Identification of Functional Subunits of the Human Cortex using Resting State fMRI

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Introduction: Since the first studies of Broca and Wernicke scientists have been trying to relate function to specific cortical areas and to generate a functional map of the cortex. Anatomic approaches based on histology (microscopic and analysis of cytoarchitecture), on morphology (anatomic parcellation of cortex), and function (task based fMRI and PET) have all previously been used to identify functional subunits within cortex and each of these approaches have strengths and limitations. Resting state connectivity mapping has been used to examine functional connections between cortical regions since the first presentation of the method by Biswal in 1995. The approach typically uses task-free time course information obtained using a blood oxygenation level dependent contrast (BOLD) acquisition and measures the temporal correlations between different regions over time. In this work, we applied a globally optimized segmentation algorithm to divide the brain into functional subunits based on resting state fMRI. We compared the results obtained using resting state data to partitions obtained based on histology and task-based fMRI.

Theory: Given a dataset $X = [x_1, x_2, ..., x_N]$, we define an affinity matrix W which measures the pairwise similarity between points. In the study of resting state fMRI, x_i corresponds to the BOLD time series at voxel i, and $W(i,j) = \exp(-\frac{(1-corr(x_i,x_j))^2}{\sigma^2})$, where $corr(x_i,x_j)$ is the correlation between two time courses x_i and x_j. Let $A = \{A_1, A_2, ..., A_R\}$ denote the R-way partitioning of the dataset X, the normalized cut[1] is given by,

$$Ncut(A) = \sum_{r=1}^{R} \frac{\sum_{i \in A_r, j \in X \setminus A_r} W(i,j)}{\sum_{i \in A_r, j \in X} W(i,j)} \quad (1)$$

Although solving for the minimum of Eq (1) is an NP hard problem, solution to a relaxed optimization problem can be obtained by solving a weighted Kmeans problem, $\min_{(\mu_1,\mu_2,...,\mu_R)} \sum_r \sum_{i \in A_r} D(i) \| y_i D^{-\frac{1}{2}}(i) - \mu_r \|^2$, where $Y = [y_1, y_2, ... y_N]$ is the new coordinate system of the original data X, which can be obtained via eigen-decomposition of W, and $D(i) = \sum_j W(i,j)$.

Method: Imaging was performed on a 3D Siemens Trio scanner at the Yale MRRC. A T1-weighted 3-plane localizer was used to localize the slices to be obtained and T1 anatomic scans were collected in the axial-oblique orientation parallel to the ac-pc line. Resting state connectivity data was obtained using a gradient echo T2*-weighted echo planar imaging sequence, 64×64 matrix, alpha/TE/TR = 80/30ms/1550ms, with 25 slices 6mm thick, slip 0mm, 22×22 cm FOV, providing whole-brain coverage with voxel size of 3.4mm×3.4mm×6mm. Eight 6-min runs of resting state data were collected. Data was motion corrected using SPM5 and slice time corrected. Physiological noise from both respiration and cardiac pulsations were removed using the RETROICOR approach. Time courses were detrended and lowpass filtered before the segmentation algorithm was applied.

Results: The segmentation results were averaged over a group of 22 subjects.

I. *Resting-State Vs. Histology*: resting state time courses from Brodmann Areas BA 17/18 were extracted from each subject. The weighted Kmeans clustering was applied with R=2. The partitioning was highly consistent across subjects. The composite map of the 2-way segmentation is shown in Fig. 1(B). Comparing to the BA map shown in Fig 1(A), we see that the two maps are in general similar to each other, while the red region in Fig 1(B) extends more medially.

II. *Resting-State Vs. Task-based*: an area in the intraparietal sulcus was discovered to be involved in working memory update/refresh tasks. Resting state data from the same region were recruited for a 2-way segmentation. The results from the resting state data show similar delineation of the functional subunits responding to different tasks (Fig 2).

Conclusion: The segmentation is driven by the resting state fMRI with no structure information. The approach generates stable functional subdivision in both sensory and cognitive regions, which show large overlap with known histology and task-based findings. The results support the idea of developing a functional brain atlas based on resting state fMRI.

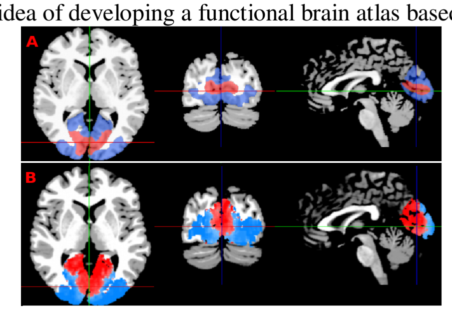

Fig 1: (A) Brodmann map of BA 17/18; (B) Composite map of the 2-way segmentation based on resting state data.

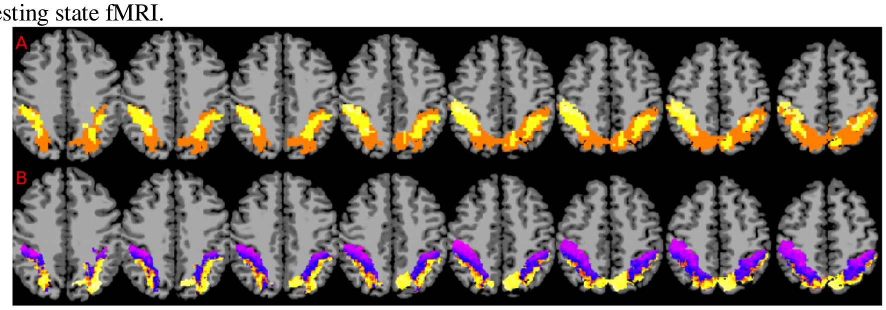

Fig 2: (A) Regions active during a working memory update/refresh experiment; (B) Composite map of the 2-way segmentation based on resting state data. The location and size of the yellow region in (A) are similar to the purple region in (B).

Discussion: The segmentation algorithm can be extended to functional parcellation of the whole brain. Two critical questions related to this extension are how to determine the number of clusters for each individual and how to combine segmentation results over a group. We are now working on an approach where segmentation of each individual is regularized by the group average.

Reference:

[1] Jianbo Shi and Jitendra Malik. Normalized cuts and image segmentation. IEEE transactions on pattern analysis and machine intelligence, 22:888–905, 2000.