

Heart-brain interactions: Is small vessel disease a link?

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PROJECT SUMMARY/ABSTRACT Small vessel disease of the brain and the heart have far-reaching clinical implications and billions of dollars in annual healthcare costs. From a pathophysiological perspective, both organs share common risk factors (e.g., hypertension, diabetes, dyslipidemia, aging, etc.) and are affected to a similar extent by systemic inflammation, ischemia due to atherosclerosis, vasospasm, micro-emboli and neuroendocrine dysfunction. Additionally, there is increasing awareness that sex differences develop and modify the interaction between the heart and the brain. Surprisingly, despite such compelling similarities between CMD and CSVD pathogenesis, divergent diagnostic and therapeutic approaches currently exist. A recent review summarizing parallels between CMD and CSVD using magnetic resonance imaging (MRI) notably did not include investigation where both conditions were simultaneously studied. In our hands, CMD is indeed associated with increased risk of stroke, and we have preliminarily linked retinal microvascular structure and peripheral vascular function to CMD, suggesting concomitant research may be useful. Given that CMD therapeutic investigation is now underway, concurrent study with CSVD may provide novel treatment targets. Our parent NHLBI-funded Women's Ischemia Syndrome Evaluation (WISE) Pre-HFpEF (1R01HL146158) is testing the hypothesis that CMD-related ischemia is a precursor of features of HFpEF in 180 women and men. The WISE subjects are deeply phenotyped, undergo repeated testing, and are typically followed for at least 10 years. An additional parent NIA-funded MAE-WEST SCORE Project 2 (1U54AG065141) adds retinal photography, peripheral microvascular reactivity, and cognitive function to the NHLBI WISE cohort to evaluate the hypothesis that microvascular disease burden is related across major organ systems. Our study will: 1) establish an at-risk cohort to allow future prospective study of heart, brain and cognitive trajectories; 2) evaluate a variety of brain MRI markers to identify those of potential use in future prospective work; and 3) provide a platform for future clinical trial planning. Specifically, should relations be identified, microvascular disease potential prevention treatment targets can be considered in CSVD-related dementia prevention trials.

Our application will concurrently and efficiently investigate small vessel disease of the brain and heart which have far-reaching clinical implications and billions of dollars in annual healthcare costs. From a pathophysiological perspective, both organs share common risk factors (e.g., hypertension, diabetes, dyslipidemia, aging, etc.) and are affected to a similar extent by systemic inflammation, ischemia due to atherosclerosis, vasospasm, and micro-scar. Understanding that dementia is likely the product of both vascular dysfunction and Alzheimer's dementia and related dementias (ADRD) pathology (so called two-hit model) suggests that concurrent heart and brain study may provide insight into treatments.