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In Search of New Protocols of Neurofeedback: Independent Components of Event-Related Potentials

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IN SEARCH OF NEW PROTOCOLS OF NEUROFEEDBACK: INDEPENDENT COMPONENTS OF EVENT-RELATED POTENTIALS

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In this article we present a method for decomposing individual multichannel event-related potentials (ERPs) into functionally meaningful components by means of spatial filtering. The spatial filters are based on topographies of components obtained by application of Independent Component Analysis (ICA) to a large collection ($n = 297$) of individual ERPs in the paired GO/NOGO task. sLORETA has been used for depicting neuronal generators of independent components (ICs). The ICs are divided into sensory-related (visual N1 and N170) and executive components presumably associated with engagement operation (P3b), action suppression (P3 NOGO) and conflict monitoring (P4 NOGO) operations. In a pilot study on 10 healthy subjects the feasibility of ICA/ERP-based neurofeedback approach has been tested. A neurofeedback protocol was implemented to test the amplitude training of the P3b independent component generated in the parietal cortex. The effect of 20 min of neurofeedback on ERPs in healthy subjects is presented. The amplitude of the P3b component did not change significantly during the training session; however, the amplitude of another component named Slow Positive Wave statistically decreased during both the training and sham conditions. We believe that this change may be sufficiently significant to warrant additional research, as it may hold promise for alternative treatments for some psychiatric illnesses.

In contrast to spontaneous electroencephalographic (EEG) oscillations, event-related potentials (ERPs) reflect stages of information processing in the human brain (Hillyard & Anllo-Vento, 1998; Näätänen, 1992). A normative database that explores parameters of ERPs together with spectral parameters of spontaneous multichannel EEG has been developed (Kropotov & Mueller, 2009). Working with patients suffering from attention deficit hyperactivity disorder (ADHD), dyslexia, schizophrenia, and some others brain disorders in our laboratory at the Institute of the Human Brain of Russian Academy of Sciences, we were struck by the fact that some of our

patients had deviations from the normative data independently either in EEG spectra or in ERPs. For example, about 50% of our schizophrenic patients showed normal EEG spectra but strongly impaired ERPs; vice versa, about 25% ADHD children showed abnormal spectra accompanied by normal ERPs.

For many years spectral characteristics of spontaneous EEG remained the main parameters for neurofeedback protocols. These parameters included (a) EEG power in specific frequency bands (such as theta, alpha, or beta; Lubar & Lubar, 1984; Sterman, 1996), (b) different types of EEG power ratio in a single electrode (such as theta/beta ratio; Kropotov et al.,

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2005), (c) asymmetry (such as the frontal alpha asymmetry measured as ratio between F7 and F8 electrodes; Allen, Harmon-Jones, & Cavender, 2001), (d) coherence, and (e) slow cortical potentials. Modern approaches used in constructing protocols of neurofeedback rely on comparing QEEG spectral characteristics with a normative database and exploring a so-called Bulldozer principle of neurofeedback (Sterman, 1996). It should be mentioned, however, that not all QEEG approaches employ the Bulldozer principle. For example, the EEG phenotype approach by Johnstone, Gunkelman, and Lunt (2005) suggests a specific neurofeedback treatment for a specific endophenotype.

Only a few attempts have been made to use ERP parameters in operant conditioning (Mnatsakanian & Dorokhov, 1995; Roger & Galand, 1981; Sommer & Schweinberger, 1992) and, recently, in brain-computer interface (Bianchi et al., 2010; Li, Sankar, Arbel, & Donchin, 2009). The difficulties that must be overcome in the ERP base neurofeedback are as follows:

1. Low signal-to-noise ratio of ERPs, making it difficult to separate an ERP component in a single trial. Even the largest ERP components in amplitude may constitute only 50% of the background spontaneous EEG. Because of the low signal-to-noise ratio, at least 30 trials are needed for averaging to obtain reliable ERP measures.
2. ERPs represent a sum of many spatially distributed sources, which determines a need for ERPs' decomposition into functionally meaningful components. A conventional method of subtracting an ERP in a "reference" task condition from an ERP in a task condition associated with a given psychological operation under study has been recently replaced by Independent Component Analysis (ICA). The literature in this field has been extended dramatically during the last few years (Makeig, Müller, & Rockstroh, 1996; Onton & Makeig, 2006).

Here we present an attempt to resolve the aforementioned problems in order to use the ERPs as one of the neurofeedback parameters.

