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Effect of neurofeedback training on auditory evoked potentials' late components reaction time: a placebo-control study

Efekat treninga nervnog sistema povratnim informacijama (*neurofeedback*) na reakciono vreme kasnih komponenti auditivnih evociranih potencijala: placebom kontrolisano istraživanje

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Abstract

Background/Aim. Neurofeedback (NFB) training of sensorimotor rhythm (SMR) contributes to improving cognitive performance and increasing attention. SMR power is increased when a person is focused and task-oriented. The shorter reaction time (RT) of the P300 auditory evoked potentials (AEPs) is associated with better attention. Hence, the increase in SMR power after NFB SMR training should decrease the RT in a cognitive task. The aim of the study was to examine the ability of healthy individuals to modulate the SMR of electroencephalographic (EEG) activity between 12 and 15 Hz during 20-day NFB training sessions. In addition, the effect of NFB SMR training on RT was investigated. **Methods.** Participants were divided into experimental and control groups, with 24 subjects (12 males and 12 females) in each group, aged between 25 and 40 years. Participants in the experimental group were trained with authentic NFB SMR training, while in the control group, false (placebo) training was applied. AEPs were registered on five occasions: before NFB training, after 5, 10, and 20 training sessions, and one month after the last training. **Results.** The results showed that a series of 20 NFB SMR training sessions increased the amplitudes of the SMR. RT in the experimental group was significantly shortened, while in the control group, it was not observed. Moreover, the increase in the power of the EEG signal of the SMR showed a negative correlation with RT, but only in a subgroup of male subjects. **Conclusion.** The obtained results indicate the effects of NFB training on the improvement of the attention process expressed by RT.

Key words:
attention; brain; cognition; electroencephalography; event-related potentials, p300; evoked potentials, auditory; feedback, sensory.

Apstrakt

Uvod/Cilj. Efekat treninga nervnog sistema povratnim informacijama – *neurofeedback* (NFB) trening senzomotornog ritma (SMR) doprinosi poboljšanju kognitivnih sposobnosti i povećanju pažnje. Snaga SMR se povećava kada je osoba usmerena na određeni kognitivni zadatak. Kraće vreme reakcije (VR) auditivnih evociranih potencijala (AEP) P300 povezano je sa boljom pažnjom. Stoga se očekuje da nakon NFB SMR treninga dođe do povećanja snage SMR i posledično do smanjenja VR u kognitivnom zadatku. Cilj rada bio je da se ispita mogućnost zdravih osoba da moduliraju SMR elektroencefalografske (EEG) aktivnosti između 12 i 15 Hz, tokom 20-dnevnih sesija NFB treninga. Pored toga, proučavan je i efekat NFB SMR treninga na VR. **Metode.** Ispitanici su podeljeni u eksperimentalnu i kontrolnu grupu, sa po 24 ispitanika (12 muškog i 12 ženskog pola) životnog doba između 25 i 40 godina. Ispitanici u eksperimentalnoj grupi trenirani su autentičnim NFB SMR treningom, dok je u kontrolnoj grupi primenjivan lažni (placebo) trening. AEP su registrovani u pet navrata: pre primene NFB treninga, posle 5, 10, i 20 sesija treninga, kao i jedan mesec nakon

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poslednjeg treninga. **Rezultati.** Rezultati su pokazali da serija od 20 NFB SMR treninga povećava amplitude SMR. U eksperimentalnoj grupi bilo je značajno skraćeno VR, dok u kontrolnoj grupi to nije zabeleženo. Takođe, povećanje snage EEG signala SMR bilo je u negativnoj korelaciji sa VR, ali samo u podgrupi ispitanika muškog pola. **Zaključak.** Dobijeni rezultati ukazuju na efekte NFB treninga na poboljšanje procesa pažnje, izraženo pomoću VR.

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

Introduction

For many years, cognitive training with neurofeedback (NFB) has proven to be a useful noninvasive and nonpharmacological method in improving numerous cognitive performances. NFB, a form of biofeedback, represents a form of neuromodulation in which individuals have information about the state of electroencephalographic (EEG) activity (brain waves) with the ability to control and self-regulate brain activity through the paradigm of operant conditioning. The modification of brain activity occurs not only through the feedback of operant conditioning but also through the modification of an individual's perception of their physiological state. Thus, two processes are involved in NFB – unconscious through operant conditioning and conscious cognitive self-perception [1].

