SALIVARY REACTIONS AFTER VENTROMEDIAL HYPOTHALAMIC LESIONS IN DOGS

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Abstract. Lesions of the ventromedial hypothalamic nucleus produced an increase of food intake and body weight, marked augmentation of intertrial salivation, and transient disinhibition of salivation to the differentiated conditioned stimulus. It is concluded that damage of the ventromedial hypothalamic nucleus produces an increase of alimentary drive.

INTRODUCTION

A review of the literature (1–3, 5, 8, 14, 26) suggests that bilateral lesions in the ventromedial hypothalamus produce hyperphagia and development of obesity. In a previous paper (23) we have shown that damage of the ventromedial hypothalamus (VMH) in dogs produces not only a marked obesity and hyperphagia but also a more or less pronounced disinhibition of the instrumental conditioned reflexes and a long-lasting increase of the number of intertrial movements. The question arises whether lesions of the VMH nucleus affect also alimentary reactions other than instrumental, in particular salivary reflexes. It is also interesting to find out which component of the salivary reaction, the conditioned or unconditioned one, will be most changed by such lesions. This may answer the question whether the inhibitory processes are disturbed or whether the alimentary motivation is increased. In order to solve these problems, a new series of experiments was undertaken in which the effects of VMH lesions upon the classical salivary conditioned reflexes were investigated.
MATERIAL AND METHODS

Training. Experiments were carried out on seven male mongrel dogs, weighing from 9.5 to 12.0 kg. The dogs were experimentally naive prior to the experiment. In all dogs chronic fistulae of the parotid gland were made by the method described by Soltysik and Zbrożyna (25). The experiments were performed in a conditioned-reflex chamber. The salivary reactions were measured by counting the drops of saliva and were recorded by the method described in our previous paper (24). The experiments were run on dogs unfed for ca. 20 hr.

Group I. In three dogs (SV1–SV3) excitatory conditioned reflexes were established. The conditioned stimulus was a sound set at a frequency of 1000 cycle/sec from a generator, reinforced by food (bread powder mixed with boiled minced meat — 50 g). A daily session consisted of six presentations of CS with intertrial intervals varying around a mean of 3 min. At the beginning of training the CS was immediately reinforced by food, and after few days the reward was increasingly delayed up to 20 sec. The CS overlapped for 10 sec with food presentation. The experiment was completed when the salivary responses were maintained at a constant level for at least 20 sessions, without further increase.

Group II. In the remaining four dogs (SV4–SV7) differentiation was trained. The procedure was as follows: after the excitatory conditioned reflex had been firmly established, an inhibitory CS was introduced which was not reinforced by food. The inhibitory conditioned stimulus was a sound from a generator set at a frequency of 700 cycle/sec, and it was presented for 20 sec. A daily session usually consisted of four excitatory and four inhibitory trials given in a random order with intertrial intervals of about 3 min.

When the full experimental training was completed and conditioned reflexes, both excitatory and inhibitory, were stable, the operation was performed.

Surgery. In all the dogs, the ventromedial hypothalamic nucleus was destroyed bilaterally by means of electrocoagulation in a stereotaxic apparatus under Nembutal anesthesia (35 mg/kg) in aseptic conditions. A 4 ma anodic d-c was applied during 1 min by means of an iridium platinium electrode. The coordinates were determined on the basis of a stereotaxic atlas by Lim et al. (16).

Measures of food and water intake. The dogs were allowed to eat ad lib. once a day for 10 days before and 30 days after the operation, as well as for 10 days after a 1 month interval. In dogs SV1–SV3 preference for quinine hydrochloride was tested.
The dogs were weighed every 4th day. Experiments were resumed on the 3rd postoperative day. Observations were carried on during 4–5 months postoperatively.

Histology. After completion of the experiments the dogs were sacrificed and their brains perfused with 10% formaline. The brains were then frozen and 40 µ thick slices were stained by the Klüver method.

RESULTS

Food and water intake. After the operation in all our dogs we observed symptoms similar to those described the previous paper (23), namely a two-, or even threefold increase in food intake, which lasted 5–16 days (Fig. 1). In this period the dogs ate very voraciously, without showing a preference for more tasteful food and not even refusing poorly tasting and bitter food with a small admixture of quinine (0.25 chloride of quinine for 1 kg of food). Gradually (after 3–4 weeks) they started to eat less and became more finicky, refusing to take poorly tasting or meatless food. On the other hand, they voraciously consumed large quantities of raw or cooked meat, up to 800–1000 g presented (larger quantities were not tested). The measurement of food intake indicated that even after 3 months postoperatively the dogs ate more than before the operation.

