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Effects of Gender, Education and Non-inverting Electrode Sites on P300 Auditory Event Related Potential in Healthy Subjects

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Abstract

Objective: Event-related potentials (ERPs) are among the most useful and dynamic tools for monitoring information flow in the brain. The auditory P300 is a well-established ERP component in the neurophysiological assessment of cognition-related processes. In this study, we evaluated effects of gender, level of education and non-inverting electrode sites on P300 ERP parameters (latency and amplitude) in healthy subjects.

Materials and Methods: In this descriptive, analytical and non-interventional study, P300 potentials were measured in oddball paradigm using two-tone burst stimuli (1000 & 2000 Hz) in 25 healthy females and 25 healthy males with different levels of education (diploma and bachelor's degree), at Fz and Cz non-inverting electrode sites.

Results: At Cz site, compared to Fz site, the mean P300 latency was significantly shorter (p=0.002) and the mean P300 amplitude was significantly larger (p=0.001) in both males and females. Amplitude, at Cz site, was significantly larger in females (p=0.039). There was no significant difference between two levels of education in both genders at both electrode sites (p>0.05).

Conclusion: Significant increase in P300 latency and decrease in its amplitude at Fz site are associated with its related neural generators. The proximity of the Cz site to these neural generators, leads to a faster auditory information processing (shorter latency) and larger amplitude.

Keywords: *Event-related Potential, P300, Amplitude, Latency, Gender, Education*

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Introduction

Event-related potentials (ERPs), as cerebral responses to various external stimuli, are associated with reception and processing of sensory information, as well as higher level cognitional events, such as selective attention and memory [1]. ERPs provide objective measurable parameters somehow reflecting cognitive functions [2].

An ERP component is defined by its polarity, latency, scalp distribution, amplitude and relation to experimental variables [1]. The latency of ERP indicates the duration of processing, and its amplitude refers to the extent of neural resources involved in cognition [1]. P300 is conventionally recorded through the oddball measurement paradigm with two different acoustic signals [3]. In this paradigm, which has been used most frequently in clinical research, presentations of frequent stimuli are interrupted by a deviant infrequent stimulus.

Generally, oddball paradigm excites two distinct responses. A positive-going waveform with relatively short peak latency, called P3a, which is followed by the frequent non-target stimulus. The second part, called P3b, is followed by the target infrequent stimulus and its peak appears about 300 milliseconds after the stimulus presentation [1, 4, 5].

P300 may be recorded simultaneously over widespread areas of the scalp by multiple and relatively independent generators [1]. The possible major foci of P300-generating centers are hippocampus, amygdala, thalamus, superior temporal sulcus, ventrolateral prefrontal cortex and probably intraparietal sulcus [1, 4].

P300 latency is thought to be an index for classification speed, which is proportional to the time required to detect and evaluate a target stimulus [4]. P300 amplitude is related to working memory updating and is also sensitive to attentional resources during a task [4]. Therefore, reduction in P300 amplitude and prolonged P300 latency may demonstrate impairment and abnormalities in cognitive performance [2].

Tsolaja et al. (2015) demonstrated that males respond faster than females [6]. Additionally, they proposed that the level and the location of the maximum intensity of sources are different between genders. However, they did not consider the effect of age accurately.

Steffensen et al. (2008) showed that females have greater P300 responses than males [7]. However, their investigation was conducted with the use of visual stimuli. In total, several studies have shown that gender can affect the response of p300.

In this study, we aimed to evaluate the effects of gender, education and non-inverting electrode sites on amplitude and latency of P300 auditory event-related potential in Iranian young healthy adults. Although several groups have directly or indirectly studied the effects of gender and electrode site on P300, based on our knowledge, effects of education has not been assessed on a homogeneous population.

Materials and Methods

Participants

This work was a descriptive, analytical and non-interventional study. Fifty healthy subjects, including 25 males and 25 females, with the mean age of 29.68 ± 5.12 years were selected using available sampling, from Akhavan Comprehensive Rehabilitation Center, Rehabilitation and Social Welfare, University of Tehran. All patients aged between 20 and 40 years old, with normal peripheral hearing (bilateral hearing thresholds ≤ 20 dBHL, bilateral tympanogram type A and normal acoustic reflexes in both ears) as well as no history of any neurological, hearing and mental disorders or traumas and right-handed. Also, those who had taken any sedatives, antidepressants or neuroleptics, 48 hours before the evaluation, were excluded from the study. All subjects were informed about the nature and purpose of the study and signed the informed consent form.

