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TASK INDUCED BRAIN ACTIVATION ANALYSIS BASED ON FNIRS DATA DURING STROOP TASK

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DECLERATION

I declare that the words and information contained in this thesis are my own except where explicitly stated otherwise in the text. I am fully aware of all the ethical rules and there are not any violation of copyright and any kind of patent.

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Burçin Tatlıeşme

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SUMMARY

The prefrontal cortex (PFC) is a brain region that plays a central and executive role in attention, cognitive processing and working memory. Therefore, examination of PFC with non-invasive functional imaging methods is crucial in understanding the dynamics of cognitive functions, also for early detection of disease-related alterations. In this study, a new technique is proposed that can be used to diagnose disorders such as hyperactivity, and attention deficiency, where PFC networks are highly involved. This method is based on recording brain hemodynamics with an fNIRS device during a Stroop task. In this study, 29 adult subjects (23,2 ± 4,5 years, 11 females) without any neuropsychiatric diseases performed a Stroop task. Attention, response control and working memory were evaluated with a 16-channel fNIRS system. For each subject, the global efficiency (GE) scores were computed for $rest_1$, test and $rest_2$ times. The ratio of test GE to rest GE scores were used to classify the subjects into two groups (Low Ratio, LR and High Ratio, HR). The HR and LR groups were found to be statistically significantly different. It was remarkable that the HR group used less time compared to LR's response time. When GE connectivity maps are analyzed, it was noticed that HRs established better direct connections during the test compared to the rest moment and showed a better focus. However, maps of the LR group, a similar focus was not observed during the test. In addition, Neural Efficiency of each participant, increased linearly with GE scores. Based on these results, it is proposed that subjects with higher GE ratios during Stroop test have "higher focus and inhibition ability" when compared to subjects with lower GE ratios. The functional connectivity seems to be more efficient in the task focused brain as higher connectivity scores are associated with higher Neural Efficiency and lower response durations. These results support the suitability of brain connectivity measures obtained from fNIRS as potential diagnostic biomarkers for differentiating and diagnosing cognitive disorders related to attention deficiency and impulsivity.

Keywords: Stroop, Function Near Infrared Spectroscopy (fNIRS), Global Efficiency, Neural Efficiency, Attention

ÖZET

Prefrontal korteks (PFK) dikkat, bilişsel işlem ve çalışma hafızasında merkezi ve yönetici rol oynayan bir beyin bölgesidir. Bu nedenle, PFK'in invazif olmayan fonksiyonel görüntüleme yöntemleriyle incelenmesi, bilişsel işlevlerin dinamiklerini anlamada ve hastalıkla ilgili değişikliklerin erken saptanmasında önemlidir. Bu çalışmada, PFK ağlarının aktif olduğu, hiperaktivite ve dikkat eksikliği gibi hastalıkların teşhisinde kullanılabilecek bir metot önerilmektedir. Bu yöntem, Stroop görevi sırasında fNIRS cihazıyla alınan hemodinamik kayıtlardan elde edilen beyin bağlantısallığına dair parametrelerin analizine dayanır. Nöropsikiyatrik hastalığı olmayan 29 yetişkin, gönüllü denekten (23,2 ± 4,5 yıl, 11 kadın) bir Stroop görevini sırasında fNIRS kayıtları alınmıştır. Dikkat, cevap kontrolü ve çalışma belleği, 16 kanallı bir fNIRS sistemi ile değerlendirildi. Her denek için, dinlenme$_1$, test ve dinlenme$_2$ anları için elde edilen HbO verileri kullanılarak global verimlilik (GV) değerleri hesaplandı. Test anındaki GV değerlerinin dinlenme anındaki GV değerlerine oranı, denekleri iki gruba sınıflandırmak için kullanıldı (Düşük Oranlılar, DO ve Yüksek Oranlılar, YO). GV oranları iki grup arasında istatistiksel olarak anlamlı bir fark gösterdi. YO grubunun DO'ın yanıt süresine kıyasla daha az olması dikkat çekiciydi. GE bağlantı haritalarında, YO'ın test sırasında, daha doğrudan bağlantılar kurduğu ve daha iyi odaklandıkları fark edildi. LR grubundakilerde, benzer bir odaklanma görülmedi. Her bir katılımcının Nöral Verimlilik miktarı hesaplandı ve GV skorları ile doğrusal olarak arttığı gözlendi. Bu sonuçlara dayanarak, Stroop testi sırasında daha yüksek GV oranlarına sahip deneklerin, daha düşük GV oranlarına sahip deneklere kıyasla "daha yüksek odaklanma ve inhibisyon kabiliyetine" sahip oldukları önerilmektedir. Daha yüksek bağlantısallık değerleri, daha yüksek Nöral Verimlilik ve daha düşük yanıt süreleri ile ilişkili olduğundan, işlevsel bağlantının görev odaklı beyinde daha etkili olduğu görülmektedir. Bu sonuçlar, dikkat eksikliği ve dürtüsellik ile ilgili bilişsel bozuklukları ayırt etmek için potansiyel tanı biyobelirteçleri olarak fNIRS verilerinin uygunluğunu desteklemektedir.

Anahtar Kelimeler: Stroop, Yakın Kızılötesi Spektroskopi (fNIRS), Global Verimlilik, Nöral Verimlilik, Dikkat

1. INTRODUCTION

The electrophysiological studies, which complement and confirm the lesion studies to a great extent, gave an idea about the role of prefrontal cortex (PFC) in sensory, motor, visceral / emotional, social and executive functions (1). Also, the PFC has an important role in sensory interest, in other words, selective control of sensory inputs' reach to higher cerebral structures, including the PFC itself. While these control mechanisms are uncertain, it can be regarded that the PFC contains interconnected links with motivation-related subcortical and limbic structures and neocortical regions associated with cognition (2).

Latest clinical observations and experimental research show that PFC injury and disease create a compelling range of cognitive deficiencies. These deficiencies could be due to but are not limited to attention problems, spatial orientation, motor control, short-term memory, temporary and resource memory, meta-memory, relational learning, creativity, persistence and ratiocination (for reviews, see Fuster, 1988; A. C. Roberts, Weiskrantz, 1998; Wise, Gerfen, 1996). (3).

In psychiatric and neurological disorders, an individual's daily activities may be seriously disrupted by the reason of structural and / or functional defects in this brain region. For this reason, studying this region by using non-invasive functional imaging methods is seriously important in comprehension of the dynamics of cognitive functions, besides for early detection of disease-related changes.

Simultaneous collection of neuropsychological test data functional neuroimaging data for the diagnosis of PFC defects and diseases has been a topic of widely investigated research over the past two decades. Neuropsychological tests are can be verbal, mathematical or visual which can involve decision-making, working memory, inhibition, short-term and long-term memory processes. During the periods of test performance, a functional activity increase is expected in a focused brain, and changes in the amount of blood supply to the brain region of interest are observed compared to the resting period. Stroop Color Word Interference Test (SCWT) (Stroop, 1935 (4)) was used in this thesis because it was intended to carry out a study on inhibition and working memory.

The aim of this study was to explore the feasibility of an fNIRS derived functional connectivity metric, namely the global efficiency as a neural correlate of cognitive processes such as attention and focus. For this purpose, a Stroop task was designed where continuous recordings of brain hemodynamics were taken with a custom made fNIRS instrument. For each subject, a functional correlation matrix was generated by partial correlation analysis of the HbO data collected via fNIRS. The strongest %10 of the correlation coefficients were used to compute the GE score and the ratio of GE score computed for stimulus duration to the GE scores computed during rest durations were used to classify the subjects into two groups as high responders and low responders. A combined analysis of behavioral and hemodynamic metrics indicated that subjects with higher GE ratios during Stroop test have “higher focus and inhibition ability” when compared to subjects with lower GE ratios. The results indicate that functional connectivity is more efficient in the task focused brain since higher connectivity scores are found to be associated with higher neural efficiency and lower response durations. The findings of the present study support the suitability of brain connectivity measures obtained from fNIRS as potential diagnostic biomarkers for differentiating and diagnosing cognitive disorders related to cognitive impairments and impulsivity (5).

2. BACKGROUND

2.1. Stroop Color Word Interference Test (SCWT)

Stroop Color Word Interference Test (SCWT) (Stroop, 1935) evaluates cognitive flexibility, cognitive inhibition, selective attention and computing speed (6). Numerous neuroimaging studies have used the Stroop test, an established neuropsychological task that measures inhibitory cognitive control, when investigating neural correlations of cognitive interference effect in healthy subjects. These works have coherently shown activations in prefrontal and cingulate cortical regions during Stroop interference (Leung et al 2000; Peterson et al 1999) (7).

The Stroop task is one of the most commonly used tasks in cognitive psychology, clinical neuropsychology, and cognitive neuroscience to examine interference and attention in the PFC (e.g., Kornblum et al., 1999; MacLeod and MacDonald, 2000). In this test, individuals should name the ink color of a word that writes a color name. When the color and word are congruent (for example, the word 'green' with green letters), the task is easy; however, when the color and word are incongruent (for example, the word 'green' with yellow letters), people experience Stroop interference effect. This effect is thought to take place since word reading is a more practical and more automated task than naming colors, therefore attention control is necessary to come through the inclination to reply to the word rather than the color (8).

