EFFECT OF BILATERAL DESTRUCTION OF SOME MEDIAL HYPOTHALAMIC STRUCTURES ON THE FORMATION OF COMPLEMENT-FIXING ANTIBODIES

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Bilateral eletrolytic injury to circumscribed areas of the medial zones of the anterior or posterior hypothalamus had no significant effect on the intensity of formation of complement-fixing antibodies. Changes in the antibody titers after a single immunization were weaker in all the groups of experimental animals than in the corresponding controls, and were not statistically significant.

In the last decade several investigations of the role of the hypothalamus in antibody formation have been published. However, these investigations are contradictory. Some workers, using the method of electrolytic destruction of different regions of the hypothalamus, obtained directly opposite results as regards the localization of the zone with the strongest action on antibody formation [3, 5, 12].

In view of the contradictory results obtained and the importance of the problem under discussion it was decided to study the character of the effect of injuries to different parts of the medial hypothalamus on the intensity of antibody formation during the primary immunological response.

EXPERIMENTAL METHOD

Chinchilla rabbits weighing 3.0-3.5 kg were used. The brain tissue was destroyed symmetrically on both sides by an electrode 0.3-0.4 mm in diameter through which a direct current of 1.0-1.5 mA was applied for 30 sec. The animals were immunized 6-7 days after the operation with a single dose of 50 mg crystalline egg albumin in 5 ml sterile physiological saline. The dynamics of antibody formation was studied by titration of the antibodies in the blood serum for 30 days after immunization by the complement-fixation test in the cold. The animals were sacrificed 30 days after immunization and histological sections of their brain were prepared and used to study the localization of the foci of injury with the aid of an atlas [10]. Depending on the localization of the foci of injury and the method of immunization (subcutaneous or intravenous) the following four groups of animals were distinguished.

Group 1 consisted of 20 animals with foci of injury in the posterior hypothalamus in the region of planes P2-P3 [10] at a depth of 12-15 mm from the brain surface, 0.5-1.5 mm laterally to the midline, at the boundaries of the caudal part of the third ventricle between transverse sections through the fibers of the fornix and mammillothalamic tract (Fig. 1). Immunization was carried out subcutaneously.

Group 2 consisted of 12 animals with foci of injury in the region of planes P1 and P2 [10], 11-13 mm from the brain surface, 0.5-1.5 mm laterally to the midline, and at the boundary between the posterior hypothalamus and thalamus (Fig. 2). The rabbits were immunized subcutaneously.

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TABLE 1. Titer of Complement-Fixing Antibodies in Blood of Rabbits with Injuries to Various Hypothalamic Structures ($\log_2$, M ±m)

Group	No. of animals	Day after immunization						
		2-	5-	7-	10-	15-	20-	30-
1-	20	—	1,20±0,36	3,57±0,52	4,10±0,49	3,85±0,41	2,41±0,49	1,20±0,41
2-	11	—	2,20±0,70	4,60±0,60	4,50±0,61	3,90±0,80	3,40±0,80	1,10±0,80
Control (subcutaneous immunization)	8	—	—	3,80±0,99	3,64±0,98	2,60±1,10	2,40±1,00	0,86±0,58
3-	10	—	0,66±0,70	2,81±1,30	4,26±0,90	4,26±0,90	3,90±0,80	2,30±1,10
4-	13	—	1,67±0,53	3,03±0,62	3,19±0,61	2,99±0,58	1,91±0,60	—
Control (intravenous immunization)	8	—	0,82±0,58	3,34±0,98	3,44±0,90	3,44±0,90	1,86±0,82	—

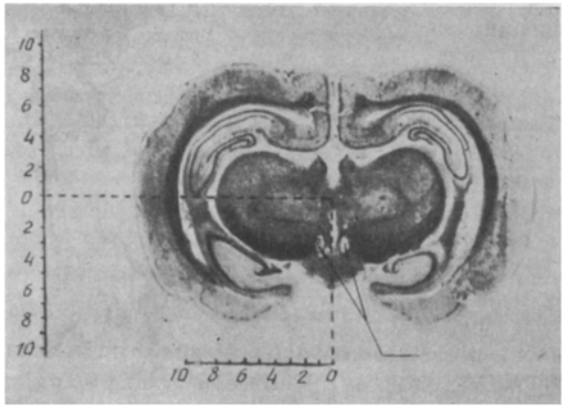

Fig. 1

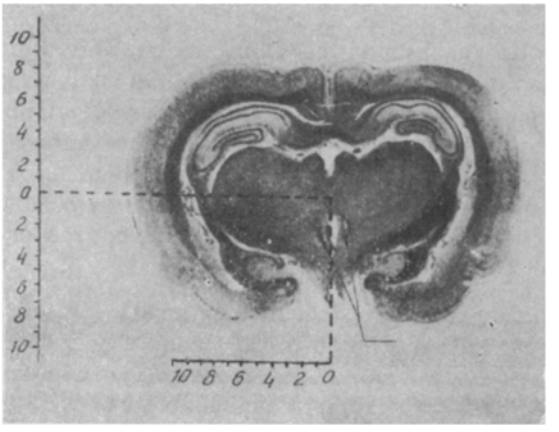

Fig. 2

Fig. 1. Localization of injuries in an animal from group 1.

Fig. 2. Localization of injuries in an animal from group 2.

