Gray to white matter signal ratio (GWR) as a novel MRI-based biomarker of longitudinal cognitive decline in cognitively normal older adults

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BACKGROUND

- Microstructural properties of cortical gray matter (e.g., mean diffusivity) are disrupted as early as the asymptomatic stage of Alzheimer's disease (AD)[1,2] and are related to changes in amyloid pathology and cognition.[3]
- The **gray to white matter signal intensity ratio (GWR)** derived from T1-weighted MRIs may reflect pathological mechanisms that precede cortical atrophy across the symptomatic and syndromic spectrum of AD.[4, 5]
- The utility of GWR for predicting longitudinal cognitive decline remains unclear.

Goal: To investigate the utility of GWR as a novel MRI biomarker for predicting the trajectory of longitudinal cognitive decline in cognitively unimpaired older adults.

Hypothesis: Greater regional GWR at baseline (i.e., blurred gray/white boundaries) would predict accelerated cognitive decline among older adults who are cognitively unimpaired at baseline.

MATERIALS AND METHODS

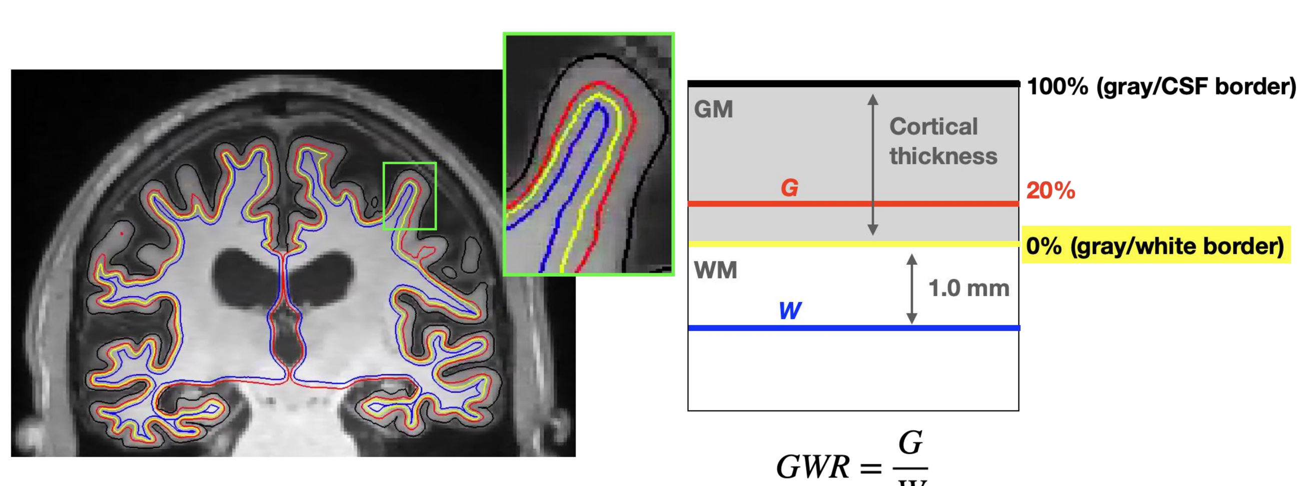
Participants: We analyzed data from 277 cognitively unimpaired individuals (CDR global scores = 0) part of the Harvard Aging Brain Study (HABS) cohort.[6]

Cognitive assessment: Longitudinal data from the Preclinical Alzheimer's Cognitive Composite Scale-5 (PACC-5).[7]

Neuroimaging: Baseline T1-weighted structural MRI data collected using the ADNI MPRAGE sequence. MRI data were processed via FreeSurfer v7.1 to derive vertex-wise estimates of GWR and cortical thickness. Global amyloid burden at baseline was estimated using ^{11}C-PiB PET.

Statistical Analysis: Linear mixed-effects models with two natural cubic spline terms were used to estimate the trajectory of PACC-5 scores over time.[8]

