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THE VARIABILITY IN P300 COGNITIVE EVOKED POTENTIAL AMPLITUDE IN THE AUDITORY ODDBALL PARADIGM

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SUMMARY

One of the best-studied responses of cognitive evoked potentials is a so-called “P300”, the late positive wave complex that occurs about 300-500 ms after the stimulus. It is obtained when the subject’s attention is focused on a signal that is rare, especially if the signal has a motivational or emotional meaning. In the study of P300 potential, we followed the variations of potential amplitude and latency, so the objective was to examine whether there is a difference in Fz and Cz amplitudes of auditory induced cognitive evoked P300 potential depending on the performance of oddball tasks, both in male and female subjects. The study included 60 subjects (30 female respondents and 30 male respondents). P300 potential is induced by the auditory "oddball" paradigm with 80% of non-target and 20% of target stimuli that are presented to the patient through headphones. The target tones are high tones of 2000 Hz. The standard, 1000 Hz tones the respondent should ignore but when he hears the target tones the respondent should press the button on the special handle. The value of Fz and Cz amplitudes both in male and female subjects obtained in the classical "oddball" paradigm when the subject reacted to the signal by pressing the key with the dominant (right) arm were statistically significantly lower ($p>0,05$) than the values of Fz and Cz amplitudes obtained when the key was pressed by the non-dominant hand. Based on this experiment it can be concluded that both in male and female subjects the performance of oddball tasks does not affect the amplitude of P300 cognitive evoked potentials.

Key words: P300, cognitive evoked potentials, oddball paradigm.

INTRODUCTION

The idea that a stimulus causes a specific response in the central nervous system was presented in 1875 by Richard Caton at the meeting of the British Medical Association, where he gave a lecture entitled "Electrical brain activity" in which he presented his observations on the changes in the brain of rabbits and monkeys under the influence of light (evoked activity). The term evoked activity denotes electrical or magnetic activity that is time associated with the stimulus, as opposed to spontaneous activity, such as the basic activity in the electroencephalogram. Evoked potentials are divided into exogenous and endogenous (cognitive) evoked potentials. Cognitive evoked potentials are defined as small phase potentials that are caused by cognitive events and can be detected by being recorded by scalp electrodes. The basic assumption with which we start the tests of cognitive evoked potentials and their links with higher brain activity is that neurophysiologic mechanisms that follow cognitive processes generate the so-called "far-field" potentials in the brain [1]. The term cognitive implies what we called "higher brain functions", such as selective attention, perception and recognition of significant stimuli, processing and retention of information, etc. Endogenous potentials have longer latency and higher amplitudes. They can not be registered during anesthesia because of the necessary co-operation with the patient. They represent a series of positive and negative waves with a wide distribution on the scalp. They are marked as waves N1, P1, N2, P2, P300. They are induced by the application of different paradigms (events), that is, by different types of tasks. Previous studies clearly show that, for now, the P300 potential induced by "oddball" paradigm is reproductible, reliable, and easy and simple to register, therefore, it is clinically applicable. Cognitive evoked potentials are used for a non-invasive measurement of the function of cortical structures responsible for cognition (understanding), i.e. further processing of sensory stimuli, which interprets the received signal. Cognitive evoked potentials are used to explore the process of selective attention and perception. P300 wave is an endogenous response to a given task that is not certain, that is, the response received for the target stimuli is not certain. It depends on the perceptual and cognitive activities. It is of positive polarity with a maximum distribution and amplitude over the central and parietal regions. It occurs 300 ms after stimulation, although the latency of this wave depends primarily on the severity of the task and stimulus type (visual, acoustic or electric) [2]. One of the best-studied responses of cognitive evoked potentials is a so-called "P300", a late positive

wave complex that occurs about 300-500 ms after the stimulus, that was first described by Sutton et al. [3]. It is obtained when the subject's attention is focused on a signal that is rare, especially if the signal has a motivational or emotional meaning. P300 is best studied in the so-called "oddball" paradigm in which the subject is faced with two different stimuli, one that occurs frequently and the other that occurs rarely ("oddball"). The subject is prepared to respond to the given example by pressing a button when an "oddball" signal occurs.

