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EFFECT OF PEPTIDE FACTORS OF THE RIGHT AND LEFT HEMISPHERES ON AMPLITUDE AND DURATION OF SOMATOSENSORY, VISUAL, AND PARIETAL EVOKED POTENTIALS IN RATS

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The important role of mechanisms of lateral specialization of the cerebral hemispheres and their mutually complementary functions in activity of the intact CNS is well recognized. This applies to questions of maturation of the brain [11, 13], cognitive activity [1, 14], emotions and perception [1, 7], mental functions [7], etc. It has also been shown that reorganization of the damaged brain is largely based on the same principles of paired function [2, 4], and that some mental disorders may be the result of a disturbance of normal interhemispheric relations. Meanwhile functional asymmetries discovered by clinical, behavioral, and electrophysiological methods, are basically neurochemical in nature [9, 10, 12]. For the correction of states induced by imbalance of the activity of the right and left halves of the brain, it may therefore be the most natural course to use endogeneous biological regulators and, in particular, neuropeptides.

The aim of this investigation was to study the characteristics of peptide regulation of the functions of the right and left cerebral hemispheres.

EXPERIMENTAL METHOD

Experiments were carried out on 30 rats and eight cats. Peptide extracts were obtained from the right and left halves of the rats' brain and their action tested by recording changes in parameters of evoked potentials (EP) in cats. The method of obtaining peptide extracts was described previously [5, 6].

The cats were anesthetized with ether or pentobarbital (30 mg/kg), the cranial cavity widely opened, the dura removed, and EP recorded in the somatosensory, visual, and parietal regions of the cortex in the left hemisphere by Ag-electrodes 0.2 mm in diameter. Before the recordings the animals were artificially ventilated after injections of relaxants. The radial nerve was stimulated by pulses 0.5 msec in duration and with an amplitude of 3-6 V (threshold value 2-2.5 V), and visual stimulation was applied in the form of flashes with an energy of 0.3 J and a duration of 0.1 msec (monocular application). Transcallosal stimuli (TCS) had a duration of 0.1-0.2 msec and an amplitude of 10-20 V. EP were led from a UBP2-03 biopotentials amplifier to a "Disa Indicator" oscilloscope, from the screen of which they were photographed by FOR-2 camera. The EP were processed collectively: 30 control and 30 after application of extracts; superposition of 5-8 responses also was used. Before the electrophysiological experiment the cats were tested by the food-getting method and animals with a dominant right forelimb were selected. The results were subjected to statistical analysis by estimation of the probability of noncoincidence of the two compared curves [3] and by Student's t test. To confirm the peptide nature of the brain extracts, control experiments were carried out with inactivation by pronase (Table 1).

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TABLE 1. Modulating Effect of Peptide Extracts on Amplitude of EP (in μV) of Various Zones of the Cerebral Cortex (M ± m; n = 30)

Experimental conditions	Object recorded				
	somatosensory		parietal		visual
	stimulus modality				
	nerve	TCS	photic	TCS	photic
Control	368±15,5	149±15,4	110± 7,6	445±21,8	422±16,6
R extract	313±15,4**	185±11,3**	159±10,8**	515±19,6**	341±28,5**
L extract	—	120±13,4*	143± 9,8*	498±18,3**	467±20,5**
R extract + pronase	338±13,6	127±10,4	112± 8,4	452±18,5	403±23,9
L extract + pronate	350±16,8	131±12,3	—	409±13,1*	—

Legend. *p 0.05, **p < 0.01.

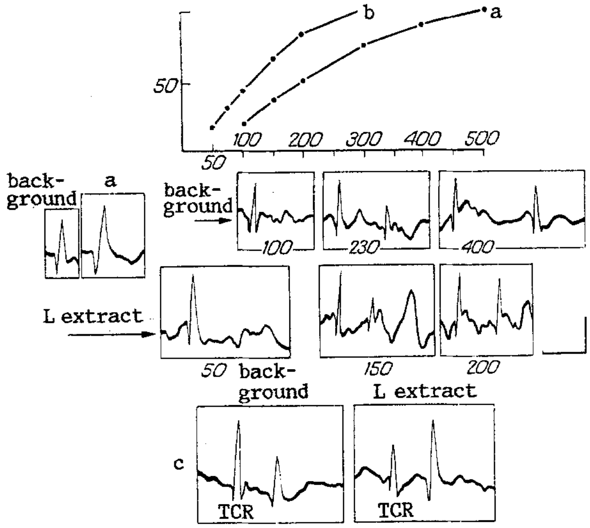

Fig. 1. Effect of paptide extracts of left hemisphere on amplitude and duration of ipsilateral EP. a) Single responses to stimulation of radial nerve, b and graph) recovery cycles of somatic EP; a) control, b) after application. Abscissa, interval between stimuli, msec; ordinate, ratio (in %) of amplitude of testing and conditioning stimuli; c) interaction of TCR and somatic EP. Calibration: 200 μV, 200 msec.

