INGESTION PATTERNS IN HYPERPHAGIC AND NORMAL RATS[1]

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Rats with lesions in the vicinity of the ventromedial nuclei of the hypothalamus become tremendously obese. This obesity results from the greatly increased food intake that each animal displays after the operation (2). A close analysis of the change in the ingestion characteristics that must accompany the increase in food intake may shed some light on the nature of the disturbance in the regulatory behavior of these animals.

An increase in the amount of food ingested daily must be achieved by an increase in either the number of meals per day, the size of each meal, or both. In addition, the rate of ingestion during each meal may be changed. In the present study, techniques were utilized which simultaneously reflected all three of these aspects of the daily food intake. In the first experiment, using a liquid diet, a drinkometer apparatus was set up in conjunction with a cumulative recorder to detect and record each time the animal licked at a tube containing the diet. In a second experiment, using a solid diet, the patterns of lever-pressing to obtain food were used to reveal the characteristics of daily food intake.

GENERAL METHOD

Subjects

Three groups of female albino rats of the Wistar strain were used in each experiment: normal, unoperated controls; obese hyperphagic animals that had been operated upon approximately two months earlier; and recently operated, nonobese hyperphagic animals (also called "dynamic hyperphagics"). They were all approximately six months old. On the average, the normal group weighed 250 gm., the obese animals weighed 600 gm., and the nonobese hyperphagics weighed 280 gm. Five normal, 5 obese hyperphagic, and 6 recently operated hyperphagic animals were used in the first experiment. The corresponding numbers in Experiment II were 6, 4, and 7.

Hypothalamic Lesions

Bilateral hypothalamic lesions were made with a stereotaxic instrument similar to that described by Stellar and Krause (8). After the animal was anesthetized and its skull exposed, it was placed in the stereotaxic instrument. Two holes were drilled in the skull with a dental trephine. Lesions were produced at points 1½ mm. posterior to the bregma, ¾ mm. lateral to the midline, and ½ mm. off the floor of the skull. A unipolar anode, 0.25 mm. in diameter and insulated except for 0.25 mm. at the tip, was used to pass a direct current of 1 ma. for 15 sec. The circuit was completed by means of a rectal cathode.

EXPERIMENT I

Method

The rats were allowed ad libitum access to a liquid diet[2] by means of a drinking tube which was fixed in a plate attached to the front of the cage. The tube was made of glass, 9 mm. in diameter, and flame-polished to an aperture of 3 mm. at the lower end. The tube was mounted to form a 30° angle with the front of the cage, and an inverted 100-ml. graduated cylinder, which served as the fluid reservoir, was connected to the upper end by flexible rubber tubing. The lower tip of the glass tube was then 4 mm. from a circular opening 12 mm. in diameter, through which the rat licked. The amount of liquid ingested during each period of time could be directly recorded by observing the change in the level of fluid in the graduated cylinder. Readings were taken twice daily, at 10 A.M. and 10 P.M., at which time the cylinders and drinking tubes were washed and fresh liquid food was put in each tube. Spillage was measured by collecting it in a small cup under the tube. This amounted to 1 or 2 ml. in 24 hr.

In addition to direct volume measurement of intake over successive 12-hr. periods, an instantaneous measure of rate of ingestion was obtained by the use of a drinkometer technique (7). By licking at the tube containing the liquid diet, the animal completed a circuit between the fluid in the tube and the plate on which the animal was standing. Each lick changed the bias on the grid of a 2050-thyratron tube and allowed the thyratron to activate a relay. The relay operated a cumulative recorder that moved a pen vertically across a

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[2] The liquid diet was prepared by mixing 250 ml. of evaporated milk, 125 ml. of 50 per cent sucrose solution, 150 ml. of whole egg, 30 ml. of Kaopectate, and 0.3 cc. of Multi-Vi Drops (White Laboratories, Inc., Kenilworth, N.J.). This mixture contains approximately 1.57 kg-cal per ml.

paper record, which moved horizontally at a speed of 22 in. per hour.

Two cages with drinking tubes mounted on them were enclosed in a relatively soundproof refrigerator shell which provided a quiet, illuminated and relatively noise-free environment. A partition between the two cages prevented each animal from seeing the other one. The animals lived in the situation all the time for seven consecutive days. The first two days were allowed as an acclimatization period, and only the measurements taken for the next five days were used as the data of the experiment. The sole source of food was the liquid diet. Tap water was available ad libitum, but it was found that the animals took practically no tap water. Normals took none, and dynamic or obese animals might consume 2 to 3 cc. of water in addition to the fluid diet.

