PARTICIPATION OF ADRENAL HORMONES IN THE GENESIS OF ARTERIAL HYPERTENSION OF HYPOTHALAMIC ORIGIN

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Continuous electrical stimulation for many hours of hypothalamic negative emotiogenic centers (the ventromedial nuclei) evoked persistent arterial hypertension with a characteristic phasic dynamics of adrenal secretory activity in waking, immobilized rabbits. Bilateral extirpation of the adrenals lowered the original level of the mean arterial pressure and inhibited the development of persistent arterial hypertension. Stimulation of the above-mentioned hypothalamic structures for many hours in adrenalectomized rabbits, in conjunction with administration of hydrocortisone and adrenalin, evoked persistent arterial hypertension again. After administration of hydrocortisone and adrenalin separately to adrenalectomized rabbits, stimulation of the ventromedial hypothalamic nuclei for many hours resulted in only a transient rise of blood pressure. It is concluded that an essential role in the formation of persistent arterial hypertension in rabbits during continuous stimulation of the hypothalamic negative emotiogenic centers for many hours is played by activation of adrenal cortical and medullary hormones.

KEY WORDS: emotional stress; adrenal hypertension; adrenal glands.

An important role in the genesis of arterial hypertension is played by continuous emotional stresses of negative character [1, 8]. Persistent arterial hypertension has been produced experimentally by prolonged stimulation of hypothalamic negative emotiogenic centers [3, 4]. Under these circumstances the source of descending pressor influences on the arteries was "static" emotional excitation arising at the level of the hypothalamic-limbic-reticular complex during stimulation of hypothalamic centers for many hours [9].

The object of the investigation described below was to study the degree to which arterial hypertension of emotional origin is produced through the hormonal mechanisms of the adrenals.

EXPERIMENTAL METHOD

Stimulating electrodes were implanted into the ventromedial nuclei of the hypothalamus of sexually mature male rabbits. After determination of the individual threshold values of electrical stimulation evoking a passive defensive response, the secretory function of the adrenals was studied and compared with the dynamics of the mean blood pressure in the femoral artery (direct method) in 15 rabbits during continuous stimulation (50-70 Hz, 3-8 V, 0.1-1.0 msec) of the hypothalamic emotiogenic centers for a period lasting several hours. Blood samples were taken through a preimplanted catheter from the femoral vein 10 min before and 20, 60, and 90 min after the beginning of stimulation for determination of the total 11-hydroxycorticosteroids (11-HCS) and of their protein-bound and free forms [7], the transcortin binding capacity (TBC) [2], and the adrenalin concentration [5]. Changes in the arterial pressure on the fifth day after bi-

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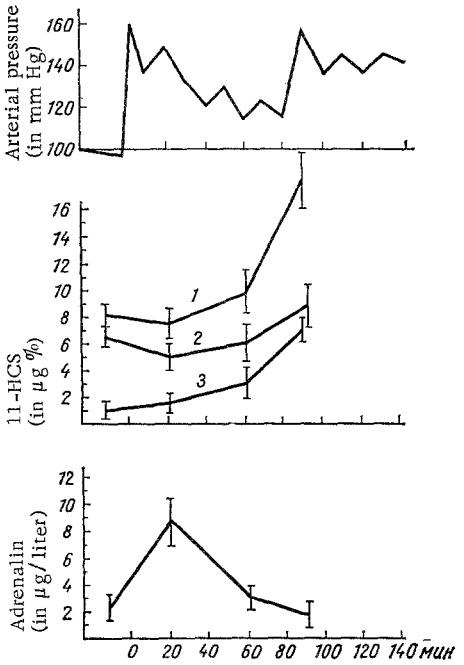

Fig. 1. Dynamics of mean blood pressure and mean plasma 11-HCS and adrenalin levels during continuous stimulation of ventromedial hypothalamic nuclei: 1) total 11-HCS fractions; 2) bound 11-HCS fractions; 3) biologically active forms of 11-HCS.

lateral extirpation of the adrenals were studied in 10 rabbits under similar conditions. The behavioral response and dynamics of the arterial pressure were tested in the animal during continuous stimulation of the ventromedial hypothalamic nuclei on the day before the operation.

In the next experiments changes in the arterial pressure were studied in 15 adrenalectomized rabbits (five in each series) during continuous stimulation of the ventromedial hypothalamic nuclei after preliminary injection of hydrocortisone and adrenalin into the animals, either separately or together. The hormones (hydrocortisone, 15-20 mg/kg/day; adrenalin 0.8-1.2 mg/kg/day) were injected intravenously immediately after control stimulation (on the third day after adrenalectomy) for 2 days. On the fifth day after the operation, prolonged stimulation of the hypothalamus was repeated, and during its course hydrocortisone (10-15 mg/kg), adrenalin (0.4-0.6 mg/kg), or both hormones together were injected by intravenous drip.

