Çocuklarda İşitsel Oddball Paradigması Esnasında Prefrontal Korteks Oksijenlenmesinde Cinsiyetin Etkileri

Gender Effects On Prefrontal Cortex Oxygenation Levels During Auditory Oddball Task In Children

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***Özetçe*—Bu çalışmada, prefrontal korteks oksijenlenmesinde cinsiyet etkileri araştırılmıştır. Bilişsel test olarak işitsel oddball paradigması uygulanmıştır. Prefrontal korteks oksijenlenmesi fonksiyonel yakın kızılötesi sprektroskopisi (fNIRS) kullanılarak kandaki oksijenlenmenin değişimine göre belirlenmiştir. fNIRS kayıtları iki uyaranın rastgele kullanıldığı (hedef ve standart) oddball paradigması ile alınmıştır. Deneklerden hedef sesleri duyduklarında butona basmaları istenmiştir. 12 sağlıklı erkek çocuk ve 9 sağlıklı kız çocuk çalışmaya dahil edilmiştir. Sonuç olarak; erkek katılımcıların işitsel oddball testi sırasında kız katılımcılardan daha fazla prefrontal aktivasyon gösterdiği gözlenmiştir. Bu sonuçlar cinsiyetin prefrontal kortex oksijenlenmesinde etkili olduğunu göstermektedir. Bu durum fNIRS kullanarak yapılan beyin fonksiyonu çalışmalarında cinsiyet eşleştirmenin önemli olduğunu göstermektedir.**

Anahtar Kelimeler—işitsel oddball paradigması; cinsiyet etkisi; fonksiyonel yakın kızılötesi spektroskopisi.

***Abstract*— In this study, our aim was to investigate gender effects on prefrontal cortex oxygenation. Auditory oddball paradigm used as cognitive task. Prefrontal cortex oxygenation is assessed by monitoring changes in blood oxygenation using functional near-infrared spectroscopy (fNIRS). The fNIRS were recorded during the 'oddball' paradigm in which two stimuli (target and standard) were presented in random order. Subjects were asked to press a button in response to the**

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target stimulus. 12 male healthy children and 9 female healthy children were included the study. As a result; it is observed that the males exhibited higher prefrontal activation during auditory oddball task than females. This results suggest that gender had an effect on prefrontal cortex oxygenation therefore gender matching is important for studies of brain function using fNIRS.

Keywords—auditory oddball paradigm; gender difference; functional near infrared spectroscopy.

I. INTRODUCTION

Noninvasive neuroimaging modalities, such as magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), positron-emission tomography (PET), functional near-infrared spectroscopy (fNIRS) and electrophysiological techniques are recently used for evaluation of gender differences during cognitive tasks. While some of these brain imaging studies described differences in response of both gender to the related cognitive tasks [1,2], some other studies illustrated no gender differences [3].

Fujimoto et al. demonstrated significant age and gender related differences in glucose metabolism of brain in healthy subjects by using [18F] fluoro-deoxy-glucose PET (FDG-PET) imaging [4]. In many studies of gender differences in brain glucose metabolism, it has been shown that female subjects showed significantly higher metabolism than in males especially in particular brain regions [5]. Speck et al. examined gender differences in brain activation by using fMRI and they found females showed activation predominantly in the left hemisphere while male subjects showed right sided dominance during working memory tasks [6].Similarly Bell et al., utilized fMRI to examine the effect of gender on regional brain activity during a motor task and three cognitive tasks including working memory, word generation task and spatial attention task, their findings showed gender differences change depending on the task [7]. In this current study we investigated neuroimaging profiles of healthy children with optical brain imaging using functional near-infrared spectroscopy (fNIRS). fNIRS measures event related hemodynamic response of the brain with concentration changes of oxygenated and deoxygenated hemoglobin. fNIRS provides advantages due to its safety, sensitivity, cost-effectiveness, tolerance to body motion thus is considered suitable for the clinical evaluations of children. Among imaging modalities, fNIRS provides robust advantages due to its compactness, cost-effective and tolerance to body motion and accessibility [8]. Izzetoğlu et al. indicated that cognitive activities such as attention, working memory, problem solving, etc.