In order to quantify the characteristics of each meal, it was necessary to define a meal. Since the animals tended to drink in bursts and then not to return to the tube for periods of 30 min. or more, an arbitrary criterion of a meal was taken to be a continuous period of drinking which was not interrupted by a pause of more than 5 min. Once this criterion had been set, the number of meals, the size of each meal, and the rate of ingestion during each meal were tabulated from the permanent record taken from the cumulative recorder. Each excursion of the cumulative recorder represented 933 licks. The rate of ingestion during each burst was recorded directly from the cumulative record by measuring the slope of each line and then averaging the slopes. The average daily meal size in milliliters was determined by dividing the total volume ingested by the number of meals ingested during that day. This measure agreed very closely with the meal size as determined by the number of licks in each burst.

Results and Discussion

Figure 1 and Table 1 summarize the results of the experiment. In the upper left part of the figure, it can be seen that dynamic hyperphagics ingest about twice as much per day as do the normal animals. Obese hyperphagics ingest just slightly more than do the normal animals. This is essentially a duplication of the phenomenon that is usually found when the intake of these types of animals

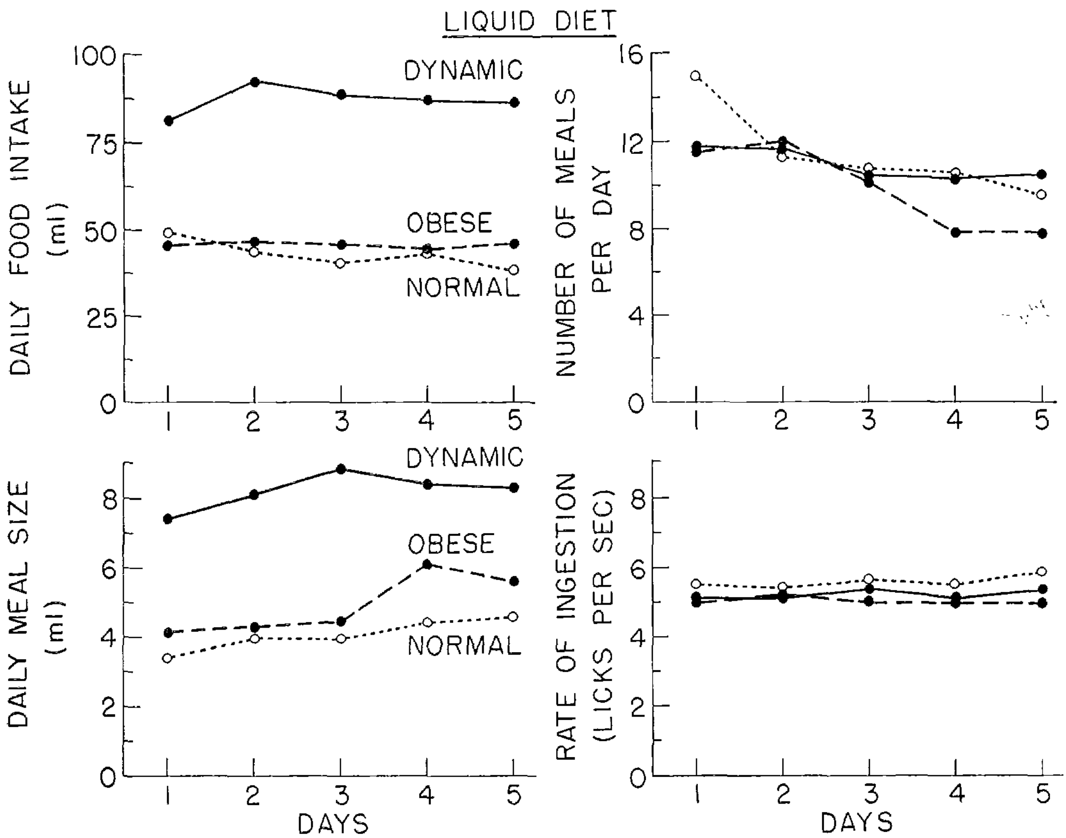

FIG. 1. Patterns of ingestion by normal, dynamic, and obese hyperphagic animals on a liquid diet. The daily meal size, number of meals per day, and rate of ingestion during each meal represent the patterns of ingestion that produced the total amount ingested daily.

