Using fMRI to Diagnose Schizophrenia

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Abstract

Diagnosis of schizophrenia is a challenging task for which diagnostic tests have yet to be developed [**?**]. Although Functional Magnetic Resonance Imaging (fMRI) methods have become more common in the diagnosis of mental disorders have become more popular, for schizophrenia diagnosis fMRI methods need to be more robust and reliable. Similar studies [**?**][**?**] have shown that fMRI can be used in conjunction with Sparse Gaussian Markov Random Field (SGMRF) to produce high accuracy in diagnosis of illness. However having a dataset with homogeneous distribution of illness makes this result less reliable and creates the need for more evidence using heterogeneous dataset in terms of illness. In this work we pursue two paths to tackle this problem. First, we evaluate performance of Sparse Gaussian Markov Random Field (SGMRF) on fMRI data brain scans, and second we study on Regions of Interest (ROI) as defined by Power *et al.* [**?**]. We used 5 fold cross validation for hyper parameter tuning and 20% holdout set for test. Accuracies that We have obtained the following accuracies using this method: for whole brain features and - for ROI features. While these result are slightly less than the results obtained by Rish *et al.*, they are on par with Rosa *et al.* results.

1 Introduction

Schizophrenia is a mental/psychiatric disorder [**?**, **?**] known affect blood flow in the brain [**?**] where those who are affected can experience hallucinations, delusions and diminished mental capacities to varying extents [**?**]. While several features of schizophrenia have proven useful for its diagnosis there are current no set of features that have sufficient sensitivity or specificity to be used in diagnostic tests [**?**]. This effectively means that subjectivity plays a role when a physician is diagnosing a patient.

Functional Magnetic Resonance Imaging (fMRI) is a tool for recording functional changes caused by neuron activity[]. When a person is doing a task, neuron activity fluctuates and in order to provide the energy needed for this activity, the blood flow increases to feed the neurons with the needed glucose, which is not stored in the brain[]. More blood flow also brings more oxygen through blood vessels. This change in the level of oxygenated blood known as oxyhemoglobin and deoxyhemoglobin (oxygenated or deoxygenated blood) changes the magnetic susceptibility of blood (BOLD signal) which is detectable through fMRI [].

fMRI is one of the most used and efficient tools in the study of psychiatric disorders such as Schizophrenia[]. An advantage of fMRI in medical diagnosis is that it is non-invasive. This means

that unlike some other imaging methods, no instruments or dyes are placed in the patients body body, this method operates without using them[].

One of the approaches that has been used for studying schizophrenia is Sparse Gaussian Markov Random Field(SGMRF) [**?**][**?**]. The primary advantage of using this method is that the functional network of the brain can be captured using the precision matrix [**?**]. By using the resulting network, healthy subjects can be differentiated from schizophrenic ones, by observing differences in the functional connectivity of the brain. Currently automated approaches to schizophrenia diagnosis have been able to yeild accuracies of 93% for data that originates from a single location [**?**] and up to approximately 80% for data that originates from multiple locations [**?**].

In this work we consider

The rest of the paper is organized as follows.

2 Background and Prior Work

2.1 Regions of Interest and Single-Voxel Analysis

Traditionally in fMRI analysis there are two main approaches for extracting information from the fMRI image. The first is a single-voxel approach and the second is to study regions of interest (ROI) [**?**]. The tradeoff between these two approaches is that a single-voxel approach requires the analysis of every voxel and is subject to the low signal to noise ratios of individual voxels, whereas a region based approach is only as effective as the regions are relevant to the fMRI task [**?**]. In 2011, Power *et al.* identified 264 putative function regions of interest derived from resting state fMRI, where no specific task being performed during data collection [**?**]. These regions contain substructures that agree that with known functional brain systems and therefore can be seen as fairly accurate representations [**?**].

2.1.1 Calculating Degrees

When analyzing fMRI data features such as voxel degrees can be extracted for use with a machine learner. Voxel degrees represent the connectedness of voxels in the brain with the other voxels and are described as "the number of voxel neighbours in a network" [**?**]. Degrees are calculated by performing multiple Pearson correlation comparisons between the i^{th} voxel and every other voxel. Once correlation values have be determined, a threshold is applied to the correlation matrix. This results in binary matrix where 1 represents a correlation value above the threshold and 0 represents a value below. Finally, for each voxel the number of 1 entries are summed (excluding the comparison against itself) and this becomes the degree of the voxel.

