SECRETORY ACTIVITY OF THE HYPOTHALAMUS – PITUITARY – ADRENAL SYSTEM IN HYPOTHERMIA

B. A. Saakov, S. A. Eremina, and É. S. Gul'yants

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Secretory activity in the hypothalamus–pituitary system during hypothermia takes place in two phases: activation followed by inhibition of neurosecretion. These changes correlate with the glucocorticoid activity of the adrenal cortex and the blood noradrenalin concentration.

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Published reports of studies of the state of the hypothalamus–pituitary–adrenal system (HPAS) in hypothermia are few in number and contradictory in nature [1, 7-9].

The object of the present investigation was to determine the relationship between the phases of experimental hypothermia and secretory activity of the HPAS.

EXPERIMENTAL METHOD

Experiments were carried out on 42 unanesthetized dogs divided into 5 groups. The dogs of group 1 were intact (controls), those of group 2 were sacrificed 5-10 min after immersion in an ice-cold bath, the dogs of group 3 were sacrificed after their body temperature had been lowered by 2-3° below its initial level, those of group 4 were sacrificed after the body temperature had been lowered to 25-26°, and the dogs of group 5 died spontaneously as a result of changes produced by hypothermia which were incompatible with life. The plasma concentration of 17-hydroxycorticosteroids (17-HCS) was determined by the Silber-Porter method as modified by Yudaev and Pankov, and adrenalin and noradrenalin were determined by the trihydroxyindole method as modified by Men'shikov [6]. Immediately after sacrifice the brain was fixed in Bouin's fluid and embedded in paraffin wax. The adrenal was fixed in 10% neutral formalin, and chromium and silver salts. Sections were stained for neurosecretion by Gomori's method as modified by Maiorova [5], for glycoproteins by the Griesbach-Purvis method; the adrenal was stained with Sudan black B by Lyson's method, for ascorbic acid by the Giroud-Leblond method, for catecholamines by the method of Hillarp and Hochfeld, and also with hematoxylin-eosin. The content of neurosecretory material in the neurons of

TABLE 1. Diameters of Neurons and Their Nuclei (in μ) in the SON and PVN of the Anterior Hypothalamus (mean for 20 cells) in the Course of Hypothermia ($M \pm m$*)

Conditions	Number of animals	SON		PVN	
		Neuron	Nucleus	Neuron	Nucleus
Intact animals (control)	3	25,3±1,4	12,8±0,4	22,7±1,0	12,5±0,8
5-10 min after immersion in ice	2	55,6±0,7	20,9±0,8	46,3±0,7	20,4±0,7
Body temperature lowered by 2-3°	2	58,8±1,4	21,7±0,7	52,1±1,7	22,1±0,9
Terminal phase of hypothermia	3	44,7±0,3	36,6±0,3	39,7±0,7	32,2±0,8

* Differences between all groups are statistically significant ($P < 0.001$).

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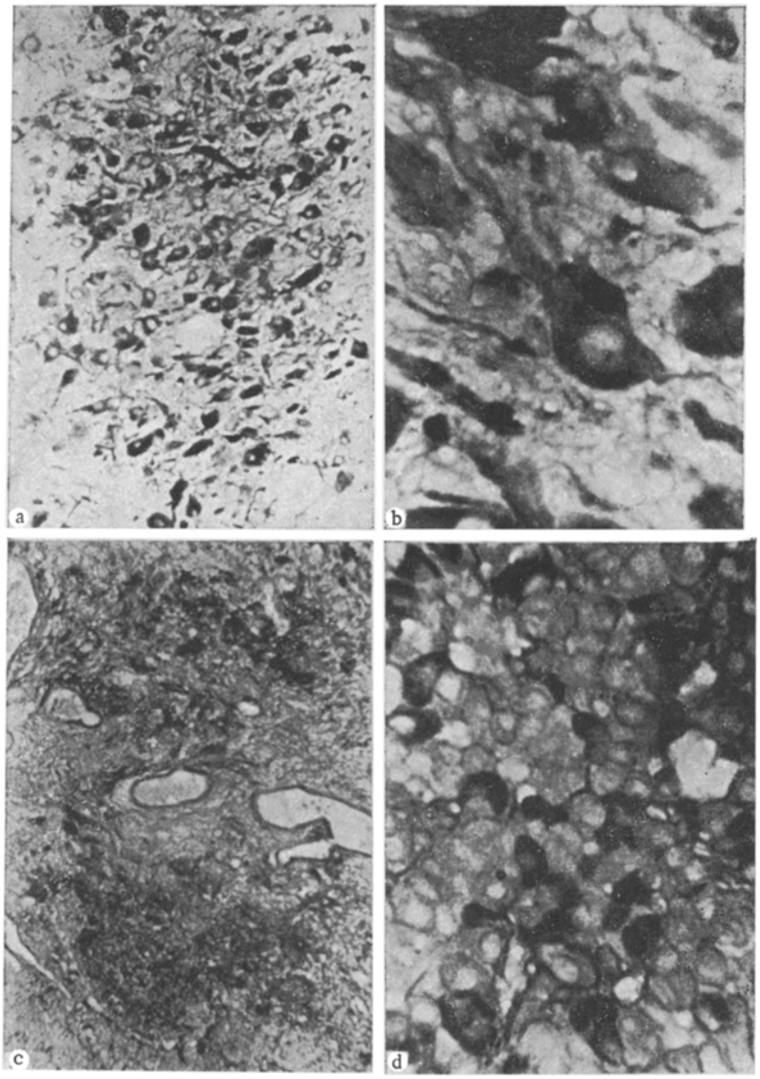

