Reproducing fMRI Data Analysis on Brain Connectivity

Li, Jie	Li, Zeyu	Yun, Chuan	Zhang, Qiangyuan
Jay4869	lizeyuyuz	ay2456	amandazhang

December 13, 2015

Abstract

In this research paper, we analyze the fMRI data from the study done by Repov and Barch exploring the relationship between schizophrenia and brain connectivity [2, 3]. Instead of reproducing ANOVA analysis of within and between brain network connectivity, we focus on analyzing fMRI scans of one subject using generalized linear model. Before data analysis, we smoothed the data spatially and corrected noise in the fMRI data. On the preprocessed data, we perform student t test to identify the voxels responding to designed stimulus. Having localized the activated voxels, we closely examine the behavior of these voxels and validated our assumptions.

1 Introduction

The paper of which our research is based is titled "Working memory related brain network connectivity in individuals with schizophrenia and their siblings" [2, 3]. Schizophrenia is a chronic, severe, and disabling brain disorder. Previous studies have shown that changes in the function of a single brain region, or even a brain system, cannot explain the functional impairments seen in this illness [1, 2]. However, Repovs and Barch attempts to show that individuals with schizophrenia have reduced connectivity within and between neural networks, which could be a forward step to understanding schizophrenia.

Repov and Barch systematically examine changes in functional connectivity across rest and different task states in order to make an inference on characteristics of schizophrenia. They asses connectivity using blood oxygen level dependent (BOLD) time series acquired using fMRI. They find four types of participates, individuals with schizophrenia, the siblings of individuals with schizophrenia, healthy controls and the siblings of healthy controls. They designed three working memory loads of an N-back task and designated four regions of interest (ROIs). The four brain networks are: (1) Dorsal fronto-parietal network (FP), (2) Cingulo-opercular network (CO), (3) Cerebellar network (CER) and (4) "Default mode" network (DMN). The objective of the study is to examine the altered functional connectivity within and between these four brain networks when the participant perform a designated N-back task. With ANOVA analysis, it is found that individuals with schizophrenia and their siblings show consistent reductions in connectivity between both the FP and CO networks with the CER network.

We narrow our focus and analysis on a single schizophrenic subject. The fMRI data in the study shows the changes in blood flow in the brain, and analyzing this data can help us understand how schizophrenic brains respond during task performance. We detail in the following the steps we take to analyze the data. We attempted both spatial and temporal smoothing on the voxels in order to reduce noise. We also performed spectral analysis on fMRI data to correct noise in the data. After preprocessing the data, we fit multiple linear regression model using two different sets of experiment conditions. Having obtained coefficient estimates, we performed Student t-tests on each voxel to examine whether the particular voxel has show significant activity subject to appropriate thresholds. Performing t-tests relying on a set of assumptions that we need to validate. We performed the Shaprio-Wilk test to check the normality assumption.

2 Data

The data used in their published paper is available on the website OpenFMRI.org. The are many data files grouped by subjects, but we will be focusing on only one schizophrenic subject–subject 001, who is male, Caucasian and Schizophrenic. The data has four dimensions (91 x 109 x 91 x 137), consisting of three dimensional voxels that are moving across time. We removed the first four outlying data along the time dimension, which leaves us 133 images. (Need to add how to come to understand the BOLD signal = signal + noise, and the necessity of remove noise)

3 Convolution and design matrix

We need a good design matrix, containing data on the explanatory variables, to be used in our linear models to explain as much variation in the observed fMRI data as possible. We studied the design of the experiment closely. fMRI scans were acquired while participants perform specified memory tasks. They are to respond for each letter shown whether it was the same as a pre-specified letter (0-back), the same as the immediately preceding letter (1-back), or the same as the letter shown two trials previously (2-back). For our subject, there were three BOLD runs, each consisting of two blocks of 0-back, 1-back, or 2-back working memory task.

We examined the seven study conditions closely. The conditions are unusual from what we are familiar with in that they are consisted of fractions of durations and negative amplitudes. The first condition consists of the start-cues, the second condition consists of the task targets (amplitudes are all one), the third condition consists of the task non-target (the positive amplitude indicates correct identification of the target and the negative amplitude indicates the non-response to the non-target), the fourth condition consists of end-cues, and the fifth condition consists of durations of the two task blocks. There is no information on what the sixth file mean, and the seventh condition consists of the erroneous responses.

Since we were only familiar with convolution for block design, we initially used only the condition one, four and five, which give us the start time, the duration, and end time of the two task blocks. Due to the delay of signal after the onset of neural activity, we make use of the hemodynamic response function (HRF). The idea is to model the signal response as the convolution of the stimulus function with the HRF. Convolving with stimulus timing allows us to get idealized response as an explanatory variable (a regressor included in design matrix). We bear in mind the limitations of this design matrix due to its omission of trials within each of two task blocks.

