Project Gamma Progress Report

Nima Hejazi, Feng Lin, Luyun Zhao, Xinyue Zhou

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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 memeory 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 nth preceeding 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 - Confition 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 nuisansance 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)

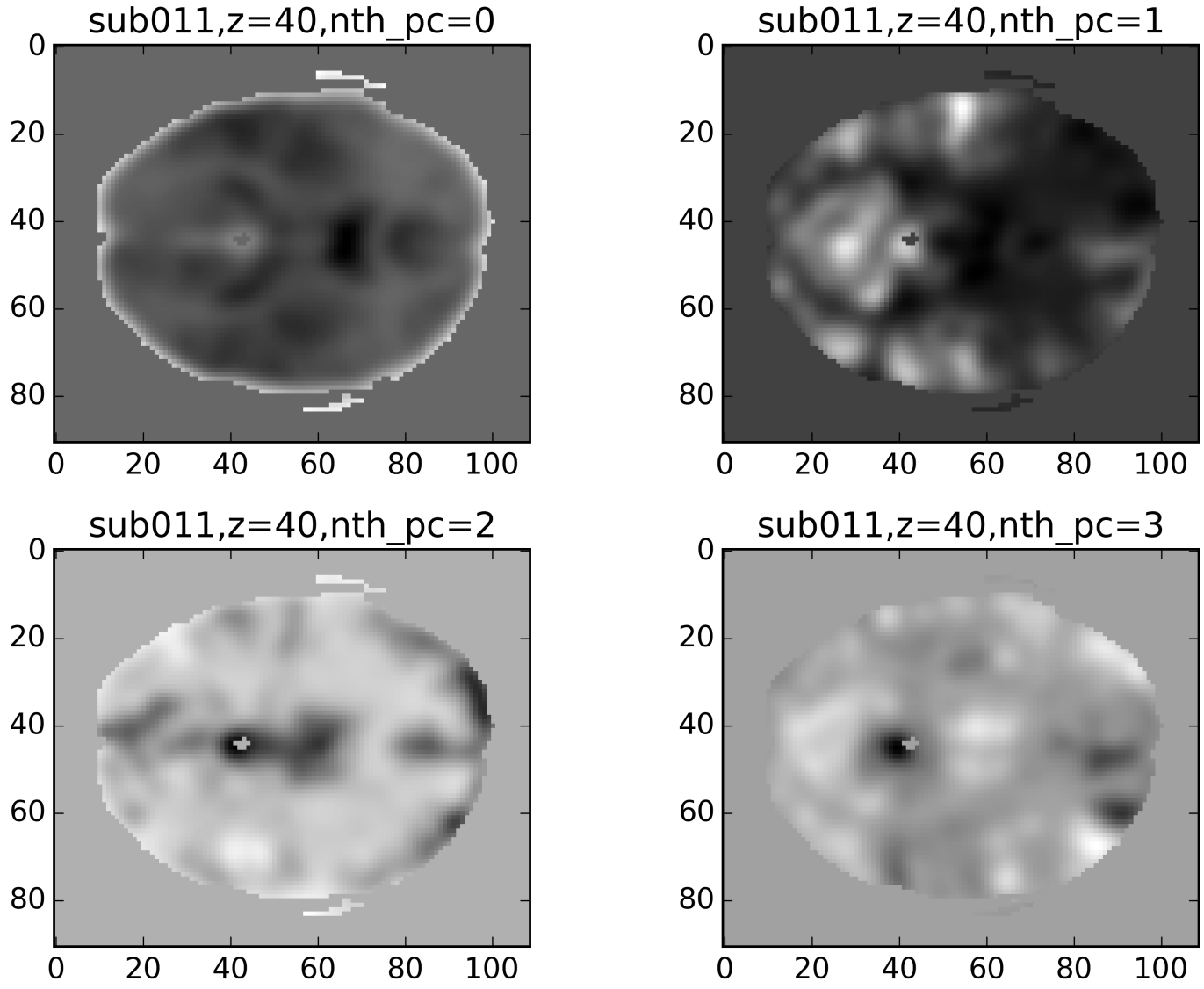

Figure 1: Control subject, First four principal components

The Method (GLM - Noise Regressors)