Fig. 1. Secretion formation in the hypothalamus–pituitary in hypothermia. a) Marked activation of secretory activity in the supraoptic nucleus (100 ×); b) neurons and their processes filled with neurosecretory material (400 ×); c) formation of "pituitary felt" in the neurohypophysis (100 ×); d) hyperplasia of β-basophils in the adenohypophysis in the terminal stage of hypothermia (400 ×). Gomori's method modified by Maiorova.

of the supraoptic and paraventricular nuclei (SON and PVN) of the anterior hypothalamus was estimated visually and by measuring the diameter of the neurons and their nuclei with a type MOV-1-15^{x} ocular micrometer (20 measurements each in the control and experimental material).

EXPERIMENTAL RESULTS

Marked activation of hypothalamic neurosecretion in the SON and less marked activation in the PVN, with increased discharge of secretion along the axons and its accumulation in the neurohypophysis, were observed 5-10 min after immersion in ice (Fig. 1a). The secretory surfaces of the cell bodies and diameters of their nuclei were significantly increased compared with intact animals (Table 1).

Moderate hyperplasia of the basophilic cells, staining intensely with aldehyde-fuchsin, was observed in the adenohypophysis.

TABLE 2. Concentration of 17-HCS (in μg%) in the Plasma and of Catecholamines (in μg/liter) in the Blood in the Course of Hypothermia (M ± m)

Index	Number of animals	Initial background	After immersion in ice				
			At initial temperature	With temperatures lowered 1-2°	30–32°	25–26°	Terminal period
17-HCS	10	12,30±1,10	22,00±2,60	22,70±3,70	24,60±2,30	32,30±4,10	14,60±2,30
P			<0,002	<0,01	<0,001	<0,001	>0,1
Adrenalin	10	1,54±0,22	0,51±0,10	3,01±0,41	3,59±0,36	1,08±0,25	22,79±7,27
P			>0,05	>0,05	<0,02	>0,1	<0,01
Noradrenalin	10	3,92±0,25	11,40±1,70	3,02±0,61	2,49±0,67	7,30±1,22	1,65±0,87
P			<0,001	>0,1	>0,1	<0,05	<0,05

After lowering of the body temperature by 2-3°, the changes described in secretory activity progressed further, the intensity of secretion production becoming equalized in the two secretory nuclei (Fig. 1b). Meanwhile in the secretory neurons marked signs of degeneration were observed.

Cooling to 26° was accompanied by an increase in the intensity of secretory processes in the SON and PVN and by the development of more severe degenerative changes in the neuron. The neurons lost their normal pear-shaped appearance and their tigroid disappeared almost completely or was hidden by the large quantity of neurosecretion. Axons and dendrites were greatly increased in width and were in contact with each other, with the bodies of the neurons, and with numerous dilated capillaries in the region of the nuclei. The paths of outflow of neurosecretion were clearly distinguishable, particularly in the hypothalamus. Along the course of the axons in the paraventriculo-supraoptic tract, numerous swellings and pools of secretory material were observed. In the pituitary stalk and neurohypophysis Herring's bodies were numerous, with the formation of a "pituitary felt" in the distal portion of the principal posterior lobe at its border with the pars intermedia (Fig. 1c).

In the terminal stage of hypothermia degenerative changes predominated in the neurons. Massive shrinking of the cells and pycnosis of the nuclei led to a marked decrease in the size of the cell bodies and to depression of their function. Characteristically, the response of the β-basophils of the adenohypophysis remained in its full extent (Fig. 1d). The content of secretion in the neurohypophysis also remained high, but the pathways of its transportation were much reduced in number.

In the adrenal cortex at all stages of hypothermia, a decrease in the ascorbic acid content and progressive delipoidosis of the zone fasciculata were observed, together with conversion of the gland cells of the zona fasciculata into cells of pale type. Morphological changes were found in phases only in the medulla, chromophilic cells of which were intensely impregnated in the experiments of groups II-IV, and appeared almost colorless in the terminal period.

The 17-HCS concentration in the plasma and the blood noradrenalin concentration increased initially during hypothermia, but decreased in the terminal period (Table 2). The blood adrenalin concentration in the terminal period was 10-15 times or more greater than normal. Comparison of these findings with the morphological changes in the HPAS shows that the stimulant action of adrenalin on hypothalamic neurosecretion [2-4] is not exhibited during deep hypothermia because of degenerative changes in the secretory neurons of the hypothalamus.

The development of hypothermia is thus accompanied by substantial morphological changes in the HPAS, by marked activation of hypothalamic neurosecretion as the body temperature falls gradually, and by a sharp decrease in its activity in the terminal stage of hypothermia. The response of the adrenal to cooling occurs in phases, the changes in hormone production taking place in opposite directions to the cortex and medulla. A parallel is observed between secretory activity of the hypothalamus–pituitary system and glucocorticoid activity of the adrenal cortex.

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