STATE OF THE HYPOTHALAMO-HYPOPHYSEAL NEUROSECRETORY SYSTEM OF RABBITS AFTER ANAPHYLACTIC SHOCK

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UDC 616-001.36-056.3-092.9-07:
[616.432+616.831.41]-008.6-0727

The neurosecretory system of rabbits was investigated 1, 3, 7, 14, and 21 days after anaphylactic shock. Morphometric methods were used to show that the dimensions of the nucleoli in the paraventricular and supraoptic nuclei of the hypothalamus increased gradually by comparison with their size at the time of anaphylactic shock but did not reach the control level. Nucleoli of the cells of the supraoptic nucleus regained their size more slowly than those of the paraventricular nucleus. The content of neurosecretory substance in the system as a whole was not reduced and remained above the control level until the 21st day. The intensity of the formation and secretion of neurohormones in the hypothalamo-hypophyseal neurosecretory system was thus reduced during the 21 days of the postshock period.
KEY WORDS: *hypothalamo-hypophyseal neurosecretory system; anaphylaxis.*

The role of the hypothalamus as a whole in sensitization processes is still far from being completely understood. Workers in this field frequently have reached contradictory conclusions [10-12]. As regards the hypothalamo-hypophyseal neurosecretory system, this has received extremely little study from this standpoint [1, 6] and the work of which the writers are aware has dealt mainly with changes in this system during the period of injection of the reacting dose of antigen.

In the investigation described below the state of the neurosecretory system was studied after anaphylactic shock.

EXPERIMENTAL METHOD

Male rabbits weighing 3-3.5 kg and aged 10-12 months were sensitized with antirabies γ-globulin. The sensitizing doses (0.1 ml/kg) were injected intravenously three times at intervals of 48 h. The reacting injection of antigen was given on the 21st day after the third sensitizing injection intravenously in a dose of 3 ml/kg. The test material was fixed at the same time of day, 1, 3, 7, 14, and 21 days after shock. Six intact animals were used as the control. All the material was collected during September and October.

The rabbits' brain and pituitary gland were fixed in Bouin's fluid. Sections were stained with paraldehyde–fuchsin by the Gomori–Gabe method and counterstained with Heidenhain's Azan, with Methyl Green and pyronine, and with gallocyanin and chrome alum by Einarson's method.

The results obtained were compared with those described by the writers previously [3, 4] characterizing the state of the neurosecretory system in rabbits surviving 5 min after anaphylactic shock.

Kemerovo Medical Institute. I. M. Sechenov Institute of Evolutionary Physiology and Biochemistry, Academy of Sciences of the USSR, Leningrad. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 81, No. 3, pp. 351-354, March, 1976. Original article submitted March 28, 1975.

TABLE 1. Some Morphometric Indices of Functional State of Hypothalamo-Hypophyseal Neurosecretory System after Anaphylactic Shock

Time of investigation	Supraoptic nucleus				Paraventricular nucleus				Neurosecretory substance in posterior lobe of pituitary (conventional units)
	Dimensions of cell body (μ^3)	Dimensions of nucleus (μ^3)	Dimensions of nucleolus (μ^3)	Number of binucleolar cells (%)	Dimensions of cell body (μ^3)	Dimensions of nucleus (μ^3)	Dimensions of nucleolus (μ^3)	Number of binucleolar cells (%)	
Control (intact rabbits)	5377±125,5	596±10,4	6,55±0,176	2	5079±95,6	656±12,3	4,97±0,137	0	3,3±0,048
Anaphylactic shock	7325±184,5	583±7,85	5,51±0,197	9	6601±185	525±7,6	2,1±0,099	11	3,9±0,109
State after shock lasting in days:									
1st	6419±277 $P_1 < 0,001$ $P_2 < 0,01$	543±6,67 $P_1 < 0,001$ $P_2 < 0,001$	3,43±0,06 $P_1 < 0,001$ $P_2 < 0,001$	3	5426±134,3 $P_1 < 0,05$ $P_2 < 0,001$	530±7,08 $P_1 < 0,001$ $P_2 > 0,5$	3,62±0,068 $P_1 < 0,001$ $P_2 < 0,001$	2	3,8±0,15 $P_1 < 0,01$ $P_2 > 0.5$
3rd	6943±147,6 $P_1 < 0,001$ $P_2 > 0,1$	685±9,58 $P_1 < 0,001$ $P_2 < 0,001$	4,23±0,138 $P_1 < 0,001$ $P_2 < 0,001$	2	5208±113,5 $P_1 > 0,2$ $P_2 < 0,001$	545±7,76 $P_1 < 0,001$ $P_2 > 0,05$	3,92±0,09 $P_1 < 0,001$ $P_2 < 0,001$	1	4,6±0,071 $P_1 < 0,001$ $P_2 < 0,001$
7th	6665±147,4 $P_1 < 0,001$ $P_2 < 0,01$	687±10,4 $P_1 < 0,001$ $P_2 < 0,001$	4,0±0,95 $P_1 < 0,001$ $P_2 < 0,001$	0,6	5005±90,4 $P_1 > 0,5$ $P_2 < 0,001$	529±6,84 $P_1 < 0,001$ $P_2 > 0,5$	3,8±0,077 $P_1 < 0,001$ $P_2 < 0,001$	0	3,8±0,086 $P_1 < 0,001$ $P_2 > 0,2$
14th	6118±113 $P_1 < 0,001$ $P_2 < 0,001$	559±6,83 $P_1 < 0,001$ $P_2 < 0,05$	4,01±0,08 $P_1 < 0,001$ $P_2 < 0,001$	0	6545±110,6 $P_1 < 0,001$ $P_2 > 0,5$	689±11,3 $P_1 > 0,05$ $P_2 < 0,001$	4,2±0,088 $P_1 < 0,001$ $P_2 < 0,001$	1	4,6±0,07 $P_1 < 0,001$ $P_2 < 0,001$
21st	6609±159. $P_1 < 0,001$ $P_2 < 0,01$	695±10,6 $P_1 < 0,001$ $P_2 < 0,001$	4,78±0,12 $P_1 < 0,001$ $P_2 < 0,001$	0,6	5516±130,0 $P_1 < 0,01$ $P_2 > 0,05$	655±10,7 $P_1 > 0,5$ $P_2 < 0,001$	4,31±0,113 $P_1 < 0,001$ $P_2 < 0,001$	0	3,9±0,097 $P_1 < 0,001$ $P_2 > 0,5$

