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ORIGINAL ARTICLE

Functional near Infrared Spectroscopy for Functional Connectivity during Stroop test via Mutual Information

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ABSTRACT
Functional near-infrared spectroscopy (fNIRS) is an optical imaging technique, which is non-invasive monitoring of human brain function by measuring the changes in the concentration of oxyhemoglobin and deoxyhemoglobin. In this study, we present a method to investigate the functional connectivity of prefrontal cortex (PFC) by applying Mutual Information via modified version of the color-word matching Stroop test. This test consists of three different stimulus conditions: Neutral (N), Congruent (C) and Incongruent (IC). A continuous wave 16 channels near-infrared spectroscopy device was used to measure the changes in HbO2 concentrations from 10 healthy volunteers and 15 Schizophrenia patients. Mutual Information (MI) values were computed for each stimulus condition in both of groups. Our analysis shows that the connectivity patterns in PFC are different from healthy to schizophrenia person and this is related with the cognitive load.
Keywords: fNIRS, Functional Connectivity, Mutual Information, Stroop test

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INTRODUCTION

Functional connectivity can be achieved through several means; several algorithms were measured with functional MRI [1]. Among these tools, our algorithm by means of fNIRS is a noninvasive, unobtrusiveness during cognitive tasks, rapidness and ease of choice. Near Infrared light from approximately 700-900 nm allows for penetration deep into tissues. Despite a lower resolution due to diffusive behavior of light propagation in tissue [2-6], this tool has been used in cognitive tasks [7-8], because of comfort, and cost-effectiveness.

Following the success of functional connectivity studies using fMRI, similar researches using fNIRS have emerged recently [9]. Many studies have investigated the relationship of brain in resting state [10-12]. In this study, we aimed to investigate the functional connectivity in the prefrontal cortex (PFC) during a modified version of the color-word matching Stroop task. This task is often used to overcome the conflict at PFC activity [13-17]. A continuous wave 16 channels near-infrared spectroscopy device was used to measure the changes in oxyhemoglobin (HbO2) concentrations from 10 healthy volunteers and 15 Schizophrenia.

Among several algorithms, we decided to investigate connectivity metric using Mutual Information (MI). The MI between two time-courses is a measure of general dependence and will detect both linear and non-linear dependencies [18]. An important contribution of our research using wavelet transform based on eliminating non-neuronal sources of noise, including cardio respiratory effects in fNIRS has been quite successful [19]. Increasing attention has been observed in patients with schizophrenia. The study of functional connectivity may contribute to a better understanding of mental illness helps to understand the mechanisms of disease. The brain is a dynamic system in which communication between regions and change is continuous [20]. The connectivity patterns obtained from healthy subjects are compared against the patterns of schizophrenia patients. This disease is dissociative disorder, meaning a lack of connectivity in brain.

MATERIALS AND METHODS

Subjects and Protocol

The data used has been collected from 10 volunteers and 15 Schizophrenia patients at Neuro-Optical Imaging Laboratory, Bogazici University Istanbul, Turkey. No psychiatric or neurological disorders were recorded in the medical history of the control subjects. Turkish versions of Zysset et al have been performed and subjects accomplished color–word matching Stroop task [14, 21]. Two words have been presented for the subjects; one of the words has been written above the other; top word written in ink color and the one in bottom in white. Subjects judged whether the word written below correctly denotes the color of the upper word or not. Subjects pressed on the left mouse button with their forefinger if color and word matched and on the right button of the mouse with their middle finger if not. The words were on the screen until the answer was given with a maximum time of 3 s. (In the time between the trials, the screen was blank. The experiment included neutral, congruent and incongruent trials. Upper word consisted of four X's (XXXX) in ink color was used in neutral condition as well as ink color of the upper word and the word itself were the same in congruent whereas in the incongruent condition; different patterns in each condition. The trials were performed in a semi blocked manner. Figure1 [17] demonstrates more details. Each block includes six trials. Inter stimulus interval within the block was 4.5 s and the blocks were placed 20 s apart in time. The trial type was homogeneous within a block (but the arrangements of false and correct trials were altering.) There were five blocks of each type. Tests were performed in a silent, lightly dimmed room. Words were shown on an LCD screen that was located 0.5 m away from subjects. Ethics Review Board of Bogazici University approved the task protocol [4, 17].

Data Acquisition

Near infrared light at two wavelengths (730 and 850 nm) can be transmitted from fNIRS device. They can penetrate through the scalp and probe the cerebral cortex. Concentration changes of oxyhemoglobin and deoxyhemoglobin in blood has been calculated based on Beer–Lambert law. The device can sample 16 different channels in the brain simultaneously by means of four LEDs and ten detectors (See Figure 2 [17] for the details of the probe).A flexible printed circuit board that was specially designed to fit the curvature of the forehead, and LEDs and detectors were placed in it.

Wavelet Transform Based Preprocessing

The signal is decomposed into wavelet coefficients by the discrete wavelet transform which may represent the signal in various frequency bands. One thing that is very important for the quality of the analysis of fNIRS signals so the decomposition was done using Daubechies (Db) wavelets is the choice of wavelet function [19].

