

26th Annual Alzheimer Day

Connectivity-Based Differentiation of Agrammatic and Logopenic Variants of Primary Progressive Aphasia Using a Whole Brain Data Driven Approach

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Background: Primary progressive aphasia (PPA) is a syndrome of progressive language impairment caused by neurodegenerative disease (Mesulam 1982). We previously showed connectivity disruptions in three specific language network nodes in people with PPA using seed-based fMRI functional connectivity analysis. The current investigation used a whole brain data driven approach to uncover signatures of resting state connectivity disruptions differentiating agrammatic PPA subtypes (PPA-G) from logopenic PPA subtypes (PPA-L).

Methodology: One hundred and six individuals participated in this study, for which 73 PPA patients were compared to 33 healthy controls. Diagnosis of PPA subtype was made by clinical consensus using established criteria (Mesulam et al, 2009). Resting state functional MRI (rsfMRI) was collected using a Siemens 3T scanner over 10 minutes with eyes open. Data were analyzed using FSL tools. A group independent components analysis generated 30 independent components (ICs). Participant's individual time series and component spatial maps were estimated using dual regression. Voxel-wise non-parametric permutation testing (n=5000) tested for significant differences in connectivity within each IC across groups. Follow-up one-way ANOVAs with Tukey post-hoc tests were conducted.

Results: Post hoc tests found PPA subgroup(s) had reduced connectivity than controls in three FSL-identified ICs showing significant group differences. PPA-L had significantly lower connectivity within IC1 in the cuneus. PPA-G had significantly lower connectivity within IC14 in Broca's area; and all three PPA subtypes had significantly lower connectivity within IC25 in the left

middle temporal gyrus (MTG).

Discussion: These results not only support previous findings, but suggest different neural network targets for therapeutic interventions for different PPA subtypes of PPA-L and PPA-G, whereas all subtypes may benefit from MTG targeting.

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