Investigating Lateralized Asymmetry as a Potential Link Between Adverse Childhood Experiences and Alzheimer's Disease Using Human Brain MRI Data

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INTRODUCTION

- Adverse childhood experiences (ACEs) include a range of incidences occurring during childhood such as emotional and physical abuse, parental separation, substance abuse, incarceration, and violence. ACES have major effects on the brain that contribute to abnormalities resulting in various diseases such as Alzheimer's disease.
- Alzheimer's disease results in the accumulation of the protein β-amyloid (amyloid β plaques) near neurons, in conjunction with twisted tangles of Tau protein developing inside neurons, causing neuronal death, resulting in symptoms of impaired memory and communication, confusion, among many others.
- Patients with Alzheimer's Disease have shown differences in brain lateralization in comparison with healthy individuals in the following areas:
  - Limbic system: Involved in sensory processing, encoding, and attentional control, contributing to the integration of thought, feeling and action.
  - Entorhinal cortex: Connectivity with the hippocampus as well as association areas of the parietal, temporal, and prefrontal cortex.

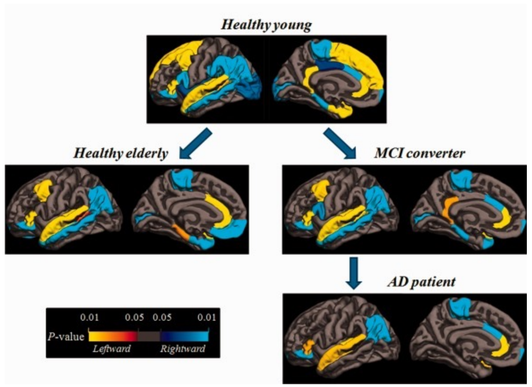

Figure 1: Evidence of differences in brain asymmetry between healthy individuals compared to those with mild cognitive impairment(MCI) and Alzheimer's Disease.

- Our study focuses on exploring the relationship between ACEs and Alzheimer's Disease by examining abnormal brain lateralization patterns as a common denominator in both maltreated individuals and Alzheimer's Disease patients.

Hypothesis

We hypothesize that individuals who have experienced ACEs will display abnormal brain asymmetry in regions comparable to those impacted in Alzheimer's Disease.

METHODS

- Study included two groups recruited from McLean Hospital, Harvard Medical School: 202 individuals with a history of maltreatment and 130 control individuals.
- Morphometric MRI data was derived from cortical parcellation and subcortical segmentation using FreeSurfer to determine volume and thickness of 82 brain regions.
- Laterality index (LI) of each region was calculated using volume and thickness values:
  - [LI=(Left-Right hemisphere)/(Left+Right hemisphere)]
    - Negative LI = Right hemisphere lateralization
    - Positive LI = Left hemisphere lateralization
  - |LI|>0.1 indicates lateral asymmetry
- Among the brain regions displaying lateral asymmetry, statistical analyses were performed:
  - Chi Square analysis was used to identify brain regions of interest (ROI) that showed different lateral asymmetries between maltreated and control adults.
  - Logistic regression, controlling for gender, was used as a follow-up test.
- Using SPSS software, graphs were generated for each of these brain regions depicting history of maltreatment in relation to laterality index.

RESULTS

Brain Region	Left Hemisphere Average Volume	Right Hemisphere Average Volume	Difference
Postcentral Gyrus (Control)	4383.19	4098.42	284.78
Postcentral Gyrus (Maltreated)	4206.69	3970.8	335.89
Intraparietal Sulcus and Transverse Parietal Sulcus (Control)	4684.12	4779.85	95.73
Intraparietal Sulcus and Transverse Parietal Sulcus (Maltreated)	4610.08	4709.6	99.52
Medial Orbital Sulcus (Control)	1440.55	1382.07	59.48
Medial Orbital Sulcus (Maltreated)	1415.06	1338.28	76.78
Pericallosal Sulcus (Control)	1511.4	2030.97	519.57
Pericallosal Sulcus (Maltreated)	1508.67	1937.6	428.93

Table 1: MRI data displaying cortical volumes and differences in each hemisphere of ROI showing abnormal asymmetry in maltreated individuals.

