REACTIONS OF THE HYPOTHALAMO-HYPOPHYSEO-ADRENAL SYSTEM TO ANTIGENIC STIMULATION OF THE AFFERENT APPARATUS OF THE ISOLATED CAROTID SINUS

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Perfusion of the carotid sinus, isolated from the general circulation of intact dogs, with heterologous blood, and perfusion of the carotid sinus of sensitized animals with normal horse serum, cause activation of the hypothalamo-hypophyseal neurosecretory system and stimulation of adrenocortical functions.

Because the posterior lobe of the pituitary obtains most of its innervation from preganglionic autonomic nerves arising from hypothalamic nuclei [3], and because of the functional unity of these structures in the processes of the neurosecretory cycle [2, 4, 10, 12], an adequate response of the hypothalamo-hypophyseal system and of the adrenocortical system connected with it, to stimulation of afferent stystems can be assumed.

With these considerations in mind, an investigation was carried out to study functional activity of the hypothalamo-hypophyseo-adrenal system (HHAS) during stimulation of afferent systems by perfusion of the carotid sinus (deprived of its connections with the remainder of the vascular system) of intact and sensitized dogs with heterologous blood and horse serum respectively. The basic fact on which this investigation was based is that manipulation of this type causes reflex changes in many organs and systems [1, 5, 6].

EXPERIMENTAL METHOD

Experiments were carried out on 25 unanesthetized mongrel dogs. Preparatory manipulations were carried out on the animals under local anesthesia with 0.25% procaine, which has no significant effect on the state of the HHAS [8]. The carotid sinus, isolated from the remainder of the vascular system, was perfused by a modification of E. A. Moiseev's method [7]. The animals were sensitized in the usual way by tripole injections of horse serum and were used in the experiment on the 14th-21st day after the 3rd injection. The same serum was used for perfusion in experiments on sensitized dogs, and rabbit blood was used in experiments on the intact animals. The concentration of 17-hydrocorticosteroids (17-HCS) was determined in the plasma from blood taken from the inferior vena cava at the level of the orifices of the lumbo-adrenal veins, by the method of Silber and Porter as modified by Yudaev and Pankov [11]. The hypothalamus and pituitary were fixed in Bouin's fluid, and the adrenal in 10% neutral formalin solution, and chromium and silver salts. Paraffin sections were stained for neurosecretion by Gomori's method as modified by Maiorova [9], and by the methods of Giroud and Leblond, Hillarp and Hochfelt, with Sudan black B by Lison's method, and with hematoxylin-eosin. The organs of 19 animals, of which 3 (intact) were the controls, were used for histological investigation. The quantity of neurosecretory material was assessed visually and also by measuring the diameters of neurons and nuclei in the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus by means of a type MOV-1-15* ocular micrometer (20 measurements in the control and 20 in the experiment).

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TABLE 1. Concentration of 17-HCS (in $\mu g\%$) in Blood Plasma of Dogs after Perfusion of Carotid Sinus with Heterologous Blood or Horse Serum

Procedure	Statistical index	Background	Time after perfusion				
			3 min	15 min	30 min	60 min	120 min
Perfusion with heterologous blood	$M \pm m$	16,1±2,3	20,0±2,7	20,7±2,4	26,4±4,2	30,2±6,1	30,0±4,3
	P		>0,05	>0,05	<0,05	<0,05	<0,02
Perfusion with serum	$M \pm m$	23,7±4,7	24,9±3,1	28,6±5,5	38,2±5,3	35,7±4,1	31,1±3,2
	P		>0,05	>0,05	<0,05	<0,05	<0,05

