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FUNCTIONAL CLUSTERS IN THE PREFRONTAL CORTEX DURING MENTAL ARITHMETIC

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ABSTRACT

Functional clustering is used to identify strongly interacting regions in the brain. In this study, functional clustering approach is applied to near infrared spectroscopy (NIRS) signals obtained during mental arithmetic task. Being a stress inducing task, mental arithmetic is known to cause a right lateral activation in the brain. We hypothesized that functional clusters would be more localized in the right prefrontal cortex. NIRS data were collected from normal healthy subjects. We found that number of functional clusters increases during task periods compared with rest and clusters are prominently located in the right prefrontal cortex. This study supports the suggestion that information theoretic approaches may be fruitful for investigating the activation patterns in the brain using NIRS .

1. INTRODUCTION

The studies on brain hemisphere asymmetry during emotion experience have suggested that relatively greater left frontal activity is associated with positive affect, whereas greater right frontal activity is associated with negative affect [1]. Consequently, it is conjectured that stress-inducing tasks like mental arithmetic (MA) should be related with right frontal cortex activation. The asymmetry of the prefrontal brain activity during MA task has been investigated by near infrared spectroscopy (NIRS) [2]. NIRS demonstrated increases of oxy-hemoglobin and total hemoglobin concomitant with decreases of deoxy-hemoglobin in the bilateral prefrontal cortices. In [2], the main objective was to investigate the relationship between brain asymmetry and heart rate during MA, and it was found that for subjects with high heart rate the activation was dominantly right lateral whereas for subjects with low heart rate it was dominantly left lateral. Several functional magnetic resonance imaging (fMRI) studies also showed the existence of various prefrontal activation patterns during MA [3,4].

In the present study, we explore the prefrontal activation patterns during MA using the concept of "functional cluster" [5]. A functional cluster in the brain can be defined as a set of neural elements that are strongly interactive among themselves but weakly interactive with the rest of the system [5]. An electroencephalography (EEG) study using photic and auditory stimuli showed the existence and different patterns of functional clusters for normal controls and schizophrenics [6]. It was also shown, using functional clustering approach, that there are specific areas in the brain engaged in the perception of 3-dimensional images [7].

Functional near infrared spectroscopy (fNIRS) is a noninvasive method to monitor brain activation by measuring changes in the concentrations of oxy- and deoxy hemoglobin (oxy-Hb and deoxy-Hb) [8]. It is simply based on measuring the transmitted and received near-infrared light in multiple wavelengths and calculating the relative concentrations of oxy-Hb and deoxy-Hb using modified Beer-Lambert law [9]. fNIRS has significant advantages over functional magnetic resonance imaging (fMRI) such as absence of radiation, higher temporal resolution, portable nature of the device, relative user-friendliness and low cost of the procedure. On the other hand, fNIRS has the shortcomings of lower spatial resolution, shallow depth of penetration and consequently some uncertainty about the probed region.

The objective of the present study is to investigate the functional clusters in the prefrontal cortex during mental arithmetic task. We hypothesize that functional clusters would be more localized in the right prefrontal cortex.

2. METHODS

2.1 Experiment

We used an experimental protocol similar to that in [2]. The experiment began with 60 seconds rest followed by 60 seconds of task period during which subjects were asked to subtract a 2-digit number from a 4-digit number as quickly as possible (self paced). After a recovery period of 90 seconds subjects performed a second task period of again 60 seconds. Experiment ended with a 60 seconds recovery period.

2.2 Subjects

NIRS data were obtained from 14 high school students (7 female, ages 15-16 years). Written consent from all the subjects were obtained from the subjects before the measurements. This study has been approved by the Ethical Review Board of Bogazici University.

2.3 Data acquisition

NIRS data were collected by a continuous wave light emitting system consisting of 4 sources and 10 detectors that can sample from 16 non-overlapping regions in the brain [10]. Light sources and optode devices were attached to the forehead of subjects by means of insulating rubber bands. The sampling rate was 1.7 Hz. NIRS data consisted of intensity measurements at three different wavelengths (730, 805 and

850 nm). Source-detector separation was 2.5 cm which allows probing the cortical activity [11] (see Fig.1 for the details of the probe). Relative oxyhemoglobin and deoxyhemoglobin concentrations were calculated by the Modified Beer-Lambert Law [9].

