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Changes in the Power Levels of Cortical EEG Rhythms in Cats during Training Using Acoustic Feedback Signals

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Chronic experiments on two conscious cats were performed to study the dynamics of the ratios of spectral power levels of beta and theta rhythms and neuron activity in the dopaminergic system of the ventral tegmentum during EEG feedback sessions. Training was performed using a model in which the level of sound signals presented to the animals decreased as the spectral power ratios of the EEG beta and theta rhythms recorded in the frontal leads increased. In a control series, the changes in the sound signal level were independent of the ongoing EEG. These experiments showed that the ratio of the spectral power levels of the beta and theta rhythms changed during feedback sessions, with increases in the spectral power of the beta rhythm and decreases in the spectral power of the theta rhythm. These changes were accompanied by increases in the activity of presumptive dopaminergic neurons in the ventral tegmentum.

KEY WORDS: dopaminergic neurons, ventral tegmentum, EEG, biological feedback, ratio of beta- and theta-rhythm power levels, neurofeedback.

Feedback (FB) based on the EEG is increasingly used in the treatment of attention deficit hyperactivity disorder. Correction of impairments is addressed by training with EEG–FB for increases in the EEG beta rhythm and decreases in the theta rhythm, which improves levels of voluntary attention and self-control in children [1, 2, 12]. According to Malone's model [13], impairments in the balance of the influences of the dopaminergic (DA) and other aminergic systems on neocortical neurons play an important role in the pathogenesis of attention deficit hyperactivity disorder. This leads to the suggestion that the effects of EEG–FB sessions are mediated by stabilization of these influences [1, 12]. However, experimental studies confirming this suggestion have not been performed. The aim of the present work was therefore to analyze changes in the EEG and in the activity of DA neurons in the ventral tegmentum (VT) during EEG–FB sessions directed to increasing differences in the ratio of the spectral power (SP) levels of the EEG beta and theta rhythms. Experimental studies of this type should allow assessment of the concrete mechanisms of formation of the effects of EEG–FB training.

METHODS

Studies were performed on two conscious cats weighing 2.5–4 kg. The animals underwent preliminary surgery under general anesthesia to implant guide cannulae into the brain; microelectrodes were inserted into these using a micromanipulator to record neuron activity in the area having the stereotaxic coordinates AP3–AP4, L1–L2, H4–H5 [14], i.e., the VT. Monopolar EEG recordings were made with the active electrode on the skull surface over the frontal area of the cortex (over field 6 of the ipsilateral hemisphere) and the reference electrode in the same area of the contralateral hemisphere. Experiments were started after 5–7 post-operative days, with parallel recording of the spike activity of VT neurons and EEG traces during sessions of EEG–FB. During experiments, the cats were placed in a hammock in the state of calm waking. Activity was recorded from single neurons using a mobile electrode consisting of a silver microwire (12 μm in diameter) in glass

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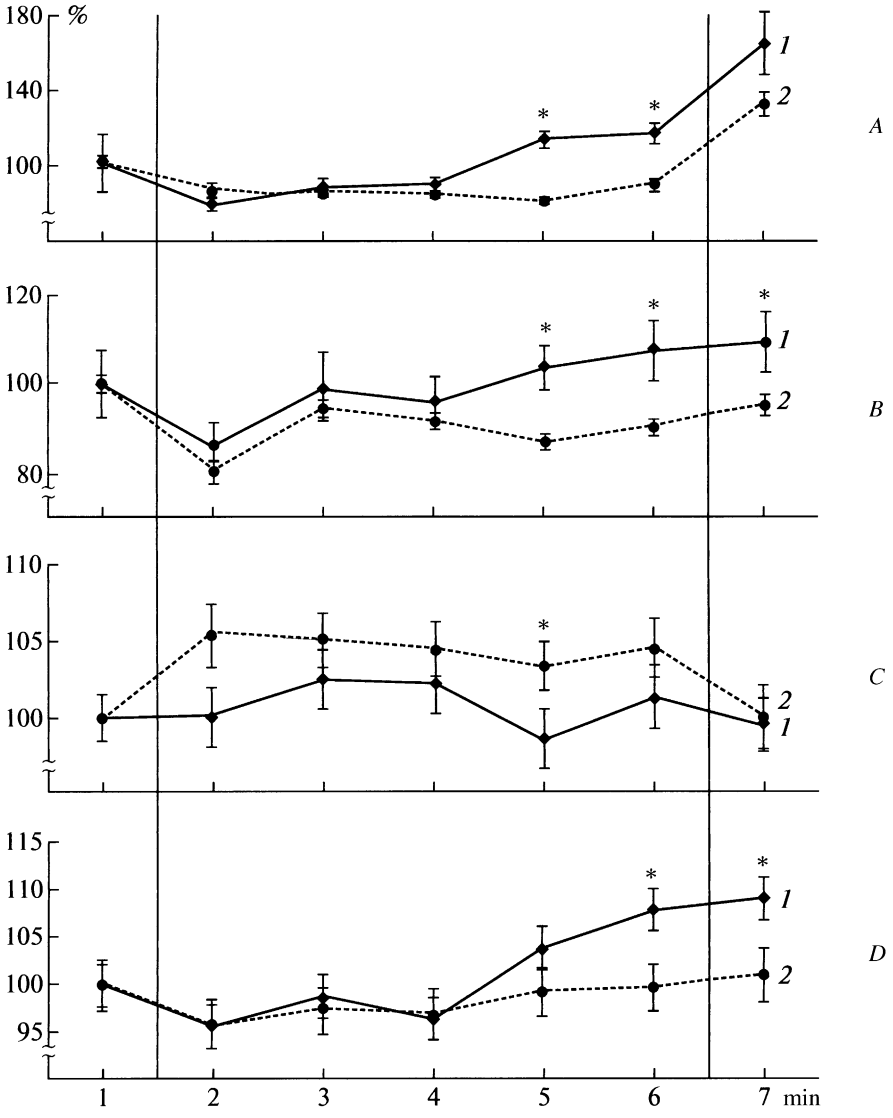

