HYPOTHALAMIC CONTROL OF FOOD INTAKE
IN RATS AND CATS*

BAL K. ANAND† AND JOHN R. BROBECK

Marked variations in food intake have been described in various species following injury to certain parts of the hypothalamus, including an increased food intake or hyperphagia caused by lesions in the medial hypothalamus, especially lesions in or ventrolateral to the ventromedial nucleus; this hyperphagia leads to obesity. 4-6, 14-15, 20, 24 A decrease or complete inhibition of food intake has also been reported as an incidental finding in animals with hypothalamic lesions, by Hetherington and Ranson 16 in rats, and by Clark, Magoun, and Ranson 19 during their study of temperature regulation in cats. Similar observations were also made in cats by Ingram, Barris, and Ranson, 19 by Ranson 22 in monkeys, and by Anand and Brobeck 24 in certain rats which were being prepared for studies of food intake and activity. The present investigation, therefore, was undertaken as an attempt to localize in the hypothalamus the areas the destruction of which leads to diminution or failure of eating with emaciation, as destruction of certain other areas leads to overeating and obesity. As a result of these studies a small, well-localized area has been found in the lateral hypothalamus; the bilateral destruction of this area is followed by a complete absence of spontaneous eating. 4 This area has been tentatively designated as a “feeding center.” An attempt has also been made to discover whether there is any correlation between different areas of the hypothalamus in the regulation of food intake.

MATERIALS AND METHODS

In a series of 94 female albino rats of the Sprague-Dawley strain, electrolytic lesions were placed in different areas of the hypothalamus with the aid of the Horsley-Clarke instrument as adapted by Clark 4 for use on the rat. Evipal was used for anesthesia (12 mg./100 g. body weight). The lesions were made with a unipolar electrode, by a direct current for 15 seconds, its intensity ranging from 0.8 to 2 milliamperes depending upon the size of the lesion desired. It should be noted here that after the milliammeter had been calibrated properly, the lesions produced with a current of 2 milliamperes were invariably found to be much larger than those reported by Brobeck, et al., 7 and by Hetherington and Ranson 16, 17 with the same current.

For placing small, well-localized lesions, the hypothalamus was divided according to the Horsley-Clarke coordinates into discrete points which were separated from each other by 1 mm. in the rostro-caudal planes, and by ½ mm. in the lateral or parasagittal planes (See Figure 18 and Table 2, below). The area between the level of the para-

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ventricular (filiform) and the supraoptic nuclei, rostrally, and the premammillary and arcuate nuclei, caudally, was divided into five planes, separated from each other by 1 mm. In female albino rats weighing about 250 g., the rostral of these planes was 8 mm. (A 8) and the caudal was 4 mm. (A 4) anterior to the plane of the ear bars. A 6 corresponded with the central portion of the ventromedial nucleus and A 7 and A 5 with its rostral and caudal limits. The five parasagittal planes (R & L $\frac{1}{2}$, 1, 1$\frac{1}{2}$, 2, 2$\frac{1}{2}$) were measured from the midline, the fourth (R & L 2) corresponding with the extreme lateral parts of the lateral hypothalamic nuclei, while the fifth (R & L 2$\frac{1}{2}$) was slightly outside the lateral limits of the hypothalamus. Horizontally, most of the points chosen were located in a plane which is about 1 mm. above the base of the brain and 1 mm. below the ear bars of the Horsley-Clarke instrument, i.e., H —1. (The base of the brain at this level is in the H —2 plane of our instrument.) A few lesions were also made in the horizontal plane of the ear bars (H 0), and others in the plane 2 mm. below the ear bars (H —2).

The rats were kept in a room where temperature was relatively constant at about 80° F. They were fed ad libitum on a high-fat diet with the addition of 10 ml. of concentrated cod liver oil, supplemented with 100 mg. of vitamin K and 300 mg. of vitamin E per 100 g. of diet. “Sure B” salt mixture (5%) was used in the diet.

A daily record was kept of food intake and the weight of the rats. Food was always present in the cages, but in order to obtain a full description of spontaneous eating behavior, none of the rats was tube-fed even though it failed to eat to the point of complete starvation.

For controls, rats of the same strain, age, and weight were kept under similar conditions.