Legend: P_1) significance of differences from results obtained in intact animals; P_2) significance of differences from results obtained on animals during anaphylactic shock.

The morphometric methods used were fully described earlier [5]. In addition, the number of binucleolar neurosecretory cells was counted (in % of 200 cells) in the supraoptic (SON) and paraventricular (PVN) hypothalamic nuclei.

EXPERIMENTAL RESULTS

Injection of the reacting dose of antigen into the rabbits was followed by the development of a symptom complex of severe anaphylactic shock, as a result of which about 30% of the experimental animals died. Rabbits which survived one week were exhausted, relatively immobile; they lost up to 10% of their body weight, and some of them died. By the 14th day after shock the experimental animals had recovered their weight and they were outwardly indistinguishable from intact animals.

Morphological changes in the neurosecretory system of the animals in anaphylactic shock, as was demonstrated previously [3, 4, 6], points to marked activation of the formation of Gomori-positive neurosecretory substance (NSS) and an increase in its transport into the posterior lobe of the pituitary, although the liberation of neurohormones into the blood stream is probably inhibited [3, 10]. During the first day after shock the dimensions of the cell bodies of SON, the volume of their nuclei and nucleoli, and also the number of binucleolar cells were appreciably reduced (Fig. 1a, b); changes of a similar character in the perikarya also were observed in PVN, whearas the nucleoli were larger than in anaphylactic shock (Fig. 2a, b) although they did not reach the control level, and the number of binucleolar cells was sharply reduced (Table 1). Granules of NSS most frequently filled the cytoplasm of the cells uniformly in both neurosecretory centers, but were more loosely distributed than in animals in a state of shock. In the region of SON 1 and, less frequently, 3 days after shock fragments of neurosecretory fibers with expansions tightly packed with NSS could be seen (Fig. 1b). Pictures of this sort were not found in the control (Fig. 1d), nor were they observed in PVN of the experimental animals.

