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Introduction

- Type 2 Diabetes Mellitus (T2DM) is a risk factor for dementia, specifically for Alzheimer’s disease and vascular dementia, as the risk of dementia increases with increase in duration and severity of diabetes (Livingston et al., 2020).
- T2DM is characterized by insulin resistance (IR) and hyperglycemia, diagnosed by fasting blood glucose (FBG) levels ≤ 100 mg/dL.
- While there is plenty of evidence showing that diabetes serves as a risk factor for pathological cognitive decline and dementia, less research has studied the effect of FBG on cognition over time in the absence of diabetes.
- High blood glucose in the absence of diabetes is generally associated with cognitive decline especially in memory and executive functioning but findings have been mixed across studies (Crane et al., 2013, Yu et al., 2020, Zheng et al., 2018).
- Anti-diabetic drugs have not been shown to lower dementia risk suggesting that the optimal risk-modifying approach is to prevent onset of diabetes (Savelieff et al., 2022).
- This study aims to examine the association between FBG on cognitive functioning in a diabetes free and cognitively healthy cohort of community dwelling individuals.

Methods

Participants: FHS Offspring cohort with no history of diabetes and dementia at baseline & follow-up

Analyses: Series of multiple linear regressions

Predictor variable: FBG collected at FHS Core Exam 7; categorical FBG ≤ 100 mg/dL

Outcome variable: Differences between the cognitive domain factor score (separately for memory, executive function, language) generated from neuropsychological tests administered closest to Exam 7 (baseline) and most recent follow up exams; continuous scores

Baseline Characteristics	Healthy/Clean Sample N=1320
Sex, Female	750(56.8%)
Age (years)	58.7 ± 8.85
Education (college graduated)	578 (43.8%)
APOE, 4 carriers	299 (22.7%)
Treated for Hypertension	302 (22.9%)
Treated for Lipids	199 (15.1%)
FBG ≥ 100 mg/dL	402 (30.5%)
FBG (mg/dL)	954 (8.91%)
BMI (kg/m ²)	27.3 ± 4.96
TC (mg/dL)	202 ± 36.0
TG(mg/dL)	122 ± 71.5
HDL (mg/dL)	56.0 ± 16.9
LDL (mg/dL)	122 ± 32.3
MMSE (range 0 - 30)	29.0 ± 1.29

APOE = Apolipoprotein 4; FBG = Fasting Blood Glucose; BMI = Body Mass Index; TC = Total Cholesterol; TG = Triglycerides; HDL = High-density lipoprotein; LDL = Low-density lipoprotein; MMSE = Mini-Mental state examination

Results

MODEL	DOMAIN	N	Beta[95%CI]	p
1	Executive Function:	1592	-0.06 [-0.11, -0.01]	0.023
	Memory:	1597	-0.03 [-0.08, 0.02]	0.29
	Language:	1574	0.04 [-0.02, 0.10]	0.15
2	Executive Function:	1591	-0.06[-0.11, -0.01]	0.026
	Memory:	1573	0.04[-0.01, 0.10]	0.13
	Language:	1596	-0.03[-0.08, 0.02]	0.31
3	Executive Function:	1591	-0.06 [-0.11, -0.01]	0.029
	Memory:	1596	-0.03[-0.07, 0.02]	0.31
	Language:	1572	-0.05[-0.01, 0.10]	0.13

Three different models were considered: Significant p value highlighted in red
Model 1: Adjusted for sex, age, education, and follow up years
Model 2: Model 1 + treatment for hypertension, and treatment for hyperlipidemia
Model 3: Model 2 + MMSE, and APOE4

Discussion

- In cognitively healthy individuals without diabetes, FBG levels were associated with declines in executive functioning over time, but not in memory, or language.
- Additional research on the association between FBG and specific aspects of executive functioning should be explored, i.e., working memory, inhibition control, and cognitive flexibility, and whether this decline impacts daily functioning.
- Active management and monitoring of FBG is imperative to prevent risk of cognitive decline.

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