

Higher short-term continuous glucose variability is associated with lower gray matter and higher white matter hyperintensity volumes in older adults: The Multi-Ethnic Study of Atherosclerosis (MESA)



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Background:

- Dysglycemia is a well-established risk factor for cognitive decline.
- The association of **short-term glucose control** with early **neuroimaging markers of dementia** remains largely unexplored.

Hypothesis:

- Higher continuous glucose variability** and **higher mean continuous glucose**, assessed by continuous glucose monitoring (CGM), are associated with **lower total** and **regional gray matter volumes (GMV)** and **higher total white matter hyperintensity volume (WMHV)**.

Methods:

- Outcomes:** MESA participants completed 3T brain MRI protocols in 2022-2024 (n=1427) for brain volumes including:
 - Total gray matter (GM), frontal lobe GM, temporal lobe GM, limbic GM, total hippocampus GM, and white matter hyperintensities volume (WMHV)
- Exposures:** MESA participants completed CGM (n=842) in 2022-2024 with ≥ 3 days of glucose variability (mean[SD] 11.7 [2.4] days).
- Standard deviation of glucose (SD)
- Coefficient of variation (CV)
- Mean continuous glucose (MEAN)
- Statistics:** We report the standardized differences in GMV and log-unit differences in WMHV per two-fold increment in short-term glucose variability (SD, coefficient of variation [CV], mean continuous glucose) with 95% confidence intervals (CI) from multivariable linear regression models adjusted for total intracranial volume, study site, age, sex, race/ethnicity, education, vascular risk factors, and APOE $\epsilon 4$ allele status.

Conclusions:

Higher continuous glucose variability was associated with **lower total GMV** and **higher total WMHV**, whereas **mean continuous glucose** was associated only with **total WMHV** in a diverse, community dwelling sample of older adults. Associations differed by diabetes status.

-For more information about the MESA study, visit <https://mesa-nhlbi.org/about/overview>

	Combined, N = 790	Normoglycemic, n = 569	Type II Diabetes, n = 221
Age, years	75.1 (6.5)	75.2 (6.8)	74.8 (6.0)
Women, n (%)	410 (51.9)	312 (54.8)	98 (44.3)
Nonwhite, n (%)	465 (58.8)	297 (52.2)	168 (76.0)
Body Mass Index, kg/m ²	28.1 (5.1)	27.3 (4.7)	30.4 (5.4)
Systolic blood pressure, mmHg	119.3 (13.5)	117.7 (13.3)	123.2 (13.2)
Hypertension, n (%)	429 (54.3)	269 (47.3)	160 (72.3)
Education attainment (> high school), n (%)	722 (91.3)	528 (92.8)	194 (87.7)

Data are means (SD) unless noted otherwise.
 Sample stratified by diabetes status by American Diabetes Association guidelines.

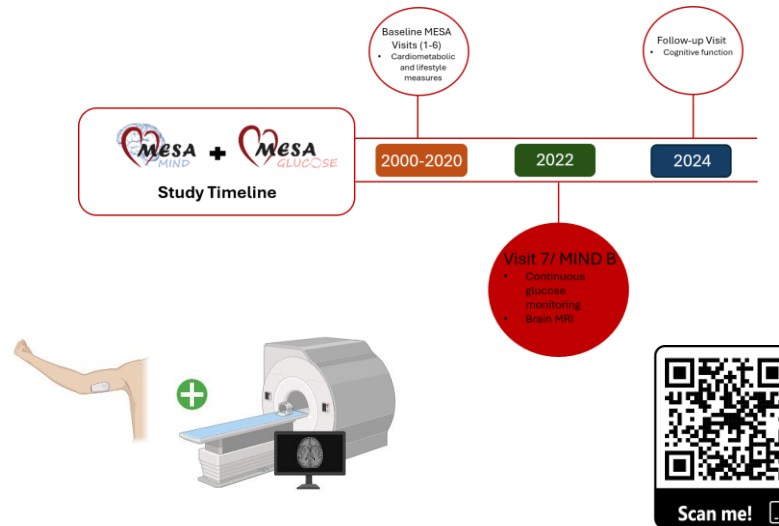
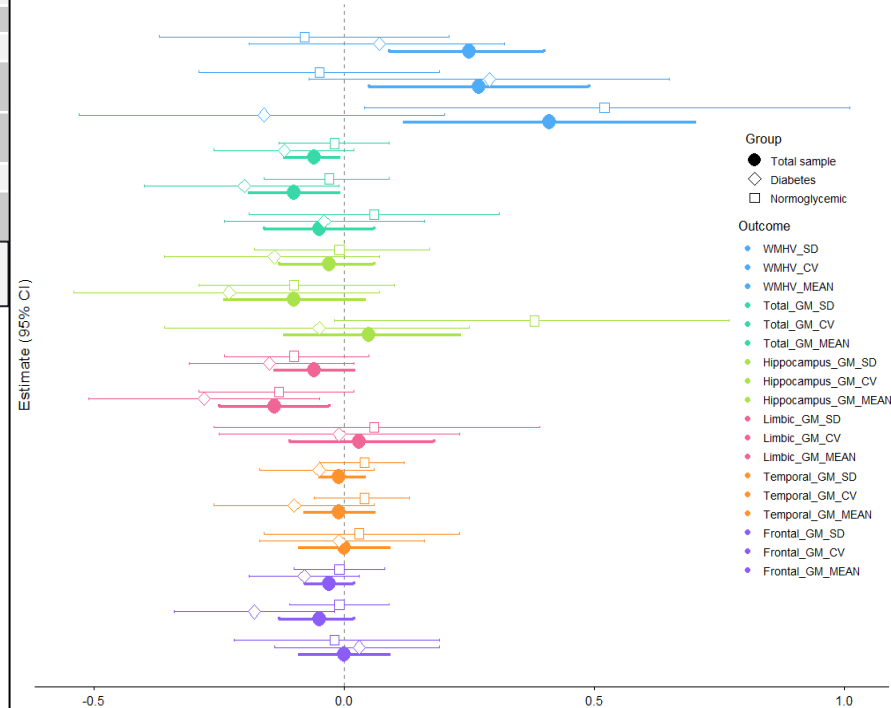


Figure 1. Higher short-term glucose variability associated with total and regional gray matter volumes and white matter hyperintensity volumes.

Standardized or log-unit difference in volume per two-fold increment in CGM variability (95% CI)



CV, coefficient of variation; CI, confidence interval; CGM, continuous glucose monitoring; GM, gray matter; SD, standard deviation; WMHV, white matter hyperintensity volume.
 Model adjusted for intracranial volume, study site, age, sex, race/ethnicity, educational attainment, mean systolic blood pressure, body mass index, HDL cholesterol, LDL cholesterol, plasma triglycerides, smoking history; lipid-lowering, anti-hypertensive, and psychiatric medication use; and APOE $\epsilon 4$ allele carrier status.
 Mean (SD) and Median [25%, 75%] of brain volumes are representative of all participants (28% Black, 12% Chinese, 19% Hispanic, 40% White). * $p < 0.05$ & ** $p < 0.01$.

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