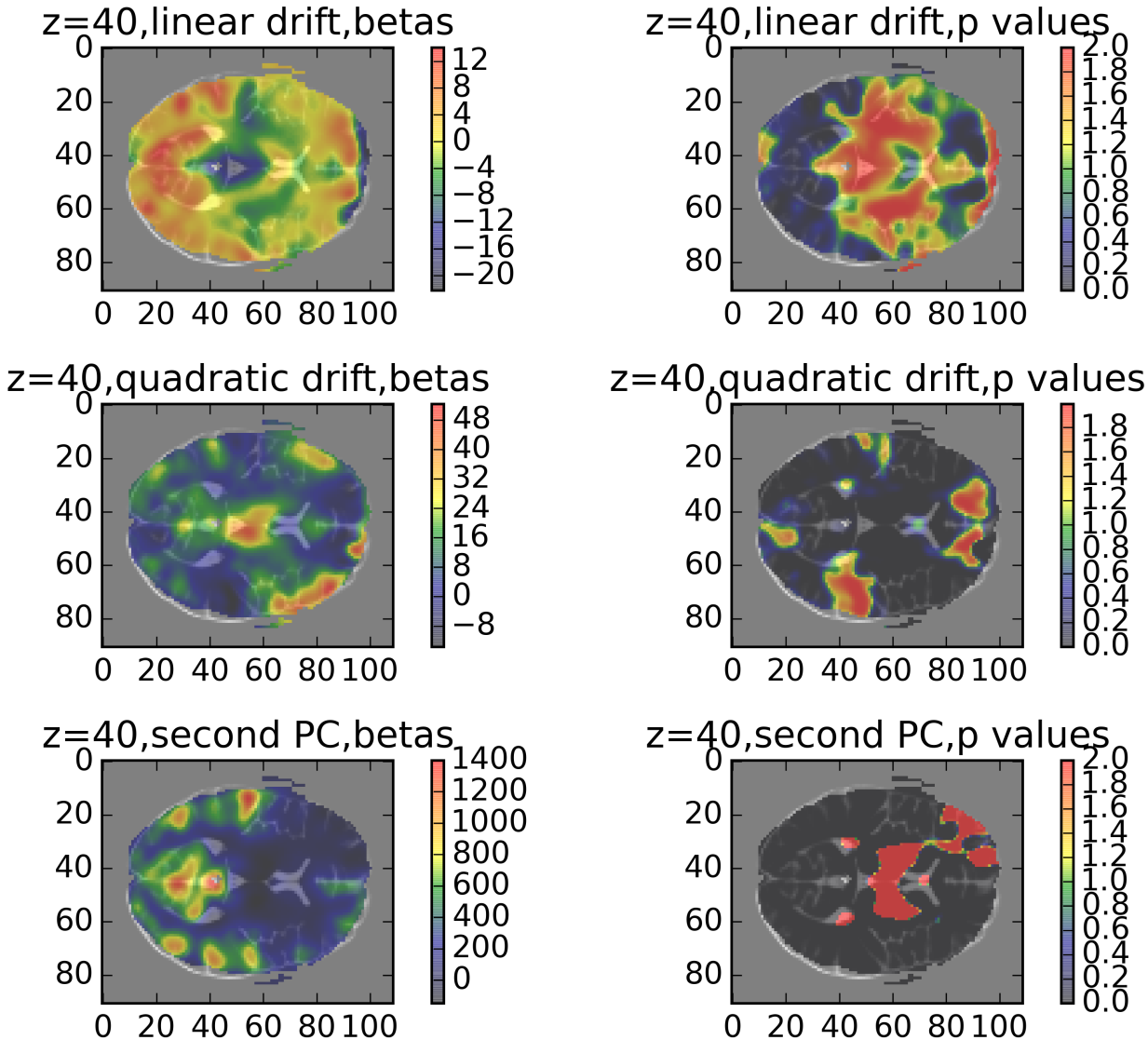

Figure 2: Noise regressors, Betas and p values

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 distribued (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)