NFB protocols are based on amplifying, inhibiting, or harmonizing certain EEG rhythms. Sensorimotor rhythm (SMR) NFB training is used as a therapeutic method in various types of disorders such as attention deficit hyperactivity disorder (ADHD) and epilepsy [2–8]. Research studies on healthy individuals, as well as on patients with brain damage, have also found positive effects of NFB SMR training protocols on cognitive functions [8–17]. NFB has also been employed in the treatment of anxiety and traumatic brain injury and in the recovery of patients with impaired motor performance [18]. Recently, the use and research in the field of EEG-NFB have expanded to a healthy population, as is the case in memory training, attention, and other cognitive abilities in young adults or the elderly population [19–22]. The method is used to improve athlete performance training, creativity, or even optimize microsurgical skills [23].

SMR or SMR waves training refers to cognitive function, better focus, and increased attention and concentration. SMR or SMR waves are beta waves in the frequency range between 12–15 Hz that occur in the sensorimotor region of the brain regulated by the thalamocortical loop [24]. SMR is observed when a person is immobile but mentally focused and attentive.

With the NFB SMR protocol, the subject trains to gain control in terms of increasing the amplitude of SMR waves, which subsequently results in improved cognitive performance in terms of increased attention and better focus. P300 cognitive evoked potential is frequently considered a neurophysiological marker of auditory attention [25]. P300 is an endogenous cognitive neuroelectric phenomenon that occurs under the influence of endogenous stimuli and depends on the state of alertness, concentration, and type of task that the subject is obliged to perform. Event-related potential (ERP) components are represented by a series of positive and negative waves (N100, P100, N200, P200, and P300) of different duration and amplitudes, of which the most significant is P300. Cognitive potentials with long latency are bioelectrical responses to thalamic and cortex activity [26]. The amplitude and latency of ERP components reflect the processes of perception, attention, cortical inhibition, memory updates, and other cognitive activities [27]. Latency [expressed in milliseconds (ms)] is defined as the time from the stimulus presentation to the point of maximum amplitude. The higher amplitudes and shorter latencies and reaction time (RT) of the P300 component are associated with better attention [28].

Studies of NFB training in a healthy young population have shown that the SMR protocol could be an effective method for improving attention and perceptual ability, reducing RT, and increasing semantic working memory [13].

Previous studies have found an association between increased SMR power and improvement of attention as well as increased SMR power and RTs in cognitive tasks, mostly in groups of participants with a variety of neurocognitive disorders. SMR power is increased when a person is focused and task-oriented. Hence, the increase in SMR power after NFB SMR training should decrease RT in a cognitive task.

So far, no studies have used a blind placebo-controlled study design in analyzing the effects of NFB SMR training on RT in auditory ERPs. Therefore, the aim of our study was to examine whether healthy subjects aged 25 to 40 years can modulate the lower-beta frequency band (12–15 Hz), called SMR, through 20 NFB SMR training sessions and influence RT compared to the placebo-control group of peers.

Methods

Participants

The study involved 48 healthy participants of both sexes (24 males and 24 females), 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, Serbia, whose Laboratory for Cognitive Research conducted the experiments. Participants were without hearing or speech disorders, with no prior or current neurological or psychiatric illness (based on the participant's verbal report). All participants were right-handed, according to the Edinburgh Handedness Inventory. Each participant gave their written informed consent before the experimental procedure. This study was approved by the Ethics Committee of the Institute for Experimental Phonetics and Speech Pathology "Đorđe Kostić" in Belgrade, on February

12, 2019 under the number 22/19 according to the Declaration of Helsinki.

Participants were divided into the control (placebo) and experimental (treatment) groups. Each group consisted of 24 subjects (12 males and 12 females) aged 25 to 40 years. Each of the 24 participants of the experimental group had 20 NFB SMR training sessions, while the participants of the control group had a placebo NFB training.

