THE INFLUENCE OF DIET AND
SEX ON THE DEVELOPMENT OF OBESITY
FOLLOWING VENTROMEDIAL HYPOTHALAMIC LESIONS

by *6¥Oφ*

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Extreme obesity was first described in human patients with pituitary tumors (Frohlich, 1901). Originally, the obesity was attributed to pituitary damage, but other investigators concluded that the deficits were due to damage to the hypothalamus (Erdheim, 1904). Smith (1927, 1930) showed that hypophysectomy, without damage to the hypothalamus, did not produce obesity in rats. Hetherington and Ranson (1939, 1942) produced hypothalamic obesity in rats by placing discrete lesions in the vicinity of the ventral portion of the hypothalamus.

Brobeck, Tepperman, and Long (1943a) observed that animals with ventromedial hypothalamic (VMH) lesions became obese because they ate more than normals. They coined the term "hypothalamic hyperphagia" and reported two distinct phases: the "dynamic" and the "static" phase. The "dynamic" phase begins immediately postoperatively. Animals consume large quantities of food and increase their body weight rapidly. In the "static" phase, the animals decrease food intake to a level near normal and maintain a high, but stable, weight.

In 1950, another aspect of the hyperphagic syndrome was observed by Kennedy. He reported that VMH lesioned animals are "finicky." When food is adulterated with cellulose or kaolin, the hyperphagic animal does not adjust its food intake to maintain a stable caloric intake, as do normal animals. The hyperphagic rat reduces its food intake as adulteration of the food increases (Teitelbaum, 1955, 1961). This phenomenon is particularly strong if the animal is in the static phase (Teitelbaum, 1955). Conversely, positive tastes (sweet) or textures (high fat diets) increase food intake in an exaggerated manner in VMH animals (Corbit & Stellar, 1964; Teitelbaum, 1955, 1961). Teitelbaum and Campbell (1958) showed that

hyperphagic rats have an altered pattern of ingestion. When eating a solid diet, hyperphagic rats eat larger meals; and they eat more frequently than normal animals. When they are on a liquid diet, they eat larger meals, but do not eat more frequently.

Experiments designed to test the possibility that VMH obesity is produced by a disturbance of metabolic functioning failed to show any disturbance of metabolism. (Brobeck, Tepperman, & Long, 1943a, 1943b; Tepperman, Brobeck & Long, 1943; Brooks, 1946; Brooks & Lambert, 1946; Brooks, Lockwood, & Wiggins, 1946; Brooks, Marine, & Lambert, 1946).

After damage to the VMH, there is an impairment of motivation. When VMH animals are required to work to obtain food, they will not work as hard as normal animals, indicating that VMH animals are not more motivated for food than normal animals, they just eat more (Miller, Bailey, & Stevenson, 1950). The suggestion that VMH animals have a deficit in motivation was further explored by Teitelbaum (1957). Three groups of animals (normals, obese hyperphagics, and non-obese hyperphagics) were required to obtain food by lever pressing on various schedules of reinforcement. When few bar presses were required for each pellet, hyperphagics pressed the bar more and obtained more food than controls. When many bar presses were required for each pellet, hyperphagics pressed the bar less and obtained less food than controls. This effect of increased work was more pronounced in obese than non-obese hyperphagic animals. It seems then, that as the animal approaches the static phase, it is decreasingly motivated to work to obtain food.

Hoebel & Teitelbaum (1966) have shown that the obese weight level is the new "normal" weight for the animal. Static VMH animals may be

force-fed enriched diets or injected with insulin each day, producing a
weight gain above the static level. When force-feeding or insulin injec-
tions cease, the animal reduces its intake, returns to its previous obese
weight and regulates at that level. If the animal is starved to its pre-
operative weight, then given ad lib. food, it will return to its obese
level and regulate there again. Thus, the weight in the static phase is
considered to be a new "normal" weight level. It has also been shown
that after an animal enters the static phase, this new weight level may
be increased by increasing the extent of VMH damage (Hoebel, 1969). When
lesions are enlarged, the animal returns to the dynamic stage, increases
its food intake until it has reached a new higher weight level, then reg-
ulates there. This phenomena is repeatable until the animal dies of
complications of obesity or old age.