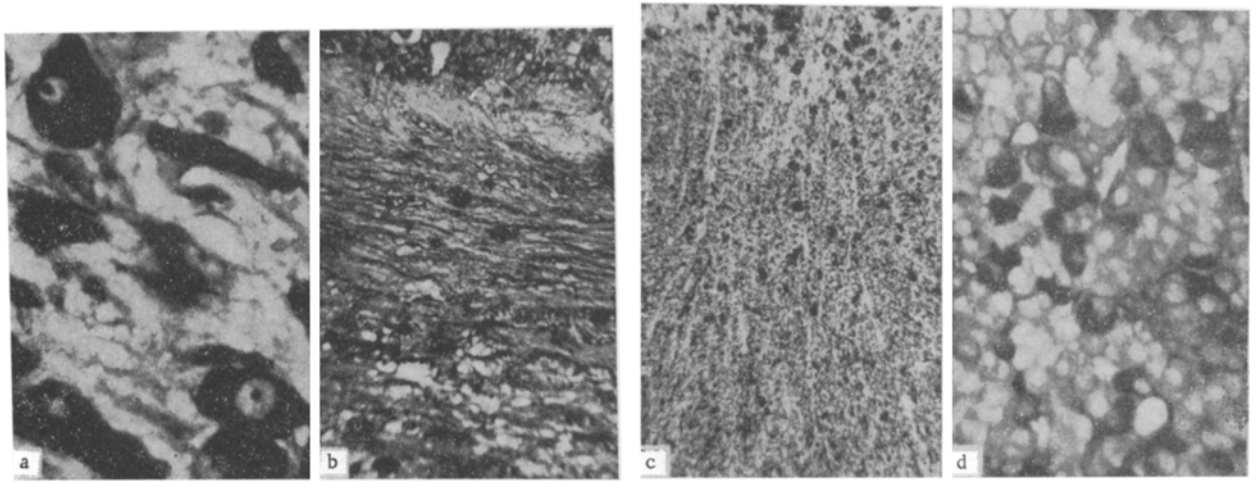

Fig. 1. Changes in hypothalamus, pituitary, and adrenal during perfusion of carotid sinus with heterologous blood and horse serum. a) Perfusion with heterologous blood. Supraoptic nucleus: marked activation of secretion formation in neurons (400×); b) pituitary stalk: accumulation of neurosecretion in endings of axons and along course of tracked fibers (100×); c) adenohypophysis: hyperplasia of β-basophils (Gomori's method in V. F. Maiorova's modification; 400×); d) perfusion with horse serum. Adrenal: marked delipoidosis of zona fasciculata of cortex (stained with Sudan black B by Lison's method; 100×).

TABLE 2. Diameters of Neurons and Their Nuclei (in μ) in SON and PVN during Perfusion of Carotid Sinus, Disconnected from the Vascular System, with Heterologous Blood and Normal Horse Serum (M±m)

Procedure	SON		PVN	
	neuron	nucleus	neuron	nucleus
Control	25,3±1,4	12,8±0,4	22,7±1,0	12,5±0,8
Perfusion with heterologous blood	55,2±0,6	32,3±0,7	49,6±0,3	28,8±0,7
Perfusion with serum	61,9±1,5	31,0±0,3	47,5±0,6	30,2±0,7

EXPERIMENTAL RESULTS

The increase in 17-HCS concentration in the plasma of the sensitized animals was due to activation of the pituitary-adrenal system [8]. Perfusion of the carotid sinus both with rabbits' blood and with horse serum evoked a pressor response, followed by lowering of the arterial pressure and a significant increase in the 17-HCS concentration in the plasma (Table 1). During perfusion of the carotid sinus with heterologous blood, neurosecretory activity was considerably increased over normal. The morphological manifestation of this increase was a marked increase in size of the neurons, as a result of the filling of their cytoplasm by numerous neurosecretory granules (Fig. 1a), which were found in the axons, along the course of the supraoptico-hypophyseal tract, and in the endings of the principal posterior part of the neurohypophysis (Fig. 1b). Focal hyperplasia of β-basophilic cells was observed in the adenohypophysis. Their cytoplasm stained strongly with aldehyde-fuchsin (Fig. 1c). During perfusion of the carotid sinus of sensitized dogs with serum, a higher level of hypothalamic neurosecretory activity was observed. The changes in size of the neurons and their nuclei observed visually were confirmed by micrometry (Table 2).

The adrenals of both groups of animals showed similar evidence of cortical stimulation, expressed morphologically by thinning and delipoidosis of the zona fasciculata (Fig. 1d), and a decrease in its ascorbic acid content, while in the medulla there was some decrease in the number and intensity of staining of adrenalin-containing cells. In the experiments to reproduce anaphylactic shock, these changes were more clearly expressed both in the cortex and in the medulla.

The difference between the distribution of neurosecretory substance in the different components of the hypothalamo-hypophyseal system is interesting. The reaction of its first two components (production and transportation of neurosecretion) corresponded to the intensity of reflex stimulation. A significant difference was found in the last (cumulative) component of this system. Whereas in experiments with perfusion with heterologous blood the neurosecretion was stored entirely in cells of the neurohypophysis, in the experiments to reproduce anaphylactic shock the posterior lobe of the pituitary contained only a small amount of neurosecretion. The excess of neurosecretory material was evidently utilized in the vessels of the portal system of the median eminence of the pituitary stalk, as indicated by data in the literature [13, 14].

The complex mechanism of functional and morphological changes taking place during perfusion of the carotid sinus, disconnected from the remainder of the vascular system, of intact and sensitized dogs with heterologous blood and with normal horse serum, respectively, is thus, in principle, of the same type, and consists essentially as follows. Stimulation of the carotid sinus receptors causes reflex activation of hypothalamic neurosecretion, which leads to stimulation of adrenocortical functions. This is reflected morphologically by an increase in production of neurosecretion in SON and PVN and elevation of the plasma corticosteroid concentration.

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