Results

I. Large lesions in the region of the ventromedial nucleus

In 18 rats, large, bilateral lesions (2 milliamperes for 15 seconds) were placed in and near the ventromedial nucleus. In 14 of these operations the electrode was localized 1 mm. lateral to the midline, about 1 mm. above the base of the brain (H —1), and in the rostro-caudal plane corresponding to the central portion of the ventromedial nucleus (A 6). Twelve of these 14 ate a very little food for a few days (2-7), and then completely stopped eating (cf. rat 11, Table 1). Their weight gradually fell, and they either died of starvation (although food was always present in the cage), or were killed when in a moribund state in order to save the brain for proper fixation. Sections revealed that all of these 12 rats had large lesions in the hypothalamus, which not only destroyed the medial hypothalamus, but also the whole of the lateral hypothalamus at the rostro-caudal level corresponding to the ventromedial nuclei (Fig. 1, rat 11).

The remaining two rats of these 14 (rats 2 and 5), on the other hand, greatly increased their food intake immediately after the operation, and gradually developed typical hypothalamic obesity (rat 2, Table 1). Sections showed that in rat 2, both the medial and lateral regions of the hypothal-

* The authors realize that these figures have meaning only when applied to the instrument as used in this laboratory, but have chosen to identify the coordinates in order to simplify the description of the operations.
mus were destroyed on the left side, but on the right side the lateral part of the lateral hypothalamus was spared (Fig. 2). In rat 5 the lateral parts of the hypothalamus were spared on both sides (Fig. 3, the medial lesions).

In the other four rats of the series of 18, the placement of the electrode was slightly different. In two of these (rats 40 and 41) the electrode was only ½ mm. lateral to the midline. Rat 40 developed hyperphagia and obesity (Table 1, result of first operation) following lesions which destroyed parts of the ventromedial nuclei and the region dorsomedial to them, while sparing the lateral hypothalamus (Fig. 4, medial lesions.) Rat 41, on the other hand, showed a greatly decreased food intake and a loss of weight for 14 days after operation; its food intake and weight then gradually returned to normal levels, but it did not develop hyperphagia and obesity (Table 1). Its lesions were more dorsal and involved the ventral thalamic and subthalamic regions, extending ventrally only as far as the dorsal limits of the dorsomedial nuclei. The lateral hypothalamus was completely spared.

In one of the two remaining rats (rat 43), the electrode was placed 1 mm. rostral, and in the other (rat 44), 1 mm. caudal to the points of placement in the 14 rats described above. Rat 44 developed hyperphagia and obesity, and the sections showed that although the lesions had completely destroyed the medial hypothalamus including the ventromedial nuclei, the lateral limits of the hypothalamus at that level were not injured. Rat 43 died on the day after the operation with a high fever (colonic temperature of 105° F.) During the one day of its survival it ate normally. Sections
### Table 1

**Daily Food Intake in Grams of Rats with Hypothalamic Lesions**

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**I. Large, medial lesions**

**II A. Small lesions in “feeding center”**

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(First operation)

(Second operation, amygdaloid nuclei)

(Killed)

(Died)

(Killed)

(Third operation)

(Asymmetrical)
Rat hypothalamus ventromedial

were around the normal nuclei showed injury to rat very early. A Study In A rat died in 2 days; in another of rats, all have shown hyperactivity when tested. A rat was found to be dead on the following day, and another one died. A rat that recovered normal eating had the lateral hypothalamus of both sides, as well as regions around the ventromedial nuclei, spared completely. Rat 43 received no injury to the lateral parts of the hypothalamus, and ate normally during the day it survived; but since the anterior hypothalamus was destroyed, the rat died of hyperthermia.

In addition to the changes in food intake, certain observations may be noted here.

(i) All of the rats within hours after the experiment showed marked hyperactivity, beginning immediately after recovery from the anesthesia and persisting for about one day.
(ii) Ten rats of this group showed from a slight to a marked somnolence, and in all of these the lesions were found to extend back to the mammillary region. 

(iii) Twelve rats of this series showed from a fair to a marked degree of irritability, and five of them were really vicious. The irritability and viciousness decreased on repeated, gentle handling, but did not disappear completely. Rat 5 was the most vicious of the group and would bite at every attempt to handle it. Its viciousness showed no decrease until a second operation was done, when large, bilateral, electrolytic lesions were placed in the lateral group of amygdaloid nuclei (Fig. 3, lateral lesions). Following this operation, surprisingly, the rat was completely tame; after that it did not bite at all.