Most of the work in hypothalamic hyperphagia has been done with fe-
male animals. Until recently, there were no studies designed to test
systematically the possibility that there are sex differences in response
to VMH lesions. Cox, Kakolewski, and Valenstein (1969) investigated
this aspect of the problem and showed that VMH-lesioned females gain
significantly more weight (percent change) than their controls, whereas
VMH-lesioned males do not. They reported that "while there is no doubt
that hyperphagia and obesity may be produced by VMH lesions in males,
the likelihood of success and the magnitude of the effect is smaller
with males." Gold (1970), however, reported that males get just as fat
as females (absolute weight gain) following VMH lesions. Males are heav-
ier than females at the same age, but in two to three weeks following VMH
lesions, females "catch up" to the weight of VMH males and then both

males and females gain weight at the same rate (Gold, 1970).

There are several major differences between the study by Gold (1970) and the one of Cox et al. (1969): (a) Cox et al. used electrolytic lesions while Gold used a method of parasagittal hypothalamic knife cuts (Albert & Storlien, 1969). (b) Cox et al. used ground food (Purina) as the post-operative food while Gold used a high-fat diet (consisting of ground food and vegetable oil). As mentioned earlier, VMH animals are finicky. Powdered chow is not highly palatable, while the high-fat diet is extremely palatable (Corbit & Stellar, 1964). Therefore, finickiness in VMH animals could explain the differences in the results of the two studies. (c) The foods were presented differently in each experiment. It has been shown (Miller, Bailey, & Stevenson, 1950; Teitelbaum, 1957) that VMH animals will not work as hard as normal animals for food when they have been deprived for the same amount of time. This observation has been made on both males and females (Miller et al., 1950, males, and Teitelbaum, 1957, females). Cox et al. used modified feeding tunnels (enlarged), and it could be argued that this would require more work than the bowl of food which was provided by Gold. (d) Gold points out that lesioned males and females gain weight at the same rate only after two or three weeks on a high fat diet. Cox et al. report data for only 21 days, and did not allow time for such an observation. (e) Since males weigh more than females of the same age, relative weight gain would have to be greater for males than for females to reach significance.

Valenstein, Cox, and Kakolewski (1969) report that, after gonadectomy of adult male and female animals without VMH lesions, the weight gain per day of the females increased from 1.8 gm. to 3.3 gm. postoperatively.

The weight gain per day of the castrated males preoperatively was 1.9 gm. but postoperatively was only 0.9 gm. per day, measured over a period of 21 days. It has also been reported (Taleisnik & McCann, 1961) that VMH-lesioned, ovarectomized female rats gain considerably more weight than those with VMH lesions alone.

Studies have been conducted using male rats exclusively (McCann, 1953; Fusco, Malvine, & Churchill, 1966; Trifaro & Mikulic, 1966); however, little or no weight gain was reported following VMH lesions. It is possible that hyperphagia and accelerated weight gain can be produced by VMH destruction in male rats (Bernardis & Skelton, 1967), but the likelihood of success is smaller than with females.

The present experiments investigated the effect of VMH lesions in both sexes, using two different diets. The method of diet presentation was that of Gold (1970); the lesions were produced electrolytically (Cox et al., 1969). An inbred strain of rats was used to reduce the variance of lesion placement. An inbred strain of rats have less variance in body weight; therefore, there would be less variance in lesion placement.

In the first experiment, the effects of sex and diet upon the development of hypothalamic obesity were investigated. In the second experiment, diets were reversed to investigate the contribution of the diet offered to the level of obesity achieved in Experiment I. Animals previously given the high fat diet were switched to ground food. Similarly, the animals given ground food in Experiment I were switched to high fat diet.

EXPERIMENT I: EFFECTS OF VENTRALMEDIAL LESIONS

Method

Subjects

Forty-eight male and female Charles River albino rats (Charles River,
Fisher Strain) were used. All animals were at least 120 days of age when
the experiment started. Rats of this strain have been bred by brother-
sister matings beyond seventy generations leading to a high degree of
homozygosity and, therefore, a reduction in the variance of body size
between subjects of the same sex. Within each sex, 2 groups of 12 rats
were formed. The groups within each sex were closely matched for body
weight. One group of animals of each sex was given a high fat diet after
lesioning; the other group was given ground laboratory chow. Of the 12
animals in each group, 4 were selected at random to serve as sham-operated
controls; 8 were given VMH lesions. Thus, the experimental design was
2 X 2 X 2, lesion by no lesion, male by female, high fat by ground food.