4 Normality Test

In our analysis part, we use linear model to fit real data. There are several assumptions on linear modeling, one of which is normality assumption on errors term. Normality of the errors can be checked by checking normality of the residuals. The usual way is plotting a Q-Q plot and check whether it forms a straight line. However in this paper, since there are around 200,000 voxels it would be hard to plot all of them and check for normality. Thus we use Shapiro-Wilk test in the paper to test for normality.

In Shapiro-Wilk test, a small p-value indicates non-linearity. We write up a function to compute p-value of each voxel and plot those p-values in three brain perspectives. There are three linear models used in the paper, the below 6 plots are p-value plots, first three of them are p-values for three different linear models using raw data. The other three plots are p-values for three different linear models using smoothed data.

kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk

llllllllllllllllllllllllllllllllllllllll

lllllllllllllllllllllllllll llllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllll lllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllll

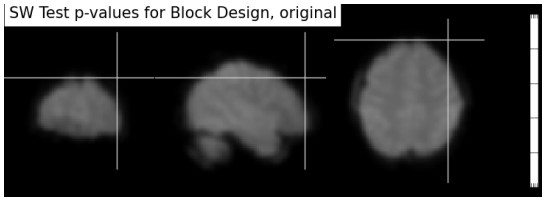
kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk

llllllllllllllllllllllllllllllllllllllll

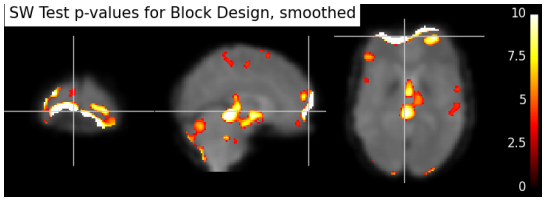
lllllllllllllllllllllllllll llllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllll lllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllll

kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk kkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkkk

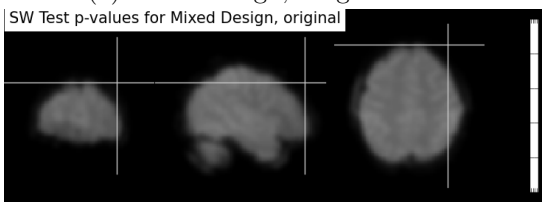
lllllllllllllllllllllllllllllllllllll
lllllllllllllllllllllll llllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllllll lllllllllllllllllllllllllllllllllllllllllllllllllllll



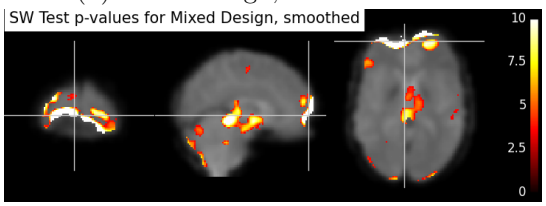
(a) Block Design, Original Data



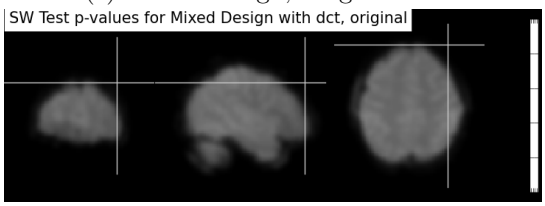
(b) Block Design, Smoothed Data



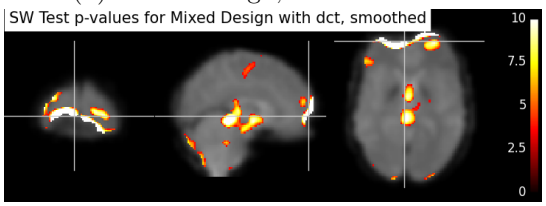
(c) Mixed Design, Original Data



(d) Mixed Design, Smoothed Data



(e) Mixed Design with DCT, Original Data



(f) Mixed Design with DCT, Smoothed Data

Figure 1: SW Test for Three Linear Models

The bright areas in the above plots means errors in that area don't follow normal distribution. We can see that data before smoothed seems to follow normal distribution well, while data after smoothed show some non-normality. This makes sense, since there should be significant points for anatomy.

References

[1] T. T. Kircher and R. Thienel, *Functional brain imaging of symptoms and cognition in schizophrenia*, Progress in brain research, 150 (2005), pp. 299–604.

[2] G. Repovs and D. M.Barch, *Brain network connectivity in individuals with schizophrenia and their siblings*, Biological Psychiatry, 69 (2011), pp. 967–973.

[3] ——, *Working memory related brain network connectivity in individuals with schizophrenia and their siblings*, Frontiers in Human Neuroscience, 6 (May 2012), pp. 1–15.