ROI Atlas Generation from Whole Brain Parcellation of Resting State fMRI Data

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Introduction

Whole brain functional connectivity (FC) analyses require specifying the functionally homogeneous regions of interest (ROIs) to be analyzed.
- Hand placed ROIs suffer from experimenter bias and error.
- ROI atlases may not correctly describe functional segregation of the brain.
- Most clustering methods (ICA, SOM, etc.) identify “networks”; this smooths out detail about the interaction between regions.

We use spatially constrained n-cut spectral clustering to identify spatially coherent and functionally homogeneous ROIs for FC analyses.

Methods

Subjects
- 41 healthy volunteers participated in accordance with IRB Policy (18F, age 28.9 +/- 7.2).

Scanning
- 3.0T Siemens Magnetom TIM Trio using 12-channel head matrix.
- Resting state data were acquired with a Z-SAGA sequence [1] to minimize susceptibility artifacts.
- TR/TE1/TE2/FA/FOV = 3000 ms/30 ms/66 ms/90°/220 mm
- 150 images acquired in thirty 4-mm axial slices, in plane resolution 3.44 mm x 3.44 mm, 7 min scan.
- Subjects were instructed to fixate on a point while clearing their minds of any specific thoughts.

Preprocessing
- Functional scans were slice timing corrected, motion corrected, written into MNI space at 4 mm x 4 mm x 4 mm resolution and spatially smoothed with a 6-mm FWHM Gaussian using SPM5.
- Data were restricted to gray matter, de-noised by regressing out motion parameters, CSF and WM time-courses and bandpass filtered 0.009 Hz < f < 0.08 Hz.

Spatially Constrained Normalized Cut (ncut) Clustering

- Represent data as an undirected weighted similarity graph, G = (V,E).
- Vertices, V, correspond to voxels.
- Edges, E, connect two voxels and are weighted by the non-negative similarity, w, between voxels.
- Spatial coherence is enforced by only connecting a voxel to other voxels in its 3D neighborhood [2].
- The algorithm cuts the graph into a specified number of clusters, K, such that intracluster similarity is greater than intercluster similarity.
- Normalized cut “balances” the sum of edge weights within each cluster.
- Practically, G is represented as an adjacency matrix W of edge weights, wij, and the ncut problem is solved by linear algebra.
- Ncut clustering was performed using a Python implementation of the algorithm presented in [3].

Similarity can be measured in many ways
- r1: Pearson correlation between voxel time-courses, threshold r1 ≥ 5.
- r2: Pearson correlation between the FC maps generated by voxel time-courses, threshold r2 ≥ 5.

Two methods for group level clustering
- Average subject specific W matrices, and cluster the results.
- Cluster each individual, combine the results, and cluster again.
- After clustering each subject, construct an affinity matrix A, where entries aij = 1 if voxels i and j are in the same cluster, aij = 0 otherwise.
- Average affinity matrices across subjects, and perform ncut clustering on the resulting matrix.

Performance Metrics

LOOCV Reproducibility
- Calculate the similarity between the clustering result from a single subject’s data to the result of group level clustering with that subject excluded.

Variation of Information

Clustering results are capable of more accurately representing resting state networks than the default mode network.

Spatially constrained spectral clustering is capable of identifying functionally homogeneous and spatially coherent ROIs for FC analysis.

Results

Spatially constrained spectral clustering is capable of identifying functionally homogeneous and spatially coherent ROIs for FC analysis.

In figure 2 results from r1 and r2 are similar, K = 50 is underclustered, and the small clusters at K = 1000 reduce interpretability.

Figure 3 shows that the accuracy of representation improves with K, clustering outperforms anatomical atlases for K > 100.

The anatomical atlases perform better for motor and visual networks than they do for the default mode network.

Figure 4 illustrates that the AAL and TT atlases do not accurately represent the anterior cingulate or frontal cortex components of the default mode network. K = 180 captures most of the detail of the voxel analysis.

Conclusion

- Spatially constrained spectral clustering is capable of identifying functionally homogeneous and spatially coherent ROIs for FC analysis.
- Results generated using r1 outperform r2, and the two-level approach performs better than averaging, although the differences are small, and the two-level approach is computationally expensive.
- No optimal choice of K was found, rather it can be chosen to optimize an experiment.
- Clustering results are capable of more accurately representing resting state networks than the explored anatomically derived ROI atlases.

References


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