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Late auditory event-related potential changes after sensorimotor rhythm neurofeedback training

Promene kasnih komponenti auditivnih evociranih potencijala nakon neurofeedback treninga senzomotornog ritma

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Abstract

Background/Aim. Neurofeedback (NFB) is a therapeutic method based on monitoring the electroencephalogram (EEG) and providing feedback on the brain activity of subjects. The aim of the pilot study was to investigate the effect of lower-beta or sensorimotor rhythm (SMR) (12-15 Hz) NFB training on amplitudes and latencies of late auditory event-related potentials (aERP) components N100, N200, P300 in Go-No go task of auditory discrimination. Methods. Each of 9 healthy participants aged 25-40 years (4 male) had 20 daily sessions of SMR neurofeedback training. The aERP was recorded 5 times: before NFB, after 5, 10, and 20 sessions, and one month after the last session. Results. The results showed a statistically significant decrease in N100, N200, and P300 latencies at Fz, Cz, and Pz regions. No significant effect of NFB training on amplitudes of components N100, N200 and N300 was found. Conclusion. The obtained results suggest that NFB training exerts its effect on the processes of auditory cognition.

Key words:

brain; cognition; electroencephalography; event-related potentials, p300; evoked potentials; evoked potentials, auditory; feedback, sensory.

Apstrakt

Uvod/Cilj. Neurofeedback (NFB) je terapijski metod zasnovan na praćenju elektroencefalograma (EEG) i omogućavanju povratne sprege moždane aktivnosti osobama. Cilj pilot studije bio je da se ispita efekat NFB treninga senzomotornog ritma (SMR), tj. niskog opsega beta ritma (12-15 Hz) na amplitude i latence komponenti kasnih auditivnih evociranih potencijala (AEP) N100, N200 i P300 tokom zadatka auditivne diskriminacije. Metode. Svaki od 9 zdravih ispitanika uzrasta od 25 do 40 godina (4 muškog pola) imao je 20 SMR NFB treninga (po jedan svakog dana), a AEP su snimani 5 puta: pre primene NFB treninga, posle 5, 10 i 20 treninga i jedan mesec posle poslednjeg treninga. Rezultati. Rezultati su pokazali statistički značajno smanjenje latenci N100, N200 i P300 komponenti u Fz, Cz i Pz regijama. Nije utvrđen statistički značajan efekat NFB treninga na amplitude ovih komponenti. Zaključak. Dobijeni podaci ukazuju na potencijalni efekat NFB treninga na poboljšanje kognitivnog procesa auditivne diskriminacije.

Ključne reči:

mozak; saznanje; elektroencefalografija; potencijali povezani sa događajima, p300; evocirani potencijali; evocirani potencijali, auditorni; povratna informacija, senzorna.

Introduction

For the last several decades, research has been dedicated to the detection, quantification, and physiological analysis of discrete electroencephalographic (EEG) changes associated with a particular event. They provide new opportunities in understanding complex brain functions, normal and pathological, that have been unexplained by classical neurophysiological paradigms. Event-related potentials (ERP) represent changes in the

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electrical activity of the central nervous system (CNS) structures that are induced (evoked) by a stimulus (exogenous potentials) or by an event (endogenous potentials).

Since the discovery of the P300 component by Sutton in 1965, much research has focused on the generation of P300 and its association with cognitive functions ¹. P300 is an endogenous cognitive neuroelectric phenomenon that occurs under the influence of endogenous stimuli and depends on the state of vigilance, concentration, type of task the subject is required to perform. The ERP components are represented by a series of positive and negative waves (N100, P100, N200, P200, and P300) of different duration and amplitude, the most significant of which is P300. The P300 is considered a manifestation of CNS involvement in processing new information when attention is engaged in memory refresh. The peak amplitude of the response signal and the latency of CNS responses to stimulation are indicators of subjects' cognitive functioning during the specific task.

Attention training is possible through a therapeutic method of learning to control brain activity by EEG recording. This process, known as NFB or EEG biofeedback, captures an aspect of physiological function and provides real-time feedback on these levels to achieve a degree of control or change in the internal state². Neurofeedback (NFB), a form of biofeedback, is a therapeutic method based on monitoring the EEG and providing feedback on the brain activity of subjects, which can be learned to regulate via operative conditioning³. The goal of the training is to practice recognizing the extent to which the brain works, how we experience what state of activity, and how to willingly transition into the state we need for a particular activity. NFB protocols are based on amplifying, inhibiting, or harmonizing certain EEG rhythms. Certain rhythms are associated with certain subjective states and behaviors.

