Effect of Semax Heptapeptide on the Human Electroencephalogram

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The effect of the new regulatory peptide Semax ($ACTH_{4-10}$ fragment) on the electroencephalogram of a healthy person was studied. Semax was administered at 0.5 mg/kg intranasally in 9 volunteers without causing any nervous system pathology. The control group comprised 6 examinees treated in the same way with distilled water. The effect of Semax manifested itself on the electroencephalogram as a boost of biopotential strength in all ranges but especially in that of the α-rhythm, the zonal differences of which were enhanced, without any pathological signs being evident.

Key Words: *neuropeptides; Semax; electroencephalogram*

Studies of the neurotropic activity of the N-terminal fragments of adrenocorticotropic hormone (ACTH) were launched at the end of the Sixties, and it was discovered that $ACTH_{1-10}$ and $ACTH_{4-10}$ effectively reverse the learning deficiency in hypophysectomized rats [3]. Intensive efforts on the part of investigators of different specialities resulted in the creation of drugs based on these fragments which improve selective attention and speed up memory consolidation. One such drug is ORG2766 analog and another it derivate Ebiratid [(0_2)MEHFdkf-NH-$(CH_2)_8$-NH_2]. Although Ebiratid is effective in low doses, the duration of its action is relatively short. Besides, a D-lysine residue was incorporated into this peptide to intensify its effect, and the D-amino acids are known not to be included in eucaryote proteins and peptides.

To devise a peptide stimulator of prolonged action it was proposed (Institute of Molecular Genetics) to protect the $ACTH_{4-10}$ fragment with proline residues, which are hard to split with peptidases. The result was Semax heptapeptide [(0_2)MEHFPGP], which is able to stimulate mnemic functions of animals and man for many hours [2]. At present Semax has passed clinical trials, the results of which testify that this peptide produces a variety of positive effects on forebrain function.

Electrophysiological manifestations of the effect of Semax on the healthy human brain were studied in the present investigation.

MATERIALS AND METHODS

The effect of Semax was examined on 9 right-handed volunteers aged from 18 to 43 years without any features of nervous system pathology. The drug was administered intranasally at 0.5 mg/kg. The general effect of Semax on the central nervous system was studied by analyzing the changes of electroencephalogram (EEG). The EEG was recorded before drug administration and 5, 15, and 25 min after it in 8 leads monopolarly. Active electrodes were placed at points O1, O2, C3, C4, F3, F4, T3, and T4, while reference electrodes were placed at points in A1 and A2 according to the 10-20 system. The examinee sat comfortably in a darkened room in a state of quite alertness with the eyes closed. The EEG parameters

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analyzed were as follows: total EEG power in the indicated leads, power of δ- , θ- , α-, β_1-, and β_2-rhythms, the expression of each rhythm in percent, the mean amplitude (μV) and frequency (Hz) of each rhythm, as well as the power of subharmonics. The coefficients of interhemispheric asymmetry and of spectrum asymmetry were measured using the formula: $K=(P_\alpha+P_{\beta1}+P_{\beta2})/(P_\delta+P_\theta)$, where P is the power of the corresponding rhythms. The coefficient shows the correlation between the fast and slow components of the EEG spectrum. The results of the spectral analysis were presented as a map of EEG rhythm power distribution over the scalp.

The control group consisted of six volunteers who were treated with the same volume of distilled water but thought they were getting Semax. The EEG analysis included the same parameters as in the experimental group.

RESULTS

Prior to Semax administration the EEGs of the majority of examinees both in the experimental and in the placebo group were normal [1].

A marked increase of the total EEG power due to a significant ($p<0.05$) increase of the α-rhythm power in the occipital leads against the background of a slight decrease of the α-rhythm power in the frontal and temporal leads was found after Semax administration in the experimental group. This resulted in an increase of the zonal differences in the α-rhythm. A decrease of the interhemisphere asymmetry was also noted. While the background (before drug administration) α-rhythm power was higher in the right (subdominant) hemisphere, the interhemispheric differences in the α-rhythm were reduced after Semax administration, especially for C3 and C4. Other EEG parameters did not undergo significant changes under the influence of the drug.

No pathological signs such as δ- and θ-waves, or high-amplitude spike fluctuations, or epileptic discharges, or focal changes were not found during the whole period of EEG recording.

It should be noted that the above effect appeared in the EEGs of the experimental group 5 min after drug administration and did not change significantly during the subsequent 15 and 30 min (Fig. 1).

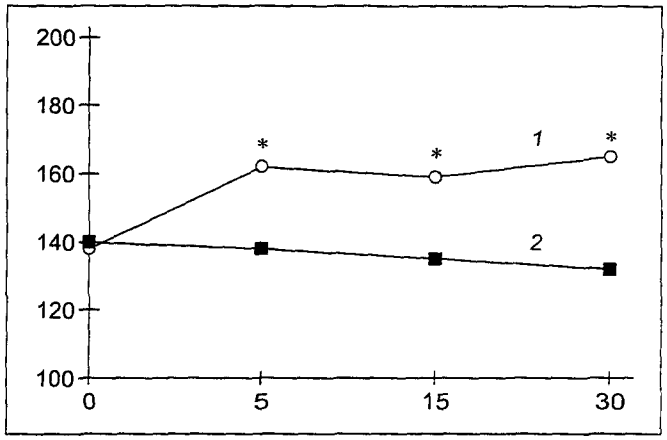

Fig. 1. Dynamic of α-rhythm power in experimental (*1*) and control (*2*) groups. Abscissa: time after Semax administration, min; ordinate: total power of α-rhythm in occipital leads, μV^2. *$p<0.05$ as compared to the control.

The EEG changes found in the experimental group were not observed in the control group. α-Rhythm power was even somewhat decreased in the occipital and central leads 15 min after the administration of distilled water, but these changes were not significantly different from the baseline parameters.

The findings testify that Semax does not cause any pathological changes of the EEG in the interval from 5 to 30 min postadministration. However, the drug reliably increases the total EEG power in all leads and the α-rhythm power especially in the occipital leads, thus making for more contrasting zonal differences of the α-rhythm.

An increase of the α-rhythm power and of its zonal differences may attest to enhanced readiness of the brain for the perception and processing of afferent signals of different modalities.

REFERENCES

1. L. R. Zenkov and M. A. Ronkin, in: *Functional Diagnosis of Nervous Diseases* [in Russian], Moscow (1991), pp. 7-146.
2. M. A. Ponomareva-Stepnaya, V. N. Nezavibat'ko, L. V. Antonova, *et al.*, *Khim.-Farm. Zh.*, № 7, 790-795 (1984).
3. D. De Wied, in: *Frontiers in Neuroendocrinology*, Oxford (1969), pp. 97-140.