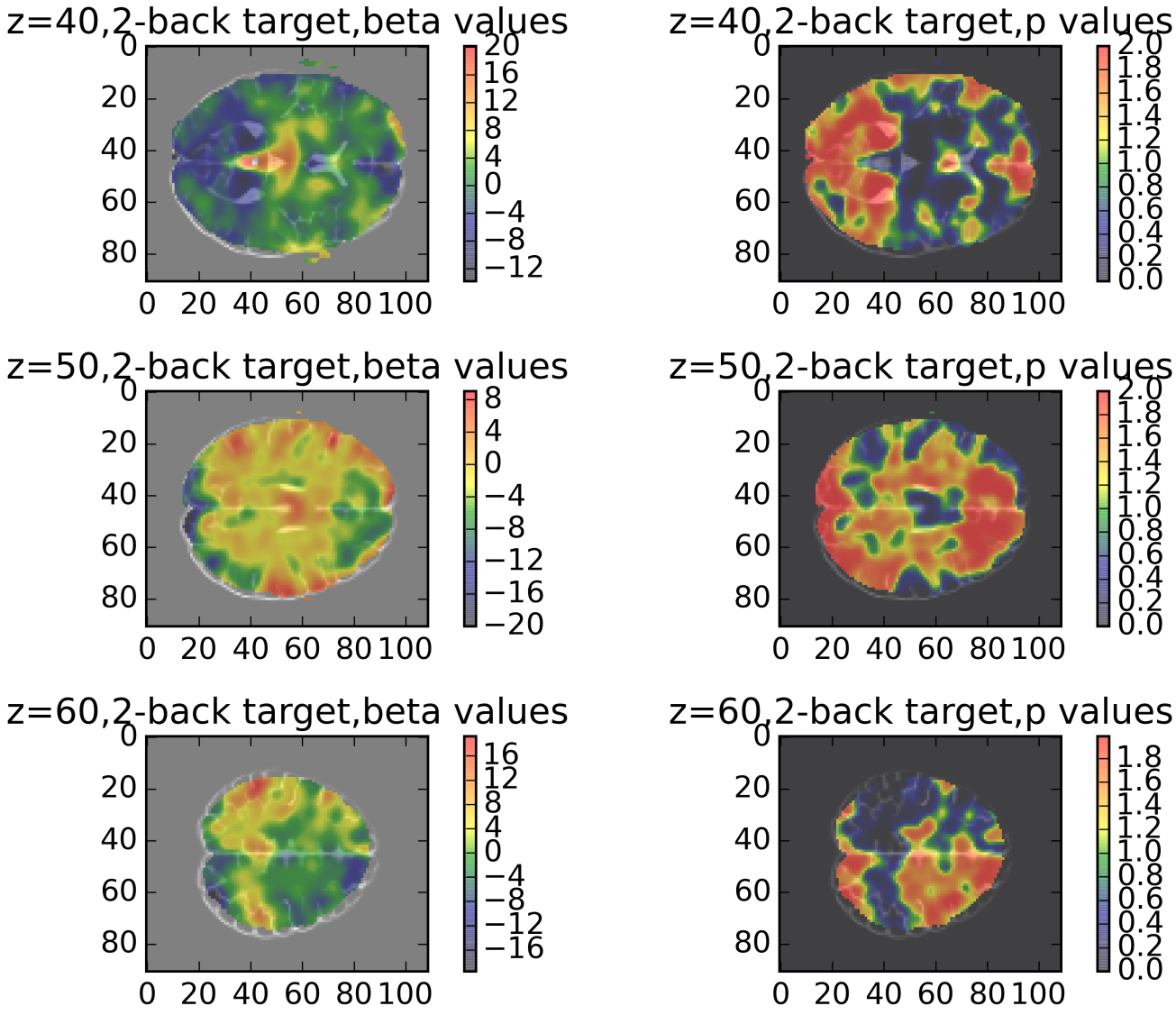

Figure 3: Betas and p-values from 2-back tasks

Results III (GLM)