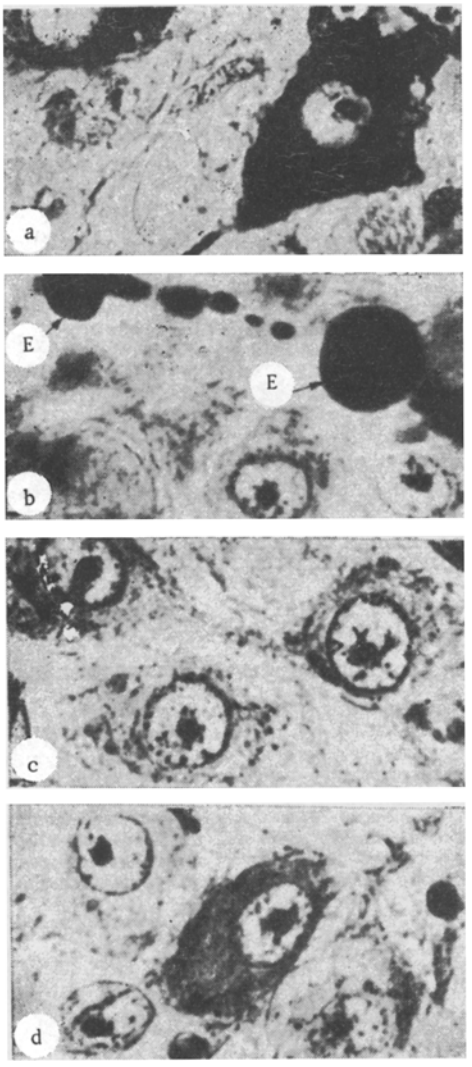

Fig. 1

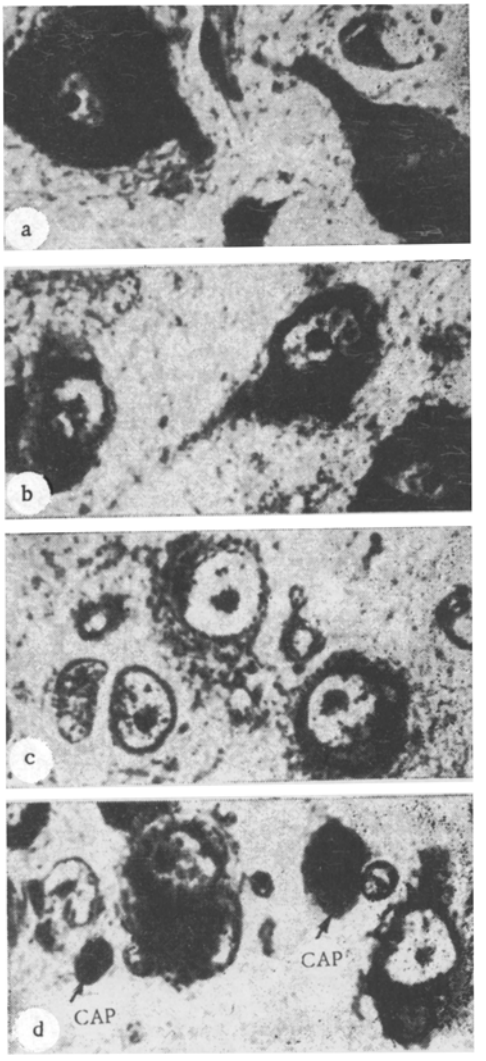

Fig. 2

Fig. 1. Supraoptic nucleus of hypothalamus: a) anaphylactic shock, b) 1st day after shock, c) 21st day after shock, d) control (intact animals); E) expansions of neurosecretory fibers packed with neurosecretion. Stained with paraldehyde–fuchsin by Gomori–Gabe method, counterstained with Heidenhain's Azan, 700×.

Fig. 2. Paraventricular nucleus of hypothalamus: a) anaphylactic shock, b) 1st day after shock, c) 21st day after shock, d) control (intact animals); CAP) capillaries. Stained with paraldehyde–fuchsin by Gomori–Gabe method, counterstained with Heidenhain's Azan, 700×.

The content of NSS in the posterior lobe of the pituitary gland remained just as high 24 h after shock as during shock (Table 1), but the volume of blood in the vessels of the neurohypophysis was only average. The content of NSS in the fibers of the hypothalamo-hypophyseal tract in the median eminence was somewhat increased. No changes were observed in the state of the outer zone of the median eminence.

It can be concluded from these observations that during the first 24 h after shock, i.e., after a very powerful degree of activation, much stronger than the ordinary physiological kind, the neurosecretory cells passed into a state of reduced intensity of secretory processes. The decrease in functional activity of the SON cells was more marked (a considerable decrease in size of the nucleoli) and in addition, transport of NSS was delayed along the fibers of this nucleus (accumulation of NSS in the expanded fibers). The functional activity of PVN was reduced by a lesser degree: On the 1st day after shock the volume of the nucleoli began to be restored, and movement of NSS along the axons evidently was not retarded.

A similarity can be seen between the response of the neurosecretory cells on the first day after anaphylactic shock and changes in other typical neurons in response to inadequately strong "fatiguing" excitation, when the RNA content in the cell falls [7-9, 11] and the size of the cell is reduced [2, 7, 9]. However, the difference between the response of the SON and PVN cells indicates that this explanation is not entirely satisfactory.

During the next 20 days the state of PVN gradually returns closer to normal (Fig. 2c, d), although the nucleoli still remain smaller in volume by the 21st day after shock than in the control. Characteristically in SON during this period the dimensions of the cell bodies and nuclei were a little increased, whereas the volume of the nucleoli and the number of binucleolar cells were considerably reduced. With respect to the content of NSS in the cells and fibers, SON was similar to the control (Fig. 1c, d). Since the dimensions of the nucleolus can be regarded as one of the principal indices of the functional state of the neurosecretory cell [7, 8], it can be assumed that the activity of secretion formation in the cells of SON was reduced. A reduction in the functional activity of both neurosecretory centers in the postshock period was also shown by the appearance of numerous pycnomorphic cells (25% by the 7th day in PVN, 13% by the 14th day in SON). The content of NSS in the posterior lobe of the pituitary remained at the same level until the 14th day and fell only a little between then and the 21st day (Table 1). This suggests that liberation of neurohormones into the blood stream was not activated.

Hence, after anaphylactic shock the hypothalamo-hypophyseal neurosecretory system probably enters into a state of lowered functional activity which persisted throughout the period of observation. The decrease in activity was most clearly marked in the cells of SON.

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