Self-stimulation and body weight in rats with lateral hypothalamic lesions

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The lateral hypothalamus (LH) and/or the fiber system of the medial forebrain bundle (MFB) which courses through this area has been viewed (19) as playing a major integrative role in the organization of the central reward system. Efforts to demonstrate a dependence of other reward structures on the integrity of this LH-MFB region have, however, been only partially successful. It appears, for example, that septal self-stimulation persists even after rather extensive damage to the LH-MFB regions (11, 28). Likewise, LH self-stimulation survives the placement of lesions at either a telencephalic or midbrain level of the MFB projections (13, 15, 27). On the other hand, there are reports of markedly attenuated rates of self-stimulation following either lesions (2, 20) or procaine anesthetization (16, 18) of the LII and/or MFB regions.

Whatever its role in the central reward system, the LH-MFB area is known to play an important role in controlling ingestive behaviors. Animals sustaining LH damage often display extended periods of aphagia and anorexia before they again accept food in quantities sufficient to maintain body weight (26). Even then, LH-lesioned animals persist in regulating their body weight at a chronically reduced level (23) and often display a permanent adipsia (6).

In the present experiment, the contributions of the LH-MFB area to central reward and to the regulation of body weight are further examined. Both the immediate and long-term effects of LH-MFB lesions upon intracranial self-stimulation (ICS) are observed. Simultaneously, daily measures of body weight and of food and water intake are also obtained. Our initial objective was to follow the changes in self-stimulation in the first several weeks after lesioning and to determine the extent to which these changes covared with the levels of food intake and body weight. Second, an effort was made in the succeeding weeks to determine whether lesion-produced changes in ICS reward are chronic in nature and, if so, how they are related to the chronic depression in body weight seen in LH-lesioned animals (23).

METHOD

Subjects and Surgical Procedures

Thirty-six male Sprague-Dawley rats, weighing 350-495 g at the time of surgery, were prepared under pentobarbital anesthesia (40 mg/kg) with three chronically indwelling electrodes. Monopolar electrodes (size 0 stainless steel insect pins, insulated with epoxylyte except for 0.5 mm at the tip) were placed bilaterally in the lateral hypothalamus at the level of the median eminence. With the skull surface horizontal between bregma and lambda, the stereotaxic coordinates for the two monopolar electrode placements were the following: 2.65 mm posterior to bregma, 1.9 mm lateral to midline, and 8.4 mm below the skull surface. The bipolar electrode, constructed of 0.25 mm diam stainless-steel wire, twisted and insulated except for the cross sectional area of the tip, was directed toward the ventral tegmental region. This electrode was placed on the midline, 5.2 mm posterior to bregma and 8.7 mm beneath the skull surface. Male Amphenol pins, crimped to the ends of the bipolar electrode, provided a means of connection to the stimulation leads. Acrylic dental cement molded around stainless steel screws tapped into the skull served to anchor the three electrodes after placement.

Apparatus

Testing for intracranial reinforcement was conducted in four 28.0 x 26.7 x 29.2 cm Skinner boxes, each equipped with a single Gerbrands rat lever. Each box was housed in a 58.5 x 42.0 x 37.0 cm sound-attenuating chamber equipped with a 15-w house light, a speaker for delivering white noise, and a ventilation fan. A two-channel commutator device attached to the ceiling of each chamber permitted the...
animal to move freely about the box without tangling the stimulation leads.

The intracranial stimulus, a train of constant-current biphasic pulses, was supplied by a Nuclear-Chicago stimulator (model 7150). Pulse duration and frequency were fixed at 0.2 msec and 50 pulse pairs/sec, respectively. Current levels, which were individually adjusted, varied from 0.1 to 1.0 ma, with a median value for all Ss of .34 ma. The stimulator was programmed to provide a 0.5 sec train of pulses following each occurrence of a lever press. Any lever responses occurring during this 0.5-sec stimulation period had no influence on the duration of the ongoing stimulus train nor were such responses recorded. The timing and control of all other experimental contingencies were programmed automatically by relay equipment.

A constant-current d-c source (C. H. Stoelting Company) was used to produce electrolytic lesions in the lateral hypothalamus.

