute to the onset and progression of mild cognitive impairment (MCI) or subtypes (e.g. amnestic MCI that primarily affects episodic memory, non-amnestic MCI that affects skills or cognitive abilities other than memory) and dementia in old age through their detrimental impacts on cerebral small blood vessels, and that susceptibility genes (e.g. APOE and obesity-related FTO genes) and drug therapy of major

VRFs (e.g. antihypertensive drugs, antidiabetic agents, statins) modify the effects of VRFs on brain SVD and cognitive decline in aging. We will test the hypothesis using data from two large-scale longitudinal population-based imaging studies supported by the Swedish government and the US National Institutes of Health: (1) The Swedish National study on Aging and Care in Kungsholmen (SNAC-K; n=3363, age 60+ years)/SNAC-K MRI study (n=555) in Stockholm; and (2) The Age, Gene/Environment Susceptibility (AGES)-Reykjavik Study (n=5764, age >65 years; 5002 persons with MRI data) in Reykjavik. Participants in SNAC-K/SNAC-K MRI were first examined in 2001-2004, and are then reexamined every 3 or 6 years. The AGES cohort was first examined in 2002-2006 and reexamined in 2007-2011. In both studies, the research approach involves epidemiology, clinical medicine, psychology, genetics, and neuroimaging. Variables include VRFs, health history, biomarkers (e.g. blood glucose, cholesterol), susceptibility genes (e.g. APOE, FTO), imaging markers of cerebral SVD (e.g. cortical and subcortical infarcts, white matter lesions, cerebral microbleeds), and neurodegeneration (e.g. volumes of hippocampus, white matter, grey matter, ventricles), and cognitive function (e.g. memory, speed, executive function). We define MCI subtypes and dementing disorders following internationally established criteria. In addition, diffusion tensor imaging in SNAC-K MRI provides additional assessments of white matter microstructure, whereas the AGES-Reykjavik Study assesses retinal microvascular signs and age-related macular degeneration (AMD), as indirect markers of brain SVD. To achieve the ultimate objective, we plan to implement 5 projects. In Project I, we develop quantitative methods to assess the burden of VRFs and cerebral SVD. In Project II, we investigate the roles of VRFs and brain SVD in cognitive decline and dementia, as well as the impact of drug therapy for VRFs and genetic susceptibility. Project III focuses on the association of SVD and short-term (3-5 years) risk for MCI and dementia. In Project IV, we explore the role of SVD in differentiating MCI subtypes (e.g. amnestic vs. non-amnestic MCI) and specific dementia forms (e.g. Alzheimer’s disease vs. vascular dementia vs. mixed dementia). Finally, we have the unique opportunity in Project V to examine whether retinal markers (e.g. retinal microvascular signs, AMD) add additional value to brain SVD in predicting risk of cognitive decline and dementia. The novel hypotheses examined will be tested using advanced statistical techniques. All studies will be carried out by a multidisciplinary team with expertise in epidemiology, neurology, psychology, biostatistics, and neuroimaging, led and coordinated by the main applicant. Findings will help improve clinical management of MCI, and facilitate the development of preventive and therapeutic approaches that seek to delay the onset of dementia. This is particularly relevant given that dementia is the major health problem in the aging society that significantly decreases quality of life and increases costs of medical and social care.

Further information available at:

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