

Vascular Abnormality is Associated with T2 FLAIR White Matter Hyperintensity & Glymphatic Dysfunction in Community Residing Older Adults

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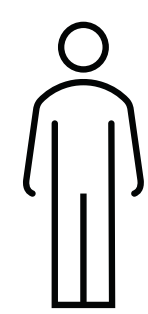
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Introduction

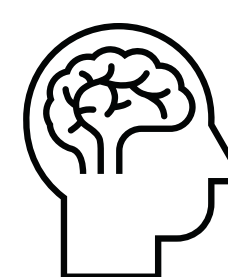
- The glymphatic system has been proposed to play a key role in the pathogenesis of dementia.
- Diffusion tensor imaging along the perivascular space (DTI-ALPS) is designed to evaluate the movement of water in the direction of the medullary perivascular spaces.
 - A lower ALPS index has been observed in conditions where glymphatic system dysfunction has been implicated, such as Alzheimer's disease.
- White matter hyperintensities (WMH), as identified on T2 FLAIR MRI, are a marker of small vessel disease, and increase in burden with age.
 - Glymphatic system dysfunction has been proposed to influence initiation and progression of small vessel disease.
- We hypothesized that in older adults:
 - WMH volume and the DTI-ALPS index would be inversely related.
 - Vascular risk factors would be associated with increasing WMH volume and decreasing ALPS index.

Methods

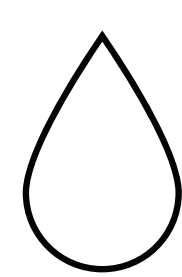
Participants were from the Einstein Aging Study, a systematically recruited, community-based cohort of adults over age 60 from the Bronx, NY.



Participants
n=154
78.2 ± 4.8 years old
36% male



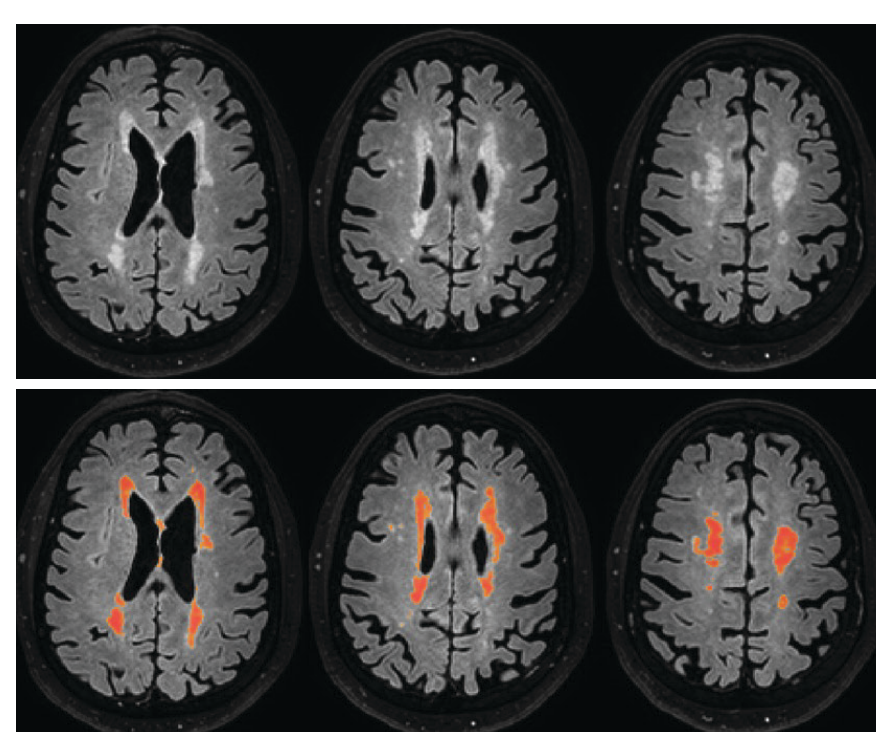
Brain MRI
• T1
• T2 FLAIR
• DTI



Blood Biomarker
• LDL cholesterol
• Glucose
• Insulin

WMH were segmented on T2 FLAIR using the Lesion Prediction Algorithm (LPA). The mean DTI-ALPS index was calculated following standard methods. FreeSurfer was used to obtain estimated intracranial volume.

Relationships were assessed via linear models between WMH volume (log-transformed) and DTI-ALPS, and with blood biomarkers, controlling for the effect of age, sex, intracranial volume, and MRI protocol.



Example of WMH segmentation with LPA.

Results

A significant negative relationship was observed between WMH volume and DTI-ALPS ($B=-0.034$, $p=0.003$).