**Self-Stimulation Procedures and Lesion Conditions**

Prelesion self-stimulation training. Within 1 week following the surgical procedure for implanting both the lesioning and stimulating electrodes, reinforcement training was initiated. In the first session, attempts were made to shape lever pressing for intracranial stimulation. Animals that could be trained were then permitted to run for 500 continuously reinforced responses, during which time the experimenter adjusted the current to levels that sustained responding at a rate of approximately 25/min.

For the next 6 days, prelesion training was provided on the test procedure that was to be employed throughout the remainder of the experiment. In the first session, a series of five 3-min self-stimulation periods, each separated by a 30-sec time out, was employed. During this session, each lever press was reinforced by a 0.5-sec train of pulses to the tegmental reward site. At the end of each 3-min period, the light in the test chamber was extinguished and the response bar was inactivated. During the time-out interval, the experimenter recorded the number of responses made in the preceding session. The beginning of the next session was signaled both by turning on the house light and by giving a single 0.5-sec train of ICS. For the next 5 pretraining days and for the remainder of the experiment, three 5-min self-stimulation sessions were employed during each day of testing.

During the first 3 days of this prelesion test procedure, the experimenter continued to make adjustments in the current level with the object of maintaining a response rate of approximately 25/min. Of the original 36 rats, nine either could not be trained to lever press or responded at low rates at all current values tested. One other animal dislodged its electrode assembly during this pretraining period. These 10 animals were dropped from the experiment at this point. For the remaining 26 animals, the individual current values thus selected in these first three pretraining sessions were then employed both in the three remaining prelesion test days and the entire postlesion period.

A response total was obtained for each of the three 5-min sessions throughout the self-stimulation test procedure, except for occasional instances in which difficulties with the stimulation leads developed within a session. In such a case, that day's self-stimulation data were based on only the number of 5-min test sessions unconfounded by such problems.

Lesioning procedure. Immediately following the last prelesion self-stimulation session, 17 animals were anesthetized with pentobarbital (40 mg/kg) and lesioned bilaterally through the implanted lateral hypothalamic electrodes with an anodal current of 1.0 ma for 11 sec applied between each monopolar electrode and an indifferent tail electrode. The remaining nine animals, comprising the control group, were anesthetized but not lesioned.

Postlesion self-stimulation test procedures. Intracranial self-stimulation testing was begun on the day following placement of the lateral hypothalamic lesions, using exactly the same procedure as that employed during the last three prelesion test days. During the 1st week postlesion, animals were tested daily, for the next week, every other day; and for the remaining 6 weeks, once a week.

Of the 26 animals completing the prelesion procedure (17 experimental and 9 controls), complete data were obtained for 18 (10 experimental and 8 controls). Four of the original group of 26 died within 1 week from lesion-produced complications. Four others dislodged their ICS electrodes at some time during the 8-week period of postlesion testing.

**General Maintenance Conditions and Diets**

Animals were individually housed in double rat cages (Wahmann Manufacturing) equipped with calibrated drinking tubes. Diets were presented in open Stender dishes placed on the cage floor.

Three diets were used for maintaining animals in the postlesion period. The first was a chocolate-chip cookie mash (24), the second was a wet mash of Purina laboratory meal (68% water by weight), and the third was dry Purina meal. With no other available source, the amount of water in the wet diets was determined to be sufficient for an intact animal to maintain or increase its body weight (22). The animals were exposed to all three diets for a period of 5 days prelesion. Water was available ad libitum with each of the three diets.

**Diet Acceptance Tests**

Food acceptance tests were 1-hr periods of free access to a diet in the home cage. All tests were preceded by 4 hr of food deprivation. Water was available during both the food deprivation and acceptance test periods.

Immediately after the lesioning procedure, all rats were deprived of food overnight and then offered the least palatable diet (dry meal). Those failing to eat an amount sufficient to maintain their body weight during the 1-hr test were then given wet mash for a 1-hr test. Finally, those not passing the acceptance criterion for the wet mash were offered the cookie mash for 1 hr. Animals failing to maintain their weight for the 1-hr period on any of these diets were given the cookie diet on an ad libitum basis; all other animals were provided ad libitum with the least palatable diet they had accepted in the tests.
responding followed an upward trend for the first 2 weeks postlesion. This can be seen in the group curve (Fig. 1A), within the first 5 days postlesion, however, and the rate of responding appeared in all surviving animals for its death. This testing procedure was continued either until the acceptance test for dry meal had been passed or until the experiment was terminated. For the first 2 weeks postlesion, diet tests were administered daily. For the 3rd and 4th weeks postlesion, they were administered once every 3rd day and then, for the remaining 4 weeks, once a week.

