Spectral embedding of the structural connectome reveals correlates of depression involving regions of the default mode network

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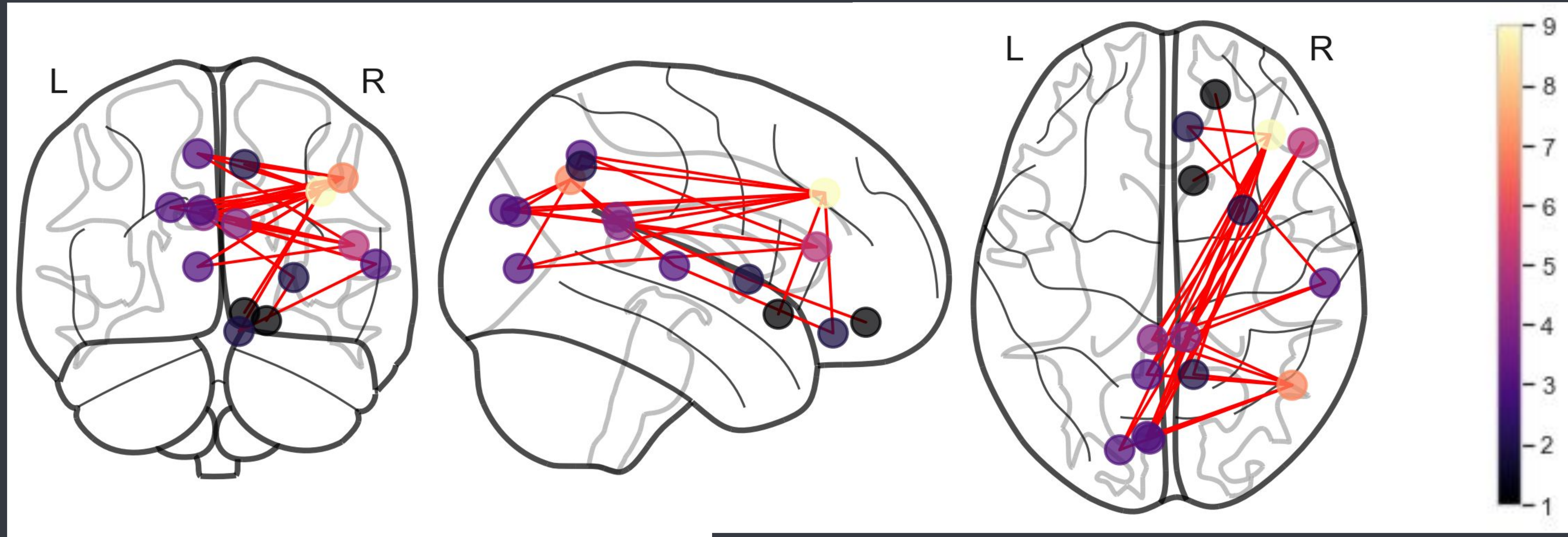
Introduction

