EFFECT OF DESTRUCTION OF CERTAIN HYPOTHALAMIC STRUCTURES ON THE COURSE OF ANAPHYLACTIC SHOCK

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The existence of regulatory influences of the central nervous system on the development of immunological processes has now been demonstrated conclusively. This applies both to the regulation of antibody formation, one of the principal immunological processes [6, 7], and to the course of other reactions of immunological nature, especially of allergic reactions including anaphylactic shock [1-5, 8].

Increasing interest has been shown in recent years in the study of the role of subcortical structures in in the regulation of protective reactions of this type, because these parts of the brain are most closely concerned with the regulation of autonomic functions.

Investigations have shown [9, 10] that massive bilateral destruction of the hypothalamus, involving the anterior, the middle and, in particular, the posterior hypothalamus, leads to the suppression of anaphylactic shock and to the depression of antibody formation. The conclusion has been drawn from this important and interesting information that the hypothalamus as a whole participates in the regulation of immunological reactions. The results described above are also confirmed by clinical observations made after massive injury to the hypothalamus (as a result of its destruction by a tumor, for example). After such extensive destruction of this region of the mesencphalon, many of the nuclear groups and connections with other parts of the brain are damaged and the connections with the pituitary are almost completely destroyed.

The discovery of the zones which are especially concerned in the regulation of immunological reactions is of fundamental importance. As earlier work has shown [6, 7], one such structure is the posterior hypothalamic nucleus.

In the present investigation the effect of local unilateral destruction of various regions of the hypothalamus on the course of anaphylactic shock was studied.

EXPERIMENTAL METHOD

Experiments were undertaken on 26 rabbits as follows. Different zones of the right side of the hypothalamus of the animals were destroyed electrolytically (the technique was fully described earlier [6, 7]). Three days afer the operation the animals were sensitized by giving them four subcutaneous injections, each of 1 ml of normal horse serum. At the end of the 14 day incubation period, the animals received the reaction dose of the antigen (5 ml) by intravenous injection. The blood pressure and respiration were recorded during the experiment.

The localization of the area of destruction of the brain was determined histologically or macroscopically. Controls were rabbits sensitized by the same method but without destruction of the hypothalamus. Other controls were intact animals each receiving 5 ml of horse serum intravenously, the reaction to the injection being recorded.

EXPERIMENTAL RESULTS

The intravenous injection of 5 ml horse serum into the unsensitized animals caused very slight changes in respiration and blood pressure (on the average by 7% of the initial level; Figs. 1 and 2).

In the sensitized rabbits the intravenous injection of the antigen led to a sharp fall of blood pressure (Fig. 1) and also to marked changes in respiration (an increase, followed by a decrease in its rate). The

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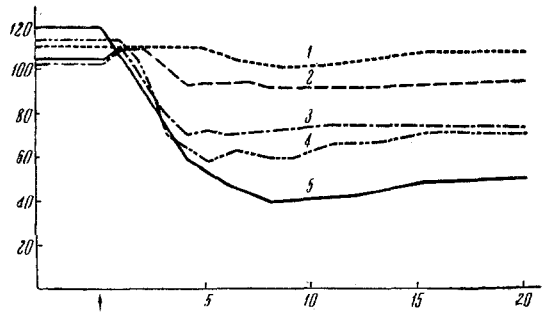

Fig. 1. Changes in the blood pressure of control animals and rabbits undergoing operation after intravenous injection of 5 ml horse serum. Along the axis of abscissas – time (in min), along the axis of ordinates – blood pressure (in mm Hg). 1) intact rabbits; 2-4) sensitized rabbits with destruction of different zones of the hypothalamus; 5) sensitized rabbits not undergoing the operation.

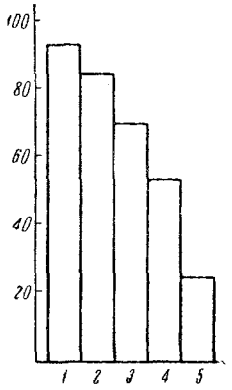

Fig. 2. Maximal fall of blood pressure arising after injection of 5 ml horse serum into rabbits of different experimental groups. Along the axis of ordinates – blood presure (in % of initial level; mean values). 1) intact rabbits; 2-5) sensitized rabbits; 2) with destroyed posterior hypothalamic nucleus, 3) destruction at the border with the posterior hypothalamic nucleus, 4) destruction outside the posterior hypothalamic nucleus, 5) rabbits not undergoing operation.

fall in the blood pressure of these animals amounted on the average to 76% of its initial value (Fig. 2). Some of the rabbits of this group died in the acute period of anaphylactic shock.

The course of the anaphylactic shock varied in the animals in which destruction of part of the hypothalamus was followed by sensitization, depending on the localization of the lesion of the subcortical zones. With respect of the strength of the developing anaphylactic reaction, the animals of this series could be divided into three groups.

Group 1 included rabbits in which practically no anaphylactic shock developed. The changes in respiration and in the blood pressure after injection of the reacting dose of antigen into these animals were slight, and resembled the reactions arising in unsensitized animals after the primary injection of horse serum (Figs. 1 and 2).

Group 2 included animals with slight changes in respiration after injection of the reacting dose of antigen and a fall in blood pressure on the average by 31% of the initial level. In other words, these were animals with weak anaphylactic shock.

Group 3 consisted of rabbits which developed changes in respiration and whose blood pressure fell by an average of 53% below the initial level. In this series of experiments the rabbits did not die in the period of anaphylactic shock, but the shock observed in the animals was little different from that found in the control sensitized animals.

Comparison between these results and those of the morphological investigation showed that in the animals of group 1, manifesting practically no sign of anaphylactic shock, the zone of destruction was localized to the posterior hypothalamic nucleus.

Where the focus of destruction lay on the border with this nucleus, the anaphylactic reaction was weak (rabbits of group 2). Destruction of other zones of the medial hypothalamus (paraventricular, supraorbital, and other nuclei included in the tuber cinereum) left the course of the anaphylactic shock essentially unchanged or had only a slight influence on it, perhaps reducing its intensity very slightly. The focus of destruction of the brain tissue was very small and localized, and it caused no particular changes in the behavior or state of the experimental animals.

It may be concluded from these results that the posterior hypothalamic nucleus is a zone with a special relationship to the regulation of immunological processes. Evidently most of the cells associated with the regulation of these processes are concentrated in it.

The fact that antibody production is depressed after destruction of the posterior hypothalamic nucleus indicates that the depression of anaphylactic shock in these animals must be associated with the absence of antibody formation.

The depression of anaphylactic shock observed in the experiments cited above [9, 10] was evidently connected with the massive nature of the focus of brain destruction, and with the loss of so many structures (the greater part of the tuber cinereum) and connections, resulting in disturbance of many autonomic processes, in most cases incompatible with life (more than 55% of the animals died in these experiments). The zone specially related to the regulation of immunological processes may be assumed to be the region of the posterior hypothalamic nucleus. In the present investigation it has been shown, in particular, that even partial destruction of the posterior hypothalamic nucleus leads to the depression of anaphylactic shock.

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