TABLE 1
Intake of a Liquid Diet

Group	N	Amount Eaten Daily (ml.)		Average Meal Size (ml.)		No. of Meals per Day		Rate of Ingestion (Licks per Second)	
		Mean	Range	Mean	Range	Mean	Range	Mean	Range
Normal	5	42.7	33.8– 53.6	4.1	2.7– 5.9	11.5	9.2–14.6	5.6	5.3–5.9
Dynamic	6	87.1	66.0–102.2	8.2	6.2–10.0	11.1	10.0–12.6	5.2	5.0–5.5
Obese	5	45.3	35.6– 66.8	4.9	3.7– 6.4	9.9	6.8–12.0	5.0	4.3–5.6

is measured (3). The other three quadrants of Figure 1 show the characteristics of the food ingestion pattern by which this increased food intake was achieved. It can be seen that in neither the rate of ingestion nor the number of meals per day are the normal animals different from the hyperphagic animals. However, the size of each meal directly reflects the increased intake of hyperphagic over normal animals.

Figure 2 shows this phenomenon graphically as it was recorded directly on the cumulative recorder. The meal chosen as typical of each group represents a meal on the third day for the median animal of each group. It is clear that dynamic hyperphagics take much larger meals than do normals or obese hyperphagics. Several of the obese animals showed the peculiar pattern of pausing within each licking period, which is shown in the pattern of the obese animal. This was attributed to the effect of the sustained work involved in maintaining a uniform licking rate for a relatively long period of time. It is possible that this is similar to the exaggerated effect of work on the performance of these animals, as demonstrated by Miller, Bailey and Stevenson (6) and by Teitelbaum (10).

The results of this experiment show clearly that, in achieving an increased ingestion of a liquid diet, hyperphagic animals do not take more frequent meals, but, rather, they tend to take a larger meal each time they eat. In other words, they do not stop eating as soon as do normal animals. This might be considered as support for the idea that hyperphagics show an impairment in the satiety mechanism (6).

In an earlier experiment, Brooks, Lockwood, and Wiggins, using a Purina Mash diet, measured the frequency of eating and the size of each meal in hyperphagic and normal animals. They found that hyperphagic animals eat larger meals. In addition, in one of their figures (Fig. 2), there was an indication that hyperphagic animals may eat somewhat more frequently (3). In order to check this point, and to see whether the ingestion patterns depended greatly on the character of the diet, a second experiment was performed in the present study which measured the ingestion patterns of hyperphagic and normal rats on a diet of solid food.

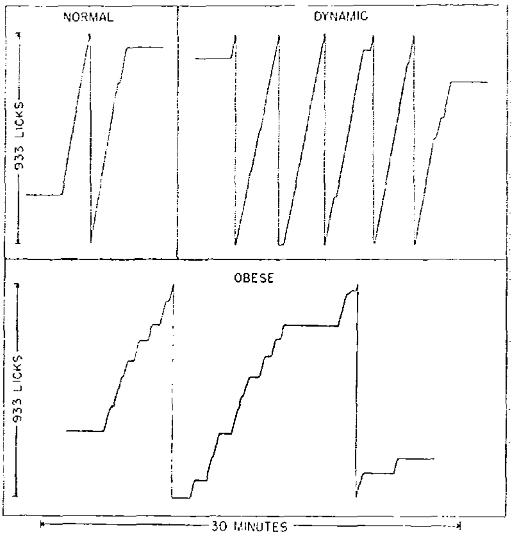

FIG. 2. Bursts of licking as recorded directly on a cumulative recorder. The pen moves upward with each lick and toward the right as time elapses. Each burst represents a typical meal on the third day for the median animal in each group.

EXPERIMENT II

The patterns of ingestion associated with a solid diet were measured by means of a Skinner box. The conditions were essentially the same as those in the first experiment, except that this time the animals were trained to press a lever once for each pellet of solid food that they received.