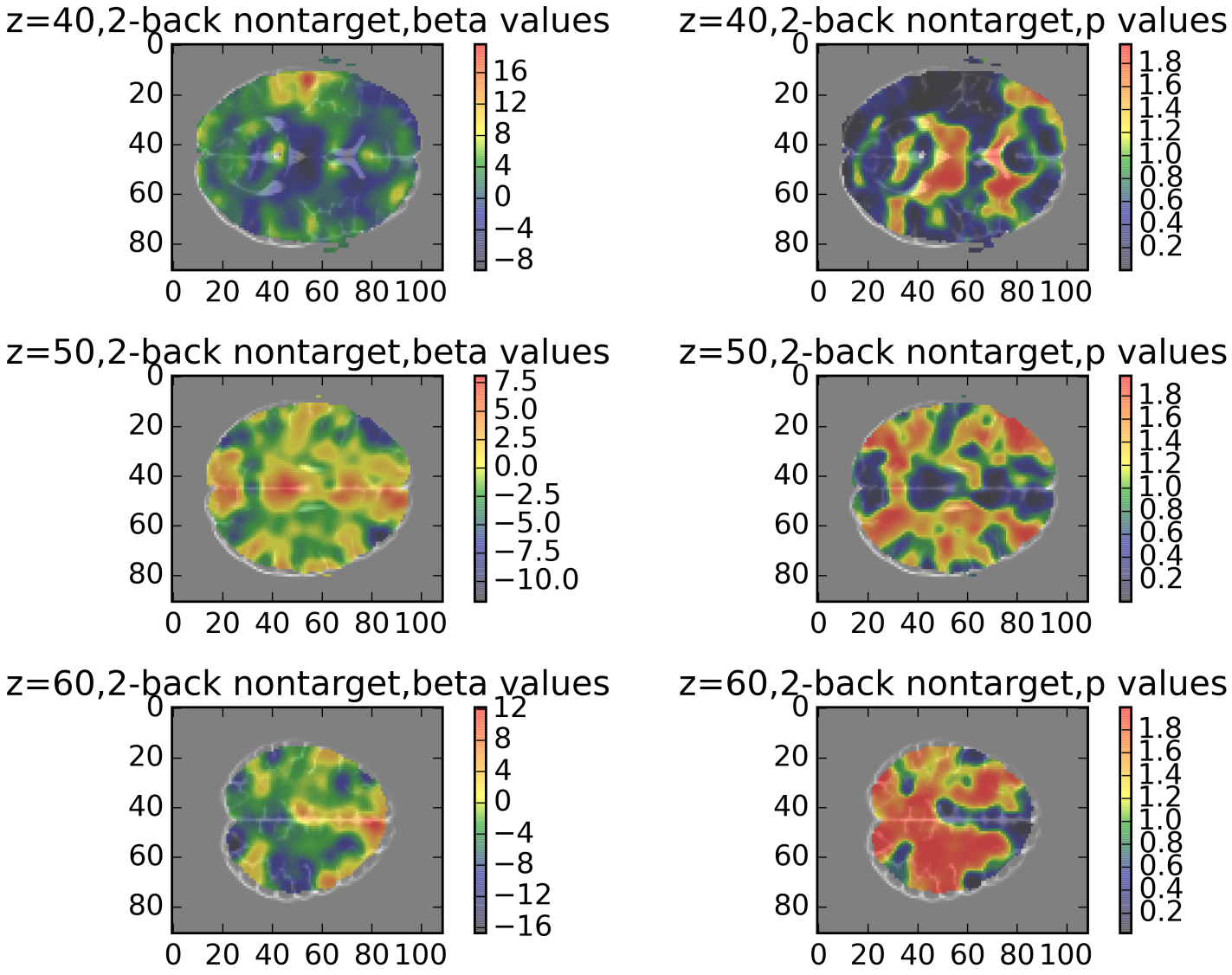

Figure 4: Betas and p-values from 2-back tasks

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