(iv) Some of the rats that had complete inhibition of eating showed pink porphyrin incrustations around the nose and eyes.

(v) A record of colonic temperatures was kept in 8 of the rats of this group. Except for rat 43, which developed hyperthermia, none showed any change in body temperature.

II. Small Lesions

In the remaining 76 rats, only small, well-localized lesions were produced.

A. Small lesions in the lateral hypothalamic area at the level of the ventromedial nucleus.

(i) In five female rats, small, bilateral lesions were produced in the extreme lateral portion of the lateral hypothalamus, using a direct current of 1 ma. for 15 sec. The electrode was placed 2 mm. lateral to the midline, about 1 mm. dorsal to the base of the brain (H -1), and at the rostro-caudal level of the central portion of the ventromedial nucleus (A 6) (Fig. 5, rat 93). As the drawings indicate, these lesions were small and well localized, and did not extend either rostrally or caudally beyond the level of the ventromedial nucleus. The operation was immediately followed by a complete cessation of eating, the body weight gradually fell, and after losing between 90 and 130 grams in weight the rats died on the eighth to twelfth postoperative day (Table 1, rats 93 and 65).

(ii) Unilateral lesions were produced in this area of the lateral hypothalamus in three rats with no effect upon eating behavior (Table 1, rat 86). When another unilateral lesion was made in the corresponding area of the opposite side, there followed immediately a complete inhibition of eating. A section from the brain of one of these rats is shown in Figure 6.

(iii) Small, bilateral lesions (Figs. 4 and 7, lateral lesions) were made in the lateral hypothalamic area in nine rats which had previously been made hyperphagic
and obese by more medial, bilateral lesions. The earlier hyperphagia at once yielded to non-eating; these animals, again, did not eat at all, and even though food was always available, they died of starvation (Table 1, rats 40 and 42).

(iv) In four rats, previously made hyperphagic and obese by bilateral, medial lesions, small, unilateral lesions were placed in this lateral area. After a day or two of diminished eating, the animals recovered and behaved as they would have if no such unilateral lesions had been present. In other words, if the rats were still in the "dynamic" stage of obesity, they continued hyperphagic and gaining weight; if they had already reached the "static" phase, they continued at that weight, eating their accustomed amount of food (Table 1, rat 63). Later, when a corresponding lesion was made also on the opposite side (Fig. 8), eating was at once abolished.

(v) In another investigation, carried out to study the effects of lesions in the amygdaloid nuclei, two rats were observed to stop eating after an attempt had been made to place large lesions in the medial group of amygdaloid nuclei. Study of sections revealed that the lesions had encroached upon the lateral hypothalamic area on both sides (Fig. 7 in Anand and Brobeck). In other animals of the series the eating remained normal; here the lesions were found to be outside the limits of the hypothalamus.

It is thus clear from these operations that bilateral destruction of the lateral portion of the lateral hypothalamus, in the same rostro-caudal and horizontal planes as the ventromedial nucleus, abolishes the food intake of rats, even in animals which have previously been made hyperphagic and obese. None of the animals in which this area of the lateral hypothalamus has been bilaterally destroyed has ever eaten any food during the entire period of its postoperative survival—and this in spite of our many attempts to put food near to or even inside the mouth. In some instances attempts to put the food cup near the mouth were resisted by the rat's pushing the cup away. Changing the diet from the high-fat mixture to "chow" pellets also failed to induce eating.

There was only one rat that recovered normal eating after an attempt had been made to produce lesions of this type in the lateral hypothalamus (Table 1, rat 123). Sections of its brainstem showed that the lesions were asymmetrical, the right one being in the lateral hypothalamus, while the
left one was outside this area (Fig. 9). Thus, in our experience, bilateral lesions in this lateral area can be said to have produced 100% of positive results in terms of failure to eat. The region is well localized and so specific with reference to the Horsley-Clarke coördinates that even small, bilateral lesions symmetrically produced using the appropriate coördinates can be expected always to lead to the desired effect of non-eating.

With the exception of the last days before death when they were emaciated and lethargic, the animals that failed to eat in their early post-operative days looked quite normal and showed a normal amount of activity and of movement about the cage. During this period they appeared to be more irritable than normal, but none of them showed any postoperative hyperactivity nor the somnolence seen after the larger lesions. During their last days some had pink porphyrin incrustations around their mouth and eyes. Colonic temperatures, measured in five of them, showed no change from normal.