Group 3 consisted of 10 animals in which the localization of the lesions was the same as in the first group, but immunization was carried out intravenously.

Group 4 consisted of 13 animals with lesions in the anterior hypothalamus in planes A2-A1 [10], at a depth of 12-14 mm from the brain surface, and 0.5-1.5 mm laterally to the midline (Fig. 3). Immunization was carried out intravenously.

The control for groups 1 and 2 consisted of eight rabbits undergoing a mock operation and immunized subcutaneously. The control for groups 3 and 4 consisted of eight rabbits undergoing a mock operation and immunized intravenously.

EXPERIMENTAL RESULTS

Examination of the histological sections through the brain of the experimental animals revealed round or oval foci of necrosis about 1 mm in diameter in the corresponding regions of the hypothalamus.

Complement-fixing antibodies appeared in all the experimental and control groups of animals on the 5th-7th day after immunization, they reached their highest titers on the 10th-15th day, and in most experiments they disappeared by the 30th day. The results of statistical analysis of the experimental data are given in Table 1. In the rabbits of groups 1 and 2 the highest antibody titers were slightly higher than in the control. The geometric mean titers in the animals of groups 1 and 2 on the 10th day after immunization

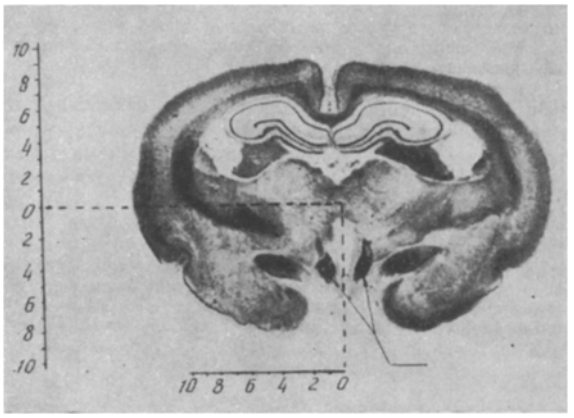

Fig. 3. Localization of injuries in an animal from group 3.

were 1 : 17 and 1 : 23 respectively, compared with 1 : 13 in the control. The antibody titer in the rabbits of group 3 on the 10th day after immunization also was somewhat higher than the corresponding control (1 : 19 and 1 : 11). By contrast to the first three groups, in the animals of group 4 the antibody titers were a little lower than in the control.

It must be pointed out that with the methods of immunization used, no complement-fixing antibodies were produced by 20-25% of the animals in both the experimental and control groups.

This may largely explain the low value of the geometric mean titers.

The results showed that injury to circumscribed areas of the hypothalamus has no significant effect on the intensity of antibody formation. Injuries within these regions of the posterior hypothalamus led to a slight increase in antibody production, while injuries to the anterior hypothalamus led to a very slight decrease in their production. Statistical analysis of the results of these experiments, by the dispersion method [9], showed that the effect of hypothalamic injury on antibody formation is not significant. If the values of the negative logarithms of the antibody titers in the period of their most intensive production (7th, 10th, 15th, and 20th days after immuization) are compared it will be seen that the value of F* for the first two groups of animals and the corresponding control was 1.4 for 2 and 148 degrees of freedom ($P > 0.05$) while for groups 3 and 4 and the corresponding control its value was 2.04 for 2 and 112 degrees of freedom ($P > 0.05$).

The results of these experiments agree well with modern views regarding the structural and functional organization of the hypothalamus. The hypothalamus is a suprasegmental apparatus of the autonomic nervous system and an organ regulating the work of the most important endocrine glands producing hormones with both catabolic and anabolic action. Zones of hypothalamic nerve cells possessing specific hormonal activity have been shown not to have sharp boundaries, just as the zones of representation of the autonomic nervous system in the hypothalamus are not sharply defined [1, 8, 6, 11]. After circumscribed destruction of individual areas of the hypothalamus it is thus most probable that only slight changes take place in the hormonal balance and in the tone of the autonomic nervous system, for zones duplicating the functions of the injured foci may exist in the intact regions. These changes in the hormonal balance and tone of the autonomic nervous system may evidently have a weak stimulatory or inhibitory action on the biosynthesis of globulins in the body in general and on antibody production as one of its manifestations.

So far as reports that "a circumscribed area with a well-marked relationship to the regulation of immunogenesis is located in the region of the dorsal hypothalamic area"† [3] or that "neuronal structures linked with the regulation of antibody production are concentrated mainly" in this zone [4], and that injury to this region of the hypothalamus leads to the complete suppression of formation of complement-fixing antibodies [3, 4] are concerned, they must be taken with considerable caution. First, in articles formulating this important conclusion there is a conspicuous absence of statistically analyzed numerical data, and second, in accordance with the published findings [2, 7] and the results of the writer's experiments, individual immunological reactivity varies within wide limits in noninbred animals. After a single immunization 20-30% of rabbits produce no precipitating or complement-fixing antibodies whatsoever.

This considerable proportion of immunologically inert animals may be a source of error unless the morphological control and the statistical analysis of the experimental material are sufficiently exact.

*F is the criterion of significance of the difference between the sets of values investigated. $F = t^2$ for equal degrees of freedom [9].

†The region injured in the animals of groups 1 and 3 in the present investigation.

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