EXPERIMENTAL RESULTS

The action of the peptide factors of the extracts was found to be dose-dependent. Variation of the dose from 40-50 ng to 3 μg per application led not only to a quantitative, but also to a qualitative change in the effects. When used in the maximal dose, both right (R) and left (L) extracts had a similar effect on EP, consisting of a three-fourfold reduction of amplitude of the sensory and interhemispheric responses; however, the general pattern of interaction between the stimuli was preserved as in the intact cortex. Reduction of the dose was accompanied by weakening of inhibitory influences, by reversal of the sign of the response, and by the appearance of differences in the actions of the R and L extracts. Figure 1 shows EP recorded in the somatosensory (S1) region of the left hemisphere before and during application of the L extract to this zone in a dose of 40-50 ng. Single somatosensory EP (a), their interaction during paired stimulation (b), and a graph and also interaction of the transcallosal responses (TCR) and EP also are shown. It will be clear from Fig. 1 that the L extract shortened the recovery cycle of the testing somatic BP to almost twice its amplitude. Before application its amplitude reached the initial value if the interval between stimuli was 500 msec, whereas after application of the L extract this interval was shortened to 300 msec (see Fig. 1b and graph; Q = 2.30, $p < 0.01$). The amplitude of the single somatosensory EP was increased by 15-40% through the action of the L extract (Fig. 1a), whereas its effect on the amplitude of TCR

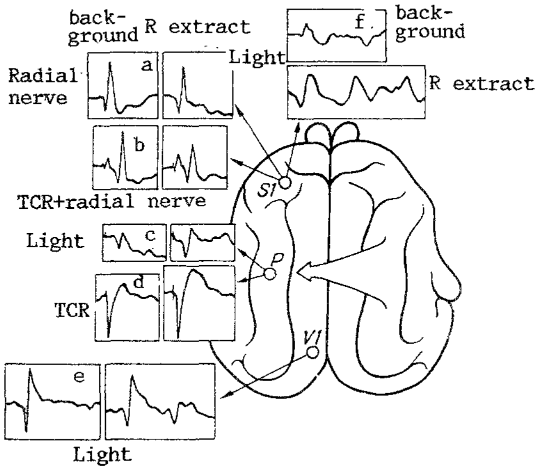

Fig. 2. Effect of "right-sided" peptide extracts on single and paired responses of projection and association cortical areas of left hemisphere. a, b, c, d, e (on left and f above) — control responses; on right — after application. Stimulus modality indicated next to figures; remainder of legend as to Fig. 1.

was opposite (Fig. 1c): it was reduced by 15-25% (Table 1). Interaction of TCR and EP also changed, the testing somatic EP being subjected to facilitatory influences. Changes in the amplitudes of the responses, incidentally, took place mainly on account of the negative phases. The experiments thus showed that extract of the left (the ipsilateral side relative to recording) hemisphere activates thalamocortical inputs into the cortex for stimuli of the adequate modality, whereas activity of the interhemispheric inputs is inhibited.

Application of the R extract had the opposite action on the amplitude of TCR and of the somatic and visual EP to that of the L extract. Figure 2 shows traces of responses recorded in the projection and parietal association (area 7) regions of the cortex of the left hemisphere. The responses are shown in pairs: before (background) and after application of the R extract, with an indication of modality of the stimulus. It was shown that the effect of the R extract is manifested as a fall in amplitude of the negative phase of the somatic and visual EP recorded in zones corresponding to stimulus modality. Besides, the positive wave of the visual EP also was inhibited in the visual cortex. During interaction between TCS and the somatic EP (Fig. 2b) against the background of the action of the R extract, facilitation of TCR was observed, its amplitude increasing by 20-40%, with a simultaneous decrease in amplitude of the somatic EP by 15-30%. Thus "right-sided" peptides lead to activation of callosal and inhibition of thalamocortical inputs into the left hemisphere.

Another particular feature of the effect of peptides from the right half of the brain must also be noted. Against the background of their application, late waves began to appear in the structure of EP with a greater degree of probability, together with sensory after-discharges with a frequency of 4-5 and 8-10 Hz, i.e., within the θ- and α-rhythm bands. Activity in the θ-band is known to reflect processes of coadjustment of different cortical regions in the period of learning and, in particular, during the compensatory process [8, 15]. Thus this fact can be interpreted to some degree as facilitation of integrative processes of the left hemisphere under the influence of peptide factor of the R extract.

When changes in the electrophysiological responses of the association cortex are described, it can be stated that the effects of the R and L extracts in this region are similar in type, and that differences between them are purely quantitative. Both extracts increased the amplitude of both TCR and the response to the photic stimulus, but the R extract had the stronger action (Fig. 2c, d).

The appearance of a response to the photic stimulus in the projection region of the somatosensory system (i.e., in a zone not corresponding in stimulus modality) against the background of application of the R extract, deserves particular attention (see Fig. 2f). The phenomenon of widening of the zones of recording of EP was demonstrated in our previous experiments during the development of compensatory processes in the cortex after unilateral damage

[4], and it was interpreted as an increase in the degree of polymodality and polyfunctionality of the structures. Pure peptide regulation may evidently be one mechanism of this process.

The action of the extracts on the primary EP complex was reversible. Only a few seconds after rinsing out the extract the amplitude changed and recovered in the course of 2-3 min. However, the phenomenon of widening of the response zones continued for 2-2.5 h. In all probability peptide factors of the right hemisphere induced a complex chain of processes leading to an increase in the polymodal properties of the neurons which lasted long enough to play an important role in certain periods of compensatory restoration of brain functions [2, 4].

The experiments thus showed that the influence of peptide factors contained in brain extracts on integral activity of the CNS is realized mainly on axodendritic synapses in the outer layers of the cortex, and it evidently controls the level of convergence of impulses of different modalities. The ipsilateral extract facilitates responses to stimuli of the appropriate modality for the given cortical region, whereas the contralateral extract activates interhemispheric inputs. The extracts studied can also potentiate the polymodal properties of neurons, and on that basis they may be effective in the processes restoring brain activity after unilateral damage.

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