EFFECT OF BILATERAL DESTRUCTION OF REGIONS OF THE MEDIAL HYPOTHALAMUS ON THE COURSE OF ANAPHYLACTIC SHOCK

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Anaphylactic shock induced in rabbits after preliminary injury to various regions of the medial hypothalamus ran a more severe course than in the control. Regardless of the location of the foci of injury, in response to injection of the reacting dose of antigen the hypotensive response was more marked and the compensatory rise of blood pressure was slower. The severity of the anaphylactic shock depended on the time elapsing after injury to the hypothalamus until injection of the reacting dose of antigen.

KEY WORDS: *Hypothalamus; anaphylactic shock.*

As the writer showed previously [1, 2] there are no structures in the hypothalamus specially concerned with the regulation of immunogenesis and injury to which would lead to significant inhibition of antibody formation, and which thus might have a significant effect on the phase of sensitization of allergic reactions of immediate type.

The object of this investigation was to study the effect of injury to different parts of the medial hypothalamus on the course of the pathophysiological phase of allergic reactions as exemplified by anaphylactic shock in rabbits, for existing information on this problem is limited in amount and contradictory in nature [3-6, 8].

EXPERIMENTAL METHOD

Experiments were carried out on 52 rabbits weighing 2.5-3 kg. Ten days after trephining of the skull the control animals, which underwent a mock operation, were immunized with ovalbumin by four injections, each of 25 mg/kg body weight, at intervals of two days. Fifteen days after the end of immunization the presence of circulating antibodies was determined by the ring precipitation test. Next day, under hexobarbital anesthesia (30 mg/kg), a cannula was inserted into the common carotid artery and the blood pressure was recorded for 10 min to establish the background values. The reacting dose of ovalbumin (30 mg/kg in 1.5 ml physiological saline) was then injected intravenously and the hypotensive response recorded for 30 min. The animals were then killed and parts of the lungs, spleen, and lymph glands were removed from them for morphological analysis. The experimental animals were divided into two groups. In the animals of group 1 electrolytic injury (current 1 mA, duration 30 sec) was inflicted on various zones of the medial hypothalamus, symmetrically on both sides, in accordance with the atlas of Sawyer et al. [7]. In nine animals of this group the anterior hypothalamus was injured between planes A-3 and A-1 at a depth of 14-15 mm from the brain surface in the region of the supraoptic nuclei. In eight animals of this group the middle part of the hypothalamus was injured between planes A-1 and B-1 at a depth of 15-16 mm from the brain surface in the region of the ventro- and dorsomedial nuclei. In ten animals of this group the posterior hypothalamus was injured between planes P-2 and P-4 at a depth of 14-15 mm from the brain surface in the region of the posterior hypothalamic zone. Ten days after the operation the animals were immunized and the reacting injection given according to the scheme described above. The animals of group 2 also underwent destruction of the anterior (five rabbits), middle (five rabbits), or posterior (four rabbits) hypothalamus and

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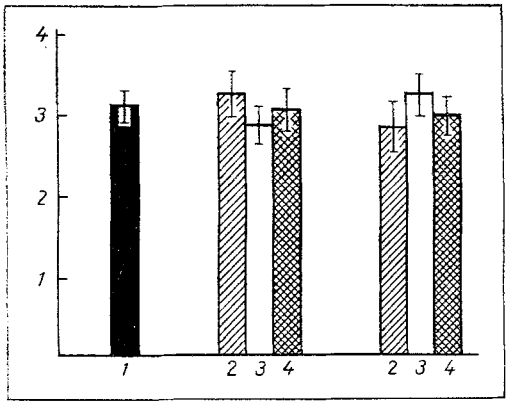

Fig. 1. Smallest concentration of ovalbumin forming precipitation rings with antibodies in animals' blood serum. Ordinate, ovalbumin concentration (in μg/ml); abscissa, group of animals: 1) control, 2) animals with injury to anterior hypothalamus, 3) to middle hypothalamus, 4) to posterior hypothalamus.

