

Hyperglycemia Does Not Add to Diabetes Status in Predicting Cognitive Decline: Results from the Atherosclerosis Risk in Communities (ARIC) Study

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Abstract

Introduction: Diabetes is associated with an increased risk of cognitive decline and dementia. It is unclear if hyperglycemia is an independent predictor of cognitive decline in persons with and without diabetes. **Hypothesis:** We hypothesized that hyperglycemia, as assessed by glycated hemoglobin (HbA1c), would be positively associated with decline in cognition in persons with and without diabetes. **Methods:** Prospective cohort study of 516 participants with and 8,442 without a history of diagnosed diabetes in the ARIC Study. We examined the association of categories of HbA1c (<5.7, 5.7-6.5, ≥6.5% in nondiabetics; <7, 7-8, ≥8% in diabetics) with 6-year change in three measures of cognition: the Digit Symbol Substitution Test (DSST), Delayed Word Recall Test (DWRT), and Word Fluency Test (WFT). Our primary outcomes were the quintile with the most annual cognitive decline for each test. **Results:** Mean age was 56 years; the participants were 56% female and 21% African American. Mean HbA1c was 5.7% overall, and 8.5% in persons with and 5.5% in persons without diabetes. In adjusted logistic regression models, diagnosed diabetes was associated with cognitive decline only as assessed by DSST (OR 1.42, 95% CI (1.14, 1.75), $p = 0.002$), but HbA1c was not a significant independent predictor of cognitive decline when stratifying by diabetes history (diabetes, p -trend = 0.320; no diabetes, p -trend = 0.566). Similarly, trends were not significant for the DWRT or WFT in either the presence or absence of diabetes. **Conclusions:** Over 6 years of follow-up, we found that hyperglycemia, as measured by HbA1c, did not predict cognitive decline beyond diabetes status in this middle-aged, community-based population. These findings are consistent with recent clinical trial data demonstrating that tight glycemic control does not prevent cognitive decline in diabetes. In conclusion, additional work is needed to identify the non-glycemic risk factors by which diabetes may contribute to cognitive decline.

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