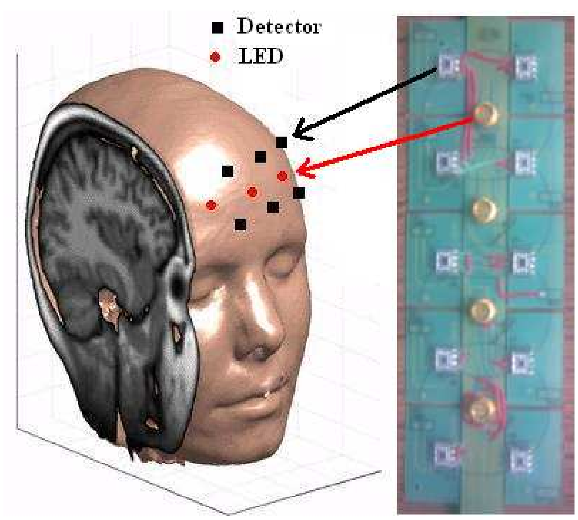

Figure 1. NIRS probe and its placement over the forehead (Head photo obtained from MATLAB® File Center).

2.4 Functional clustering

For a system X with n elementary components, mutual information *(MI)* between the j^{th} subset consisting of k elements $\left(X_j^k\right)$ and its complement $\left(X - X_j^k\right)$ is defined as,

$$MI\left(X_j^k; X - X_j^k\right) = H\left(X_j^k\right) + H\left(X - X_j^k\right) - H\left(X\right) \quad (1)$$

where $H(.)$ denotes entropy of the system. We also make use of the concept of integration, which is the generalization of mutual information to multivariate case [12]. Integration of the system X, denoted as $I(X)$, is defined as the difference between the sum of the entropies of all individual components $\{x_i\}$ considered independently and the entropy of the system X considered as a whole:

$$I\left(X\right) = \sum_{i=1}^{n} H\left(x_i\right) - H\left(X\right). \quad (2)$$

If subsets, X^k, composed of *k-out of-n* components are considered, the average integration for these subsets may be denoted as $\left\langle I\left(X_j^k\right)\right\rangle$, where the average is taken over all $n!/k!(n-k)!$ combinations of k-components. Recall that a functional cluster was defined as a group of units, which are more interactive among themselves than with the rest of the system [5]. A convenient indicator of functioning in clusters would be the cluster index *CI*, defined as the ratio of the integration of the cluster to the mutual information between that cluster and the rest of the system:

$$CI = \frac{I\left(X_j^k\right)}{MI\left(X_j^k; X - X_j^k\right)} \quad (3)$$

For a cluster to be qualified as a functional one, its cluster index should be greater than 1. Since *CI* increases with cluster size, we should normalize it in order to compare the significance of clusters of different size [5]. Normalizing can be achieved by generating random samples of the same cluster size and overall integration but with no functional clustering. A Student's *t*-like statistics was calculated by subtracting the mean *CI* of these random samples from the *CI* of the NIRS data and dividing by the standard deviation of the *CI* of the random samples. 1000 random samples were used in this study and the significance threshold was determined as 0.05. In order to interpret the pattern of functional cluster, using the procedure described in [7], for each detector we calculated the proportion of significant clusters that they were included in. Hence, a value between 0 and 1, showing the "probability" of that detector being a member of a functional cluster, was obtained. This procedure was applied to each subject and a mean probability value was derived for each detector position

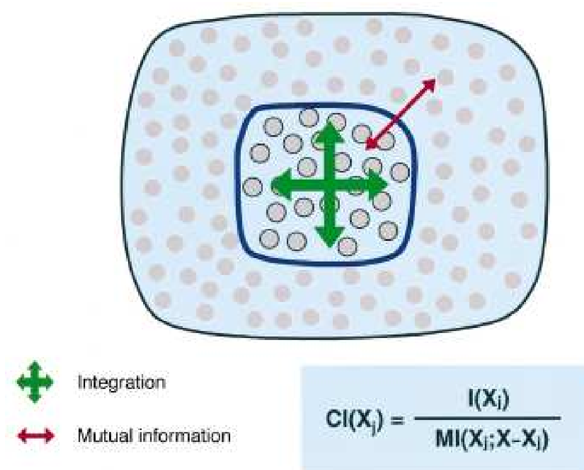

Figure 2. Illustration of functional clustering (image obtained from [13]).

