Impact of Glycemic Control and Cardiovascular Disease Measures on Hippocampal Functional Connectivity in African Americans with Type 2 Diabetes: a resting state fMRI Study

Afarin Famili[1], Gowtham Murugesan[1], Benjamin C. Wagner[1], S. Carrie Smith[2], Jianzhao Xu[2], Jasmin Divers[2], Barry I. Freedman[2], Joseph A. Maldjian[1], and Albert Montillo[1]

[1] University of Texas Southwestern Medical Center, Dallas, TX

[2] Wake Forest School of Medicine, Winston-Salem, NC

Purpose:

This study tests the hypothesis that inadequate Type 2 diabetes (T2D) management, including fine gradations of glycemic control, increasing measures of cardiovascular disease (CVD) and renal disease, leads to decreased hippocampal connectivity in African Americans (AA).

Materials and Methods:

The study includes 155 AA with T2D, 57% female with mean age of 59.2 years for whom diabetes management was quantified. Subjects had a mean diabetes duration of 14.5 years, hemoglobin A_{1c} (HbA_{1c}) of 7.97%, estimated glomerular filtration rate (eGFR) of 86.6 mL/min/1.73m^2, and coronary artery calcium (CAC) score of 475.4mg. An 8min resting state fMRI was acquired and structural and functional MRI were co-registered, normalized to MNI space, and mean fMRI time courses per region were computed, and then pairwise region connectivity using Pearson's correlation was computed. The regions and connections form a graph of nodes and edges. Correlation was thresholded to retain the top 10% edges. The degree of each region which represents the overall connectivity of the region to the rest of the brain was computed to form a brain health measure. A linear support vector regression model was fit to predict the brain health measure using 10-fold cross-validation, while permutation testing was used to compute model reliability. The predictor set consists of diabetes measures: HbA_{1c}, renal disease measures: eGFR, c-reactive protein (CRP), and urine albumin-to-creatinine ratio (ACR), and CVD measure: CAC. Our model is fully adjusted for education, age, sex and BMI.

Results:

The functional connectivity of the hippocampus was found to be significantly impacted by HbA_{1c} and CAC with R^2=1.9%, p=0.00047. Lower functional connectivity of right hippocampus (hippocampal degree) was associated with poor glycemic control (higher HbA_{1c}) and greater calcified plaque (higher CAC) as shown in Fig. 1. The results complement previous research demonstrating an inverse association between CAC and Montreal Cognitive Assessment test scores [Freedman et al, Diabetes Care, 2015].

Conclusion:

This work provides new evidence that elevated HbA_{1c} and CAC are associated with decreasing functional connectivity of the right hippocampus in AAs with T2D.

Clinical Relevance:

The results suggest that maintaining fine degree of glycemic control and cardiovascular health may support optimal hippocampal function, a structure critical for successful memory retrieval.

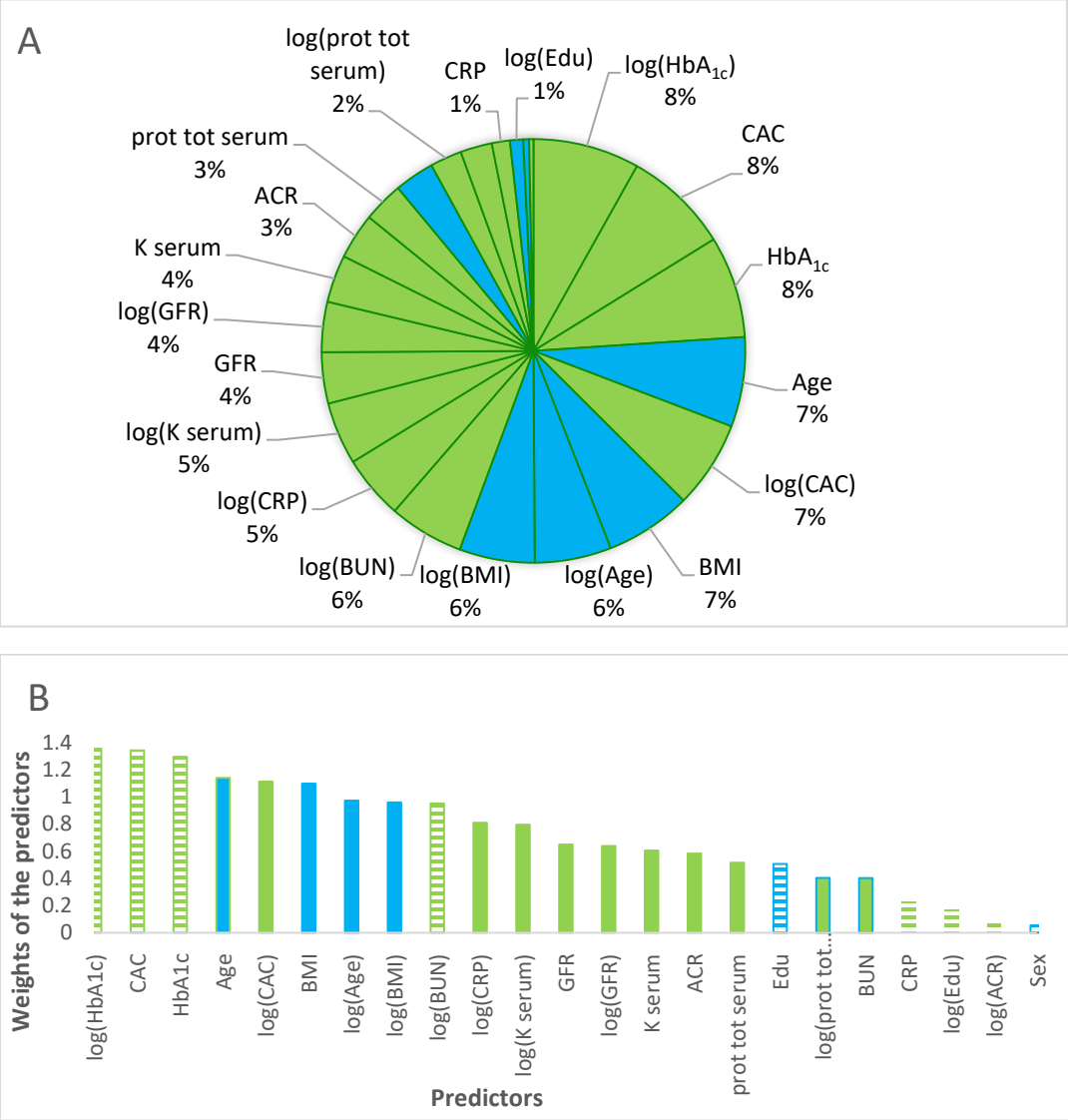

Figure1: Association between right hippocampal functional connectivity and diabetes. These 16 normalized diabetes, renal, and CVD related measures (green), and 8 normalized confounders (blue) combine to predict the functional connectivity of right hippocampus, with an effect size of R2 = 1.9%. A) Relative distribution of predictor weight B) Absolute predictor weight; solid and hatched bars indicate the direct and inverse association of variables with functional connectivity of hippocampus respectively. (Freedman et al, Diabetes Care, 2015)

References

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