

# Longitudinal relationship between depression and hippocampal subfield volumes in cognitively unimpaired older adults

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## Introduction

- Depression and Alzheimer’s Disease are both linked to hippocampal atrophy<sup>1,2</sup>
- Previously, depression was associated with smaller CA23DG volume cross-sectionally<sup>3</sup>
- We examined: 1) How depression relates to hippocampal volume across diverse ethnoracial groups and 2) How this relationship looks longitudinally?

## Methods

- Hippocampal high-resolution MRI scans (Vida or Skyra scanners) (Figure 1)
- Automatic Segmentation of Hippocampal Subfields software → subiculum, CA1, and CA23DG (region including CA2, CA3, and dentate gyrus)
- Depression = history of depression or a Geriatric Depression Scale score of ≥10
- Health and Aging Brain Study – Health Disparities (Table 1)
- Covariates: age, sex, years of education, ethnoracial group, intracranial volume, slices segmented, scanner (Table 2)
- P-values were FDR-corrected across 3 subfield regions

Table 1. Demographics by Depression Status

|                         | Depressed          | Not Depressed       |
|-------------------------|--------------------|---------------------|
| N                       | 319                | 720                 |
| Sex (n)*                | 65M/254F           | 270M/450F           |
| Mean age (years)        | 64.0 ± 7.8         | 64.7 ± 8.2          |
| Mean education (years)* | 12.8 ± 4.5         | 14.1 ± 4.0          |
| Ethnoracial group (n)   | 34NHB/128H/157 NHW | 112NHB/264H/34 4NHW |

Table 1. Demographics by depression status. M=male, F=female, NHB=non-Hispanic Black, H=Hispanic, NHW=non-Hispanic White

Table 2. Statistical Models

|                                  | Additional Covariates                               |
|----------------------------------|-----------------------------------------------------|
| Linear Regression Model          | Baseline HHR volume, months between clinical visits |
| Linear Mixed Effects Model (LME) | Random intercept for subject variability            |
| LME with Additional Timepoints   | Random intercept for subject variability            |

Table 2. Linear regression and linear mixed effects models (LME) were used to examine the relationship between depression and hippocampal subfield volumes across two timepoints. Another LME was run to test the relationship across additional timepoints.

## Results

Linear Regression:

- Depression at baseline was associated with smaller follow-up CA23DG (B=-0.095, p=0.043) when controlling for baseline volume. Depression at baseline was associated with smaller follow-up CA1 (B=-0.074, p=0.077) and subiculum (B=-0.077, p=0.082) volumes at trend levels. (Figure 2)

LME:

- Depression was not associated with change in CA23DG volume over time (B=-0.007, p=0.429).

Figure 1. Hippocampal High-Resolution Image

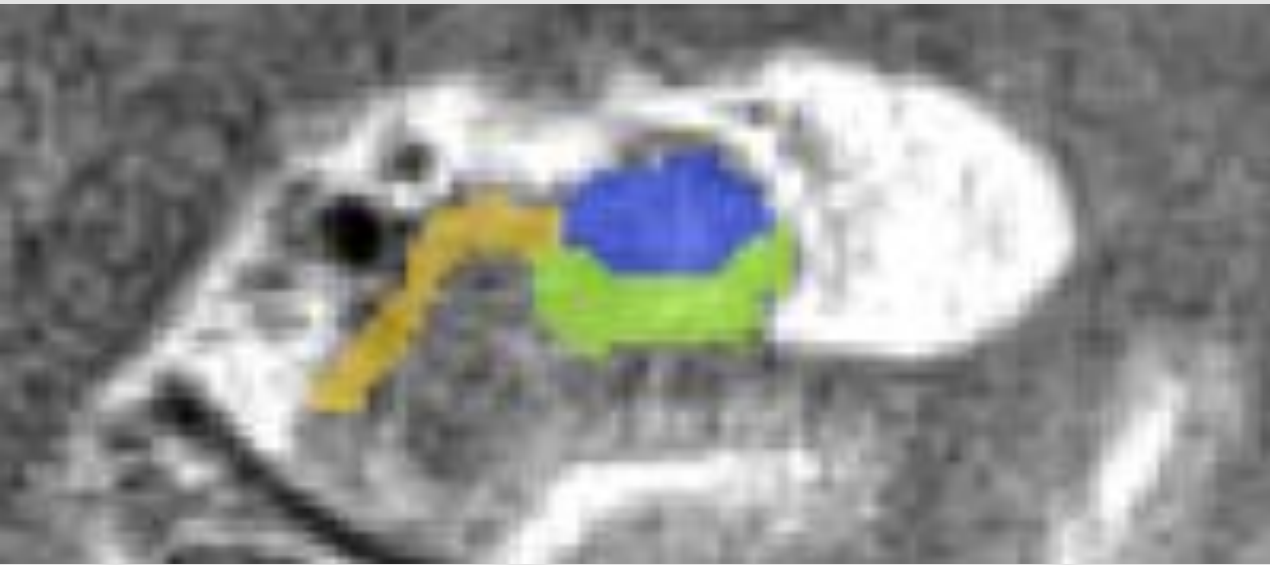


Figure 1. Hippocampal high resolution brain image, showing segmentations of the CA1 (green), CA23DG (blue), and subiculum (yellow).

