

# THE EFFECT OF DESTRUCTION OF THE POSTERIOR HYPOTHALAMUS ON THE BASAL METABOLIC RATE OF RABBITS

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A study of the changes in patients due to damage to the diencephalon from tumors or inflammatory processes has led to the conclusion that the hypothalamus must inevitably be involved in metabolic regulation. Experiments on animals in which the thalamus had been partially destroyed, or stimulated, have demonstrated the correctness of this conclusion. There is a very extensive literature on this subject; we will point out merely that according to many authorities [1, 2, and others], the principal role in the regulation of metabolism is played by the anterior and midline region of the thalamus. Information concerning the involvement of the posterior hypothalamus is scarce. In experiments on rabbits we have shown that stimulation of certain structures of the posterior hypothalamus leads to a marked or even complete suppression of the production of complement-binding antibodies [3,4]. Destruction of other structures localized for example in the anterior hypothalamus, thalamic nuclei, and caudate nucleus caused no such reaction.

Immunogenesis, which is also impaired to the same extent by hypothalamic stimulation of the posterior hypothalamic field at the level P-3, P-4 (atlas of Soier and others), depends upon the metabolic rate.

The object of the present investigation has been to determine how destruction of certain regions of the posterior hypothalamus affects metabolism.

## EXPERIMENTAL METHOD

The experiments were carried out on 15 rabbits before and after operation. The metabolic rate was determined by the absorption of oxygen (method of Regnault and Rayzet, as modified by P. N. Veselkin). Before the start of the experiment, the animals were made familiar with the conditions; next 2-3 measurements were made lasting 10 min each. At the same time, thermocouples were used to measure the rectal temperature.

The absorption of oxygen was measured after 1-2 days or 1-2 months after destruction of the brain tissue. As a rule, the experiments took place at intervals of 2-3 days, and the change in the oxygen consumption was observed for several weeks.

Some of the experiments were carried out on rabbits in which the basal metabolic rate was measured before the operation, and observations were continued after the brain operation. In other animals the metabolism was determined only postoperatively, and was compared with the results obtained for oxygen consumption on intact animals.

Parts of the brain were destroyed under stereotaxic control. A unipolar electrode, insulated for the whole of its length except for a bare region 0.5-1 mm from the end, was inserted into the brain into a position defined by coordinates in the atlas of Soier, et al. The indifferent electrode was placed on the ear. Destruction was produced by a dc current of 1mA acting for 30 seconds, which enabled a restricted region of the tissue to be destroyed.

## EXPERIMENTAL RESULTS

A study of the oxygen requirements before operation showed that this quantity was fairly constant, although there was a certain variation in any one animal. As a rule, the amount of oxygen demanded was 9-12 ml per kg per

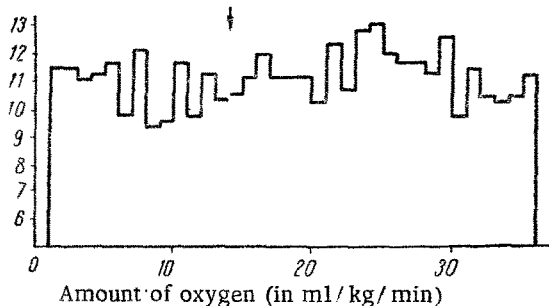


Fig. 1. Oxygen consumption by a rabbit before and after destruction of a portion of the posterior hypothalamus. Ordinate—amount of oxygen (in  $\text{mm}^3$  per kg per minute); abscissa—days after operation. The arrow indicates the time of operation.

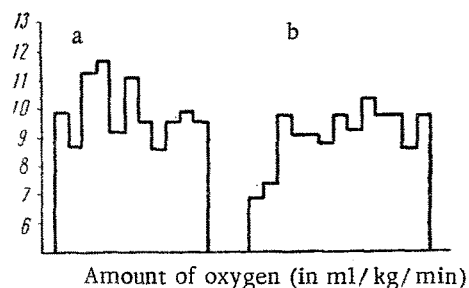


Fig. 2. Oxygen demand by (a) normal and (b) operated rabbits of the same weight ( $\approx 3$  kg). Indications as in Fig. 1.

Figure 3 shows the position of the necrotic areas. Parts of the damage lie chiefly in the region of the posterior hypothalamus. Histological control (M. V. Kovalenkova) allowed us to conclude that in most animals the region of destroyed tissue was extremely restricted.

