Associations Among Early-Life Adversity, Hippocampal Volume, and Cognitive Performance in Non-Demented Individuals with Autosomal Dominant Alzheimer's Disease

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Introduction

- Latino children are disproportionately exposed to early-life adversities.
- Elevated incidences of early-life adversity have been linked to reduced hippocampal volume and heightened deficits in cognitive functioning in older individuals.
- The associations between early-life adversity and risk for Alzheimer's Disease (AD), specifically, remain unclear.
- Investigating the relationship between early-life adversity, hippocampal volume, and cognitive performance may inform us about the clinical trajectory of AD in this population

Objective

- We examined early-life adversity and its relationship with hippocampal volume and cognitive performance in cognitively-impaired and –unimpaired individuals from Colombia who belong to families with autosomal dominant AD (ADAD).

Methods

- 57 cognitively-impaired (34) and –unimpaired (23) participants from the Massachusetts General Hospital (MGH) Colombia-Boston (COLBOS) Biomarker Study were included (mean age = 39.9 years, SD = 6.38).
- Cognitive performance was measured using the Mini-Mental State Examination (MMSE) and the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word List Delayed Recall (WLDR).
- Cognitive impairment was measured using the Functional Assessment Staging Tool (FAST).
- Early life adversity was measured using the stress and anxiety inventory (STRAIN), specifically the time limited: Total count of early adversity (EATotCT) measure (range: 0-10).

  Example questions:
  - Have you experienced bullying (e.g., name calling, humiliation, rejection) during childhood?
  - You separated from parent or caregiver for at least one month during childhood?

- Structural MRI scans were conducted at MGH and processed with FreeSurfer (v6.0).
- Pearson correlations and regression models, adjusted for sex, age, carrier status, and intracranial volume, were used to elucidate associations among early-life adversity, hippocampal volume, and cognitive performance.

Hypotheses

- We hypothesized that:

  1) Greater instances of early-life adversity will be associated with diminished hippocampal volumes

  2) Measures of hippocampal volume will be associated with cognitive performance

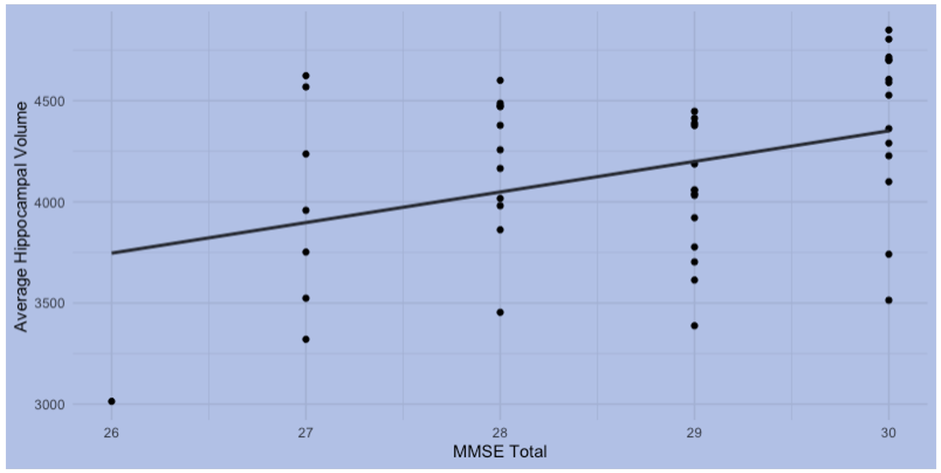

Figure 1: Total MMSE scores are significantly correlated with average hippocampal volume (r=0.43, p=0.002).

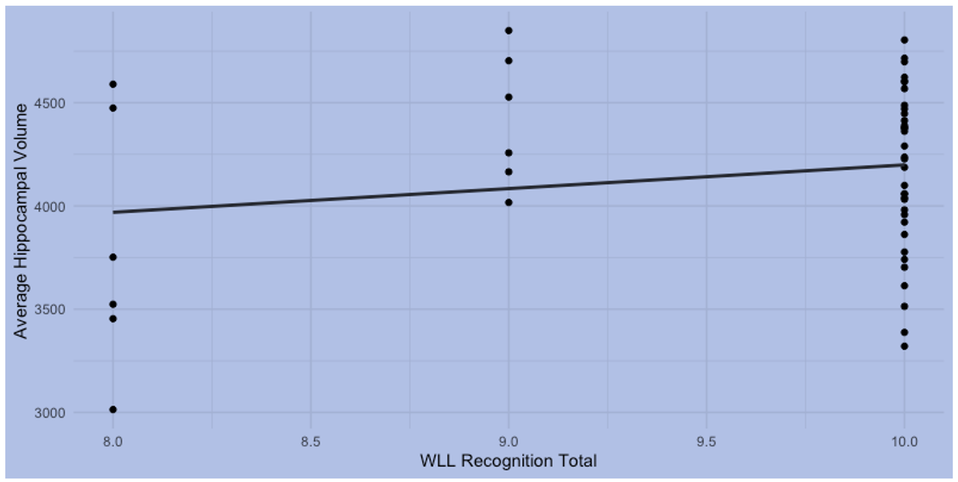

Figure 2: Total WLL Recognition scores are significantly correlated with average hippocampal volume (r=0.35, p=0.014).

Results

TABLE 1. Demographics, Cognition, and EATotCT

	Mean (SD)
Age	39.5 (6.04)
MMSE	28.6 (1.29)
EATotCT	3.79 (2.75)
WLDR	12.9 (7.44)
Avg Hippocampal Volume	4120 mm^3 (465 mm^3)

- There were no significant associations among early-life adversity, hippocampal volume, and cognitive performance in cognitively-impaired and -unimpaired individuals (all Ps>0.05).
- Hippocampal volume was positively correlated with both total MMSE score (Figure 1) and WLDR (Figure 2) scores.
- Results from regression models were consistent with correlation analyses, showing that higher hippocampal volume was associated with higher MMSE and WLDR scores.

Conclusions

- Early-life adversity did not exhibit significant associations with either hippocampal volume or cognitive performance in adults who belong to families with ADAD.
- Cognitive performance was associated with hippocampal volume, a marker of neurodegeneration, a few years before dementia onset (typically age 49 in these individuals).
- Limitations in the STRAIN such as cultural bias, subjective and retrospective reporting, and response bias may have influenced these results. This inventory also does not consider neuroprotective factors.

Future Directions

- Future investigations that address current limitations through the implementation of multiple measures of early-life adversity and which utilize a larger sample size are warranted to further examine the relationship among early-life adversity, neurodegeneration, and cognitive decline in those at increased risk for AD.

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