



Associations Of Inflammatory Processes And White Matter Hyperintensities In Community-dwelling Older Adults

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INTRODUCTION

- ❑ Inflammatory processes are associated with Alzheimer's disease and related dementias (AD/ADRD)¹.
- ❑ Higher peripheral inflammation (e.g., hs-CRP) is associated with greater white matter hyperintensities (WMH) in older adults².
- ❑ Glial fibrillary acidic protein (GFAP), indexing astrocyte reactivity and neuroinflammation, is linked with greater WMH and AD pathology³.
- ❑ APOE-ε4 carrier status, a risk factor of AD, is linked to both peripheral and neuroinflammation.
- ❑ **Key Questions:** 1. Do peripheral and neuro inflammation have distinct contributions to WMH burden in community-dwelling populations? 2. Do they interact with APOE-ε4 status?

METHODS

Participants: 372 U.S. community-dwelling dementia-free men from the Vietnam Era Twin Study of Aging (VETSA)

- ❑ Mean age: 67.38 years, SD=2.66; Range: 61-72

MRI Acquisition: 3TGE Discovery MR750, 8-channel coil, 3DT1 FSPGR, 2DT2 FRFSE-XL, 2DPD FRFSE-XL

MRI Processing: Multi-channel segmentation approach for global WMH volume⁴ (**Figs. 1 & 2**).

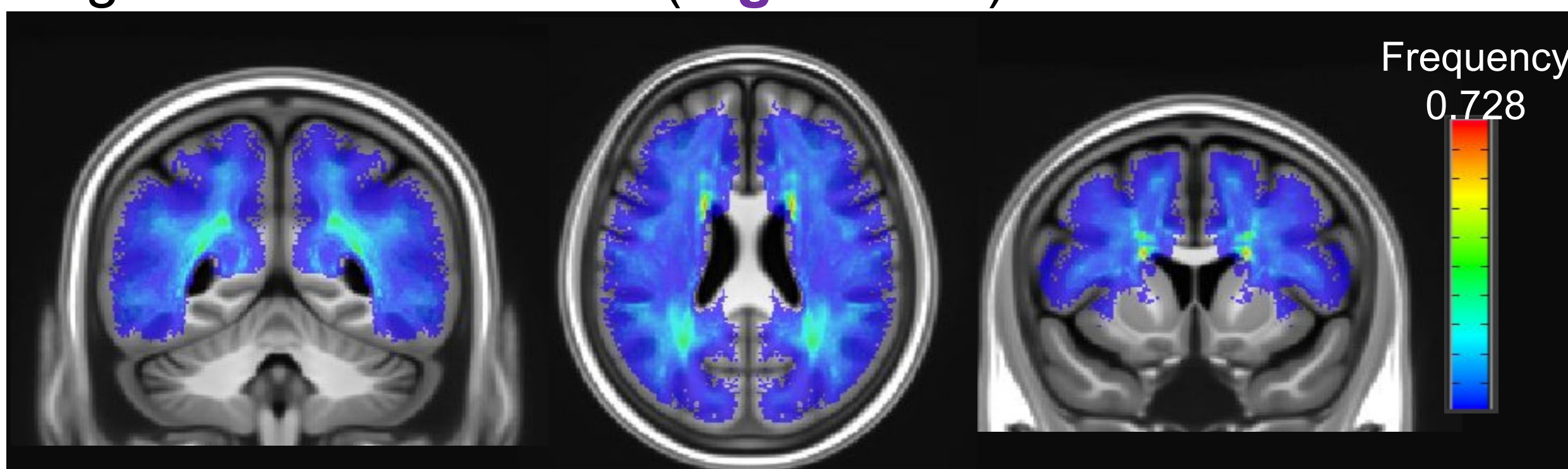


Fig. 2. WMH frequency atlas reflects the spatial distribution and common areas of WMH in this cohort. Colors reflect the frequency of the sample with WMH in the given voxel.

Blood Collection and Processing (fasting):

- ❑ Plasma GFAP: Simoa HD-X platform by Quanterix
- ❑ Serum hs-CRP: Spectrophotometry by Quest

Statistical Analyses: Biomarkers and WMH volume log transformed, GFAP adjusted for site & storage time

- ❑ Global WMH Volume ~ Age + biomarker*APOE-ε4 status + health comorbidities + total WM volume + (1|Family ID)

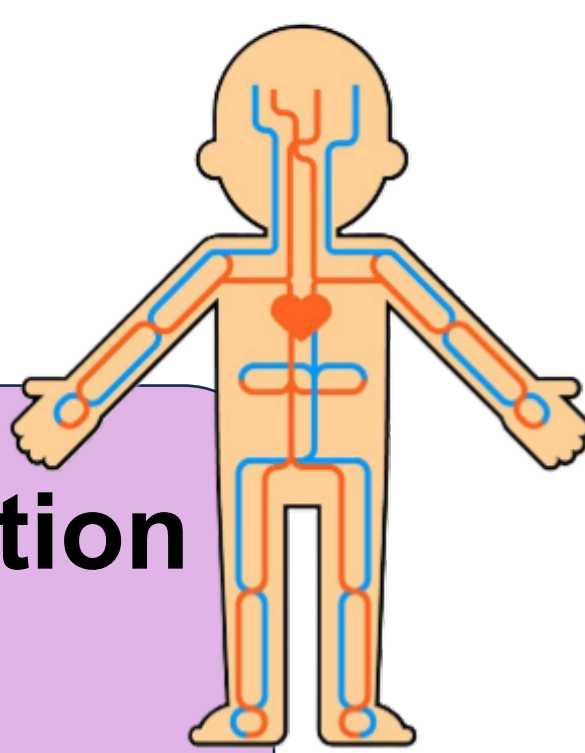
RESULTS

- ❑ With hs-CRP and GFAP together in same model:
 - ❑ Higher hs-CRP and GFAP were both significantly associated with greater WMH volume
- ❑ There were no interactions of either biomarkers with APOE-ε4 carrier status, and no main effect of APOE-ε4