In dogs SV2 and SV4 an increased daily water intake (800–1500 ml) was also observed.

During the first 2–3 postoperative weeks an increase of body weight was observed in all the dogs. The average weight gain was 2.6 kg. As seen in Fig. 2, the dogs were gradually losing their weight as the experiments progressed; nevertheless, even 2 months after the operation their weight was slightly higher than before the operation.

![Fig. 1. Mean food intake in individual dogs during 10-day periods before operation (A), after operation (B) and 2 months later (C).](image-url)
General behavior. After the operation the dogs displayed a strong motor excitation before each feeding; they barked, ran around, and voraciously attached the offered food. After the meal they became calm and quiet. The dogs were generally very friendly. Only three of them seemed to be more fearful, and for about 10 days just after the operation they were afraid to approach strangers. Nevertheless, if such persons offered them a morsel of food, they ran up, snatched it and ran away. We never observed any signs of aggression.

![Fig. 2. Mean body weight in all dogs during the 16 days before operation, 36 days after operation, and a 16 day period 2 months later.](image)

Salivary reflexes. Group I. In dogs SV1-SV3, in which only excitatory classical conditioned reflexes were established, the secretion of saliva to both conditioned and unconditioned stimuli was maintained around the preoperative level following electrocoagulation of VMH (Fig. 3). There were no statistically significant changes found as to the quantities of saliva secreted both to CS and US. In dogs SV2 and SV3, copious salivation in the intertrial intervals was observed, which lasted in dog SV2 for 15 sessions, and in dog SV3 for 17 sessions (Fig. 3). In dog SV1 only a slight increase of salivation in the intertrial intervals was noticed, the enhanced secretion having lasted only for nine sessions. After a few weeks (2 or 3 weeks) the amount of saliva secreted in the intertrial intervals markedly diminished and approached, but did not return, to the preoperative value.

Group II. In dogs SV4–SV7, in which both excitatory and inhibitory salivary conditioned reflexes were established, a very slight increase of salivation to conditioned and unconditioned stimuli was observed after electrocoagulation of VMH (Fig. 4). On the other hand, intertrial salivation markedly increased, and in addition salivation to the inhibitory stimulus appeared (Fig. 4). Salivation to the inhibitory conditioned stimulus lasted for 17 days in SV4, for 25 in SV5, for 19 in SV6 and for 8
The effects of ventromedial hypothalamic lesions in dogs SV1–SV3 on salivation during 20 sec of CS (perpendicular stripes), 20 sec of US (white) and salivation during 2 min of intertrial intervals (black). Each block represents mean value of salivation during 10 sessions before the operation (A), 10 sessions after the operation (B), and 10 sessions 2 months later (C). Arrow indicates the operation.

in SV7. At the end of the observation period (after about 4 months) we did not notice any changes as compared with the preoperative condition in the salivary reactions to both excitatory and inhibitory conditioned stimuli, and intertrial salivation had also nearly reached the preoperative level. This effect of abnormal increase of intertrial salivation was demonstrated very clearly in all dogs (SV1–SV7), as seen in Fig. 4. Usually the augmentation of salivation achieved its maximum about 10 days after operation and then decreased gradually.

To verify the differences between preoperative and postoperative salivation, analysis of variances (mixed design type IV, Lindquist (17)
and t-test were used. The data were collected in three blocks mean of each of 10 sessions: before operation, just after operation and 2 months after operation. It was found that these three blocks of sessions did not differ statistically in the mean absolute number of drops of saliva secreted during the excitatory conditioned stimulus and during the un-
Fig. 5. Photographs of representative frontal sections of the brains of dogs SV1–SV7 with ventromedial hypothalamic lesions.
conditioned stimulus. However, the three periods differed as to the mean absolute numbers of drops of saliva secreted during intertrial intervals \((p < 0.01)\) as well as to the amount of salivation during the inhibitory conditioned stimulus \((p < 0.01)\). The t-test showed that the differences between the preoperative and early postoperative blocks both in the amount of salivation during intertrial intervals and during the inhibitory conditioned stimulus were much more pronounced \((p < 0.001)\) than that between the preoperative and the late postoperative blocks \((p < 0.01)\).

Comparison of the mean absolute quantities of food intake in these three periods has revealed statistically significant differences between the periods \((p < 0.02)\). The preoperative and early postoperative periods showed the greatest difference \((p < 0.001)\); whereas the preoperative and the late postoperative periods did not differ statistically at all.

**Anatomical verification.** In all dogs the lesions were bilateral and included almost the whole ventromedial hypothalamic nucleus. In addition in dogs: SV1, SV2 and SV3 small ventral parts of nucleus dorsomedialis were damaged. In dogs SV5 and SV7 the ventrolateral nucleus and the medial part of the fornix were partially damage (Fig. 5).