Procedure

Animals were housed individually in standard wire-mesh rat cages.
Food was presented in an 8-cm. diameter glass sponge cup. Each diet was
available to the animals for one 3-day period two weeks prior to lesion-
ing. In the week prior to lesioning the animals were given fresh pellets
daily. Animals were weighed daily for 7 days prior to surgery. They
were deprived of food 24-72 hr. after lesioning. Since animals with VMH
lesions begin to eat before completely recovering from the anesthetic,
inhalation of food particles during this period may result in death
(Brobeck, Tepperman, & Long, 1943). When food was returned, ground food
(Purina Lab Chow) was presented to two of the groups (one male and one

female), while the other two groups were given a high fat diet. The high fat diet consisted of two parts of ground food (Purina Laboratory Chow) by weight to one part of Crisco vegetable shortening (Corbit & Stellar, 1964). Papers were placed under each cage to catch spillage. Food, water, and body weight measures were taken every 3 days for 63 days after lesioning. The colony room was kept at about 26° C (79° F).

Surgery

After baseline measures of body weight were obtained and the animals were exposed to both diets, experimental animals received bilateral electrolytic lesions aimed at the VMH. Control animals received a sham operation in which the electrode was lowered 4 mm. into the brain and withdrawn without lesioning. Stereotaxic coordinates for the placement of VMH lesions were 2.3 mm. to 2.7 mm. posterior to bregma. More posterior coordinates were used for larger animals. With the frontal bones parallel to the table on the stereotaxic instrument, lesions were made .5 mm. lateral to the mid-sagittal sinus and 1.2 to 1.5 mm. above the floor of the skull. Smaller animals received lesions closer to the ventral limit of the brain. Atropine sulfate was administered five minutes prior to the administration of the anesthetic. Surgery was performed under Equithesin anesthetic, using a Kopf stereotaxic instrument. The lesioning electrode was a platinum-iridium alloy wire (.012 in. in diameter) insulated except for a cross-section at the tip. Lesions were made by passing 2 ma. d.c. anodal current for 20 sec., using a rectal cathode. Experimental and control animals were lesioned in a random sequence, but all males were lesioned before lesions were begun in females. All operations were completed within 48 hr. Seventy-two hr. after lesioning began, all animals

were given the diet appropriate for their group.

Data Analyses

The data were analyzed using an analysis of variance (ANOVA) for two different measures: percent change scores and absolute difference scores. The percent change score was the weight on day 63 divided by the preoperative weight multiplied by 100. The absolute difference score was obtained by subtracting the preoperative weight from the weight on day 63. Analyses were performed using both measures across days (repeated measures). Analyses of the data were done on animals who completed Experiment I. Two experimental male animals died, one in the ground food (GF) diet group and one from the high fat (HF) diet condition. Data from these animals was not included in the analysis.

Food intake was transformed to kcal/gm of food. According to Corbit & Stellar (1964), the high fat diet has 5.5 kcal/gm and the ground food diet has 3.61 kcal/gm.

Results

Body Weight

The mean body weight for each group is plotted in Figure 1. The ANOVA's on end point data yielded the results shown in Table 1. There was a significant effect of VMH lesions on body weight for both the percent change scores and the absolute difference scores. The diet provided produced significant effects on obesity; the HF groups were heavier than those on ground food. The analysis showed no significant main effect of sex. There were significant interactions, with the percent change score data, between lesion-control and male-female (A x B), i.e., there is a differential effect of sex after lesions. Lesioned females show a larger percent

Figure Caption

Fig. 1. Body weight for animals in Experiment I (days 0-63) and
Experiment II (days 64-90). Legend applies to diet in
Experiment I; in Experiment II, the diets were reversed,
but the same symbols were retained. Results from experi-
mental animals of both sexes on the high fat diet are
indicated by "HF E"; experimental animals of both sexes
on the ground food diet are indicated by "GF E." Control
animals of both sexes on the high fat diet are indicated
by "HF C"; control animals of both sexes on the ground
food diet are indicated by "GF C."

