THE CONTRIBUTION OF OROPHARYNGEAL SENSATIONS TO HYPOTHALAMIC HYPERPHAGIA

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Finickiness accompanies the overeating and obesity that are produced by ventromedial hypothalamic lesions. Decreases in the palatability of the food that do not affect the normal rat will depress feeding in the hyperphagic rat (Kennedy, 1950), and can even render the animal aphagic (Teitelbaum, 1955; Corbit & Stellar, 1964). Improvements in the taste and texture of the diet exaggerate food intake in both the dynamic (Corbit & Stellar, 1964) and the static (Teitelbaum, 1955) phases of the phenomenon and elevate the level of obesity in the static phase (Corbit & Stellar, 1964). Clearly, the vigour of the hyperphagia and the level of the obesity reached are functions of the palatability of the diet.

To what extent does the phenomenon of hypothalamic hyperphagia depend on palatability? Will the rat with ventromedial hypothalamic lesions overeat and become obese if it cannot taste or smell its food? The question can be answered with a technique described by Epstein (1960). Rats will eat food that does not pass through the mouth and pharynx.They feed themselves by pressing a bar for the delivery of food into their own stomachs through a chronic gastric tube. Normal animals feed themselves for months with this method and regulate food intake with precision (Epstein & Teitelbaum, 1962b). The following is a report of hypothalamic hyperphagia in rats feeding themselves in this manner.

Methods

Subjects

Intragastric feeding was studied in eight adult female rats of the Sherman albino strain. The animals weighed between 250 and 290 g. at the beginning of the experiment. In six of the animals, ventromedial hypothalamic lesions were made prior to the beginning of training for intragastric feeding. All gained at least 75 g. before being introduced to the experiment. The seventh and eighth animals were fitted with chronic ventromedial hypothalamic electrodes before training and the lesions were made after intragastric feeding was well established. Hypothalamic placements were at stereotaxic coordinates A:6, RL:0·75, Down: 9·0–9·5 mm. from the surface of the cortex. In all cases, the sagittal sinus served as the reference midline. In the six animals made hyperphagic before training, bilateral lesions were made with a nichrome anode (1 mA., d.c. for 30 seconds). In the seventh and eighth animals a pair of insulated platinum electrodes was fixed to the skull (Hoebel, 1964) and the lesions were made subsequently under light ether anaesthesia (3 mA., d.c. for 40 seconds).

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Diets

Two types of liquid diet were employed. The first was an enriched eggnog (Williams & Teitelbaum, 1959) that contains 1·55 k.cal. per ml. This diet contains insoluble material and tends to clog the intragastric tubing. It was replaced during the experiment by a completely soluble diet for the rat supplied by General Biochemicals Incorporated (Chagrin Falls, Ohio) as their soluble diet No. 116 EC. It is a less expensive version of the Greenstein L-amino acid diet (Greenstein, Winitz, Birnbaum & Otey, 1957). It contains casein hydrolysate instead of the amino acids, sucrose instead of glucose, and the vitamins, minerals, "Tween" emulsifier, and essential fatty acids as described by the original authors. It is a 50 per cent. solution that contains 2 k.cal. per ml.

Intragastric Feeding

The essential elements of the intragastric feeding technique are a chronic gastric tube, a diet delivery-system controlled by a bar available to the animal, and automatic programming and recording equipment which permits uninterrupted study of the animal's behaviour. The technique has been described in detail elsewhere (Epstein & Teitelbaum, 1962 a and b).

The rats were first trained to press the bar to obtain liquid diet for oral consumption. The number of bar presses required for each delivery was increased by steps to six. The initiation of

intragastric self feeding was accomplished by switching the diet supply line from the food cup to the inlet of the gastric tube. The next time the animal pressed the bar six times, 2·5–3·0 ml. of liquid food was injected (0·1 ml./sec.) directly into the stomach instead of into the cup. In one animal (IGM-1), the method was modified to give the rat complete control of the size as well as the frequency of its meals. The pump was activated by depression of the bar and remained active as long as the bar was held down. The rate of delivery was fixed at 3·4 ml. per 10 seconds. A recording circuit was devised that translated the duration of bar press into vertical excursions of a cumulative pen. Water was available at all times from a graduated cylinder fitted with a drinking spout.

