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RESPONSES OF THE ADRENAL CORTEX AND THYROID GLAND OF HYPOPHYSECTOMIZED RATS TO COOLING

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Animals deprived of their pituitary gland continue to survive for a long time although the state of their endocrine glands does not completely recover [2, 4]. Polenov [3], as the result of an analysis of the formation of the Gomori-positive hypothalamo-hypophyseal neurosecretory system during vertebrate phylogeny and ontogeny, postulated the regulatory influence of nonapeptide neurohormones (vasopressin – VP, oxytocin) directly on peripheral endocrine glands without the participation of adenohypophyseal hormones, i.e., by the para-adenohypophyseal route. This method of regulation assumes its greatest importance in stress situations, and in states approaching the pathological. Evidence of the possible direct effect of VP on the adrenal cortex has recently been published [6, 13, 16]. However, the only evidence of this kind of regulation of the thyroid gland has been obtained by research undertaken more than 20 years ago [9, 11]. The study of rats in the early period (during the first week) after total hypophysectomy (HE) made it possible to examine the response of an animal deprived both of the posterior lobe of its pituitary gland (PLP) and of its adenohypophysis. Regeneration of PLP takes place 4 weeks or more after HE, with the formation of a miniature neurohemal organ [14], so that the responses of an animal deprived of its adenohypophysis alone can be investigated.

The aim of the present investigation was to obtain further data on the importance of adenohypophyseal hormones and nonapeptide neurohormones of PLP in the response of the adrenal cortex and thyroid gland of hypophysectomized rats to stress in the form of cooling.

EXPERIMENTAL METHOD

Experiments were carried out on 86 male Wistar rats weighing 130-150 g. The pituitary gland was removed by the trans-sphenoidal approach under ether anesthesia. Completeness of removal of the gland was verified by examination of the sella turcica region after decapitation of the rats. The animals were divided into the following groups: 1) intact (control), 2) 7 days after HE, 3) 7 days after mock HE, 4) 4-7 weeks after HE, 5) 4-7 weeks after mock HE. The mock HE operation involved all stages of HE except extirpation of the pituitary. The animals of all the above groups were used for comparison with animals of the same groups

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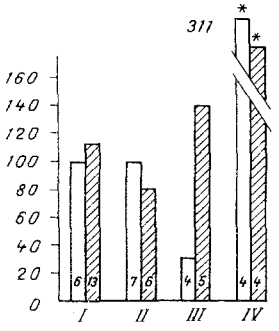

Fig. 1

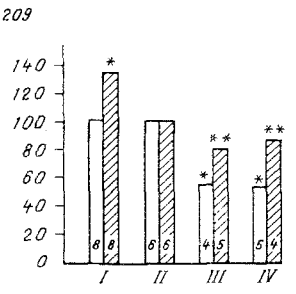

Fig. 2

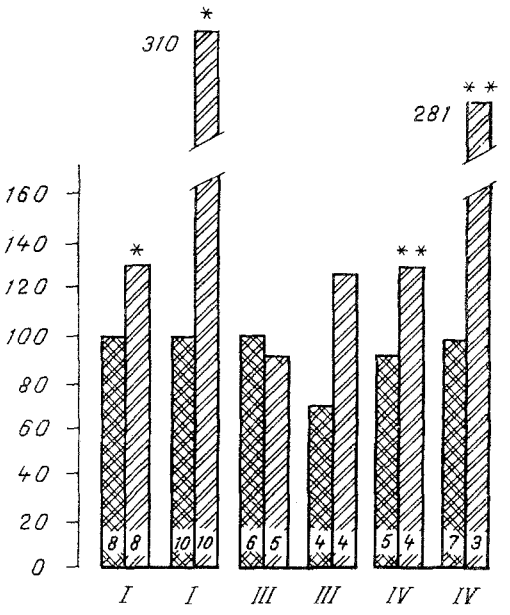

Fig. 3

Fig. 1. VP concentration in blood (in % of intact control, taken as 100%). I) Intact animals (control); II) 4-7 weeks after mock HE; III) 7 days after HE; IV) 4-7 weeks after HE. Unshaded columns – without cooling, shaded – after cooling. Numbers inside columns indicate number of animals. *$p < 0.05$ compared with control.

Fig. 2. Height of thyrocytes (in % of intact control, taken as 100%). Here and in Fig. 3: **$p < 0.05$ compared with animals of the same group not exposed to cooling. Remainder of legend as to Fig. 1.

