THE HYPOTHALAMO-ADENOHYPOPHYSEO-ADRENAL NEUROSECRETORY SYSTEM IN HYPERTHERMIA

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Experiments on albino rats showed that in exogenous hyperthermia the functional activity of the hypothalamo-hypophyseo-adrenal neurosecretory system is increased. In animals surviving after heat shock the production of corticotropin-releasing factor of the hypothalamus and the quantity of ACTH liberated from the pituitary gland are greater than in rats which die.

There are only a few communications on the effect of a high external environmental temperature on the neurosecretory nuclei of the hypothalamus and the neurohypophysis, and the results they contain are chiefly morphological in character [2, 3, 8, 11, 17]. So far as the state of adrenocortical function in hyperthermia is concerned, it has been investigated by many workers but conflicting results have been obtained. Some workers have found an increase in adrenocortical activity [1, 4, 5, 14], while others found no significant changes in the corticosteroid concentrations in the blood and urine during moderate hyperthermia [7, 10]. Data in the literature show [9] that the thermostability of adrenalectomized rats is reduced, while exogenous administration of corticosteroids increases the resistance of animals to heating [6, 13]. It was accordingly decided to investigate the state of the hypothalamo-adenohypophyseo-adrenal system during the development of hyperthermia, for this endocrine system undoubtedly plays an important role in the pathogenesis of hyperthermia.

The object of the present investigation was to study the effect of exogenous hyperthermia of varied duration on the corticotropin-releasing activity (CRA) of hypothalamic extracts, the ACTH concentration in the pituitary gland, and functional activity of the adrenals.

EXPERIMENTAL METHOD

Four series of experiments were carried out on 132 adult rats weighing 150-200 g. Hyperthermia was induced in a hot chamber with an air temperature of 50-51°C and was evaluated by noting changes in the rectal temperature (TÉMP-60 electric thermometer). The heating was stopped on the appearance of convulsions and the animals were subsequently kept at room temperature (18-20°C).

The state of adrenocortical function was judged from the ascorbic acid concentration in the glands determined by the method of Roe and Kuether, and the ACTH concentration in the pituitary gland was determined by Skebel'skaya's method [12]. The CRA of the hypothalamus was estimated by the method of Arimura et al. [15]. This consists essentially of obtaining hypothalamic extracts and then testing them on recipient rats, the function of whose hypothalamo-hypophyseo-adrenal system has previously been suppressed by chloropromazine, morphine, and pentobarbital. To determine the CRA of the extracts the ascorbic acid concentration was compared in the left (before injection of the extract) and right (1 h after intravenous injection of the extract) adrenals of recipient rats. The operation of removal of the left adrenal and the injection of isotonic solution were not accompanied by any statistically significant changes in the ascorbic acid concentration in the right adrenal.

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EXPERIMENTAL RESULTS

The first series of investigations includes the results of 30 control experiments. The initial body temperature of these animals averaged 37.3 ± 0.21°, and the ascorbic acid concentration in the left adrenal was 440 ± 15.16 mg% and in the right 403 ± 15.49 mg%.

Injection of hypothalamic extract into the intact animals led to a decrease in the ascorbic acid concentration in the adrenals of the recipient rats on the average by 125 ± 2.30 mg%. The ACTH concentration in the pituitary gland was 19.8 + 1.05 milliunits (mu)/100 μg acetone powder of the gland tissue.

In the 34 experiments of series II the rats were heated for 10-15 min. Their body temperature was raised on the average to 40.6 ± 0.26°C, i.e., by 3.3°C. The ascorbic acid concentration in the adrenal was not significantly changed from its initial level (393 ± 16.3 mg%) and its mean value was 373 ± 7.43 mg%. The CRA of the hypothalamus was lowered. Intravenous injection of hypothalamic extracts from hyperthermic animals into recipient rats was accompanied by a decrease in the ascorbic acid concentration on the average by 85 ± 5.87 mg%, which is statistically significant ($P > 0.01$). The ACTH concentration in the pituitary was significantly lower ($P < 0.001$) and its mean value was 12.4 ± 1.00 mu. During this period of hyperthermia, despite the decrease in CRA of the hypothalamus and the decrease in ACTH concentration in the pituitary glands, the ascorbic acid concentration in the adrenals of the hyperthermic animals was not significantly reduced although it showed a tendency in that direction.

Series III included all the animals whose heating was interrupted with the onset of heat stroke and which survived for 1 h when subsequently kept at room temperature (18-20°C). Their mean body temperature at the moment of heat stroke was 41.8 ± 0.13°C, i.e., it was significantly increased by 4.5°C ($P < 0.001$) compared with initially. During the subsequent hour when they were kept at room temperature the rectal temperature returned to its initial value (mean 37.0 ± 0.33°C), the mean ascorbic acid concentration in the adrenal at this time was 300 ± 15.64 mg%, and was not significantly changed by comparison with the previous values (298 ± 15.2 mg%), but it was 26% lower than initially (403 ± 15.5 mg%; $P < 0.001$). The CRA of the hypothalamus was significantly lowered (to 43 ± 39 mg%) compared with its initial level ($P < 0.01$). The ACTH level in the pituitary was 5.8 ± 0.41 mu, significantly lower than normally ($P < 0.001$) and with the previous period ($P < 0.001$).

Series IV included animals which died after the onset of heat convulsions during observations in the course of the first hour. Their rectal temperature at the time of heat stroke averaged 41.8 ± 0.08°C, i.e., it was 4.5°C above its initial level ($P < 0.001$) and was the same as in the animals in the experiments of series III. Keeping these animals at room temperature for 1 h ended in their death, when the rectal temperature of some of the rats showed a further rise by 0.2-0.4°C, but in some animals the rectal temperature was below its initial level. The mean ascorbic acid concentration in the adrenals of the rats which died was 327 ± 3.42 mg% and it did not differ significantly from the concentration in series III, but it was 19% lower than the initial value ($P < 0.001$). CRA of the hypothalamus (64 ± 2.1 mg%) was significantly lower than initially ($P < 0.001$), but higher than in the experiments of series III ($P < 0.001$). The mean ACTH concentration in the pituitary was 9.9 ± 0.87 mu, definitely below the initial level ($P < 0.001$), but higher than in the animals of series III ($P < 0.001$).

Comparison of the results showed that in exogenous hyperthermia the functional activity of the hypothalamo-hypophyseo-adrenal neurosecretory system is increased. In the animals which survived heat shock for 1 h both the CRA of the hypothalamic extract and the amount of ACTH liberated from the pituitary gland were higher than in rats which died. This result suggests that the level of functional activity of the hypothalamo-adenohypophyseo-adrenal neurosecretory system, along with its other properties, plays an important role in maintaining the resistance of the organism to the action of a high external environmental temperature.

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