Self-stimulators were then tested for the effects of hunger drive on the rate of self-stimulation. In almost all cases, animals stimulated themselves faster after 24 hours of food deprivation. However, deprivation caused a much greater increase in the eaters than the non-eaters (see Fig. 1).

Thus, although there are self-stimulation points which are not also feeding points, when we do get an electrode into the feeding area of the lateral hypothalamus, it appears to be always in a strong self-stimulation area. Furthermore, hunger seems to augment the self-stimulation response derived from this area (*6*).

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22 November 1961

Hypothalamic Control of Feeding and Self-Stimulation

Abstract. Hypothalamic sites which control feeding exert a corresponding control over lateral hypothalamic self-stimulation. This was demonstrated in rats bearing four, intrahypothalamic electrode-cannulas for electrical stimulation or chemical injection. Self-stimulation of the lateral hypothalamus was inhibited by ventromedial excitation or by excessive feeding. Both self-stimulation and feeding were accelerated (disinhibited) by ventromedial ablation or anesthetization. Thus food acts via the ventromedial hypothalamus to inhibit not only feeding, but also lateral hypothalamic self-stimulation.

Feeding is under the control of a dual neural mechanism in which the lateral hypothalamus excites feeding and the ventromedial hypothalamus inhibits it (*1*). In the lateral hypothalamus, electrical (*2, 3*) or chemical stimulation (*4, 5*) induces feeding, and anesthetization (*4*) or destruction of this region (*1*) depresses it. In the ventromedial hypothalamus the situation is reversed; stimulation (*3, 6*) suppresses feeding, and anesthetization (*4*) or destruction (*7*) augments it.

Stimulation in certain areas of the brain is reinforcing; in other areas it induces aversion. For instance, a rat will press a lever repeatedly to stimulate its lateral hypothalamus, but will work to avoid stimulation of its ventromedial hypothalamus (*8*). Thus, the tissue in the lateral hypothalamus which excites feeding lies within a system where stimulation is reinforcing, whereas the inhibitory "satiety center" lies within an aversive region. This anatomical overlap suggests that there might be a functional correlation between feeding and self-stimulation. If so, the hypothalamic systems which regulate feeding should exert a similar control over self-stimulation; moreover, food should decrease the rate of self-stimulation as it satiates hunger.

To explore these possibilities, we devised an electrode-cannula assembly which made it possible to excite or depress the medial and lateral hypothalamus, both bilaterally and simultaneously, in waking rats. Monopolar, hollow electrodes, insulated except at the tip, were constructed from 24-gauge platinum tubing (*9*). Four tubes were implanted simultaneously in the hypothalamus of each rat. Implantation was perpendicular to the surface of the cortex in a frontal plane 6 mm anterior to the ear bars of the stereotaxic instrument. The lateral hypothalamic electrode-cannulas were 2 mm lateral to the midsagittal sinus and 7.5 mm below the surface of the cortex (symbolized: A-6, L-2, D-7.5). Ventromedial electrode-cannulas were implanted at A-6, L-0.75, D-8.5. An indifferent electrode was secured under the scalp.

The electrical stimulus was a 0.5-second train of 100-cy/sec, monophasic, negative, 0.1-msec pulses from a Tektronix 161 square-wave generator. The intensities used were between 0.1 ma and 0.6 ma per electrode. Chemical injections were made from a remote microsyringe via a length of PE-10 tubing fitted onto a 31-gauge stainless-steel tube which was inserted inside the full length of the platinum electrode. The chemical injections used were 5 to 10 μl of a 2- to 5-percent solution of sodium chloride for local excitation, and 5 to 10 μl of 1-percent procaine hydrochloride for local anesthetization.

In this report "self-stimulation" always means lever pressing to trigger electrical stimulation of the lateral hypothalamus. Figure 1 summarizes the effects upon feeding and self-stimulation which were obtained by exciting or depressing the hypothalamus. Each arrow represents the results of experiments on five or more female, Sherman albino rats. In brief, when feeding was elicited or increased, so was self-stimulation. When feeding was inhibited, self-stimulation was also inhibited.

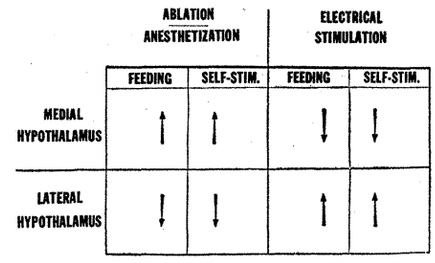

Fig. 1. The relationship between hypothalamic control of feeding and self-stimulation. An upward arrow means start or increase of feeding or self-stimulation, as indicated; a downward arrow means stop or decrease of these activities. Each hypothalamic manipulation that had an effect on feeding had a similar effect on lateral hypothalamic self-stimulation.

