

ARTS and Brain Age Gap Across the Brain–Vascular Aging Continuum in Relation to Cardiovascular risk behaviors and Brain Maintenance

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KEY MESSAGE

- ARTS is associated with older-appearing brains, reflecting cumulative vascular burden.
- Viewed through a resilience lens, BAG offers a promising tool for quantifying brain maintenance.
- By identifying individuals who maintain younger-appearing brain structure in the presence of vascular risk, BAG provides a complementary framework for distinguishing vulnerability from resilience along the brain-vascular aging continuum.
- Clarifying the cognitive consequences across this continuum remains the key next step.

BACKGROUND

Individuals age biologically at different rates despite similar neuropathological burdens. Some show accelerated cognitive decline, others maintain brain structure into late life. The Brain Age Gap (BAG) captures this variability and relates to dementia risk factors. From a resilience perspective, BAG may reflect brain maintenance, indicating preserved, “younger-appearing” brain structure despite age-related insults. ARTS aptures in vivo microvascular damage, but its contrubution to BAG—and whether microvascular injury signals reduced resilience—remains unclear.

AIMS

To examine associations between ARTS and BAG, postmortem athero-/arteriolosclerosis, and cardiometabolic conditions to clarify whether vascular microstructural injury relates to diminished brain maintenance in older adults.

METHODS

Study population. We included 1,134 dementia-free individuals (85% women) from the Rush ADRC cohorts (ROS, MAP, MARS, LATC, Clinical Core) with brain MRI at baseline (cross-sectional design).



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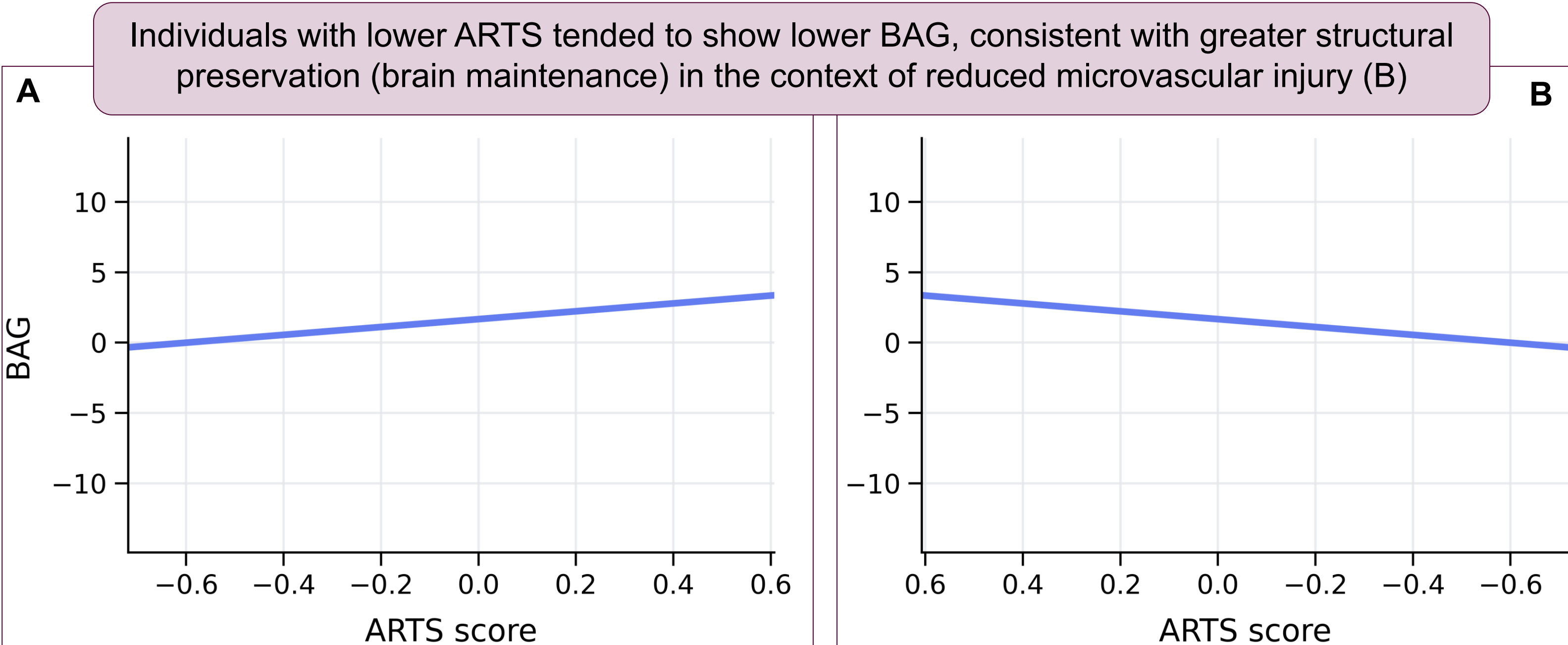
My team’s research focuses on understanding vascular contributions to cognitive disorders, particularly linked to cerebral small vessel disease, as well as mechanisms of cognitive resilience and sex-related differences.

RESULTS

1—Association between ARTS and BAG.