Test for Regulation

Regulation was tested during intragastric feeding in five animals by diluting the diet to half its concentration with tap water. Regulation was achieved if the animal maintained a constant daily food intake, *i.e.*, doubled the volume of its intake on days of 50 per cent. dilution and halved its volume of intake upon return to full strength diet.

Oral Incentive

In three animals, a small amount of solution was delivered into the cup in the cage simultaneously with the intragastric load. In two this incentive was the eggnog diet, and in one it was 0·1 per cent. sodium saccharin solution (w/v in water). In all three animals the volume of the incentive was one-ninth the volume of the concurrent load.

Results

Five of the eight animals were hyperphagic while feeding themselves without taste and smell. In the three others the addition of oral incentives was necessary to maintain bar-pressing during intragastric feeding. The results for the five rats that did not require oral incentives are summarized in Table I. In two rats (IGM-1 and IGM-7) hyperphagia was produced *after* intragastric feeding was established. The others were hyperphagic before they fed themselves intragastrically. Table I shows the animal's body weight at the time intragastric feeding began, the maximum weight reached after hypothalamic lesions, average daily food intake and weight gain during intragastric hyperphagia (dynamic phase only), and the total number of days of intragastric feeding. All animals overate and gained weight steadily to moderate levels of obesity.

The detailed data of one rat (IGM-1) are shown in Fig. 1. In this animal both meal size and frequency were self-controlled. The pump ran as long as the bar was held down. Note first that a sustained hyperphagia leading to more than 200 g. increase in body weight was produced by medial hypothalamic lesions while the animal fed itself by injecting food into its own stomach. A first set of lesions on day 9 in the figure produced only three days of overeating. On day 34 a second set produced the sustained phenomenon. After each pair of lesions, the hyperphagia was expressed initially as an increase in meal size resulting in a clear doubling of daily food intake.

In all five of the animals in Table I, food intake was regulated in the face of abrupt changes in the concentration of the diet. This is shown on days 37 to 43 of Fig. 1. After 50 per cent. dilution of the diet, indicated by the division of the histograms into filled and open halves, the volume of liquid consumed doubled within three days. The adjustment to dilution is made precisely but

Table I. Hypothalamic Hyperphagia and Weight Gain to Moderate Levels of Obesity in Rats Feeding themselves without Taste or Smell.

Subject	Initial weight	Maximum weight	Daily IG* food intake	Daily IG* weight gain	Total days IG feeding
IGM—1	260	488	64·2	5·4	58
IGM—7	282	390	53·7	4·0	50
IGM—19	247	414	96·5	7·6	48
IGM—10	325	423	55·6	2·7	73
IGM—25	295	348	42·7	2·8	26

*Mean values during dynamic phase.