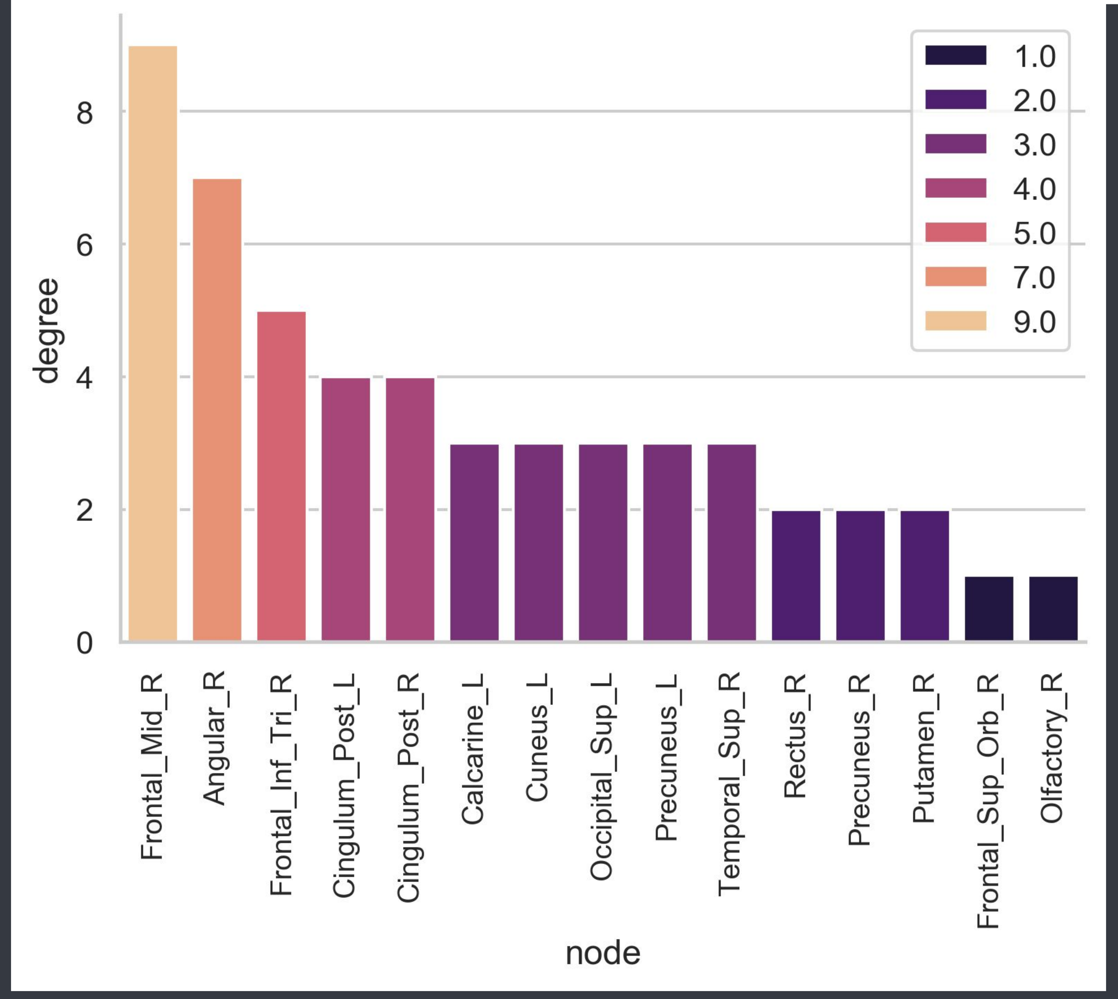
Graph theoretical models of brain networks are extensively studied in the field of psychiatry. Such networks are represented as a set of vertices (brain regions) and edges (connections between brain regions), which are defined based on imaging modality. Commonly, white matter tractography based structural connectomes are used directly for either edge-based or graph theoretical analysis. However, edge-centric studies are limited to pairwise comparison, and predefined graph features limit access to potentially informative latent network structure. Alternatively, the mathematical properties of connectome graph laplacian can be utilized to model the “heat” or “information” diffusion characteristics, which take into account the entire network topology, of brain networks. In this study, we propose a novel method for representing the structural connectome by defining edge weights between nodes as a distance metric based on the spectral embedding of each subject’s brain graph. We then apply the network-based statistic (NBS) framework to identify subnetworks that correlate with clinical traits of interest.

Methodology

Data used are diffusion tensor imaging based structural connectomes from an Research Domain Criteria (RDoC) study, with N=66 patients (PT, mean age=27.5, male/female=20/46) with any form of internalizing psychopathology (e.g., major depressive disorder, generalized anxiety disorder, social anxiety disorder, post-traumatic stress disorder) and N=23 age and sex matched healthy controls (HC, mean age=24.7, male/female=8/15). The Depression Anxiety and Stress (DASS) questionnaire was administered to each subject. The symmetric normalized laplacian is computed and eigen-decomposed to obtain the eigenmodes (eigenvectors of the laplacian matrix) for each subject’s structural adjacency matrix. Each element of an eigenmode corresponds to the spectral embedding of a node such that diffusion occurs more quickly between nodes with similar eigenmode values. Brain network eigenmodes are then used to determine the euclidean distance of all nodes to one another in the embedding space. Next, an NBS-based framework is applied to the newly defined structural connectomes to identify subnetworks that either positively or negatively correlate with clinical traits of interest.

Results





In a preliminary analysis, one subnetwork was found to correlate positively with the DASS depression subscale, indicating that slower diffusion within the subnetwork is positively associated with this scale. This subnetwork is includes the bilateral precuneus, posterior cingulate cortices, and right frontal cortical regions. (rho threshold =0.4, p<0.001). Edges in this subnetwork were predominantly adjacent to right frontal and parietal regions, as well as the posterior cingulate. The later, as well and the precuneus, are hubs of the default mode network, a major functionally defined subnetwork that has previously been implicated in depression and anxiety.

Spectral embedding of the structural connectome reveals diffusion-based brain subnetwork correlates of clinical measures in a transdiagnostic psychiatric cohort.

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