3. RESULTS

NIRS parameters exhibit their expected patterns during the MA task, i.e., oxy-Hb and total-Hb increase and deoxy-Hb decreases (see Fig. 3). The change during the second MA task is always smaller than the first one for all of the variables of interest. There may be two reasons for this phenomenon: First, a pause of 90 seconds may not be enough for recovery and second, the following task period may take place with an elevated baseline. Although, the figures show that the values return to their baseline values in the recovery period, this possibility cannot be totally eliminated. Second, subjects may get used to the experiment and therefore experience less stress during the second task period. Our study cannot rule out any of these possibilities.

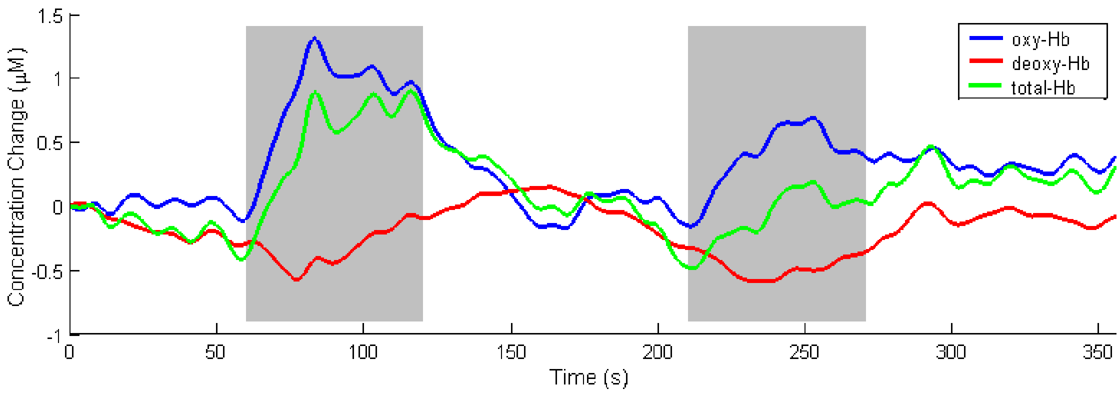

Figure 3. Typical examples of changes in NIRS parameters during MA. Gray areas denote the task periods.

To be able to evaluate the lateralization of the brain within the information-theoretic framework, we identified functional clusters during the experiment. Figure 4 shows the total number of functional clusters for oxy-Hb and deoxy-Hb.. Our prediction was that number of clusters would increase during trial blocks and decrease during rest blocks. The results for oxy-Hb are consistent with this prediction whereas those of deoxy-Hb do not show convincing evidence. The number of functional clusters increases monotonically till it reaches a maximum during the rest between the two trial blocks, and there is a slow decrease afterwards. For oxy-Hb, the lowest number of functional clusters is attained during the first rest period. The number of clusters is slightly higher during the first task period with respect to the second task period, but the standard deviation is also higher. An interesting observation is that the number of clusters does not decrease after the second trial block.

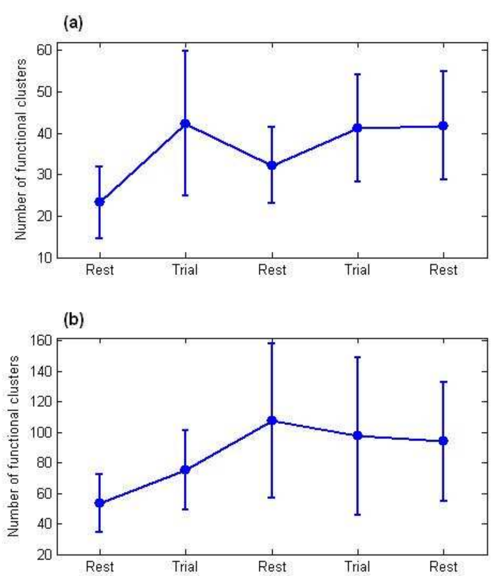

Figure 4. Total number of clusters for a) oxy-Hb, b) deoxy-Hb.

