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ANALYSIS OF HEMODYNAMIC RESPONSES TO HYPOTHALAMIC STIMULATION IN WAKING ANIMALS

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Experiments on waking cats showed that electrical stimulation of "protective" zones of the hypothalamus leads to development of hypertension and inhibits baroreceptor reflexes. In animals with divided carotid sinus and aortic nerves, threshold hypothalamic stimulation leads to the appearance of depressor responses, whereas above-threshold stimulation evoked depressor-pressor responses. It is suggested that depression of baroreceptor reflexes is one of the mechanisms of the development of hypertension in response to hypothalamic stimulation.

KEY WORDS: Hypothalamic stimulation; hypertension; baroreceptor reflexes.

Electrical stimulation of "protective" zones of the hypothalamus is known to evoke hypertension due to an increase in cardiac output and constriction of regional vessels. Acute experiments have shown [2, 4] that the developing hypertension is accompanied by inhibition of baroreceptor reflexes.

The object of this investigation was to study the character of hemodynamic responses and to analyze the mechanisms of onset of hypertension during hypothalamic stimulation in chronic experiments on waking animals.

EXPERIMENTAL METHOD

Altogether 25 experiments were carried out on 14 cats. A week before the experiment, under sterile conditions, nichrome electrodes 150-180 μ in diameter were inserted into the ventromedial nucleus of the hypothalamus, and fluorine-plastic catheters filled with heparin were introduced into the external jugular vein and aorta (through the carotid artery). The distal ends of the catheters were brought out under the skin and fixed in special cocks, secured to the skull. The following were measured: the arterial pressure (BP, by a manometer incorporating mechanotrons), the interval between two adjacent systoles (by a cardiotachometer), and respiration (with a carbon detector); the baroreceptor reflexes were tested by the method described previously [3, 6] at rest and also during electrical stimulation (0.5-1.5 msec, 80-100 stimuli/sec, 50-500 μA,

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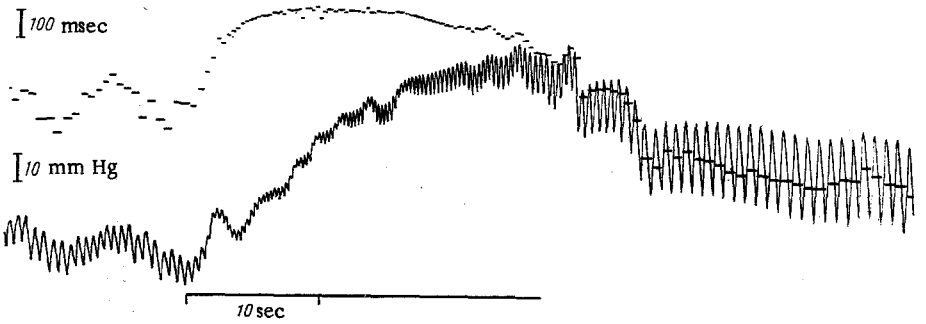

Fig. 1. Changes in period of cardiac contractions and BP during hypothalamic stimulation. From top to bottom: period of cardiac contractions, BP. Straight line shows duration of stimulation with time marker (10 sec).

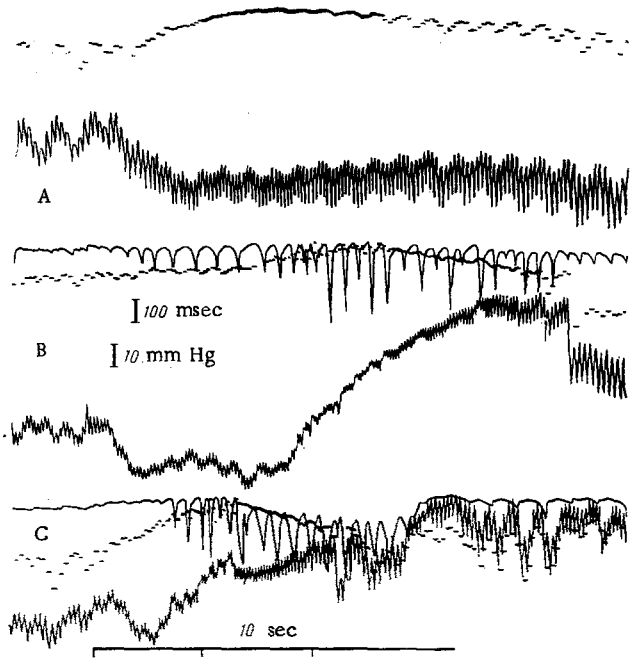

Fig. 2. Changes in respiration, period of cardiac contractions, and BP in cat during hypothalamic stimulation after deafferentation of carotid sinus and aortic reflexogenic zones. A) Threshold hypothalamic stimulation on third day after deafferentation; B) above-threshold stimulation; C) threshold hypothalamic stimulation on 9th day after division of nerves. From top to bottom, in A: period of cardiac contractions, BP; in B and C: Respiration, period of cardiac contractions, BP. Straight line shows duration of hypothalamic stimulation. Time marker 10 sec.