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can be assessed by fNIRS technology robustly [9]. Because the prefrontal cortex (PFC) is associated with the level of alertness and attention, in these attention related task we focused on alterations in PFC activity with fNIRS. Gender differences observed during cognitive tests, including emotional activation task [2], maze tasks [10], n-back tasks [11], spatial-based working memory tasks [12]. Marumo et al investigated characteristics of hemodynamic response during an emotional activation task and evaluated gender differences. They found females showed significantly increased change in oxy-hemoglobin relative to men in the right prefrontal cortex [2]. Li et al. investigated gender differences during verbal n-back tasks by using fNIRS and emphasized the importance of gender in hemodynamic response evaluations of PFC [12].

In this study, we used fNIRS to provide new insights into the evolution of distinction between genders in terms of oxygenation of PFC during an auditory oddball attention task.

II. METHODS

A. *Participants*

The study was conducted on 12 male healthy children with a mean age of 9.63 (SD 2.06, range 7-12 years) and 9 healthy female children with a mean age of 10.35 (SD 1.40, range 7-12 years). Participants underwent a standard clinical assessment comprising neurological, endocrine and psychiatric evaluations and no history of psychiatric or neurological disorder, were enrolled in the study. The Wechsler Intelligence Scale for Children-Revised (WISC-R) [13]. full IQ scores of subjects were all over 80. All subjects were right-handed had normal hearing functions. The hearing functions tested with Rinne and Weber test. The research protocol was approved by the ethics committees of the University of Erciyes, and was in accordance with the latest version of the Declaration of Helsinki. All participants assented to participate in the study. Written consent was obtained from the parents.

B. *Stimuli and Protocol*

fNIRS recordings were obtained while participants performed the auditory ‘oddball’ paradigm. In this study 160 auditory stimuli that contain standard (2000 Hz) and target (1500 Hz) trials were presented in a random order. The target trials comprised 20% of the whole stimuli. The inter-stimulus intervals were randomized between 1250 and 2500 msec. Prior to the first run of the experiment, the participants were asked to respond target trials by pressing the button. During the experiment the participants instructed not to move, speak, or blink too much in order to avoid noises and stabilize the blood flow in fNIRS channels.

C. *fNIRS Data Acquisition*

In this study, we used a 16 channel (CH) continuous wave fNIRS system that has four sources with two different wavelengths (730 and

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850 nm) and ten photo detectors. Figure 1 shows the CH locations on the fNIRS probe. Hemodynamic changes were calculated using the modified Beer–Lambert law [14]. The sampling frequency was 2Hz. First, the raw fNIRS intensity measurements were low-pass filtered with a cut-off set to 0.14 Hz [15] to remove noises derived from movement artifacts, heart pulsation and respiration. Then data of each channel were averaged across 32 target responses for each subject. Target responses identified 3 s before the target stimuli period onset to 10 s after the target stimuli. Grand average of oxy-Hb responses of one male and one female showed in Figure 2.

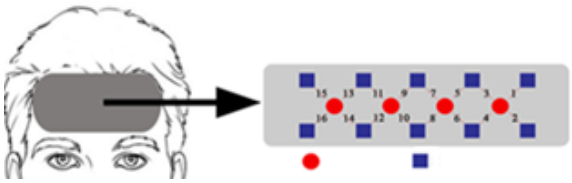
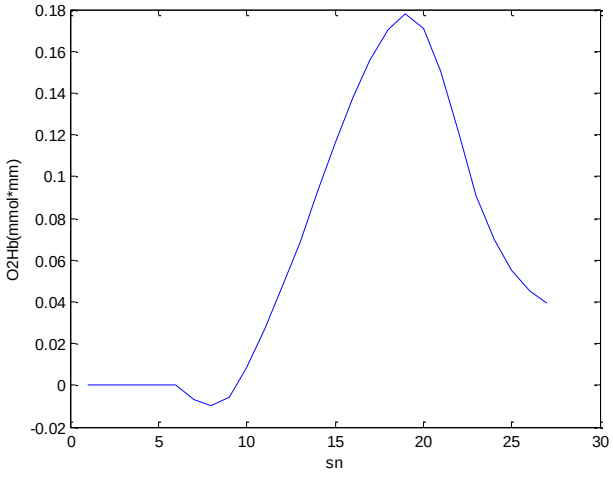