B. Small lesions in adjacent areas. Small, symmetrical, bilateral lesions were placed in areas adjacent to and all around the area described above and designated as a "feeding center."

(i) In three rats, bilateral lesions were placed ½ mm. lateral to the above mentioned point, i.e., 2½ mm. from the midline. Two of these rats stopped eating for one day, and one did not eat for five days, after which they began to eat and gradually increased their intake to preoperative levels in 5-7 days (Table 1, rat 98). Food intake and body weight then remained comparable to those of normal controls. Sections revealed that the lateral hypothalamus was completely spared on both sides in all three rats, and that the lesions involved variable amounts of injury to fibers of the internal capsule and optic tract, as well as to the tips of the pyriform lobes (Fig. 10).

(ii) In four rats, bilateral lesions were placed ½ mm. medial to the "feeding center," i.e., 1½ mm. from the midline. Two of these rats ate something on each day, although their intake was decreased for 3-5 days, after which it returned to preoperative levels (Table 1, rat 103). In another, feeding ceased for one day and then gradually recovered, while in the fourth rat that ate practically no food for 7 days, feeding then gradually returned to preoperative levels in another 4 days (Table 1, rat 133). When their
postoperative food intake is carefully compared with that of controls (Table 1, rat 118), one can see that the rats with these lesions eventually ate somewhat more than normal, since in unoperated female rats of the Sprague-Dawley strain the daily food intake diminishes when the animal attains a weight of about 250 grams and "plateaus" at this level. In this group of animals with lesions the food intake neither decreased,

nor did the weight become stationary but went on gradually increasing for some 3 months as the rats slowly became obese. Sections from three of these rats revealed lesions in the lateral hypothalamus which did not reach out to its extreme lateral parts (Fig. 11). In one rat (rat 103) the lesion on the left side had, in fact, encroached upon the extreme lateral part of the hypothalamus; but on the right side this area was spared.

(iii) In three rats, bilateral lesions were placed in a plane 1 mm. rostral to the "feeding center." All of these animals stopped eating for one or two days, and then gradually recovered (Table 1, rat 94). Postoperative food intake and weight were otherwise comparable to those of controls. Sections revealed lesions in the extreme lateral limits of the hypothalamus in its anterior portion, extending anteriorly to the level of the paraventricular nuclei; but caudally the lesions did not extend back to the level of the ventromedial nucleus (Fig. 12).

(iv) Similar bilateral lesions were placed in three rats in a plane 1 mm. caudal to the "feeding center." Two of these rats stopped eating for one day and then gradually recovered, while one had only a decreased food intake for 3-4 days, followed by normal eating (Table 1, rat 92). Postoperative food intake and weight were then comparable to those of the controls. Sections revealed localized lesions in the extreme lateral parts of the hypothalamus in its caudal portion; the lesions did not extend rostrally as far as the level of the ventromedial nucleus (Fig. 13).

(v) In two rats, bilateral lesions were placed in a plane $\frac{1}{2}$ to 1 mm. dorsal to the "feeding center." These rats also stopped eating for two days and then gradually recovered (Table 1, rat 116). Sections revealed lesions which were dorsal to the
lateral area of the lateral hypothalamus; ventrally the lesions did not reach beyond the ventral limits of the dorsomedial nuclei (Fig. 14).

(vi) In two rats, on the other hand, bilateral lesions were placed in a plane ½ to 1 mm. ventral to the “feeding center.” In one rat there was an immediate and complete cessation of eating. The other rat stopped eating for two days after operation; for the next three days it ate small and gradually diminishing amounts of food, and then once more completely failed to eat (Table 1, rat 117). Sections revealed lesions in the lateral part of the lateral hypothalamus, which ventrally reached the base of the brain, and dorsally extended up to the level of the dorsomedial nuclei (Fig. 15).

It thus appears that bilateral destruction of areas adjacent to the region described above (A), and as near as ½ to 1 mm. in all directions around it except ventrally, does not produce the same cessation of eating. As a result of these nearby lesions the feeding may either stop or diminish for a few days and later return to normal levels. Or, if the destruction involves the medial areas adjacent to the “feeding center,” the animal eats more than normal and gradually becomes obese (see below). Destruction of regions ventral to the “feeding center,” on the other hand, also produces cessation of eating, but we have not been able to make lesions that were confined to the base of the brain using this particular technique, since the injury always spreads dorsally along the needle tracks (Fig. 15). Thus, the ventral limits of the “feeding center” cannot be clearly established from our data. The fact that rat 117, with lesions near the base of the brain, did eat some food for each of three days may suggest that the dorsal extension of the lesions rather than their more ventral components was responsible for the failure to eat.