30 sec) of the hypothalamus. After the main series of observations a second operation was performed on the cats, involving bilateral division of the carotid sinus and aortic nerves. After the end of the postoperative period the animals were again used in the experiments.

EXPERIMENTAL RESULTS

In waking cats BP was 70-90 mm Hg, the mean period of cardiac contraction 350-550 msec, and the regression coefficient reflecting the relationship between the rate of artificial elevation of BP (intravenous

injection of phenylephrine) and the developing bradycardia, a quantitative indicator of the magnitude of the baroreceptor reflexes [6], was 4.4-11.7 msec/mm Hg. During threshold (as regards emotional reaction) stimulation of the hypothalamus a nonspecific "alerting reaction" of the animals developed, with changes in the rate and depth of respiration, mild tachycardia developed (the pulse interval was reduced by 30-60 msec), and BP increased (by 5-10 mm Hg). With an increase in the intensity of stimulation the character of the emotional responses differed in different cats and was manifested as active- or passive-defensive behavior.

An active defensive response of "rage" type consisted of the adoption of a threatening posture, growling, hissing, baring the teeth, piloerection, and dilatation of the pupils. The animals responded to provocative action (threatening) by actively attacking. Autonomic manifestations appeared after a minimal latent period (1-2 sec) and were maintained persistently throughout the period of stimulation (Fig. 1). Tachycardia (a decrease in the pulse interval by 200-300 msec) began virtually simultaneously with the rise in BP, which was increased by 40-50 mm Hg.

In a "fright – flight" response of passive defensive type the cat pressed itself against the floor with its tail uplifted, and sometimes micturition was observed. In response to provocation the animal pressed itself more closely against the floor, stretched out its head, and hissed. Autonomic changes during passive defensive behavior were similar to those in animals with a response of "rage" type but there intensity was rather less.

Testing the baroreflex during the time of the emotional behavioral response (artificial rise of BP) showed that baroreflex bradycardia was either absent or was much less than in the resting state. During established hypertension (irrespective of the type of emotional-behavioral response) the regression coefficient fell to 0-2 msec/mm Hg.

Immediately after division of the carotid sinus and aortic nerves, BP increased by 30-50 mm Hg and marked tachycardia developed: The initial cardiac frequency was 230-250 beats/min. The hypertension lasted 6-20 h, after which BP fell to normal. On the 3rd or 4th day after deafferentation of the baroreceptor zones BP did not exceed on average 80-90 mm Hg, but the cardiac frequency remained higher than initially (the pulse interval was 250-330 msec).

Threshold stimulation of the hypothalamus on the 3rd-5th day after division of the carotid sinus and aortic nerves against the background of more marked emotional-behavioral responses led to a decrease in BP by 10-20 mm Hg, which lasted throughout the period of stimulation (Fig. 2). The cardiac frequency was virtually unchanged or slight tachycardia was observed. With an increase in the intensity of hypothalamic stimulation a character of the emotional responses remained the same as before division of the "buffer" nerves but significant changes took place in the dynamics of BP. As Fig. 2 shows, the initial change in BP in the deafferented animals was hypotension, which was replaced 10-20 sec after the beginning of stimulation by a pressor response of BP. The changes in BP described above took place against a background of tachycardia which disappeared after injection of the beta-adrenoblocker Obsidan (propranolol) in a dose of 2 mg/kg.

It was shown previously [3] that 8-11 days after division of the carotid sinus and aortic nerves baroreceptor reflexes are restored. As Fig. 2C shows, hypothalamic stimulation in the cat 9 days after carotid sinus and aortic deafferentation gives rise to the same changes in BP as before division of these nerves. The changes are manifested primarily as disappearance of the hypotensive phase, and the pressor response of BP is obtained even with hypothalamic stimulation of threshold strength.

The results of these experiments showed that electrical stimulation of the hypothalamus, leading to the onset of hypertension, inhibits baroreceptor reflexes in waking animals. Threshold hypothalamic stimulation in cats with divided carotid sinus and aortic nerves does not cause BP to rise. The development of the hypertensive response both in a natural stress situation [3] and during low-intensity electrical stimulation of the hypothalamus is thus evidently due to inhibition of baroreceptor reflexes. Stimulation of diencephalic structures at a higher intensity probably leads to elevation of BP also through excitation of suprasegmental structures which directly activate spinal vasomotor neurons.

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