2.2. Functional Near-Infrared Spectroscopy (fNIRS)

Several neuroimaging studies performed by functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have demonstrated specific brain activation in the anterior cingulate cortex (ACC) and lateral PFC (LPFC) during occurring the Stroop interference effect (Egner, Hirsch, 2005; MacDonald, 2000; Taylor et al., 1997; Zysset et al., 2001) (9). Near-infrared spectroscopy (NIRS) is a method of enabling functional imaging of brain activity (10). Functional near-infrared spectroscopy (fNIRS), a hemodynamics based technique, is used for non-invasive evaluation of human cortical brain activation (for detailed reviews Obrig, Villringer, 2003; Hoshi, 2003). Unlike traditional neuroimaging methods, for instance fMRI and PET, fNIRS technology provides a portable device that does not require a user's body or head restriction and can therefore be used for brain monitoring tool in everyday environments (11). fNIRS allows to measure differences in the concentration of oxygenated (O_2Hb) and deoxygenated (HHb) hemoglobin. Moreover, fluctuation of total hemoglobin may be calculated by adding of O_2Hb and HHb. The typical fNIRS activation signal is the decrease in HHb with comparable O_2Hb increase over time, which gives the shape of the blood oxygenation level- dependent (BOLD) signal in fMRI (Logothetis, Wandell, 2004). Unlike other neuroimaging methods, fNIRS uses optics as a more practical and non-side effected way instead of putting to use radioactivity (PET) or magnetic properties (fMRI) of cerebral blood. This eliminates the requirement for complex technical appliances (e.g. on-site cyclotron (PET), huge magnet (fMRI)) or the use of contrast agents. This subsistent advantage and the disadvantages that other methods have, such as noise disturbances, small movement constraints, resolution problems and relatively high costs have accelerated the adoption of fNIRS as an alternative and complementary functional neuroimaging tool to fMRI (12).

fNIRS has several advantages compared to other imaging techniques, such as flexibility, portability, low cost and biochemical specificity (13). As compared with fMRI and PET, the external appearance of fNIRS is more like an electroencephalogram (EEG). Therefore, data collection is comfortable for subjects (patients and children can be reexamined repeatedly), possibly because of less constrictive measuring conditions (eg. less movement restriction, no noise disturbance) that cause more ecologically valid conditions than other neuroimaging methods (e.g. Suzuki et al., 2004). Rapid advances in technology such as the transition from single-channel to multi-channel systems and the development of methodology such as event-related study designs, time series analysis methods have allowed fNIRS to easily engage in psychological, psychiatric and basic research on children, adults and the elderly subjects (e.g. Ehlis et al., 2005; Fallgatter, Strik, 1997, 1998; Schroeter et al., 2004). There are few published studies focusing on quality criteria or reliability and reproducibility of fNIRS in contrast with the extensive use of it (14).

Modern brain mapping methods like diffusion MRI, fMRI, EEG and MEG form increasingly broad datasets of anatomical or functional linkage patterns. In a similar way, large connectivity data sets in biological, technological, social and other scientific fields are formed by simultaneous technological advances. Over the past decade, efforts to characterize these data sets have led to the emergence of a new, multidisciplinary method to examining of complex systems (Strogatz, 2001; Newman, 2003; Boccaletti et al., 2006). The principle of this method, known as complex network analysis, is to explain the significant properties of complex systems by measuring the topologies of their relevant network representations. The origin of complex network analysis is derived from the mathematical study of networks known as graph theory. Nevertheless, distinct from classical graph theory, this analysis first of all concentrates on random or unregulated real-life networks that are large and complicated (15).

2.3 Global Efficiency (GE)

This branch of mathematics, which focuses on the definition, examination and analysis of complicated networks, is known as graph theory. The spread of graphic theory to real-world systems emerged in the 1950s in the context of questions in the social sciences. It was only in recent years, neuroscientists began to grip the huge potential of these tools for examining brain organization and function and studying them from an integrative, mathematically meticulous and statistically principled perspective (16).

Vertices or node clusters (also called V) connected to edges (also called E links) constitute networks or graphics. Connections in large-scale brain networks represent anatomical, functional, or effective connections based on the data set (Friston, 1994), while nodes generally symbolize brain regions. A network can be prevalently defined with an adjacent matrix A, in that the ij_{th} input provides the strength of the edge between node i and node j. All networks are expressed by their adjacency or in other words connectivity matrices. In these matrices, rows and columns indicate nodes while matrix entries show connections. Edges may either be directed ($A_{ij} \neq A_{ij}$) or undirected ($A_{ij} = A_{ij}$) and also be weighted or unweighted. In unweighted or binary networks, if they are present, edges carry the weight 1 and if they are absent, the weight 0. The edges in the weighted networks carry any numerical weight as a symbol of the strength of the connection between the two nodes to which they are connected. The most common elements of networks commonly used in neuroscience are seen when it comes to connection types with different characteristics, e.g. those with more than one edge type or vertex (16).

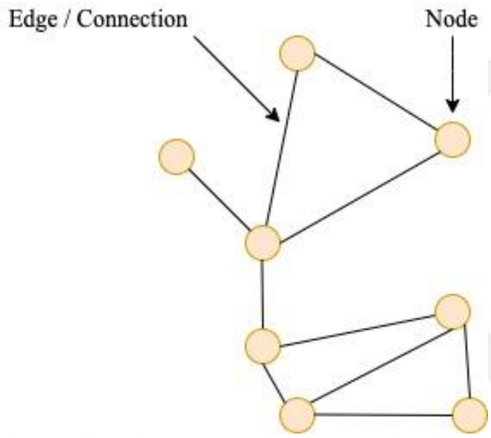


Figure 1: *Visual Example of Edges (Vertices) and Nodes*

During brain activation, functional connections show the magnitudes of temporal correlations, and can take place between anatomically unconnected region of interest (ROI) pairs. Depending on the measurement, the functional connection can indicate linear or nonlinear interactions as well as interactions at different time intervals (Zhou et al., 2009). Effective connections indicate the direct or indirect causal effects of one region on another and can be predicted from observed distortions (Friston et al., 2003).

Whereas binary connections indicate the presence or absence of connections, the weighted connections also include information about the connection forces. While weights in functional and effective networks indicate magnitudes related to correlation or causal interactions, weights in anatomical networks indicate the size, density, or consistency of anatomical pathways. Moreover, connections can also be distinguished by the presence or absence of directionality. Thereby, anatomical and effective connections can be represented by conceptually directed connections. Directed effective connection patterns can be understood from changes in functional activity following local perturbations.

The lengths of the paths eventually predict the potential for functional integration between the brain regions, and shorter paths indicate a stronger potential for integration. The most widely used measure of functional integration is known as the characteristic path length of the network and is the average shortest path length between all node pairs in the network (eg. Watts and Strogatz, 1998). The average inverse shortest path length is a relevant measure known as 'global efficiency' (17). The length of characteristic path is mainly affected by long paths, whereas global efficiency (GE) is fundamentally affected by short roads. Some researchers defended that this could make GE a superior measure of integration (Achard and Bullmore, 2007). Link lengths are inversely proportional to link weights, this is because large weights characteristically indicate strong connections and close proximity (15).

The distance d(i, j) between any two vertices i and j in a graph is the number of edges in a shortest path between i and j. If there is no path connecting i and j, then d(i, j) = ∞ (18). In this thesis, Latora and Marchiori's (17) was used because it enables us to work with weighted connection graphs. In this case, the GE is computed as

$$GE = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{d_{ij}}$$

where d_{ij} is defined as the smallest sum of physical distances along all possible paths in the graph from i to j (17).

The interpretation of this equation can be made as "stronger link weights correspond predictably to shorter lengths". The GE values obtained from the equation are in the range of [0; ∞]. This value may be normalized to the [0; 1] range by dividing it into randomly generated networks with the same number of nodes. This analysis gives an idea of the robustness of the network and its proximity to small network characteristics (19). Hence, connections with longer paths have higher global efficiency. Longer or, in other words, direct paths are expected to emerge at the time of a focused task. Because a particular task forces the nodes in different regions of the brain to communicate with each other.

Even in the absence of explicit tasks or stimuli, research has shown that spontaneous fluctuations in brain activity have occurred (20). This phenomenon can be examined through blood oxygen level-dependent (BOLD) signals measured by a fMRI (Biswal et al., 1995; see Fox and Raichle, 2007 for review) and hemoglobin oxygenation signals measured by fNIRS (21). In this study, GE analysis based on fNIRS measurements was performed in absence of overt tasks and task related processes. Then, a meaningful difference between rest and task conditions were assessed in terms of the GE metric.

In this thesis study, a new technique was proposed that can be used to diagnose the failure of executive function disorders such as characterized by inattention, hyperactivity, and impulsivity like Attention-deficit/hyperactivity disorder (ADHD) (22). This method is based on recording brain hemodynamics with the fNIRS device during the resting state and performing Stroop task then analyzing hemodynamic signals with global efficiency theory for the quantitative determination of functional connectivity of PFC. The study hypothesizes that the functional connections in the human brain are shorter in terms of GE metric at rest, when it is not focused on anything, compared to the moment when the task is given. In other words, during resting state, we expect a lower global efficiency score than the task moment. The ratio of test to rest GE scores of a healthy individual are expected to be greater than 1. Otherwise, it may be a signal for a disorder (23) such as inattention, hyperactivity, and impulsivity.