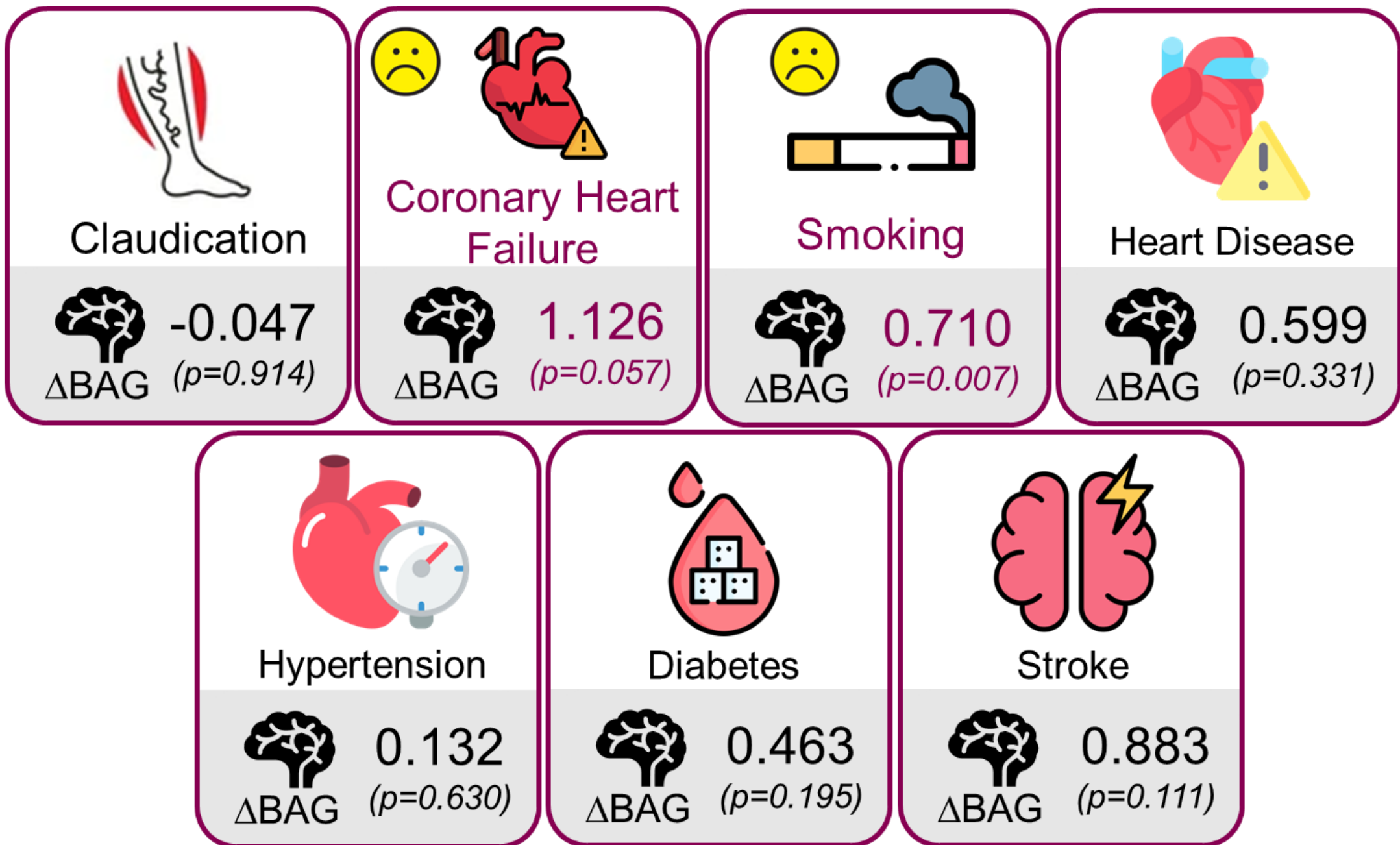
Greater ARTS score was associated with greater BAG (older-looking brains) (A) [$\beta=2.79$, $SE=0.66$, $p<0.001$]

Chronological age	78.8 ± 6.8 (range 59.8–96.3)
Predicted brain age	79.0 ± 7.5 (range 59.1–101.3)
BAG	-0.12 ± 4.7 (range -14.9–14.5)
ARTS score	-0.06 ± 0.21 (range -0.72–0.61)



2 —BAG, vascular brain pathology, vascular conditions, and ARTS.

Atherosclerosis showed a borderline association with BAG ($\beta = 1.11$, $SE = 0.60$, $p = 0.064$); no other associations were observed postmortem.



Adjusting for ARTS attenuated the association between heart failure and BAG, whereas the association with smoking persisted.

ARTS is an MRI-based classifier that estimates the likelihood of arteriolosclerosis in vivo, using T1w, FLAIR, and DTI data as input. The model was trained on ex vivo MRI data and subsequently translated to in vivo application (Makinejad et al *Neuroimage Clin* 2021).

BAG was estimated from structural T1-weighted MRI using convolutional neural networks with a hold-out validation approach (Leonardsen et al., *NeuroImage*, 2022). BAG was calculated as predicted brain age minus chronological age.

Postmortem vascular pathology & in-vivo vascular conditions. In vivo vascular risk factors included self-reported smoking, heart failure, hypertension, and diabetes. Postmortem assessments included cerebral amyloid angiopathy, large-vessel atherosclerosis, gross infarcts, and small-vessel arteriolosclerosis.

Statistical analysis. Generalized linear model adjusted for age at MRI, sex, and education



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