



MIND Diet Adherence Attenuates the Effects of Cerebrovascular and Neurodegenerative Disease Burden on Cognition

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Background

The MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet is associated with reduced Alzheimer's disease dementia risk and cognitive decline (Morris et al. 2015, *AlzDem*), but its role in moderating pathology-cognition relationships in high-risk populations remains unclear.

This study examined **whether adherence to the MIND diet moderated the impact of brain pathology on cognitive performance.**



Methods

Cohort

- 66 participants were included; they were drawn from the MINDSpeed randomized controlled trial (Clark et al. 2019, *AlzDem*) (baseline data only; cross-sectional analysis).
- The cohort was at high risk for dementia. Eligibility criteria: 60+, no evidence of dementia, completed high school education or less, residing in the Indianapolis metropolitan area; majority Black females.
- All participants completed cognitive assessments, the online VioScreen food frequency questionnaire (FFQ), and structural MRI.

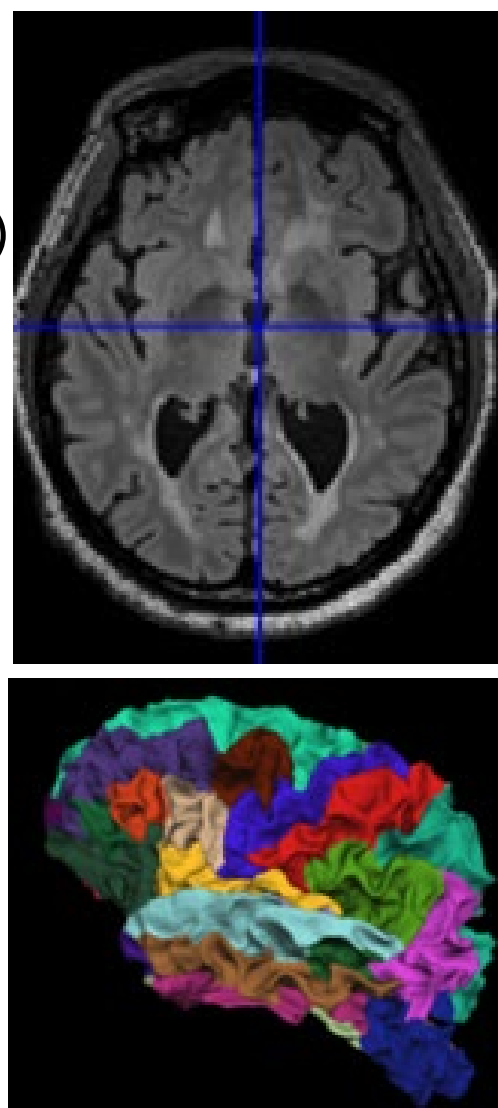
N=66 participants	
Age	65 ± 5 (60-82)
Sex, Female	73%
Race	65% Black; 30% White; 5% Other
Education	11.6 ± 1.6
APOE ε4 +	44%
BMI	33 ± 8 (21-55)
Hypertensive	80%
Diabetic	44%
Heart attack/MI	11%
Stroke or TIA	15%
MIND diet score	5.6 ± 1.9 (2-11.5)
HEI-2020 score	59.5 ± 11.4 (34.1-88.4)
Table 1. Participant demographics. Presented as mean ± standard deviation (range) for continuous variables and percentage for categorical variables.	

MIND diet score

- The VioScreen FFQ (Viocare, Inc) was converted to a MIND diet score (Dempsey et al. 2025, *AlzDem*).
- Briefly, the MIND diet has 15 dietary components, including 10 'brain-healthy' food groups, and 5 'unhealthy' food groups which are reverse scored. Each of the food categories were coded into high, medium, or low intake using predetermined cutoffs (Morris et al. 2015, *AlzDem*) and given a score of 0, 0.5, or 1, and summed to a total of 15, with higher scores indicating greater adherence.

Structural MRI

- Measurements of brain pathology:
 - Total white matter hyperintensity (WMH) volume, a marker of cerebrovascular disease, was estimated from T2 FLAIR using the LST-LGA algorithm in SPM12
 - WMH was cube-root transformed.
 - Hippocampal volume & cortical volume were estimated from the T1 MP-RAGE scan using FreeSurfer v7
 - Hippocampal volume and cortical volume were adjusted for intracranial volume (ICV) using the residual method.



Cognition

- Multiple cognitive assessments were used to create a memory composite and an executive function composite; the two were averaged to create the overall cognition composite (Clark et al. 2025, *AlzDem*).

