DYNAMICS OF INDIVIDUAL CARDIOVASCULAR RESPONSES IN RABBITS IN ACUTE EXPERIMENTAL EMOTIONAL STRESS

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The averaged dynamics of cardiovascular disturbances in rabbits during experimental emotional stresses caused by continuous stimulation of the negative emotiogenic centers of the hypothalamus for many hours while the animals were immobilized, has been investigated [2, 3]. Meanwhile, no attempt has been made to analyze individual cardiovascular responses of animals under similar experimental conditions.

Individual types of dynamics of cardiovascular responses of animals during acute experimental emotional stress were studied in the present investigation.

EXPERIMENTAL METHOD

Experiments were carried out on 40 male Chinchilla rabbits weighing 2.5 kg with stimulating electrodes implanted beforehand into the region of the ventromedial nucleus of the hypothalamus. Only those animals which responded to stimulation of the ventromedial hypothalamus (2-8 V, 50 Hz) with a passive defensive reaction were used for the experiments.

During the experiments, the rabbits were tied to a frame and exposed for 3 h to irregular, alternating, and simultaneous brief electrical stimulation of the ventromedial nuclei of the hypothalamus and of various regions of the skin. Aperiodic emotiogenic stimulation, as several workers have shown [1, 4, 6], has the most powerful stressor action.

Electrical stimulation of the skin was applied through needle electrodes inserted into the skin of the fore and hind-limbs, and also through special clips to the rabbits' ears. Stimuli which caused a rise of arterial blood pressure (BP) by 20-30 mm Hg without any marked motor response of the animal also were used. Each animal was stimulated six times in the course of 10 min. A pulsed current with a voltage of 10-50 V and frequency 50 Hz was used for nociceptive stimulation. Each stimulation lasted on average 5-10 sec.

BP and the heart rate were recorded in each animal, through a catheter introduced into the femoral artery, by means of a strain gauge and Siemens-Elema Mingograph.

EXPERIMENTAL RESULTS

Individual analysis of the changes in BP during exposure to the stimuli used revealed several groups of experimental animals irrespective of the initial type of hemodynamic parameters (Fig. 1).

Group 1 consisted of five animals whose BP remained at the initial level throughout the period of stimulation, and the changes in heart rate were not of the typical character for the whole group: This index showed either an increase or a decrease.

In the animals of group 2 (nine rabbits) various changes in BP were observed, but they were not accompanied by death of the animals. Depending on the character of the changes in BP, the animals of this group were divided into two subgroups. In the animals of the first subgroup, BP at the beginning of stimulation was reduced by 17 ± 11.3 mm Hg and the heart rate at this time was usually increased by 50 beats/min. The de-

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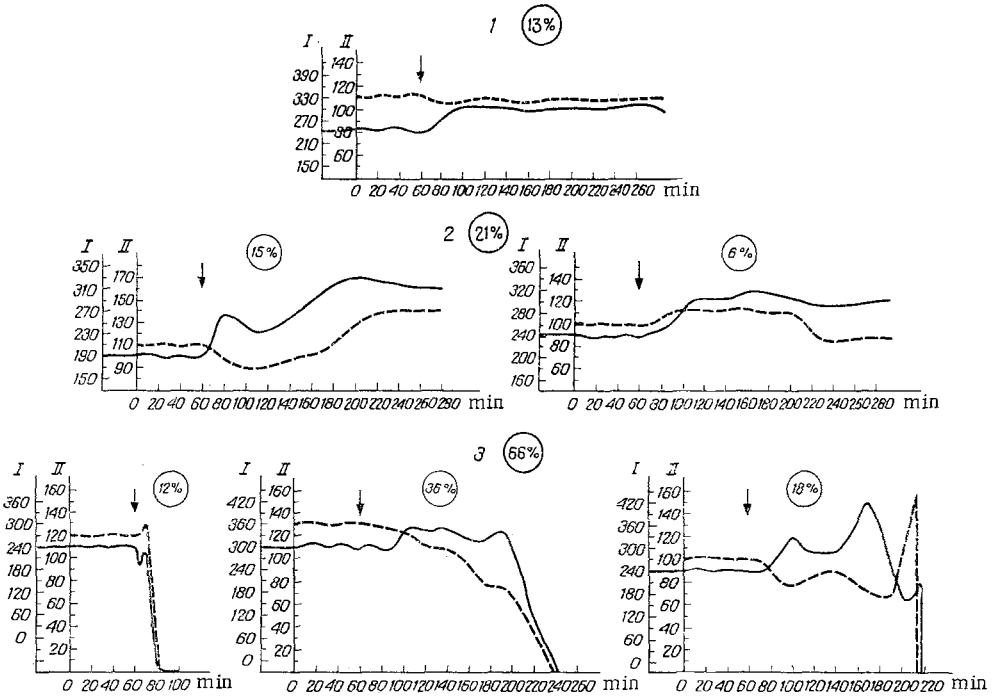

Fig. 1. Types of cardiovascular responses of rabbits during acute emotional stress. 1-3) Dynamics of changes in BP and heart rate of animals of different groups. Abscissa, time (in min); ordinate: I) heart rate (beats/min), II) BP (in mm Hg). Arrows indicate beginning of stimulation. Number of animals in each group and subgroup (in % of total number) are circled.

crease was followed by a gradual rise of BP and by some reduction in heart rate, but 1.5-2 h after the beginning of the experiment BP was increased by 28 ± 20.6 mm Hg compared with its initial level, and the heart rate was increased on average by 90 beats/min (three rabbits). In the animals of the second subgroup, BP was raised at the beginning of the experiment by 5.8 ± 3.2 mm Hg, but after 1.5-2 h it showed a steady reduction by 23.3 ± 2.7 mm Hg relative to the initial level. The heart rate rose in the course of the experiment by 50-80 beats/min (six rabbits).

