Functional Near Infrared Spectroscopy to Investigation of Functional Connectivity in Schizophrenia Using Partial Correlation

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Abstract  Functional near-infrared spectroscopy (fNIRS) is an optical imaging method which monitors the brain activation by measuring the successive changes in the concentration of oxy- and deoxyhemoglobin in real time. 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 among schizophrenia and healthy persons. fNIRS data were band-pass filtered using a wavelet algorithm with frequency range of 0.003-0.08Hz. Partial correlation (PC) values were computed for each stimulus condition. Our analysis shows that the functional connectivity of PFC is highly relevant with the cognitive load and it is different from healthy to schizophrenia person.

Keywords  Connectivity, fNIRS, Partial Correlation, Schizophrenia, Stroop Task

1. Introduction

Functional Near infrared spectroscopy (fNIRS), a non-invasive optical imaging method that measures concentration change of hemoglobin in vivo, is an increasingly popular tool for functional neuroimaging. fNIRS has several advantages over functional magnetic resonance imaging (fMRI), including low cost, portability, unobtrusiveness, and higher temporal resolution. However these advantages come with a cost of being prone to motion artifacts and other physiological noises. Any advanced analysis of fNIRS data should first take into account the necessity of removal of motion artifacts and elimination of irrelevant physiological noise. One these advanced analysis techniques is the functional connectivity approach which is fairly new in fNIRS literature [5].

In this study, we investigate the effect of motion artifact on fNIRS data and propose a method to reduce noise. We aimed to investigate the functional connectivity in the prefrontal cortex (PFC) during a modified version of the color-word matching Stroop task. Since fNIRS signals are known to be affected heavily with the fluctuations in the skin layer, a functional connectivity analysis should also consider the removal of such a dominant feature in the signal. To address this issue we propose the use of the partial correlation approach. The connectivity patterns obtained after these steps from healthy controls are then compared against the patterns from schizophrenia patients. This disease is hypothesized to be a dissociative disease, meaning a lack of connectivity in brain regions.

2. Materials and Methods

2.1. Subjects

Data were collected from 11 healthy volunteers recruited from college students and 16 schizophrenia subjects with a similar age distribution at the Pamukkale University, Denizli, Turkey.

2.2. Stroop Task

Subjects were asked to perform color–word matching Stroop task whose trials are the Turkish versions of Zysset et al. [6]. Subjects were presented with two words, one written above the other. The top one was written in ink color whereas the bottom one was in white. Subjects were asked to judge whether the word written below correctly denotes the color of the upper word or not. If color and word match, then subjects were to press on the left mouse button with their forefinger, and if not, on the right mouse button with their middle finger. Subjects were informed to perform the task as quickly and correctly as possible [7].

The words stayed on the screen until the response was given with a maximum time of 3 s. The screen was blank
between the trials. The experiment consisted of neutral, congruent and incongruent trials. In the neutral condition, upper word consisted of four X’s (XXXX) in ink color. In the congruent condition ink color of the upper word and the word itself were the same, whereas in the incongruent condition, they were different. The trials were presented in a semi blocked manner. See Fig. 1 for the details. Each block consisted of 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 within a block was homogeneous (but the arrangements of false and correct trials were altering). There were five blocks of each type. Experiments were performed in a silent, lightly dimmed room. Words were presented via an LCD screen that was 0.5 m away from the subjects. The task protocol is approved by the Ethics Review Board of Bogazici University [3].

![Figure 1. Stroop Task [4]](image)

### 2.3. Measurement

fNIRS data were previously collected by the NIROXCOPE 301 system developed at the Neuro-Optical Imaging Laboratory with a 16 channels continuous wave dual wavelength fNIRS system.

![Figure 2. Details of Probe [3]](image)

The device is capable of transmitting near infrared light at two wavelengths (730 and 850 nm), which are known to be able to penetrate through the scalp and probe the cerebral cortex. Calculation of concentration changes of oxy-Hb and deoxy-Hb in blood is based on Beer–Lambert law. Employing four LEDs and ten detectors, the device can sample 16 different channels in the brain simultaneously. See Fig. 2 for the details of the probe. LEDs and detectors were placed in a flexible printed circuit board that was specially designed to fit the curvature of the forehead.

Sampling frequency of the device was 1.7 Hz. Stimulus onset vectors for each type of stimulus (neutral, congruent and incongruent) were formed and convolved with the canonical hemodynamic response function [3].