Methods

Statistical Analysis

- Multivariate linear regression models were used to test:
 - The relationship between each MIND diet score and cognitive performance.
 - Significant associations (p<0.05) were further tested including neuroimaging measures to test whether the associations were independent of structural brain pathology.
 - The relationship between brain pathology (WMH, hippocampal, & cortical volume) and cognitive performance.
 - Interaction models then tested whether diet modifies associations between brain pathology and cognition.
 - Post-hoc simple slopes analysis was used to facilitate interpretation for significant interactions (p<0.05).
- All models were adjusted for age, sex, and years of education.

Results

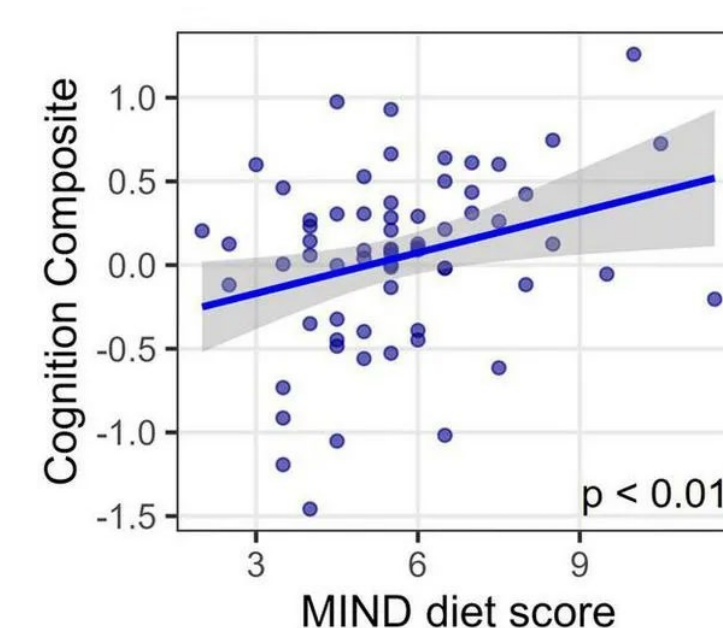


Figure 1. Association between MIND diet score and cognitive performance.

MIND diet score was positively associated with the cognition composite ($\beta = 0.32$, 95% CI: 0.09 to 0.54, $p = 0.008$) when adjusted for age, sex, and education.

When analyzed by domain, the MIND diet positively associated with memory ($\beta = 0.34$, 95% CI: 0.11 to 0.58, $p = 0.005$), but not executive function performance ($\beta = 0.16$, 95% CI: -0.08 to 0.40, $p = 0.19$).

The association between the MIND diet score and memory remained significant after additional adjustment for each brain pathology measure.

Direct relationships between structural brain pathology and cognition.

Greater white matter hyperintensity volume (WMH) was associated with worse cognitive performance ($\beta = -0.34$, 95% CI: -0.57 to -0.11, $p = 0.004$). Neither hippocampal volume nor cortical volume were significantly associated with the cognition composite.

	β (95% CI)	p-value
WMH volume	-0.15 (-0.35, 0.05)	<0.001
Diet score	0.42 (0.22, 0.61)	0.08
WMH volume x Diet score	0.47 (0.28, 0.66)	<0.001
Hippo volume	0.13 (-0.11, 0.38)	0.66
Diet score	0.21 (-0.03, 0.45)	0.08
Hippo volume x Diet score	-0.03 (-0.36, 0.30)	0.86
Cortex volume	0.19 (-0.04, 0.43)	0.01
Diet score	0.21 (-0.01, 0.44)	0.06
Cortex volume x Diet score	-0.30 (-0.56, -0.04)	0.02

Table 2. Interactions between brain pathology and MIND diet scores predicting cognition.

The MIND diet score was a significant moderator of the relationships between WMH volume and cortical volume and cognition, but not hippocampal volume and cognition.

Shown are the main effects for diet and brain pathology and their interaction term from models adjusted for age, sex, and education. The values reported are the standardized beta estimate (B), the 95% confidence interval (CI), and p-values. Boldface indicates a significant relationship ($p < 0.05$).

Greater white matter hyperintensity volume and lower cortical volume significantly associated with cognitive performance only at the low MIND diet score, but not medium or high MIND diet scores.

