SEX EFFECT IN THE ASSOCIATION BETWEEN FASTING BLOOD GLUCOSE AND TOTAL GREY MATTER VOLUME IN THE 60s

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THE AIM OF THIS STUDY WAS TO INVESTIGATE ASSOCIATIONS BETWEEN FASTING BLOOD GLUCOSE LEVELS, TOTAL BRAIN, GREY MATTER, WHITE MATTER, AND LATERAL VENTRICLE VOLUME IN A LARGE GROUP OF OLDER INDIVIDUALS.

INTRODUCTION

Past research has demonstrated that type 2 diabetes (T2D) is cross-sectionally and longitudinally associated with overall brain atrophy, and increased cerebrospinal fluid volume [1]. This pattern of atrophy is associated with cognitive decline and dementia [2]. Moreover higher blood glucose levels in the normal range have also been associated with hippocampal atrophy[3], and a 1.4 fold increased risk of developing dementia in non-diabetic Individuals [2]. It remains to be established whether the effects of high blood glucose are mainly limited to the hippocampus, or affect cerebral structures more broadly. This is particularly Important in an ageing context, because glucose metabolism becomes less efficient with age, and high blood glucose levels may exacerbate normal moderate age-associated brain atrophy [4]. This is also pertinent in the context of sex differences, as women have smaller brains and different grey to white matter ratios [5-7], higher incidence of T2D [8], and greater risk from health factors that impact both brain and blood glucose metabolism like greater increase in adiposity with age [6, 9].

METHOD

Individuals (*n*=288) with blood glucose and MRI data were selected from the PATH through life project [10].

Fasting blood glucose and MRI data was available across three time points, across a 12-year follow-up for 288 participants (aged 60-66 years at baseline, 46% female).

T1-weighted scans were acquired with a Fast-Field Echo sequence up to 4 times 4 years apart. Scans were corrected for head tilt and alignment and intensity inhomogeneity using rigid-body transformations, and were processed using the longitudinal pipeline functionality of Freesurfer 5.3 (http://www.freesurfer.net) [11].

Associations between blood glucose and the volume of four topical brain areas were investigated using multilevel models, while controlling for age, intracranial volume, hypertension, sex, and scanner effects. Alpha was set at 0.05.

RESULTS

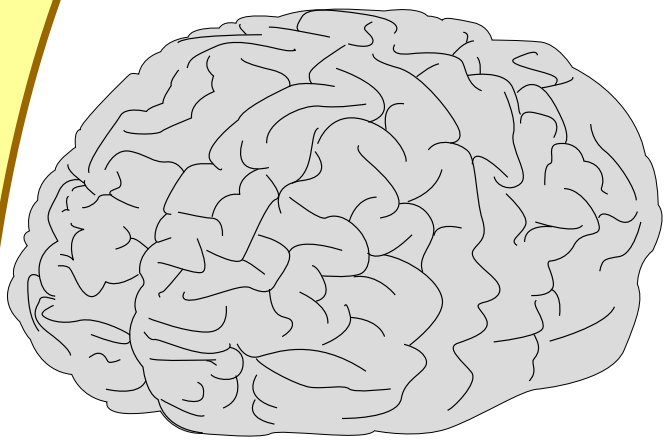
Mean participant age at baseline was 63 years (SD=1.43), and at final assessment was 75 years (SD=1.36).

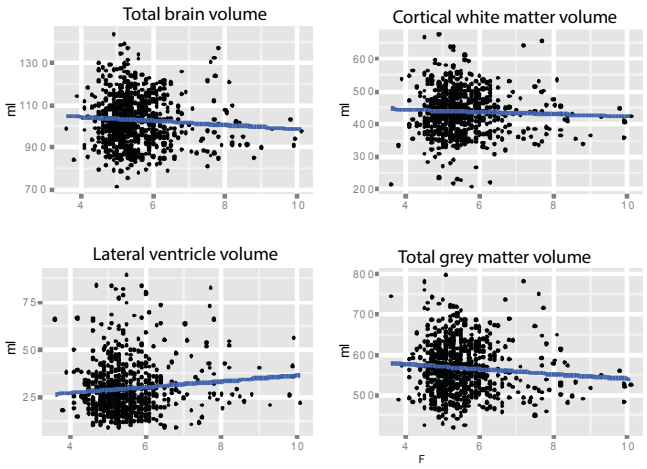
Fifteen percent (*n*=44) of participants had diabetes. For each additional year, there was a decrease of 4.11ml/yr in total brain volume, 3.00ml/yr in grey matter, 0.79ml/yr in cortical white matter, and an increase of 0.81ml/yr in lateral ventricle volume.

There were no significant associations between fasting blood glucose and total brain volume, cortical white matter volume, or ventricle volume. Higher glucose levels (glucose x time interaction) or increasing glucose levels over time (random effects) were not significantly associated with volume change in any area.

Fasting blood glucose was significantly associated with total grey matter volume. Every additional 1mmol/L in fasting glucose was associated with 1.54ml lower grey matter volume.

The effect was not significant in females, but in males, each 1mmol/L in fasting glucose was associated with 2.04ml lower grey matter volume. Significance in all analyses did not survive Bonferroni adjustment.





CONCLUSION

HIGHER FASTING BLOOD GLUCOSE IS ASSOCIATED WITH LOWER TOTAL GREY MATTER VOLUME, AND MORE SO IN MALES. THESE FINDINGS STRESS THE IMPORTANCE OF MANAGING BLOOD GLUCOSE LEVELS EARLIER IN ADULTHOOD, PARTICULARLY IN MALES, THROUGH EDUCATION, POPULATION HEALTH INTERVENTIONS, AND POLICY.

(1) Manschot, S.M., et al., Brain magnetic resonance imaging correlates of impaired cognition in patients with type 2 diabetes. Diabetes, 2006. 55(4): p. 1106-1113. (2) Crane, P.K., et al., Glucose levels and risk of dementia. New England Journal of Medicine, 2013. 369(6): p. 540-548. (3) Cherbuin, N., P. Sachdev, and K.J. Anstey, Higher normal fasting plasma glucose is associated with hippocampal atrophy: The PATH Study. Neurology, 2012. 79(10): p. 1019-26. (4) Fink, R.I., O.G. Kolterman, and J.M. Olefsky, The physiological significance of the glucose intolerance of aging. Journal of gerontology, 1984. 39(3): p. 273-278. (5) Király, A., et al., Male brain ages faster: the age and gender dependence of subcortical volumes. Brain imaging and behavior, 2015: p. 1-10. (6) Lemaître, H., et al., Age-and sex-related effects on the neuroanatomy of healthy elderly. Neuroimage, 2005. 26(3): p. 900-911. (7) Gur, R.C., et al., Gender differences in age effect on brain atrophy measured by magnetic resonance imaging. Proceedings of the National Academy of Sciences, 1991. 88(7): p. 2845-2849. (8) Australian Bureau of Statistics, Diabetes in Australia: A Snapshot, 2007-08 2011. (9) Legato, M.J., et al., Gender-specific care of the patient with diabetes: review and recommendations. Gender Medicine, 2006. 3(2): p. 131-158. (10) Anstey, K.J., et al., Cohort Profile: The PATH through life project. International journal of epidemiology, 2012: p. dyr025. (11) Reuter, M., et al., Within-subject template estimation for unbiased longitudinal image analysis. Neuroimage, 2012. 61(4): p. 1402-1418.

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