Working Memory Related Brain Network Connectivity in Individuals with Schizophrenia and Their Siblings

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Abstract

A recent study shows that schizophrenia reflects a "dysconnection" syndrome, which means schizophrenia can result in damaging functional brain connectivity in neural networks. We are interested in schizophrenia, so we decide to look into their studies to see if their conclusion makes sense. Therefore, we download the data they got during their tests and redo their analysis by following their steps in the paper. Even though we aren't able to go through all the analysis they did, we expect to get the same result for the analysis we do.

1 Introduction

Schizophrenia is a chronic, severe, and disabling brain disorder that has affected people throughout history. Or you can just think it as an illness that causes abnormal social behavior and failure to recognize what is real. Previous studies showed that changes in the function of a single brain region, or even a brain system, cannot explain the functional impairments seen in this illness. This means that the causes of schizophrenia is much more complicated than we think. A recent study shows that individuals with schizophrenia have reduced connectivity between neural networks, which could be a forward step to solve the cause of this illness.

The paper suggests this conclusion is "Working memory related brain network connectivity in individuals with schizophrenia and their siblings" [1], and the data they used is available on OpenFMRI.org under "Working memory in healthy and schizophrenic individuals". The paper thinks that neural networks which are critical for cognitive function might be affected by schizophrenia, because individuals with schizophrenia have severe cognitive issues. In particular, these neural networks are (1) Dorsal fronto-parietal network (FP), (2) Cingulo-opercular network (CO), (3) Cerebellar network (CER) and (4) "Default mode" network (DMN).

In total 102 participants in the paper's experiment and they were divided into 4 groups: (1) individuals with Schizophrenia (SCZ; N = 19); (2) the siblings of individuals with schizophrenia (SCZ-SIB; N = 28); (3) healthy controls (CON; N = 10); and (4) the siblings of healthy controls (CON-SIB; N = 17). In order to assessing functional brain connectivity, they used blood oxygen level dependent (BOLD) time series acquired using fMRI.

The paper's objective is finding connectivity within and between each ROI on different tasks. They extracted these ROIs and worked directly on them. Since we do not have the knowledge about partition the brain into ROIs, we could not do the same analysis as them. Therefore, we will simply focus on the entire brain and find the region related to these tasks. Also, they worked on all subjects and did comparisons between different groups. Since we don't have time to go through all of the subjects, we choose the first subject from SCZ group. If we have time, we will work on another subject from CON group and do a comparison between these two.

Our goal is to use the paper's data to do some statistical analysis, and see if our analysis could come up with the same conclusion as the paper. We understand the fact that we couldn't reproduce the whole analysis part of the paper due to the limitation of knowledge and time. However, with the analysis we designed for this data, we will finally get a great result.