None of the animals belonging to this group, i.e., those with small lesions in areas adjacent to the “feeding center,” showed any postoperative hyperactivity, somnolence, irritability, or viciousness. Their colonic temperatures were normal.

C. Small lesions in other areas of the hypothalamus. As described in Methods, the area of the hypothalamus in the horizontal plane 1 mm. above the base of the brain, bounded (a) medially by the midline, (b) laterally

![Figures 14 and 15](https://example.com/figures.png)

**Fig. 14.** Lesions dorsal to “feeding centers” of lateral hypothalamus. Rat ate less for a few days, then ate normally.

**Fig. 15.** Position of lesions placed 1 mm. ventral to others of this series at level of ventromedial nucleus. Injury extended dorsally along needle tracts. Feeding was almost abolished.
by a parasagittal plane 2½ mm. from the midline (this plane passes somewhat lateral to the limits of the hypothalamus), (c) rostrally by a plane passing through the region of the paraventricular and supraoptic nuclei, and (d) caudally by a plane passing through the premammillary and arcuate nuclei, was divided into 25 points on each side for placing small, localized, bilaterally symmetrical lesions. The effects of some of these lesions have already been reported under (A) and (B); the operations not already described above yielded the following results.

(i) Lesions producing overeating and obesity. Bilateral lesions in the areas situated in the tuberular portion of the hypothalamus, between ½ to 1½ mm. from the midline, but not destroying both of the areas in the lateral hypothalamus which we have called the "feeding center," lead to increased eating and a gradual development of obesity, provided that the lesions encroach upon this area at the level of, that is, within the rostro-caudal limits of the ventromedial nucleus (Table 1, rats 102, 109, and 112). Thus, small, bilateral lesions placed ½ mm., 1 mm., and 1½ mm. lateral to the midline,

![Fig. 16. Lesions in region of ventromedial nuclei, producing moderate hyperphagia and obesity.](image)

![Fig. 17. Lesions which induced hyperphagia and obesity although ventromedial nuclei were not directly injured.](image)

and within the rostro-caudal limits corresponding to the A 5, A 6, or A 7 coordinates of the Horsley-Clarke instrument, led to obesity. Although the food intake was definitely more than that of unoperated controls, the increase was not as marked as the hyperphagia produced by the larger lesions described in an earlier paper. In rats with the smaller lesions the development of obesity was also slower, and the body weight did not reach the higher limits attained by rats with larger lesions. For example, in the group of rats with small lesions (see above), where care was taken to see that all of the animals were of the same strain and age, as well as of comparable weight and food intake before operation, certain of the rats after operation showed greater hyperphagia and earlier obesity than others, with no good correlation between these phenomena and the coordinates at the time of operation. Yet when the sections were studied, the differences in food intake could then be correlated with the size of the lesion in this particular area; the larger the lesion, the more marked the increase in food intake. Rat 109 showed the best hyperphagia, was the earliest to develop obesity, and exhibited the largest lesions (Fig. 16). Next in order in this group was rat 102 (Fig. 17).

(ii) Lesions followed by normal eating. Bilateral lesions outside the limits of the area associated with hyperphagia, and which also did not affect the "feeding centers" in the lateral hypothalamus, did not produce any change in eating (Table 1, rats 111 and 100). For example, none of the rats with bilateral lesions in the more rostral plane of the paraventricular and supraoptic nuclei (A 8) or in the more caudal plane of premammillary and arcuate nuclei (A 4) showed any change in food intake or
increase of weight beyond the normal limits, when the lesions were confined to that particular level. Two animals (rats 106 and 101) with lesions in the more caudal plane (A 4), which did show some increase of food intake, were found at autopsy to have lesions extending rostrally up to the caudal limits of the ventromedial nuclei. Again, bilateral lesions in the lateral planes 2 mm. and 2½ mm. from the midline did not cause any change in food intake except for the bilateral lesions in the “feeding center.”