Group 3 consisted of animals (conventionally described as "predisposed") which died in the course of the experiment (26 rabbits). This group of animals was divided into three subgroups. The first consisted of five animals which died between 15 and 40 min after the beginning of the experiment. In these animals, in response to the first stimulations BP rose by 16 ± 9.4 mm Hg, but the heart rate showed only a very small increase, or it was reduced. These changes were followed by a sharp decrease in the heart rate and BP, and by death of the animal. The second subgroup consisted of 14 rabbits, characterized by a gradual decrease in BP immediately after the beginning of stimulation, which ended in death in the course of 1.5-2 h. The heart rate of the animals of this subgroup in the course of the experiment was higher than initially on average by 55 beats/min and it fell sharply at the time of the animal's death. The third subgroup consisted of seven rabbits in which a unique phase dynamics of BP was found in response to stimulation. Immediately after the beginning of stimulation there was a very small increase or no change in BP. The heart rate of these animals remained at its initial level. BP then fell by 13 ± 4.7 mm Hg below its initial level, and remained at the new level for 1-1.5 h. Under these circumstances, the heart rate was usually raised by 50-100 beats/min. This was followed by a second rise of BP by 40 ± 11.3 mm Hg, accompanied by a decrease in heart rate on average to the initial level. At the height of the increase in BP the animals died.

The individual types of cardiovascular responses of the rabbits to acute emotional stress thus revealed correspond fully to the results of experiments on rats [5] under conditions of immobilization stress. This, in turn, is evidence that the mechanisms of emotional stress are the same in animals of different species.

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CONTRACTILE PROTEINS OF NERVE ENDINGS AS A POSSIBLE TARGET FOR THE PRESYNAPTIC ACTION OF TETANUS TOXIN

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Tetanus toxin (TT) is known to have a presynaptic action, leading to inhibition of mediator secretion in central and peripheral synapses [5]. It has also been shown that TT binds selectively with gangliosides of nerve ending membranes [6]. However, the mechanism of its toxic action has not yet been explained. It has been suggested that there are three centers in the TT molecule: receptor, binding with gangliosides, antigenic, and toxophore [6]. The results of electrophysiological investigations indicate that the action of TT is aimed at the final stage of exocytosis – interaction between synaptic vesicles (SV) and complementary regions of the presynaptic membrane [5]. Elucidation of the biochemical target for TT is important for the understanding not only of the pathogenesis of tetanus, but also of the process of mediator secretion itself. It has recently been postulated that mediator secretion is based on mechano-chemical processes in which a cytoskeletal network of microtubules, neurofilaments, and active microfilaments associated with the presynaptic membrane takes part [2, 9]. These structures may be responsible both for transporting SV to the active zone of the synapse and for complementary contact between SV and the presynaptic membrane, with subsequent exocytosis. Accordingly, it can be suggested that the target for TT may be the contractile proteins of nerve endings. It was shown previously [4] that TT depresses the ATPase activity of the actomyosinlike protein (AMLP) of the rat brain. The object of the present investigation was to study the effect of TT on the AMLP superprecipitation reaction and on interaction between actin-like protein (ALP) and isolated SV.

EXPERIMENTAL METHOD

The TT was purified by gel-filtration on Sephadex G-100 [8]. TT with a toxicity of $1.25 \cdot 10^5$ MLD for mice/mg protein was used in the experiments. AMLP was isolated from bovine cerebral cortex by the method in [12] with certain modifications. The tissue was homogenized in 2 volumes of isolation medium (0.9M KCl, 1.5 mM dithiothreitol, 5 mM $MgCl_2$, 50 mM Tris-HCl; pH 9.2) at 0-4°C. The homogenate was treated with 0.5% Triton X-100 and kept in the cold for 18 h, after which it was centrifuged (1 h, 10,000g). The supernatant was diluted with 1 mM $CaCl_2$ solution in the ratio of 1:5, the pH of the medium was adjusted to 6.25-6.3 with acetic acid, and centrifugation was repeated under the same conditions. The residue was washed and suspended in isolation medium, the final KCl concentration being adjusted to 0.6M. After centrifugation (30 min, 100,000g) the supernatant was diluted sixfold with dionized water, the pH adjusted to 6.25-6.3 with acetic acid, after which centrifugation was carried out for 1 h at 100,000g. The residue, consisting of AMLP, was dissolved in 0.6M KCl containing 1 mM dithiothreitol and 20 mM Tris-HCl, pH 7.4, and kept at 0-4°C for 1-2 weeks. The yield of AMLP was 10 mg protein/g wet weight of tissue. Protein was determined by Lowry's method.

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