MA703 Final Project Proposal
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Introduction: One of the main goals of human cognitive neuroscience is to be able to prescribe function to brain regions, either in isolation or in their communication with others. The lack of direct measurements of neuronal activity (e.g. single-cell electrophysiology) makes this a tough problem in humans, one that nowadays relies mostly on functional MRI (fMR) data. In my lab, we are particularly interested in determining the unique neural attributes of the medial prefrontal cortex (mPFC), in particular in its relation to how humans evaluate prospects and make decisions. The challenge lies in that this region has been related to a variety of functions, the most popular being its activity when subjects are not engaged in any behavior or stimulation. This is called resting state (RS), and the areas that underlie this state have been named the default mode network (DMN). Unfortunately, the mPFC is especially tough to image, as the oxygen-related signal recorded by fMRI is contaminated by the oxygen in the sinuses.

An ever-growing trend in human neuroimaging has been to apply network statistics to tackle these functional challenges. For example, a region's function might depend on its connectivity at any given time with one community or another. One great advantage of network science is the ability to characterize connectivity that allows comparisons among individuals in a meaningful way. Therefore, I propose to use some of the statistics that we have learned in class to estimate intrinsic functional subdivisions of the mPFC at the individual subject level. Particularly, I would like to distinguish communities related to DMN from others, so that we can generate more informed topographic targets for future studies of decision making.

I would like to address my question at 3 levels of granularity: 1) across the literature (meta-analysis); 2) full-brain connectivity, using a pre-specified brain atlas; and 3) characterizing the connectivity of surface vertices (small units of function that contain oxygen-dependent information across time--unfortunately the nomenclature overlaps) for the regions that I'm interested in. I will perform the last two steps at an individual level for 3 subjects, hoping to find some commonalities among them.

Proposed Methods: To perform the first step, I will use data from a metanalysis that gathered peak brain coordinates of activity from studies of valuation and DMN. These are the surviving areas post-statistical thresholding from each study. I have partially analyzed this data by mapping the peak coordinates to an atlas of the human cortical surface. This produced a list of standardized parcels that were reported on each study. I will thus generate an undirected, weighted graph in which each vertex is a brain parcel, and edges will correspond to the number of times each of them co-occurred across studies. The advantage of utilizing this atlas is threefold: first, it reduces the number of functional vertices from 60,000 (cortical surfaces) to 360 (cortical parcels). Second, it standardizes the vertices from the first to the second stage of my project. Finally, it will allow me to project each area on a brain space without much clutter. While I plan to use other visualizations, I expect to mostly take advantage of the brain's topographical information that I do have.

Once I have this meta-analytic graph, I plan on computing descriptive measures to capture each parcel's centrality in the literature. I am thinking of using the strength of each vertex, as well as their betweenness centrality. With these I hope to select a couple of regions of interest (ROI) from mPFC and other brain areas that are central to valuation and DMN literatures. These ROIs will inform the next two steps.

In order to actually quantify the intrinsic connectivity of these ROIs, I will use data from the Human Connectome Project. Specifically, I will acquire resting-state fMRI activity from 3 subjects, all of whom have been preprocessed according to industry standards to allow for group-level comparisons. Each data set contains around 1 hour of signals represented as 4800 time points, and again each subject contains 60,000 vertices. I will parcellate each subject's brain according to the atlas mentioned above, so that each parcel contains the mean time series from its vertices, and will correlate the mean time series among all parcels. This will produce a weighted adjacency matrix for each subject, where each vertex is a parcel, and edges the correlations among all of them. Finally, I will take the exponential of these weights, Fisher transform them (i.e.

tanh) so that all weights are positive while maintaining the shape of the original correlation distribution, and retain the edges whose adjusted p-values remain significant (FDR < 0.05).

Again, I will quantify each parcel's strength and betweenness, average them across subjects, and examine how well these statistics correspond with the occurrences in step one. Second, I will maximize the strength-based modularity metric as a community detection method, so that I can check if the whole-brain communities somewhat match the standard DMN ones. While this measure has resolution problems at large and low scales, if it does extract a close match to standard DMN networks, it could act as a good method for the final stage of the project. Additionally, from previous experience in fMRI, very small communities are unlikely in this context. This step is meant to examine whether the ROIs from step 1 can be subdivided into DMN and non-DMN regions at this level of granularity.

For the final stage, I will "zoom in" by computing the correlation among all of the cortical vertices from each ROI across all the ROIs, and apply the same correction as in step two. This will produce a graph with anything from hundreds to thousands of vertices (since each parcel contains around 200 cortical vertices). This time, I will only compute the modularity to see if mPFC can be subdivided at this finer level of resolution, and compare the resulting communities across subjects. Additionally, I will estimate communities by using sensory areas with mPFC ROIs. This will act as a control, since sensory areas should not produce refined communities with vmPFC due to their relatively independent functionality (unlike DMN areas). I will visualize all the community affiliation of each vertex across subjects in a sort of heatmap, to see if this method results in similar communities. I am also interested in trying quantitative methods to characterize how stable these communities are across, such as stability or promiscuity (Garcia et al., 2018).

Depending on the time I have left, I would also like to probe the temporal dynamics of these networks. My idea would be to divide each subject's data into six 10 minute bins and re-compute the analyses in stage 3. This would help me address the intuition that mPFC shifts functionality from DMN to non-DMN dynamically, thus explaining why studies that summarize activity fail to capture its components. Finally, I thought about using ERGM to get the probability of each edge in being DMN or not, but this seems more suitable to brain activity that can compare resting state and subjective value tasks (perhaps a future follow-up).

Reference

Garcia, J. O., Ashourvan, A., Muldoon, S. F., Vettel, J. M., & Bassett, D. S. (2018). Applications of community detection techniques to brain graphs: Algorithmic considerations and implications for neural function. *Proceedings of the IEEE*.