Experimental protocol

All subjects underwent an ear, nose, and throat examination and pure-tone audiogram was recorded, using an AC40 audiometer (Interacoustics, Denmark) in a soundproof booth (TDH-39). Middle-ear function and acoustic reflexes were also tested (Madsen Tympanometer, model Zodiac 901, Denmark).

Electrode sites were cleansed and reference (inverting) electrodes were placed on the right and left mastoids, connected to input 2 of channels 1 and 2 of the pre-amplifier. Active (non-inverting) electrodes were placed on Cz and Fz sites and connected to input 1 of channels 1 and 2 of pre-amplifier. Finally, the ground electrode was placed on Fpz site.

In order to eliminate the ocular movements and blinking artefacts, subjects were asked to close their eyes and try to keep their eyes fixed during the recording. The impedance of each electrode was maintained below 5 kiloohms and the impedance between electrodes was kept below 2 kiloohms. The subjects lied down comfortably with response keypads placed in right hand and the ER-3A earphones on both ears.

We used tone burst signals with alternating polarity and a hearing sound level of 75 dBHL. We applied auditory oddball paradigm with two stimuli and different frequencies. Target stimulus, at a frequency of 2000 Hz and with a probability of 20%, was represented randomly between a background repeated standard stimulus with a frequency of 1000 Hz and a probability of 80%.

Electroencephalograms were recorded through a band-pass filter (0.1 to 30 Hz), at a rate of 0.9/sec, with 200 sweeps (160 standard stimulus sweeps and 40 target stimulus sweeps). The subjects were asked to pay attention to the target stimulus and were instructed to press the response key as soon as hearing that. A short practice trial was tried before each main session. In this study, P300s were recorded using ICS Charter Evoked Potential, GN Otometrics (USA).

Statistical analysis

Statistical analysis was performed using IBM SPSS 16 software. Mean and standard deviation of the P300 potentials were calculated. Kolmogorov-Smirnov approach was applied to test the normal distribution. Absolute latency and amplitude of P300 in Cz and Fz sites were compared between males and females using independent t-test. The effect of electrode site on latency and amplitude of P300 potentials in both groups was evaluated using paired T-test. The P300 parameters (latency and amplitude) in Cz and Fz sites were compared between subjects with diploma and bachelor degrees, using independent t-test.

Results

The average age of participants (25 males and 25 females) was 29.68 ± 5.12 years, with a minimum of 26 and a maximum of 28 years. Among the participants, 22 (44%) persons had diploma and 28 (56%) persons had bachelor's degree.

Absolute latency and (millisecond) and amplitude (microvolt) of P300 at Fz site were 286.43 ± 20.64 and 8.22 ± 1.97, respectively. At Cz site, the values were 282.29 ± 20.21 and 11.97 ± 2.99, respectively.

The effect of non-inverting electrodes site on latency and amplitude of P300 was analyzed using paired T-test and results showed that both in females and males, P300 latency (p=0.041 in females and p=0.018 in males) and amplitude (p<0.001 in females and p<0.001 in males) are different between Cz and Fz sites. This difference was more obvious between the amplitudes (Table 1).

The comparison of P300 parameters (latency and amplitude) between male and female subjects using independent t-test in both electrode sites showed that gender affects only the amplitude at Cz site (Table 2).

The comparison of P300 parameters between education levels using independent t-test showed no significant effect of education level on p300 latency and amplitude (Table 3).

The effect of gender and educational level on latency and amplitude of P300 was analyzed using regression and results are shown in Table 4.

Table 1. Analysis of the effect of the electrode sites on P300 parameters

Female	Mean±SD	(*p*-value)
Cz latency	277.42±42	
Fz latency	282.10±25.59	0.041*
Cz Amplitude	13.13±3.16	
Fz Amplitude	8.41±1.99	<0.001*
Male	**Mean±SD**	**(*p*-value)**
Cz latency	287.56±14.06	
Fz latency	291.138±12.98	0.018*
Cz Amplitude	10.72±2.29	
Fz Amplitude	8.02±2.02	<0.001*

*statistically significant.

