

# Watershed Microinfarct Pathology and Cognition in Older Persons

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## BACKGROUND

### What is known:

- Watershed border zones lie at the distal territories of the anterior, middle, and posterior cerebral arteries
- Watershed regions are more vulnerable to hypoxia-ischemic events.
- Microinfarct lesions are pathological markers of a hypoxic-ischemic environment
- Microinfarcts are related to cognitive impairment and dementia.

### What Is Not Known:

- Are watershed regions vulnerable to microinfarct lesions?
- Are these lesions associated with cognition?
- Is there regional variability?

## OBJECTIVE

- Examine the relationship of microinfarcts in watershed and non-watershed regions with cognition.

## RESULT

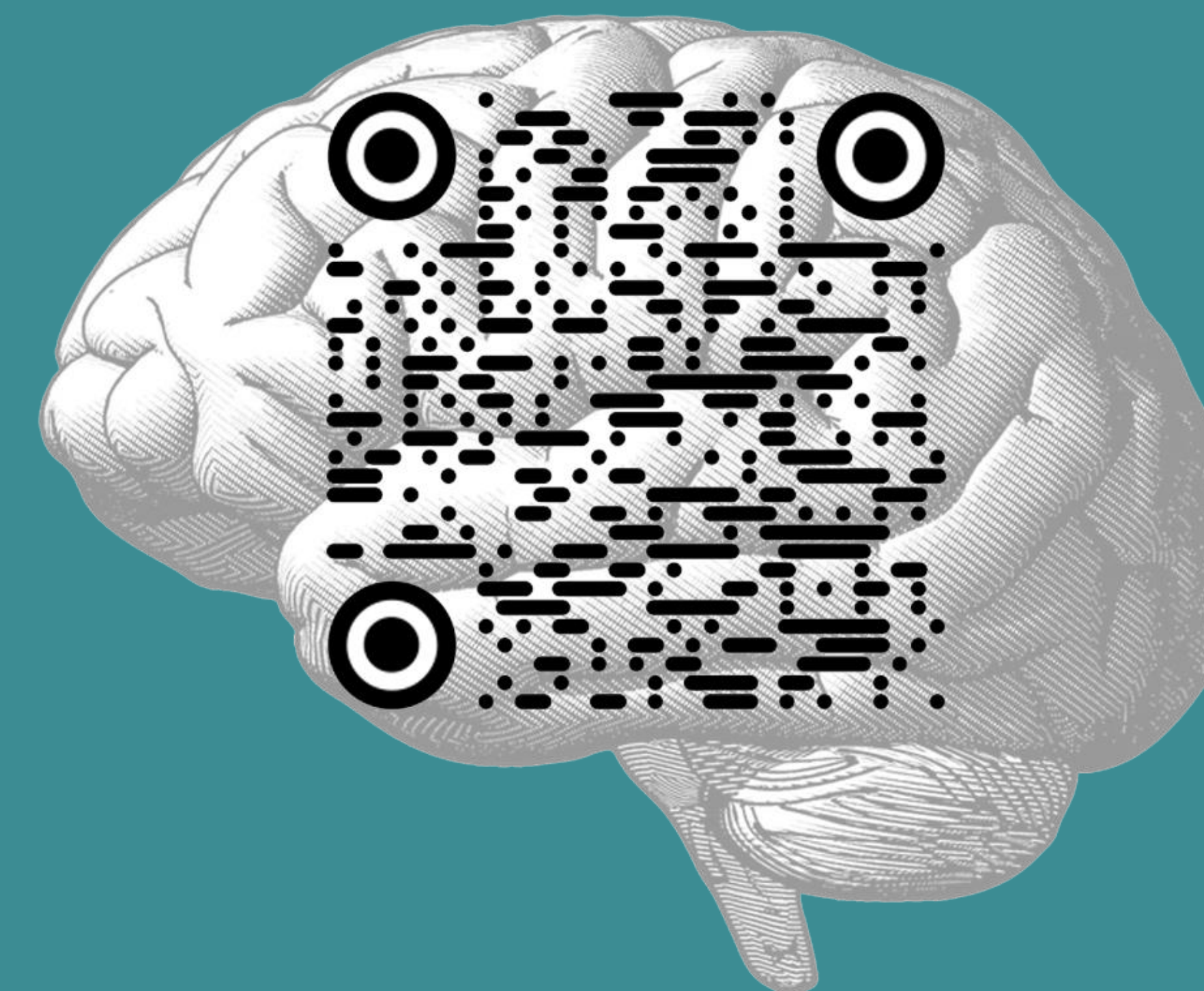
- Participants (n=356):** Rush Memory and Aging Project (mean age-at-death, 91 years; 28% men).
- Microinfarct Pathology:** 15% had watershed microinfarcts and 30% had microinfarcts in non-watershed regions.
- Analysis:** Linear regression models adjusted for demographics, macroinfarcts, and AD pathology

Brain Region	Global Cognition	Episodic Memory	Semantic Memory	Working Memory	Visuospatial Ability	Perceptual Speed
<b>Watershed Microinfarcts</b>	<b>-0.56</b> (0.26, 0.03)*	-0.35 (0.29, 0.22)	-0.50 (0.31, 0.10)	<b>-0.58</b> (0.27, 0.03)*	<b>-0.57</b> (0.27, 0.03)*	-0.08 (0.24, 0.75)
<b>Non-Watershed Microinfarcts</b>	-0.22 (0.19, 0.25)	-0.19 (0.21, 0.37)	-0.17 (0.23, 0.46)	-0.24 (0.20, 0.22)	0.13 (0.20, 0.50)	-0.15 (0.18, 0.41)

## DISCUSSION

- Watershed microinfarcts are associated with lowered cognitive function.
- Microinfarcts in non-watershed regions were not associated with cognition.
- Watershed regions may serve as the proximate marker of global cerebral ischemia.

# Vascular Pathologic Changes in Watershed Brain Regions are Associated with Neurodegeneration and Cognitive Impairment



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Kapasi et al., Watershed Microinfarct Pathology and Cognition in Older Persons. *Neurobiol Aging*. 2018 May; 70:10-17

## WATERSHED SMALL VESSEL DISEASE AND PHF-TAU TANGLES

- Prior Evidence:** Hypoperfusion or ischemia may contribute to AD pathogenesis.
- Objective:** Examine association between small vessel disease (SVD) with AD pathology (n=796)
- Analysis:** Linear regression models adjusted for demographics and common age-related neuropathologies
- Preliminary Data:** Arteriolosclerosis in watershed regions is associated with higher levels of PHF-tau tangle burden (Estimate = 0.13; SE=0.05; p=0.01).

## FUTURE WORK

- Develop a watershed MRI imaging atlas to examine structural/functional changes.
- Utilize digital pathology to capture additional SVD-related pathogenic changes.
- Examine proteomic changes associated with SVD.

## TRAINING PLAN FOR CAREER DEVELOPMENT (K) AWARD

- Clinical assessment of Alzheimer's and vascular dementia
- Assessing cerebral SVD with neuroimaging
- Digital neuropathology
- Small vessel disease biology
- Systems biology
- Epidemiology and biostatistics