# Features of the resting-state functional network in patients with major depressive disorder: mutual information analysis in fMRI data

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***Abstract*—In this work, we conducted the analysis of the functional magnetic resonance imaging data in healthy subjects and patients with major depressive disorder that were obtained during experimental research when subjects were resting. The signals that have undergone preprocessing and filtration were used to find the functional connectivity between the brain regions. Results demonstrate significant changes between functional connections based on the mutual information measure. We obtained five significantly changed connections, four of which increased more in cotrol group over patients.**

***Index Terms*—fMRI; functional connectivity; mutual information; brain networks; connectivity; major depressive disorder; depressive episode;**

## I. Introduction

The use of functional magnetic resonance imaging (fMRI) technology and near-infrared spectroscopy (fNIRS) is a contemporary and noninvasive approach to studying the brain in its natural environment [1]–[6]. The detection of blood oxygen levels within active areas of the brain aids in our comprehension of the particularities of their structural integrity under normal and pathological conditions, as well as during various activities (as opposed to rest state).

In the relevant body of literature, it has been established that the rise in regional blood flow within the brain (BOLD effect) can function as a marker for the activity of neurons. Functional magnetic resonance imaging is typically regarded as a suitable instrument for the identification of sites of brain activity. Furthermore, fMRI is commonly considered to be an optimal method for generating spatial maps of activated neural clusters [8], [9]. Within the last few years, the utilization of the fMRI technique has expanded to analyzing the functional connectivity between various regions of the brain, during the execution of specific tasks. However, insufficient focus has been given to a thorough examination of the functional networks beyond the scope of the region of interest paradigm, even though the analysis of these networks has been demonstrated to be beneficial [10]–[17].

The study of MDD is an important and urgent problem due to the prevalence of this disorder. A promising approach for studying this disorder is to analyze the features of functional connectivity in patients using fMRI data. It should also be noted that a linear connectivity measure (Pearson correlation) is often used to reconstruct functional connectivity, but it is important to analyze nonlinear relationships due to the nonlinearity of the data. We apply this approach in our current work using mutual information, which allows us to take into account both linear and nonlinear interactions.

The objective of this study was to examine the variations in functional connectivity throughout the brain between healthy individuals and patients diagnosed with MDD, by means of the mutual information calculation.

## II. Design of the experiment

The experimental data was obtained from 97 healthy volunteers and 72 patients with major depressive disorder. In order to take part in the study, the following criteria were required to be met: aged between 18 and 65 years; the absence of metal implants and similar; no presence of other psychiatric conditions (addictions, anxiety and similar); and no occurrence of severe neurological pathologies or a concussions.

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Patientsṕsychiatric histories were also taken into consideration for purposes of determining the inclusion criteria. Every subject provided written informed consent in accordance with the Declaration of Helsinki. (Ethics Comittee approval P-369 of 29.05.2015).

3 Tesla magnetic resonance imaging system (GE Discovery 750) was used for the magnetic resonance imaging procedure. The process involved using a structural scan of big resolution as part of the imaging protocol. The thickness of a slice was 1 millimeter, matrix 256 squared, time of relaxation 7.2 milliseconds, Time of reflection 2.3, angle of flip 12 degrees, and resting-state volume — two dimentional stack with width about 3 millimeters, matrix 64 squared, repeat time 2 thousand milliseconds, reflection time 30 milliseconds, number of images 36, straight angle, a total of 192 volumes. Before the procedure commences, the subjects are given the instruction to remain in a state of tranquility. They were instructed to keep their eyes closed, as well to avoid engaging in any particular thoughts or thought processes.