METHODS

Subjects

Ten healthy subjects 20 to 61 years of age participated in the study in which the P3b component of ERPs was used as a neurofeedback parameter. Subjects were selected from the staff of the Institute of the Human Brain. The study was approved by the local Ethical Committee.

Behavioral Task

A modification of the visual paired GO/NOGO paradigm was used. Three categories of visual stimuli were selected: (a) 20 different images of animals, referred to as "A"; (b) 20 different images of plants, referred to as "P"; (c) 20 different images of people of different professions, and this was presented together with an artificial "novel" sound, referred to as "H+Sound." All visual stimuli were selected to have similar size and luminosity. The randomly varying novel sounds consisted of five 20-ms fragments filled with tones of different frequencies (500, 1000, 1500, 2000, and 2500 Hz). Stimulus intensity was about 70 dB SPL, measured at the patient's head.

The trials consisted of presentations of paired stimuli with interstimulus intervals of 1 s. Duration of stimuli was 100 ms. Four categories of trials were used (see Figure 1a): A-A, A-P, P-P, and P-(H+Sound). The trials were grouped into four blocks with 100 trials each. In each block a unique set of five A, five P, and five H stimuli were selected. Each block consisted of a pseudo-random presentation of 100 pairs of stimuli with equal probability for each stimulus category and for each trial category. Participants practiced the task before the recording started. Subjects rested for a few minutes after each 200 trials.

Subjects sat upright in an easy chair looking at a computer screen. The task was to press a button with the right hand to all A-A pairs as fast as possible and to withhold from button pressing to other pairs (Figure 1a).

ERP-Based Neurofeedback Procedure

An ERP-based neurofeedback protocol was implemented in software written by one of

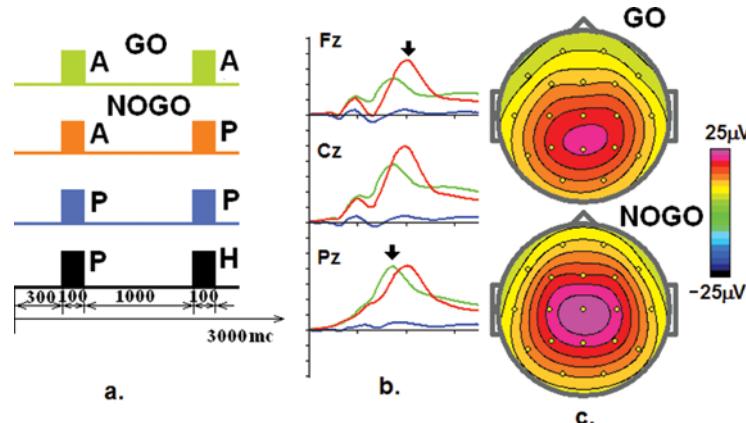


FIGURE 1. Grand average event-related potentials (ERPs) in response to GO and NOGO cues. Note. (a) Schematic representation of the two-stimulus GO/NOGO task. From top to bottom: time dynamics of stimuli in four categories of trials. A, P, H stimuli = “Animals,” “Plants” and “Humans.” GO trials occur when A-A stimuli require the subject to press a button. NOGO trials are A-P stimuli, which require suppression of a prepared action. GO and NOGO trials represent “Continue set.” Ignore trials are pairs beginning with P, which require no preparation for action. Novel trials are pairs requiring no action, with presentation of a novel sound as the second stimuli. Ignore and Novel trials represent “Discontinue set.” Time intervals are depicted at the bottom. (b) Grand average ($n = 297$) ERPs to GO (green line), NOGO (red line) and Ignore (blue line) cues in the two-stimulus GO/NOGO task. Montage-linked ears reference. Position of electrodes is according to the International 10-20 system. X-axis = time in ms, Y-axis = potential in μ V. Positivity is up. (c) Maps of scalp potentials at peak latencies (marked by arrows) of late positive waves in response to GO, NOGO cues. Amplitude and mapping scales are presented on the right.

the authors (MPV). In this software 19 channels of EEG were recorded, whereas GO and NOGO trials were presented in a sequence of pairs of stimuli (Ignore/P-P, Novel/P-H+S, GO/A-A, NOGO/A-P) on the screen located in front of the subject. The trials were identical to the two stimulus GO/NOGO task previously described, but the probabilities for trial categories were different: Go trials were 3 times more frequent than other categories. The test used for determining the baseline of the individual component consisted of 60 Go trials, 20 NoGo trials, 20 Ignore trials, and 20 Novel trials with a total duration of 8 min. The tests for both the training and the sham condition were twice as long and consisted of 120 Go trials, 40 NoGo trials, 40 Ignore trials, and 40 Novel trials. The subject was instructed to press the button as fast and accurately as possible. In both the sham and control conditions the subject was asked to observe the neurofeedback parameter (an amplitude of the selected component) depicted on the screen 700 ms after the second stimulus presentation.