Higher-frequency wave training refers to better focus and increased attention and concentration, such as the socalled training of the lower beta activity segment (12–15 Hz), also called sensorimotor rhythm (SMR)⁴. Sensorimotor rhythm or SMR waves (12–15 Hz) are beta waves that occur in the sensorimotor region of the brain regulated by the thalamocortical loop⁵. They reflect a state of alertness and alertness without tension⁶. With the NFB-SMR protocol, the subject trains to gain control in terms of increasing the amplitude of the SMR wave, resulting in increased attention and better focus. Literature data indicate that normal healthy individuals can learn to control and modify the components of their EEG activity and thus contribute to improving attention and cognitive function.

This pilot study aimed to investigate the effect of the lower-beta frequency band (12–15 Hz) called sensorimotor rhythm (SMR) NFB training on amplitudes and latencies of event-related potentials (N100, N200,

P300) in a Go/No go auditory task discrimination in healthy adult participants.

Methods

Participants

The study involved 9 participants, 25 to 40 years old. The participants were recruited from the Institute for Experimental Phonetics and Speech Pathology and the Life Activities Advancement Center in Belgrade, whose Laboratory for Cognitive Research conducted the experiments. Participants were healthy individuals of both sexes (4 male and 5 female), without hearing or speech disorders, with no prior and current neurological or psychiatric illness (based on the participant's verbal report). All participants were right-handed, according to the Edinburg Inventory. Each participant gave his/her written informed consent before the experimental procedure. This study was approved by the local Ethics Committee according to the Declaration of Helsinki (22/19).

Auditory event-related potentials recording

The auditory ERPs (aERP) were recorded using a standard oddball Go/No go paradigm. The EEG data were recorded using a Nihon Kohden Electroencephalograph (model EEG-4314 F) and Neuroscan Acquire 4.0 software.

The participants had a task to react by pressing a control button with the right hand's thumb each time they hear a tone that differs from other tones that are mostly presented. A total of 80% of each presented tone had a frequency of 1,000 Hz, and 20% of tones were the oddballs with the frequency of 2,000 Hz. The tones were randomly presented to the participants. The participants listened to the tones using earphones. Three Ag/Ag-Cl ring electrodes for aERP registration were positioned according to 10-20 International system for electrode placement at the Fz (frontal midline), Cz (central midline), and Pz (parietal midline) regions. The reference electrode was set to the ear lobes and the ground electrode on the forehead. The impedance was kept below 5 k Ω with no more than 1 k Ω difference between electrodes. The software has its own implemented tool for artifact rejection. Each recording section that had more than 20% of rejected trials due to excessive artifacts was discarded and done again. Each participant underwent the experimental procedure in the morning hours (9-11 am). Participants were instructed to have 8 hours of sleep before ERP recording. Additionally, they used no medication or alcohol and no caffeine drinks before recording at least 24 h and 12 h respectively. The participants were nonsmokers. For each participant, averaged amplitude (µV) and latency (ms) of N100, N200, and P300 waves were obtained for each electrode (Fz, Cz, and Pz).

Neurofeedback SMR protocol training

The experimental task for participants was to perform an NFB SMR training - increasing the amplitude of SMR. Each participant participated in 20 sessions of NFB SMR protocol training, three times a week for 33 min: 2 minutes of the resting-state period (watching a blank computer screen) at the beginning, 4 training trials each lasting 6 min, and 2 min resting-state at the end. During the trials, a participant observes physiological responses on a screen in the form of pictures and video games. The information that comes from this process is feedback, which is reflected in changes in the image or sound of the video game used for training. The games are designed to let the participant advance in the game if he or she can bring the physiological function that is being rehearsed to the desired level. After each trial, the participants had a one-min break. The NFB SMR training was performed using BioTrace software for Nexus - 10B2015. The electrode was set to a Cz region (central midline-vertex region).

After 5, 10, and 20 NFB SMR training sessions, as well as one month after the last session, participants were reregistered with aERP using the same procedure as at the beginning.

Statistical analyses

Due to the small sample size, the comparisons of amplitude and latency differences before and after NFB SMR training were analyzed using nonparametric statistics: the Kruskal-Wallis test for exploring the effect of time point (before NFB, after 5, 10, 20 sessions, and one month after the last training session) and Wilcoxon signed ranks test for *post hoc* multiple comparisons reporting *Z* score and *p*-value. In each comparison, a 95% confidence interval was used.