Calculation of GWR and cortical thickness



$$GWR = \frac{G}{W}$$

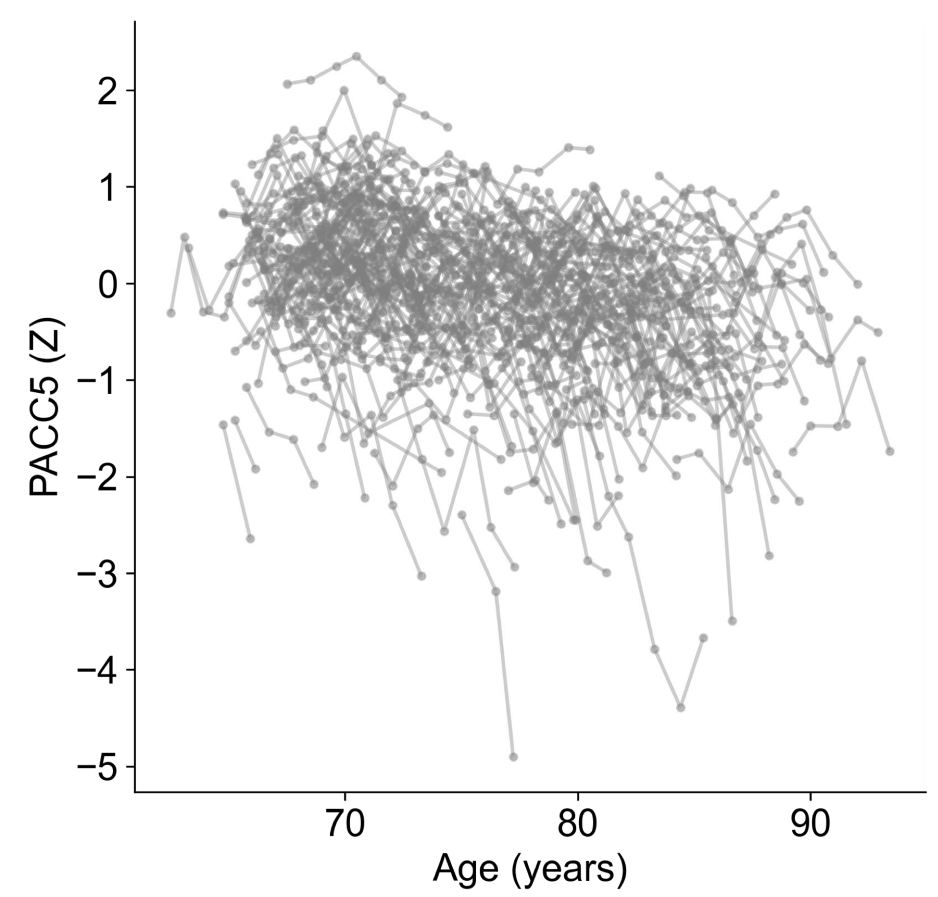
RESULTS

Sample characteristics

Variable	
Count (%)	
Female	167 (60.3%)
White/non-Hispanic	223 (81.0%)
Baseline amyloid positivity*	73 (26.4%)
APOE-ε4+	77 (27.8%)
Mean (SD)	
Baseline age, years	73.6 (6.1)
Years of education	15.8 (3.1)
Baseline MMSE	29.0 (1.1)
Baseline PACC5	-0.02 (0.7)
# follow-up cognitive assessments	4.5 (1.0)