The general procedure of the neurofeedback protocol was as follows: From each EEG epoch after either the GO or NOGO cue

(depending on the training component) a spatial filter (see Methods section) was applied online. Maximal amplitude of the resulting signal (an amplitude of independent components [ICs]) in a given time interval was computed online and was presented as feedback immediately after computation. The time interval was defined on the basis of temporal parameters of the component.

In particular, for the P3b component (which was trained in the present study) the time interval was between 200 and 700 ms. Consequently, the feedback was provided immediately 700 ms after the GO stimulus. The baseline amplitude parameters of the selected IC were defined during 8 min of the task in which no feedback was presented—or the baseline recording. After determining the baseline of the individual component, the control and sham ERP neurofeedback sessions were run.

The sequence of control and sham sessions were selected randomly and blinded for each subject. In the control session the amplitude of the component was online compared with the baseline parameter. If the current amplitude exceeded the baseline, the subject was

presented a sign “+” on the screen, otherwise the sign “−” appeared. In addition, the dynamics of the neurofeedback parameters were depicted at the bottom of the screen as a curve. As a sham condition a yoked control was used (the EEG of another subject in the control condition was fed back).

EEG Recording and Correcting Artifacts

EEG was recorded from 19 scalp sites, band-pass filtered between 0.53 and 50 Hz, and digitized at a rate of 250 samples per second per channel. Electrodes were applied according to the International 10-20 system. The EEG was recorded referentially to linked ears, allowing computational rereferencing of the data (remontaging). For decomposing ERPs into independent components, the EEG was computationally rereferenced to a common average montage. Electrooculography (EOG) was recorded from two electrodes placed above and below the right eye. All electrode impedances were below 5 kOhms.

Eye blink artifacts and horizontal eye movements were corrected by zeroing the activation curves of individual ICA components corresponding to the artifacts (Jung et al., 2000; Vigário, 1997). Comparison of this method with an EOG regression technique is described elsewhere (Tereshchenko, Ponomarev, Kropotov, & Müller, 2009). In addition, epochs with excessive amplitude of nonfiltered EEG and/or excessive faster and/or slower frequency activity were automatically marked and excluded from further analysis. The epoch exclusion thresholds were set as follows: (a) 100 μ V for nonfiltered EEG, (b) 50 μ V for slow waves in 0–1 Hz band, and (c) 35 μ V for fast waves filtered in the band 20–35 Hz.

Decomposition of the Collection of ERPs into Independent Components

The goal of ICA is to utilize the differences in scalp distribution between different generators of ERP activity to separate the corresponding activation time courses (Makeig et al., 1996). Components are constructed by optimizing the mutual independence of all activation time curves, leading to a natural and intuitive

definition of an ERP component as a stable potential distribution, which cannot be further decomposed into independently activated sources.

In the present study, ICA was performed on the full *ERP scalp location x time series matrix*. Assumptions that underlie the application of ICA to individual ERPs are as follows: (a) summation of the electric currents induced by separate generators is linear at the scalp electrodes, (b) spatial distribution of components' generators remains fixed across time, and (c) components vary independently from each other across subjects and task conditions (Makeig et al., 1996; Onton & Makeig, 2006).

Briefly, the method implemented in this article is as follows: The input data are the collection of individual ERPs arranged in a matrix P of 19 channels (rows) by T time points (columns). The ICA finds an “unmixing” matrix (U) that gives the matrix S of the sources (ICs) when multiplied by the original data matrix (P),

$$S = UP$$

where S and P are $19 \times T$ matrices and U is 19×19 matrix. $S(t)$ are maximally independent.

In our article, matrix U is found by means of the Infomax algorithm, which is an iteration procedure that maximizes the mutual information between S . According to the linear algebra,

$$P = U^{-1}S,$$

where U^{-1} is the inverse matrix of U (also called mixing matrix) and the i -th column of the mixing matrix represents the topography of i -independent component; S_i represents time course of the i -independent component.