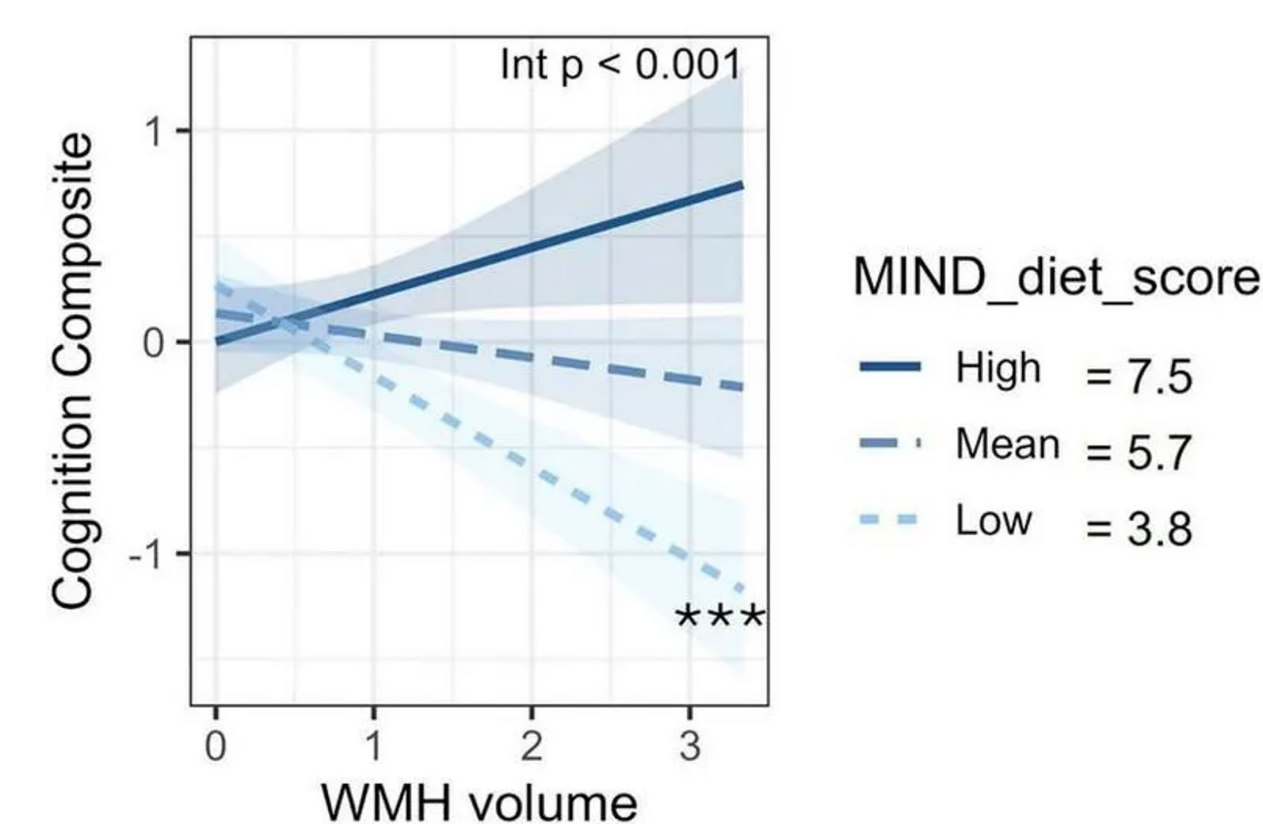


Figure 2. White matter hyperintensity volume x MIND diet interaction on cognition.

WMH volume was significantly negatively associated with cognition at the low MIND diet score ($\beta = -0.62$, 95% CI: -0.86 to -0.30, $p < 0.001$). However, at the mean or high MIND diet scores, WMH was not significantly associated with cognitive performance ($p > 0.05$).

