Northwestern Medicine
Feinberg School of Medicine

Mesulam Center for Cognitive
Neurology and Alzheimer's Disease

26th Annual Alzheimer Day

Relationship Between Whole-Brain Resting Connectivity, Cortical Thinning, and Symptoms in Primary Progressive Aphasia

Kyla Guillaume[1], Marsel Mesulam[1], Elena Barbieri[2], Jordan Behn[1], Emily Rogalski[1], Borna Bonakdarpour[1]

[1]*Mesulam Center for Cognitive Neurology and Alzheimer's Disease, Northwestern University Feinberg School of Medicine*

[2]*Department of Communication Sciences and Disorders, Northwestern University*

Background

The goal of this study was to observe the neural mechanisms underlying primary progressive aphasia (PPA) on a whole-brain level. PPA is a progressive language disorder due to underlying neurodegenerative disease (Mesulam, 1982). Previous PPA research has shown areas of atrophy within the 3 subtypes of PPA
– agrammatic (PPA-G), logopenic (PPA-L), and semantic (PPA-S). Our previous research also showed decreased connectivity between three major nodes of the language network. However, interaction between resting connectivity and cortical thinning at a whole-brain level remained to be determined. In this study, we used whole-brain resting state analysis and voxel-based morphometry (VBM) to observe the relationship between functional connectivity and cortical volume in PPA as compared to controls.

Methods

Twenty five right-handed PPA individuals and 10 controls participated in this study. The inferior frontal gyrus triangularis (IFG), middle temporal lobe (MTG), and anterior temporal lobe (ATL) were used in whole brain functional connectivity analysis to measure the connectivity between each region to the other voxels in the brain in PPA compared to controls using a t-test. VBM analyses were conducted by comparing, using independent-sample t-tests, the segmented and smoothed gray matter maps derived from the PPA and the control groups, with the goal to measure the difference in the amounts of cortical brain matter between groups. The resulting images were thresholded at $p < 0.001$ (uncorrected). Resting connectivity and atrophy maps were rendered upon each other to determine areas of overlap. Additionally, the gray matter volumes and functional connectivity maps were then correlated with patients' behavioral scores on the Boston Naming Test (BNT), Northwestern Anagram Test and Northwestern Assessment of Verbs & Sentences (NATNAVS), repetition test, and Peabody Picture Vocabulary Test (PPVT). These results were thresholded at $p < 0.001$ (uncorrected).

Results

The PPA-G subtype displayed significant atrophy in the superior temporal gyrus and IFG pars triangularis. PPA-G also showed decreased connectivity between the IFG seed and non-atrophied areas and in the right frontal lobe. PPA-S displayed significant cortical atrophy in the left ATL, and decreased connectivity was found between the ATL seed and non-atrophied regions in both the left and right frontal lobes. The PPA- L group presented significant atrophy in the left posterior temporal region, with decreased functional connectivity found in the temporoparietal region across all seeds. Cortical volume in the left ATL was correlated with BNT and PPVT scores at $p<0.01$. Cortical volume in the left frontal lobe correlated with NATNAVS, while the volume of the angular gyrus region correlated with repetition scores. In all cases, there were areas of decreased resting connectivity that were outside regions of atrophy.

Discussion

All subtypes showed atrophy patterns consistent with what has been reported in literature. The regions of cortical volume that were significantly correlated with BNT, PPVT, and repetition scores across all subtypes are consistent with the areas that have been shown to be involved in naming, word comprehension, and repetition. The existence of functional abnormalities outside of atrophic brain regions demonstrates that decreased connectivity beyond areas of atrophy also contributes to language impairments in PPA.

This research was presented as part of the 26th Annual Alzheimer Day hosted by the Northwestern University Mesulam Center for Cognitive Neurology and Alzheimer Disease on September 24, 2020.

brain.northwestern.edu