Fig. 3. 11-HCS concentration in adrenal tissue and in blood plasma (in % of intact control, taken as 100%). Remainder of legend as to Fig. 1.

but additionally exposed to cooling at 4°C for 1.5 h. After decapitation of the rats the brain, pituitary and thyroid glands, and one adrenal gland were fixed in Bouin's fluid. Paraffin sections through the brain and pituitary were stained with paraldehyde-fuchsine by the Gomori–Gabe method with counterstaining by Heidenhain's azan. Sections through the thyroid and adrenal glands were stained with Ehrlich's hematoxylin. The state of the thyroid function was assessed by examination of the height of the follicular epithelium in central sections and the ratio of epithelium-colloid-connective tissue under magnification of 90 × 16. Using a standard grid with magnification of 40 × 10, the relative dimensions of the zona glomerulosa, zona fasciculata, and zona reticularis of the adrenal cortex and the adrenal medulla, expressed as percentages, were estimated in 10 central sections from one adrenal gland. The other adrenal was frozen in liquid nitrogen. The concentration of 11-hydroxycorticosteroids (11-HCS) in the tissue of this adrenal gland and in the blood was determined fluorometrically. Concentrations of VP, ACTH, and TSH were determined in the blood plasma by radioimmunoassay. The last two hormones were determined only in rats hypophysectomized 7 days before decapitation. The significance of the difference between the results was estimated by Student's t test and by the Mann–Whitney–Wilcoxon nonparametric test.

EXPERIMENTAL RESULTS

Histological investigation of the region of the median eminence of the hypothalamus and of part of the pituitary stalk remaining behind after HE showed that 7 days after HE no sign of regeneration of PLP was present. The histological picture of the median eminence remained characteristic of intact animals, but in the region of division of the pituitary stalk traces of hemorrhages were visible. A miniature equivalent of PLP was formed 4-7 weeks after HE in the form of a reorganized pituitary stalk. The regenerating PLP was rich in vessels, surrounded by terminal portions of fibers filled with Gomori-positive neurosecretory material. Both in the control animals and in rats undergoing HE and the mock HE the quantity of neurosecretory material in PLP was somewhat reduced after cooling, and this difference was seen more clearly at the periphery of PLP, where oxytocin-containing fibers predominate in rats [1].

The blood VP level fell 7 days after HE, in some animals below the level of sensitivity of the method (control 1.72 ± 0.2 pg/ml, HE 0.53 ± 0.44 pg/ml; $p < 0.01$). In the same period the blood ACTH concentration also fell below the level of sensitivity of the method (control 30.7 ± 15.3 pg/ml, HE 0.0 pg/ml; $p > 0.05$). The TSH concentration in the blood of the hypophysectomized rats was virtually unchanged, possibly due to the preserved function of the thyrocytes in the tuberal part of the anterior lobe of the pituitary, which is adherent to the median eminence. Unlike the rats of group 1, in those with HE 4-7 weeks after the operation the blood VP level reached 311% compared with the control (5.6 pg/ml + 2.0 pg/ml; $p = 0.01$). Neither in animals undergoing the mock operation nor in the hypophysectomized rats at this period was any significant change found in the blood VP level after cooling (Fig. 1).

In the thyroid gland 7 days and 4-7 weeks after HE morphological signs of depression of its function were clearly distinguished. A similar effect of HE was described previously [2, 4]. Under the influence of cold, signs of activation of hormone synthesis and secretion were observed in the thyroid gland of the animals of all groups. The height of the thyrocytes in animals of all groups was increased compared with the initial state almost by the same degree (Fig. 2). Signs of intensive hyperemia of the gland were observed, resorption vacuoles appeared in the follicular colloid, and intracellular droplets appeared in the thyrocytes. Despite the fact that thyrotropocytes are preserved in the tuberal part of the anterior lobe of the pituitary [10] in rats with HE, and probably maintain the blood TSH level thyroid function remained depressed 1 and 4-7 weeks after HE. Consequently, the level of function of these thyrotropocytes was insufficient to maintain the normal level of thyroid gland activity. Nevertheless, the possibility cannot be ruled out that the response of the thyroid gland to cooling in hypophysectomized rats is effected through the function of these thyrotropocytes. The response to cooling in the thyroid gland of the hypophysectomized rats may also be induced by the stimulating effect of the sympathetic innervation [12] or by the direct action of TSH releasing hormone on thyrocytes [5]. Since the concentration of TSH of hypothalamic origin was unchanged after HE, its participation in regulation of the response of the thyroid gland is unlikely [7]. Changes in the blood VP level in rats at different times after HE were not reflected in the response of the thyroid gland to cooling.