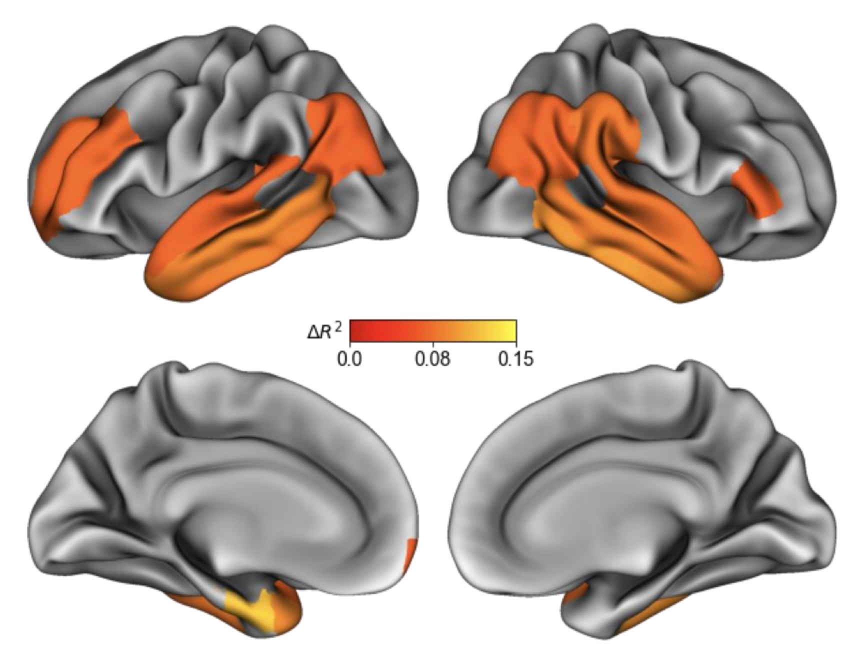
*PiB FLR DVR > 1.2

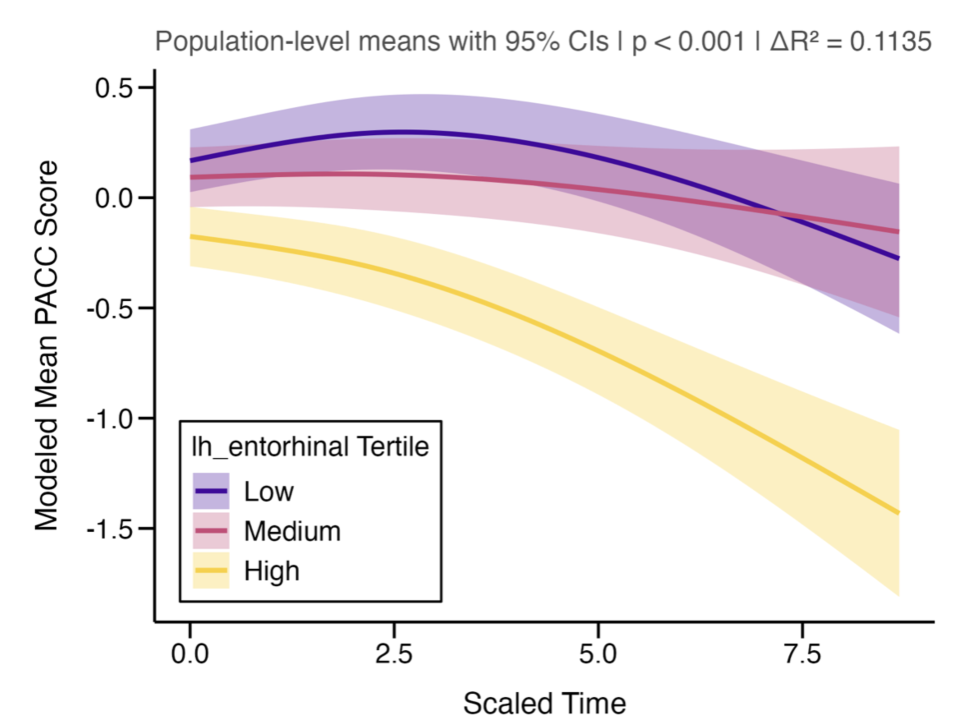
Longitudinal changes in PACC scores across individual participants



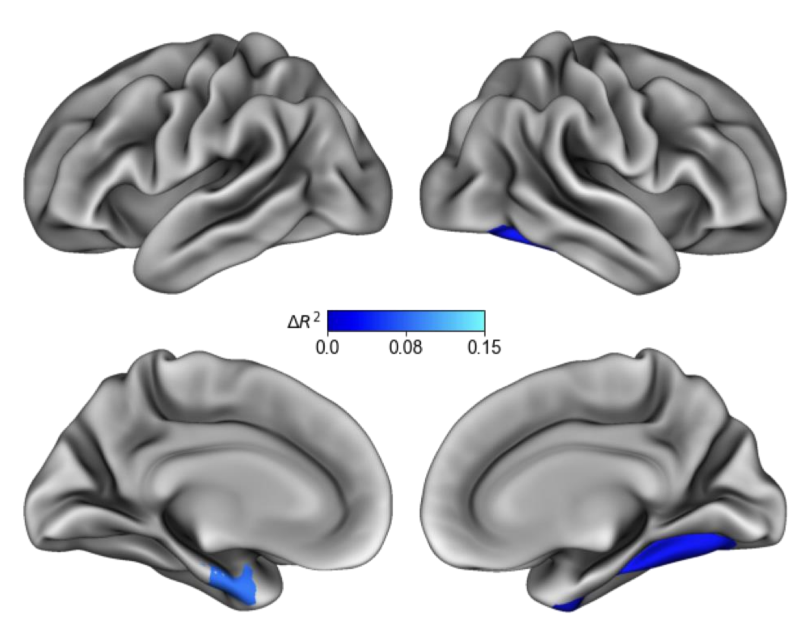
Baseline MRI features predicting longitudinal trajectories of PACC change