We can present potential P as a sum of potentials generated by single independent components,

$$P = \sum P_i = \sum U_i^{-1}S_i,$$

where U_i^{-1} is the i -th column of the mixing matrix U^{-1} and represents the topography of

i-independent component; S_i – is the time course of the i-independent component.

The topographies of the independent components are presented as topographic maps, while time courses of the components (also called “activation time courses”) are presented as graphics with time corresponding to x-axis. The “power” of the components is characterized by a variance $\text{VAR}_i = \sum \sum (U_{ij}^{-1} * S_{ik})^2 / (N_{\text{samp}} * N_{\text{chan}})$ where N_{samp} – number of time points and N_{chan} – number of channels.

ICA was performed on a collection of ERPs computed to the second stimulus in 1-s time intervals after the second stimulus presentation. The ICA method (Makeig et al., 1996) was implemented in the analysis software written by one of the authors (PVA). The topographies and activation time courses of the components were tested against the corresponding results obtained by means of “InfoMax” software in EEGLAB, a freely available interactive Matlab toolbox for processing continuous and event-related electrophysiological data (<http://sccn.ucsd.edu/eeglab>).

Decomposition of Individual ERPs into Independent Components

The i-th independent source S_i can be found as

$$S_i = U_{zi}P,$$

where U_{zi} – is matrix U in which all rows are zeroed except the i-th row.

According to linear algebra,

$$P_i = U^{-1}U_{zi}P,$$

where $U^{-1}U_{zi}$ is a filter for extracting the i-th component from the vector P of potentials. In our study, we used this filter for extracting the P3b component from EEG fragments following GO cues.

sLORETA Imaging

The sLORETA imaging method was used for localizing the generators of the ICA components extracted in this study (ICs). The free software is provided by the Key Institute for Brain-Mind Research in Zurich, Switzerland

(<http://www.uzh.ch/keyinst/loreta.htm>). For theoretical issues of this method, see Pascual-Marqui (2002).

Statistical Analysis of ICA Data

Amplitudes of the components were computed for each condition and each subject separately. Student’s *t* test was used for assessing statistical significance of the difference between conditions.

RESULTS AND DISCUSSION

Grand Average ERPs

Visual inspection of grand average ERPs to GO and NOGO cues (Figure 1b) demonstrated that these trials in comparison to Ignore trials evoke late positive fluctuations with different peak latencies, amplitudes, and distributions. Topographic mappings of potentials at peak latencies of positive waveforms are presented at the bottom of Figure 1c. The late positivity for GO stimuli peaks at 340 ms and reaches 20.5 μ V at Pz, the late positive fluctuation in response to NOGO stimuli peaks at 400 ms and reaches 24.6 μ V at Cz. These are classical findings commonly observed in previous studies in GO/NOGO tasks for the executive components (Bokura, Yamaguchi, & Kobayashi, 2001; Falkenstein, Hoormann, & Hohnsbein, 1999; Fallgatter & Strik, 1999; Simson, Vaughan, & Ritter, 1977).

Sensory-Related Independent Components

Application of ICA to the HBI collection of 297 ERPs of healthy subjects revealed 19 independent components (Kropotov & Mueller, 2009; Kropotov & Ponomarev, 2009). Two of those components were associated with radial and horizontal eye movement artifacts and were excluded from analysis. Here we present only the largest IC components, that is, those that constitute more than 90% of the signal variance. These components, in turn, can be separated into sensory and executive components.

Sensory components were present in GO/NOGO conditions as well as in Ignore

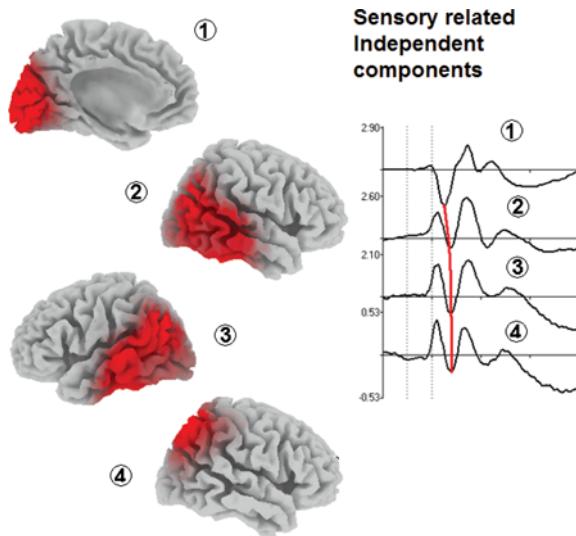


FIGURE 2. Sensory-related independent components in GO/NOGO task. Note. Right: time dynamics of the sensory related components, that is, the components that do not depend on continue (GO/NOGO) or discontinue (Ignore/Novel) sets. Components are aligned according to the latency of N1 fluctuation. Y-axis = amplitude in standard units; X-axis = time in ms. Left: sLORETA images of the components built up on the basis of their topographies (not presented). Positivity is up.

conditions and appear to reflect stages of visual processing. These components are presented in Figure 2. As was shown in the Methods section, each component is characterized by topography and time dynamics. sLORETA images were constructed on the basis of these topographies.