THIS BOOK CONTAINS NUMEROUS PAGES WITH DIAGRAMS THAT ARE CROOKED COMPARED TO THE REST OF THE INFORMATION ON THE PAGE.
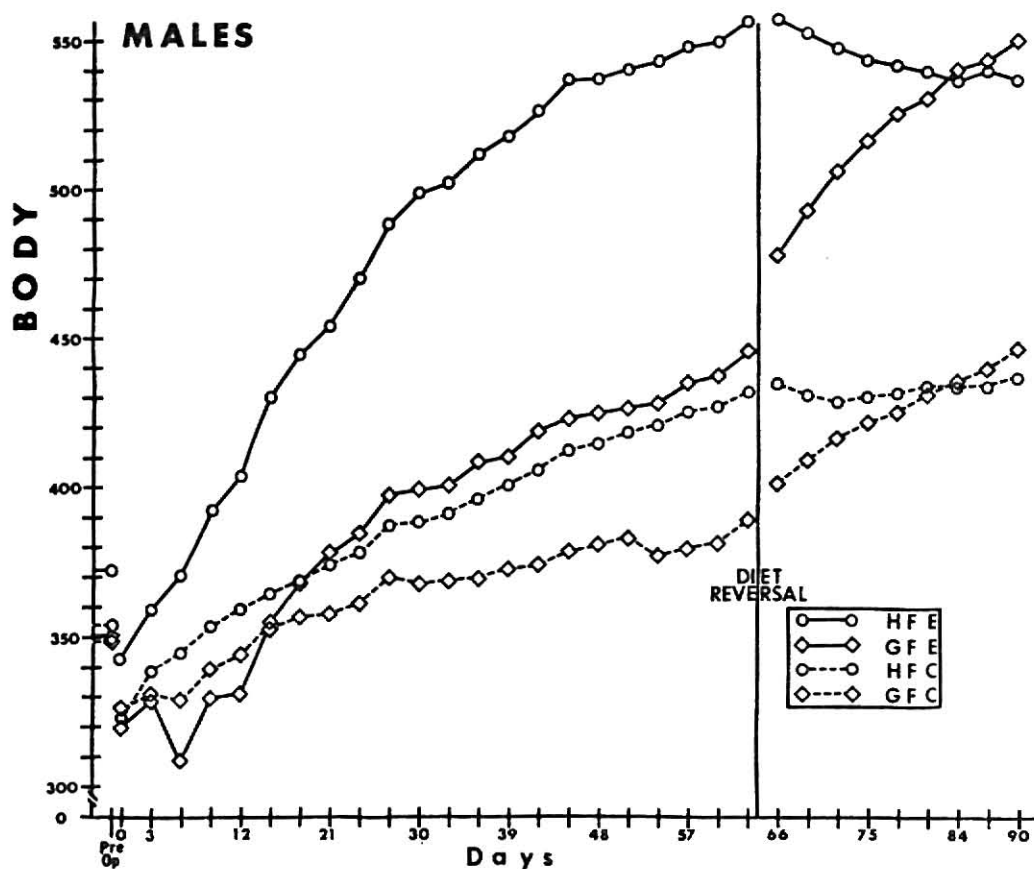
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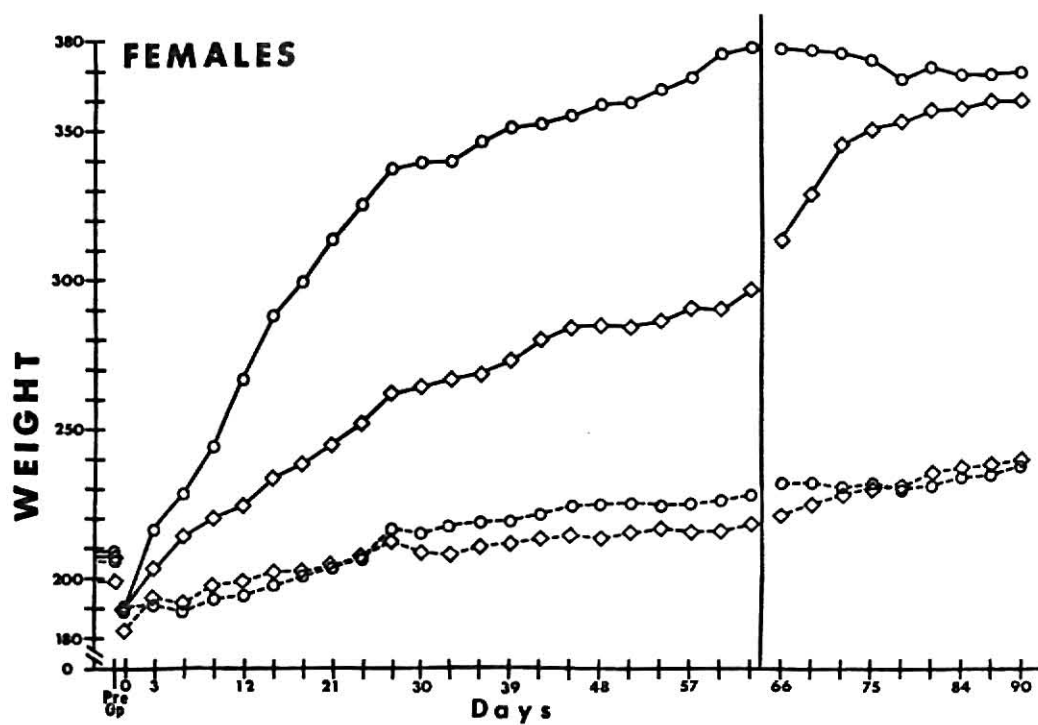
Table 1