Histological Procedures

Following the 8-week period of postlesion testing, all animals were sacrificed under pentobarbital anesthesia by intracardial perfusion of a 10% Formalin solution. The brain was then removed, fixed for 1 week or more in the Formalin solution, frozen, and sectioned frontally at 40 μ. Every second section through the hypothalamus and all sections containing evidence of the tegmental electrode tract were saved and later stained with a cresyl violet-luxol fast blue technique. Sections were examined microscopically, and lesion extent was estimated with reference both to control sections and the König and Klippel (14) rat stereotaxic atlas.

RESULTS

Effects of LH Lesions Upon Posterior Hypothalamic and Ventral Tegmental Self-Stimulation

The effects upon intracranial self-stimulation of lesioning the LH-MFB area are represented in Fig. 1A. Over the last 2 days of prelesion testing, both the experimental and control animals self-stimulated at a mean rate of 36/min. The response rate of the sham-lesioned group remained at approximately the same level for the first several postlesion sessions and then increased gradually over the remainder of the 8-week test period to a value of 50/min (see Fig. 1A). Responding by the lesioned animals, in contrast, fell in the first postlesion session to a group mean of only 2/min. Eight of the 10 lesioned animals responded at rates less than 1/min in this session and three of this number failed to respond at all. Some responding appeared in all surviving animals within the first 5 days postlesion, however, and the rate of responding followed an upward trend for the first 2 weeks postlesion. This can be seen in the group curve (Fig. 1A), which increases steadily from the low level seen after lesioning until reaching a value approximately half that of the control rate by the end of the second postlesion week. Relative to the control animals, the self-stimulation rate of the lesioned group subsequently displays little or no change after the 2nd week postlesion and remains at roughly a constant percentage of the control rate for the remainder of the 8-week testing period.

A postlesion self-stimulation score was obtained for each LH-lesioned animal by first determining the mean rate of responding across four weekly test periods. The four postlesion test periods chosen for this purpose (test days 14, 21, 28, and 35) were chosen so as to bracket the period (week 4 postlesion) used to calculate the new weight regulation level in these animals. After adjusting for the increase in response rate of the control animals during this same postlesion period, each lesioned animal's self-stimulation rate was expressed as a percentage of its prelesion value. As a group, the self-stimulation rate of the lesioned animals was reduced to 55% of the prelesion value, with individual scores varying from 11 to 102%. Compared to the eight control animals, the mean self-stimulation score for the experimental animals was significantly reduced by the LH lesions ($t = 2.46; df = 16; .025 > P > .01$).

Effects of LH Lesions Upon Food Intake

Diet testing was begun on the day immediately following placement of the LH lesions. All rats were first food deprived for 4 hr and then tested for 1-hr periods on one or more of the three diets. Of the eight sham-operated controls, all but one accepted the dry meal diet and gained weight during the first postlesion session. The single exception accepted the wet mash diet and then passed the acceptance test for the dry meal on the following day. In contrast, none of the lesioned animals initially accepted either the dry meal or wet mash diets, and only two took any of the cookie diet. The remaining 11 lesioned animals were initially both aphagic and adipsic.

Three of the lesioned animals died within 8 days of the operation. Two of these lost weight steadily for 6–8 days and appeared to be totally aphagic to the point of death, at which time their body weights were 230 and 243 g. Compared to the mean weight of the nonlesioned controls during this same period (390 g), their terminal weight was approximately 60% of normal. This value corresponds closely to that at which nonlesioned animals normally die under a starvation schedule (3), and it seems reasonable to assume that starvation was the principle cause of death in these two subjects. The third animal, however, died at a weight level approximately 80% that of the control group, suggesting that factors other than a lack of food intake were responsible for its death.