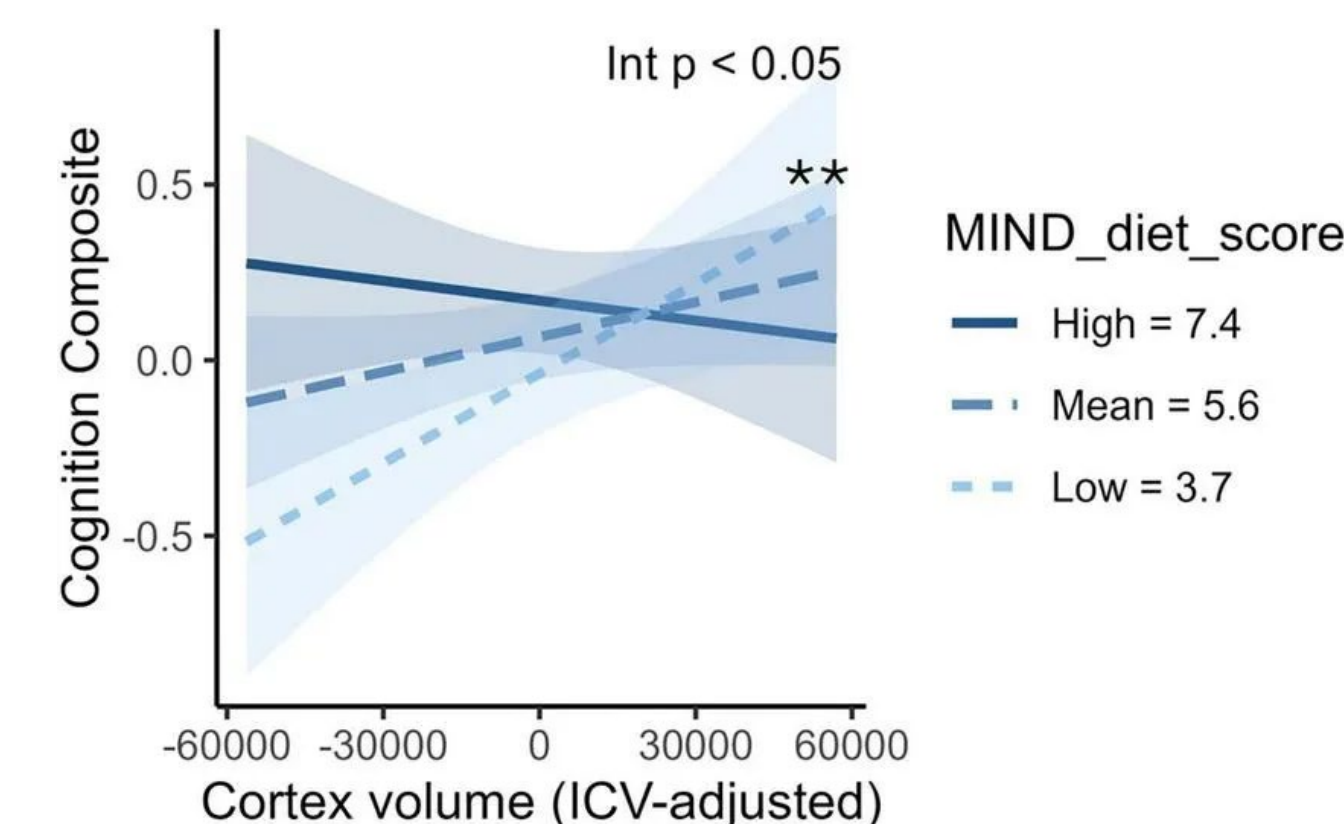


Figure 3. Cortical volume x MIND diet interaction on cognition.

Lower cortical volume was significantly associated with worse cognition at the low MIND diet score ($\beta = 0.44$, 95% CI: 0.12–0.77, $p = 0.008$) but was not significantly associated with cognition at the mean or high MIND diet scores ($p > 0.05$).

Conclusions

- In this cross-sectional study of older adults at high risk for dementia:
 - Greater adherence to the MIND diet was associated with better memory performance independent of brain pathology.
 - MIND diet adherence substantially moderated relationships between structural brain pathology and cognition.
 - At the low MIND diet score, greater WMH volume was strongly associated with poorer cognitive performance. However, these negative associations were markedly attenuated and no longer significant at the average and high MIND diet scores. A similar, but weaker effect was seen for cortical volume.
 - MIND diet adherence did not significantly modify the relationship between hippocampal volume and cognition, and dietary influence on AD-specific processes remains less clear.
- Higher levels of white matter disease and diffuse cortical neurodegeneration may have less impact on cognition in individuals with higher adherence to the MIND diet.**
- These moderation effects support a cognitive resilience or compensation framework, whereby adherence to the MIND diet enhances the brain's capacity to compensate for structural damage—particularly cerebrovascular pathology and cortical changes—without proportionate cognitive impairment.
 - This supports other studies on cognitive resilience (Dhana et al. 2021, *J Alzheimers Dis*; Wagner 2023 et al. *AlzDem*; Bauer et al. 2025, *Front Neuro*).
- These findings highlight the MIND as a promising, accessible strategy to support cognitive health and resilience in vulnerable populations. Further studies are needed.

Limitations

- Limitations include modest sample size and cross-sectional design, which precludes causal inference. All individuals were recruited from the Indianapolis metropolitan area, limiting the generalizability of results. Diet and other health factors were self-reported and thus subject to bias. The absence of an AD-specific biomarker (e.g., A β or phosphorylated tau) limited our ability to disentangle vascular and AD contributions to cognitive function.

Future Directions

- Future studies should examine dietary resilience across varying types and severities of brain pathology and explore other reserve-related factors.
- Longitudinal and interventional studies incorporating in vivo biomarkers of cerebrovascular disease, AD pathology, and neurodegeneration will be essential to clarify temporal relationships and causal mechanisms.

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