STATE OF THE HYPOTHALAMIC–PITUITARY NEUROSECRETORY SYSTEM IN RABBITS WITH ANAPHYLACTIC SHOCK

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The hypothalamic–pituitary neurosecretory system of rabbits with anaphylactic shock was investigated by morphometric and histochemical methods. The volumes of the perikarya were increased and the dimensions of the nuclei and nucleoli of the neurosecretory cells were reduced, and the content of neurosecretory substance throughout the neurosecretory system was increased. In rabbits dying from shock the volumes of the nuclei and nucleoli were reduced by a lesser degree, the dimensions of the perikarya were changed, and the content of neurosecretory substance in the posterior lobe of the pituitary was reduced. In animals surviving shock the synthesis of neurohormones by the neurosecretory cells was thus sharply stimulated, but liberation of neurohormones from the posterior lobe was inhibited. In animals dying from shock hormone formation in the neurosecretory cells was stimulated to a lesser degree, but the processes of liberation of neurohormones from the posterior lobe of the pituitary were probably intensified.

KEY WORDS: *anaphylactic shock; neurosecretion; hypothalamic–pituitary system.*

Division or destruction of various parts of the hypothalamus is known to lead to changes in the response of the sensitized organism to injection of the reacting dose of antigen [5, 9, 12, 15].

A useful purpose would thus be served by studying the state of the hypothalamic–pituitary neurosecretory system, one of the most important integrative centers of the body [2, 6], in anaphylactic shock. The problem is all the more interesting because of the few investigations of the neurosecretory system that have been undertaken [1, 4, 8]. Furthermore, in none of the investigations cited above was any attempt made to compare the state of the neurosecretory system in animals dying from shock and in survivals.

EXPERIMENTAL METHOD

Male rabbits aged 10-12 months were sensitized by a triple injection of anti-rabies γ-globulin (0.1 ml/kg). The reacting injection of antigen (3 ml/kg) was given on the 21st day after the last sensitizing injection. Altogether 38 animals were used: group 1 (control), rabbits on the 21st day of sensitization; 2) rabbits surviving 5 min of anaphylactic shock; 3) rabbits dying after 3-5 min of anaphylactic shock. Material from three rabbits from each group was studied.

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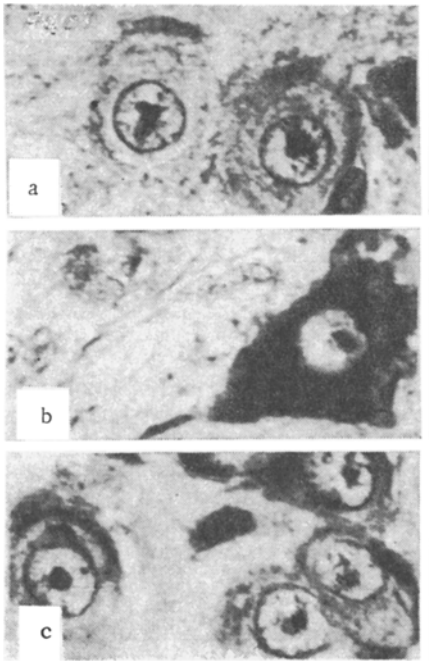

Fig. 1

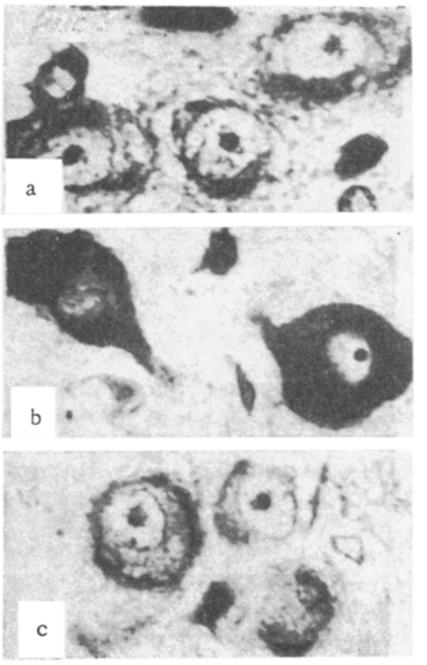

Fig. 2

Fig. 1. Supraoptic nucleus of hypothalamus. Neurosecretory cells. Here and in Fig. 2: a) rabbits of group 1; b) rabbits of group 2 (cells filled with neurosecretory substance); c) group 3. Stained with paraldehyde–fuchsin by Gomori–Gabe method and counterstained with Heidenhain's azan; 100X.

Fig. 2. Paraventricular nucleus of hypothalamus. Neurosecretory cells.

The brain and pituitary gland were fixed in Bouin's fluid and sections, 6 μ in thickness, were stained with Einarson's gallocyanin, with methyl green–pyronine, and in the main series with paraldehyde–fuchsin by the Gomori–Gabe method and counterstained with Heidenhain's azan. The morphometric techniques used in the investigation were described earlier [3].

EXPERIMENTAL RESULTS

Injection of the reacting dose of antigen was followed by the development of a symptom-complex of severe anaphylactic shock, from which about 30% of animals died. Death occurred most often between the third and fifth minute of shock.