Associations with greater WMH volume



Neuroinflammation
GFAP
 $\beta=.06, p=.024$



Peripheral inflammation
hs-CRP
 $\beta=.08, p=.004$

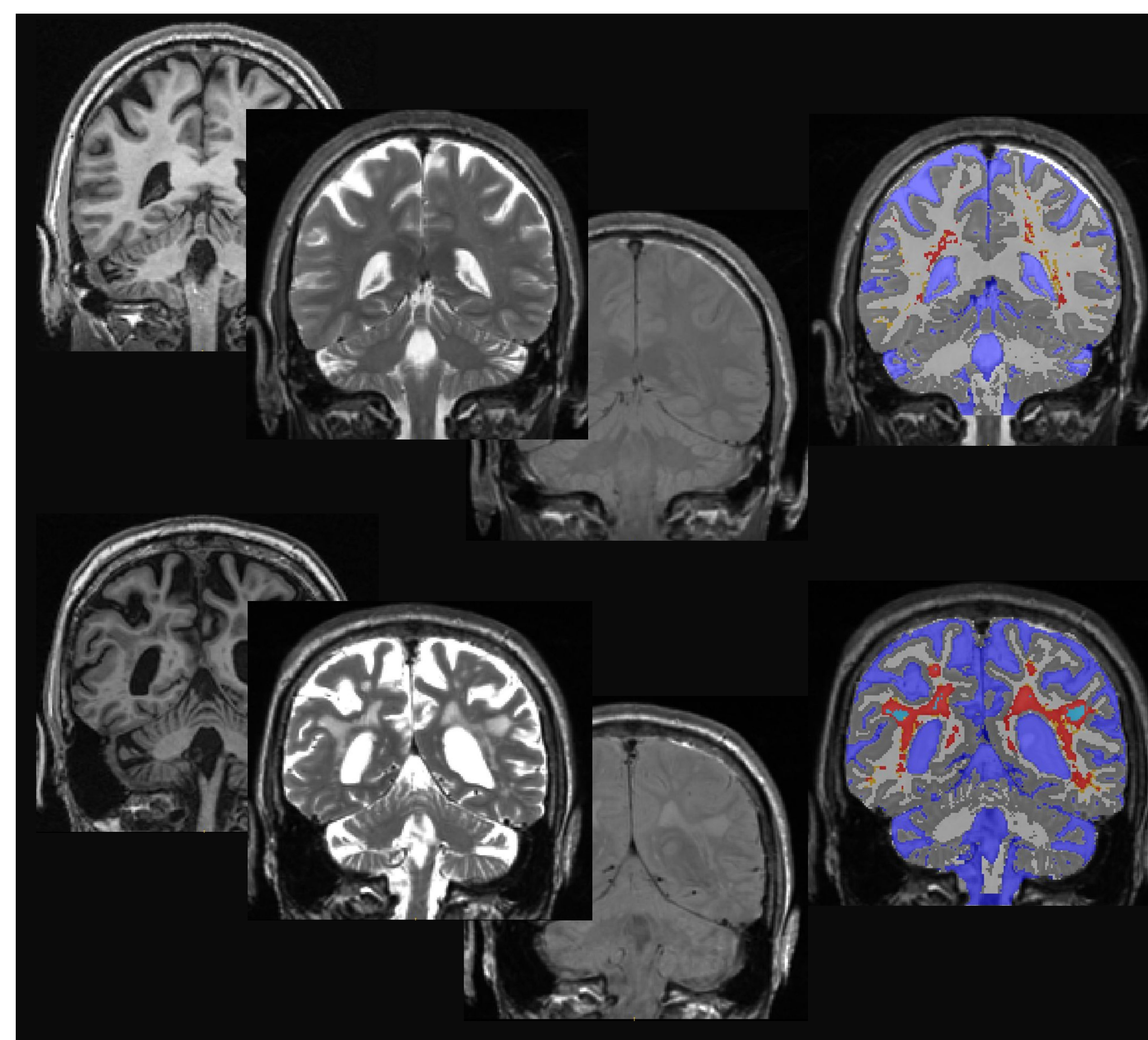


Fig. 1. WMH segmentation⁴. T1 (first), T2 (second), PD (third) volumes using ITK statistical classification framework, Scott's L2E method, anatomical considerations via ITK's morphological operators⁴. Segmented images (fourth): CSF=dark blue; gray matter=gray; normal white matter=light gray; WMH=red, baby blue.

- ❑ **Sensitivity Analyses:** Results remained unchanged when controlling for Body mass index (BMI). BMI is considered a confound of biomarker levels (i.e., more dilution, lower biomarker level).

DISCUSSION

- ❑ Peripheral inflammation and neuroinflammation are distinct biological pathways associated with WMH burden.
- ❑ WMH may arise from multiple inflammatory mechanisms in the peripheral and central nervous systems simultaneously.
- ❑ Targeting both inflammatory processes may be beneficial for treating WMH burden and related neurodegenerative diseases.

REFERENCES

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