Feeding in the remaining 10 lesioned animals displayed the postoperative pattern previously described by Teitelbaum and Epstein (26). Following a period of total aphagia, animals would accept the cookie diet, although they ordinarily failed at first to ingest sufficient amounts to maintain body weight. Within several days, however, intake levels were adequate to maintain body weight and acceptance of the wet mash diet ordinarily followed within the next...
week or two. The mean length of total aphagia was 2.5 days, with a range of 0.3-5.5 days. The mean number of days from lesioning to the end of the anorexic period was 3.7 days, with a range of 1.5-6.5 days. By the end of 1 month postlesion, all but one of the surviving animals had passed the acceptance test for wet mash and two were maintaining their weight on dry food and water.

Effects of LH Lesions on Body Weight

The mean weight of the lesioned and sham-lesioned subjects over the first 8 weeks postlesion is represented in Fig. 1-B. Immediately following placement of the LH lesions, the weight of the experimental animals dropped sharply for several days before leveling off at a value substantially below that of controls. It can also be seen that the weight differences between the lesioned and control animals which developed during this initial postlesion period are maintained during the remainder of the 8-week observation period.

This transition to a reduced level of weight regulation can be represented by expressing the mean weight of the lesioned animals as a percentage of the control level over the 1st month postlesion (see Fig. 2). After dropping rapidly over the first several days, the weight level then declines more slowly before reaching a minimum of 82.6% on day 16 postlesion. It then stabilizes at approximately 83%. Note that the weight level of the lesioned animals (i.e., their weight as a percent of control) declines for over 2 weeks postlesion (Fig. 2); yet their actual body weight falls for only 4-5 days (see Fig. 1B). What this indicates is that the lesioned animals, though no longer losing weight, fail to display the daily weight gain characteristic of the intact animals during this period. It is not until the 3rd week postlesion that their rate of weight gain is sufficient to maintain their body weight at a constant percentage of the control level.

For purposes of the present analysis, each lesioned animal’s new regulation level or “set point” was calculated by taking its average adjusted weight across the fourth postlesion week and expressing this value as a percentage of the average weight of the nonlesioned control animals. As a group, the lesioned animals regulated their weight at 83% of the control value, with individual set-point values ranging from 65 to 97%. Statistical analysis confirmed that the postlesion level of weight regulation of the experimental group was significantly lower than that of the control group (t = 4.28, df = 16, P < .01).

Histological Analyses

Lateral hypothalamic lesions. A computer-assisted procedure was previously developed for determining those areas of the lateral hypothalamus whose destruction contributes to the reduction in the regulated level of body weight (22). This analysis, run initially on a sample of 110 LH-lesioned animals, revealed a critical area for weight regulation of approximately 4.7 mm³ in the medial plane of the lateral hypothalamus, extending from the level of the anterior hypothalamus to the level of the premammillary nuclei and dorsally into the subthalamic region. Amount of damage to this functionally defined area was linearly and inversely related to the body weight set point (r = -.85).

This procedure was employed in evaluating damage to the LH weight regulation region in the present animals.1 First, serial sections of each brain were examined and the lesion-produced damage was represented on reproductions of Figs. 28, 30, 32, 34, 37, and 39 from the König and Klippel (14) rat atlas. A transparent grid of 0.5-mm squares was then placed over each of the reconstructed lesions, and a square was judged to have been lesioned if damage appeared in more than half of the 0.5-mm area. The König and Klippel frontal sections were chosen so as to be each separated by approximately 0.5 mm, consequently, damage to any cube represented destruction to a cubic area of about 0.125 mm³. In the initial determination of the LH area critical to the lesion-produced weight reduction, a bilateral system comprised of 78 cubes was derived. For the purposes of the present analysis, LH damage in each lesioned animal was described in terms of the percentage of these 78 critical cubes that were destroyed.

The photomicrographs in Fig. 3 are of brain sections taken at a midhypothalamic level from two lesioned animals. The bilateral damage represented in the top section was the most extensive found among the 10 experimental animals, and it was calculated that 78% of the critical LH area was destroyed. The postlesion weight regulation level or set point for this animal was 65%, and its stable postlesion rate of self-stimulation was 33% of the prelesion rate. Fifty-one percent of the critical LH area was destroyed in the brain from which the section shown in the bottom of Fig. 3 was taken. Following lesioning, this animal regulated its body weight at 83% of normal and self-stimulated at 55% of its prelesion rate. With the parameters employed, lesions causing less than 50% damage to the critical LH area tended to be asymmetrical, with one or, in a single case, both electrodes deviating somewhat from the intended locus.