After determining the total number of functional clusters, The spatial partitioning of these clusters over the prefrontal cortex was then investigated. Using the procedure described in Section 2.4, we calculated the probability of each detector being a member of a functional cluster. Figures 5 and 6 show the results for oxy-Hb and deoxy-Hb, respectively.

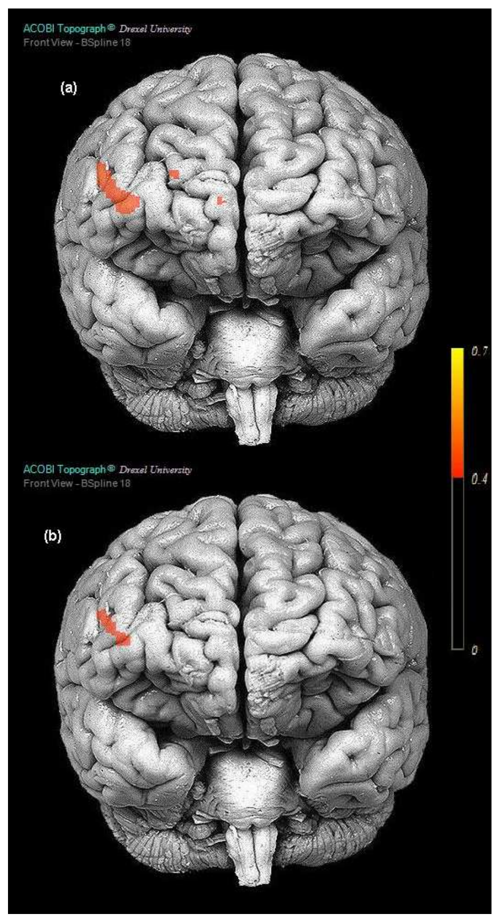

Figure 5. The pattern of functional clusters for oxy-Hb during a) First task period, b) Second task period

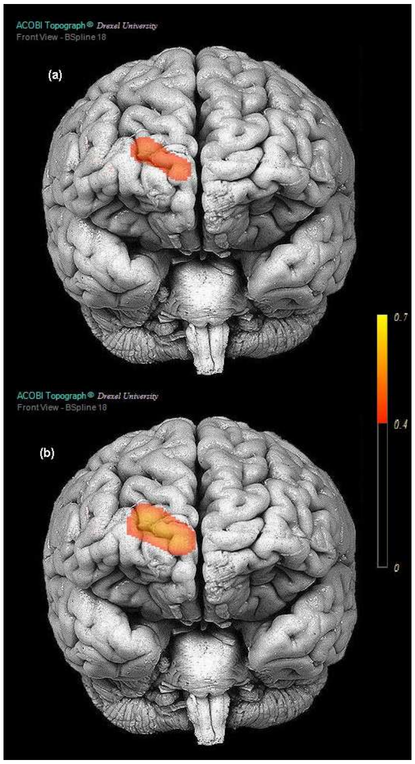

Figure 6. The pattern of functional clusters for deoxy-Hb during a) First task period, b) Second task period.

The distribution of the functional clusters is dominantly right-lateral for HbO2 for both of the task periods. The clusters are more concentrated for the second task period. This may be associated with our observation on the time-series data. This result may again be the consequence of habituation of the subject. The clusters for deoxy-Hb are also located at the right hemisphere but with a less pronounced lateralization.

4. DISCUSSION

The functional clustering approach confirmed the dominancy of the right hemisphere during MA. Analysis of oxy-Hb data has shown that there is an increase in the number of clusters during task periods, and that these clusters are concentrated in the right prefrontal cortex. The number of clusters in the deoxy-Hb case does not follow the expected pattern, and moreover, its reaching the highest value during the rest block between the trials is hard to explain. This may be the result of inconsistency of deoxy-Hb data, which has been already pointed out by other researchers [14]. These types of discrepancies were also noted by other researchers [7]. An interesting observation is that clusters become weaker for oxy-Hb in the second task period, whereas they become wider for deoxy-Hb.

Functional clustering provides a comprehensible framework for studying interactions within units within a neural system. Since it is not model-based any type of relationship may be sought by functional clustering. NIRS is a new technique for studying neural activations. Information-theoretic approaches, like functional clustering, may be effective in probing out the activation patterns from NIRS data.

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