Method

The Skinner box consisted of a cage, 8 in. high, 8½ in. wide, and 9 in. long. The two sides and the floor were made of ⅛ in. steel bars placed ½ in. apart and mounted in two Bakelite strips. The front and back were made of aluminum and the top lid of clear Plexiglas to permit observation of the animal's behavior. Three inches above the floor a lever projected ½ in. out into the cage through a slot in the front wall. The lever was 1⅞ in. wide and could be depressed by a force of at least 10 gm. A small food cup, 1 in. square by ½ in. deep, projected from the front wall at a point 2½ in. below the bar and 1½ in. to the left of it. Each time the animal pressed the bar and moved it through an arc of ⅛ in., a microswitch was closed, and a feeder automatically delivered a 45-mg. pellet of Purina Chow.[3] A water tube in the cage allowed free access to water at all times. The pattern of ingestion was recorded by means of a cumulative recorder similar to that used in the first experiment. Each Skinner box was housed in a relatively soundproof refrigerator shell. As in the previous experiment, the animals lived for seven days in the Skinner box, and their patterns of ingestion were measured by recording each time they pressed the bar and obtained a pellet of food. The same criterion of a meal was used in this experiment, that is to say, any burst of food intake of at least five pellets separated by at least 5 min. from any other burst constituted a single meal. The minimum of five pellets per burst was used to exclude accidental bar presses which sometimes occurred when the animal was exploring the cage. These were rare, amounting to perhaps three or four per day. Thus, the number of meals and the number of pellets per meal were obtained directly. In addition, the rate of ingestion during each meal was measured by counting the number of pellets obtained in that meal and measuring the time it took to obtain them. This then gave a rate of ingestion in terms of pellets per minute. The ingestion patterns during the last five days of the seven-day period were used as the data of the experiment.

It is essential, in order to get an accurate representation of the patterns of ingestion of the pellets, to prevent the animal from piling up pellets and eating them at some other time. This was accomplished in the present experiment by having each bar press send a short pulse through the normally closed contacts of the microswitch. The pulse operated a relay which stepped a stepping switch 11 times and at the end of the cycle activated a feeding mechanism, which dropped a pellet into the tray in the animal's cage. If the animal pressed the bar again while the stepper was cycling, this delayed the delivery of the pellet until the animal released the bar and allowed the stepping switch to finish its cycle. This device quickly trained the animal to press and release the bar and then to drop down to the food cup and eat the pellet. The cycling time of the stepper (about 1 sec.) was such that the pellet delivery closely coincided with the return of the animal to the food cup after releasing the bar. The animal was in this manner trained to press the bar and to eat the pellet after each bar press. Thus, the animal would eat a number of pellets in a burst and then would not return to the bar for a long time, usually at least a half-hour. The cycling of the stepper was also used to step the cumulative recorder 11 times for each bar press. By this means a clearly visible displacement occurred for each single bar press on the cumulative recorder (see Fig. 4) and the number of pellets per meal could be counted directly from the record.

Results and Discussion

Figure 3 and Table 2 summarize the results of this experiment on the ingestion patterns associated with a solid diet. The upper left portion of the graph shows again that dynamic hyperphagic animals eat nearly twice as much as do normal animals, and obese hyperphagics only slightly more than normal. From the lower left-hand graph it is clear that dynamic hyperphagic animals in this situation eat larger meals than do normal animals, while the upper right-hand graph shows that they also have a tendency to eat more frequently, but this is not statistically significant. The obese hyperphagic animals tend to eat larger meals, but they eat less frequently. These results confirm in general the previous findings of the first experiment and are also in agreement with the data reported by Brooks, Lockwood, and Wiggins (3). The difference between the findings with solid and liquid diets suggests that the character of the diet may affect food-ingestion patterns.

An interesting finding, shown in Figure 4, is the fact that the rate of ingestion is very rapid in obese animals and curiously slow in dynamic hyperphagics. This rate is indicated by the number of pellets per minute that a rat will obtain by pressing the bar. The obese animals appear to gobble each pellet and go right back to the bar for the next. Recently operated animals seem to linger over each pellet and to chew it much longer than do normal or obese hyperphagic animals. This phenomenon was most marked during the first two or

[3] The pellets of food are manufactured by the P. J. Noyes Co., Lancaster, New Hampshire. According to their specifications, each 45-mg. pellet contains 80 per cent Purina Laboratory Chow, 8 per cent bleached flour, 9.5 per cent glucose solids from liquid glucose USP, 1.5 per cent Type A USP gelatin, and 1 per cent tricalcium phosphate. Each pellet contains 0.163 kg-cal.