Results

Figure 1 presents the averaged amplitudes of N100 (left panel), N200 (middle panel), and P300 (right panel) waves for Fz, Cz, and Pz electrodes at different time points. Using the Kruskal-Wallis test for exploring the effect of time point and *post hoc* Wilcoxon signed ranks test for multiple comparisons, no significant differences were found in N100, N200, or P300 amplitude among five-time points for Fz, Cz, and Pz electrodes.

Figure 2 presents the averaged latencies of N100 (left panel), N200 (middle panel), and P300 (right panel) waves for Fz, Cz, and Pz electrodes at different time points. The







Fig. 2 – Average latency value (ms) of N100 (left panel), N200 (middle panel), and P300 (right panel) waves at Fz, Cz, and Pz electrode location at five-time points: before neurofeedback sensorimotor rhythm (NFB SMR) training and after 5, 10, and 20 sessions as well as one month after the last session. Statistically significant differences are marked with asterisks.

p < 0.05, p < 0.01.

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Kruskal-Wallis test found a statistically significant effect of time point on N100 latency at Fz: H(40) = 7.695, p < 0.01, Cz: H(40) = 7.760, p < 0.01, and Pz: H(40) = 9.418, p < 0.01; N200 latency at Fz: H(40) = 5.144, p = 0.02, Cz: H(40) = 8.165, p < 0.01, and Pz: H(40) = 6.727, p = 0.018; and P300 latency at Fz: H(40) = 9.118, p < 0.01, Cz: H(40) = 10.638, p < 0.01, and Pz: H(40) = 8.119, p < 0.01. The *post hoc* Wilcoxon signed ranks test found that this effect was driven by the significantly shorter latencies after the NFB SMR trainings (after 5, 10, and 20 sessions) and one month after the last session compared to the period before training (p < 0.05). No differences in latency of N100, N200, or P300 were found among different sessions (5, 10, and 20 sessions).

Discussion

This study explored the effect of NFB-SMR training on the amplitude and latency changes of aERP recorded at Fz, Cz, and Pz regions during the standard auditory oddball discrimination task. An effect of NFB SMR training was found for aERP latencies. NBF SMR training caused a decrease in latencies of auditory ERP N100, N200, and P300 waves. However, no differences in amplitudes were found. To generate P300 potential, the oddball paradigm was used. It is the acoustic oddball discrimination test, the most commonly used, which involves the use of two types of tone: high-frequency arrhythmic tone and low-frequency rhythmic tone. The difference between the two tones is in frequency and intensity ⁷. The respondent is presented with two types of auditory stimuli: the "rare" or "unexpected" arrhythmic tone, which represents the target stimulus and differs in frequency from the "standard" or "expected" tone and occurs in random order. The participant is required to respond to an "unexpected" tone (by counting, pressing a key), and to ignore the "standard" tone, ie, to recognize target stimuli in a series of stimuli that differ in a characteristic (volume, duration), and are less likely than standard ones. Oddball experimental requires paradigm the attention and concentration of respondents.

Over the last several decades, a large number of studies in healthy individuals as well as in patients with brain damage have shown that SMR NFB can lead to cognitive improvements, mainly in memory functions and attention $^{8-14}$.

Latency is usually interpreted as the speed of processing sensory stimuli as a consequence of distinction from the other stimuli. Therefore, shorter latencies are considered to reflect more effective mental performance compared to longer latencies. Kober et al. ¹⁵ showed in a study in healthy young adults that training with the NFB SMR protocol leads to cognitive improvements associated with changes in the electrophysiological parameters of evoked potentials. The experimental but not the control group showed a linear increase in SMR strength during training, which was associated with improvements in attention, to more pronounced processing of stimuli, as indicated by increased N100 and P300 amplitude after

training compared to the pre-training condition. We found a similar result regarding a sample of healthy individuals. The amplitude of this potential is related to the amount of attention given to a task and the refreshment of working memory content. The P300 latency reflects the speed of stimulus classification, that is, the information evaluation time. ERP waveforms are quantitatively described by amplitude level, latency length, and topographic distribution. The amplitude reflects the magnitude of neural activity and typically ranges from 1 to 30 mV ¹⁶. Latency represents the time interval, that is, the period from the moment of stimulation to the appearance of maximum amplitude, *ie*, peak of ERP, and ranges from several hundred milliseconds.