Figure 2. CA23DG Volume by Depression Status

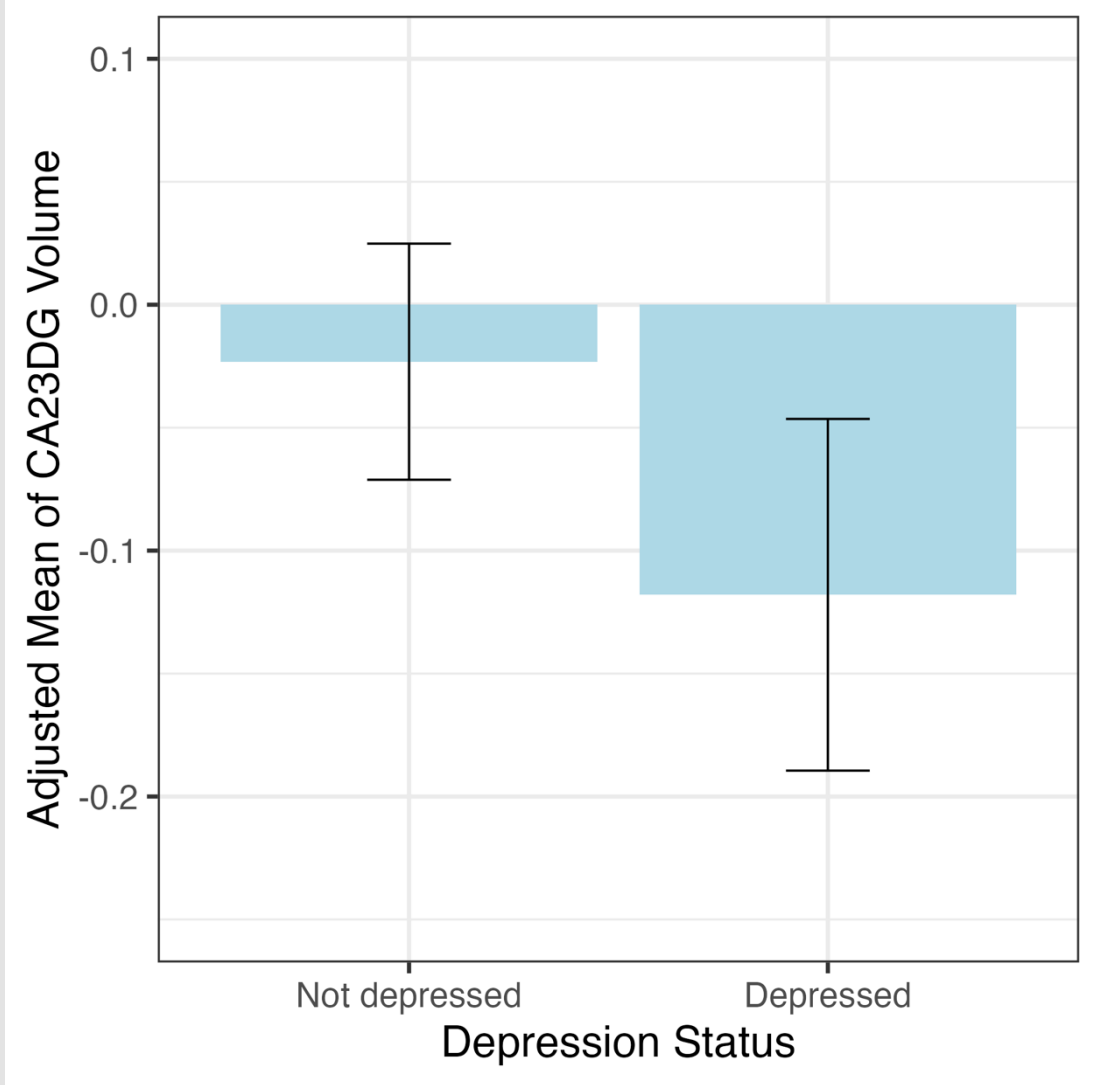


Figure 2. Bar plot showing the adjusted mean of CA23DG volume by depression status.

## Discussion

- Using linear regression and controlling for baseline volume, depression predicted lower CA23DG volume at timepoint 2. However, depression was not associated with CA23DG change using LME.
- There may be a potential external variable or insufficient timepoints for optimal LME.
- Future studies should include larger sample sizes and more timepoints.

## Key Point

When controlling for baseline hippocampal subfield volume, a depression diagnosis predicted a smaller CA23DG volume two years later.

## References & Acknowledgements

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