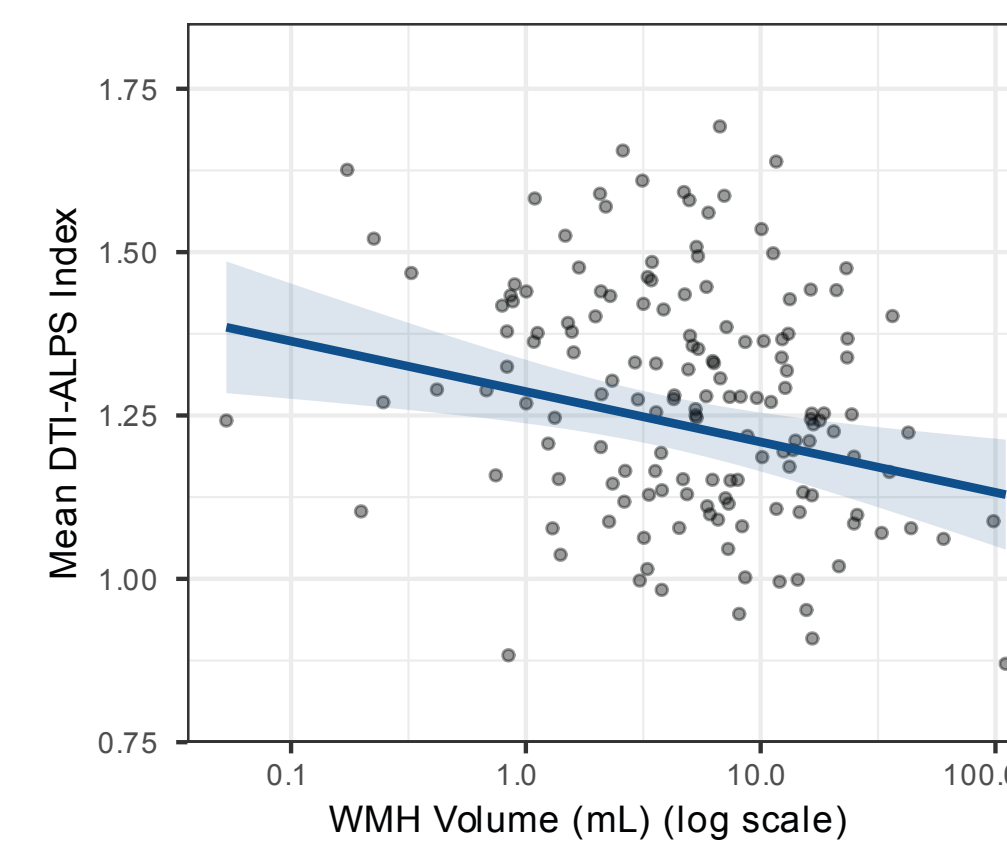


Figure 1. WMH volume vs. mean DTI-ALPS index with a model-predicted line and 95% confidence interval, controlled for covariates.

A significant positive relationship was observed between fasting insulin and DTI-ALPS ($B=0.004$, $p=0.027$) and between fasting insulin and WMH volume ($B=0.031$, $p=0.010$).

