

Arterial Stiffness is Related to Indices of Blood Brain Barrier Breakdown and Brain Volume in a Middle-aged Cohort at Risk for Alzheimer's Disease

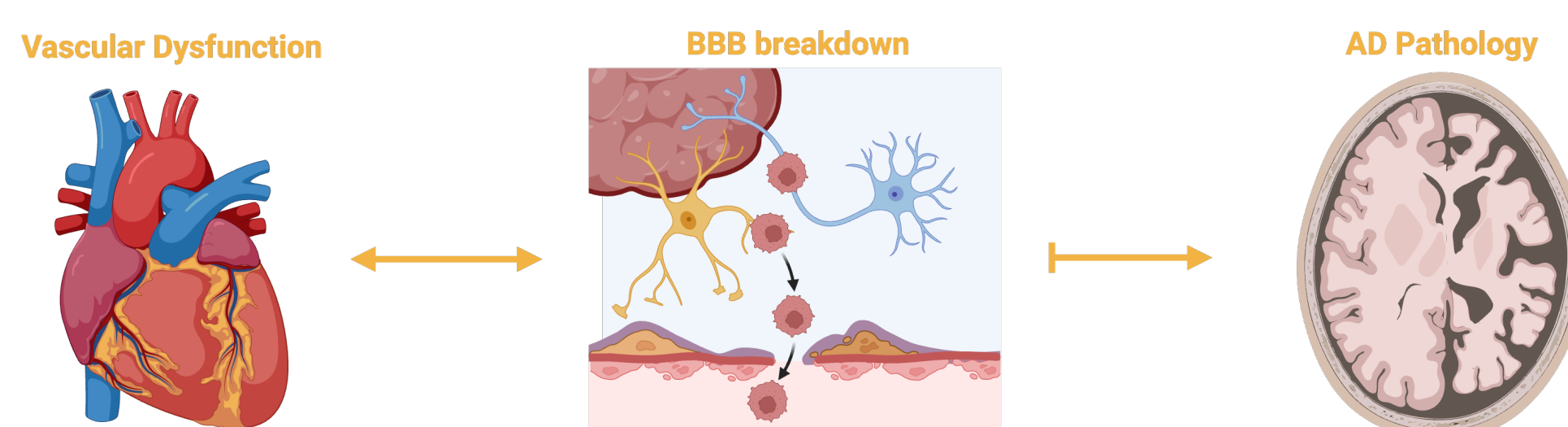
Jordan Watson¹, Maria Misura, PhD², Jordan Pelkmans¹, Brittany Butts PhD, RN¹, Enid Swatson, MPH¹, Chloe Park¹, Danielle D. Verble, MA¹, Elizabeth Flynn¹, Scott Miners, PhD³, Patrick Gavin Kehoe, PhD³, Whitney Wharton, PhD¹

¹ Emory University, Atlanta, GA, ² Georgia State University, Atlanta, GA, ³ University of Bristol, Bristol, UK

This study examines the relationship between systemic arterial stiffness, blood-brain-barrier integrity, and brain volume in a racially diverse cohort of middle-aged adults.

Background

- Systemic and brain vascular dysfunction and blood brain barrier breakdown strongly influence AD pathology.
- With a growing prevalence of Alzheimer's disease (AD), there is an increased need to identify biomarkers that can indicate disease at the earliest stage possible.



Methods

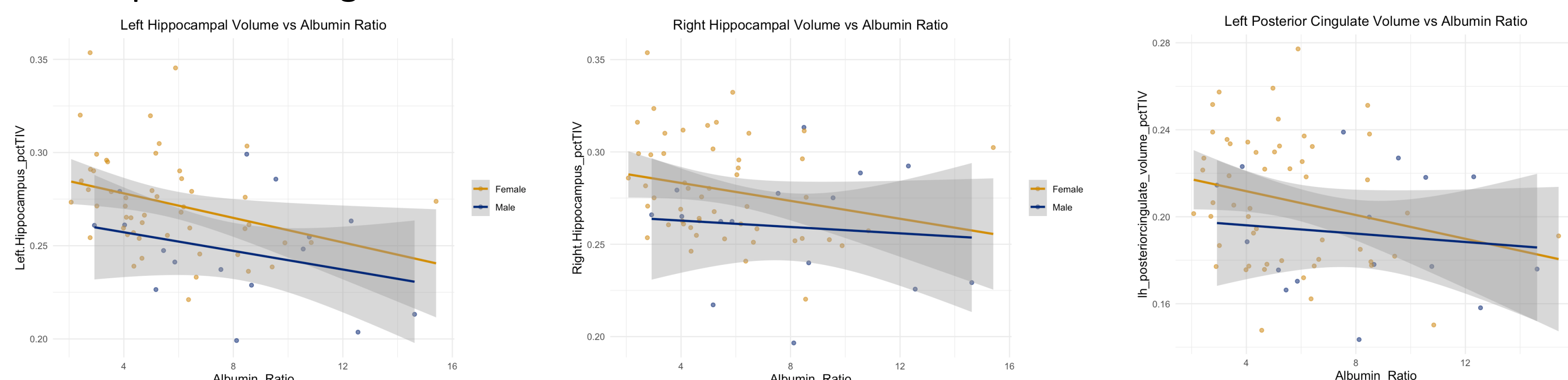
- Baseline data from the larger NIH-funded E2 Study, which included middle-aged, cognitively normal participants, were used.
- Participants underwent neuroimaging, lumbar puncture, blood draw, and vascular ultrasound.
- Arterial stiffness was measured using cfPWV.
- The ratio of cerebrospinal fluid to serum albumin was used as a marker of BBB integrity.
- Participants were scanned on a 3T MRI machine.
- Subcortical nuclei volumes were derived from T1-weighted images and processed with FreeSurfer.
- Brain volumes were calculated as a percentage of intracranial volume.
- The relationships were investigated using linear regression adjusting for sex.
- An interaction term was added to investigate if the relationship between percent of inter-cranial volume and biomarkers varied by sex.