Analysis of Variance of Body Weight Changes

(Percent Change and Absolute Difference)

from Prelesion Weight to Day 63

Source	df	Percent change F	Absolute difference F
Lesion vs. control (A)	1	40.55**	48.25**
Male vs. female (B)	1	1.81	3.24
High fat vs. ground (C)	1	10.24**	14.58**
A x B	1	6.41*	1.03
A x C	1	4.94*	5.33*
B x C	1	< 1	< 1
A x B x C	1	1.38	< 1
Error	38		

* p < .05

** p < .01

change in body weight than lesioned males, while control females show a smaller percent change than do control males. The lesion-control and high fat-ground food (A x C) interaction was also significant, i.e., there is a differential effect of diet following lesions. Experimental animals on the HF diet increased their weight, both on the percent change scores and the absolute difference scores, more than experimental animals on the GF diet. Control animals on the high fat diet gained more weight than control animals on the ground food diet, however, there is a larger difference in body weight between experimental groups than control groups. The absolute difference scores yielded about the same result for the A x C interaction but showed no significant effect of an A x B interaction.

The analysis was extended to examine individual effects (e.g., control GF males vs. experimental GF males). VMH males on GF differ significantly from their controls (F = 4.30, df = 1/38, p < .05) i.e., experimentals are heavier than their controls. The differences are more marked when VMH males on HF diet are compared to their controls (F = 14.88, df = 1/38, p < .01). The same results hold for comparisons between control and experimental groups of females (GF, F = 6.57, df = 1/38, p < .05; HF, F = 29.14, df = 1/38, p < .01). There was a significant difference between VMH males on HF diet and VMH males on the GF diet (F = 9.99, df = 1/38, p < .01). This effect also holds for the females (F = 8.68, df = 1/38, p < .01). There are no significant differences between the sham-lesioned control groups within either sex; however, control groups across sexes do differ significantly (F = 7.93, df = 1/38, p < .01). The male controls showed a greater gain, typical of normal males.

The ANOVA's with repeated measures across days are summarized in Table 2. For the analysis, the data were collapsed into 9 day blocks, except for

Table 2

Analysis of Variance of Body Weight Changes

(Percent Change and Absolute Difference)

with Repeated Measures over Days

Source	df	Percent change F	Absolute difference F
Lesion vs. control (A)	1	39.90**	42.97**
Male vs. female (B)	1	3.36	< 1
High fat vs. ground food (C)	1	12.04**	14.72**
A x B	1	7.99**	1.55
A x C	1	8.30**	8.65**
B x C	1	< 1	< 1
A x B x C	1	1.38	< 1
Error	38		
Days (D)	6	138.8**	16.36**
A x D	6	31.65**	3.51**
B x D	6	< 1	< 1
C x D	6	8.43**	< 1
A x B x D	6	2.73*	< 1
A x C x D	6	3.18**	< 1
B x C x D	6	< 1	< 1
A x B x C x D	6	1.17	< 1
Error	228		