The lower-right quadrant in Fig. 1 indicates that unilateral or bilateral electrical stimulation of the lateral hypothalamus caused the rats to eat. This effect was observed from the time stimulation was begun on the day after implantation. Eating was stimulus-bound: satiated rats began to eat within 10 seconds of stimulus onset and continued eating for only a few seconds after the stimulus was turned off. The same rats did not begin self-stimulation until approximately a week after the electrodes were implanted. Once they began, the rate of self-stimulation by rats fed ad libitum was typically 3000 lever presses per hour.

The upper-right quadrant in Fig. 1 indicates that the rats stopped eating when they were stimulated in the ventromedial hypothalamus. They were induced to eat either by 2 days of starvation or by stimulation of the lateral hypothalamus; under both conditions they voraciously ate a liquid diet (*10*) or Purina laboratory chow until medial stimulation was applied. During weak medial stimulation, on either side of the brain, eating slowed or stopped completely. The same was true for self-stimulation; the rats stopped lever pressing when each press stimu-

lated the medial as well as the lateral area. Higher currents induced aversion and simply disrupted feeding or self-stimulation.

The lower-left quadrant in Fig. 1 indicates that unilateral anesthetization or destruction of the tissue under the self-stimulation electrode stopped self-stimulation. Bilateral destruction produced aphagia.

Most interesting is the fact that anesthetization or ablation of the ventromedial hypothalamus accelerated not only feeding, but also self-stimulation (upper-left quadrant in Fig. 1). Data illustrating this result are shown in records *A* and *B* of Fig. 2. The rate of lateral hypothalamic self-stimulation was increased after destruction of the ventromedial hypothalamus on both sides of the brain (first arrow in *A*). This effect is emphasized in record *B* in which lateral self-stimulation was suppressed by injecting hypertonic saline into the ventromedial regions; then the effect was completely reversed by ventromedial anesthetization; indeed, self-stimulation was accelerated to a new high.

In such experiments the effect of bilateral anesthetization lasted 5 to 30 minutes. In three rats, unilateral depression of the ventromedial region, even contralateral to the self-stimulating electrode, produced a transient, 3- to 5-minute acceleration of self-stimulation. Therefore, destruction or anesthetization of a site at which a rat will avoid stimulation (*8*) can enhance self-stimulation at a distant, reward site. This suggests that the normal neural activity of an aversive system can inhibit a reward system. Like feeding, self-stimulation is under inhibitory control.

Does this correlation between hypothalamic control of hunger and self-stimulation extend to the natural effects of food? Does food decrease the rate of self-stimulation as it satiates hunger? Record *C* (Fig. 2) shows that self-stimulation was slowed to about half the normal rate by a stomach load of 18 ml of liquid diet. The same amount of water had only a transient effect, suggesting that some consequence of food intake other than taste or stomach distension was responsible for prolonged inhibition. This agrees with the finding of Margules (*11*) and Olds (*12*) that hungry rats press faster for hypothalamic self-stimulation than satiated ones. In our experiment inhibition of self-stimulation typically lasted ½ to 2 hours. Sometimes lever pressing decreased relatively uniformly; other times, as in records *B* and *C*, there were repeated interruptions of self-stimulation by other activities such as grooming or rubbing the chin along the floor. In some cases, self-stimulation stopped completely. The inhibition of self-stimulation produced by food in the stomach could be eliminated within 2 minutes by destroying or anesthetizing the ventromedial hypothalamus. This suggests that the inhibitory effect of food on self-stimulation is exerted by way of the ventromedial hypothalamus.

We conclude from these results (*13*) that within the medial and lateral hypothalamus, the feeding systems control self-stimulation in a manner analogous to their control of feeding. Stimulation of the ventromedial area or satiety induced by excessive feeding inhibits lateral hypothalamic self-stimulation; ventromedial destruction disinhibits it. When an animal is hungry, lateral hypothalamic self-stimulation is more reinforcing; when satiated, it is less so. It may be that the pleasure of lateral hypothalamic self-stimulation is similar to the gratification obtained by eating.