Table 2. Analysis of the effect of the gender on P300 parameters

P300 Parameters	Female*Male (*p*-value)
Cz latency	0.210
Cz Amplitude	0.039*
Fz latency	0.275
Fz Amplitude	0.633

*statistically significant.

Table 3. Analysis of the effect of the education level on P300 parameters

P300 Parameters	Diploma*Bachelor (*p*-value)
Cz latency	0.212
Cz Amplitude	0.568
Fz latency	0.927
Fz Amplitude	0.323

Table 4. Analysis of the effect of gender and education on P300 parameters

		B	(*p*-value)
P300 latency at Cz electrode site	Constant	9.139	0.266
	Gender	282.40	0.00*
	Education level	−8.72	0.29
P300 latency at Fz electrode site	Constant	279.23	0.00
	Gender	8.62	0.318
	Education level	−3.56	0.679
P300 amplitude at Cz electrode site	Constant	16.24	0.00
	Gender	−2.46	0.043*
	Education level	−0.402	0.731
P300 amplitude at Fz electrode site	Constant	10.343	0.00
	Gender	−0.492	0.548
	Education level	−0.890	0.285

*statistically significant

Discussion

In this study, in order to understand the effects of gender, level of education and non-inverting electrode sites on P300 parameters, we evaluated 50 healthy adult subjects (25 male and 25 female) with two different educational levels, diploma and bachelor's degree.

Our results showed significant differences between P300s at Cz and Fz sites. At Fz position, P300 latency was greater and its latency was shorter. Additionally, at Cz position, P300 amplitude was significantly different between males and females. This finding may show the faster and greater ability of women's brain in updating the working memory and allocating more attentional resources during active tasks.

Our results are in contrast with Polish et al. study (1986) which assessed P300 parameters in 100 healthy subjects (50 male and 50 female) and reported no significant differences between genders and electrode sites [8]. In this regard, one of the most probable reasons could be the nature of applied tasks.

Polish et al. instructed the subjects to move the index finger of their right hand whenever they detected a target tone, while in our study, the subjects were asked to press the button as soon as they detected the target tone. It is argued that different methods are associated with varying cognitive processes and attention demands [3].

Furthermore, unlike Polish et al., we homogenized our sample in term of handedness, because the hand dominance is associated with the speed of information processing in the brain hemispheres [9]. Also, the differences between the results may be attributed to the difference in stimulus (intensity and duration) and acquisition parameters (bandpass filters).

In another study by Franco et al. (2001), 25 healthy individuals with ages between 22 and 58 years were evaluated and no significant differences were reported between P300 parameters, based on gender and non-inverting electrode sites [10]. However, in our study, P300 parameters were significantly different between Cz and Fz sites. This contradiction may be due to the difference in the used tasks. In Franco's study, subjects were instructed to count the target stimulus which is more difficult than pressing a button upon detecting the target stimulus [3].

In a study by Costa et al. (2002), P300 was investigated in 75 healthy subjects (50 females and 25 males) with ages between 8 and 11 years. Contrary to our results, they demonstrated that there were no statistically significant differences in P300 latency and amplitude between females and males [11]. In this case, one possible reason could be the difference in the studied age range.

The average P300 latency changes approximately 20 ms per year. In the young population, due to increased data processing speed, P300 latency is reduced [3]. On the other hand, Costa et al. asked subjects to respond to counting the target stimuli silently which is different from our task. When the subjects silently count the targets, P300 latency and amplitude are larger than when they press a button [3].

Generally, it is likely that the different results between our study and studies mentioned above, is due to the impact of menstrual cycle on late event-related potentials, so it is recommended to consider this factor in future studies in this field.

Duarte et al. (2009) reported significant differences between P300 latency and amplitude at Cz and Fz sites. Although they did not control the effect of age, their results are in accordance with ours. It can be justified that in younger individuals the scalp distributions of P300 response are greater in central/parietal regions. However, it should be borne in mind that as age increases, the topography of the P300 response expands to the frontal regions [3].

We investigated the effects of education level on P300 parameters, and according to our knowledge, this is the first time that this issue is investigated. In this case, although the results were not clear, however, it suggests that in the wave-based assessments, several factors must be considered.

Conclusion

Our results showed that P300 auditory event-related potential is influenced by miscellaneous factors, such as age, gender, recording electrodes position and maybe, education level. More detailed studies will elucidate the impact of these factors better.

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