2. METHODS

2.1. Experimental Design

2.1.1. Participants

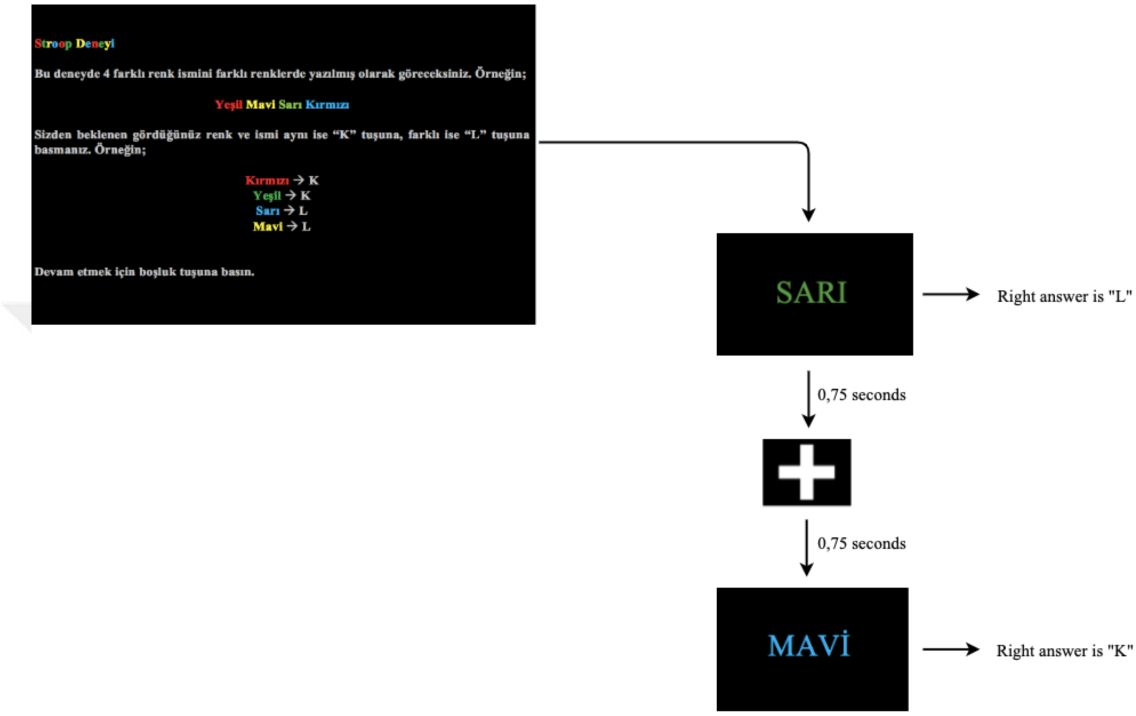
29 young adults (11 females, 15 males) were enrolled in the study. No subject had a history of neurological, major medical or psychiatric disorders; none were taking medication at the time of measurement. All subjects were right handed as assessed by the Edinburgh Handedness Inventory. The subjects were 18 – 26 years old (mean 23,2 ± 4,5). The research protocol was approved by the Ethics committee at the Acibadem Mehmet Ali Aydinlar University and Acibadem Healthcare Organizations Medical Research Ethical Committee (ATADEK) (Decision No. 3 of ATADEK dated October 11, 2018). Written informed consent was obtained from all subjects after complete description of the study to the subjects before the session.

2.1.2. Experimental Protocol

The task used for the current study was a modified and computerized version of the Stroop task that is used for evaluating attention, response control and working memory. During experimental protocol design, "Psytoolkit.org" and its web based experiment library were used. This website gives the user an interface where s/he can write his/her own code. The web-based library of the site contains open source code for many prominent neuropsychological experiments. For the scope of this study, a simple version of Stroop neuropsychological test was used which includes only one word to be shown on the screen in a trial. Gijsbert Stoet's open source Stroop (24) was our starting point. Then, a different version of this experiment was designed (*Flowchart 1*). The Stroop task stimuli consisted of the Turkish words KIRMIZI, MAVİ, YEŞİL and SARI (Turkish for RED, BLUE, GREEN and YELLOW). Each word was written in one of these three colors and was presented in the center of a black screen. Here only in the incongruent, congruent conditions were presented. During the incongruent condition, the color in which the presented word was written was incongruent with the meaning of the word, i.e., the word was displayed in a color that did not match its meaning (i.e., “BLUE” in RED, “RED” in GREEN, “GREEN” in BLUE). In the congruent condition, words and their colors matched in terms of meaning and color (i.e., “RED” in RED, “BLUE” in BLUE, “GREEN” in GREEN) *(Figure 2)*).

Figure 2: *Four Different Examples of Stroop Task Trials*

For the conditions where the color name and its color are the same, subjects pressed the “K” button, otherwise they were asked to press the “L” button. When determining the keys to be pressed, it was considered that they should not be distant buttons and not be familiar to subjects like up and down buttons or space. After the participant registered the response, the screen progressed to the next word. An experimental run consisted of 40 congruent and incongruent trials presented in random order with an interstimulus interval of 750 milliseconds. Each word was shown at the center of the screen for 750 milliseconds, and participants had 750 milliseconds for pressing a key, and if they don't press any key, the new word will appear after 1500 milliseconds. Between the trials, a white "+" was shown as fix point, on a black background (*Flowchart 1*).



Flowchart 1: *Flowchart of an Example Experimental Procedure*

Prior to placement of the fNIRS probe, subjects were briefly informed about the details of the Stroop task. They did practice until they ensured that they understood and were capable of completing the task. The experiment was performed in a room that had less light and sound isolation. During data acquisition, subjects were asked to use a visual display from a 13-inch laptop computer. Subjects were instructed to sit on a comfortable chair and to relax and remain calm (*Photo 1, 2*).

Photo 1*: The Experimental Setup. From left to right: The computer on which the data collection box is connected and on which the Brain - Info program is running, the stimulation computer used by subjects during Stroop task, Arges Cerebro Niroxcope 301*

Photo 2: *Experiment Process: The experiment designer on the left controls the experiment from the data computer, while the participant on the right does the Stroop task*

When the participant was ready for the experiment, the fNIRS probe was placed on the person's head and measurements began to be taken. Before starting the Stroop test, they were asked to look at the empty wall without focusing on anything, while for 30 seconds “Resting State - 1” recording was performed. Resting state optimization is a problem that is still sought in the literature. How long is enough and necessary for the brain to go into rest has not been found in an optimal way. The results should be examined and decided as it is not known whether the participants were actually in rest or not focusing on any issues during the measurements. In this study, 2 resting state measurements were taken 30 seconds before and after the test, taking into account other resting state studies in the literature. The 30-seconds Restı were kept on the stopwatch and the subject was audibly stimulated 3 seconds before the end of the countdown. When the time expired, the participant initiated the Stroop test by pressing the space key on the laptop’s keyboard. Then the experiment process was named “Test State” began, this process was completed by each participant at different times. This was because each participant's process of understanding and reacting to the test worked differently. Even though they had 750 milliseconds to answer, there were also participants who responded much earlier, as well as those who could not exceed the answer time and dial in time. At the moment, the subject pressed the button for starting the test, a marker indicating the start of the “Test State” was inserted from the computer where the fNIRS measurement was taken simultaneously. A second marker was used for the moment when the test was completed by monitoring the computer screen where the experiment was performed. After the experiment, while subjects looked at the empty wall and focused on nothing, “Resting State - 2” measurement was done for 30 seconds. At the end of the 30 seconds, fNIRS measurement was terminated and the device was removed from the participant's head. During the analysis process, we compared the resting state -1, test state and resting state -2 data.

At the end of the experiments, fNIRS measurements were taken from 29 different participants before, during and after the Stroop task. It was observed that some of the detector outputs could not be used due to serious motion artifacts or occasional defects of the sensor. Rejection criteria based on visual examination were determined, such as errors in signal amplitude due to the saturation of the sensors and outliers caused by the subjects ' head movements. It was also observed that in some cases the sensors did not make any measurements due to hair coming in front of them. After eliminating outlier measurements, data analysis was performed with the remaining 25 young adults' (9 females, 16 males) data.

2.1.3. fNIRS Data Acquisition

While the subjects were doing the Stroop task, data acquisition was performed by an fNIRS system that consisted of a 16-channel continuous-wave dual wavelength. Thus, oxy-Hb data of 16 different regions on PFC for each time series can be measured. The fNIRS probe (ARGES Cerebro NIROXCOPE 301, Hemosoft Inc., Turkey), that is designed to be a compact, reliable data acquisition and display system based on a microcontroller operating with the functional near-infrared spectroscopy (fNIRS) method (*Photo 3*). The system, consisting of two different wavelengths which are 730 and 850 nm from four light sources and ten photo-detectors, offers an innovative and unique approach to brain researchers (*Photo 4)*. NIROXCOPE 301 is designed for research clinics and laboratories. The system can be used in normal laboratories as well as in hospital and home environments and can find a wide range of applications with ease of use. Active detection technology provides a fully wearable neuro-imaging solution (25).

Photo 3: *ARGES Cerebro NIROXCOPE 301 Data Collection Box*

Photo 4: *Head probe of NIROXCOPE 301: There are ten photo-detectors in total, five at the top and five at the bottom, while there are four light sources in the middle line.*

The source and detectors are equidistantly placed on the probe with a source detector separation of 2.5 cm. A source–detector distance of 2.5 cm provides a penetration depth of 1.25 cm in tissue. Previous works demonstrated that with a source–detector distance equal to approximately 2.5 cm, the fNIRS equipment is capable of detecting effectively the Hb and HbO concentration changes on the surface of the cerebral cortex (26). LEDs and detectors were placed in a rubber band that was specially designed to fit the curvature of forehead.

The probe is positioned such that its base aligns with the eyebrows of the subject and the middle with the Fz location from 10 to 20 EEG electrode placement and a sports bandage is used to secure it on its place and eliminate background light leakage (*Figure 3*). Sampling frequency of the device was 1.7 Hz. The concentration changes in Hb and HbO signals are calculated from the Beer–Lambert law using two wavelengths. This gadget was able to transmit near infrared light at two wavelengths, which are assumed to have the power to pierce the scalp and examine the cerebral cortex (27).