None of the animals of this (C) group, whether they developed obesity or not, showed any postoperative hyperactivity, somnolence (not even those with the caudal lesions), irritability, or viciousness. Regarding their body temperature, all rats had normal colonic temperatures except the animal (rat 83) that died on the day after the operation with a fever of 104.5° F. Sections showed bilateral destruction of a large part of the anterior hypothalamus from the paraventricular nuclei up to the rostral limits of the supraoptic nuclei. This result is analogous to the course of rat 43 (see above) which also died of hyperthermia, with much larger, bilateral lesions in the same area. In the remainder of the animals, showing only small lesions of these rostral areas and injury to only a part of the anterior hypothalamus, there was no change in

\[
\text{Table 2}
\]

**Average Rate of Daily Change in Body Weight during the First Thirty Days after Operation in 25 Rats with Lesions and 3 Controls**

<table>
<thead>
<tr>
<th>Controls</th>
<th>R &amp; L ½</th>
<th>R &amp; L 1</th>
<th>R &amp; L 1½</th>
<th>R &amp; L 2</th>
<th>R &amp; L 2½</th>
</tr>
</thead>
<tbody>
<tr>
<td>115 &amp; 110</td>
<td>+1.3 g.</td>
<td>+1.0 g.</td>
<td>+1.0 g.</td>
<td>+1.0 g.</td>
<td>+1.2 g.</td>
</tr>
<tr>
<td>120 &amp; 114</td>
<td>+1.0 g.</td>
<td>+2.1 g.</td>
<td>+5.0 g.</td>
<td>+2.4 g.</td>
<td>+1.3 g.</td>
</tr>
<tr>
<td>119 &amp; 113</td>
<td>+1.3 g.</td>
<td>+2.0 g.</td>
<td>+3.0 g.</td>
<td>+2.5 g.</td>
<td>-9.0 g.</td>
</tr>
<tr>
<td>118 &amp; 112</td>
<td>+1.2 g.</td>
<td>+3.0 g.</td>
<td>+2.5 g.</td>
<td>+3.6 g.</td>
<td>+0.9 g.</td>
</tr>
<tr>
<td>111 &amp; 106</td>
<td>+1.3 g.</td>
<td>+2.0 g.</td>
<td>+2.3 g.</td>
<td>+1.3 g.</td>
<td>+1.3 g.</td>
</tr>
</tbody>
</table>

R & L denote the lateral coordinates, in millimeters from the midline. A denotes the distance anterior to the plane of the ear bars, in millimeters. * Survived only 8 days.

In another rat (rat 80), a large, unilateral lesion was placed on the right side in the anterior hypothalamus; there was no change in colonic temperature. After 20 days another large, unilateral lesion was placed in the same area of the opposite side, but this did not lead to hyperthermia and the rat survived. Sections revealed large lesions in the same regions as those of rat 83.

Table 2 shows the average rate of daily increase or decrease in body weight during the first thirty postoperative days in a group of 25 animals of the same weight and age, operated upon on the same day, with small, bilateral lesions in each of the 25 areas mentioned above. The table also includes data from three normal rats of the same group which served as controls.
In Figures 18 and 19 an attempt has been made to project the results of bilateral lesions in these various regions onto a diagrammatic representation of one side of the hypothalamus (taken from Krieg*).

**III. Hypothalamic lesions in cats**

During the course of another study, bilateral, electrolytic lesions were produced by means of the Horsley-Clarke instrument in certain areas of the hypothalamus in cats. The following pertinent observations were made concerning food intake.

(i) In two cats, large, electrolytic lesions were produced bilaterally (4 ma. for 30 sec.) in and around the central and medial nuclei of the amygdala**; a complete cessation of eating was observed immediately after the operation in one of these cats. She was kept alive for 6 weeks by tube feeding and during this period showed no abnormal somnolence, was quite active, and did not develop rage. Neurological examination revealed no abnormality; vision and smell likewise appeared to be normal. Not only was there no spontaneous eating, but even attempts to put food into the mouth did not elicit eating or swallowing—on the contrary, the food was always ejected from the mouth. The animal was autopsied after 6 weeks, and sections revealed large, bilateral lesions which, in addition to destroying the amygdala, spread medially into the lateral regions of the hypothalamus on both sides. The second cat did not eat spontaneously for 7 days, during which time it was tube-fed. Then she began to eat a little food spontaneously, but the food intake was much less than before operation. Her behavior was in other respects quite normal. Sections showed much less destruction of the lateral hypothalamus than in the first cat.