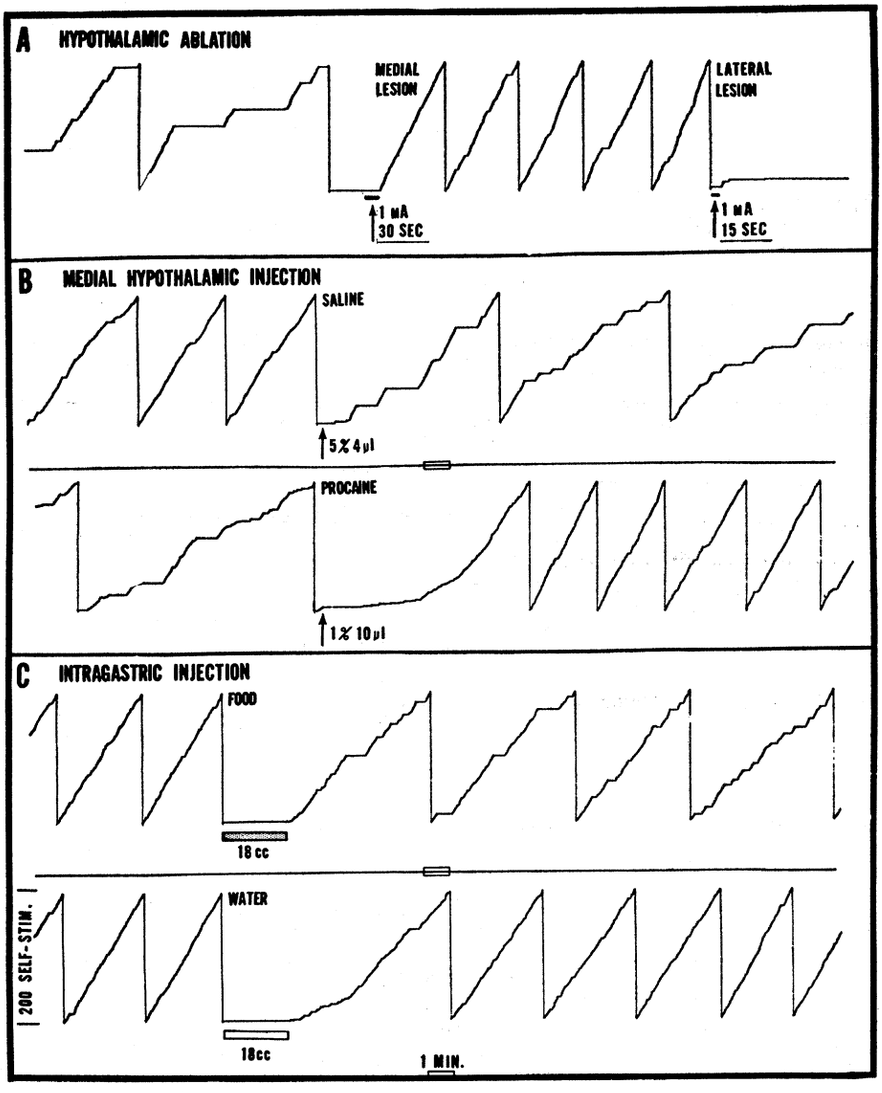

Fig. 2. Representative cumulative-recorder records showing the changes in lateral hypothalamic self-stimulation rate produced by experimental influence of the hypothalamus or by feeding. *A*, Acceleration of self-stimulation caused by destruction of both ventromedial regions. *B*, Inhibition of self-stimulation by chemical excitation of both ventromedial regions, and subsequent disinhibition of self-stimulation by anesthetization of these regions. *C*, Prolonged inhibition of self-stimulation by tube feeding a liquid diet (top) but only transient inhibition by tube feeding an equal volume of water (bottom).

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13. A 10-minute movie is available. It shows the major effects that have been reported here. Special thanks are extended to Drs. Alan N. Epstein and Eliot Stellar for their valuable suggestions. This research was supported by the National Science Foundation (grant No. G-9792).

13 October 1961

Self-Regulated Exposure to Light by Dark- or Light-Treated Rats

Abstract. Rats allowed to expose themselves to light do so for a rather constant length of time each day. This duration of exposure depends upon both the brightness of the light used for testing and the illumination in which the rats were maintained before testing.

The albino rat had long been characterized as aversive to light (*1*) when Marx (*2*) showed in 1955 that onset of light was positively reinforcing. This unexpected effect has been repeatedly confirmed, and the current interpretation is that onset of light is reinforcing because of the change in stimulation (*3*). An alternative hypothesis is that there exists a preference function across luminance which reaches a maximum in the "dim" region and then decreases as luminance is increased. In this report I attempted a direct test of the preference hypothesis by allowing rats to choose between darkness and one of a number of illuminations of the cages in which they were maintained.

