Spatial alteration of resting state networks in generalized anxiety disorder

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Background: Generalized anxiety disorder (GAD) is one of the most prevalent but less studied anxiety disorders of late-life. Our previous research has documented changes in resting state connectivity associated with GAD. Although the fluid spatial representation of resting state networks is described in the literature, previous studies have focused on changes in the strength of network connectivity. In this study, we investigated changes in spatial representation of resting state networks by allowing each network to vary spatially (within each subject), while controlling for the overall size of the network. We then calculated how the spatial representation of the resting state networks differed in late-life GAD compared to elderly healthy participants (HC).

Methods: Resting state functional magnetic resonance (fMRI) scans were collected in 17 (10 F, mean age 64) participants with GAD and 20 HC (10 F, mean age 68). Previous work (Smith et al) used a cohort of nearly 30,000 healthy resting state scans to establish 20 group networks. We used seven of these networks to perform a dual regression on the current dataset. After slice-time/motion correction, spatial normalization, and smoothing, we performed dual regression (via FSL) to extract individual networks for each subject. We then threshold each group network using Z-values greater than 3 and min cluster size of 50 voxels. We counted the number of voxels (K) in each group network, and then created a binary subject level network map that took the top K voxels for each subject. This controls for the size of the network, while allowing each network to be more fluid in its representations. For each network, we tested (Fisher’s exact test) whether there was a significant (p<0.05, cluster size greater than 100) difference between the proportions of subjects that have this voxel in the network in HC compared to GAD. We then plotted the mean likelihood (number of subjects that have the voxel in the network divided by number of subjects in the group) for each group and 95% confidence intervals.

Results: The middle cingulate and right middle temporal gyrus were more likely to be in the dorsal default mode network (dDMN) in HC compared to GAD [HC: 33 (30, 36) & GAD: 3 (1, 5) and 5 (3, 7)]. However, the left inferior parietal was less likely to be in the dDMN in HC than GAD [HC: 11 (5, 16) and GAD: 43 (35, 52)]. The anterior cingulate was less likely to be in the ventral DMN in HC than GAD [HC: 18 (14, 22) and GAD: 56 (51, 61)]. The right inferior frontal (orbital) was more likely to be in the right executive control network (rECN) in HC than GAD [HC: 35 (31, 39) and GAD: 4 (2, 7)], while the right supramarginal was less likely in HC than GAD [HC: 21 (15, 26) and GAD: 60 (53, 66)]. The left middle frontal was more likely to be in the left ECN in HC than GAD [HC: 50 (45, 55) and GAD: 13 (9, 17)].

Conclusions: We found that the variability in the spatial representations of each network may provide important information suggesting that the recruitment of various regions of interest in the canonical resting state network may be a marker of specific disorders.