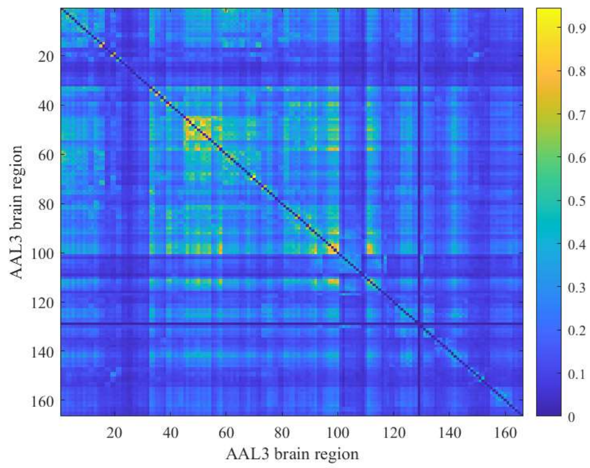


Fig. 1. Averaged mutual information matrix for brain areas

## III. Methods

The analysis of the fMRI data was carried out using the Statistical Parametric Mapping; version 12) employed on MATLAB software for Windows. T1 were preprocessed including, segmenting and and normalization. The images were realigned, excluding effects of movement, aligned with the initial high-quality image, estimated to match the Montreal Neurological Institute volume space, and cleaned down with an 8 millimeter Gauss distribution kernel. We matched Montreal Neurological Institute voxels to the Anatomical Atlas Labels 3 [21] regions of the volumed aligned each subject quality image slice. We proceeded to calculate the average activity levels across the regions for each of the subjects. After that, we used mutual information approach to calculate the connectivity between the brain regions on each averaged region activities. Mean mutual information matrix can be easily seen in the Fig. 1 [24].

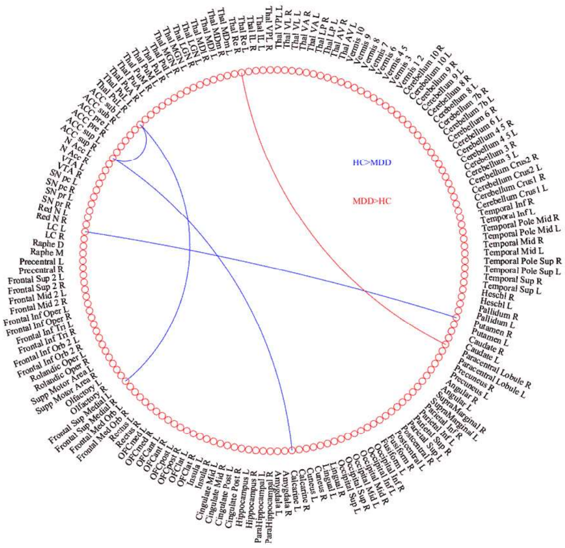


Fig. 2. Significant connection changes between the healthy control group (HC) and patients with MDD

## IV. Results

In our work we were looking for the difference between HC and MDD groups. To assess the presence of significant variations among the obtained mutual information connectivity 2D structures, the FDR method with a significance p=0.025 together with 100 thousands permutations were employed [22], [23]. In the obtained results, only connections of significance were considered and displayed in the following graphical connectogram (Fig. 2).

Easy to see that three out of five significantly changed connections include thalamic regions. Change in the thalamic connections was reported in the recent research [25], [26]. However results showed that stronger thalamic connections in comparison to the baseline were found in both patients and control group while almost all other interconnections got weaker [26]. These findings hint that whole brain resting-state interconnectivity could be useful but relatively not good biomarker [25].

Decreased activity between the Anterior cingulate cortex and Calcarine has also being reported, providing further evidence of disruptions in impulsivity and decision making underlying suicidal behavior [27].

## V. Conclusion

Thus, we performed functional analysis of fMRI data in healthy subjects and patients with major depressive disorder that were obtained during experiment, based on the false discovery rate method on the mutual information matrices. We discovered that the most significant changes in functional network connectivity in the direction HC>MDD include connections: Thalamus PuL R — Frontal Superior Medial R, Thalamus PuL R — Anterior cingulate cortex Superior Medial R, Anterior cingulate cortex Superior Medial R — Calcarine L. However only one significant connection was found for the opposite direction MDD>HC: Thalamus Re R — Parecentral Lobule R.

There are also great prospects for applying proposed method based on the evaluation of mutual information-based network metrics to the diagnosis of other neural diseases, including autism and Alzheimer's disease [28]–[30].

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