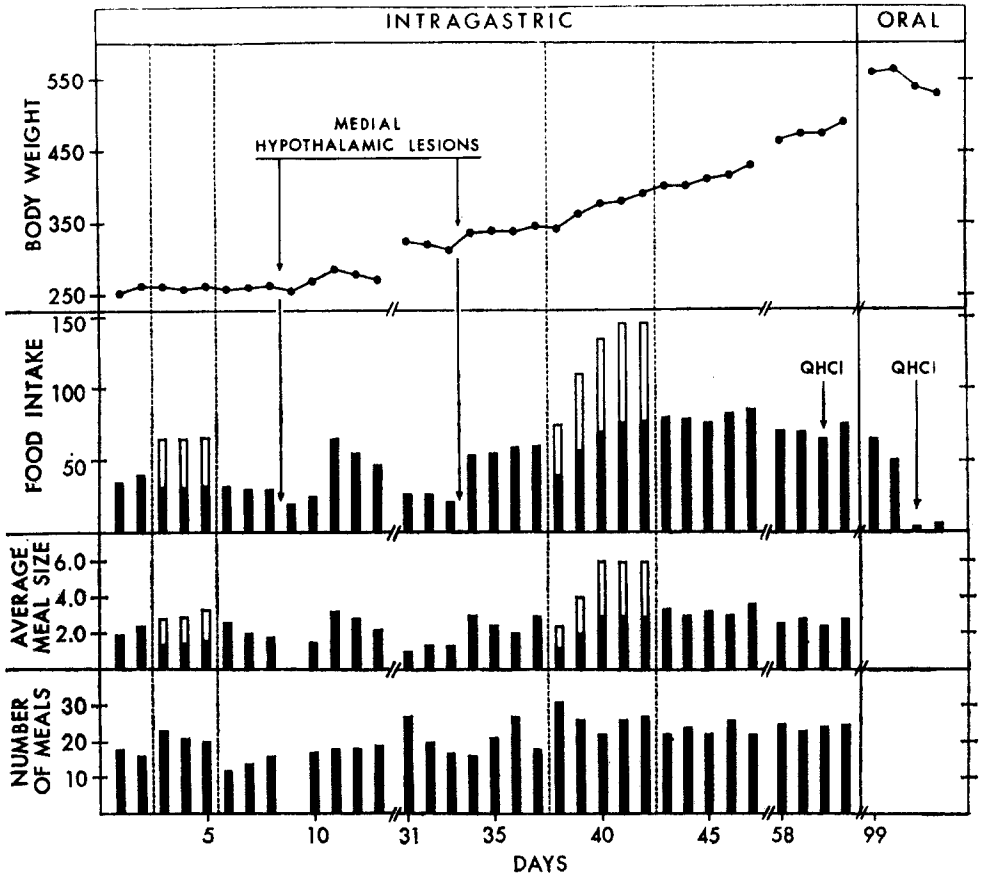

Fig. 1. IGM-1: Hyperphagia and moderate obesity in a rat feeding itself without taste and smell. Body weight in grams, food intake in millilitres. QHCL indicates days of adulteration of the diet with 0·03 per cent. quinine hydrochloride.

slowly (compare it with the adjustment made on days 2 to 6 before lesions). This delay in adjustment to dilution was seen in all five rats. The converse adjustment to concentration was equally precise and as rapid as in normal animals (Epstein & Teitelbaum, 1962b).

All the animals that were hyperphagic *before* intragastric feeding was instituted decreased their bar-pressing and food intake during the transition from oral to intragastric feeding (see IGM-10, Fig. 7, Teitelbaum & Epstein, 1963). The animals included in Table I (IGM-19, 10, and 25) adjusted to the change by increasing their intake and became hyperphagic. The remaining three animals became severely anorexic. These were the animals that required an oral incentive. All were vigorous hyperphagics when eating by mouth. Bar-pressing and hyperphagia were restored in these animals by the introduction of a small oral incentive (eggnog in two, 0·1 per cent. saccharin in one animal) delivered into a cup for oral ingestion concurrently with the delivery of the food into the stomach.

These phenomena are shown in Fig. 2. When eating eggnog by mouth the animal is vigorously hyperphagic, consuming over 100 ml. per day. On transition to intragastric feeding, bar-pressing and food intake drop immediately. On the fifth day the animal is aphagic. The introduction of saccharin (0·1 per cent. w/v) incentive restores bar-pressing. Food intake rises to hyperphagic levels, and once begun, the overeating and weight gain continue at a slower rate after the withdrawal of the incentive (days 14 to 30). A second and more sustained dynamic phase is produced by reintroducing the saccharin incentive (day 45 in Fig. 2) when the animal's weight had stabilized