Figure 1. The source-detector locations on the fNIR probe.

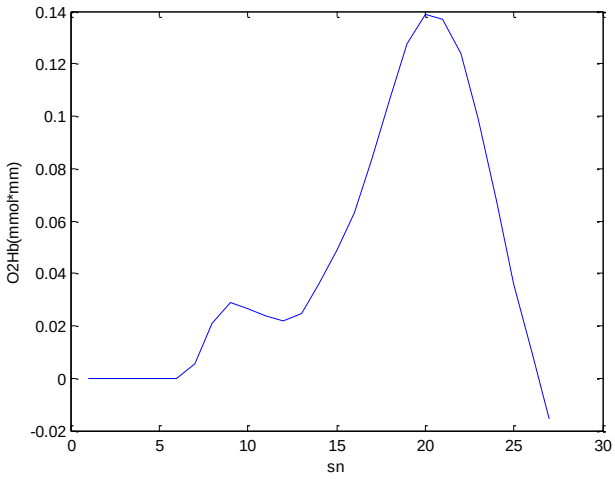
D. fNIRS Data Analysis

In this study because of its high sensitivity and reliability, we focused on the oxy-Hb signal [16]. The average of the integral value of oxy-Hb was calculated for covered all channels in PFC (CH 1 to CH 16).

Grand average of each CHs for 12-male and 9-female group calculated. For statistical analysis, among the groups we performed Mann Whitney U test because there were two independent groups and the data were not normally distributed. In each channel we assessed the integral value of oxy-hbo signal.



(a)



(b)

Figure 2. Grand average of oxy-Hb target responses of a male (a) and female (b) subject.

	Male	**Female**	**p**
Int- oxy-hbo	1,838 ± 0,54	1,219 ± 0,25	0,023

Table I. Mean, standard deviation and statistical analysis of integrated oxy-Hb for each ROI.

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III. RESULTS

We assessed the group difference in integral value of oxy-Hb signals with Mann Whitney U test. Table 1 shows concentration change of integral values of oxy-hbo among with group statistics. Descriptive values obtained by data analysis were expressed as means±S.D. (standard deviation). Differences were considered to be statistically significant if they had a probability of less than 0.05 ($p<0.05$).

IV. DISCUSSION

This study was designed to determine effects of gender on brain oxygenation patterns during auditory oddball paradigm. We found that males exhibited higher prefrontal activation during auditory oddball task than females in prefrontal cortex. So gender influenced performance on auditory oddball task. The reasons for this finding may be attributed to functional or structural differences in brain for both groups. Also researchs have demonstrated that sex hormones were implicated in general cognitive status, specifically in executive functions [17].

In literature, a range of cognitive tasks evaluated for investigating gender influences on prefrontal cortex oxygenation levels. While some of these studies showed females' oxy-hbo levels were higher than males' some other studies illustrated males' oxy-hbo levels were higher than females. It was depending on cognitive task. For instance, females showed better performance in emotional tasks [2], while males show better performance in maze tasks [11]. We selected an easy, short task contains standard and target paradigm with random sequence that can be appropriate for children. The test is related to attention so appropriate for assessment of prefrontal cortex.

Because of the increased number of children with psychosomatic, behavioral, and psychiatric disorders visiting outpatient clinics, in this study we choose children participants. This results suggest that gender had an effect on individual variability of fNIRS signals in response to auditory stimuli therefore gender matching is important for studies of brain function using fNIRS.

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