

Elevated Plasma P-tau217 Levels in Older Adults with Enlarged Perivascular Spaces

Arunima Kapoor, MSc¹, Allison C Engstrom, BS¹, Melanie Quiring², John Paul M. Alitin, BA², Trevor Lohman, PhD², Aimee Gaubert, BA², Amy Nguyen², David Robert Bradford, BS³, Angel Charity Leslie³, Lorena Sordo⁴, Kathleen Rodgers, PhD³, Elizabeth Head⁴, Daniel A Nation, PhD^{2,5}

¹Department of Psychological Science, University of California, Irvine, Irvine, CA, USA; ²Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA, USA; ³Center for Innovations in Brain Science, Department of Pharmacology, University of Arizona, Tucson, AZ, USA; ⁴Department of Pathology and Laboratory Medicine, University of California, Irvine, Irvine, CA, USA; ⁵Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.

INTRODUCTION

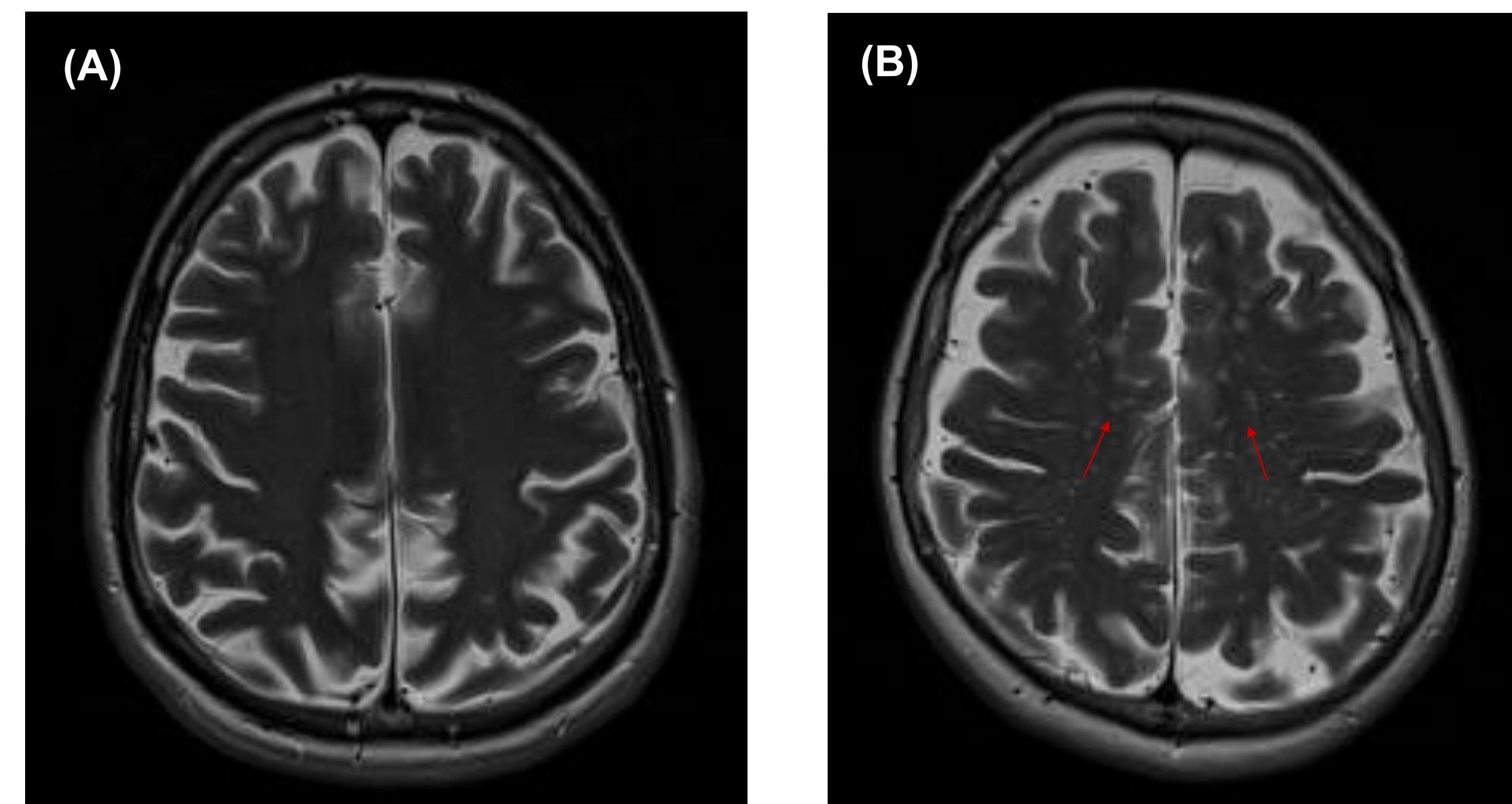
- Perivascular spaces (PVS) are fluid-filled spaces surrounding arterioles and venules in the brain, which enable clearance of waste and maintain flow of fluids and substances
- Lower plasma amyloid-beta ($A\beta$) 42/40 ratio, which indicates higher cortical amyloid deposition, is associated with greater PVS dilation
- Given recent advancement in plasma biomarkers, p-tau217 has emerged as an improved biomarker for Alzheimer's disease (AD) and is more closely associated with cortical amyloid deposition
- However, there are limited studies examining the association between plasma p-tau217 levels and PVS enlargement.