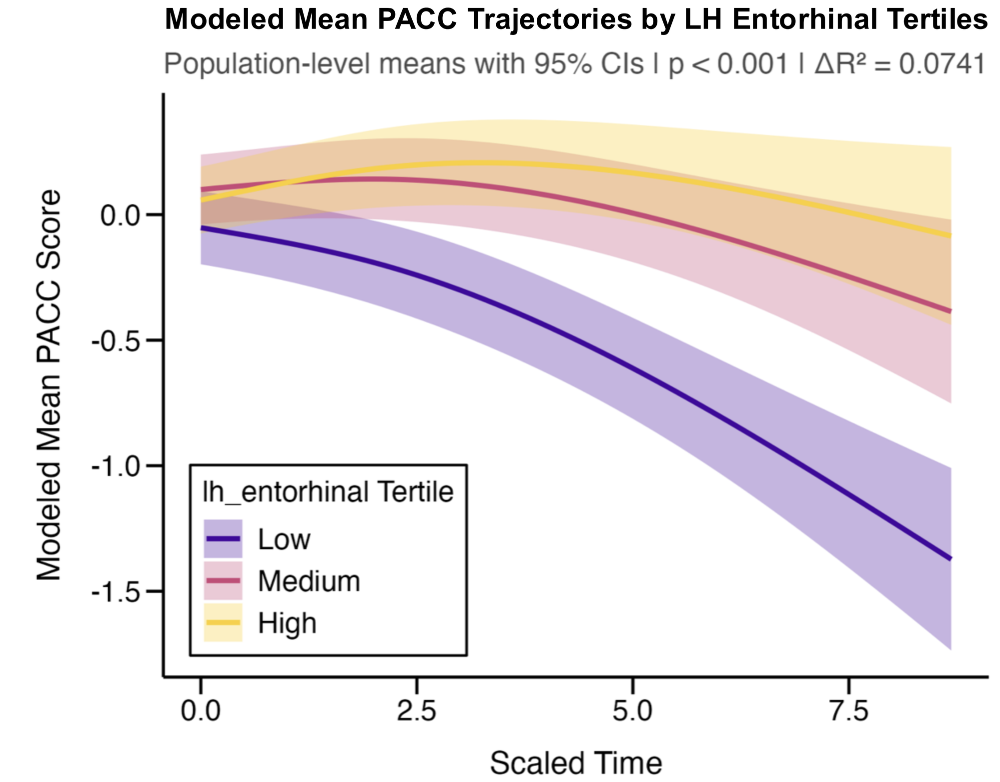
A. GWR



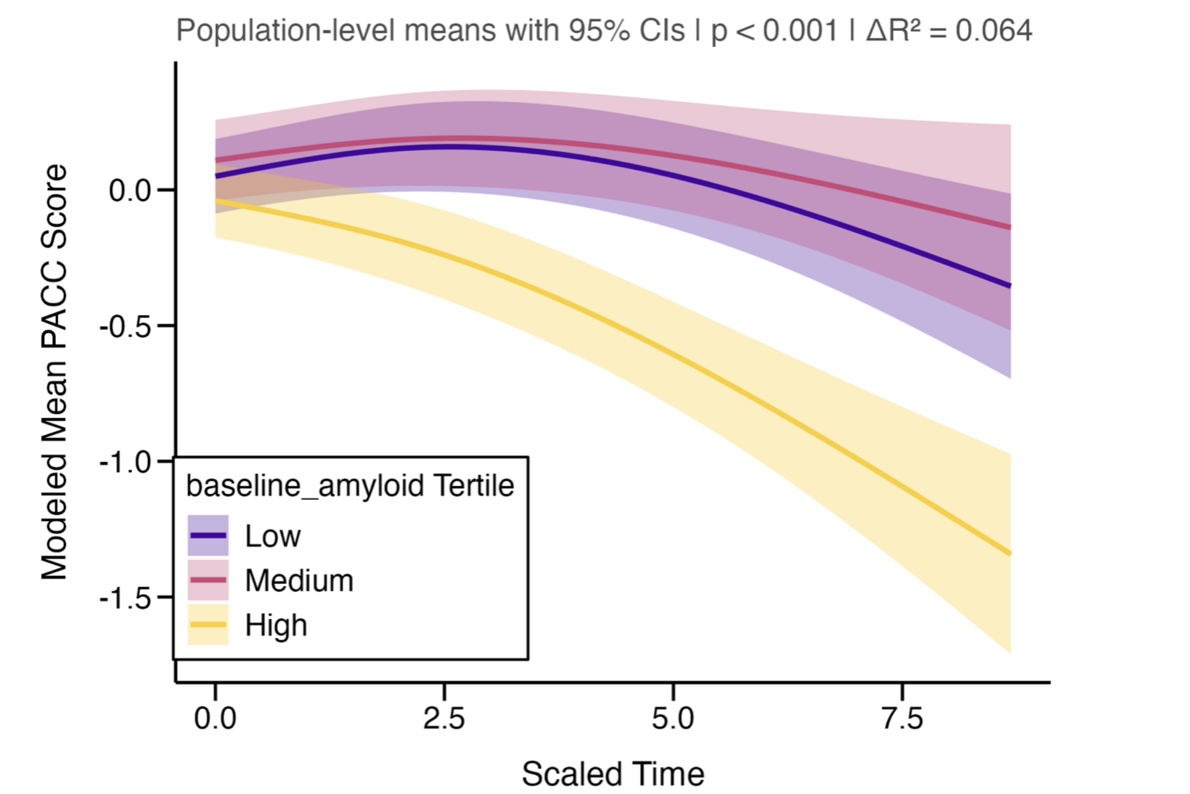


B. Cortical Thickness

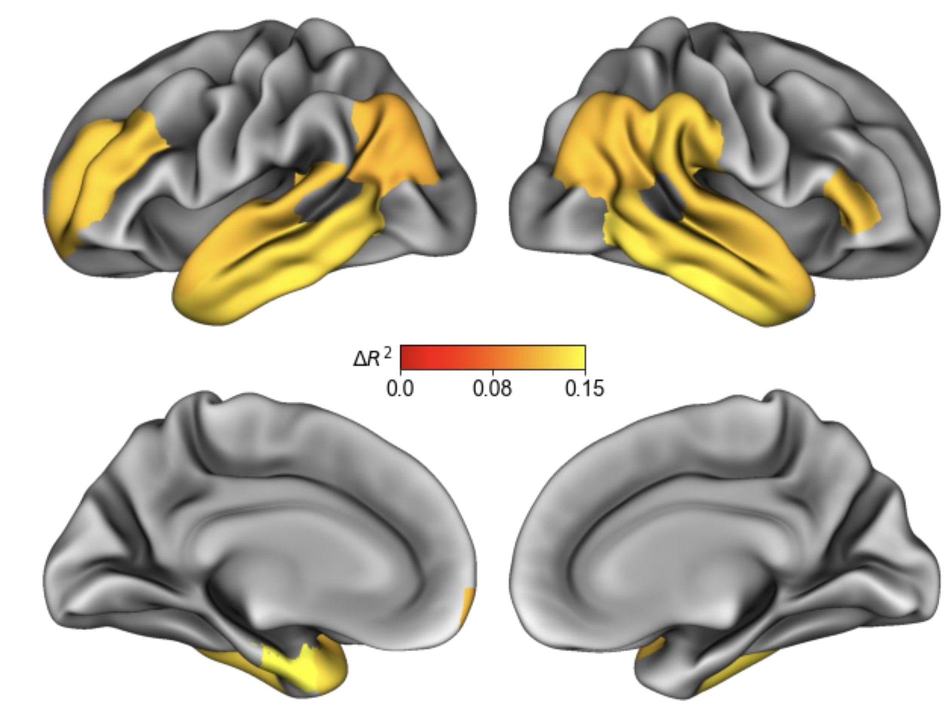




Modeled Mean PACC Trajectories by Baseline Amyloid Tertiles



Additive Effects of Baseline GWR and Amyloid



CONCLUSIONS

- In cognitively unimpaired older adults, baseline GWR is a stronger predictor of longitudinal cognitive decline than cortical thickness.
- Although GWR is associated with cortical amyloid accumulation[9], it may capture unique aspects of AD-related neuropathologic and/or neurodegenerative change relative to amyloid accumulation, thus leading to improved model performance when coupled together.
- These findings support the utility of conventional T1-weighted MRI for multi-scale assessment of brain structural integrity, with potential applications in diagnosis, prognostication, and outcomes monitoring in neurodegenerative diseases.

REFERENCES & ACKNOWLEDGMENTS

[1]Montal et al. (2018). *Alzheimers. Dement.*; [2]Spotorno et al. (2024). *Brain*; [3]Spotorno et al. (2023). *Brain*; [4]Salat et al. (2011). *Neuroimage*; [5]Putcha et al. (2023). *Neuroimage Clin.*; [6]Dagley A, et al. *Neuroimage* 2015.; [7]Papp et al. (2024). *J Prev Alzheimers Dis.*; [8]Sperling et al. (2024). *J Prev Alzheimers Dis.*; [9]Jang et al. (2024). *Neurobiol Aging.*

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