EXPERIMENTAL RESULTS

The original arterial pressure in the rabbits was 96 ± 14 mm Hg, the total 11-HCS concentration was 7.48 ± 0.7 μg% (protein-bound fractions 6.3 ± 0.75 μg% and biologically active fractions 1.04 ± 0.1 μg%), and the adrenalin concentration was 2.02 ± 0.4 μg/liter; the TBC was 9.9 ± 1.3 μg%.

When the ventromedial hypothalamic nuclei were stimulated the arterial pressure rose after 2-3 sec to 145-155 mm Hg and then gradually returned to normal during the next 30-40 min. The 11-HCS concentration remained virtually unchanged at these times but the adrenalin level was 330% higher than initially. Later transient fluctuations of arterial pressure were observed, with predominantly depressor effects. The combined 11-HCS concentration at the 60th minute of hypothalamic stimulation was 25% higher than initially. The adrenalin concentration was back to normal. Starting from the second to third hour of stimulation of the ventromedial hypothalamic nuclei a second rise of arterial pressure took place (150-160 mm Hg) and this continued throughout the period of stimulation. At the 90th minute of the experiment the concentration of total 11-HCS and of their free forms was increased by 122 and 611% , respectively, compared with initially. The adrenalin concentration remained close to its original values (Fig. 1). The TBC remained unchanged throughout the experiment. Continuous electrical stimulation of the ventromedial hypothalamic nuclei over a period of hours, combined with immobilization (the animal was fixed to a frame), thus in-

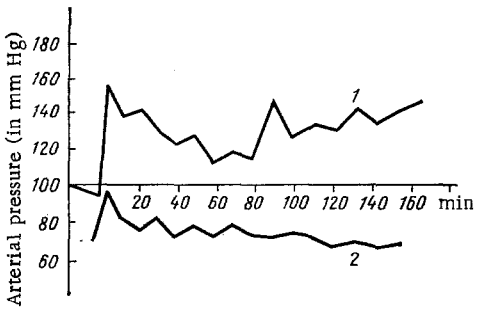

Fig. 2

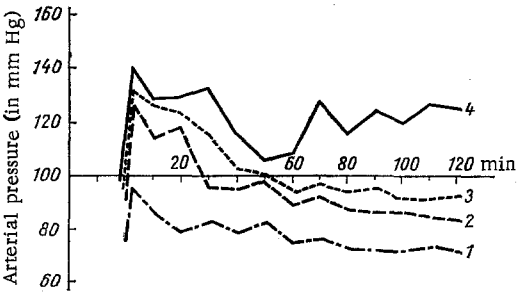

Fig. 3

Fig. 2. Dynamics of mean blood pressure in intact (1) and adrenalectomized (2) rabbits during continuous stimulation of ventromedial hypothalamic nuclei.

Fig. 3. Dynamics of mean blood pressure in adrenalectomized rabbits during continuous stimulation of ventromedial hypothalamic nuclei after preliminary injection of hydrocortisone and adrenalin: 1) adrenalectomized rabbits; 2) the same after injection of adrenalin; 3) the same after hydrocortisone; 4) the same after hydrocortisone and adrenalin.

duced changes in the secretory function of the adrenals in unanesthetized rabbits. The dynamics of the blood adrenalin level in these experiments resembled that in patients with essential hypertension in the various stages of its course [6, 10].

Bilateral extirpation of the adrenals in rabbits caused the blood pressure to fall to 76 ± 10 mm Hg. Stimulation of the ventromedial hypothalamic nuclei against this background caused a less marked (to 90-100 mm Hg) and shorter (10-15 min) hypertension (Fig. 2).

After injection of hydrocortisone into adrenalectomized animals the initial level of the mean arterial pressure rose to 91 ± 3 mm Hg. Subsequent hypothalamic stimulation led to hypertension (125-130 mm Hg) only during the first 30-40 min. After preliminary injection of adrenalin, hypothalamic stimulation led to an even smaller (120-125 mm Hg) and shorter (25-30 min) rise of arterial pressure. After combined injection of hydrocortisone and adrenalin into the adrenalectomized rabbits, the mean arterial pressure was restored (95 ± 5 mm Hg). Hypothalamic stimulation under these conditions led to an increase of arterial pressure to 135-140 mm Hg. During the next 30-40 min it gradually returned to normal. During the next 15-20 min of stimulation very small fluctuations of pressure were observed, but 50-60 min after the beginning of stimulation there was a second rise of the arterial pressure to 130-140 mm Hg, which persisted throughout the next hour of stimulation (Fig. 3).

Only the combined injection of hydrocortisone and adrenalin into the adrenalectomized animals thus restored the dynamics of the mean arterial pressure during continuous prolonged stimulation of the ventromedial hypothalamic nuclei as characteristically observed in intact animals.

It can be concluded from these results that an essential role in the formation of persistent arterial hypertension during prolonged activation of the negative emotiogenic centers of the hypothalamus is played by increased function of the adrenal cortex and medulla.

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