We examined plasma p-tau217 levels in individuals with low and high PVS burden

METHODS

- Independently living older adults (N = 154, mean age = 69.1 years; SD = 6.9; age range 55-89 years; 33.1% male) free of dementia or clinical stroke were recruited from the community and underwent brain MRI, and blood draw
- PVS were qualitatively scored using a 5-point scale in the basal ganglia (BG), and centrum semiovale (CS). Scores were dichotomized to low enlarged PVS burden (scores of 0-1, none or mild) or high enlarged PVS burden (score >1, moderate-severe)
- Plasma was assayed using the Quanterix Simoa® ALZpath Assay to determine p-tau217 levels
- One-way ANCOVA was conducted to compare p-tau217 between low and high enlarged PVS burden controlling for age and sex

RESULTS



Plasma levels of p-tau217 and total tau by low (A) versus high (B) enlarged perivascular spaces burden in the centrum semiovale (C, D) and basal ganglia (E, F)

CS = centrum semiovale; BG = basal ganglia; PVS = perivascular spaces

- 57.3% participants had high burden of CS-PVS, and 27.3% had high burden in the BG
- There was a significant difference in plasma p-tau217 levels between low and high CS-PVS burden, controlling for age and sex ($F(1,133) = 5.76$ $p = 0.018$, $\eta^2 = .04$), with higher levels in the high PVS burden group (estimated marginal mean = .136) compared to low (estimated marginal mean = .111)

DISCUSSION

- Prior studies have demonstrated that elimination of toxic proteins from the brain occurs via perivascular spaces and hypothesized that failure to eliminate $A\beta$ may contribute to the pathogenesis of AD
- Our findings suggest that higher plasma p-tau217 levels, which may indicate higher cortical amyloid and tau accumulation, is associated with greater PVS dilation
- Similar to $A\beta$, p-tau217 may rely on clearance through PVS, suggesting a role for vascular damage in the pathogenesis of AD
- The findings of this study suggest that cerebrovascular dysfunction is associated with AD pathophysiological changes and that future studies are warranted to directly study this disease mechanism.

References: Bakker et al., 2016; Doubal et al., 2010; Perosa et al., 2022; Vilor-Tejedor et al., 2021; Kapoor et al., 2023. **Acknowledgements:** National Institutes of Health (DAN: R01AG064228; R01AG060049; R01AG082073; P01AG052350), American Heart Association (AK: 23PRE1014192)