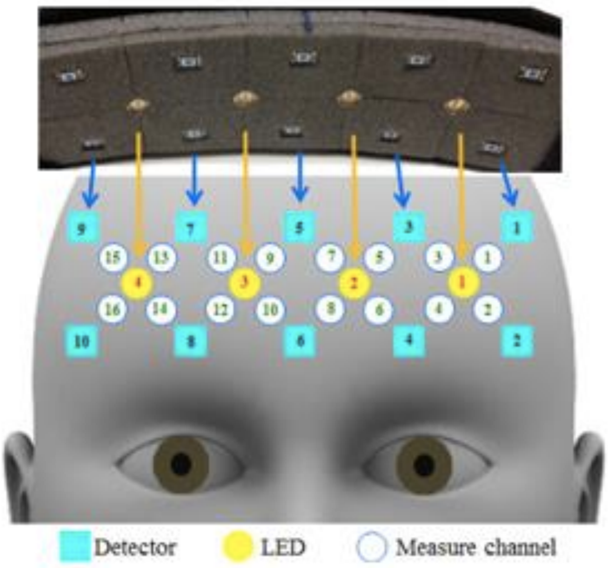


Figure 3: *Location of the light sources and photo-detectors on the forehead. fNIRS probe with ten photo-detectors and four light sources on the forehead for recording sixteen different channels. Blue squares are photo-detectors, yellow circles are light sources and white circles represent channels (28).*

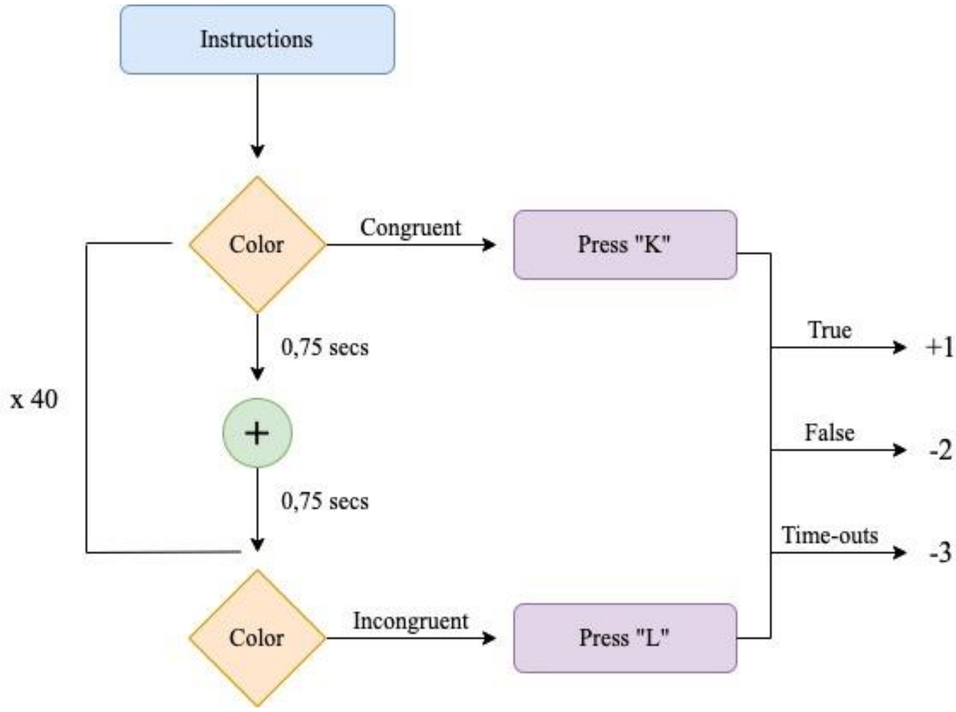
2.2. Data Analysis

2.2.1. Behavioral Data Analysis

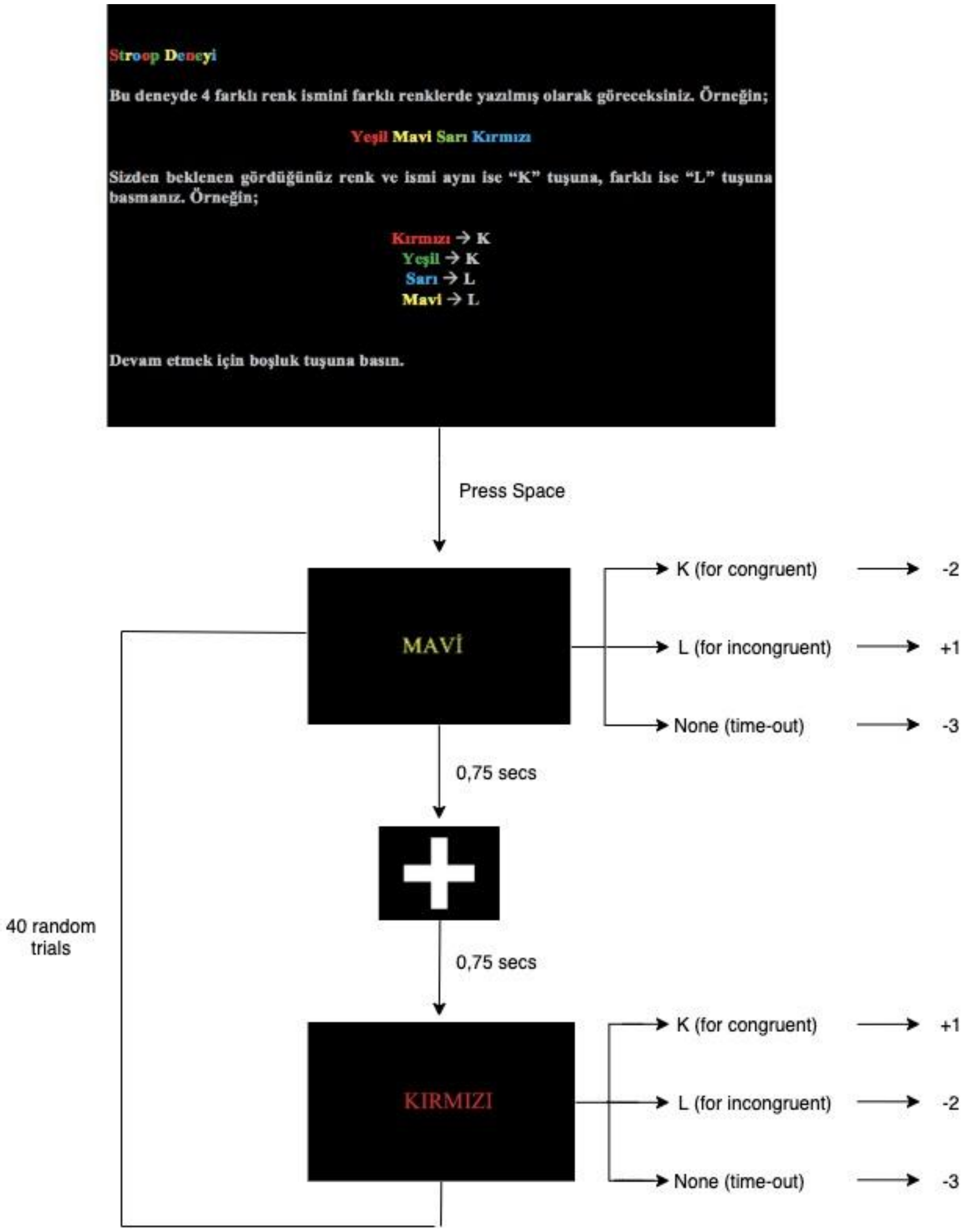
At the end of each measurement, Psytoolkit automatically generates a separate data table for that experiment. The results can either be created online and transferred to an archive, or downloaded for later use. During this study, after each participant completed the online Stroop task, their marks were downloaded onto an Excel file (*Table I*) and prepared for analysis.

The web-based library of Psytoolkit website provides information on how to read this table prior to analysis. Column 1 only provides information about the status of the experiment (i.e. whether it is tested or not). Column 2 (Name of the Word) indicates the color name typed on the screen. Column 3 (The Color the Word is Printed in) specifies the color in which the typed word appears on the screen. In Column 4, (Stroop Color Match), the color name written on the screen and the matching status of the type color are indicated. If the color name (Column 2) and the color in which the word is written (Column 3) are the same, Column 4 writes 1; whereas, if the meaning and color of the printed word do not match, it writes 2. Column 5 (Table row Number) refers to the line where the printed word is found in the test code (see the Figure, this information is not used in the analysis). Column 6 (The Pressed Key Number) indicates which key the participant pressed. If the participant concludes that there is a congruent case between the color and meaning of the printed word and presses the “K” key, digit 1 is typed to the corresponding row in Column 6. Similarly, the “L” key, is pressed in the case of incongruent stimuli (i.e. the meaning and color of the printed word do not match) and digit 2 is typed to the corresponding row in Column 6. Column 7 depicts whether the participant responded correctly to the trial or not. In this column, the number 1 is used for a correct answer and the number 2 is used for a wrong answer while the number 3 is used for key presses not completed within 750 milliseconds. Finally, Column 8 (Reaction Time) specifies the amount of time the subject has spent for that trial in milliseconds.

In the first step of the analysis, total duration of the experiment for each participant was calculated. Column 1 was excluded from the table because it had no significance in terms of analysis. Afterwards, a scoring system was established for a total of 40 trials, taking into account the numbers indicated in Column 7. According to this system, the participants would earn 1 point for each correct answer, while for each incorrect answer they would lose 2 points and lose 3 points as much as the number of time-outs. As a result, a person who answered all trails correctly would receive 40 full points. A sample data sheet of a participant whose analysis has been completed is demonstrated in *Table II*.



Flowchart 2: *Behavioral Data Analysis Steps*



Flowchart 3: *Behavioral Data Analysis Steps with Trials*

2.2.2 fNIRS Data Analysis

All data analysis of this study was done over MatLab R2017a (9.2.0.538062) version. A major concern with fNIRS measurements is the presence of strong spontaneous fluctuations or physiology-based systemic interferences in the signal due to cardiac pulsation, respiration and a variety of spontaneous low frequency oscillations (LFOs) occurring (Obrig et al., 2000; Payne et al., 2009; Toronov et al., 2000). Such systemic interferences are present in both the cerebral and superficial layers (i.e. scalp and skull) of the head and reduce the accuracy of fNIRS for detecting brain activation (Tian et al., 2011). Several methods have been proposed in the literature to reduce the systemic interference in fNIRS signals (29, 30). In this thesis, an fNIRS data analysis methodology which my advisor had previously developed was adapted to the data sets (31).