Executive Independent Components

The executive components were those that were elicited in GO/NOGO conditions and were absent in Ignore condition (Kropotov & Mueller, 2009; Kropotov & Ponomarev, 2009). They appear to reflect stages of information processing in the executive system of the brain. These components are presented in Figure 3. Each component is characterized by distribution of its generators and by time dynamics. According to sLORETA imaging, generators of the components are distributed over the middle parietal cortex, supplementary motor cortex, frontal eye fields of the frontal lobe, and anterior part of the cingulate cortex. In Figure 3 the executive components are

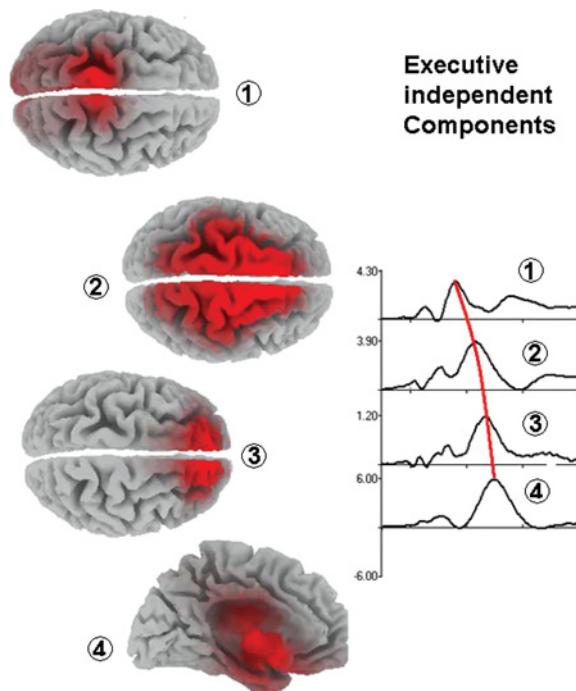


FIGURE 3. Executive independent components in GO/NOGO task. Note. Right: time dynamics of the executive components, that is, the components that are elicited only in continue set (GO/NOGO). Components are depicted for NOGO condition and are aligned according to the latency of late positive fluctuations. Y-axis = amplitude in standard units; X-axis = time in ms. Left: sLORETA images of the components built up on the basis of their topographies (not presented). Positivity is up.

aligned from top to bottom according to the latency of late positive fluctuations.

ICA/ERP-Based Neurofeedback

Are humans able to change ERP components by means of a neurofeedback procedure? To answer this question we implemented a pilot study with 10 healthy subjects.

For the study we selected the P3b component generated in the GO condition. Subjects performed a two-stimulus GO/NOGO task while viewing a computer screen. The screen presented the + (plus) sign immediately after the trial if the amplitude of the current ERP component was larger than the baseline, otherwise a - (minus) sign was shown. At the bottom of the screen a graph of the component dynamics over trials was depicted. The subjects performed two sessions: one with a real neurofeedback (named training or control), and the

