Reports

Relationship between Feeding and Satiation Centers of the Hypothalamus

Abstract. Electrodes were implanted in the hypothalamus of five goats in which an alimentary instrumental conditioned reflex had been previously established. Electrical stimulation of the ventromedial hypothalamus inhibited the conditioned movements and food intake in hungry goats. This also occurred in those satiated goats in which eating and conditioned movements were elicited by stimulation of the lateral hypothalamic area. Withdrawal of the stimulation of the medial hypothalamus evoked a short aftereffect in the form of a recovery or increase in the trained movements and food intake.

It is known that two hypothalamic centers are involved in the regulation of food intake. These are: the lateral hypothalamic area, the electrical stimulation of which produces hyperphagia (*1*) and whose destruction leads to aphagia (*2*), and the medial part of the hypothalamus, mainly the ventromedial nucleus, whose stimulation decreases food intake (*3*) while destruction results in hyperphagia and obesity (*4*). Anand and Brobeck (*2*) postulated that the lateral hypothalamic area, a "feeding center," contains a basic mechanism for food intake, while the ventromedial nucleus, a "satiation center," contains an inhibitory one. The present study was undertaken to get a better understanding of the relations between feeding and satiation centers during elicitation of alimentary instrumental conditioned reflexes in unanesthetized animals in which electrical stimulation of the hypothalamus was applied.

Five adult goats were used. First an instrumental conditioned reflex of putting the left foreleg on the food tray was established in all goats. The reflex was elaborated to the experimental situation without the use of a sporadic stimulus; every conditioned movement was reinforced by food. After several weeks of the daily training, three unipolar electrodes were put into the medial part of the hypothalamus in all goats, under local anesthesia (Polocain, 2 percent), according to the Hess method (*5*) adapted for goats by Andersson (*6*). In two goats three further electrodes were placed in the lateral hypothalamic area, ipsilaterally in one goat and contralaterally in the other (Fig. 1). The indifferent electrode was attached to the skin of the head. Immediately after insertion of the electrodes, the animal was brought to the experimental pen where, as was usual, it began to perform the conditioned movements and eat the food given as reinforcement. Then the electrical stimulation (0.5 to 1 volt, 50 pulses/sec) was applied.

We found that stimulation of a number of points in the medial part of the hypothalamus caused cessation of the act of eating in hungry animals. In many cases the reaction was a defensive one and the animal not only jumped back from the food tray but also manifested fear and restlessness which lasted for several minutes after the withdrawal of the stimulation.

On the other hand, there were other points of the medial hypothalamus, which we call "inhibitory" points, whose stimulation evoked cessation of eating and sudden ejection of the food from the mouth, without any defensive reaction. The trained movements were also absent during stimulation, and the animal stood quietly before the food tray. In some cases only a decrease in the intensity of eating and in the frequency of conditioned movements was observed. When the stimulation lasted more than 1 minute, the goats usually went away from the food tray and sometimes lay down. However, when the stimulation was switched off, the animals almost immediately returned to the food tray, performed the trained movements, and again began to eat food. In two goats (Nos. 16 and 17) an increase in the frequency of the trained movements, after the withdrawal of the stimulation, was observed (Fig. 2*a*).

When stimulation of an "inhibitory" point was applied to completely satiated goats that did not want either to perform conditioned movements or to eat (Nos. 13, 14, and 15), no visible effect was observed during stimulation. However, just after the current was switched off, the animals, in spite of being fully satiated, came to the food tray, performed several trained movements, and consumed the portions of food which were presented (Fig. 2*b*). This effect, especially striking in two goats (Nos. 13 and 15), lasted usually some seconds, and then the animals left the food tray.

In two satiated goats (Nos. 14 and 15) stimulation of the lateral hypothalamic area was applied. This elicited the trained movements and eating (*7*). When, on the background of this "alimentary" stimulation, an "inhibitory" point was stimulated, eating became less intense or ceased altogether. The trained movements were less frequent or else disappeared. After the "inhibitory" stimulation was switched off, a transitory increase in the frequency of the conditioned movements was often observed (Fig. 2*c*).

The results obtained seem to support the hypothesis of Anand and Brobeck (*2*) on the hypothalamic mechanism of the regulation of food intake. There is no doubt that in our experiments electrical stimulation of some medial parts of the hypothalamus, called here "inhibitory" parts, exerted an inhibitory

Fig. 1. Frontal section of the hypothalamus of goat No. 14. *Al*, site (coagulated) of electrical stimulation which evoked conditioned reaction and food intake in satiated goat; *In*, point at which inhibition of conditioned reaction and food intake was evoked by electrical stimulation; *F*, col. fornicis descendens; *TMT*, mammillothalamic tract.

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Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].