In contrast, a study by Arns et al. ¹⁷ showed an increase in N200 and P300 amplitudes in participants who had the SMR protocol. Increasing the amplitude of N200 and P300 indicates the normalization of neural circuits associated with discrimination of stimuli and updating of attention ¹⁷. In a study by Reichert et al. 18, an increase in N100 and P300 amplitude was observed in a poststroke patient in an experimental group who had SMR training, whereas the control group showed no difference. This finding is in line with our study that found no differences in N100 and P300 amplitude in healthy participants after SMR NFB training. The earliest wave in the sequence arises about 100 ms from stimulation and is designated as wave N100 due to the negative polarization. The second wave occurs about 150 ms from stimulation, is positive polarity, and is designated P100. Of the early components, the most important is the negative wave, the N200 component, which occurs 200 ms from stimulation and is associated with the process of sensory discrimination. The role of N200 today is mainly focused on "cognitive controls", a concept that encompasses monitoring and control of motor responses ^{19, 20}. The longest latency and the highest amplitude registered above the central and parietal regions of the cerebral cortex is the P300 wave. The time span of this P300 component by Coles and Rugg²¹ can range from 250 ms to 900 ms, with an amplitude ranging from at least 5 μ V to the usual limit of 20 μ V for auditory and visually evoked potentials, even though amplitudes up to 40 µV have also been recorded. The P300 component is thought to be a cognitive neuroelectric indicator of CNS activity that involves processing new information when attention is directed to updating memory performance ²². P300 latency can be considered a measure of the relative duration of the stimulus evaluation process, which is an upper bound on the time of stimulus categorization and evaluation ²¹, or the time it takes to allocate resources and update memory. It is an endogenous response to a task that is not known, i.e., response to target stimuli ²³. Late potentials are used to study multiple modalities of cognition but are most commonly related to memory and attention. Extension of the P300 latency, which reflects the time of assessment and categorization of stimuli, indicates a slowdown in mental functions. The P300 ERP is a determinant of alertness and active attention. The lack of attention causes a decrease in the P300 amplitude or the absence of a P300 wave. Insufficient attention and concentration also make it difficult

to distinguish between standard and target tone, which directly affects P300 latency ²⁴.

In a study by Kropotov et al.²⁵ in children with attention-deficit/hyperactivity disorder (ADHD) after beta and SMR training sessions, differences in pretreatment and posttreatment ERP were observed. Successful performers received positive components evoked within 180-420 ms. Differences are distributed in the frontal/central parts and appear to reflect activation of the frontal cortical areas. The use of NFB as an operative conditioning paradigm by the SMR protocol in a study by Kaiser and Othmer ²⁶ showed a significant clinical improvement in attention and impulsivity control in 85% of subjects after NFB training ²⁶. In the Lubar and Lubar 27 study in children after SMR and beta wave training, all children increased SMR or beta values and decreased slow EEG activity, which was also evident in their spectral strengths regarding increased beta and decreased slow activity and improved school success. Normalization of ERP components in participants with ADHD after NFB training is also described by several other authors ^{28, 29}. These results indicate the possibility of using SMR NFB as a therapeutic method for attention improvement. Several authors have shown that the latency and/or amplitude values of P300 in normal adults are reproducible and stable without statistically significant differences in retesting state at different time intervals 30-35. This is in line with our finding that P300 latency is stable even one month after the last training. This might point to a plastic change of the brain's electric activity that can last for a longer period of time. This is important because in generating endogenous potentials, selective attention is paramount. That is, directing alertness and willing activity to complete the information processing.

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Selective attention occurs when processing information in situations where it is necessary to select one from several messages to be further processed while the others are ignored. Achieved long-lasting enhancement of selective attention using NFB might be a promising field of research towards its application in neurotherapy in children with developmental disorders as well as adults with neurological cognitive impairments.

Our study has a limitation regarding the small sample size. Hence, the generalization of the results should be done with caution. However, this study showed that participants gained a shorter reaction time – shorter latencies in the auditory discrimination task, after NFB SMR training. This finding implies that NFB might be a useful method of neuromodulatory therapy in improving the auditory processes. Further research should comprise a much bigger sample size in order to explore the potential effect of NFB training on cognitive processes.

Conclusion

The obtained results suggest that NFB training produces its effect on the processes of auditory cognition.

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