Auditory event-related potentials recording

The auditory event-related potentials (aERP) were recorded using a standard oddball go/no-go paradigm. To obtain the P300, an auditory "oddball" paradigm with two tones was used, with 80% of non-target and 20% of target stimuli. Participants had a task to react by pressing a control button with the right hand's thumb each time they heard a tone that differed from other tones that were mostly presented. A total of 80% of each presented tone had a frequency of 1,000 Hz, and 20% of tones were oddballs with a frequency of 2000 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 the International 10–20 System of 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 was on the forehead. The impedance was kept below 5kΩ with no more than 1kΩ 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 redone. Each participant underwent the experimental procedure in the morning hours (9–11 am). For each participant, averaged amplitude (μV) and latency (ms) of N100, N200, and P300 waves were obtained for each electrode (Fz, Cz, and Pz). The aERP were recorded at the beginning (t1), after 5 (t2), 10 (t3), and 20 (t4) NFB SMR treatments, as well as one month after the last NFB SMR treatment (t5). The aERP were recorded using a Nihon Kohden Electroencephalograph (model EEG-4314F) and Neuroscan Acquire 4.0 software.

Neurofeedback sensorimotor rhythm protocol training

The task for participants of the experimental group was to perform NFB SMR training, thus increasing the amplitude of SMR. Each participant took part in 20 sessions of NFB SMR protocol training three times a week for 33 min: 2 min of the resting-state period (watching a blank computer screen) at the beginning, four training trials, each lasting 6 min, and 2 min resting state at the end.

During the trials, the participants look at the physiological responses on the 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. For the control group, the games are designed to let the participants advance in the game if they can bring the physiological function being rehearsed to the desired level. After each trial, participants had a one-minute break. While the experimental group had to improve the amplitude of the SMR during 20 instrumental conditioning sessions, the control group received false feedback. The control group had the same test protocol and amount of treatments. The training design of the control group was identical and differed only in the frequency setting where the respondents did not receive feedback related to their achievement. For a detailed description of the placebo control study design, see Lansbergen et al. [29].

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 re-registered with aERP using the same procedure as at the beginning.

Statistical analysis

This study had a small sample with the obtained data that did not have a normal (Gaussian) distribution. Hence, the groups (experimental and placebo) were compared for NFB SMR power and RT using nonparametric statistics – 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. The Wilcoxon signed ranks test was used to compare male and female participants. Finally, we have used the Pearson correlation coefficient to probe an association between RT and NFB SMR power in the Cz region in the experimental group. In each comparison, a 95% confidence interval was used.

Results

The first level of analysis was to explore the effect of group (experimental – treatment vs. control – placebo) on NFB SMR power. The Kruskal Wallis test found a significant effect of group on NFB SMR power in the Cz region after 10 sessions: H (47) = 3.244, $p < 0.01$, and 20 sessions: H (47) = 4.205, $p < 0.001$. No differences between the experimental and control group were found after 5 sessions. In addition, in the experimental group, the *post hoc* Mann Whitney *U* test found a statistically significant difference in NFB SMR power between the 5th and 10th session: Z = 3.776, $p < 0.01$; between 5th and 20th session: Z = 4.713, $p < 0.001$; as well as between 10th and 20th session: Z = 2.859, $p = 0.02$. The results show a statistically significant linear increase in NFB SMR power as a result of NFB SMR training sessions in the Cz region in the experimental (treatment) group. No such trend was found for the placebo control group (Figure 1).

The next level of analysis was to explore the effect of NFB SMR training on average RT in both groups (experimental – treatment vs. control – placebo). The Kruskal Wallis test found a significant effect of group on RT at the following time points: t1 – H (47) = 2.672, $p = 0.02$; t2 – H (47) = 3.165, $p < 0.01$; t3 – H (47) = 3.822, $p < 0.001$; t4 – H (47)

= 3.047, $p < 0.01$. The next level of analysis was to explore the effect of NFB SMR training sessions on RT in the experimental and placebo group separately. In the experimental group, *post hoc* Mann Whitney *U* test found a statistically significant difference in RT between t0 and t1: Z = 2.427, $p = 0.02$, between t1 and t2: Z = 2.344, $p = 0.03$, and between t2 and t3: Z = 2.859, $p < 0.01$.

The results show a statistically significant linear decrease in RT as a result of NFB SMR training sessions in the Cz region in the experimental (treatment) group. No such trend was found for the placebo control group (Figure 2).

