DOI: 10.1002/alz.046338

BIOMARKERS

POSTER PRESENTATIONS

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Neuroimaging / differential diagnosis

Neurodegeneration in the Longitudinal Evaluation of Early Onset Alzheimer's Disease Study (LEADS) sample: Results from the MRI core

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Abstract

Background: Approximately 5% of the 5.6 million (~280,000) Americans with Alzheimer's disease (AD) develop symptoms at age 65 or younger and are classified as having early-onset AD (EOAD). Although EOAD and late-onset AD (LOAD) share the same pathologic substrate, there are notable differences in their clinical and biological phenotypes. The Longitudinal Early-onset AD study (LEADS) is a multi-site, observational clinical and biomarker study of EOAD. In the present study we utilized the currently available LEADS imaging data to explore the spatial extent and magnitude of neurodegeneration EOAD

Method: 95 amyloid positive patients with EOAD, 37 amyloid negative cognitively impaired patients (EOnonAD) , and 55 cognitively unimpaired controls (CNs) were included in the analysis. The magnitude of cortical thinning in the EOAD and EOnonAD groups was estimated using whole-brain GLMs compared to the CN group. In addition, w-scores were derived for each EOAD patient for these ROIs: average cortical thickness, hippocampal volume, AD-signature cortical thickness (typically used in LOAD), and precuneus cortical thickness controlling for age, sex, and acquisition site. The utility of each ROI to differentiate EOAD patients from CNs was assessed by calculating the percentage of patients falling below a W-threshold of -1.5.

Result: In EOAD, a distributed pattern of cortical thinning was observed in lateral temporal, parietal, and frontal cortex ($p<.01$), and was most prominent in the precuneus (Cohen's d' = 1.5). In the EOnonAD group, cortical thinning was observed but was highly variable across individuals. The w-score analysis in the EOAD group yielded the following results: Mean Cortical thickness: Mean = -3.34, SD = 2.97, Classification = 72%.; Hippocampal volume: Mean = -2.96, SD = 2.39, Classification = 74%; AD Signature: Mean = -4.63, SD = 3.07, Classification = 80%; Precuneus: Mean = -5.98, SD = 4.1, Classification = 90%.

Conclusion: Our results are consistent with previous findings demonstrating cortical thinning in lateral parietal, precuneus, and lateral temporal lobes in EOAD with relatively less involvement of the medial temporal lobes. Our results also suggest that the precuneus may be especially vulnerable to neurodegeneration in patients with EOAD and may serve as a useful biomarker for patient classification.