

# HIGHER FASTING PLASMA GLUCOSE LEVELS IN THE NORMAL RANGE ARE ASSOCIATED WITH HIPPOCAMPAL ATROPHY IN COGNITIVELY HEALTHY COMMUNITY-BASED OLDER ADULTS IN THEIR 60S

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## BACKGROUND

Substantial research showing associations between type two diabetes (T2D), the metabolic syndrome, obesity and brain atrophy and cognitive decline is already available. The mechanisms involved are not completely understood but include chronic inflammation, which is known to be associated with neurodegeneration and dementia; over-activation of the pro-thrombotic pathways, which can increase the risk of atherosclerosis and cardiovascular disease thus leading to cerebral hypoperfusion; and pathological activation of the stress response, particularly via the HPA axis, which is also associated with neurodegenerative processes and neurogenesis inhibition. In addition, insulin resistance has also been shown to be associated with pathological brain changes and cognitive impairment. However, little is known about the effect higher blood glucose levels within the normal range have on brain health in cognitively healthy individuals without T2D.

## AIMS

The aim of this study was to investigate the association between plasma glucose levels and the atrophy of a cerebral structure particularly sensitive to pathophysiological stressors, the hippocampus, in cognitively healthy individual who do not suffer from T2D and have glucose level within the normal range.

## METHOD

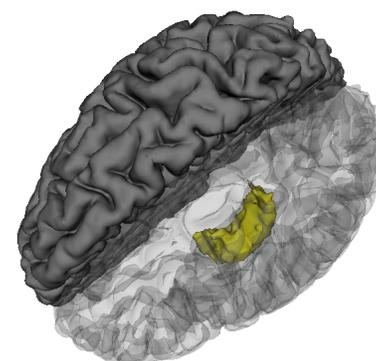
Participants were selected from the PATH Through Life cohort, a longitudinal study of ageing and mental health which surveys community-based individuals randomly selected from the population of Canberra and surroundings. Exclusion criteria included dementia and other neurological disorders, history of T2D or stroke, and fasting plasma glucose levels higher than 6 mmol/l. 266 cognitively healthy participants with an available MRI scan at the first wave of data collection and at follow-up were considered in the present investigation. The hippocampus was manually traced by an expert neuroscientist on the coronal section of T1-weighted MRI scan. Change in hippocampal volume over a 4-year follow up was investigated with hierarchical multiple regression analyses. Covariates controlled for included age, sex, education, body mass index, hypertension, APOE E4 genotype, smoking, and alcohol intake.

## RESULTS

Participants had a mean age of 62.6 years at first assessment (range 60-65), were 44.7% female, and had an average plasma glucose level of 4.93 mmol/l (range 3.2-6.0). Linear regression analyses showed plasma glucose levels were significantly associated with Left (beta = -0.190, p = 0.001,  $\Delta R^2 = 0.32$ ) and Right (beta = -0.216, p = 0.001,  $\Delta R^2 = 0.42$ ) hippocampal atrophy.

## DISCUSSION

The present results suggest that higher fasting glucose levels within the normal range are associated with a faster rate of hippocampal atrophy in cognitively healthy community-based individuals. Fasting glucose levels explained between 3-4% of the variance in hippocampal volume change over 4 years in the surveyed cohort. Implications for public health will be discussed.



3D Reconstruction of a segmented hippocampus