

Project Gamma Progress Report

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Background

Essential Background

- ▶ “Working memory in healthy and schizophrenic individuals”
- ▶ Accession number: ds000115 (from the OpenFMRI.org website)
- ▶ The paper(s) used ANOVA to explore within/between network connectivity wrt working memory measures.
- ▶ The goal was to identify regions contributing to impaired cognitive function in schizophrenics.
- ▶ The method was fcMRI, collecting activation and connectivity (resting) fMRI data.
- ▶ 102 subjects: individuals with schizophrenia, their healthy siblings, and controls.
- ▶ N-back memory tasks

Goals (GLM)

- ▶ A target is the event that the current letter that is the same as the n th preceding letter
- ▶ A non-target is the opposite of a target, in which the current letter is not the same
- ▶ An activation cluster: to a group of neighboring voxels activated beyond certain statistical threshold (t-test p value) by defined events
- ▶ Goal of GLM: detect the activation clusters of target and non-target events in one subject in the control (healthy) group
- ▶ Subgoals:
 1. Compare 0-back and 2-back tasks for one subject
 2. Identify noise regressors so that we can remove them in data for connectivity analysis

Goals (Connectivity)

- ▶ The goal of connectivity analysis is to compare the functional brain connectivity, measured by ROI-ROI correlations of 2-back task data between the four networks of the brain (DMN,FP,CO,CER), across CON and SCZ groups.
 1. 2-back task: difficult to perform, requires highest memory load, more likely to reveal the difference
 2. four networks: DMN,FP,CO,CER are thought to be critical for cognitive function and defined in the paper
 3. CON: control and their siblings SCZ: schizophrenia and their siblings

The Method (GLM - Confiton Files)

- ▶ cond001: Start cues for both blocks of the run
- ▶ cond002: The letters presenteed to the subject. The intensities are all one becasue there is only one homogeneous event type
- ▶ cond003: The target and non-target events during the run
- ▶ cond004: Done cues for both blocks of the run
- ▶ cond005: Start and durations of the two blocks with a rest (i.e. fixation) period in between the blocks.
- ▶ cond006: Excludede; Unknown and unexplained in the paper
- ▶ cond007: Errors made by the subject when responding for each letter shown whether it was the same as a pre-specified (0-back) or preceding (1,2-back) letter

The Method (GLM - Regressors)

- ▶ Condition file on-off time course at a time unit of 0.01 TR with a gamma function and take the convolved values at the start of each TR
- ▶ reg001: Convolution of target events
- ▶ reg002: Convolution of non-target events
- ▶ reg003: On-off time course for the two blocks
- ▶ reg004: Convolution of start cues. Separated from the target and non-target regressors because it is not likely to involve heavy working memory load compared to task regressors
- ▶ reg005: Convolution of done cues
- ▶ reg006 and reg007: A linear drift term and a quadratic drift term as potential nuisance regressors. Their significance is investigated below [graph]
- ▶ reg008 and reg009: The first two principal components of the data. Based on the projections shown below, we decide that the first two are not functional features. [Control subject, First four principal components]
- ▶ reg010: Intercept term.

The Method (GLM - Analysis)

- ▶ Standard processed brain -> pad brain boundary -> pass through Gaussian filter of $\sigma=2$ -> GLM
- ▶ For each β on each voxel time course, a linear regression two-tailed t-test
 1. null hypothesis: $\beta = 0$
 2. alternative hypothesis: $\beta \neq 0$
- ▶ Assumptions:
 1. Residuals of each linear model are independent and identically distributed (i.i.d)
 2. Residuals for the model are normally distributed
 - 2.1 Shapiro-Wilk Test per voxel: 37703 out of 207766 voxels failed
 - 2.2 Test normality of several models together. perform Hochberg (6 / 207766 voxels failed) and Benjamini-Hochberg tests (all passed)

Method (Connectivity)

- ▶ Remove noise regressors identified in the GLM from the voxel time series
- ▶ Extract the voxels per ROI and validate: given the center index and the diameter
 1. ROIs are non-overlapping
 2. regions vs cubic regions

Method (Connectivity)

- ▶ Compute the ROI-ROI correlation
 1. for each ROI, get the average time series;
 2. for any two networks, obtain the correlation matrix containing the r-values of any two ROIs for the two networks;
 3. for each subject, we get the correlation matrix;
 4. for several subjects, group the r-values into CON and SCZ group based on the category of the subjects pic to explain the process

Results (GLM)

Results (Connectivity)

- ▶ Analyze on 20 subjects, 12 SCZ and 8 CON
- ▶ the individuals with schizophrenia and their siblings (SCZ) showed an overall reduction in connectivity between the cognitive control networks as compared to CON

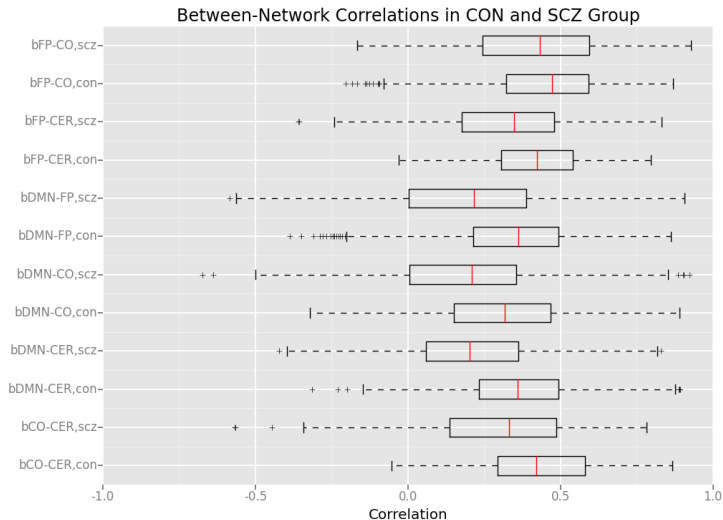


Figure 1: Boxplots of the r-values

Discussion

- ▶ Expand the number of subjects
- ▶ Perform permutation test to statistically validate the difference of connectivity between SCZ and CON