A second variable investigated was the effect of luminance of maintenance quarters prior to testing. With few exceptions, experimenters have tested the reinforcing or aversive effects of light without regard to pretest conditions of luminance. Since past results show that a given luminance can be reinforcing in one study and aversive in another, it seemed possible that this inconsistency could be due to differences in lighting between different animal maintenance quarters.

Male albino rats were kept in either darkness or bright light (100 mlam) in identical cages for 12 days, then put, one to a chamber, into test chambers with two levers. When the animal pressed one lever, the chamber's diffused overhead light came on and stayed on until the other lever was pressed. Each animal could thus control how long its light was on. Different chambers had lights of 0.01, 0.1, 1.0, 10, or 100 mlam (*4*). Each animal was left in a given chamber for 12 consecutive days without disturbance. Food and water were always available by feed-through tubes. Athough 40 rats were pretreated and tested, seven were discarded for nonresponding and three more to allow a balanced statistical analysis.

The number of minutes that each chamber's light was left on each day was recorded. Figure 1 shows the mean daily duration that each light was kept on by the dark- or light-treated animals tested with it. Each of the ten functions shown is the mean performance of three animals across 12 days.

When tested in chambers that had a very dim light, rats kept in darkness for 12 days before testing showed no significant difference from light-treated animals in the daily durations of self-exposure to light. When given control of a 1-mlam light, however, dark-treated rats soon shifted to durations significantly shorter than those of the light-treated group ($p < .001$) (*5*). In 10 and 100 mlam, both groups eventually chose very short daily durations of light, but the dark-treated animals did so sooner in both cases ($p < .05$). Furthermore, the differently pretreated groups showed a small but consistent difference between the asymptotes of their light-duration functions for the last 6 days in 10 mlam ($p < .01$) and the last 3 days in 100 mlam ($p < .05$).

The long daily durations of light chosen by rats in 0.01 and 0.1 mlam show that dim light is somewhat preferred over darkness. Short durations in higher luminances show the reverse, that is, darkness preferred over light. Thus the reinforcing properties of the onset of dim light are at least partly due to the preference value of the absolute luminance produced by the response, and not entirely to the change in stimulation. Similarly, the reinforcing properties of the offset of bright light (*1*) reflect the preference for darkness shown by rats of the present study tested in 10 and 100 mlam. The finding of Barnes (*6*), that a change of dim lights from "on" to "off" is not reinforcing, further strengthens the preference hypothesis. Furthermore, this hypothesis unites the results of the earlier light-aversion studies with the later light-reinforcement studies, suggesting a single and quantifiable theory of luminance-controlled behavior.

The finding that dark-treated rats strongly prefer darkness to 1.0 mlam while light-treated ones keep the 1-mlam light on for substantial periods introduces a complication in the determination of a preference function across

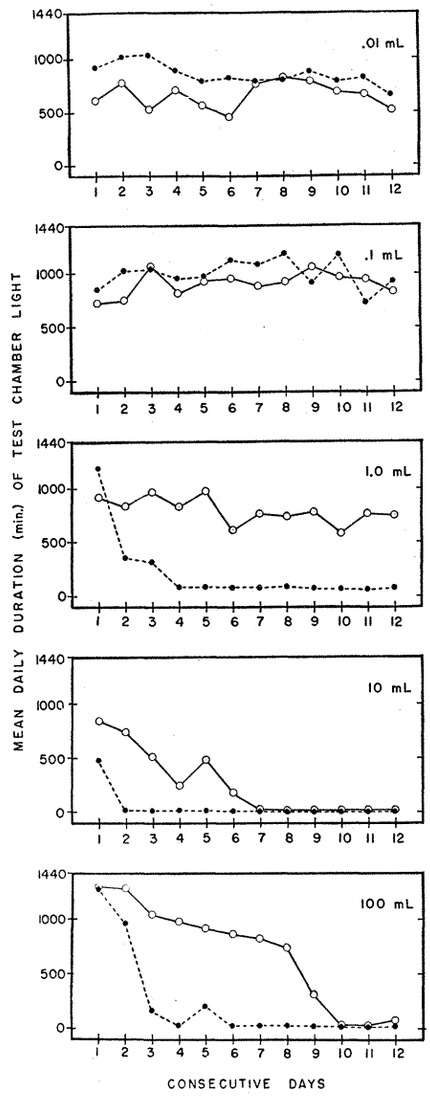

Fig. 1. Mean daily duration of albino rat's self-exposure to various luminances (indicated at upper right of each plot) as a function of time. Dark circles indicate rats kept in darkness for 12 days prior to testing; open circles, rats similarly kept in 100 mlam. (1440 min = 24 hr).