The "oddball" paradigm is commonly used in clinical practice because it is acceptable, understandable and accessible to subjects of various ages and degrees of mental ability. It is an auditory stimulation composed of two tones: "rare" or "unexpected", arrhythmic tone that is the target stimulus, and the "frequent", standard, rhythmic tone, to which the respondent does not pay any attention. The rare tone is different in frequency and intensity from the second standard tone. The "oddball" paradigm represents a task that requires respondent's attention and concentration. The amplitude of the P300 wave is higher for the significant informative stimulus which requires more attention. P300 amplitude variations are a manifestation of a redirected attentional capacity, and the latency variations of the same wave reflect the redirection speed of these capacities. Latency of P300 corresponds to the speed of stimulus classification based on discrimination of two events when the mental model of the stimulus structure adapts to the current condition.

STUDY OBJECTIVE

Regarding the fact that cognitive evoked potentials depend on endogen stimuli such as state of mind, concentration, attention and physiological states the aim of research was to examine whether there is a difference in Fz and Cz amplitudes of auditory induced cognitive evoked P300 potential depending on the performance of oddball tasks, both in male and female subjects.

MATHERIAL AND METHODS

RESPONDENTS

The study included 60 subjects (30 female respondents and 30 male respondents). All responders were between ages 19 and 21. All were free of neurological or psychiatric disorders and with no recent usage of any medications.

METHOD

P300 potential is induced by the auditory "oddball" paradigm with 80% of non-target and 20% of target stimuli that are presented to the patient through headphones. Two tones of 1000 and 2000 Hz, with 90 dB intensity are used as stimulus. The target tones are high tones of 2000 Hz. The standard tones of 1000 Hz the respondent should ignore, but when he hears the target tones the respondent should press the button on the special handle. P300 is registered when the participants pressed the button on the handle first by their dominant and then their non-dominant hand.

MATERIAL

Cognitive evoked potentials are detected by silver disk electrodes. The electrodes are 1 cm in diameter, with a small opening in the center through which the contact paste is applied. It enables the transmission of signals from the skin to the electrode via ionic interactions that occur between the electrolyte paste and the skin surface on one side, and between the electrolyte paste and inner electrode surface on the other side. Electrodes are placed according to the 10-20 international system, and the positions for each electrode are defined as percentages (10-20%) of the distances between orientation points such as nazion- inion and the ear lobe. Electrodes are placed along the midline scalp and marked with the letter z (Cz and Fz). We registered P300 cognitive evoked potential using a far-field technique, because in this way the electrodes have a lower impact on the size and shape of the potential, compared to the near-field recordings. The amplitude is given as μV, and it was measured from the isoelectric line to the top of the wave.

STATISTICAL ANALYSIS

All obtained data was statistically analyzed. The following variables were examined: Fz and Cz amplitudes when the button is pressed by the dominant and then by the non-dominant hand.

The presence of a normal distribution of values for all variables was checked individually and in all groups and subgroups of respondents using the Kolmogor-Smirnov test. The continuous variables with normal distribution values were expressed by the arithmetic mean and standard deviation (x ± SD). To determine the existence of statistically significant differences in the values of continuous variables with normal distribution in dependent samples, a parametric T-test for dependent samples was used.

RESULTS

The study was conducted on 60 subjects, divided into 2 groups of 30 subjects according to gender. The following parameters were examined: the difference in Fz and Cy amplitudes when the button was pressed by a dominant as opposed to a non-dominant hand when performing oddball tasks, both in male and female subjects. In all cases the right hand was dominant compared to the left.