In the experimental group, the *post hoc* Mann Whitney *U* test found a statistically significant difference between male and female participants in RT at each time point: t0 – Z = 2.105, $p = 0.02$; t1 – Z = 2.237, $p = 0.018$; t2 – Z = 2.336, $p = 0.018$; t3 – Z = 2.291, $p < 0.01$; t4 – Z = 2.341, $p < 0.01$.

Male participants had shorter RT compared to females (Figure 3).

In the experimental group, *post hoc* Mann Whitney *U* test found a statistically significant difference between male and female participants in NFB SMR power in each of three-time points – after 5 sessions: Z = 4.236, $p < 0.01$; after 10 sessions: Z = 2.382, $p = 0.018$; as well as after 20 sessions: Z = 2.116, $p = 0.018$. Male participants had higher NFB SMR power compared to females (Figure 4).

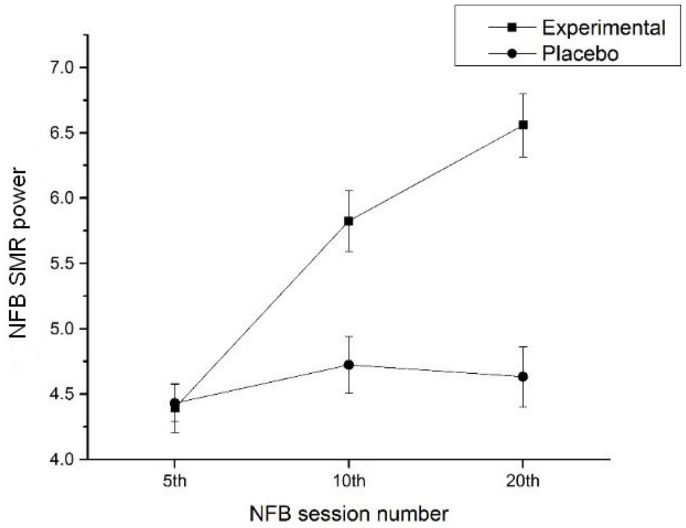

Fig. 1 – The effect of neurofeedback (NFB) sensorimotor rhythm (SMR) training on the NFB SMR power after 5, 10, and 20 NFB sessions in experimental and placebo groups.

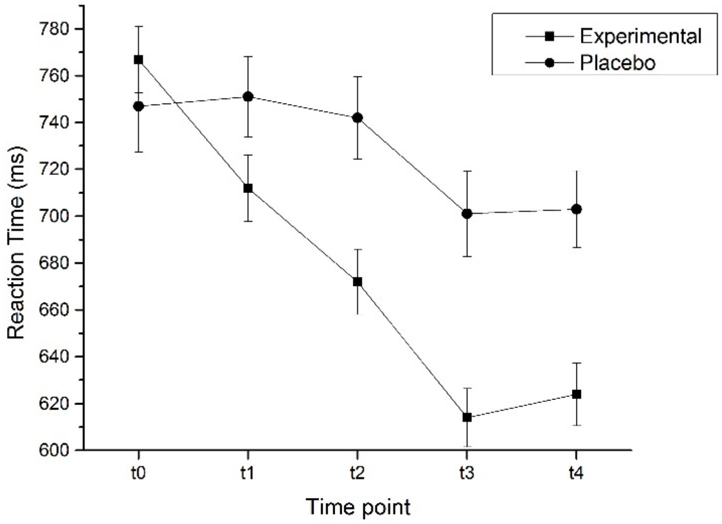

Fig. 2 – The effect of neurofeedback sensorimotor rhythm training on average auditory evoked potentials reaction time in the central midline region for each group (experimental and placebo) and at each time point.

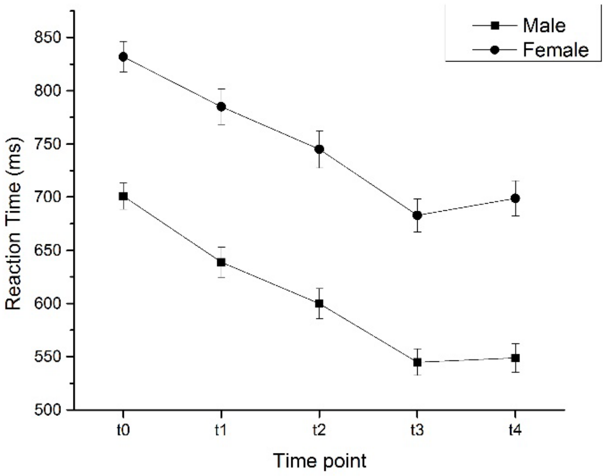

Fig. 3 – The effect of neurofeedback sensorimotor rhythm training on the average auditory evoked potentials reaction time in the central midline region in male and female participants from the experimental group.