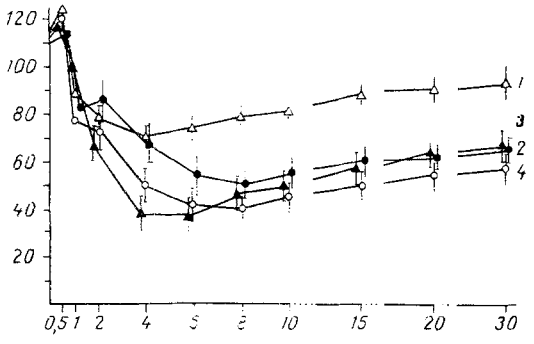

Fig. 2

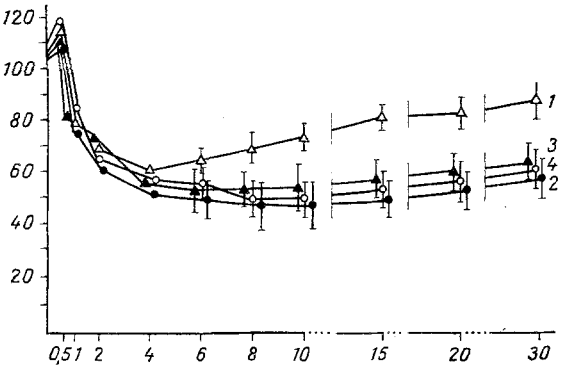

Fig. 3

Fig. 2. Changes in arterial pressure of animals of group 1 after receiving reacting dose of antigen. Ordinate, arterial pressure (in mm Hg); abscissa, time after injection of antigen (in min). 1) control; 2) animals with injury to anterior hypothalamus; 3) to middle hypothalamus; 4) to posterior hypothalamus.

Fig. 3. Changes in arterial pressure of animals of group 2 after injection of reacting dose of antigen. Legend as in Fig. 2.

were tested four months later by the scheme described above. After the end of the experiment the brain was removed from all animals undergoing the operation in order to localize the foci of injury.

EXPERIMENTAL RESULTS

In all animals of the control and experimental groups, irrespective of the location of the foci of injury, antibodies forming clear precipitation rings with ovalbumin solution in a minimal concentration of 2-6 μg/ml were found in the blood serum 15 days after immunization (Fig. 1). In preparations from the spleen and regional lymph glands there were features characteristic of intensive immunogenesis, marked proliferation of plasma cells in the follicles of the spleen with the appearance of many cells of the plasma series in the lymph gland. Just as in the previous investigations, injury to different zones of the hypothalamus thus had no significant effect on the intensity of antibody formation.

The reacting dose of antigen was chosen so that its injection did not cause death of any of the control animals from anaphylactic shock. Injection of the reacting dose of antigen caused a transient rise of blood pressure followed by a sharp hypotensive reaction in most of the animals of the control group (Fig. 2). The mean background level of the blood pressure in this group was 116±4 mm Hg. Immediately after injection of the reacting dose of antigen the blood pressure rose to 124±12 mm Hg, falling after 4 min to minimal values (70±11 mm Hg). A compensatory rise of blood pressure began 5-6 min after injection of the antigen, and toward the end of the period of observation it reached 90±9 mm Hg.

The study of histological preparations of the lungs was of special interest, for anaphylactic shock develops in rabbits as a result of spasm of the arterioles of the pulmonary circulation. Comparatively minor changes, expressed as some thickening of the interalveolar septa and filling of individual alveoli with serous contents, were observed in the lungs taken from the control animals after the end of the experiment. In the animals of group 1, irrespective of the localization of the foci of injury, the course of the anaphylactic shock was more marked (Fig. 2). The minimal values of the blood pressure were 40-50 mm Hg. The compensatory rise of blood pressure began later and was less marked than in the control. Toward the end of the experiments the blood pressure was 55-65 mm Hg. About 25% of the animals of this group died from anaphylactic shock. Morphological changes in the lungs were much more severe than in the control animals. Besides filling of many alveoli with serous contents diapedesis of erythrocytes was observed both into the cavity of the alveoli and into the swollen interalveolar septa, pointing to much more severe circulatory disorders than in the control.

In the animals of group 2 the hypotensive reaction was less marked than in group 1, and it differed from the reaction in the control group by delay in the compensatory rise of blood pressure (Fig. 3).

The hypothalamus is known to play an important role in the maintenance of homeostasis in the body, especially in critical situations. Anaphylactic shock naturally followed a more severe course in the animals with hypothalamic injury, and this was reflected in particular in the level of compensatory rise of the blood pressure. The difference in the severity of the anaphylactic shock in the animals of group 1 and 2 suggests that the magnitude of the effect of hypothalamic injury depends on the time elapsing after injury to the hypothalamus and before injection of the reacting dose of antigen and it is evidence of the compensatory powers of this part of the CNS. The absence of any significant difference in the course of anaphylactic shock in animals with injuries to different parts of the hypothalamus indicates that normal functioning not only of the individual structures of the medial hypothalamus, but of the hypothalamus as a whole, including the numerous fiber tracts to higher and lower levels of the nervous system, is important for the compensation of the hemocirculatory disorders.

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