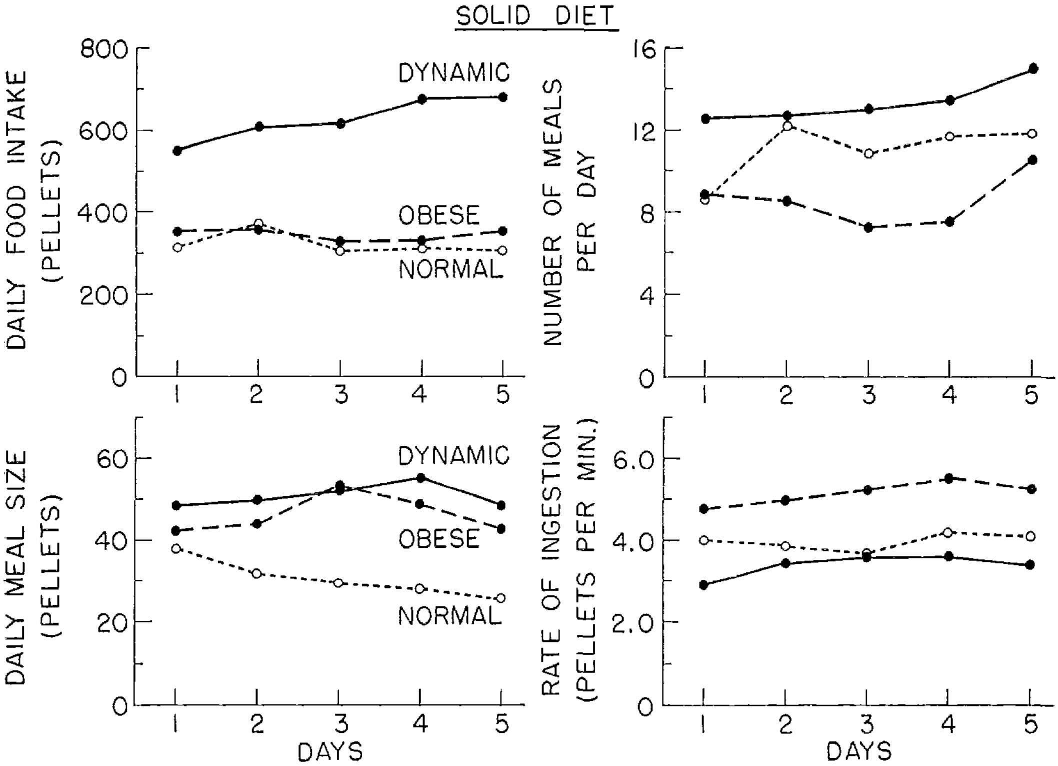

FIG. 3. Patterns of ingestion by normal, dynamic hyperphagic, and obese hyperphagic animals on a solid diet. The daily meal size, the number of meals per day, and rate of ingestion during each meal represent the patterns of ingestion that produced the total amount ingested daily.

TABLE 2
Intake of a Solid Diet

Group	N	Amount Eaten Daily (No. of Pellets)		Average Meal Size (No. of Pellets)		No. of Meals per Day		Rate of Ingestion (Pellets per Min.)	
		Mean	Range	Mean	Range	Mean	Range	Mean	Range
Normal	6	323.1	279.4–376.6	30.8	20.7–39.6	11.0	9.4–15.2	4.0	2.9–5.1
Dynamic	7	625.7	513.0–749.6	50.9	37.9–78.3	13.3	8.5–16.8	3.4	2.1–4.9
Obese	4	344.9	338.4–352.0	46.3	29.6–71.5	8.3	5.2–11.4	5.1	4.4–6.1

three days after operation and then tended to disappear. Brooks, Lockwood, and Wiggins found that hyperphagic animals appeared to eat the freshly prepared wet mash very rapidly. The rate of ingestion of a solid diet in the present experiment does not indicate this ravenous quality of eating. The rate was, of course, limited by the bar-pressing situation, but observation of the animals as they ate each pellet clearly showed that they chewed each pellet longer. It is possible that the dryness of the pellets promoted slower ingestion and perhaps more pausing during each meal to obtain water.

It has also been reported that a change in the feeding cycle goes along with a change in the day-night activity rhythm. A normal rat is more active at night and tends to eat more at night than during the day. A hyperphagic animal tends to eat as much during the day as during the night (3). Recently, Anliker and Mayer recorded cumulatively the curve for the amount ingested during each 24 hr.