An average of 49.2% of the critical LH area was destroyed in the 10 lesioned animals. The weight regulation level of this group was 83.3%. This set-point value (83.3%) corresponds well with the value of 83.8% predicted by the linear equation (y = -.43x + 105) determined in the original analysis of this relationship (22). Individually, the bilateral

1The animals in the present experiment were also included in the analysis from which the LH area critical to the level of regulated body weight was originally derived (22).
Fig. 3. See facing page for legend.
damage to the critical LH area ranged in the 10 lesioned animals from 9 to 78%.

Locus of self-stimulation electrodes. The self-stimulation electrodes in the 18 control and experimental animals were distributed within a region approximately 2 mm in length extending from the posterior hypothalamic area to the ventral midbrain. Specific electrode sites included the ventral tegmental area of Tsai and the ventral tegmental decussation, the mammillary peduncle and supramammillary decussation, including two placements appearing to terminate in the mammillary bodies and the posterior hypothalamic nucleus. The distribution of placements within the control and lesioned groups was roughly equivalent. Within the lesioned group, an attempt was made to relate the degree of lesion-produced suppression of self-stimulation to the electrode locus, but no consistent pattern could be detected. Apparently, the loss to the reward system resulting from LH damage is fairly widespread, with the areas affected extending to the deep ventral regions of the midbrain as well as to the more proximal posterior hypothalamic area.

Relationships Between Feeding, Body Weight, and Self-Stimulation

It is evident from a comparison of Fig. 1A and B that both the direction and temporal course of the lesion-produced changes in intracranial self-stimulation are closely related to the postlesion changes in body weight. During the immediate postlesion period of rapid weight loss (i.e., during the period of total aphagia), responding for ICS was severely depressed or totally absent. From this low level, however, responding gradually increased until reaching a stable level between the 2nd and 3rd week postlesion (see Fig. 1A). During this period, the surviving animals passed through the stages of aphagia and anorexia during which their level of maintained body weight (expressed as a percent of the control value) declined until reaching a stable level of 83% by the 3rd week postlesion (see Fig. 2).

As previously reported (22), a high negative correlation exists between percent damage to a critical LH area and the postlesion level of regulated body weight. Running this analysis on the 10 lesioned animals in the present experiment yielded an r value of -.86 (P < .01). Additionally, an attempt was made to determine the extent to which damage to this very same LH area predicted the extent of lesion-produced depression in self-stimulation. For the 10 lesioned animals, percent damage to the LH area critical to weight regulation was found to be significantly and inversely related to the stable rate of postlesion self-stimulation (r = -.79, P < .01).

Taken together, the above observations suggest a high degree of anatomical correspondence or overlap between the weight regulation and self-stimulation systems. This relationship can more clearly be demonstrated, however, by examining the degree to which the lesion-produced reduction in self-stimulation rate covaries with the reduction in the level of maintained body weight. The scatterplot (Fig. 4) of postlesion body weight and self-stimulation scores for the 10 lesioned animals determined in the manner previously described, provides a graphical representation of this close relationship. Analysis of these data yielded a correlation coefficient (r) of +.79 (P < .01).

DISCUSSION

Several investigators (11, 28) have reported that self-stimulation in septal or olfactory sites survives bilateral transection of the MFB. Others (13, 15, 27) have found that lateral hypothalamic self-stimulation persists after lesions of the basal forebrain or tegmental projections of the MFB. Still others (2) have reported self-stimulation decreases following placement of lesions at different levels of the MFB, but stress that there is usually partial to complete recovery over time. Taken together, these observations fail to indicate a crucial role for the MFB in a central system of reward and are certainly consistent with Valenstein and Campbell’s (28) characterization of the reward system as one with a highly redundant pattern of organization.

