ROLE OF INDIVIDUAL HYPOTHALAMIC STRUCTURES IN CERTAIN IMMUNOBIOLOGICAL PROCESSES

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Bilateral electrolytic coagulation of the posterior hypothalamus in rabbits inhibits some of the factors of natural immunity: the bactericidal activity and complementary activity of the blood serum, and the titers of lysozyme and normal typhoid agglutinins.

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Many investigations have been carried out to study the role of the nervous system in immunobiological processes. However, the role of subcortical structures in regulation of the processes of infection and immunity has been inadequately studied. It is only recently that reports have been published of investigations of regulation of allergic [1, 2, 11] and immunologic reactions [3, 4, 6, 8, 9] by the hypothalamus.

The object of the present investigation was to study the relative participation of individual hypothalamic structures (especially structures of the posterior hypothalamus located in the posterior and dorsal hypothalamic areas) in regulation of certain reactions of natural immunity: 1) bactericidal activity of sera, 2) their complementary activity, 3) the lysozyme titer, and 4) the titer of normal typhoid agglutinins.

EXPERIMENTAL METHOD

Experiments were carried out on 57 rabbits, 25 of them forming the control group.

Selected areas of the brain were destroyed bilaterally by an electrolytic method, using a stereotaxic apparatus of the Dell type, by means of a direct current (2 mA, 1 min) applied through a monopolar electrode. Coordinates were determined from the atlas of Sawyer and co-workers [10]. Coagulation was carried out in the posterior and dorsal hypothalamic areas at the level P-1. The animals were anesthetized with nembutal (40 mg/kg). Before the operation the initial immunologic indices of the animals were repeatedly determined. On the 7th day after the operation and every 7th day thereafter blood was taken from the rabbits' ear to determine changes in the test reaction of natural immunity over a period of 6 weeks.

The bactericidal titer of the serum was determined by the micromethod of Mironov and Svital'skaya [5], lysozyme in the rabbits' blood serum was determined by the usual indirect method of qualitative indication of this enzyme in liquids, based on high sensitivity of the bacteria Micrococcus lysodeikticus to the action of lysozyme, complementary activity of the sera was determined by E. P. Shuvalova's method [7], and the titer of normal typhoid agglutinins in the usual manner.

The control in all series of experiments consisted of frequent determinations of analogous indices in rabbits in which destruction was carried out in another part of the brain (subcortical white matter). The subcortical white matter was coagulated in order to determine whether the changes in natural resistance of the animal observed after destruction of appropriate hypothalamic structures were specific to the hypothalamus alone, or whether similar changes could take place after destruction of other parts of the brain.

After the end of the experiments the size, character, and localization of the focus of destroyed brain tissue were verified histologically. The brain to be examined was fixed in 10% formalin and embedded in paraffin wax; serial frontal sections (20 μ) were cut and stained by Nissl's method.

The numerical results were subjected to statistical analysis by Student's method.

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TABLE 1. Humoral Factors of Natural Immunity after Coagulation of Posterior Hypothalamus and Subcortical White Matter

Character of brain damage	Day of investigation	Lysozyme titer		Titer of normal typhoid agglutinins		Titer of complement		Bactericidal titer	
		M±m	P	M±m	P	M±m	P	M±m	P
Experimental rabbits before operation		88±5,57		22,8±2,58		0,15±0,0087		625±43,6	
Coagulation of posterior hypothalamus	7	704±41,5	<0,001	16,2±1,16	=0,02	0,278±0,018	<0,001	1250±110	<0,001
	14	104±5,67	<0,05	13,1±0,87	<0,01	0,191±0,027	<0,01	500	=1
	21	54±2,66	<0,001	16,2±0,86	<0,02	0,340±0,01	<0,001	2317±201	<0,001
	28	28,5±1,18	<0,001	14,3±0,99	<0,002	0,273±0,01	<0,001	1091±51	<0,001
	35	25±1,42	<0,001	12,5±0,82	<0,001	0,18±0,01	<0,002	500	=1
	42	54±2,66	<0,001	16,5±0,85	<0,02	0,277±0,01	<0,001	2078±238	<0,001
Experimental rabbits before operation		51±3,2		42±11,9		0,141±0,009		500	
Coagulation of subcortical white matter	7	410±18,08	<0,001	74±10,8	>0,05	0,124±0,005	>0,1	500	=1
	14	205±12,7	<0,001	42±11,9	=1	0,107±0,003	<0,001	500	=1
	21	171±12,5	<0,001	42±11,9	=1	0,107±0,003	<0,001	500	=1
	28	106±3,67	<0,001	42±11,9	=1	0,132±0,007	<0,05	500	=1
	35	61±3,2		42±11,9	=1	0,132±0,006	<0,05	500	=1
	42	51±3,2		42±11,9	=1	0,141±0,01	>0,1	500	=1

EXPERIMENTAL RESULTS

The experiments showed that the mean bactericidal titer of the experimental rabbits before the operation was 625, while in rabbits with coagulated subcortical white matter its value was 500, remaining unchanged during the 6 weeks after the operation.

The serum bactericidal activity was reduced by half in rabbits with coagulated posterior hypothalamas on the 7th day after the operation, the greatest decrease being found on the 21st day after operation. However, on the 14th and 35th day after operation the serum bactericidal activity increased.

The serum complementary activity of rabbits with destruction of the posterior hypothalamus was reduced on the average by 50% below the initial level on the 7th day after the operation and by 55% compared with rabbits in which the subcortical white matter was destroyed. The decrease in complementary activity was greatest on the 21st day, but on the 42nd day after operation it was still 55% below normal.

Coagulation of the posterior hypothalamus also led to a consideration decrease in activity of serum lysozyme and in the titer of normal agglutinins. On the 7th day after operation the serum lysozyme activity was increased to 8 times the control level, and the same was observed after coagulation of the subcortical white matter. However, in contrast to rabbits of the control group, the lysozyme titer subsequently fell below the initial level. The serum lysozyme activity fell to its lowest level of 29% of the initial activity on the 35th day after operation.

The titer of normal typhoid agglutinins was reduced 1.3-1.8 times after coagulation of the posterior hypothalamus, compared with the initial value, and remained at this level throughout the 6 weeks after operation; this effect was not observed after destruction of the subcortical white matter (Table 1).

The facts described show that bilateral destruction of the posterior hypothalamus inhibits the studied reactions of natural immunity.

What is the mechanism of the observed phenomena? The hypothalamus, as is well known, is intimately connected with the pituitary, and through the pituitary hormonal system it influences the adrenal cortex, hormones of which have an important influence on immunologic reactions. Our operations on the hypothalamus must therefore have caused disturbances of immunologic reactions.

Disturbance of the hormonal function of the adrenal cortex and associated immunologic reactions may be connected with disturbance of the regulatory function of the autonomic nervous system directed toward the adrenals, and also, indirectly, of the reticulo-endothelial system as a result of coagulation of the hypothalamic nuclei.

Finally, the disturbances of immunologic processes may also be connected with a disturbance of central mechanisms,

namely, regulatory mechanisms of the cerebral cortex, certain hypothalamic nuclei, and the reticular formation of the brain stem.

It is difficult at present to decide which of these mechanisms is the most important. The most likely explanation is that all these factors play a part.

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