Table 1. Arithmetic mean and standard deviation of the Fz amplitude in both studied models

Gender	N	Parameters	x±SD	Mediana	Min-Max
Male	30	Fz amplitude of the right hand	12,35 ± 10	9,20	4,9 - 53
Male	30	Fz amplitude of the left hand	11,43 ± 6,35	10	5,3 – 29,20
Female	30	Fz amplitude of the right hand	10,91±7,61	8,95	4 – 37,1
Female	30	Fz amplitude of the left hand	9,95 ± 6,09	9	3,9 – 28,6

Table 2. The difference in Fz and Cz amplitude values between the right and left hand in male subjects

Parameters	X ± SD	N	SE	Sig. (p)
Difference in Fz amplitude	0,918 ± 8,83	30	1,57	0,56
Difference in Cz amplitude	1,24 ± 6,37	30	1,12	0,27

Table 3. The difference in the value of Fz and Cz amplitude between the right and left hand for female subjects

Parameters	X ± SD	N	SE	Sig. (p)
Difference in Fz amplitude	0,96±5,60	30	1,05	0,36
Difference in Cz amplitude	0,03±5,84	30	1,10	0,97

Fz amplitude value in male patients, obtained in the classical "oddball" paradigm when the subject reacted to the signal by pressing a button by a dominant (right) hand, was significantly lower than the value of Fz amplitude obtained when the button was pressed by a non-dominant hand (Table 1 and 2).

The next followed parameter is the difference of Cz amplitude in the performance of the oddball tasks by a dominant and a non-dominant hand in male subjects, where we observe that there is no statistically significant difference ($p>0.05$) between the right and the left hand (Table 2).

The value of Fz amplitude in female subjects obtained in the classical "oddball" paradigm when the subject reacted to the signal by pressing the button with the dominant (right) was not statistically significantly different ($p>0.05$) from the values of Fz amplitudes obtained when the button was pressed by the non-dominant (left) hand (Table 3).

There was also no statistically significant difference found in any of the values of Cz amplitude in task performance by the dominant hand and the non-dominant in female subjects (Table 3).

DISCUSSION

Covington and Polich тhey analyzed the influence of stimulus intensity on latency and amplitude of P300 wave [4]. The P300 amplitude was not significantly changed with the change of the intensity of auditory stimuli as opposed to visual stimuli, while the P300 latency fell significantly during the increase in the intensity of stimuli, and the auditory stimulus showed a shorter latency than the visual. In our research the amplitude shows the existence of significant inter-individual variations that ranged from 4.9 to 53 in male subjects when the button was pressed by a dominant hand and from 5.3 to 29.20 when pressed by a non-dominant hand, and in female subjects the values ranged from 4 to 34.10 ms when the button was pressed by a dominant hand, and from 3.9 to 28.6 when the button was pressed by a non-dominant hand. Also there were observed variations in the same subject if the measurement was repeated. Nishida S et al. published a study of 12 young, healthy subjects and observed that P300 wave latency varies from subject to subject, and the standard deviation of the measured peak latencies was 27.5 [6]. Physiological variability of variables also appeared in the individual data, and the span of physiological variability that existed between the respondents ranged between 17 and 57. If the detection of P300 complex was made with a difficulty, due to a small number of subjects included in the study, the physiological variability could not be tested. One of the most serious problems in estimating the P300 latency in clinical and experimental research, is to assess whether each measured latency is within normal limits, as the range of normal values is relatively wide and has not yet been precisely defined. P300 variability among normal subjects can be categorized in the interindividual or intraindividual variability. For the interindividual variability, the most studied and distinguished factor is the age factor [6-8], where the greatest variability appeared in subjects younger than 50 years of age and older than 55, but it was much smaller in subjects between 30 and 40 years of age. While the most familiar example is the intraindividual variability, the fact is that the given probability of the target stimulus manifestation can change the amplitude and latency of the P300 complex, because in the repeated recordings, the changes in the probability of the target stimulus manifestation changed the amplitude and also the latency of the P300 wave complex [5,9,10]. Nishida S. et al. presents a hypothesis that the width of the physiological variability interval between subjects, and in the same subject, may be reduced by increasing the number of target stimuli with the restriction of habituation or exhaustion of the subject due to the frequent scanning repetition [6]. In contrast to the uncertainty regarding the neural origin of P300 responses, there is more information about the factors that influence the amplitude and latency of P300 waves. Duncan-Johnson and Donchin reported that the amplitude of P300 waves was sensitive to the probability of the target stimulus manifestation, which means that the stimulus is relevant to a given task [9]. If the target stimulus occurs while the subject performs another task then even the rare stimuli do not induce a P300 response [9]. Further research shows that there is a more subjective than objective probability of P300 wave amplitude occurrence and control when the subject is presented with rare but not target stimuli compared to the target stimuli [11]. In addition to this there is a fact that the P300 response may be induced by the stimulus or stimuli in any scanning modality and the stimulus may be very different, as long as the subject is able to classify it as being different [12]. In other studies Donhin et al. demonstrated that the P300 waves amplitude is associated with sources which are responsible for processing and differentiating stimuli [13,14]. In this study where we have two tasks, P300 amplitude increases with the cognitive demands of information processing, while P300 response to a secondary task decreases.

