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Epicenters of cortical atrophy in primary progressive aphasia differ by underlying neuropathology

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Introduction: Primary progressive aphasia (PPA) is caused by neurodegenerative disease that selectively targets the (usually) left hemisphere language network. Recent studies suggest that the epicenter of cortical atrophy can be identified based on healthy resting state networks. With this method, typical amnestic Alzheimer disease dementia (ADD) tends to have posterior network epicenters while frontotemporal dementia (FTD) tends to have anterior epicenters. We hypothesized that individuals with PPA would show differential epicenters based on their underlying neuropathology: frontotemporal lobar degeneration (FTLD) or Alzheimer disease neuropathologic change (ADNC).

Methods: Analysis included PPA participants that had undergone structural T1-weighted MRI and had either autopsy, CSF, or PET imaging that indicated AD or FTLD neuropathology. We calculated the most likely epicenter of cortical atrophy for each PPA participant using the Human Connectome Project (HCP) multi-modal parcellation, the average resting state fMRI connectivity from 337 healthy HCP participants, and the PPA participant's FreeSurfer-derived cortical thickness w-scored for age. The frequency of atrophy-epicenters between anterior and posterior networks was compared between the PPA-FTLD and PPA-ADNC groups.

Results: We found a significant difference between the frequency of 64 PPA-FTLD participant's anterior and posterior epicenters (51 anterior, 13 posterior) compared to 53 PPA-ADNC epicenters (15 anterior, 38 posterior) with a 2-sided Boschloo's exact test ($p < 0.0000001$). As expected, cortical epicenters were mostly found in the left hemisphere (n=109/117).

Conclusion: This study further demonstrates the selective vulnerability of AD or FTLD neuropathology in a group of well-characterized PPA participants with overlapping clinical deficits but divergent pathology.

Conflicts of interest

The authors have no releveant disclosures.