Functional connectivity analysis

[Hb] and [HbO] data collected simultaneously from all channels throughout the experiment were passed through a high pass filter to obtain HBO_R^i and HB_R^i, where "i" represents channel number. Eight order Butterworth (fc = 0.09 Hz) was chosen as the high pass filter. The regressor used in functional connectivity (FC) analysis based on partial correlation (PC) is obtained by taking the average of all channels of this signal. Therefore, $\overline{HBO_R} = \sum_i HBO_R^i$ ($\overline{HB_R} = \sum_i HB_R^i$) is used to reduce systemic physiological effects from the correlation of the raw [HbO] ([Hb]) signals from two channels. After the regressor is calculated, the pre-test (Rest1), test and post-test (Rest2) parts are combined to form separate time series for these stimuli. The FC matrices calculated for the individual time series are therefore called F_{REST1}, F_{TEST} ve F_{REST2}. (30).

Global efficiency

The graphic-based network analysis, described in detail in Section 2.3, is one of the most advanced methodologies in brain connectivity studies. The channels are considered as a set of vertices (V) and the PC coefficients are considered as weights assigned between the vertices on the set of edges (E) to create an undirected full weight graphic (*Figure 4*). FC metrics derived from each channels PC with the rest of the channels were investigated for each type of stimulus.

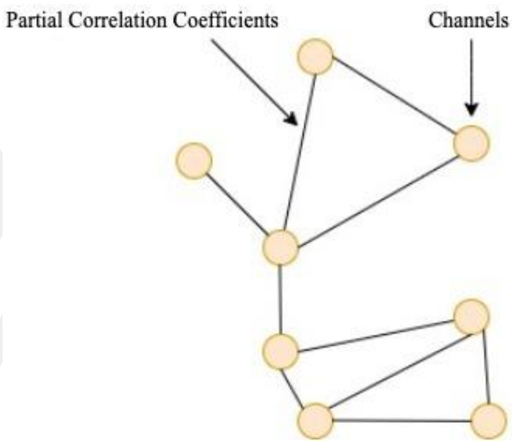


Figure 4: *Visual demonstration of Neural Connectivity*

Global efficiency (GE) can be evaluated for a wide variety of networks, including weighted graphs. The maximum possible GE occurs when all edges are present in the network. Since GE value is valid for working with weighted connections, in our case GE is calculated as,

$$GE = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{d_{ij}}$$

where dij is defined as the smallest sum of physical distances along all possible paths in the graph from channel i to channel j. For weighted graphs, stronger connection weights correspond to shorter lengths. Equation (1) generates values of GE in the range of [0,1].

4. RESULTS and DISCUSSION

In order to perform task induced brain activation analysis with GE metric, hemodynamic measurements were taken from the PFC with an fNIRS device while the Stroop task designed as described in previous Section 2.1 was performed. The experiment was completed by using 40 trials consisting of images of 4 different color names written in their own colors or in other colors. The images randomly and automatically appeared on the screen by using the Stroop code on Psytoolkit. Participants got 1 point for each correct match answer and hence the highest score was 40. They lost 2 points for each wrong answer while lost 1 points if they could not dial within the time (0,750 secs) required to answer between the two trials. While analyzing the parameters, firstly Stroop test results of each participant were downloaded from Psytoolkit.com as described in Section 2.2.1 and total score and experiment duration were calculated. After the scores of all subjects were calculated, the mean of Stroop task was 37,66 ± 2,11 points. The mean of response time (RT) was 30,78 ± 5,35 seconds. Then, the code used for GE calculation was run on MatLab for each participant. This code provides three different GE values for $Rest_1$, Test and $Rest_2$ periods. *Table 1* demonstrates behavioral and hemodynamic parameter results obtained during the experiment for all the participants.

Table 1: *Mean and Standard Deviation Values for Behavioral and Hemodynamic Parameters of All Subjects*

Parameters	Stroop Score	Response Time (s)	GE for HbO_2 $Rest_1$	GE for HbO_2 Test	GE for HbO_2 $Rest_2$
Mean	37,66	30,78	0,121	0,118	0,121
Std. Dev.	2,11	5,35	0,018	0,019	0,024

Considering the many studies that GE is associated with intelligence (32,33), cognitive ability (34, 35), and working memory (36*)*, each healthy individual was expected to have a higher GE value during the test compared to the resting moment during the test. After analyzing the parameters of all participants, it was realized that although there were no disease diagnoses, there were two different groups of participants. According to this, a group (2 female, 8 male) of participants had higher GE during the Test period compared to $Rest_1$ state; the other group (7 female, 8 male) had a lower GE amount in the testing state compared to the $Rest_1$. Because there is expected to be an increase in focus and working memory function during the Stroop task, seeing a relatively higher GE value during the Test time means that the expected increase in cognitive workload has occurred. However, seeing a relatively higher GE during the $Rest_1$ period could be a precursor to a number of disorders. Based on this, in our experiment that we wanted to do among healthy participants, it was realized that there may be a group that had not been diagnosed yet, but may have a neuropsychological disorder or focus problem. Therefore, the analysis was continued by making sure that there were two different groups. In order to distinguish these two groups precisely, the ratio (GE_{Test} / GE_{Rest1}) of the amount of GE obtained during the test (GE_{Test}) to the GE amount obtained during the $Rest_1$ (GE_{Rest1}) was calculated for each participant. The first group of those above 1 was called the High Ratio (GE ratio mean for HR = 1,198 ± 0,161), while the second group of those below 1 was called the Low Ratio (GE ration mean for LR = 0,859 ± 0,090). When Two Sample Independent T-Test was performed, the ratios showed statistically significant differences between these two groups (*Table 2*, $p= 6{,}8 \times 10^{-3}$). Moreover, when the $Rest_1$ and Test GE values of both groups were analyzed, a statistically significant difference was found again. Based on these hemodynamic data, it can be concluded with certainty that there are two different groups of participants in term of performance. It was explained in Section 2.3 that higher GE scores are associated with higher brain activity and more focused functioning. Based on this, it can be concluded that, the participants in the HR group focused on the task better because they had higher GE scores during the Test period; however, those in the LR group are relatively less focused as they have higher GE scores at $Rest_1$.

In order to associate the difference in hemodynamic activity to cognitive performance, a parameter named Neural Efficiency was computed. The neural efficiency hypothesis shows that some individuals must use a certain amount of mental resources for a given task, while others will achieve the same results with less mental effort. Thus, for the same output performance, two people can show different brain activities and, conversely, for the same brain activity, two people can show different output performances (37). In this research, Neural Efficiency of each participant was computed by dividing the total Stroop score to the total duration of the experiment. Hence, a calculation was made based on the time spent for a correct answer. When the distribution of GE_{Test} / GE_{Rest1} ratio was examined with Neural Efficiency, it was observed that a qualitative distinction existed between the two groups. Moreover, a linear relationship exists between Neural Efficiency and GE ratio parameter which implied that higher behavioral performance is associated with higher hemodynamic connection strength (*Figure 5*).

Table 2: *Comparison of Behavioral and Hemodynamic Data for Rest and Test Conditions Between High and Low Ratio Groups. The fifth column denotes the ratio of GE_{Test} to GE_{Rest1}. The P values indicate statistical significance between HR and LR for each parameter.*

High Ratio Group's Parameters						
	Stroop Score	**Response Time (s)**	**Neural Efficiency**	**GE for HbO_2 $Rest_1$**	**GE for HbO_2 Test**	**GE_{Test} / GE_{Rest1}**
Mean	37	27,607	1,357	0,111	0,133	1,198
Std. Dev.	2,539	3,678	0,152	0,010	0,021	0,161

Low Ratio Group's Parameters						
	Stroop Score	**Response Time (s)**	**Neural Efficiency**	**GE for HbO_2 $Rest_1$**	**GE for HbO_2 Test**	**GE_{Test} / GE_{Rest1}**
Mean	38,2	31,812	1,218	0,129	0,110	0,859
Std. Dev.	1,859	4,294	0,142	0,015	0,010	0,090

P Value	0,185	0,019	0,036	0,003	0,002	$6{,}8 \times 10^{-3}$

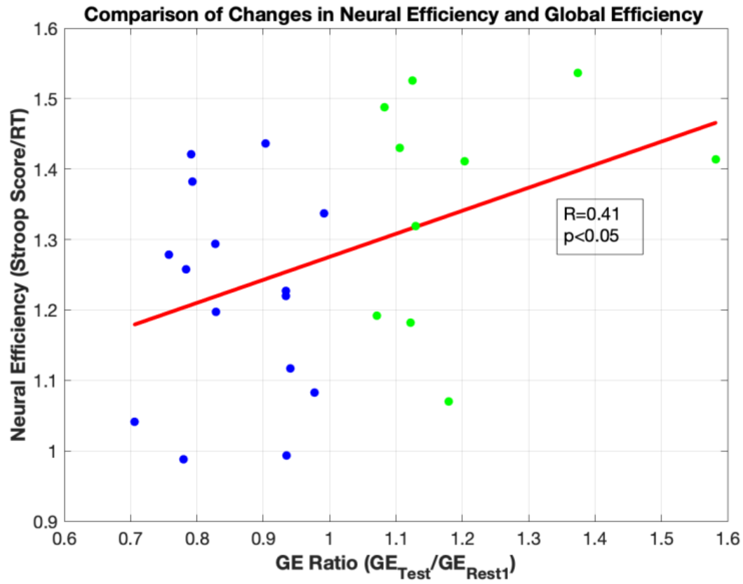


Figure 5: *Comparison of Changes in Neural Efficiency and Global Efficiency for All Participants. The graph shows clearly linear relationship exists between Neural Efficiency and GE ratio parameter.*

During this classification, the GE score obtained during $Rest_2$ was not taken into consideration, since it did not show any significant change. This may be because the brain that focused on the test was unable to disperse immediately this focus or stress within 30 seconds after the test. The control of this can be done by extending the duration of the $Rest_2$ period in subsequent studies.

When the behavioral and fNIRS (hemodynamic) results of these two groups were examined in detail, remarkable points were noticed. The experiment duration of the participants in the HR group (27,60 ± 3,67 seconds) was shorter than the total experiment time of the LR's (31,81 ± 4,29 seconds), and also these two time-series are statistically significantly different (in Two-Sided Unpaired T-test the p value is 0,018) (*Table 2*). This was a fairly significant one, because it was evidence that the group with higher GE values gave faster responses during testing. In other words, based on the GE score, the group with higher focus rate is able to give answers in a shorter time. Similarly, individuals with focusing problems are expected to spend longer periods for responses.