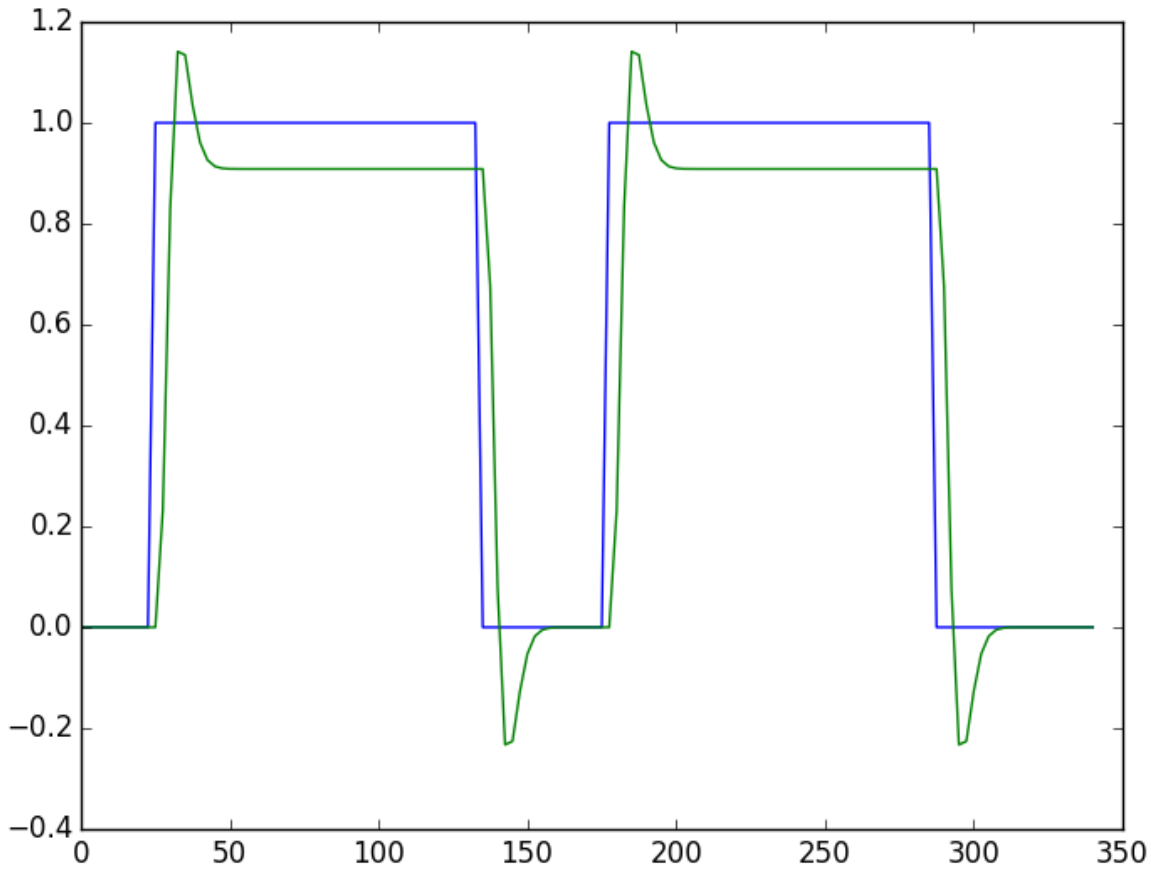
2 Data

We went to OpenFMRI.org and looked through all the files it has for this paper. The are many data files grouped by subjects and we only downloaded "ds115-sub001-005.tg", which contains the brain image of the first five subjects, and the "ds115-metadata.tg", which contains metadata for the paper. Since we only chose one subject, which is sub001, we only need his part in the data file.

First, we checked all the files for sub001 and found there are three tasks for our subject. We realized that these were "N - back" working memory task in the paper. This task was 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.

Second, we found that under each task there are four brain images. We thought one of them should be the raw image and the others were some-how processed by the authors. Therefore, we plotted these four brain images and chose the most blurred one (This is probably because it is after smoothing), which is "BOLD-mcf-brain.nii".

Then, similar to what we did in class, we used HRF function to convolve our neural prediction, This will give us a hemodynamic prediction, under the linear-time-invariant assumptions of the convolution. This is a very important step because we will use convolution data in our linear modeling process in the future. Here is the comparison between the original neural prediction and convolved.



3 Methods

3.1 Linear Modeling

First of all, we did a muti-variables linear regression on convolving response (design matrix X) and blood pressure(response Y). We constructed the design matrix X, which dimension is (133, 2) and reshaped our blood pressure data from 4 dimension to 2 dimension.

Second, under the assumption of constant variance and normality of our data, we use OLS method to calculate $\hat{\beta}$, the formula is $\hat{\beta_{ls}} = (X^T X)^{-1} X^T Y$. We plug in X and Y to get our $\hat{\beta_{ls}}$, which is a 2 by 147456 matrix. Then we reshaped it into 4 dimension. Based on the $\hat{\beta_{ls}}$ we got from muti-variables linear regression, we compute the fitted value $\hat{Y}$, which equals $X\hat{\beta_{ls}}$. The residual $\hat{e}$, which equals $Y - \hat{Y}$. The residual sum of squares RSS, which is $\hat{e}^T\hat{e}$. The covariance matrix of $\hat{\beta_{ls}}$ is $cov(\beta_{ls}) = \sigma^2(X^T X)^{-1}$. Here σ^2 is unknown, we use $\hat{\sigma}^2 = \frac{RSS}{n-r}$, which is an unbiased estimate of σ^2. Thus the covariance matrix $cov(\beta_{ls}) = \frac{RSS}{n-r}(X^T X)^{-1}$.

Then, we generated our null hypothesis test:$\hat{\beta} = 0$.

By using t-test and set our significance level as 10%, we found there are 1507 out of 147456 voxels that have the significant effect between our task and blood pressure, so we defined the sub-area of brain contains the most significant voxels by plotting a p-value map.

4 Results

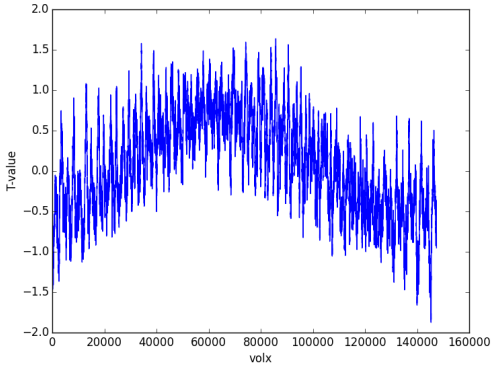


Figure 1: Plot of T values.

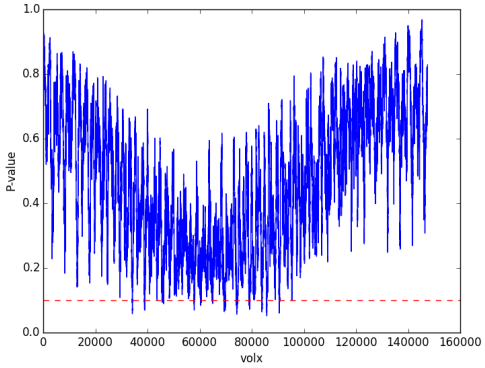


Figure 2: Plot of P values.

5 Discussion

References

[1] G. Repovs and D. M.Barch, *Working memory related brain network connectivity in individuals with schizophrenia and their siblings*, Frontiers in Human Neuroscience, 6 (May 2012).