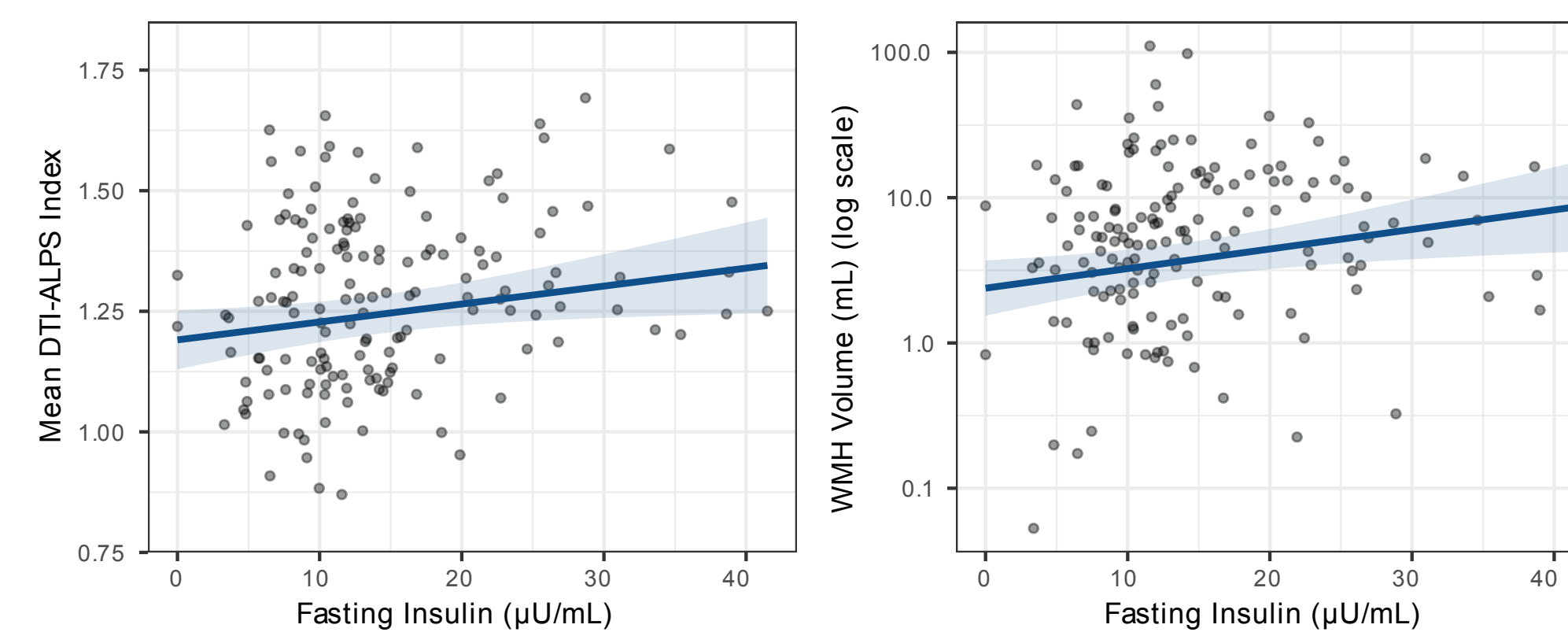


Figure 2. (Left) Fasting insulin vs. mean DTI-ALPS index and (Right) Fasting insulin vs. WMH volume. Both scatterplots show a model-predicted line and 95% confidence interval, controlled for covariates.

A significant negative relationship was also seen between LDL cholesterol and WMH volume ($B=-0.008$, $p=0.006$; Figure 3). All figures show a model-predicted line and 95% confidence interval, controlled for covariates.

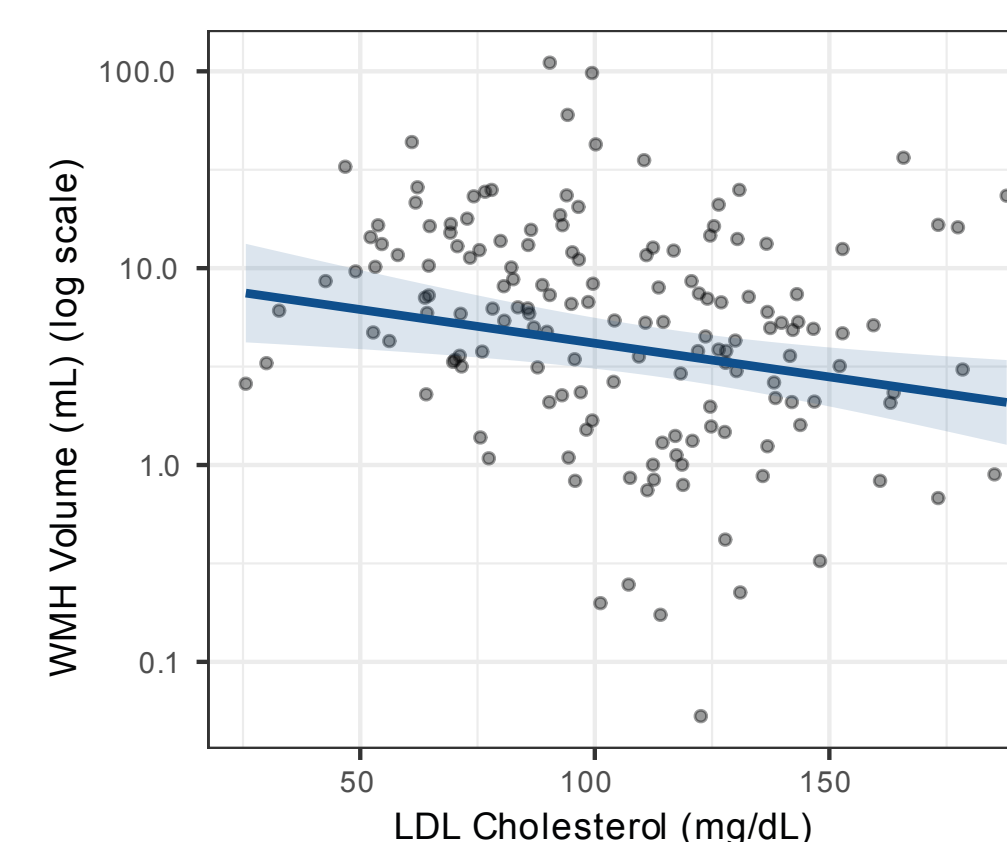


Figure 3. LDL cholesterol vs. WMH volume with a model-predicted line and 95% confidence interval, controlled for covariates.

Conclusions

- We identified a significant negative relationship between WMH volume, a marker of vascular disease, and the DTI-ALPS index, aligned with literature.
- Consistent with our hypothesis, increasing fasting insulin, a potential measure of insulin resistance, was associated with increasing WMH volume.
- However, increasing insulin levels were associated with increasing glymphatic function and increasing LDL cholesterol was associated with lower WMH volumes.
- Future work will explore a broader set of cardiovascular risk factors and the potential confounding effect of treatment.

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