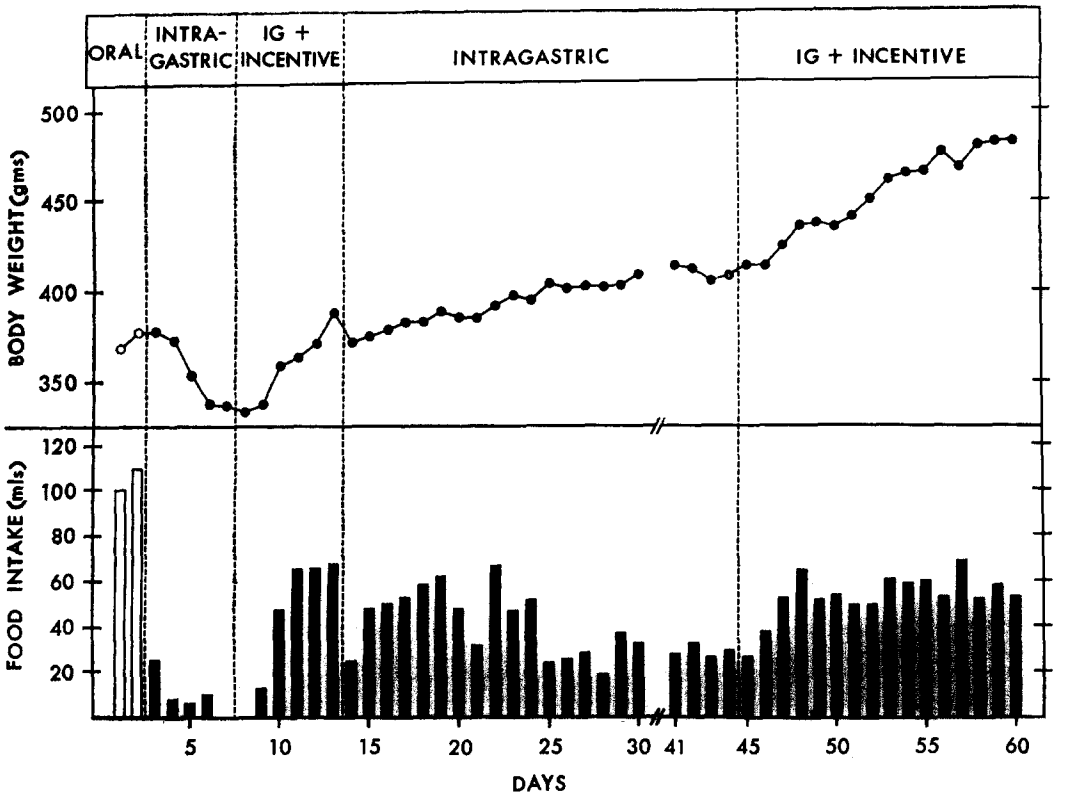

Fig. 2. The addition of a saccharine incentive restores bar-pressing and hyperphagia (days 8 to 24), and produces a second dynamic phase and a higher level of static obesity (days 45 to 60) in a rat that was vigorously hyperphagic when eating by mouth.

at 410 g. and food intake had fallen to non-hyperphagic levels. A higher level of obesity (480 g.) is quickly reached. With the oral incentive (days 45 to 60) the animal ate 53·3 ml./day and gained 70 g. in 15 days. Without the incentive (days 14 to 30), the animal ate only 41·8 ml./day and gained only 40 g. It should be noted that in this case the incentive is a completely non-nutritive solution.

The two other rats that required oral incentives were the most obese animals studied at the time intragastric feeding began (425 g. and 484 g.). Both animals ate less and lost weight when taste and smell were withdrawn. In both, hyperphagia and rapid weight gain returned when the small oral incentive was added to the intragastric load.

Discussion

These results show that high palatability of the diet is not necessary for hypothalamic hyperphagia. Rats overeat and become obese while feeding themselves foods that do not pass through the oropharynx. The overeating cannot be simply the result of exaggerated responsiveness to the taste and smell of patalable foods.