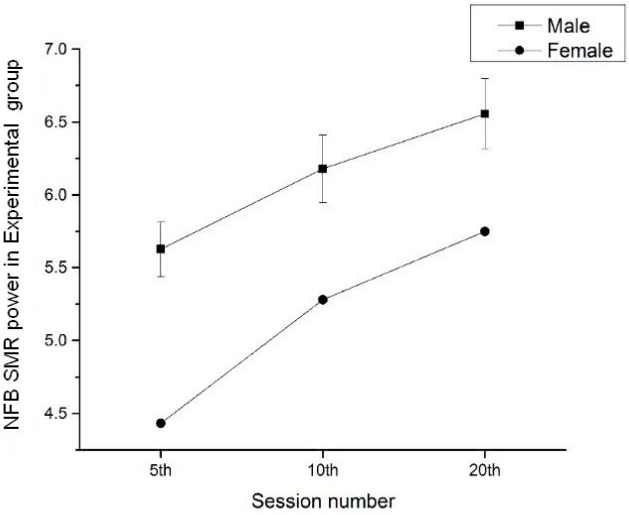

Fig. 4 – Comparison of neurofeedback (NFB) sensorimotor rhythm (SMR) power between male and female participants in the experimental group.

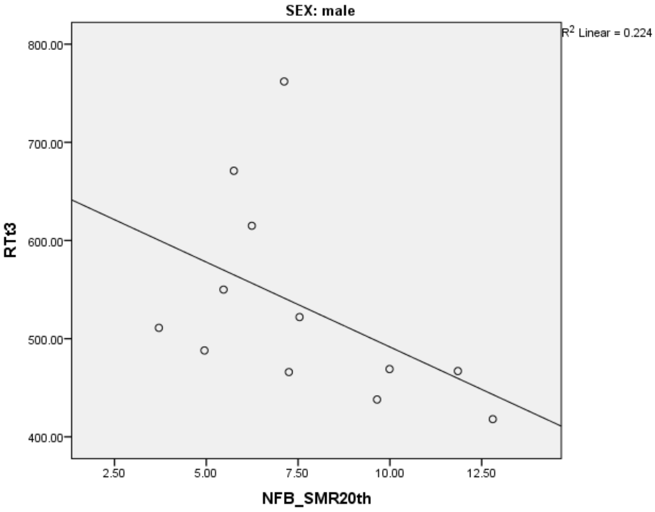

Fig. 5 – Correlation between neurofeedback (NFB) sensorimotor rhythm (SMR) power and reaction time (RT) after 20 NFB SMR sessions in male participants from the experimental group.

The final level of analysis was to probe a potential association between NFB SMR power and RT after 20 NFB sessions in male participants from the experimental group (Figure 5). A Pearson correlation coefficient (linear R^2) showed a significant negative correlation between NFB SMR power in the Cz region and RT after 20 NFB sessions: $R^2 = 0.024$, $p = 0.02$. Results showed a linear reduction of RT with the increase in NFB SMR power in male participants from the experimental group.

Discussion

The aim of this study was twofold. We first examined whether healthy subjects could modulate their EEG activity using NFB training. Second, we examined the effect of NFB SMR training on RT. Finally, we examined the correlation between NFB SMR power and RT.

The study showed that the subjects of the experimental group were able to increase their EEG activity within NFB training in the trained frequency range of 12–15 Hz.

Several studies have shown that subjects can learn to self-regulate different parameters of EEG activity (amplitude and coherence of EEG signals) through NFB training [30–32.]

