Reproducing fMRI Data Analysis on Brain Connectivity

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

November 15, 2015

Abstract

In this research paper, we attempt to reproduce fMRI data analysis done by Repov and Barch in their paper exploring the relationship between schizophrenia and brain connectivity [1, 2]. In addition to the reproducing the ANOVA analysis of within and between brain network connectivity, we analyze the given fMRI data using linear modeling, time series as well as machine learning to explore various characteristics of voxel behaviors in response to N-back tasks.

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" [1, 2]. 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]. 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.

In their paper, the writers try to systematically examine changes in functional connectivity across rest and different task states in order to make an inference on characteristics of schizophrenia. The authors found 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 performing a designated N-back task. After analyzing the data using ANOVA, the authors found that that individuals with schizophrenia and their siblings showed consistent reductions in connectivity between both the FP and CO networks with the CER network.

In our attempt to reproduce the analysis done by Repovs and Barch, we first examine the validity of their use of ANOVA methods to assess functional connectivity. On top of that, we will make necessary simplifications and model the data using various analysis methods such as linear modeling, time series, as well as machine learning.

2 Data

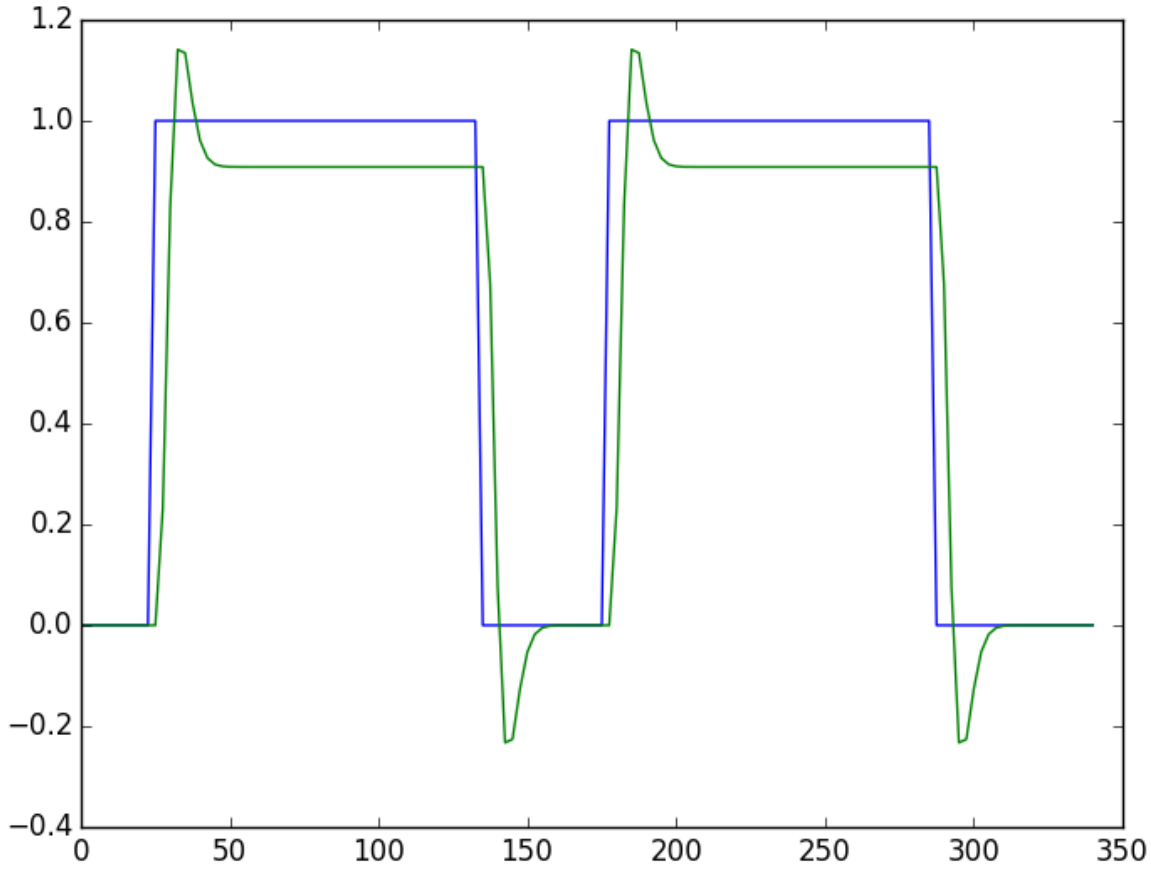
The data used in their published paper is available on the website OpenFMRI.org. The are many data files grouped by subjects, but we will be focusing on only a few subjects due to time and resource constraints. We start off analyzing a single subject, subject 001, who is male, Caucasian and Schizophrenic. If we have time, we will extend our analysis on comparing two subjects, one with schizophrenia and one healthy control. Each subject contains four folders, and for our analysis, we focus on the folder containing blood oxygen level dependent (BOLD) time series.

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 $cov(\beta_{ls}) = \sigma^2(X^TX)^{-1}$. 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 $cov(\beta_{ls}) = \frac{RSS}{n-r}(X^TX)^{-1}$.

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

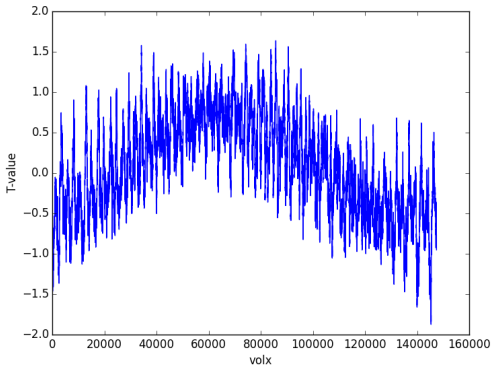


Figure 1: Plot of T values.

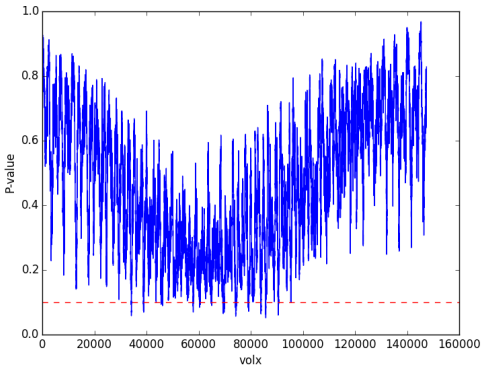


Figure 2: Plot of P values.

4.1 Data Preprocessing

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.

5 Discussion

5.1 Obstacles

The hardest part of the project is understanding which direction we should go given the time constraint and limited knowledge on the subject.

References

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

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