As the Stroop scores of both groups were examined, the average score of the HR group was 37 ± 2,53, whereas the average of the LR group was 38,2 ± 1,85. It was observed that these two-data series did not differ statistically significantly from each other (p = 0,184) (*Table 2*). However, when looking at Neural Efficiency values to calculate the time per correct response, the mean was 1,357 ± 0,152 for HR group and 1,218 ± 0,142 for LR group and they differed significantly between the two groups (p= 0,036). Neural Efficiency is a better indicator for distinguishing the two groups instead of taking consideration directly response time. The reason why the total experiment times of two groups is not significantly different may be because in our sample there were fewer (10 people) in the HR group and relatively more (15 people) in the LR group. In the future studies, the accuracy rate should be investigated again by taking more participants from the HR group and comparing the statistics. From another point of view, the Stroop task used was relatively easy as it was intended to be a version that every level could easily understand and do. Increasing the number of trials combined with a more compelling version in future studies could help achieve statistically clearer results.

In addition to parameter analysis, the code used in the GE score calculation also provides GE maps. The fNIRS device used during the experiments takes measurements from 16 channels and each of these 16 channels corresponds to a region on the PFC. The maps generated by the code were based on these 16 points, and the connectivity strength between each channel pair can be demonstrated in 16 x 16 matrices with colors. The colors are from navy to orange, orange indicates the strong connectivity while navy represents weak connectivity (*Figure 6*). There are some points to consider when reading these maps. Most regions (or in this case channels) in the brain of a healthy individual, who is not focused on anything, are in communication with each other; which can be resembled to common background neural activity. However, whenever the individual focuses on a topic or task, activation is expected only in regions that will take part in decision-making, background neural activity is suppressed (38*)*. If this otherwise it can be said that the focus is not fully occurred. Based on this, in the analysis of HR participants' maps, less yellow and orange were expected compared to resting periods during the test period. Similarly, during the map analysis of LR participants, less yellow and orange were expected during resting states, while more connectivity was expected to occur during the test. *Table - 3* and *Table - 4* contain representative GE map examples for both groups and these images support the focus schemes described above.

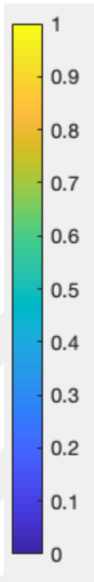


Figure 6: *Connectivity Values Corresponding to Colors in GE maps*

Table 3: *Representative Map Images for High Ratio Group*

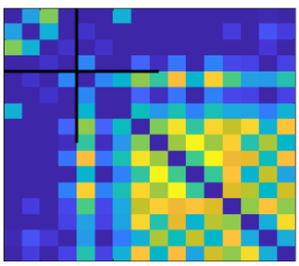
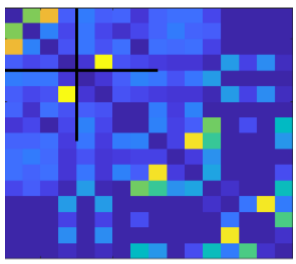
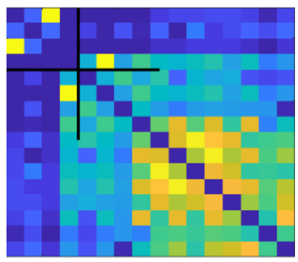
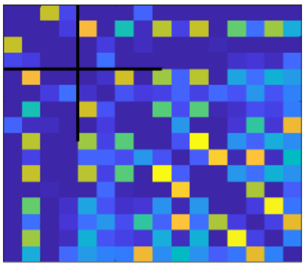
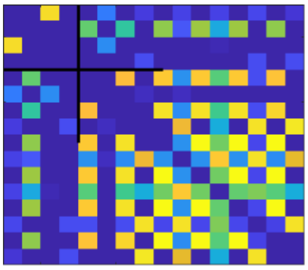
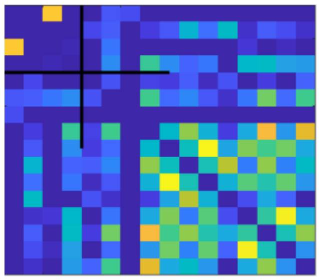
GE Map for Rest$_1$	**GE Map for Test**	**GE Map for Rest$_2$**
		
GE Score for Rest$_1$: 0,13	GE Score for Test: 0,15	GE Score for Rest$_2$: 0,14

Table 4: *Representative Map Images for Low Ratio Group*

GE Map for Rest$_1$	**GE Map for Test**	**GE Map for Rest$_2$**
		
GE Score for Rest$_1$: 0,16	GE Score for Test: 0,11	GE Score for Rest$_2$: 0,13

When the GE maps of all participants were examined, most of them were found to be consistent with the map reading method and analysis described above. In other words, in the maps of the HR group, there were fewer yellow and orange colors compared to resting states, as there were more direct connections during the test. In the map analysis of the LR group, more yellow and orange colors were seen during the test. These results support the results of previous studies and support the inferences made based on the changes in GE scores. Despite all these, no significant differences were observed in the GE maps of few participants. The reason for this may be different causes such as different focusing processes of individuals during the test, or focusing problems, hunger, sleeplessness etc. In the future studies in order to determine the true reason, measurements can be taken again from the same participants but different conditions, or the same metrics can be investigated in a larger cohort of subjects.

The consistency and significance of the results we obtained as a result of the Stroop test can be checked by adding another test to the protocol and interpreting it together. A second test will strengthen our results.

5. CONCLUSION

The Prefrontal cortex is a brain region that plays a central and executive role in attention, cognitive processing, and working memory. In psychiatric and neurological diseases, the daily activities of the individual can be seriously impaired in case of structural and / or functional disorders in this brain region. Therefore, examining this region with non-invasive functional imaging methods is crucial for understanding the dynamics of cognitive functions and also for early detection of changes related to the disease. In this study, a modified version of the color-word matching Stroop task was employed during fNIRS data collection from PFC. The aim was to explore the feasibility of an fNIRS derived functional connectivity metric, namely the Global Efficiency as a neural correlate of cognitive processes such as attention and focus.

During the experiments, fNIRS measurements were taken from 29 volunteer participants between the ages of 18-27, who were not diagnosed with any psychological or neurological diseases, while performing Stroop task (3 outlier participants' data eliminated). These hemodynamic results were analyzed by GE analysis and three different GE scores were obtained for $Rest_1$, Test and $Rest_2$ periods. Neural Efficiency metric was computed from behavioral performance data which integrates test score and reaction time in one metric. Neural Efficiency during Stroop performance was found to be linearly related to the functional connectivity strength of the PFC during the task. Overall, the results are demonstrated the sensitivity of fNIRS derived connectivity metrics to variations in cognitive performance. In many studies where GE and brain imaging methods were used together, it was expected that GE was directly proportional to the characteristics such as intelligence, working memory, cognitive ability. Therefore, a higher GE value was expected during the test compared to the rest time. During the analysis, it was noticed that participants were divided into two different groups based on whether their GE_{Test} scores were larger or smaller than their GE_{Rest1} scores. For a more precise classification, it was examined that the GE_{Test} / GE_{Rest1} ratio was below or above 1. As a result of the analysis, it was noticed that the participants in the group with a GE ratio above 1, called High Ratio group, completed the task in a shorter time on average. Conversely, participants with a GE ratio below 1, called Low Ratio group, were found to spend longer on the for the same task. Unfortunately, this divergent difference in experiment duration was not seen in the experimental scores. The average Stroop score of the participants in the LR group was higher than the HR's score. However, in these types of studies, we recommend using another score-related metric, such as Neural Efficiency, rather than analyzing using the experiment score directly. Neural Efficiency values, i.e. the time spent per correct answer, of these two groups are significantly different.

Moreover, when the GE connectivity maps that come from GE analysis code, of both groups were examined, it was observed that HR's were relatively more focused at the time of testing than resting states. However, in the maps of LR's, this focus is more often seen in resting states. In other words, if the first grouping method made according to whether the GE_{Test} value is greater or smaller than the GE_{Rest} value, the HR group, where direct connections and therefore focus were more visible, could be clearly distinguished when the GE maps were examined.

In the light of all these analyzes, it was concluded that the HR group, which has a higher GE score at the time of testing than the one in $Rest_1$, shows higher focus and completes the task faster. The group LR and whose GE score at the time of the test was lower than that of $Rest_1$, completed the task in a longer period of time, showing a lower focus. Similarly, when the Neural Efficiency values of the two groups were examined, the two groups were significantly different from each other. Based on these results, it is proposed that subjects with higher GE ratios during Stroop test have "higher focus, cognitive and inhibition ability" when compared to subjects with lower GE ratios. The functional connectivity seems to be more efficient in the task focused brain as higher connectivity scores are associated with higher Neural Efficiency and lower response durations. These results support the suitability of brain connectivity measures obtained from fNIRS as potential diagnostic biomarkers for differentiating and diagnosing cognitive disorders related to attention deficiency and impulsivity. Hence, we propose the GE metric and GE maps as a promising quantitative hemodynamic measure for the diagnosis and recognition of disorders, related to inhibition and attention such as cognitive impairments, impulsivity, learning difficulty while applying Stroop or similar tasks (5).

6. FUTURE WORK

In our future studies;

- A similar task-related study can be performed in different age groups to observe GE score changes in young, adult, and older individuals.
- Eye tracking can be added to the experimental design to identify problems with focusing.
- A similar study involving participants with and without the diagnosis of cognitive impairments can be observed and the GE score change can be observed.
- Before and after the use of methylphenidate from the participants diagnosed with cognitive impairments, a change in the GE score can be observed.
- Other neuropsychological tests, such as Stroop task, may be included in the study and the results may be reviewed together with psychiatrists. It can be investigated whether another test gives answers that support the current results. Thus, while physicians make an opinion about the diagnosis of the participants, it is observed whether the GE scores obtained as a result of the test support them.

