

Project Gamma Progress Report

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Essential Background

- ▶ “Working memory in healthy and schizophrenic individuals”
- ▶ Accession number: ds115 (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)

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

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: Letters presenteed to the subject
- ▶ cond003: Target and non-target events during the run
- ▶ cond004: Done cues for both blocks of the run
- ▶ cond005: Start times and durations of the two blocks
- ▶ cond006: Excluded; Unknown and not explained in the paper
- ▶ cond007: Errors made by the subject: misidentifying either a target or a non-target

The Method (GLM - Functional Regressors)

- ▶ Convolve neural predictions rescaled at a time unit of 0.01 TR with a gamma function
- ▶ Take the convolved values at the start of each TR
- ▶ Regressors:
 1. reg001: Convolution of target events
 2. reg002: Convolution of non-target events
 3. reg003: On-off neural predictions for the two blocks: account for block differences
 4. reg004 & reg005: Convolution of start cues and done cues: Not likely to involve heavy working memory load compared to task-related regressors

The Method (GLM - Noise Regressors)

- ▶ reg006 & reg007: A linear drift term and a quadratic drift term as potential nuisance regressors
- ▶ 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
- ▶ reg010: Intercept

The Method (GLM - Noise Regressors)

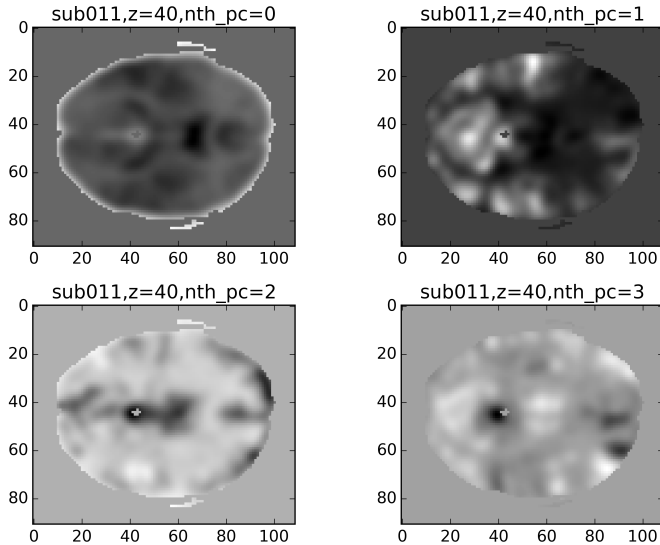


Figure 1: Control subject, First four principal components

The Method (GLM - Noise Regressors)

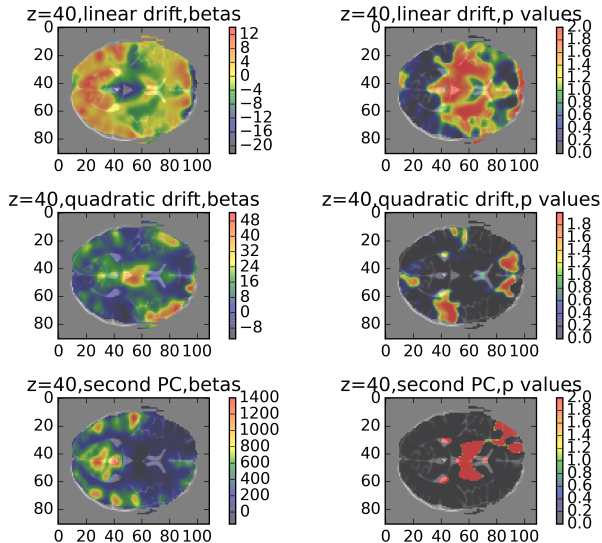


Figure 2: Noise regressors, Betas and p values

The Method (GLM - Analysis)

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

Method (Connectivity)

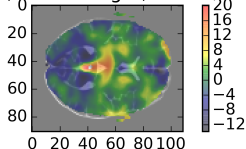
- ▶ Compute the ROI-ROI correlation
 1. for each ROI, get the average time series;
 2. for any two networks, obtain the correlation matrix containing the r-values of any two ROIs for the two networks;
 3. for each subject, we get the correlation matrix;
 4. for several subjects, group the r-values into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

