A Comparative Analysis of Functional Connectivity Data in Resting and Task-Related Conditions of the Brain for Disease Signature of OCD

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Abstract— **Obsessive Compulsive Disorder (OCD) is a frequent, chronic disorder producing intrusive thoughts which results in repetitive behaviors. It is thought that this psychological disorder occurs due to abnormal functional connectivity in certain regions of the brain called Default Mode Network (DMN) mainly. Recently, functional MRI (FMRI) studies were performed in order to compare the differences in brain activity between patients with OCD and healthy individuals through different conditions of the brain. Our previous study on extraction of disease signature for OCD that is determining the features for discrimination of OCD patients from healthy individuals based on their resting-sate functional connectivity (rs-FC) data had given encouraging results. In the present study, functional data extracted from FMRI images of subjects under imagination task (maintaining an image in mind, im-FC) is considered. The aim of this study is to compare classification results achieved from both resting and task-related (imagination) conditions. This research has shown quite interesting and promising results using the same classification (SVM) method.**

I. INTRODUCTION

Obsessive Compulsive Disorder is a mental disease which is characterized by obsessions triggered by compulsions [1, 2]. Recent studies [3] hypothesized that brain activity pattern during resting-state or cognitive task-related conditions differ between OCD and healthy cases. Additionally, it speculated that obsessive thoughts might affect function of the right posterior parietal region of the brain. MRI or other conventional imaging tools can not differentiate many psychiatric disease such as OCD accurately in early stage of the disease because only structural abnormalities of the brain can be distinguished by these methods [4].

This study is focused on investigation of brain activity under resting state and cognitive control task called imagination for detection of patients with OCD. For this purpose, pattern recognition approaches are applied on FC data collected from regions of brain that may have difference between OCD and healthy cases under different brain conditions.

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In our previous study two main approaches are followed for this purpose. As a first method, similarity values of rs-FC test data to the mean of the healthy and OCD groups were computed separately and then these two values were classified using SVM classifier. In the second approach, feature extraction methods based on dimension reduction as Linear Discriminant Analysis (LDA), Principal Component Analysis (PCA) and Kernel PCA (KPCA) were implemented on subsampled rs-FC data and the same classifier were used for classification. The SVM method defines a hyper surface, a separating boundary, to discriminate two cases [5, 6]. In previous study [3], it was shown that OCD patients can be discriminated from healthy group with 69% accuracy by applying similarity measure methods for feature extraction and SVM classifier on resting-state FC (rs-FC) data [7].

In this study the same mentioned procedure will be applied on FC data between regions of interest (ROIs) and all voxels of the brain, but this time the brain is under a cognitive control task called imagination. The results obtained by imagination state FC (im-FC) will be compared with those obtained by rs-FC previously This research is important since it can show whether FC analysis during cognitive control state of the brain is able to improve the discrimination power compared to previous study or not.

II. MATERIAL

A. Data Acquisition

High-resolution T1-weighted functional scans obtained by a 1.5 Tesla MRI system at Integra Imaging Center, Ankara, Turkey [3] was used to collect the data. Besides resting state, four different tasks which are free imagination, suppression, erasing and imagination were performed by participants while FMRI were being collected.

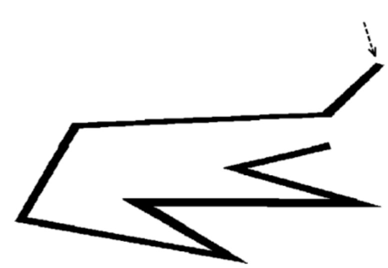

Figure1. The figure shown to the participants [3]

In this study we focused on imagination cognitive control task which is an active maintenance task that belongs to working memory.

The following instructions were given to the participants for this task: imagine continuously the shape, shown in Fig 1, until another command is given [8].