### 2.4. Wavelet Algorithm

Several types of noise including systemic artefacts like blood pressure oscillations, respiration related, cardiac pulsation, and motion artefacts are known to be included in the fNIRS signal. Systemic artefacts generally correspond to frequencies higher than 0.08Hz while neuronal activity related signals in fNIRS data occupy the frequency range of 0.003-0.08Hz. Wavelet algorithm was used to denoise [2] the fNIRS signal.

Since the sampling rate of our data is 1.7 Hz the available frequency range is 0 to 850 mHz, We chose a decomposition tree for the discrete wavelet transform (DWT) with 8 levels. See Fig. 3. According to the frequency band of interest (0.003-0.08Hz), the details at levels 1, 2, 3 and the approximation at level 8 must be zero. The coefficient corresponding to the low pass filter are called as Approximation Coefficients (CA) and similarly, high pass filtered coefficients are called as Detailed Coefficients (CD). Furthermore, the CA and CD are divided into new approximation and detailed coefficients. This decomposition process is done until the required frequency response is achieved from the given input signal.

Wavelet decomposition can be regarded as projection of the signal on the set of wavelet basis vectors. Wavelet algorithm seems to be a promising tool to eliminate the artefacts in fNIRS data while preserving the temporal dynamics of the hemodynamic response. DWT based denoising should be adapted as a standard preprocessing step for fNIRS data analysis [2].

The sampling rate of our data is 1.7 Hz, so the available frequency range is 0 to 850 mHz. In this work, first of all, 8 levels decomposition using DWT has been done to effectively remove the low frequency fNIRS. Hence, the corresponding wavelet coefficient on CA8 is changed into zero. Therefore, we have reconstructed the signal on each level by using Inverse Discrete Wavelet Transform (IDWT) to obtain fNIRS signals [10].

Stroop task, which requires responding to a particular stimulus dimension while suppressing a competing stimulus dimension, is commonly used to evaluate PFC function. This 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 [9].

Figure 3. Wavelet Tree

Fig 4 shows comparison of the original signal and the processed signal using wavelet algorithm.

Figure 4. Comparison of the original signal and the processed signal in healthy subject

2.5. Partial Correlation

Partial correlation (PC) values were computed for each stimulus condition [1]. Since PC analysis helps to remove the effect of indirect paths, by applying this method, the PC between two channels is correlated, with the activity at all other 14 regions regressed out [8,9].

A correlation between two variables when the effects of one or more related variables are removed.

This is the relationship between two variables after removing the overlap completely from both variables. For example, in the diagram above, this would be the relationship between y and x2, after removing the influence of x1 on both y and x2. In other words, the partial correlation determines the variance represented by section 1, while the variance represented by sections 2, 3, and 4 are removed from the overall variances of the variables. Below is the formula for calculating a partial correlation (See Fig 5).

\[
 r_{12,3} = \frac{r_{12} - r_{13} r_{23}}{\sqrt{(1-r_{13}^2)} \sqrt{(1-r_{23}^2)}}
\]

3. Results

We report the major significant PC change in two pairs of channels for controls with an interhemispheric link: 1st and 12th with F(2,33) = 4.1, p = 0.025 and 5th and 14th with F(2,33) = 3.84, p = 0.031. Figure 6 displays the change in PC values for these pairs. In contrast, the major significant PC change for schizophrenia subjects were found in two pairs of channels that reside again on an interhemispheric link: 7th and 16th with F(2,45) = 3.58, p = 0.036 and 5th and 13th with F(2,45) = 3.65, p = 0.034. These results are graphically presented in the following figures.

Figure 5. Partial Correlation

Figure 6. Healthy (5th and 14th) & Schizophrenia (5th and 13th)
4. Conclusion

The major finding of this study is that the trend of PC values calculated for interhemispheric channel pairs for different stimulus types are reversed in schizophrenics. In Control group PC values are negative for C condition, meaning a reversal of the temporal dynamics between those two channels, while they are positive for IC condition, representing a synchronous contribution of those two channels to the suppression of irrelevant stimulus dimension and decision making effort, but In schizophrenia patient PC values are opposite for C condition, meaning a completely different neurobiological system is activated (or lost its synchronization).

The PC method is preferable to standard cross correlation due to its inherent elimination of the most common and underlying activity in all the channels and highlighting only the actual correlation between the two channels.

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