At the same time, evidence is accumulating that, even if not abolished, central self-stimulation can be markedly attenuated by LH-MFB lesions. A strong, though temporary, suppression of septal, preoptic, and ventral tegmental self-stimulation is seen following injection of procaine into the MFB-LH area (16, 18). Longer-lasting effects have been reported following electrolytic lesions. Olds and Olds (20) observed that self-stimulation of the anterior hypothalamus was only 22% of control levels as long as 8 weeks following placement of MFB lesions at a posterior hypothalamic level. They also found posterior hypothalamic self-stimulation to be chronically reduced by lesions at an anterior hypothalamic level of the MFB, although the reduction (to 80% of control levels) was quantitatively smaller. The results of the present experiment both confirm and extend these observations. Lesions of the LH-MFB area reduced posterior hypothalamic and ventral tegmental self-stimulation to a degree that was directly proportional to the extent of the LH damage. Furthermore, the stability of the responding from the third postlesion week to the experiment’s end at 8 weeks.
supports the impression that this attenuation is chronic in nature. Thus, although self-stimulation may well survive even quite extensive LH-MFB damage, both the present data and those of Olds and Olds (20) indicate that its level is attenuated.

The lesions employed in this work produced all the essential features of the LH feeding syndrome described by Teitelbaum and Epstein (26). Lesioned animals were aphagic and anorexic for up to 1 week before they again accepted food in sufficient quantity to maintain their body weight. Even then, many remained adipsic and accepted only hydrated diets throughout the postlesion observation period. Support is also provided by the present data for the recent claim (23) that the level of regulated body weight is chronically lowered in LH-lesioned male rats. Throughout the 8-week observation period, the lesioned animals maintained their body weight at a level significantly below the control range. Furthermore, despite small but regular weight gains, the mean weight of these animals remained at essentially a constant percentage of the control weight from early in the 3rd week postlesion. For the 10 lesioned animals, the correlation between damage to the lateral hypothalamic region critical to weight regulation and the postlesion body weight set point was highly significant \( r = -0.86 \).

A covariance of feeding and/or body weight with lateral hypothalamic self-stimulation has been a frequent finding in previous investigations (8). There are reasons for expecting a similar relationship(s) to exist at posterior hypothalamic and ventral tegmental reward sites. First, the LH area critical to the lesion-produced reduction in body weight (22) is related anatomically by way of the MFB to these more caudal reward areas. Likewise, both electrically elicited feeding (31) and self-stimulation (21, 29, 30) has been observed in the ventral tegmental area. Further support is provided by the observation that lesions made through electrodes situated in ventral tegmental self-stimulation sites produce both a period of aphagia and a lowering of body weight (25).

The above observations suggest that the ventral tegmental region may represent a caudal extension of the LH feeding-reward system. Two sets of observations from the present work offer support for this view. First, in the immediate postlesion period, the duration and temporal course of the changes in feeding and self-stimulation show a good correspondence. Both self-stimulation and feeding are either absent or very severely depressed for several days following placement of the LH lesions; but, as the animal passes successively through the postlesion periods of aphagia and anorexia, the self-stimulation rate progressively increases.

Second, evidence of a close relationship between the level of weight maintenance and the rate of responding for intracranial self-stimulation is seen throughout the postlesion observation period. Over the first 2 weeks, during which time the weight maintenance level of the lesioned animals is declining (see Fig. 2), the rate of self-stimulation steadily increases (see Fig. 1A). By the time the body weight level has reached its minimum (day 16), the self-stimulation rate also appears to have reached a stable level. At these stable levels, the percentage reduction in the rate of self-stimulation correlates highly with the magnitude of the lesion-produced reduction in regulated body weight \( r = +.79 \).

In interpreting these results, attention should be given to the role of body weight in determining the levels of both food intake and self-stimulation. It is well known that animals whose body weight has been elevated by force feeding will either cease to feed or reduce their intake until their weight is returned to its normal level (4). Even a rat already obese as a result of ventromedial hypothalamic damage will, if force fed above its maintained level of body weight, display this reduced intake and concomitant weight loss (9). In a similar manner, elevation of body weight by force feeding will cause the rate of LH self-stimulation to be reduced (10).