B. Participants

Totally, 24 right-handed volunteers with minimum age of 18 years attended to this research project. 12 (6 male and 6 female) out of total 24 attendants had OCD for 6 months to 7 years and the remaining 12 participants (6 male and 6 female) were healthy volunteers, similar in terms of sex and education level (control group). 3 of OCD subjects had checking obsession, 8 of them had cleaning obsession, and one was with damaging obsession. No psychiatric disorder was recognized in patients other than OCD. Neither neural system nor psychiatric disorder was detected in control group attendant [4, 9].

C. Preprocessing For Image Enhancement and Registration

Statistical Parametric Mapping (SPM) software which is a toolbox of Matlab was used to preprocess FMRI data. In this study 5 main preprocesses including Realignment, Slice Timing, Co-registration, Normalization and Smoothing were applied on data for head motion correction, spatially normalizing images with respect to a reference template and removing the noise [9].

D. ROI Selection

Recent researches on FMRI data [3] and functional connectivity analysis [9] of patients with OCD during different brain states have demonstrated that OCD influence remote regions of brain called default mode network (DMN) like left and right posterior lobes (LIPL, RIPL) and post cingulate corpus (PCC) [4, 9]. We considered LIPL, RIPL and PCC regions as regions of interest (ROIs) in this study.

E. Functional Connectivity Analysis

CONN software, a functional connectivity estimation toolbox, was implemented so as to examine FMRI data for FC analysis [10]. CONN applies Pearson's correlation coefficient method to calculate the correlation coefficients between ROIs and other voxels of the brain. At the end of the FC analysis, the correlation coefficient map under imagination condition (im-FC) for each ROI were constructed for each subject. The resting state FC (rs-FC) data for the same subjects and ROI's were constructed previously.

As it will be explained in detail in following sections, discriminating features needed for classification of OCD and healthy cases were extracted from these FC images (3D maps having 91×109×91 voxels).

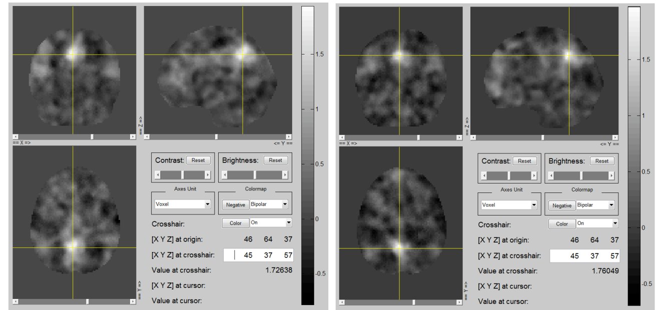

Figure2. Resting-state FC between PCC ROI and all brain voxels (a) for a healthy subject and (b) for a patient subject.

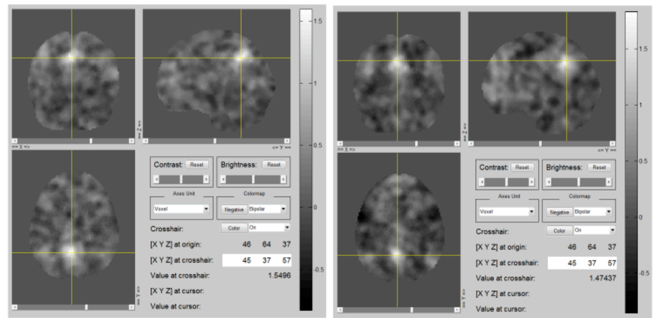

Figure3. Task-related (imagination) state FC between PCC ROI and all brain voxels (a) for a healthy subject and (b) for a patient subject.

Fig 2 shows functional connectivity map between PCC ROI and all voxels of the brain while brain is in resting-state whereas Fig 3 shows the FC image of the same ROI, while the mind is maintaining the image demonstrated in Fig 1.

III. Methods

A. Feature Extraction

It is noteworthy that the same feature extraction methods with the same parameters were applied to FC data of both resting and imagining conditions in order to be able to compare the classification results obtained from both conditions.