The relative sizes of the zona glomerulosa of the adrenal cortex of the rats after HE remained unchanged (control 17.0 ± 0.87%, HE 17.8 ± 0.38%, $p > 0.05$), in agreement with the widely held view, and it can probably be explained on the grounds that the regulatory function of the zona glomerulosa of the renin-angiotensin system is not impaired after HE. Dimensions of the zona fasciculata and zona reticularis were reduced only 7 days after HE, and remained approximately unchanged thereafter until the end of the experiment (control 67.01 ± 0.76%, 7 days after HE 59.65 ± 3.3%, $p = 0.05$). The 11-HCS level, reflecting under these circumstances the total concentration of aldosterone and corticosterone, in the adrenal remained close to normal (control 0.39 ± 0.03 µg per adrenal gland, 7 weeks after HE 0.36 ± 0.04 µg per adrenal, $p > 0.05$). Maintenance of the 11-HCS level in the adrenals after HE was probably due to a compensatory reaction of cells of the zona glomerulosa. The blood 11-HCS concentration, which was significantly lowered 1 week after HE (3.63 ± 0.97 µg%; $p < 0.05$), later was restored to its initial value (6.56 ± 1.08 µg%; Fig. 3). A similar trend in the state of the adrenals in hypophysectomized rats was described previously [15].

In the control rats cooling caused a significant rise in the 11-HCS level both in the adrenals (0.50 ± 0.04 µg per adrenal gland; $p < 0.05$) and in the blood (20.54 ± 2.7 µg%; $p < 0.01$). It must emphasized that 7 days after HE cooling did not cause any change in the blood 11-HCS level (4.63 ± 1.49 µg%; $p > 0.05$), whereas when a long time had elapsed after HE cold induced an adrenal response just as in the control rats (Fig. 3). The absence of a response of the adrenal cortex to cold 7 days after HE, when the blood VP level was low, and the appearance of such a response in rats with a regenerating PLP and with a high VP level, do not rule out the suggestion that in hypophysectomized rats a high blood VP level is an essential condition for the adrenals to respond to cooling. However, a raised blood VP concentration (Fig. 1) alone is insufficient to lead to a raised 11-HCS level, and it can accordingly be postulated that the response of the adrenals to cold in hypophysectomized rats is stimulated by some other factor (possibly by catecholamines), whose effect is observed when the blood VP concentration is high. The absence of ACTH-cells in the tuberal part of the adenohypophysis in hypophysectomized rats [10] suggests that the elevation of the 11-HCS level described above is the result of the direct action of VP on adrenocortical cells, more especially since there is evidence that receptors for VP exist in the adrenal cortex [6, 8, 13, 16].

The response of the adrenals to cooling in hypophysectomized rats may therefore take place in the absence of the adenohypophysis, but when the blood VP level is sufficiently high. The state of the thyroid gland and its response to cold in hypophysectomized rats are independent of the blood VP concentration.

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PREVENTION OF DISTURBANCES OF ACTIVITY OF THE MONOOXYGENASE SYSTEM AND OF HEPATOCYTE ULTRASTRUCTURE AFTER ACUTE HEPATIC ISCHEMIA BY α-TOCOPHEROL AND LIDOCAINE

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Prevention of postischemic disturbances of the detoxication function of the liver arising as a result of certain surgical procedures or pathological states is an urgent problem in medical practice. Intensification of peroxidation processes [3, 6] and activation of endogenous phospholipases [5] are the leading factors in the development of postischemic disturbances of hepatic structure and function.

The aim of the present investigation was to study activity of microsomal monooxygenases and hepatocyte ultrastructure in rats at different stages of the postischemic period, and the effect of combined prophylactic administration of the antioxidant α-tocopherol (TP) and the phospholipase inhibitor lidocaine (L) on them.

EXPERIMENTAL METHOD

Experiments were carried out on 200 male Wistar rats weighing 150-240 g. Total ischemia of the liver for 30 and 60 min was produced by the method described previously [2]. The effectiveness of combined administration of TP and L was assessed by noting the survival rate of the animals after total hepatic ischemia for 60 min. All biochemical investigations were

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