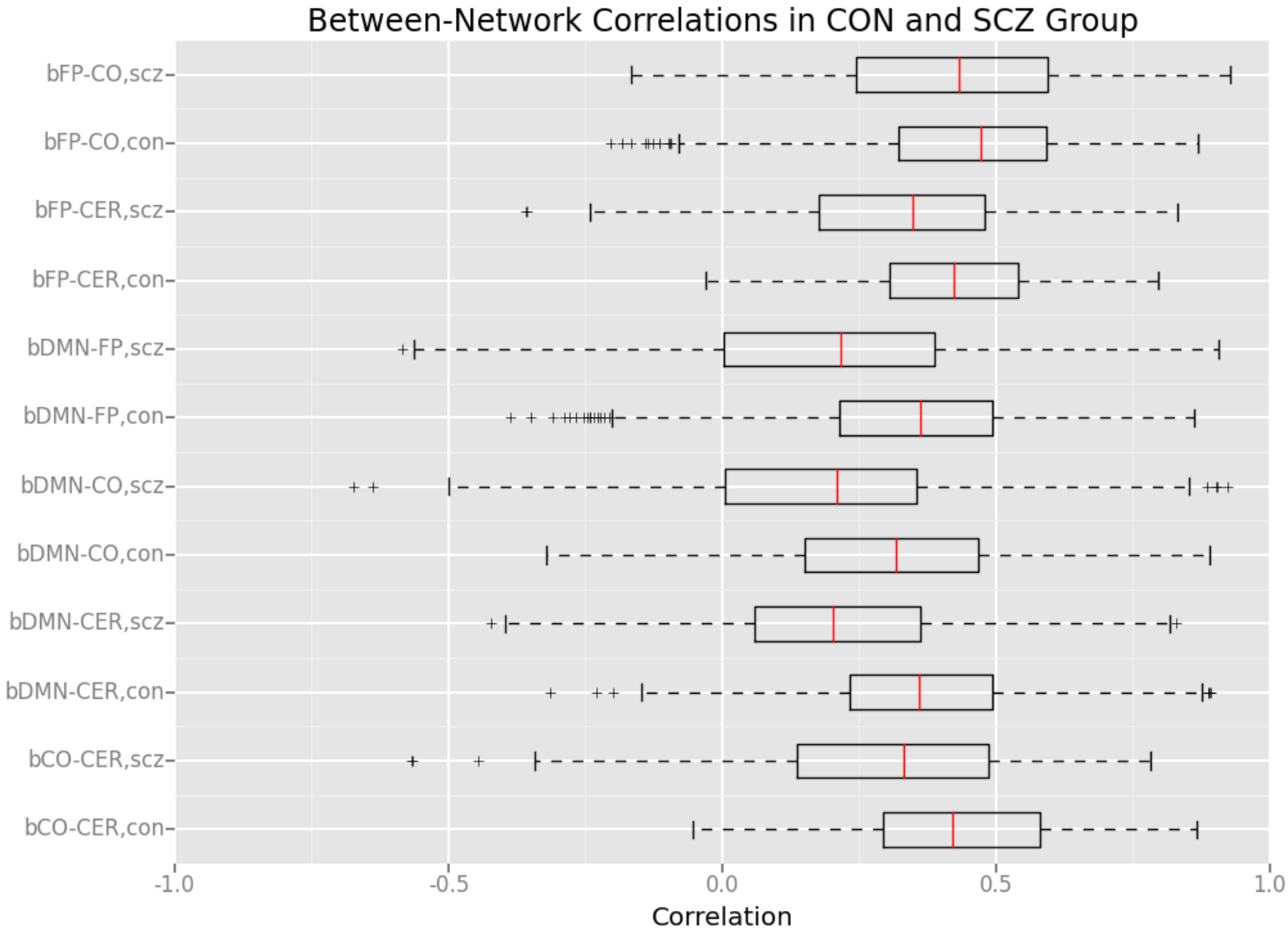

Figure 5: Boxplots of the r-values

Discussion

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