1) Dimensionality Reduction methods:

Here, principal component analysis (PCA), kernel PCA and linear discriminant analysis (LDA) methods were used for dimensionality reduction.

a) Principal Component Analysis

Using this method, FC data that consists of set of $\{\mathbf{x_1},\ldots,\mathbf{x_n}\}$ samples is projected from d-dimensional subspace into lower-dimension subspace determined by the principal components, which are the eigenvectors of the covariance matrix **C:**

$$\mathbf{C} = \sum_{k=1}^{n} (\mathbf{x_k} - m)(\mathbf{x_k} - m)^t \qquad (1)$$

Here m is the mean vector of the samples in the training set [11, 12]. Principal components (PCs) consist of $\boldsymbol{M}$ largest eigenvectors of the covariance matrix $\boldsymbol{C}$ corresponding to the largest eigenvalues. The dimensionality of each sample vector of d-dimensional functional connectivity data, $\mathbf{x} \in \mathbf{R}^d$ is reduced to M-dimensional vector, $\mathbf{x_r} \in \mathbf{R}^M$ using:

$$\mathbf{x_r} = \mathbf{A}\mathbf{x} \tag{2}$$

b) Kernel PCA

Using nonlinear transformation, each d-dimensional sample vector $\mathbf{x}_k$ is projected into an M-dimensional feature space $\varphi(\mathbf{x}_k)$ such that $\varphi : \mathbf{R}^d \rightarrow f^M$. The kernel function is expressed as:

$$k(\mathbf{x_i}, \mathbf{x_j}) = \varphi(\mathbf{x_i})^T \varphi(\mathbf{x_j}) \tag{3}$$

c) Linear Discriminant Analysis

The main goal of this approach is to find an optimal projection direction, vector **w**, for optimal discrimination of the OCD and healthy samples [12] such that:

$$J(\mathbf{w}) = \frac{\mathbf{w^t s_B w}}{\mathbf{w^t s_w w}} \tag{4}$$

$$S_1 = \sum_{x \in c_1} (\mathbf{x} - m_1)(\mathbf{x} - m_1)^t \tag{5}$$

$$S_2 = \sum_{x \in c_2} (\mathbf{x} - m_2)(\mathbf{x} - m_2)^t \tag{6}$$

Where $\mathbf{s_B}$=S_1+S_2 is the between-class scatter matrix while $\mathbf{s_W}$=$(m_1$-$m_2)(m_1$-$m_2)^t$ is within-class scatter matrix [12]. Afterwards, the dimension of d-dimensional sample vectors of the data are reduced by projecting samples through **w** direction, which are called discriminant variables, so that the cost function $J(\mathbf{w})$ given become maximum.

2) Similarity Measure

The feature vectors based on similarity measures are produced by computing the similarity of the FC data of the individual subjects to the mean of the remaining FC data of OCD and healthy individuals, therefore having only 2 components.

a) Dot (inner) product similarity measure

This feature extraction method finds the square of Euclidean distance between two vectors **x** and **y** and it is defined as [13]:

$$dot(\mathbf{x}, \mathbf{y}) = \mathbf{x}.\mathbf{y} = \sum_{i=1}^{d} x_i y_i \tag{7}$$

b) Cosine similarity measure

The cosine similarity gives the cosine of the angle between **x** and **y** vectors which is computed as [14]:

$$\cos(\mathbf{x}, \mathbf{y}) = \frac{\mathbf{x}.\mathbf{y}}{\|\mathbf{x}\| \|\mathbf{y}\|} \tag{8}$$

c) Correlation similarity measure

The only difference between inner and correlation similarity measure is that the mean of the sample vector is subtracted from itself. The mean of $\mathbf{x}, \mathbf{y} \in \mathbf{R}^d$ vector components and the correlation similarity between them is computed as follows [13]:

$$\bar{x} = \frac{1}{d} \sum_{i=1}^{d} x_i , \quad \bar{y} = \frac{1}{d} \sum_{i=1}^{d} y_i \tag{9}$$

$$corr(\mathbf{x}, \mathbf{y}) = \sum_{i=1}^{d} (x_i - \bar{x})(y_i - \bar{y}) \tag{10}$$