Results I (GLM)

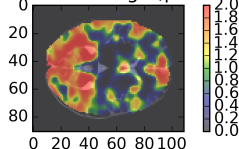
- ▶ Use of the GLM approach reveals that the 2-back task activate occipital and prefrontal regions more, as would be expected based on the higher cognitive load associated with these tasks.
- ▶ The coefficient and p-value maps displayed in the following slides illustrate the activations across several axial slices.
- ▶ The target 2-back task seems to activate many of the regions we would expect by a task associated with both visual processing and working memory.
- ▶ The non-target 2-back task activates a wider variety of regions, highlighting a difference in the neural dynamics between the two different types of tasks.

Results II (GLM)

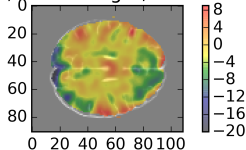
z=40, 2-back target, beta values



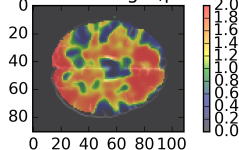
z=40, 2-back target, p values



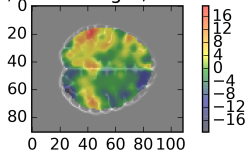
z=50, 2-back target, beta values



z=50, 2-back target, p values



z=60, 2-back target, beta values



z=60, 2-back target, p values

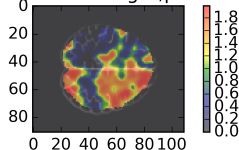
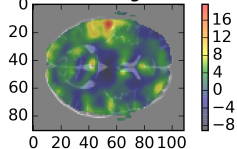


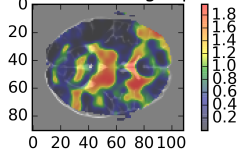
Figure 3: Betas and p-values from 2-back tasks

Results III (GLM)

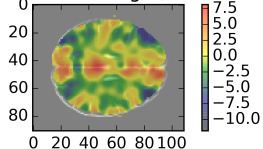
z=40,2-back nontarget,beta values



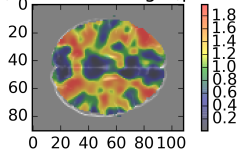
z=40,2-back nontarget,p values



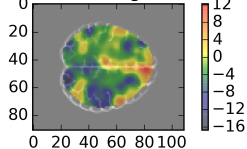
z=50,2-back nontarget,beta values



z=50,2-back nontarget,p values



z=60,2-back nontarget,beta values



z=60,2-back nontarget,p values

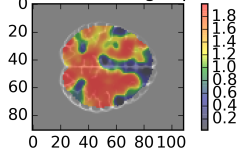


Figure 4: Betas and p-values from 2-back tasks

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

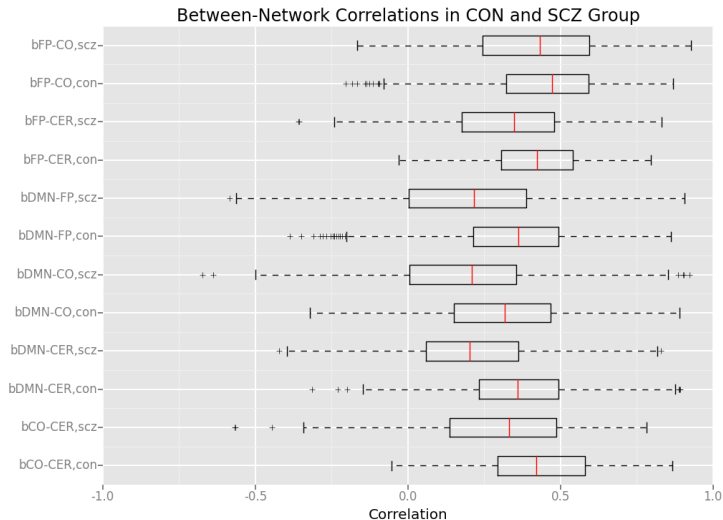


Figure 5: Boxplots of the r-values

Discussion

- ▶ get better result on more subjects
- ▶ Perform permutation test to statistically validate the difference of connectivity between SCZ and CON