

**Intra-individual asymmetries in distinct regions of interest are associated with each variant of primary progressive aphasia**

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State of the Art:

Primary progressive aphasia (PPA) variants are distinguished by area of greatest atrophy, measured by voxel-based morphometry or cortical thinning: left inferior frontal gyrus (IFG) and insula in nonfluent agrammatic PPA (nfaPPA); left temporal pole (TP) and inferior temporal gyrus (ITG) in semantic variant PPA (svPPA); and left superior temporal gyrus (STG), angular gyrus (AG) and supramarginal gyrus (SMG) in logopenic variant PPA (lvPPA). However, these distinctions depend on comparing scans to age and sex-matched controls, which is complicated by individual differences in brain size and shape.

We sought to quantify the area of greatest atrophy in individuals with PPA without this complication. We hypothesized that greatest left-right differences within individuals are: IFG and insula in nfaPPA; TP and ITG in svPPA; and STG, AG, and SMG in lvPPA.

Methodology:

Participants with PPA (n=36; 13 nfaPPA, 8 svPPA, 15 lvPPA) had MRI automatically segmented through MRICloud (<http://www.MRICloud.org>) to determine volume of cortical regions of interest (ROIs): IFG, insula, STG and MTG poles, ITG, STG, AG, SMG. We used logistic regression to determine asymmetry of ROIs that best identified each variant.

Results

Each variant was independently associated with left-right difference in one ROI for each variant: insula for nfaPPA ( $z=2.3$ ;  $p=0.02$ ); middle temporal gyrus pole for svPPA ( $z=2.0$ ;  $p=0.04$ ); and STG for lvPPA ( $z=2.31$  0.021), after controlling for asymmetries in other ROIs.

Conclusions:

PPA variants differ by area of greatest atrophy defined by the greatest intra-individual left-right difference across regions of ROIs, identified automatically through MRICloud.

**Conflicts of interest**

N/A