**DISCUSSION**

The present results have clearly shown that bilateral ventromedial hypothalamic lesions produce transient augmentation of salivation mainly during intertrial intervals and inhibitory trials, i.e. disinhibition.

As shown by Rożkowska and Fonberg (23) and Rożkowska (22) ventromedial hypothalamic lesions also produce transient disinhibition of instrumental differentiation and marked increase of intertrial movements. These results may be due both to the increase of alimentary motivation and the impairment of inhibitory mechanisms caused by releasing the "hunger center" from an inhibitory influence from the VMH "satiety center".

Our present results show that the marked increase of intertrial secretion as well as disinhibition of inhibitory trials were rather short-lasting, occurring only immediately after the surgery, i.e. when the animal exhibited pronounced voraciousness and hyperphagia. Disinhibition of salivation during the inhibitory trials was probably due to the increase of alimentary motivation. An impairment of discriminatory functions is much less probable because the observed disinhibition was transient and shortlasting and closely connected with the increase of food intake. In addition the reaction of the dogs from the first postoperative session showed that they reacted differently to the positive and differential CSi and that these reactions were the same as before the opera-
tion. It appears that after a VMH lesion the hunger drive transiently increases. The rather rapid compensation probably occurs as the result of the interception of functions by the cerebral cortex or lateral amygdala (9, 11).

Several authors (8, 18, 19, 27, 28) emphasized that animals with ventromedial hypothalamic lesions exhibited preference for more flavorful food and became more sensitive to both positive and negative gustatory qualities of their diet. Taste becomes a very strong motivational stimulus. According to Konorski's theory (15), the gustatory protopathic sensations play the main role in the regulation of food intake after lesion of the ventromedial nucleus.

In our cases, however, taste disturbances do not seem to be responsible for the increase of salivation because the preference for tastier food (especially meat) appeared in the later period after the operation (2 or 3 weeks) at a time when salivation had already returned to the normal level. It is necessary to stress that increased salivation in the intertrial intervals may be considered as a prolongation of the unconditioned reaction (the act of eating) because the dogs many times licked out and smelled the bowl after they finished eating. These observations may indicate that the animals with such lesions display increased hunger, but it also may be attributed to a prolonged act of consumption.

The changes in salivary reflexes after VMH exhibit some similarity to those observed after prefrontal ablation (6, 7). Brutkowski has found that after ablation of gyrus proreus, anterior part of orbital gyrus and also some part of gyrus compositus anterior the salivary secretion to unconditioned stimuli and in intertrial intervals is augmented.

The experiments of Balińska et al. (4) are especially interesting due to the remarkable similarity of behavior disturbances following lesions of the frontal cortex and the hypothalamus in rabbits. After lesions of the medial hypothalamus and medial frontal cortex hyperphagia occurred in conjunction with overreactivity and disinhibition of the inhibitory CR. The similarity between the effects of lesions of the ventromedial hypothalamus and frontal cortex may be easily explained by the anatomical results (20) which showed an association between the medial frontal cortex and the hypothalamus.

Żernicki and Santibañez-H. (30) have found that after ablation of the anterior composite gyrus the conditioned reflexes are more affected than the unconditioned ones, and acid reflexes are more affected than the alimentary reflexes. According to these authors lesions of the anterior composite gyrus mostly impair fear and appetite, affecting much less the hunger drive (see 30). The experiments on the effect of lateral hypothalamic lesions on the salivary reactions reinforced by food (24) and acid (21) showed opposite relations to the lesions of gyrus composite
anterior, i.e. the acid-salivary reflexes were less affected than the food-salivary reflexes.

The effects of all these types of lesions may reflect different functions of these various parts of brain and different mechanisms acting upon the alimentary salivary reflexes. Damage of the frontal cortex may mostly impair the inhibitory mechanisms which is reflected in the most pronounced disturbances in inhibitory reflexes; damage of the hypothalamus may in turn produce an increase of alimentary drive and may therefore lead to the increase of the intertrial reactions; whereas lesions of the anterior composite gyrus may affect alimentary reactions by changing the taste values of the food.

It is interesting to note that effects similar to those produced in the present experiments were found by Fonberg (11–13) after lesions of the lateral amygdala. The latter produced hyperphagia, increase of body weight, increase of salivary reactions to the unconditioned stimuli as well as intertrial salivation. This proves once more the similarity between functions of the ventromedial part of the hypothalamus and lateral amygdala (9–11, 13).

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REFERENCES


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