BIBLIOGRAPHY

1. Foy H.J., Runham P., Chapman P., Prefrontal Cortex Activation and Young Driver Behaviour: A fNIRS Study, Plos One | doi: 10.1371/journal.pone.0156512, May 26, 2016

2. Joaquín M. Fuster, The Prefrontal Cortex, Fourth Edition 2008 Elsevier, p.267

3. Kane M. J., Engle R. W., The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective, Psychonomic Bulletin & Review 2002, 9 (4), 637-671

4. Stroop R. J., Studies of Interference in Serial Verbal Reactions, Journal of Experimental Psychology, 18, 643-662., 1935

5. Tatlıeşme B, Akın A., Test Correlated Brain Function Analysis with Global Efficiency During Stroop Task, http//fnirs.org, fNIRS 2018 meeting, Tokio, UK, 2018, https://fnirs2018.org/wp-content/uploads/2018/09/fNIRS2018_abstract.pdf, I-33

6. Rognoni T., Casals-Coll M., Sánchez-Benavides G., Spanish normative studies in young adults (Neronorma young adults project): Norms for Stroop Color—Word Interference and Tower of London-Drexel University tests, Neurologia. 2013 Mar;28(2):73-80. doi: 10.1016/j.nrl.2012.02.009. Epub 2012 May 30.

7. Wagner G., Sinsel E., Sobanski T., Köhler S., Cortical Inefficiency in Patients with Unipolar Depression: An Event-Related fMRI Study with the Stroop Task, Biol Psychiatry. 2006 May 15;59(10):958-65. doi: 10.1016/j.biopsych.2005.10.025. Epub 2006 Feb 3.

8. Veen V., Cameron S Carter C. S., Separating Semantic Conflict and Response Conflict in the Stroop Task: A functional MRI study, Neuroimage. 2005 Sep;27(3):497-504. doi: 10.1016/j.neuroimage.2005.04.042.

9. Byun K., Hyodo K., Suwabe K., Positive Effect of Acute Mild Exercise on Executive Function via Arousal-Related Prefrontal Activations: An fNIRS Study, NeuroImage 98 (2014) 336–345

10. Villringer A. and Chance B., Non-Invasive Optical Spectroscopy and Imaging of Human Brain Function, Trends Neurosci. (1997) 20, 435–442

11. Holper L., Scholkmann F., Wolf M., Between-Brain Connectivity During Imitation Measured by fNIRS, NeuroImage 63 (2012) 212–222

12. Plichta M.M., Herrmann M.J., C.G. Baehne, Fallgatter A. J., Event-Related Functional Near-Infrared Spectroscopy (fNIRS) Based on Craniocerebral Correlations: Reproducibility of Activation, Human Brain Mapping 28:733–741 (2007)

13. Zysset S., Schroeter M. L., Near-Infrared Spectroscopy Can Detect Brain Activity During a Color–Word Matching Stroop Task in an Event-Related Design, Human Brain Mapping 17:61–71(2002)

14. Plichta M.M., Herrmann M.J., C.G. Baehne, Fallgatter A. J., Event-related Functional Near-Infrared Spectroscopy (fNIRS): Are the Measurements Reliable?, Neuroimage. 2006 May 15;31(1):116-24. doi: 10.1016/j.neuroimage.2005.12.008. Epub 2006 Jan 30.

15. Rubinov M., Sporns O., Complex Network Measures of Brain Connectivity: Uses and Interpretations, Neuroimage. 2010 Sep;52(3):1059-69. doi: 10.1016/j.neuroimage.2009.10.003. Epub 2009 Oct 9.

16. Urs Braun U., Muldoon S. F.,Bassett D. S., On Human Brain Networks in Health and Disease, Curr Opin Neurol. 2009 August; 22(4): 340–347. doi: 10.1097/WCO.0b013e32832d93dd

17. V. Latora V., Marchiori M., Efficient behavior of small-world networks, Phys. Rev. Lett. 87(19), 198701 (2001)

18. Eka B., VerSchneiderb C., Narayana D.A., Global Efficiency of Graphs, AKCE International Journal of Graphs and Combinatorics 12 (2015) 1–13

19. Einalou Z., Maghooli K., Setarehdan S. K., Akin A., Graph Theoretical Approach to Functional Connectivity in Prefrontal Cortex via fNIRS, Neurophotonics 4(4), 041407 (Oct–Dec 2017)

20. Fox M. D., Raichle M. E., Spontaneous Fluctuations In Brain Activity Observed with Functional Magnetic Resonance Imaging, Nature Reviews | Neuroscience, 700 September 2007 | volume 8

21. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th Ed. Washington (DC): American Psychiatric Association; 2000, p.332

22. Berlot R., Metzler-Baddeley C., O'Sullivan M. J., Global Efficiency of Structural Networks Mediates Cognitive Control in Mild Cognitive Impairment, Frontiers in Aging Neuroscience, December 2016 | Volume 8 | Article 292

23. Zhang J., Wang J. Wu Q., Disrupted Brain Connectivity Networks in Drug-Naive, First-Episode Major Depressive Disorder, Biological Psychiatry, 2011-08-15, Volume 70, Issue 4, Pages 334-342

24. https://www.psytoolkit.org/experiment-library/stroop.html Date of Access: 15.11.2019

25. http://www.hemosoft.com.tr/en/page/products/electro-mechanical-systems/arges-cerebro-86.html#.XuGckEX7SUk Date of Access: 15.11.2019

26. Boas D. A., Gaudette T., Mandeville J. B., The Accuracy of Near Infrared Spectroscopy and Imaging during Focal Changes in Cerebral Hemodynamics, NeuroImage 13, 76-90 (2001)

27. Dadgostar M., Einalou Z., Setarehdan S. K., A. Akin A., Comparison of Denoising Algorithms in fNIRS, http//fnirs.org, fNIRS 2012 meeting UCL, London, UK, 2012; Functional Near Infrared Spectroscopy to Investigation of Functional Connectivity in Schizophrenia Using Partial Correlation, Universal Journal of Biomedical Engineering 2(1): 5-8, 2014

28. Dadgostar M., Einalou Z., Setarehdan S. K., A. Akin A., Classification of Schızophrenia Using SVM via Fnırs, Biomedical Engineering: Applications, Basis and Communications, Vol. 30, No. 2 (2018) 1850008 (8 pages) DOI: 10.4015/S1016237218500084

29. Erdoğan S. B., Yücel M. A., Akın A., NeuroImage 87 (2014) 490–504, p.490, 491

30. Dadgostar M., Einalou Z., Setarehdan S. K., A. Akin A., Functional connectivity of the PFC via partial correlation, Optik 127 (2016) 4748–4754, p.4750

31. Akın A., Partial correlation-based functional connectivity analysis for functional near-infrared spectroscopy signals, Journal of Biomedical Optics 22(12), 126003 (December 2017))

32. Li Y., Liu Y.., Jun Li J., Jiang T., Brain Anatomical Network and Intelligence, PLoS Computational Biology | www.ploscompbiol.org 2 May 2009 | Volume 5 | Issue 5 | e1000395

33. Heuvel M. P., Stam C. J., Kahn R.S., Efficiency of Functional Brain Networks and Intellectual Performance, Journal of Neuroscience, 2009 Jun 10;29(23):7619-24. doi: 10.1523/JNEUROSCI.1443-09.2009.

34. Gong G, He Y, Concha L, Mapping Anatomical Connectivity Patterns of Human Cerebral Cortex Using In Vivo Diffusion Tensor Imaging Tractography. Cereb Cortex 2009; 19:524–536.

35. Hagmann P, Cammoun L, Gigandet X, Mapping The Structural Core of Human Cerebral Cortex. PLoS Biol 2008; 6:e159

36. Bassett D.S., Bullmore E.T., Meyer-Lindenberg A., Cognitive Fitness of Cost-Efficient Brain Functional Networks. Proc Natl Acad Sci U S A 2009; 106:11747 – 11752

37. Neubauer, A.C., Fink, A., 2009. Intelligence and neural efficiency. Neurosci. Biobehav. Rev. 33, 1004–1023. http://dx.doi.org/10.1016/j.neubiorev.2009.04.001

38. Rubinov M., Sporns O., Complex network measures of brain connectivity: Uses and interpretations, NeuroImage 52 (2010) 1059–1069, p.1062

APPENDIX

```
bitmaps
  instruction1
  instruction2
  fixpoint
  yellowyellow
  yellowgreen
  yellowblue
  yellowred
  redyellow
  redgreen
  redblue
  redred
  greenyellow
  greengreen
  greenblue
  greenred
  blueyellow
  bluegreen
  blueblue
  bluered

table stroop
  "yellow yellow 2" yellowyellow 2
  "yellow green 1" yellowgreen 1
  "yellow blue   1" yellowblue   1
  "yellow red    1" yellowred    1
  "red yellow    1" redyellow    1
  "red green     1" redgreen     1
  "red blue      1" redblue      1
  "red red       2" redred       2
  "green yellow 1" greenyellow 1
  "green green   2" greengreen   2
  "green blue    1" greenblue    1
  "green red     1" greenred     1
  "blue yellow   1" blueyellow   1
  "blue green    1" bluegreen    1
  "blue blue     2" blueblue     2
  "blue red      1" bluered      1

task stroop
```

```
  table stroop
  keys l k
  delay 750
  show bitmap fixpoint # stimulus 1
  delay 750
  show bitmap @2 # stimulus 2
  readkey @3 750
  delay 750
  save BLOCKNAME @1 TABLEROW KEY STATUS RT
message instruction1
message instruction2
block test # this block is called "test"
  tasklist
    stroop 40 # run the stroop task 40 trials.
  End
```

Code of the Turkish version of the Stroop Task on Psytoolkit.org (https://www.psytoolkit.org/cgi-bin/psy2.6.1/edit?e=stroop_en_son)

