

# Effects of Glycaemic Control on Memory Performance, Hippocampal Volume and Depressive Symptomology

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## Background and Purpose

Haemoglobin A1c (HbA1c) in blood plasma is commonly utilised biomarker of glycaemic control, and impaired glycaemic control has been linked to poor cognitive function (Ravona-Springer et al., 2012; Repple et al., 2019) and elevated depressive symptomology (Chiu & Du, 2019; Schmitz, Deschenes, Burns, & Smith, 2016). However, the underlying neurobiological mechanisms behind these associations remain unclear. Hippocampal atrophy, which has been linked to poorer memory, and depression risk, has also been associated with impaired glycaemic control (Gold et al., 2017; Zhang et al., 2015). The negative effects of HbA1c levels on hippocampal volume might be an underlying mechanism explaining the relationships between impaired glycaemic control, cognition and depressive symptomology. However, no study has to date examined all these factors together in a non-clinical sample. Therefore, the present study aimed to examine whether hippocampal atrophy might have a role in explaining the associations between HbA1c levels, cognition, and depressive symptomology, in a large sample.

## Hypotheses

- Higher HbA1c levels would be associated with lower memory performance, elevated depressive symptoms, and lower hippocampal volumes
- Lower memory performance, and more depressive symptoms, would correlate with lower hippocampal volumes
- As a follow-up analysis, we explored whether these associations might be stronger amongst participants aged 50 and older.

## Method

### Design of the study

The data came from the Baependi Heart Study which is a longitudinal cohort study into environmental and genetic effects on cardiovascular disease risk factors (Eagan et al., 2016). Participants were drawn from Baependi, a small town in Brazil.

### Sampling and Measurements

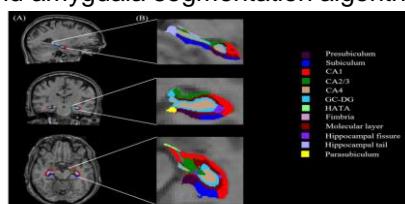


| Whole Sample<br>(N = 1322)   |
|--|
| <ul style="list-style-type: none"> <li>HbA1c</li> <li>Word List Recall Test</li> </ul> |

| MRI Sample<br>(N = 392)  |
|--|
| <ul style="list-style-type: none"> <li>HbA1c</li> <li>Depressive Symptoms</li> <li>MRI data</li> </ul> |

- Sociodemographic variables included age, gender and education level (in years).
- For depression: subscale of the Hospital Anxiety and Depression Scale (HADS)
- Word List Memory Recall Task. Participants were presented with 10 unrelated words, recall performance summed over 3 recall attempts (immediate, plus delayed)
- Hippocampal volumes were calculated using Freesurfer's automated hippocampal and amygdala segmentation algorithm (Iglesias et al., 2015).

From Zheng et al. (2018)



### Analysis

Due to non-normal distribution, HbA1c data were log<sub>10</sub> transformed. Partial Correlation analyses were conducted to examine the relationship between normalised HbA1c levels, depressive symptoms, memory performance, and hippocampal volume (total, right, and left). All correlational analyses were adjusted for age, gender, and years of education. The analyses into the association between HbA1c levels and hippocampus volume also adjusted for depressive symptoms.

## Results

- There was a negative association between normalised HbA1c values and total word list recall performance ( $r(1317) = -.061, p = .027$ , see Figure 1).
- Higher normalised HbA1c levels were associated with lower **left** hippocampus volume ( $r(386) = .100, p = .049$ , see Figure 2).
- There was a negative association between normalised HbA1c levels and depressive symptoms ( $r(387) = .120, p = .018$ , see Figure 3).
- Follow-up analyses showed associations of HbA1c levels with **left** ( $r(155) = -.212, p = .008$ ), **right** ( $r(155) = -.177, p = .027$ ) and **total** hippocampal volume ( $r(155) = -.200, p = .012$ ) were stronger in participants aged >50.
- Also, the association between HbA1c levels and depressive symptoms ( $r(156) = .193, p = .015$ ) was more pronounced in participants aged >50.

Figure 1

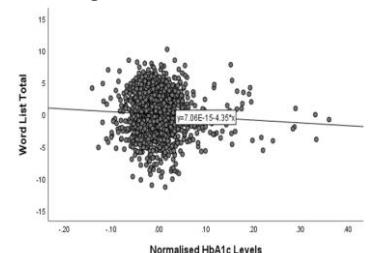


Figure 2

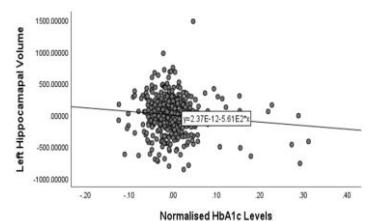
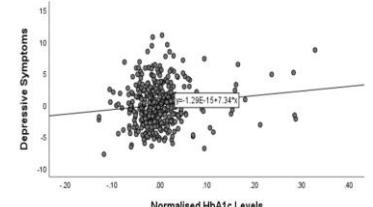


Figure 3



## Discussion

- Poor glycemic control was found to be related to higher depressive symptoms and poor word list memory performance in the whole sample. It also associated with lower hippocampus volume, particularly in those aged over 50.
- Although recall and depression did not correlate with hippocampal volume, its correlation with HbA1c levels does suggest that hippocampal atrophy might have some role in how HbA1c impacts cognition, and depressive symptoms.
- Effects of elevated cortisol levels, and neuroinflammation could be important in this.

## References

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