Powley and Keesey (23) have interpreted LH aphagia and anorexia in the same vein. They propose that the primary consequence of LH lesions is to lower the maintained level or set point for body weight. Thus, rather than reflecting a loss of neural control over feeding, LH aphagia and anorexia are viewed as indicative of an active neural inhibition which persists until the lowered body weight set point is finally achieved. That is, eating is inhibited in an LH-lesioned animal by the same means that feeding is suppressed in a normal animal force fed to supranormal weight levels. Accordingly, the absence or lower level of both feeding and self-stimulation seen in the present work immediately after lesioning the LH can be interpreted as the active inhibition of a feeding-reward system in an “overweight” animal. But, as body weight is lowered to the new regulation set point, this inhibition should diminish and both feeding and self-stimulation should reappear, as the present data indicate they do. Indeed, as can be seen by comparing Fig. 1A and Fig. 2, the self-stimulation rate appears to reach its stable postlesion level at the same time (approximately 2 weeks postlesion) that body weight reaches its new maintenance level or set point.

The one observation seemingly at odds with the preceding analysis is that the ratio of self-stimulation, though increasing from the low levels seen immediately postlesion, remains below normal levels even after the animal has successfully reduced its body weight to the new maintenance level and has returned to a stable pattern of feeding. Several possibilities are suggested by this result. One is that the attenuated levels of self-stimulation may be indicative of a more general motivational deficit in LH-lesioned animals. It is useful to note in this regard that others have contended that the LH animal does exhibit a chronically reduced level of food motivation (5, 26). This possibility is important to the analysis of the LH feeding syndrome proposed by Powley and Keesey (23), since it raises the question of whether the lower levels of weight maintenance in LH animals might be the result of a reduced level of food motivation. The results of several experiments specifically designed to examine this possibility do not, however, favor such an interpretation. Not only do LH-lesioned animals appear motivated to maintain their body weight at a reduced level, but they are quite successful in doing so. If presented with a highly palatable diet (23) or an unpalatable diet (12), the LH-lesioned animal displays the expected weight increase and decrease. However, their weight remains at a reduced level and any changes are proportional to those shown by intact animals. As a consequence, their maintained weight level remains at essentially a constant percentage of the control value.
throughout such a series of diet manipulations. Likewise, when presented with diets differing in caloric density, the LH-lesioned animal makes whatever adjustments in intake are required to maintain its body weight at this same fixed percentage of the normal level (23). It is conceivable, of course, that test procedures other than those employed in these studies may reveal deficits in the LH animal’s ability to defend its new set point. But on the basis of the evidence now available, it appears that both LH and intact male rats respond to challenges to their weight maintenance levels in similar ways, with the only major difference being that the former is attempting to maintain a lower-than-normal weight level.

A second possibility is that the factor(s) responsible for the chronic reduction in the self-stimulation rate fails to exert similar long-lasting effects upon free feeding. It might be noted in this regard that, although a close correspondence between feeding and self-stimulation has been demonstrated under a variety of conditions (8) and although the present data are generally consistent with these earlier observations, there are circumstances when this relationship breaks down. It was noted in a previous report (1), for example, that both self-stimulation and food intake are elevated in the period immediately following ventromedial hypothalamic nucleus lesions; but, by the next day and for the remainder of the 6-day postlesion period during which testing was conducted, the degree of hyperphagia and the rate of LH self-stimulation were found to be negatively correlated. Thus, the present finding of a persistently lower level of self-stimulation in an LH-lesioned animal displaying an apparently normal ability to defend its new weight level may represent just another instance in which the long-term effects of central nervous damage on the reward and feeding systems are divergent.

The possibility should also be considered that factors other than a loss in the reward properties of the intracranial stimulation contribute to these chronically reduced rates of self-stimulation. It is worth noting, for example, that damage to lateral hypothalamic regions can cause motor (1) and/or sensorimotor (17) deficits. Though it is unlikely that the sensorimotor demands of pressing a lever for electrical stimulation are any greater than those associated with feeding, it should be recalled that the self-stimulation measures we employed were rate dependent and would likely be sensitive to such deficits. In contrast, we placed no similar time constraints on the feeding behavior, and even an animal with certain motoric deficits should well have been able to ingest the amounts of food necessary to regulate body weight at its set point level. Unfortunately, it is not possible to estimate from the present data the degree to which the chronically lower levels of self-stimulation are related to such sensorimotor dysfunctions and the extent to which they may reflect genuine motivational deficits. Thus, any further evaluation of the relative merits of these various possibilities will require a more detailed analysis of the long-term behavioral consequences of LH lesions.

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