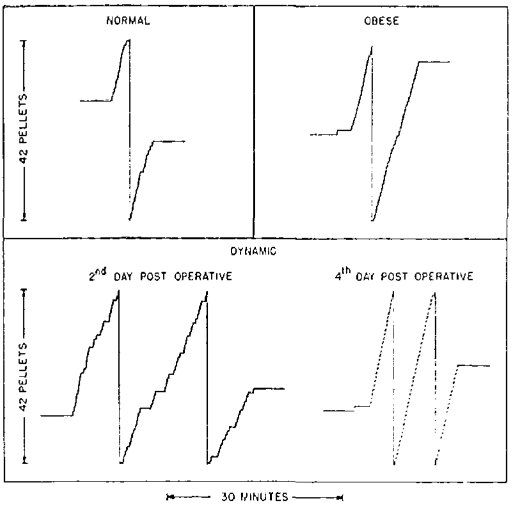

FIG. 4. Cumulative response records showing typical meals obtained by pressing a lever once for each pellet of food. Each discrete step upward represents a single pellet.

by normal and obese mice in a bar-pressing situation (1). They demonstrated that the curve shows marked leveling-off periods when the normal animal eats relatively little. Hypothalamic, obese mice, in contrast with normal mice, do not show these leveling-off periods, but tend to obtain food steadily, as much during the day as during the night. Similar results with hyperphagic rats were found in the present experiment, that is to say, normal animals tended to eat more at night than during the day. Hyperphagic animals, both dynamic and obese, ate as much during the day as during the night, although in some cases the obese animals showed some tendency to revert to the normal pattern of eating more at night.

The fact that hyperphagic animals increased their consumption of a liquid diet merely by increasing the size of each meal and not by increasing the number of meals appears to be related to the caloric content of the diet and the stomach capacity of the animal. In an average meal of the liquid diet, dynamic hyperphagic animals obtained more calories (12.86 kg-cal) than in an average meal of dry pellets (8.56 kg-cal). It is likely then that they increased the number of meals on a dry bulky diet in order to obtain a greater over-all intake of calories. Obese animals, with an increased stomach capacity, ate larger meals rapidly but, in keeping with their approximately normal total intake, ate less frequently.

This finding that obese hyperphagic rats eat less frequent meals is in agreement with the recently published results of Larsson and Strom (5), who showed that goldthioglucose obese mice eat larger but less frequent meals than normal mice. The apparent lack of accord between the findings of Anliker and Mayer (1) and those of Larsson and Strom with respect to the number of meals eaten daily may be attributed to the fact that the obese mice of Anliker and Mayer had not yet reached a static obese plateau. Thus, they would be more like dynamic hyperphagic animals: on a solid diet, they eat larger and more frequent meals than normal animals.

As a follow-up to the first experiment, the caloric content of the liquid diet was halved by mixing it with an equal volume of water. Under these circumstances the dynamic and obese hyperphagic animals doubled their intake of the liquid diet. They did this mainly by greatly increasing the frequency of bursts of licking. This is in accordance with the findings of Brooks, Lockwood, and Wiggins that when the size of the stomach is surgically reduced in hyperphagic rats, they continue to eat more than normal rats, but they do this by eating small meals very frequently. It appears then that hyperphagic animals do maintain an increased caloric intake. When the caloric content per unit volume of the diet is high, as in a liquid diet, they appear to do this primarily by an increase in the size of each meal. When the caloric content is lower, they increase both the size and the frequency of their meals. If, however, the palatability or the bulk of the diet changes markedly, they may not maintain this increased caloric intake, especially if they are obese (4, 9).

The increased food consumption of hyperphagic rats seems most closely related to whether or not they are obese. Once having become obese, hyperphagic animals will limit their food intake to practically the same as normal animals and will maintain a relatively even weight level. If they have not yet become obese, or have been forced to lose weight by restriction in their food intake, they will overeat when allowed food ad libitum (4). This indicates that it may be fruitful to investigate more directly the relation of obesity to food intake in these animals.

SUMMARY

The patterns of food ingestion displayed by normal rats, obese hyperphagic, and dynamic (nonobese) hyperphagic rats were studied. In two experiments, using a liquid diet and a solid diet, measures were utilized which recorded the amount eaten daily, the number of meals, the size of each meal, and the rate of ingestion during each meal.

The results showed that:

1. When eating a liquid diet, dynamic hyperphagic animals ate about twice as much as normals. Obese hyperphagics ate just slightly more than normal animals. The increased food intake shown by hyperphagic animals was reflected entirely by an increase in the size of each meal. There was no increase in the frequency of eating or in the rate of ingestion during each meal.

2. When eating a solid diet, dynamic hyperphagic animals revealed their increased food intake in an increased meal size and a tendency to eat more frequent meals. The rate of eating was slower than normal in recently operated hyperphagic animals, and tended to become faster as the animals became obese. The increased frequency of eating the solid diet was related to the fact that fewer calories were obtained in each meal of the solid diet than of the liquid diet. Obese hyperphagics ate larger meals but less frequently than normal animals.

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