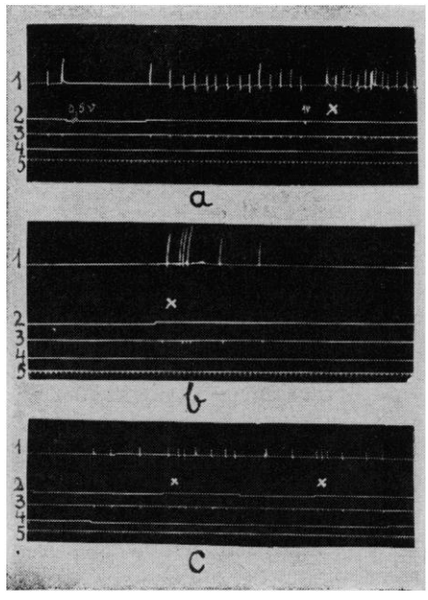

Fig. 2. Kimograms of experiments with goat No. 16 (*a*), No. 15 (*b*), and No. 14 (*c*). 1, conditioned reaction; 2, electrical stimulation of medial part of the hypothalamus ("inhibitory" stimulation); 3, food giving; 4, electrical stimulation of the lateral hypothalamus ("alimentary" stimulation); 5, time (5 seconds); *x*, moment of increase or reappearance of reaction after switching off the "inhibitory" stimulation.

effect on the act of eating as well as on the alimentary instrumental conditioned reflexes. Moreover, a noteworthy "off effect" was observed, which may be considered as a kind of rebound phenomenon. It should be stressed that this latter was present only at "inhibitory" points; it was not observed at those points where the stimulation evoked defensive reactions.

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Stimulation of Postirradiation Recovery of Cells by Cutting

Abstract. X-rays and ultraviolet radiations delay regeneration and division of *Blepharisma undulans*. Irradiated blepharisma which have not been cut divide once or twice fairly soon after the controls, then they cease dividing for a period of time (stasis) which may last for many hours or even days. Once they recover from stasis they divide at a rate comparable to controls. Cut, irradiated blepharisma, on the other hand, having to replace lost parts, start to divide later than the uncut irradiated individuals, but little if any stasis occurs. As a consequence, although irradiated with the same dosage, cut individuals recover a normal rate of division sooner than uncut ones.

In the course of studies on the effects of x-rays and ultraviolet radiations on the regeneration of *Blepharisma undulans* it was noted that individuals which had been cut just before or after irradiation appeared to divide faster than uncut irradiated individuals, inasmuch as after a lapse of time more were present in cultures from cut, irradiated individuals than in cultures from uncut, irradiated ones (*1*).

To determine whether, by itself, amputation of part of a protozoan stimulates division of the cell, the division rate of blepharisma from which the hypostome had been removed was determined. The results show that the operation does not stimulate division, rather it delays division by 8 to 12 hours; that is, by about the time it takes for an individual to reconstitute the lost oral structures necessary for feeding (5.5 hours) plus the time required to rebuild the mass of protoplasm removed (3 to 7 hours). Regeneration occurs at the expense of nutrients stored in the cell and is completed even in the absence of external food sources. When these internal stores are reduced by several days of starvation preceding cutting, regeneration takes several hours longer than in unstarved individuals, indicating that it is now more difficult to mobilize the materials required for regeneration. Once division starts after cutting, it goes on at the same rate as in uncut controls (Fig. 1).

A study of the postregeneration division of blepharisma showed that the divisions which immediately follow irradiation are delayed in both cut and uncut irradiated individuals. However, the uncut blepharisma exposed to substantial doses of either x-rays or ultraviolet radiations divide once or twice, then stop dividing for a period (stasis) which may last for many hours or even days (Fig. 1). Blepharisma cut after irradiation usually show little or no stasis. Therefore, even if the first few divisions of cut irradiated individuals are delayed as compared to uncut irradiated ones, they soon catch up with and then surpass them (Fig. 1).

This is most clearly shown in Table 1, which summarizes the differences in generation time for the first and third divisions in cut and uncut individuals. For controls (unirradiated) this is about the same for both divisions. For the irradiated blepharisma one might expect the same value as for the controls if both cut and uncut individuals were equally affected by the radiations and cutting did not affect their sensitivity. Actually the difference in generation time for the first division is greater for cut and uncut irradiated animals than for the two controls, suggesting initial compounding of the damage resulting from radiation and cutting. Much more striking is the subsequent reversal of the relative positions of cut and uncut individuals, for with few exceptions, by the third division after irradiation, the progeny of cut, irradiated blepharisma are well ahead of the uncut, irradiated ones, as indicated by the negative values.

The upshot of these experiments (*2*) is that in some way cutting seems to enable the animals to bypass the reactions which cause stasis. Kimball *et al.* (*3*) postulate that division delay in ciliates, and possibly in all cells, consists of at least two phases: (i) retardation of the first and sometimes the second postirradiation division, from which the cell soon recovers, and (ii) a long but not permanent cessation of division (stasis). The first phase of division delay they consider to result from an effect of the radiations on the mitotic apparatus; the second phase, from failure to synthesize cell materials. When the synthetic apparatus of the cell is finally repaired, the cell once again begins to grow and divide. Once division starts, the irradiation injury has been overcome. The site of protein and protoplasmic synthesis is thought to be in the ribonucleic acid–rich microsomal component of the cytoplasm (*4*). If the microsomes are inactivated (for example, by ribonuclease), synthesis ceases until more microsomes (ribosomes) are reformed. The division delay registered as stasis after irradiation may correspond to the period of replenishment of ribonucleic acid microsomes.

Cutting blepharisma is known to induce macronuclear reorganization which has been described by Suzuki (*5*) and has been verified here for both varieties of *Blepharisma undulans* (*americanus* and *japonicus*). In the present study irradiation was observed to retard the reorganization of the macronucleus required for regeneration