To concentrate on the functional association between brain regions subtended by activity in a defined frequency interval, the wavelet domain is beneficial. Neuronal activity related signals in fNIRS data are demonstrated to occupy the frequency range of 0.003-0.110Hz [2, 15]. The approximation at level 3 (CA3) must be selected according to the frequency band of interest (0.003-0.110Hz), so that the input signals were decomposed. Db5 is the best mother wavelet for this purpose [22]. The coefficients were nulled at very low and higher frequency values and then the filtered fNIRS signal was reconstructed for each detector.

MUTUAL INFORMATION

Information theory of Shannon is a method for measuring the information in a random variable based on entropy. The other method like correlation coefficient analysis linear relationship between coefficients but information theory's methods consider nonlinear relationship of the random variables. Equation 1 defined mutual information between 2 variables.

$$MI(X,Y)=\sum_{x,y}P(x,y)\log\left(\frac{P(x,y)}{P(x)P(y)}\right) \quad (1)$$

P(x, y) is the joint probability distribution function of random variables. Mutual information measures the information that x and y share, it means how much knowing one of these variables reduce uncertainly about the other. When x and y are independent, knowing about X variable doesn't give any information about y and vice versa, therefore mutual information is zero. If X is a function of Y then MI(X, Y) is a function of X, and if Y is a function of X then MI(X, Y) is a function of Y. The result of MI(X, Y) always is nonnegative. Also, MI is a symmetric criteria (MI(X, Y) =MI(Y, X)). If mutual information between 2 variables is high, it indicates high dependence among them [23].

Functional Connectivity
Stroop task consists of three different stimulus conditions: Neutral (N), Congruent (C) and Incongruent (IC). The measured data are separated according to each stimulus type and sorted with respect to the time because connectivity patterns obtained from hemodynamic response to each stimulus is expected to be different because of the contribution of partially different neural networks. We propose a normalized MI measure for assessing connectivity and a new measure which provides increased delectability to linear dependencies while still capturing non-linear dependencies.

RESULTS
ANOVA was used to test the statistical significance between groups since the group variances were different. The statistically significant level of difference was considered to be at $p < 0.05$. We report in Table 1 the major MI change in a pair of channel that reside on two hemispheres: 8th and 14th with $F(2, 24) = 3.41$, $p=0.049$. Table 1 is shown the significant differences of ANOVA for healthy subjects. Although very small in value, the significant MI change observed in bilateral PFC regions is a marker of Stroop effect while the rest of the channel pairs have MI values in the range 0.287 ± 0.023 for N condition, 0.240 ± 0.016 for C condition and 0.523 ± 0.031 for IC condition. The matrix of connectivity in HbO2 signal for schizophrenia is shown in Figure 3.
Table 2 is shown the significant differences of ANOVA ($p<0.05$) for schizophrenia. In HbO2 signals, we found the major MI change in some pairs of channels that reside on side hemispheres of the PFC: 3th and 7th with $F(2, 42) = 3.29$, $p=0.047$. The matrix of connectivity in HbO2 signal for healthy subjects is shown in Figure 4.

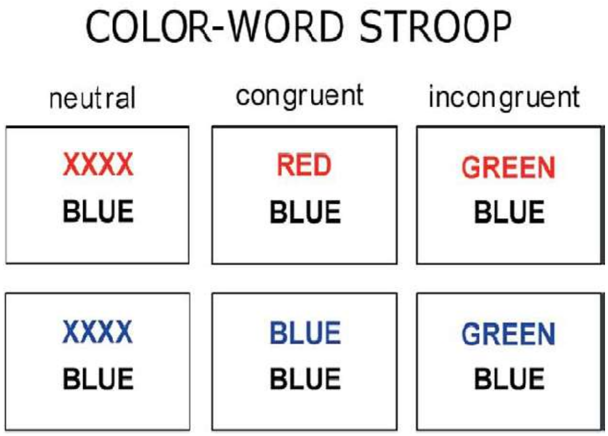

Figure 1. Stroop task protocol [17]

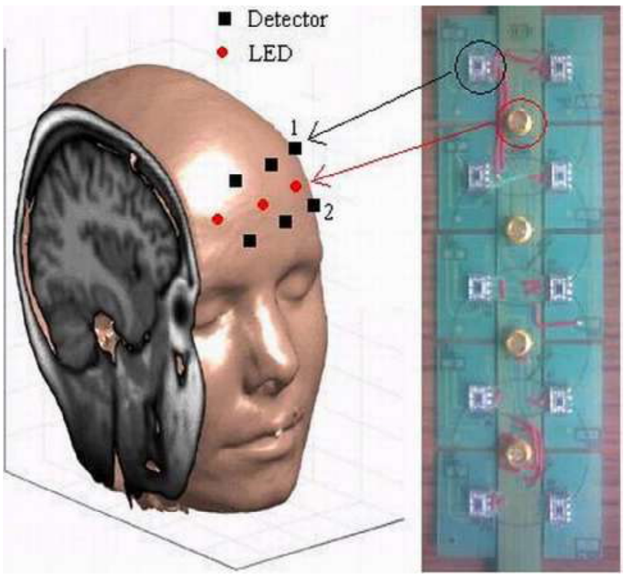

Figure 2. Details of the fNIRS probe and its approximate placement on the forehead [17]