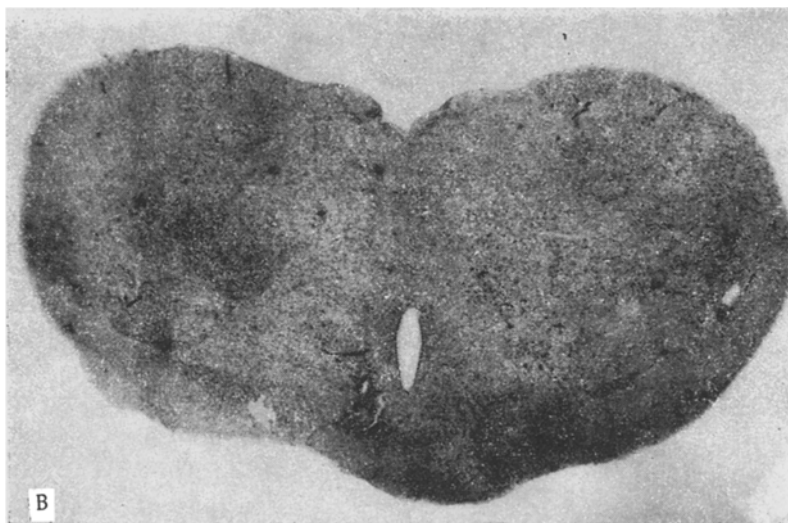
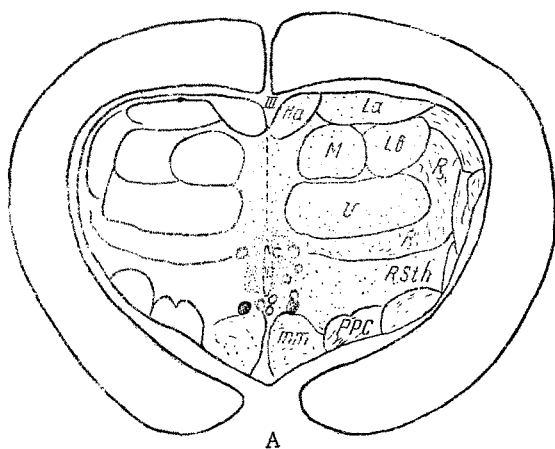


Fig. 3. Diagram showing the position of the damaged zones (A). Microgram of rabbit brain with area of destruction in the posterior hypothalamus (B).

minute. We must note that the continuous temperature recording made before the experiment in some cases enabled an increase or decrease in the rate of absorption of oxygen to be related to body temperature.

Soon after the operation (1-5 days) in some animals we were able to observe a brief change in the oxygen consumption.

In the days which followed, oxygen consumption returned to the original level (Fig. 1).

Apparently the brief changes in the metabolic rate after the operation result from operative trauma, and not from destruction of a particular part of the brain. This conclusion is supported by the fact that the change in the oxygen consumption takes place in rabbits independently of which part has been destroyed.

In our experiments there was a marked relationship between oxygen demand and weight: the greater the weight, the less the oxygen consumed per kg. This result is well known, but in our experiments it was particularly important. To observe the rabbits long after the operation (1-2 months), we used heavy rabbits (3-3.5 kg) and observed the visible reduction of the metabolic rate. In order to ascertain definitely the reason for the loss of weight and to determine to what extent it was due to hypothalamic damage, we carried out special experiments on intact animals of the same weight. As can be seen from Fig. 2, we were unable to find any appreciable differences in the metabolic rates as between the intact animals of the same weight and rabbits examined at considerable times after the electrolytic lesion in the hypothalamus.

Because in our previous experiments we had shown that in the region of the posterior hypothalamus there is a restricted zone whose destruction involves a marked suppression of the process of immunogenesis [3, 4], we were particularly interested to determine the role of this particular part of the thalamus in the regulation of metabolism. Following up this idea, to analyze the facts obtained we grouped the animals in which the destroyed zone was in the region of the posterior hypothalamus in a single group; rabbits in which the destruction was localized elsewhere formed a second group. We then treated the results statistically.

A statistical analysis of the results of the experiments showed that the difference between the mean values of oxygen requirement by the intact and operated animals was  $1.3 \pm 0.6$ , i. e., it was statistically significant. However, taking into account the greater weight of the operated animals, we calculated the linear coefficient of correlation between weight and oxygen consumption ( $r$ ), and it was found to be  $0.719 \pm 0.116$ . The high and statistically significant value of the correlation confirmed that in rabbits with the smaller weight the oxygen demand per kg was higher than that in the heavier group.

There is, however, no reason to suppose that the differences we have disclosed in the oxygen requirements of intact and operated rabbits were due to operative interference. They are evidently due to the difference in weight.

The results we have reported allow us to conclude that portions of the posterior hypothalamus which were damaged at operation are not zones responsible for regulation of oxygen consumption. Although it is improbable that this regulation of metabolism as a whole is brought about by a strictly localized structure, which we may refer to as a "center" in the classical sense of the word, nevertheless it is quite probable that destruction of portions of brain tissue participating in the regulation of this process would bring about considerable changes in it.

The negative results obtained are of special interest because they allow us to raise the question of the specific influence exerted by the posterior hypothalamus on the process of immunogenesis. At the present time, we may very tentatively state that the marked or even complete suppression of the production of antibodies observed after destruction of an area in the posterior hypothalamic field is not the result of a clearly marked reduction of metabolic rate.

However, we must take into account that the basal metabolic process is integrative, and is made up of phenomena which play an unusual part in the production of the final quantity. In particular, a relatively small proportion of the oxygen consumed is expended in protein metabolism. At the same time, it is precisely the reduction of protein metabolism which might be important in connection with the impairment of the immunological reaction. Therefore, we can form a final opinion of the mechanism of the influence of the hypothalamus on immunogenesis only by studying protein metabolism in animals after destruction of the portions of the hypothalamus concerned.

#### SUMMARY

The role of the posterior hypothalamus in the control of the BMR was studied in experiments on rabbits. The BMR was measured by the amount of oxygen taken up per kg of body weight per minute (Regnault-Rayzet methods, modified by Veselkin). Oxygen uptake was determined in intact rabbits and in animals after an electrolytic destruction of cerebral tissue. The position of the damage was verified histologically. The results were treated statistically. It was found that destruction of an area in the posterior hypothalamus did not lead to any changes in the BMR.

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