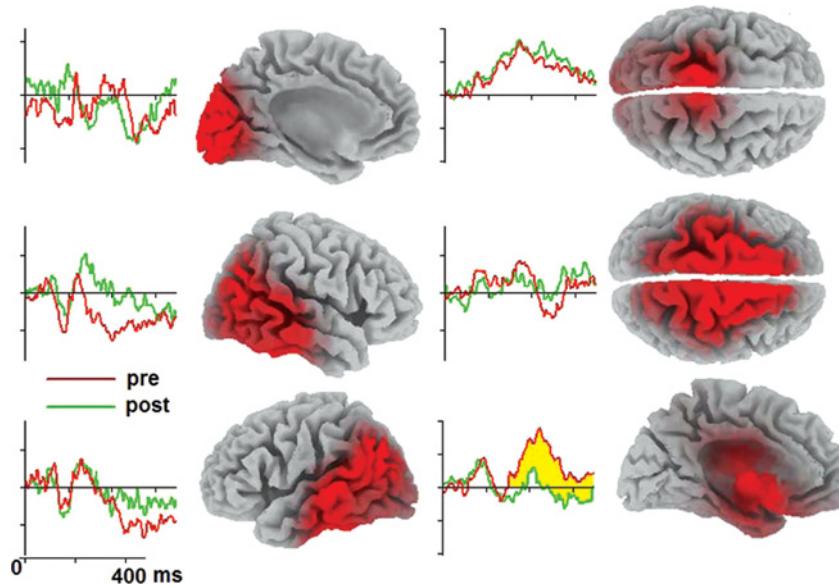


FIGURE 4. Neurofeedback training of the P3b component. Note. (a) Group average ($n = 10$) of P3b and Slow Positive Wave independent components during baseline recording (red), neurofeedback, control session (green), and sham session (blue). Neurofeedback consisted of presentation of amplitude of the P3b component after each GO trial. Asterisk shows statistically significant ($p < .01$) difference between “baseline” and “neurofeedback.” (b) Individual P3b and Slow Positive Wave independent components in one subject during baseline recording (red), neurofeedback, control session (green), and sham session (blue). Each bin corresponds to $2 \mu\text{V}$. X-axis = time in ms. (c) sLORETA images of the P3b and Slow Positive Wave components.

other one with sham feedback. The sequence of control and sham sessions was counterbalanced across subjects.

The results of the group analysis are shown in Figure 4. As a group, subjects were not able to discriminate between the neurofeedback and sham conditions. They also were not able to voluntarily increase the P3b component as was required by the task. As can be seen from Figure 4, grand averages of the P3b component did not differ from baseline for both the training and sham conditions. Two subjects were able to increase the required component ($p < .05$) and were able to discriminate between control and sham conditions.

The most intriguing fact was that the Slow Positive Wave (SPW) component generated in parahippocampal gyrus was significantly ($p < .05$) enhanced during both sham and training sessions in comparison to the baseline, alas without differentiation between training and sham conditions.

The results of this pilot study show that it is quite difficult to learn to train the selected P3b component in one session. It might be that one

session of the ERP neurofeedback is not enough to learn the skill. However, the results show that the efforts made by the subjects during both the training and sham sessions did lead to a significant change of the SPW component.

CONCLUSION

In clinical electroencephalography we are looking at the brain through two different windows. These windows consist of spectral characteristics of the spontaneous EEG and by components of ERPs. This article deals with possibilities opened by the second window in the field of neurofeedback.

There are at least two problems in ERP-based neurofeedback: correction of eye movement artifacts, and selection of functionally meaningful ERP components. Ways of solving these problems have been presented in this article. In particular, we propose a method for decomposing individual multichannel ERPs into functionally meaningful components by means of spatial filtration. The spatial filters

are obtained by application of Independent Component Analysis for collection of individual ERPs. When applied for ERPs in a GO/NOGO paradigm, two groups of ERP components were extracted: sensory and executive components. Each component is characterized by a specific localization of generators and by a specific time course.

GO trials were associated with late positive wave of ERPs with latencies around 300 ms and a localization to the centro-parietal cortex. This wave reflects the operation of action engagement. Application of Independent Component Analysis for ERPs in such trials allowed us to separate two independent components: The P3b (Verleger, 1988) and an SPW. According to sLORETA, the source of the P3b component is localized to the parietal cortex and the source of the SPW is localized to the parahippocampal gyrus. In our study we examined whether subjects were able to voluntary control their P3b amplitude by means of ERP neurofeedback.

Unfortunately, we did not find any reliable indications that healthy subjects were able to learn during 20 min how to voluntarily increase the P3b amplitude. Also, as a group they were not able to discriminate between sham and training sessions. This observation could indicate the stability of the P3b component in healthy subjects. It could also indicate that possibly one session is not enough for a subject to learn the skills of voluntarily increasing the P3b amplitude.

However, our data demonstrate that another component of the ERPs, namely, SPW, could be changed as a result of the efforts made by the subjects in both the training and sham conditions. It may be suggested that storage of new condition demands alteration in hippocampal neurons causes significant change in the amplitude of the SPW independent component during both biofeedback and sham conditions, hence reflecting a nonspecific effect.

It should be stressed that in some psychiatric patients abnormalities in ERPs are accompanied by practically normal EEG spectra. In such cases ERP-based neurofeedback might be investigated further, using more sessions.

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