Fig. 1. Dynamics of study parameters during feedback sessions (*1*) and control sessions (*2*): *A*) ratio of spectral power levels of the beta and theta rhythms; *B*) spectral power of the beta rhythm; *C*) spectral power of the theta rhythm; *D*) activity of ventral tegmentum dopaminergic neurons. Data were averaged for 45 experimental sessions and 31 control sessions. Vertical lines identify the period of sound signal presentation (from minute 2 to minute 6). *Significant differences compared with controls, $p < 0.05$; the baseline level of each parameter was taken as 100%.

insulation (70 μm in diameter) with a sharply pointed tip resembling an injection needle. Microelectrode resistance was 0.8–1 MΩ. After amplification, signals were passed to the input of a computer sound card (sampling frequency $4 \cdot 10^4$ Hz). Study neurons were regarded as presumptive DA cells on the basis of published electrophysiological criteria allowing the discharges of DA and non-DA neurons to be discriminated: relatively low baseline activity frequencies (1–8 spikes/sec), the multiphasicity and long durations (2.5–5.0 msec) of action potentials, and positioning of the cells in the VT area of the brainstem [9]. EEG recordings were made using a Bioscrypt BST-112 (Germany) electroencephalograph, the signal being passed through an SDI–ADC16-16 laboratory interface to a computer with a sampling frequency of 200 Hz. The main EEG rhythms were discriminated, including the theta (4–7 Hz) and the beta (14–30 Hz) rhythms.

EEG–FB sessions were performed using the following protocol: baseline recording (first minute), delivery of the FB sound signal (white noise, minutes 2–6), aftereffects (minute 7). The dependent parameter was the intensity of the white noise, which changed depending on the ratio of the SP of the beta rhythm to the SP of the theta rhythm (to 70–80 dB), with greater values of this ratio producing

smaller loudness levels for the white noise (experimental sessions, experimental series). The animals were initially trained to control their EEG rhythms and 50–70 sessions were performed without recording of spike activity. This was followed by sessions in which parallel recordings were made of EEG traces and neuron activity in the VT. After 7–10 such sessions, control sessions were performed (control series). In this series, the loudness of the sound signal was not associated with the ongoing EEG pattern and was the sound signal from one of the traces made previously in an experimental session. Attempts were made to record a given neuron during one experimental session and one control session. When, during the recording of the activity of a particular neuron, the experimental session was performed first and the control session subsequently, spike activity traces of the next neuron were made with the control session first. This experimental model was developed to identify differences in the responses of individual neurons to the sound signal changing chaotically or depending on the animal's ongoing EEG pattern, with simultaneous evaluation of the possible contribution of the activity of the DA neurons being studied to forming the effects of FB.

Experimental data were recorded in computer memory and were subsequently processed. SP levels of EEG rhythms were calculated using a fast Fourier transform. Neuron activity was evaluated by counting the numbers of action potentials per unit time. Experimental data were summed for each minute. Each animal was used for 2–3 months. After experiments, animals were euthanased and the neuron activity recording zone was verified on brain sections prepared by standard methods. Further processing of experimental data was performed by unifactorial analysis of variance (ANOVA). Our studies were restricted to two animals on humanitarian grounds.