(ii) In two other cats, bilateral lesions were first made in and around the ventromedial nuclei, resulting in increased food intake and obesity. One of these cats developed a marked degree of hyperphagia, with an average daily food intake (canned dog food) which rose from a preoperative level of 80-90 g. to 400-500 g. She became markedly obese, her weight increasing from 2.2 kg. to 5.8 kg. She was the only cat which developed obvious rage reactions.** Eight weeks after the first operation, bilateral lesions were placed in the lateral portions of the lateral hypothalamus in the rostro-caudal plane of the ventromedial nucleus. The animal remained alive for 8 days after operation, and during this period there was a complete failure of eating as well as of drinking. In addition, she showed some degree of somnolence. She was not tube-fed, and died on the eighth day, after her weight had fallen from 5.8 to 4.3 kg. She exhibited no rage during this period. The other cat showed much less increase in its daily food intake following the first operation, its weight increasing from 2.2 to 3.4 kg. in 24 days. She remained friendly and manifested no rage. Lateral lesions were then made, but she lived only for one day after this second operation and suddenly died. During this one day she did not eat or drink.

**DISCUSSION**

The present study appears to show that both increased food intake (hyperphagia) and decreased food intake or even complete cessation of eating can be produced as a result of certain bilateral hypothalamic lesions. The region the bilateral destruction of which produces hyperphagia and obesity, as localized by the studies of Hetherington and Ranson** and Hetherington,** includes some parts of the ventromedial nuclei or the adja-
cent areas of the lateral hypothalamus. Lesions more rostral or dorsal which completely spare these nuclei do not lead to hyperphagia and obesity. Those authors have also reported that these nuclei need not be completely destroyed to produce obesity. The results of our study with well-localized, small lesions generally confirm their observations, although we have found that bilateral lesions placed lateral to those nuclei, and completely sparing the nuclei themselves, also bring about obesity. Hetherington and Ranson have observed obesity following bilateral lesions placed caudally—dorsolateral to the prefrontal and mammillary regions—which they attributed to the destruction of efferent fibers running from the ventromedial nucleus, or its neighborhood, into the brainstem. Ruch, Patton, and Brobeck likewise obtained obesity in monkeys from still more caudally placed lesions of the ventral part of the thalamus and the rostral portion of the mesencephalic tegmentum. We have not been able to obtain similar results in rats from small caudal lesions in the particular horizontal plane which we have chosen. Of six animals in which caudal lesions were made, only two (rats 106 and 101) showed slight increases of food intake, and sections from the brain of these two revealed lesions extending rostrally up to the caudal limits of the ventromedial nuclei (see group C, (ii), above).

Another, more highly circumscribed, area has been found in the extreme lateral portion of the lateral hypothalamus at the same rostro-caudal plane as the central part of the ventromedial nucleus, bilateral destruction of which leads to complete inhibition of food intake. Unilateral destruction of this area does not produce this effect, and this is in conformity with the observations that unilateral injury to the medial hypothalamus does not lead to obesity, and that stimulation of either side of the hypothalamus usually affects both sides of the visceral nervous system, and probably of the somatic, as well.

As noted above, failure of spontaneous eating for variable periods following hypothalamic injury has already been reported incidentally by
Hetherington and Ranson\(^8\) in rats, by Clark, Magoun, and Ranson\(^5\) and by Ingram, Barris, and Ranson\(^9\) in cats, and by Ranson\(^6\) in monkeys. Although they did not localize the regions responsible for eating, their results in general corroborate ours.

This particular lateral area of the hypothalamus not only contains some portion of the large stellate cells constituting the lateral hypothalamic nucleus, but in addition has in it a large group of fibers from the medial forebrain bundle, from the stria terminalis, and direct amygdalo-hypothalamic fibers, as well as fibers from the ansa lenticularis.\(^9\) Since these same fibers are likely to be destroyed in lesions of the adjacent medial, lateral, rostral, caudal, and dorsal areas, which in our experience did not disturb eating, it is difficult to believe that these particular fibers make up the "feeding center." It may well be that this "center" is composed of neurons lying among these fibers, as the cells of the respiratory center are thought to lie in the reticular formation of the medulla. Adjoining the area of the "feeding center" are other important structures, such as the internal capsule, optic tract, tip of the pyriform lobe, and, a little more laterally, the medial group of amygdaloid nuclei; still further dorsal and lateral are the basal ganglia. Since lesions which have been confined to the lateral hypothalamus without direct injury to these other structures (Fig. 5) have completely inhibited eating, while lesions which destroyed the adjoining structures at the same time sparing at least one lateral hypothalamic area have not abolished eating (Fig. 10; cf. also Anand and Brobeck\(^4\)), it can be inferred that this effect is probably due solely to lesions in the lateral hypothalamus. The behavior of these rats and cats suggests that the lesions have in some manner removed what Adolph has called the "urge to eat."\(^1\)