2.2 Multi-site Comparisons

Although, there were several prior work on the classification of schizophrenia patients using fMRI, most of them are based on data from a single site. However, in [**?**], a multi site data set was analyzed. Here, the data comes from five different sites with different machines. They analyzed the data set using SVM and obtained accuracies in the range of $73.53 - 80.92\%$. In this research we will try to obtain results with similar accuracies, but using probabilistic graphical methods.

2.3 Principal Component Analysis

2.4 Support Vector Machines

What is an SVM and how does it work

2.5 SGMRF

What is a SGMRF and how does it work

One variation of Markov Random Field is Gaussian Random which is mostly being used for continuous space of variables and has well-defined mathematic properties that can be computed. Multi-

variate Gaussian density function over set of random variables X is defined as below:

$$p(X) = (2\pi)^{-n/2}|\Sigma|^{-1/2}\exp\left\{-\frac{1}{2}(X-\mu)^t\Sigma^{-1}(X-\mu)\right\}. \quad (1)$$

Where μ is mean and Σ is the covariance matrix. We can set the μ to zero and replace Σ^{-1} with C the equation (1) can be written as the following form.

$$p(X) = (2\pi)^{-n/2}|C|^{1/2}\exp\left\{-\frac{1}{2}(X-\mu)^t\Sigma^{-1}(X-\mu)\right\}. \quad (2)$$

3 Methodology

3.1 Data Set

Data used for this study were downloaded from the Function BIRN Data Repository (http://fbirnbdr.birncommunity.org:8080/BDR/). The original data contained nine sites and 235 subjects. However, during the preprocessing steps some of the subjects were removed and we had 95 subjects and five sites. Data were preprocessed by Dr. Mina Gheiratmand by using FSL software (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). Our data contained 46 schizophrenic subjects and 49 healthy subjects. Each subject had four runs so effectively our data set had 380 subjects. Each run had 137 time slices and each time slice had the signal amplitude of over $100,000$ voxels. The voxels were referred using the 3D coordinates and thus the dimensionality of a single run was $\mathcal{R}^{N_1\times N_2\times N_3\times 137}$.

We removed 80% of subjects from each site as our holdout set and used the remaining set as our training set. Furthermore, we made sure that the holdout set is also balanced, so that the ratio between the patients and healthy subjects is same in the holdout and training sets for each site. Also we made sure that all the runs from the same subject either belonged to the holdout set or to the training set. The training set is used for finding the hyper parameters of the systems using five-hold cross validations. After finding the hyper parameters we used the full training set to train the system with the selected hyper parameter and obtained the accuracy on the hold out set. Furthermore, we repeated this procedure five times for different hold out sets to get an average accuracy.

3.2 Your Approach? Mario

First, we ran the approach proposed by Rish *et al.* [**?**] on our data set. Here, we obtained the log degrees of each voxel for each subject. Thus we had a matrix of size 380×28720. However, using all the available voxels resulted in computation difficulties and thus selecting the best voxels to separate the healthy and schizophrenic subjects is very important.

To select the best voxels out of the possible 28720 voxels, we experimented multiple approaches. These include

1. Selecting the voxels based on the t-test.
2. Selecting the voxels based on the absolute differences between the mean degrees of a voxel between schizophrenic and healthy subjects.
3. Selecting the voxels based on the differences between the mean degrees of a voxel between schizophrenic and healthy subjects.
4. Selecting the voxels based on the differences between the mean degrees of a voxel between healthy and schizophrenic subjects.

Out of the above four approaches we obtained the highest accuracy on our cross validation set by the third approach. Also the number of voxels to select k was decided by running the same approach for different k values. And we found the optimum k value as 20 for our cross validation set. By using the selected voxels we obtained the precision matrices for schizophrenic and healthy subjects. Similar to the value of k, the sparsity coefficient λ was also obtained through a hyper parameter serach on our cross validation set.

3.3 Methods using Power *et al.*'s ROIs

3.3.1 ROI with Patient Concatenation

3.3.2 ROI with Fouier Coefficients

3.3.3 Region Degrees and SVMs

3.3.4 Individual MRF Structure Classification

3.4 Your Approach? Farhad

Describe your experiments

4 Results

4.1 Your Approach? Mario

With the Rish et al. code we obtained a 69% cross validation accuracy on our cross validation sets and 75% accuracy on the hold-out set.

4.2 Methods using Power *et al.*'s ROIs

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4.2.4 Individual MRF Structure Classification

4.3 Your Approach? Farhad

Report your results

5 Conclusions

6 Acknowledgements

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