RESULTS

Activity was recorded from 45 neurons (which on the basis of the criteria identified above were presumptively regarded as DA cells) and 45 experimental sessions and 31 control sessions were performed. The results of these experiments showed that in the experimental series, the ratio of the SP of the beta rhythm to the SP of the theta rhythm increased from the second half of the session as compared with that in controls (Fig. 1, *A*). This increase was significant at minutes 5 and 6. A tendency to an increase in the ratio of the SP of the EEG beta rhythm to the SP of the theta rhythm as compared with controls persisted during minute 7.

This change in the SP ratio was associated with an increase in the SP of EEG beta activity. This frequency range of EEG oscillations showed statistically significant changes (increases relative to controls) at minutes 5, 6, and 7 (Fig. 1, *B*). The SP of the theta rhythm, conversely to the dynamics of beta-rhythm SP, decreased throughout EEG–FB. However, these changes were mainly tendencies and were statistically significant only in minute 5 (Fig. 1, *C*).

The activity of DA neurons during EEG–FB sessions increased (Fig. 1, *D*). Statistically significant changes relative to controls were seen in minutes 6 and 7. Attention is drawn to the similarity of beta-rhythm SP dynamics and changes in VT DA neuron activity throughout EEG–FB sessions.

DISCUSSION

The data obtained here on EEG changes are consistent with results obtained not only in animals, but also in humans. Amzica et al. [8] showed that cats could be trained to generate faster (20–50 Hz) oscillations on acquisition of an operant conditioned reflex. In these experiments, cats showed spatially selective increases in the generation of groups of fast oscillations in the motor cortex (field 4) to 140%. Studies reported by Grin-Yatsenko et al. [1, 2] showed that subjects could increase the ratio of the power of beta1 rhythms to the power of the rest of the EEG spectrum by 30–100% during 4-min training periods. Increases in this ratio were found to result from decreases in the power of the low-frequency parts of the EEG spectrum and simultaneous increases in the level of beta1 activity.

In addition, our experiments showed that the activity of DA neurons was in fact modified during EEG–FB sessions. What is the possible role of these changes in forming the effects of training?

There are several hypotheses for the mechanisms of the correcting effects of neurotherapy. Sterman [16] proposed that EEG–FB sessions might restore the regulatory function of the thalamocortical mechanisms involved in supporting attention processes. A similar point of view was espoused by Abarbanel [7], who suggested that the mechanisms of EEG–FB were based on the plasticity of thalamic and limbic neural networks. Lubar [12] proposed that changes in the efficiency of signal transmission in subcortical-cortical and cortical-cortical neural circuits might result from modification of the activity of brain aminergic systems. Rearrangements of the system of resonating loops in cortical-subcortical formations, which are accompanied by changes in EEG rhythm patterns, are tightly linked with these modifications.

At the same time, there is convincing evidence that DA neurons in the midbrain VT provide dense innervation of limbic system structures and the cortex (particularly the prefrontal area) [11], modulate glutamatergic signal transmission in the neocortex [15], and play important roles in triggering and maintaining the processes supporting attention [13], in inducing long-term potentiation, which is a key mechanism of attention [10], and in forming conditioned reflexes [4, 5]. In addition, data have been obtained indicating a direct relationship between the activity of the DA system and the power of the EEG beta rhythm [3, 6].

Integrating existing theories of the mechanisms of neurotherapy sessions and results obtained in studies of the functional role of the brain DA system with the data obtained here suggests the following scheme for the involvement of the DA system in the mechanisms of EEG–FB. The VT DA system, which modulates the activity of the neural networks of the thalamus, limbic system, and cortex, is involved in maintaining a variety of processes leading to increases in the synaptic efficiency of these networks. This is apparent in the pattern of ongoing EEG activity as an increase in the SP of the beta rhythm. Thus, the decisive factor determining the effectiveness of EEG–FB sessions is the creation of an increased neurotransmitter level (in our case DA) in quite extensive areas of the brain, leading to simultaneous modification of the state of large neuron ensembles linked with the formation of the EEG beta rhythm. Plastic changes occurring in these neural networks on repeated EEG–FB training sessions become structural and persist for long periods of time.

CONCLUSIONS

1. The ratio of the power levels of the beta and theta rhythms increases during EEG–FB sessions because of increases in the spectral power of the beta rhythm and decreases in the spectral power of theta activity.

2. The spike activity frequency of neurons in the dopaminergic system of the ventral tegmentum increases during EEG–FB sessions.

3. The use of acoustic feedback signals based on EEG measures allows animals to be trained to control their EEG rhythms, which occurs because of, among other factors, rearrangements in the activity of dopaminergic neurons in the ventral tegmentum.

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