Brain ROI	No History of Maltreatment (N=130)	History of Maltreatment (N=202)	Total (N=332)	p value*
Postcentral Gyrus |LI| >0.1	19 (14.6%	48 (23.8%)	67 (20.2%)	0.0427
Intraparietal Sulcus and Transverse Parietal Sulcus |LI| >0.1	29 (22.3%)	27 (13.4%)	56 (16.9%)	0.0337
Medial Orbital Sulcus |LI| >0.1	28 (21.5%)	66 (32.7%)	94 (28.3%)	0.0279
Pericallosal Sulcus |LI| >0.1	91 (70.0%)	118 (58.4%)	209 (63.0%)	0.0329

Table 2: Tabulation of subjects (n,%) with |LI|>0.1, stratified by history of maltreatment for ROI with p value < .05.

RESULTS CONTINUED

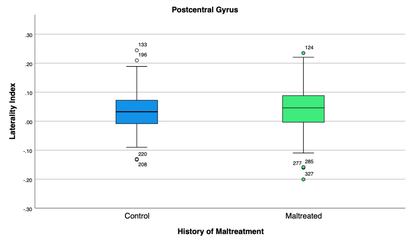

Figure 2: Maltreated (N=202)(x̄= 0.05) significantly more left lateralized than controls (N=130)(x̄= 0.03) (CI= 1.013, 3.263)(P=<.05)

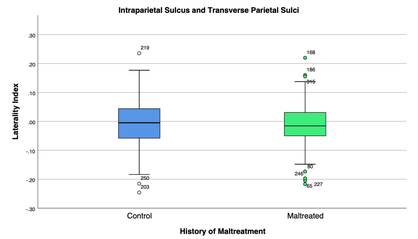

Figure 3: Maltreated (N=202)(x̄= -0.02) significantly less left lateralized than controls (N=130)(x̄= 0.00) (CI= 0.301, 0.957)(P=<.05)

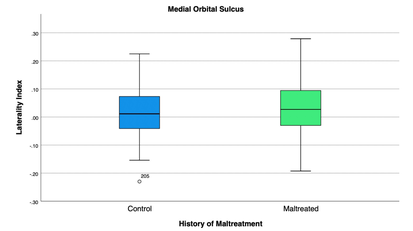

Figure 4: Maltreated (N=202)(x̄= 0.03) significantly more left lateralized than controls (N=130)(x̄= 0.01) (CI= 1.057, 2.943)(P=<.05)

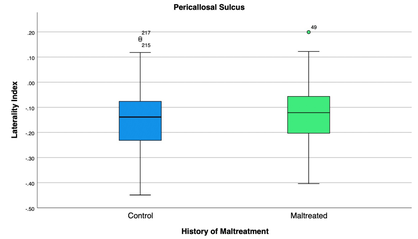

Figure 5: Maltreated (N=202)(x̄= -0.12) significantly more left lateralized than controls (N=130)(x̄= -0.14) (CI= 0.378, 0.964)(P=<.05)

Abnormal asymmetry is seen in the following regions in maltreated individuals:

- Postcentral Gyrus: Perceives somatic sensations from the body.
- Intraparietal Sulcus and Transverse Parietal Sulcus: Used in attention tasks, and maintenance of information in the working memory.
- Medial Orbital Sulcus: Auditory processing and integration of olfactory information.
- Pericallosal Sulcus: Separates the cingulate gyrus from the corpus callosum.

CONCLUSIONS

Lateralization is vital in certain neuronal functions. However, abnormal asymmetry in maltreated individuals indicates structural compensation occurring, potentially causing harm. The commonality of abnormal lateralization in maltreated individuals and Alzheimer's Disease Patients provides insight to possible mechanisms by which ACEs predispose individuals to developing Alzheimer's Disease. The regions highlighted in this study show to be particularly susceptible to being impacted by maltreatment and can be studied in future research.

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