It further appears from these observations that the more medial hypothalamic structures (where lesions cause hyperphagia) exert their influence on food intake through the "feeding center," possibly by means of inhibitory fibers running laterally into that center. Thus, an animal fails to eat following destruction of the "feeding centers" of both sides, while if the "feeding centers" (or even one of them) are intact and the more medial mechanism is removed by destruction of the ventromedial nuclei or their efferent fibers, the animal exhibits a state of hyperphagia. This concept is also in accord with the observation that the degree of hyperphagia and the rapidity with which obesity develops depend upon the size of the lesions in the more medial region, in other words, upon the number of inhibitory fibers damaged. On the other hand, combined bilateral lesions of the medial and lateral mechanisms, together, produce the same effect as lateral lesions alone, that is, failure to eat.*

**Summary**

A small area has been localized in rats in the extreme lateral part of the lateral hypothalamus, in the rostro-caudal plane corresponding to the central
part of the ventromedial nucleus. Bilateral destruction of this area leads to a complete cessation of eating. A unilateral lesion has no such effect. Bilateral lesions involving either the ventromedial nuclei, or the region between them and the lateral area (but not involving the lateral area), produce hyperphagia and obesity. Bilateral lesions in other areas of the hypothalamus do not produce a change in food intake, with the exception that injury to regions adjacent to the lateral area may induce diminished eating for a few days after operation. If the animal is made obese by medial lesions, eating ceases when the lateral areas are destroyed bilaterally. This lateral area has been called a "feeding center"; it may be responsible for the central hunger reaction or the urge to eat, while the ventromedial nucleus or some structure in its neighborhood may be capable of exerting an inhibitory control over the "feeding center" through fibers which run laterally into the lateral hypothalamic area.

Similar observations have been made in cats.

**Abbreviations for all Figures**

- **ANT,** nucleus hypothalamicus anterior
- **ARC,** nucleus arcuatus
- **DM,** nucleus hypothalamicus dorso-medialis
- **F,** fornix
- **IC,** internal capsule
- **LAT,** nucleus hypothalamicus lateralis
- **ME,** median eminence
- **MFB,** medial forebrain bundle
- **ML,** nucleus mammillaris lateralis
- **MML,** nucleus mammillaris medialis pars lateralis
- **MMM,** nucleus mammillaris medialis pars medialis
- **MP,** nucleus mammillaris posterior
- **MPL,** nucleus mammillaris prelateralis
- **MT,** mammillo-thalamic tract
- **OC,** optic chiasma
- **OT,** optic tract
- **PC,** pyriform cortex
- **PMD,** nucleus premammillaris dorsalis
- **PMV,** nucleus premammillaris ventralis
- **POST,** nucleus hypothalamicus posterior
- **PS,** pituitary stalk
- **PV,** nucleus paraventricularis (filiformis)
- **SCH,** nucleus suprachiasmaticus
- **SO & SUP. O,** nucleus supra-opticus
- **V,** third ventricle
- **VM,** nucleus hypothalamicus ventromedialis
- **I, II, & III OP.,** first, second, and third operation respectively
- **A4 to A8,** 4 to 8 mm. anterior to the ear bars of Horsley-Clarke instrument
- **L ½ to 2½ mm. lateral to the midline**
- **H-½ to 2 mm. ventral to the ear bars of the Horsley-Clarke instrument**

*Confirmative evidence in support of the existence of a "feeding center" in this region has been obtained by Anand and Delgado (1951) in cats. The appropriate area of the lateral hypothalamus has been stimulated chronically in unanesthetized animals by means of implanted electrodes. Food intake increased greatly during the days when the stimulation was carried on, and then fell once more to normal levels when the stimulation was discontinued.*
REFERENCES


15 Hetherington, A. W.: Non-production of hypothalamic obesity in the rat by lesions rostral or dorsal to the ventromedial hypothalamic nuclei. J. Comp. Neur., 1944, 80, 33.