Compared with the control (group 1), the number of darkly stained neurosecretory cells with a high content of neurosecretory substance was appreciably greater in the supraoptic (SON) and paraventricular (PVN) nuclei in the animals of group 2. In the control, for instance, there were 4% of these cells in SON and 24% in PVN, but in group 2 there were 24% and 37% respectively (Figs. 1a, b and 2a, b). The bodies of the neurosecretory cells were considerably enlarged but the volumes of the nuclei and nucleoli were reduced (Table 1). The diffuse staining of the cytoplasm with gallocyanin was less strong, but the rim of Nissl's substance was wider and brighter than in the animals of group 1. Many neurosecretory fibers packed with neurosecretory substance appeared. Cells with two nucleoli were frequently seen in both SON and PVN (in group 1: 1% in SON, 2% in PVN; in group 2, 9, and 11%, respectively). The content of neurosecretory substance in the posterior lobe of the pituitary was increased from 2.5 ± 0.7 points in group 1 to 3.9 ± 0.1 points.

All these changes in the neurosecretory system can be regarded as evidence of a

TABLE 1. Dimensions of Neurosecretory Cells of Supraoptic and Paraventricular Nuclei (in μ^3)

Group of animals	Supraoptic nucleus			Paraventricular nucleus		
	cell body	nucleus	nucleolus	cell body	nucleus	nucleolus
1-	6202±175,6	666±12	6,32±0,17	5179±110,2	601±12	3,69±0,065
2-	7325±184,5	583±7,85	5,5±0,2	6601±185,5	525±7,6	2,1±0,099
P_1	<0,001	<0,001	<0,001	<0,001	<0,001	<0,001
3-	5890±136,3	552±7,88	3,87±0,07	4922±98,4	542±8,7	3,67±0,06
P_1	>0,05	<0,001	<0,001	>0,05	<0,001	>0,05
P_2	<0,01	<0,001	<0,001	<0,001	<0,1	<0,001

P_1 — significance of difference from results obtained in group 1.
P_2 — significance of difference from results obtained in group 2.

sharp increase in secretion-forming activity and in the intensity of transport of neurohormones along the axons, but no considerable discharge of neurohormones evidently took place from the posterior pituitary. These marked changes in the state of the neurosecretory system took place within a period of only 5 min, but this does not seem improbable, considering observations by other workers who described similar changes in the neurosecretory system a few minutes after exposure to extremely strong stressors [7, 10, 11, 13, 14].

In the rabbits of group 3 darkly stained neurosecretory cells were predominant in SON and PVN, but there were appreciably fewer cells rich in neurosecretory substance among them (15% in SON, 26% in PVN) than in the animals of the previous group. Compared with the initial state, the content of neurosecretory substance in the cells was not significantly changed (compare Figs. 1c and 2c). The volumes of the bodies and nuclei of the neurosecretory cells in SON and PVN and the volumes of the nucleoli in SON were reduced, but the size of the nucleoli of the PVN cells was unchanged (Table 1). Cells with two nucleoli were rare (0.3% in SON, 1% in PVN). The intensity of staining of the cytoplasm with gallocyanin was lowered. Besides cells with clearly defined Nissl's substance, other cells which stained extremely palely with gallocyanin and with single granules of Nissl's substance, giving them an "exhausted" appearance, also were seen. These cells were perhaps a certain stage of degeneration of the neurosecretory cells of the "melting" type [2]. Only solitary expansions of the neurosecretory fibers, loosely filled with granules of neurosecretory substance, were seen in the region of SON and PVN. The content of neurosecretory substance in the posterior lobe of the pituitary in the animals of this group was reduced to 1.7 ± 0.2 points, and in some of them it had almost completely disappeared from the neurohypophysis.

The picture described above suggests that in animals dying from shock activation of synthesis of neurohormones in the neurosecretory cells is inadequate in degree, whereas liberation of neurohormones from the posterior lobe is intensified, with the result that the content of neurosecretory substance in the system as a whole falls.

In animals surviving anaphylactic shock processes of synthesis and transport of neurohormones along the axons are thus intensified extremely rapidly. In rabbits dying from shock only the first stage of activation of neurohormonal synthesis probably takes place, and the process subsequently develops insufficiently for some reason or other. The state of the posterior lobe of the pituitary also differs in the animals of the two groups, but in this case the relationship is opposite: the liberation of neurohormones is intensified in the animals dying from shock but weakened in the animals surviving shock. This last result is contrary to the widely held view that the liberation of neurohormones from the posterior lobe of the pituitary is intensified in stress [6], but under the conditions of anaphylactic shock, the absence of active liberation of neurohormones is probably of special physiological significance, for it is observed only in animals that survive after shock.

It is interesting to note that the neurosecretory cells respond somewhat differently from other neurons to anaphylactic shock. For instance, the nuclei of pyramidal neurons in the temporal region of the cortex increase a little in size during shock ($627 \pm 30.7\ \mu^3$ compared with $556 \pm 14.7\ \mu^3$ after sensitization; $P < 0.03$), whereas the changes in the neurosecretory cells are different in character (Table 1).

The results of this experiment also demonstrate the high reactivity of the neurosecretory cells, for within a few minutes they were able to synthesize large quantities of neurosecretory material, to undergo sharp changes in the size of their perikarya, nuclei, and nucleoli and in the number of nucleoli in the nucleus, and not merely, as was already known [2, 6], to liberate large quantities of neurohormones quickly from their terminals.

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