CONCLUSION

All the above can lead us to the following conclusions: that, both in male and female subjects the performance of oddball tasks does not affect the amplitude

of P300 cognitive evoked potentials because there is no statistically significant difference in the Fz and Cz amplitude values of P300 potential when the task is performed by the dominant compared to the non-dominant hand. These results can indicate practic importance of standard recording of event related potentials when using the oddball paradigm.

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SRPSKI

VARIJABILNOST AMPLITUDE KOGNITIVOG EVOCIRANOG P300 POTENCIJALA DOBIJENOG AUDOTIRNOM ODDBALL PARADIGMOM

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SAŽETAK
Jedan od najbolje proučavanih odgovora kognitivno evociranih potencijala je tzv. "P300", kasni pozitivni talasni kompleks koji se javlja oko 300-500 ms posle stimulusa. Dobija se kada je pažnja subjekta usmerena na signal koji se retko javlja, naročito ako taj signal ima neko motivaciono ili emotivno značenje. Pri proučavanju potencijala P300, pratimo varijacije amplitude i latence potencijala, pa je i cilj rada bio ispitati da li postoji razlika u Fz i Cz amplitudi auditivno izazvanog kognitivno evociranog potencijala P300 u zavisnosti od načina izvođenja oddball zadatka , kako kod osoba muškog pola tako i kod osoba ženskog pola. U istraživanju je bilo uključeno 60 ispitanika (30 ispitanika ženskog i 30 ispitanika muškog pola). P300 potencijal izazvan je auditivnom "oddball" paradigmom sa 80% neciljnih i 20% ciljnih stimulusa koji su pacijentu prestavljeni pomoću slušalica. Ciljni tonovi su tonovi visine 2000 Hz, a standardne tonove od 1000 Hz ispitanik treba da ignoriše i kada čuje ciljne tonove ispitanik treba da pritisne dugme na specijanoj ručici. Vrednost Fz i Cz amplitude kako kod osoba muškog tako i kod osoba ženskog pola dobijene u klasičnoj "oddball" paradigmi kada je subjekt na signal reagovao pritskom na taster dominantnom (desnom) rukom nisu bile su statistički značajno kraće ($p>0,05$) od vrednosti Fz i Cz amplitude koje su dobijene kada je taster pritiskan nedominantnom rukom. Na osonovu ovog istraživanja može se zaključiti da ni kod osoba muškog ni kod osoba ženskog pola način izvođenja oddball zadatka ne utiče na amplitudu P300 kognitivno evociranog potencijala.

Ključne reči: P300, kognitivno evocirani potencijali, oddball paradigma