The study of Doppelmayr and Weber [33] showed that subjects who had SMR training were able to modulate the EEG in the trained frequency bands as opposed to the control and theta/beta ratio groups. In addition, only the SMR group was able to achieve better results in RT tasks. In a study by

Vernon et al. [13], healthy subjects were able to increase SMR activity after only eight NFB sessions, which was associated with an improvement in memory tasks. Gadea et al. [34] showed that healthy women were able to improve SMR waves, and this was positively associated with improved performance in a test that measures executive attention. In the study by Parsaei et al. [35], there was an increase in SMR waves and a significant improvement in RT in the experimental group of older men but not in the control group, which had a false NFB. In our study, the effect of NFB SMR training was examined in the experimental group on RT. NFB SMR training caused a reduction in RT in both male and female participants observed as a group. However, the increase in NFB SMR power had a statistically significant negative correlation with the RT only in male participants. That is probably the explanation for the shorter RT in male participants compared to female ones.

The oddball paradigm was used to generate P300 potential. It is the auditory discrimination test, which involves the use of two types of tones: high-frequency arrhythmic tone and low-frequency rhythmic tone. The difference between the two tones is in frequency and intensity [36]. 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 about it in random order. The participant is required to respond to an “unexpected” tone (pressing a key) and ignore the “standard” tone, i.e., to recognize target stimuli in a series of stimuli that differ in one feature (volume, duration) and are less probable than the standard ones. The oddball experimental paradigm requires the attention and concentration of respondents.

Components can be analyzed in terms of their latency and amplitude. Registration of these potentials shows a sequence of peaks with negative-positive-negative-positive polarity (N1-P2-N2-P3) at intervals of 80 and 350 ms after stimulation [25].

Latency represents the time interval, that is, the period from the moment of stimulation to the appearance of maximum amplitude, i.e., the peak of ERP. Latency reflects the speed of processing of 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.

A large number of studies talk about the positive effects of NFB SMR on selective attention, auditory attention, phonological awareness [37, 38], RTs, and memory [39, 40]. Bielas and Michalczyk [41] demonstrated an improvement in attention capacity after the beta protocol of NFB training (12–22 Hz), with an active electrode set to Cz in the elderly population. Analysis of RT of the subjects after NFB training showed a significant improvement. In contrast, the difference in RT in the control group that did not have NFB training was not significant. In children and adolescents with focal epilepsy, SMR training significantly reduced RT [42]. In the Kober et al. [11] study of subjects after stroke, the experimental but not the control group showed a linear increase in SMR strength during training, which was associated with improvements in memory and attention. In addition, the increase in SMR led to a more pronounced stimulus processing, which is shown by the increased amplitude of N1 and P3 evoked potential. In an extensive Kaiser and Othmer [43] study, NFB training on a large number of subjects produced significant improvement in attention and impulse control in 85% of subjects. Egner and Gruzelier [44] investigated the different effects of SMR (12–15 Hz) and beta (15–18 Hz) NFB training on different performances. In their research, SMR training resulted in increased perceptual sensitivity and better attention, and low beta rhythm training gave faster RT. In this study, as in ours, the differentiation of cognitive performance in relation to gender shows that male subjects had a faster RT compared to female subjects, which is consistent with the results of Adam et al. [45] and Botwinick and Thompson [46].

Much research has been devoted to studying the effects of gender differences in RT, and it is often stated that men have faster and less variable RT than women. One possible explanation is that gender differences in RT variability may be due to the influence of sex hormones on the brain and, implicitly, can be expected in adults but not in children [47, 48]. Recently, interest in RT has been focused on medium RT and intraindividual RT variability, i.e., the consistency of an individual’s response. Intraindividual variability, although highly correlated with mean RT, is a discrete measure of cognitive performance. A small number of studies have investigated gender differences in intraindividual variability in RT and show that women are less consistent than men [49]. Our study is in line with these findings. After NFB SMR training, healthy male subjects showed a significant association between NFB SMR power and cognitive evoked potential RT.

EEG-NFB training is a promising technique that helps an individual learn to modulate brain activity in order to achieve cognitive and behavioral enhancement.

Conclusion

This study showed the possibility of increasing the power of SMR by using the NFB training protocols. This result was confirmed using a placebo-control study group that showed no such effect. Further, the increase in the SMR power was followed by a decrease in RT in auditory evoked potentials. However, these results are limited to a positive effect of NFB SMR training on auditory attention only. Further studies should include different modalities of attention (visual, for instance) as well as different age groups (including children and adolescents).

Conflict of interest

The authors declare no conflict of interest.

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