However, taste and smell are potent energizers of feeding in the normal and particularly in the hyperphagic rat. Palatable diets have been shown to be essential for the onset of hyperphagia, for maximum rates of food intake and weight gain in the dynamic phase and for maximum weight levels in the static phase (Corbit & Stellar, 1964). The experiments reported here supplement these findings by showing that without the taste and smell of palatable diets the hyperphagic rat will not eat as vigorously. This is strikingly demonstrated by the experiments shown in Fig. 2. The animal was one of our maximal hyperphagics when pressing a bar to eat by mouth. It quickly stopped pressing and became aphagic when it could no longer taste or smell its food. But when a non-nutritive sweet-tasting incentive was offered with each gastric load, the animal was once again motivated to overeat. These excessive reactions to

taste and smell are additional demonstrations of the finickiness of the hyperphagic rat, that is seen in both the dynamic (Graff & Stellar, 1962) and static (Teitelbaum, 1955) phases of the phenomenon.

These experiments also show that as rats become obese, high palatability becomes essential for sustained hyperphagia and maximum obesity. Our rats did not reach high levels of obesity when they could not taste or smell their food. When the obese level was reached the mere addition of a small, sweet incentive restored hyperphagia and weight gain. This is reminiscent of the increased oral food intake of obese hyperphagics when sugar is added to their diet (Teitelbaum, 1955).

Additional evidence for the importance of palatability for sustaining hyperphagia in the obese rat comes from our finding that our most obese hyperphagic rats did not overeat and lost weight when switched from oral to intragastric feeding. Their body weight had apparently already exceeded the level at which food intake in the absence of palatability is depressed by obesity. Hoebel and Teitelbaum (in Teitelbaum, 1961) have already shown that obesity curbs hypothalamic hyperphagia. They described a rat which was subjected to ventromedial hypothalamic lesions, after it had become obese as the result of overeating in response to chronic insulin hypoglycaemia. It did not display maximum hyperphagia until it was deprived of food and forced to lose more than 230 g. in weight. Obesity also depresses food intake in the neurologically normal rat. Cohn & Joseph (1962) have shown that rats, whose body weight has been raised to twice the normal level by forced feeding, do not eat spontaneously for as long as 16 days after the forced feeding have been stopped. In the rat feeding itself intragastrically without the incentives of palatability, the depressing effect of obesity on food intake operates at lower weight levels.

The importance of taste and smell as energizers of feeding behaviour is further shown by the slow regulatory adjustments made by our hyperphagic animals. In previous experiments neurologically normal rats feeding themselves intragastrically (Epstein & Teitelbaum, 1962b) and hyperphagic rats eating by mouth (Williams & Teitelbaum, 1959) increased food intake to changes in dilution rapidly, usually within the first night of feeding after the change. In all animals tested in the present experiment, intragastric food intake was doubled in response to 50 per cent. dilution of the diet, and food intake was halved when full-strength diet was returned. But the adjustments to dilution were much delayed. Food intake was never doubled during the first night and typically the regulation was not achieved until the third night of dilution.

These findings support the view that motivation is essential for the regulation of food intake (Teitelbaum & Epstein, 1933). The taste and smell of food are powerful reinforcing stimuli that serve to motivate the behaviour involved in feeding. Normal animals, with adequate motivation, can largely ignore taste and smell and regulate their food intake in the face of wide variations in palatability and dilution (Adolph, 1947). But in animals with hypothalamic damage, where motivation is impaired, regulation will be delayed or will not be achieved unless high palatability is operating to motivate food intake.

Summary

Hypothalamic hyperphagia was studied in rats that fed themselves food they could not taste or smell. Overeating persisted in the absence of oropharyngeal sensations. However, high levels of obesity were not reached. The addition of small oral incentives produced new bouts of overeating and rapid weight gain. Excessive responsiveness to highly palatable foods is not the cause of hypothalamic hyperphagia but oropharyngeal sensations determine the rate and duration of the overeating and are essential for maximum levels of obesity.

Acknowledgements

Supported by grants USPHS NB-03469 to Alan N. Epstein and NSF G-24386 to Philip Teitelbaum. The authors are grateful to Mr. Robert Glassman who conducted the experiments with IGM-1, and to Miss Sandra Lee who prepared the figures.

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(*Accepted for publication* 27*th July*, 1965; *Ms. number*: 585).