Analyzing Cortical Volume Asymmetry in Preclinical Alzheimer's Disease

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INTRODUCTION

- Alzheimer's disease is the 6th leading cause of death in the United States.

- AD is process of progressive neurodegeneration, or progressive deterioration, of structure and function.

- Cerebral amyloid plaques are a hallmark of AD pathology and are associated with neurodegeneration (i.e., atrophy)

- The early stage of significant amyloid accumulation without overt cognitive dysfunction is known as preclinical AD

- Cerebral amyloid does not deposit symmetrically between the hemispheres; some hypothesize that neurodegeneration would also occur asymmetrically.

CORTICAL VOLUME ASYMMETRY

- Asymmetry is not always pathological (i.e. language – left lateralized)

- In AD, degree of asymmetrical cortical volumes/thickness has been associated with disease severity in some regions such as the hippocampus, a hub for long-term memory

OBJECTIVE

This study aims to analyze patterns in asymmetry of cortical volume as potential marker for AD progression.

HYPOTHESIS

Greater hippocampus asymmetry would be associated with more advanced AD pathologies (i.e., high cerebral amyloid and low cerebral glucose metabolism).

MATERIALS & METHODS

PARTICIPANTS AND DATA

Cross-sectional data from ongoing large center study (PI: Klunk & Aizenstein, 2RF1AG 025516)

Participants were 93 cognitively healthy individuals (mean age=76.4 years, sd = 6.1, 26% Male) with varying levels of cerebral beta amyloid

Multimodal neuroimaging data:
- structural MRI (3T)
- Positron Emission Tomography (PET) with Pittsburgh compound B (PiB cerebral amyloid)
- FDG (cerebral glucose metabolism)

Freesurfer was used to segment the structural MRI and extract cortical volume of the hippocampus

ASYMMETRY INDEX (AI)

$$\text{Asymmetry Index (AI)} = \frac{(L-R)}{(0.5(L+R))} * 100$$

2 types of AI:
1. ±AI: negative scores indicate leftward & positive scores indicate rightward asymmetry
2. |AI| : absolute value of AI (i.e., degree of asymmetry regardless the direction)

STATISTICAL ANALYSIS

4 linear regression models:

- Outcomes: asymmetry index (±AI), degree of asymmetry |AI|, L&R Hippocampal volumes
- Predictors: cerebral amyloid deposition status, cerebral glucose metabolism (FDG).
- Covariates: intracranial volume (ICV) and the demographic variables (age, race, sex, and education)

RESULTS

1. Both asymmetry indices (±AI, |AI|) did not show an association with any of the predictor variables

2. The left and right hippocampal volume did not show any association with cerebral amyloid deposition (PiB)

3. Greater age were associated with lower left and right hippocampal volume

   (Right: β=-43.9, p=0.001), [F(8, 57) = 9.2, p < 0.001]; Left: β=-44.7, p=0.001), [F(8, 57) = 7.60, p < 0.001)

4. Greater cerebral glucose metabolism (FDG) was associated with greater right hippocampal volume (β=911.20, p=0.01)
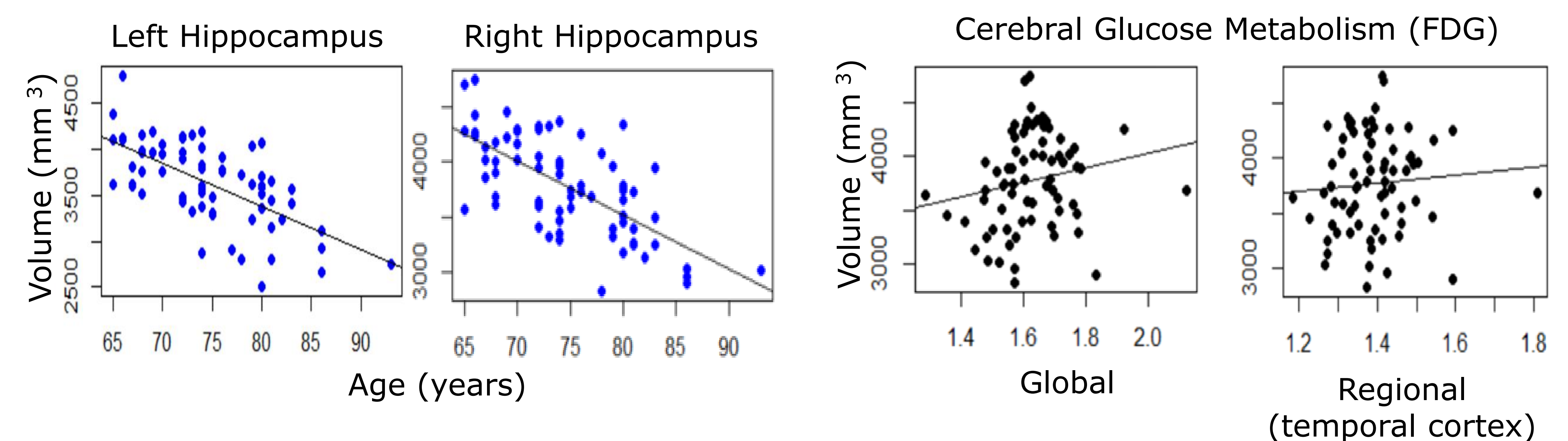
DISCUSSION

At this early stage, preclinical AD individuals might have more symmetric changes in hemispheric atrophy, and we expect at later stages of AD to transition to more asymmetric cortical volume changes. Our analysis directs us to the rate of asymmetry in longitudinal data rather than asymmetry index (AI) in cross-sectional data as a potential marker for AD progression.

These results suggest symmetric atrophy changes will stop at some point and transition to asymmetric atrophy, at this later stage during AD progression cognitive impairment might be present along with lower glucose metabolism, and more asymmetric volume changes.

FUTURE DIRECTIONS

- Conduct a Voxel-Wise analysis focusing on subcortical substructures of the Hippocampus (i.e., Fimbria and Parasubiculum)
- Calculate the asymmetry in cerebral glucose metabolism (FDG) and in cerebral beta amyloid (Aβ) (PiB) and find associations.
- Longitudinal Study

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