Demographics

Characteristic (n=162)	Mean ± SD
Age (years)	64 ± 9
Female (%)	73.5%
Black or African American (%)	49.4%
Highest Level of Education (years)	16.4 ± 2.4
Diabetes (%)	11.7%
Hypertension (%)	50.6%
Hyperlipidemia (%)	66.9%

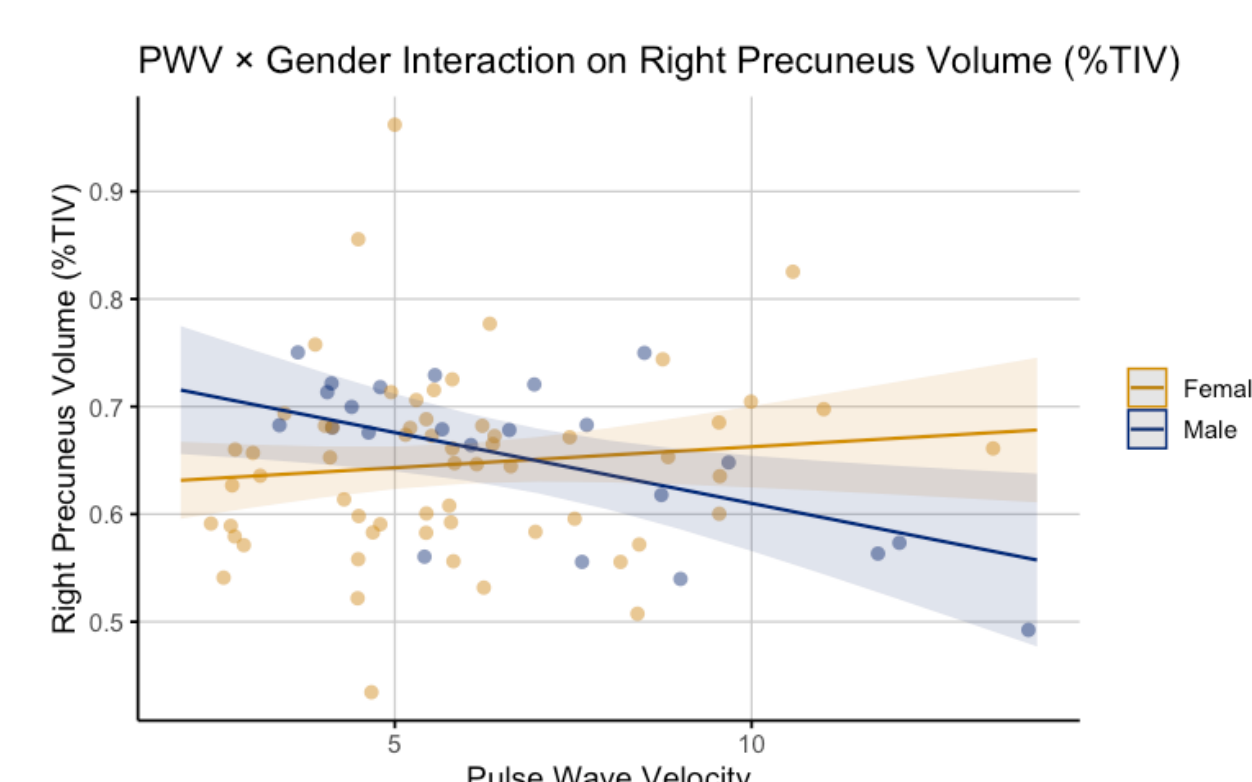
Results

- CSF/serum albumin ratio was inversely associated with left and right hippocampal volume, and left posterior cingulate volumes



- The association between arterial stiffness and right precuneus volume differed significantly between males and females.

Characteristic (n=162)	Male (n=43)	Female (n=119)
Age (years)	63 ± 9	68 ± 9
Pulse Wave Velocity (m/s)	6.06 ± 2.45	7.32 ± 2.97
Right Precuneus Volume (%TIV)	0.65 ± 0.08	0.65 ± 0.07



Discussion

- Preliminary analyses from this ongoing study found regional interactions between arterial stiffness and BBB integrity in a middle-aged cohort at risk for AD by virtue of parental history.
- A higher CSF blood brain barrier marker was associated with smaller hippocampal and posterior cingulate volumes. This finding is consistent with other preclinical AD work highlighting early BBB breakdown in the medial temporal lobe.
- In males we found that greater arterial stiffness was associated with smaller right precuneus volume. No significant association was seen in females. This suggests that vascular contributions may have differential effects on preclinical brain changes according to sex.
- Longitudinal work will examine the CSF to serum albumin ratio and sPDGFRβ over two years, to clarify how systemic vascular function and BBB integrity may influence pathogenic mechanisms underlying brain structure and blood flow.

Acknowledgements



- This project was supported by the National Institute of Health 5R01AG066203-05.
- Thank you, Dr. Wharton and Dr. Butts, for all your support!