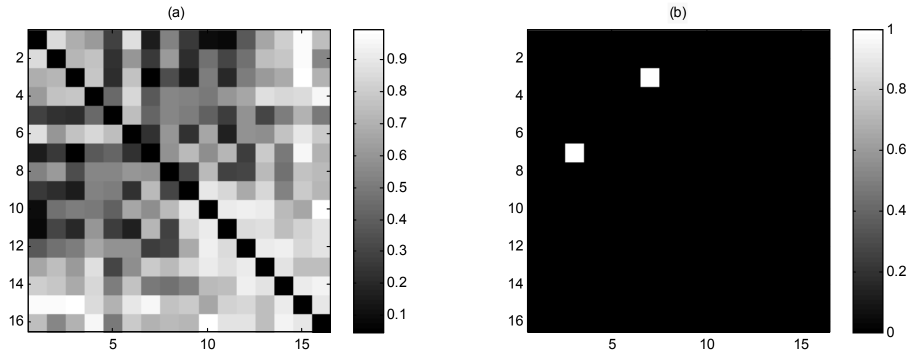

Figure 3. (a) Mutual Information matrix of HbO2 signal for Schizophrenia, (b) functional connectivity map of HbO2 signal via ANOVA results (p<0.05) (Einalou et al)

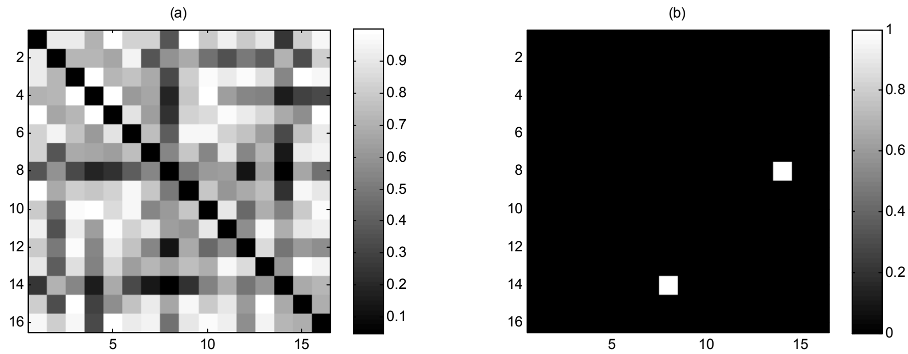

Figure 4. (a) Mutual Information matrix of HbO2 signal for Healthy, (b) functional connectivity map of HbO2 signal via ANOVA results (p<0.05)

Table 1. Statistical properties of mutual information in HbO2 (Healthy)

Stimulus Type	**Channels: 8th and 14th**
	Mean ± Std
Neutral	0.287 ± 0.0232
Congruent	0.240 ± 0.0164
Incongruent	0.523 ± 0.0316
P-Value	0.049

Table 2. Statistical properties of mutual information in HbO2 (Schizophrenia)

Stimulus Type	**Channels: 3th and 7th**
	Mean ± Std
Neutral	0.041 ± 0.0093
Congruent	0.045 ± 0.0067
Incongruent	0.162 ± 0.0227
P-Value	0.047

DISCUSSION AND CONCLUSION

In this study a new method proposes to identify the functional connectivity of the brain using mutual information in fNIRS signals. FNIRS is an emerging imaging technology with important applications in the study of disorders of the brain [24]. Okada et al report the first study of schizophrenia fNIRS. Differences

in activity patterns compared with healthy subjects have shown [25]. Previous studies have shown that patients with schizophrenias have impaired in PFC activity. [26, 27]. Taniguchi et al measured the brain activity decreases in PFC in schizophrenia patients during the Stroop task [28, 29] in comparison with healthy subjects. The results were consistent with previous studies. Network-based analysis of functional connectivity in the resting state FMRI method to study the topological organization of schizophrenia have shown by Zhang et al. Pair of opposite hemispheres contribute 80% change in functional connectivity[30]. Our results are consistent with these studies. We have shown that connectivity maps generated with MI algorithm have identified Stroop effect for HbO2 signal, significant connectivity change was observed between hemispheres in healthy persons and left intrahemispheric in schizophrenia patients. The important findings of this study indicate that by decreasing distance between the channel pairs in schizophrenia, MI as a measure of functional connectivity strength increases in healthy subjects. All the analysis proposed here could be used for other tasks in other domains.
Future research to determine the difference fNIRS in various stages of clinical, longitudinal changes, the effects of drugs, and changes in the work of paradigm is needed to develop more accurate biomarkers that can be used to aid in the differential diagnosis, understanding the current situation, predict, and decisions about treatment options for schizophrenia. fNIRS future research environments need to be standardized measurement procedures, explorer settings, and analytical methods tools, description, and data base systems in fNIRS Society.

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