Table I: *An example of the Stroop task data set of a participant downloaded from Psytoolkit*

test	red	yellow	1	5	1	3	750
test	blue	red	1	16	1	3	750
test	red	red	2	8	2	1	715
test	red	green	1	6	1	3	750
test	yellow	red	1	4	1	3	750
test	red	blue	1	7	1	1	682
test	green	blue	1	11	1	1	745
test	blue	red	1	16	1	1	673
test	yellow	green	1	2	1	1	680
test	blue	red	1	16	1	1	697
test	blue	blue	2	15	2	1	621
test	yellow	green	1	2	1	1	746
test	yellow	yellow	2	1	2	1	744
test	green	green	2	10	1	3	750
test	red	green	1	6	1	3	750
test	yellow	blue	1	3	1	3	750
test	green	yellow	1	9	1	3	750

test	green	green	2	10	1	3	750
test	yellow	blue	1	3	1	3	750
test	yellow	red	1	4	1	3	750
test	red	yellow	1	5	1	3	750
test	yellow	green	1	2	1	3	750
test	blue	yellow	1	13	1	3	750
test	green	yellow	1	9	1	3	750
test	blue	blue	2	15	2	1	625
test	blue	red	1	16	1	1	646
test	blue	blue	2	15	2	1	665
test	blue	red	1	16	1	1	719
test	green	green	2	10	1	3	750
test	yellow	red	1	4	1	3	750
test	yellow	green	1	2	1	3	750
test	green	green	2	10	1	3	750
test	green	yellow	1	9	1	3	750
test	yellow	red	1	4	1	1	696
test	blue	blue	2	15	1	3	750
test	yellow	red	1	4	1	3	750
test	green	green	2	10	1	3	750
test	red	green	1	6	1	3	750
test	blue	blue	2	15	1	3	750
test	green	red	1	12	1	3	750

Table II: *An example of the Stroop task data set of a participant that analyzed*

Name of the Word	**The Color the Word is Printed in**	**Stroop Color Match**	**Table Row Number**	**The Pressed Key Number**	**Correctness**	**Reaction Time**
yellow	blue	1	3	1	1	706
red	yellow	1	5	1	1	609
red	blue	1	7	1	1	499
green	yellow	1	9	1	1	493
green	yellow	1	9	1	1	497
green	green	2	10	2	1	603

green	red	1	12	1	1	585
yellow	yellow	2	1	2	1	669
green	blue	1	11	1	1	560
yellow	yellow	2	1	2	1	616
yellow	yellow	2	1	2	1	464
red	green	1	6	1	3	750
yellow	red	1	4	1	1	605
green	red	1	12	1	1	742
red	blue	1	7	1	1	659
yellow	blue	1	3	1	1	654
blue	yellow	1	13	1	1	661
green	yellow	1	9	1	1	554
blue	red	1	16	1	1	500
yellow	green	1	2	1	1	650
blue	red	1	16	1	1	576
red	green	1	6	1	1	552
blue	blue	2	15	2	1	564
blue	green	1	14	1	1	590
green	green	2	10	2	1	736
green	red	1	12	1	1	569
green	red	1	12	1	1	500
yellow	yellow	2	1	2	1	654
red	yellow	1	5	1	3	750
green	blue	1	11	1	1	555
green	red	1	12	1	3	750
red	green	1	6	1	1	730
blue	green	1	14	1	1	639
red	yellow	1	5	1	1	455
green	blue	1	11	1	1	542
blue	red	1	16	1	1	559
red	red	2	8	1	3	750
red	red	2	8	2	1	470
red	red	2	8	2	1	434
blue	blue	2	15	1	2	479
Wrong	**(-2) x1 = - 2**					
Time-out	**(-1) x 4 = - 4**					

Total Score	40 – 6 = 34				Total Time	23930

Table III: *All the behavioral and hemodynamic data set of all the participants*

Subject Code	Score	Time (s)	Neural Efficiency	GE for HBO2 REST1	GE for HBO2 TEST	GE for HBO2 REST2
1	38	26,58	1,430	0,104	0,115	0,092
2	34	23,93	1,421	0,121	0,096	0,108
3	35	23,81	1,470	0,132	0,100	0,108
4	38	36,51	1,041	0,160	0,113	0,133
5	37	42,58	0,869	0,100	0,113	0,121
6	36	32,23	1,117	0,118	0,111	0,104
7	40	28,94	1,382	0,140	0,111	0,108
8	36	33,64	1,070	0,096	0,113	0,165
9	38	26,87	1,414	0,110	0,174	0,132
10	40	26,89	1,488	0,121	0,131	0,104
11	32	27,08	1,182	0,131	0,147	0,138
12	37	30,16	1,227	0,121	0,113	0,104
13	38	28,82	1,319	0,100	0,113	0,113
14	38	31,40	1,210	0,092	0,092	0,096
15	40	27,86	1,436	0,114	0,103	0,096
16	34	22,29	1,526	0,104	0,117	0,119
17	40	31,81	1,258	0,117	0,092	0,104
18	36	30,07	1,197	0,146	0,121	0,100
19	39	41,55	0,939	0,153	0,148	0,156
20	40	32,80	1,220	0,107	0,100	0,092
21	38	28,43	1,337	0,115	0,114	0,163
22	40	30,92	1,294	0,139	0,115	0,114
23	40	40,28	0,993	0,124	0,116	0,158
24	38	26,92	1,411	0,113	0,136	0,153

25	36	23,44	1,536	0,115	0,158	0,119
26	40	33,55	1,192	0,113	0,121	0,103
27	38	29,72	1,279	0,132	0,100	0,133
28	38	35,09	1,083	0,133	0,130	0,113
29	38	38,45	0,988	0,150	0,117	0,169
Mean	37,66	30,78	1,253	0,121	0,118	0,121
St, Dev	2,11	5,35	0,182	0,018	0,019	0,024

Table IV: *Parameters for High Responders*

Subject Number	**Stroop Score**	**Time (s)**	**Neural Efficiency**	**GE for HbO_2 $Rest_1$**	**GE for HbO_2 Test**	**GE_{Test} / GE_{Rest1}**
1	38	26,58	1,430	0,104	0,115	0,092
8	36	33,64	1,070	0,096	0,113	0,165
9	38	26,87	1,414	0,110	0,174	0,132
10	40	26,89	1,488	0,121	0,131	0,104
11	32	27,08	1,182	0,131	0,147	0,138
13	38	28,82	1,319	0,100	0,113	0,113
16	34	22,29	1,526	0,104	0,117	0,119
24	38	26,92	1,411	0,113	0,136	0,153
25	36	23,44	1,536	0,115	0,158	0,119
26	40	33,55	1,192	0,113	0,121	0,103
Mean	37	27,607	1,357	0,111	0,133	0,124
Std. Dev.	2,539	3,678	0,152	0,010	0,021	0,023

__Table V:__ Parameters for Low Ratio Group

Subject Code	Stroop Score	Time (s)	Score/Time	GE for HbO_2 $Rest_1$	GE for HbO_2 Test	GE_{Test} / GE_{Rest1}
2	34	23,930	1,421	0,121	0,096	0,108
4	38	36,510	1,041	0,160	0,113	0,133
6	36	32,230	1,117	0,118	0,111	0,104
7	40	28,940	1,382	0,140	0,111	0,108
12	37	30,157	1,227	0,121	0,113	0,104
15	40	27,858	1,436	0,114	0,103	0,096
17	40	31,807	1,258	0,117	0,092	0,104
18	36	30,071	1,197	0,146	0,121	0,100
20	40	32,797	1,220	0,107	0,100	0,092
21	38	28,426	1,337	0,115	0,114	0,163
22	40	30,916	1,294	0,139	0,115	0,114
23	40	40,282	0,993	0,124	0,116	0,158
27	38	29,719	1,279	0,132	0,100	0,133
28	38	35,092	1,083	0,133	0,130	0,113
29	38	38,449	0,988	0,150	0,117	0,169
Mean	38,2	31,812	1,218	0,129	0,110	0,120
Std. Dev.	1,859	4,294	0,142	0,015	0,010	0,025

RESUME

Personal Information

Name	Burçin	Surname	Tatlıeşme
Birth Place	Ankara	**Birth Day**	01/01/1994
Nationality	T.C	**Phone Number**	0535 024 51 97
E-mail	burcin.tatliesme@acibadem.edu.tr ; burcintatliesme@gmail.com		

Education

	Institution	Graduation Year
Undergraduate	Istanbul Bilgi University	2017
High School	Bahçelievler Anatolian High School	2012

Experience

Position	Organization	Duration (Year – Year)
1. Covid-19 Project Personnel	Health Institutes of Turkey	2020-Present
2. Business Development	Respo Gadgets	06.2018 – 10.2018
3. Export, Import and Purchasing Manager	Sitopsi Medical & Pharmaceutical Co. Ltd.	01.2018 – 04.2018

Language	Reading	Speaking	Writing
English	Very Good	Good	Very Good

Foreign Language Examination Grade									
KPDS	ÜDS	IELTS	TOEFL	TOEFL IBT	TOEFL CBT	CAE	CPE	YÖKDİL	YDS
								81,250	

KPDS: Kamu Personeli Yabancı Dil Sınavı; ÜDS: Üniversitelerarası Kurul Yabancı Dil Sınavı; IELTS: International English Language Testing System; TOEFL IBT: Test of English as a Foreign Language-Internet-Based Test TOEFL PBT: Test of English as a Foreign, YDS: Yabancı Dil Seviye Tespit Sınavı

Language-Paper-Based Test; TOEFL CBT: Test of English as a Foreign Language-Computer-Based Test; FCE: First Certificate in English;

CAE: Certificate in Advanced English; CPE: Certificate of Proficiency in English

	Quantitative	Equally Weighted	Verbal
ALES Note	75,72923	80,83011	78,52606

Computer Skills

Program	Ability to use
Microsoft Office Programs	Very Good
Latex	Good