B. Data Classification using SVM Classifier

Let $\{\mathbf{x}_1,..,\mathbf{x}_n\}$ be a training data set of n sample vectors of each d-dimension correspond to classes $\{c_1,...,c_n\}$ where $c_k \in \{+1, -1\}$, k=1, 2, .. n. A linear model of a 2-class classification problem is defined as [11]:

$$y(\mathbf{x}) = \mathbf{w}^T \varphi(\mathbf{x}) + b \tag{11}$$

Where $\varphi(\mathbf{x})$ is a fixed transformation vector, $\mathbf{x}$ denotes the input vector, **w** is the vector showing the direction of the separating hyperplane and b is a scalar parameter. The sign of $y(\mathbf{x})$ determines to which class the test data is belonging.

$$C_k = \begin{cases} +1 & if \quad y(\mathbf{x_k}) > 0 \\ -1 & if \quad y(\mathbf{x_k}) < 0 \end{cases} \qquad k = 1,...,n \tag{12}$$

IV. Results

The results obtained by the method explained in this study for resting and imagination conditions are summarized in Table I, which shows the mean of classification performance of 12 healthy subjects and 12 patient subjects using double leave-one-out cross-validation as explained in [3].

In obtaining these results, SVM classifier was applied on the feature vectors obtained by similarity measure (cosine, dot and correlation similarities) and dimensionality reduction (PCA, KPCA and LDA) methods on FC data in both resting and imagination states.

It is noteworthy that all feature extraction and classification parameters are the same for all brain regions and brain conditions.

TABLE I. CLASSIFICATION ACCURACY RESULTS OF SVM IN RESTING AND IMAGINATION CONDITIONS

Feature		**Brain Condition**					
		Resting State			**Imagination**		
		ROI Type			**ROI Type**		
		PCC	*LIPL*	*RIPL*	*PCC*	*LIPL*	*RIPL*
Similarity measures	Cosine	55.5	68.5	64.0	**74.0**	39.0	43.0
	Dot	66.5	65.0	68.0	56.0	35.0	40.0
	Correlation	57.0	**69.0**	64.5	57.0	28.0	41.0
Dimension reduction	PCA	55.5	44.5	62.5	28.0	47.5	61.0
	Kernel PCA	56.5	41.5	55.0	29.0	45.0	55.0
	LDA	56.0	42.0	66.5	29.0	67.0	57.0

The results related to resting state of the brain shown in Table I were obtained in previous study [3]. It can be seen from Table I that the best classification accuracy result of SVM for resting condition obtained as 69% on LIPL ROI when correlation similarity was used as feature vector.

SVM classification results under imagination condition which is considered in present study are also given in Table I. The same feature extraction and classification methods with same parameters were used to compare classification accuracy results for both resting and imagination conditions. SVM classification results of imagination condition show that using cosine similarity as feature vector gives the best SVM classification result as 74% in PCC ROI.

According to Table I, SVM classification results obtained using dimension reduction methods during resting condition had better performance than imagination condition in PCC ROI however classification results in left and right IPL were slightly the same in both brain conditions.

V. CONCLUSION

Comparing classification accuracy results of SVM under resting and imagination conditions shown in Table I, represents high discriminative power of features obtained by similarity measures for both resting and imagination conditions in contrast with features obtained by dimension reduction methods instead they are more complicated and time consuming. So,the similarity measure feature extraction is the most appropriate method for detection of OCD in both brain conditions.

This study recommended that functional connectivity differences in IPL and PCC ROIs of OCD brain were appropriate brain regions to detect this disease in a way that supports the hypothesis by Koçak et al. [3, 9] based on existence of functional abnormalities in right fronto-parietal brain regions especially PCC and IPL of patients with OCD under resting or task-related conditions.

We are expecting better performance when more appropriate feature extraction methods, e.g. independent Component Analysis (ICA), and classifiers, e.g. Gaussian Mixture Model (GMM) or deep learning, are used. Also we are planning to classify OCD according to type of disease (checker, cleaner or harming obsessions).

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