$*\ \underline{p} < .05$

$**\ \underline{p} < .01$

the last block which had 12 days. Results were similar to those found in the analysis at day 63: there was a significant effect of the lesion, the diet, the length of time spent in the postoperative condition; however, there was not a significant effect of sex. Similarly, there was a significant effect of the lesion across days and a significant effect of diet across days, while sex across days did not yield a significant effect. Thus, over the period of Experiment I, diet and lesion effects influence weight gain across days, while sex has no significant influence on weight gain across days. The same interactions noted in Table 1 appeared in the repeated measures ANOVA. There was also a significant lesion by sex by days interaction and the lesion by diet by days was also significant.

The lesions are effective in all experimental groups in either sex, on either diet. The effect of diet is significant on the production of obesity over days. Either end-point or repeated measures ANOVA's using percent change or absolute differences showed the same main effects.

An additional ANOVA was performed on the data taken at 21 days since this was the termination point of the Cox et al. (1969) study. At this point, the data did yield an overall significant effect of the lesion (F = 31.95, df = 1/38, p < .01), and a significant effect of the diet (F = 9.62, df = 1/38, p < .01), but no difference due to sex. Once again, there was a significant interaction between lesion and sex (F = 6.49, df = 1/38, p < .05). There was also a significant interaction between lesion and diet (F = 10.22, df = 1/38, p < .01), but there was no significant interaction between sex and diet. With individual comparisons, VMH males on GF were not significantly different from their sham-operated controls at 21 days, nor were lesioned females different from their controls. Males and females on the HF diet were significantly different from their

controls (F = 5.98, $\underline{df}$ = 1/38, $\underline{p}$ < .05; F = 41.65, $\underline{df}$ = 1/38, $\underline{p}$ < .01, respectively.

Mann-Whitney Tests were run on successive points on the body weight data for females on the GF diet to determine when lesioned females became significantly different from their controls. Lesioned females became significantly different from their controls at day 27 (U = 5, $\underline{p}$ < .036). According to the Mann-Whitney test, males on the GF diet never significantly differ from their sham-operated controls; however, an ANOVA did show that males on GF were significantly different from their controls on day 63.

Food Intake

Mean food intake, transformed to kilocalories per gram of food (kcal/ gm), is shown in Figure 2. ANOVA's were performed on the data at a point of maximum food intake (days 15-18) and at the end of the experiment (days 60-63). The data were further transformed to kcal. per 100 gm. body weight (kcal/100 gm).

In the analysis performed at the point of maximum food intake, there was a significant effect of the lesion (F = 32.21, $\underline{df}$ = 1/38, $\underline{p}$ < .01), a significant effect of sex (F = 8.15, $\underline{df}$ = 1/38, $\underline{p}$ < .01), and a significant effect of diet (F = 8.68, $\underline{df}$ = 1/38, $\underline{p}$ < .01). That is, males were eating more than females, males and females consumed more on the HF diet than on the GF diet, and experimental animals were consuming more than their controls. None of the interactions were significant at this point. An analysis performed on kcal/100 gm body weight showed the same effects: the effect of the lesion (F = 24.77, $\underline{df}$ = 1/38, $\underline{p}$ < .01) and the effect of the diet (F = 6.70, $\underline{df}$ = 1/38, $\underline{p}$ < .05) were significant, however, females ate significantly more than males when intake was converted to kcal/100 gm body weight (F = 17.20, $\underline{df}$ = 1/38, $\underline{p}$ < .01). When the food intake data were

Figure Caption

Fig. 2. Mean food intake over 3 days, expressed in kilocalories. Legend applies, as in Fig. 1, to Experiment I; in Experiment II, the diets were reversed, but the same symbols were retained.

transformed to kcal/100 gm body weight, none of the resulting interactions was significant.

Sixty-three days after lesioning, there were no significant differences in food intake (either kcal or kcal/100 gm) between experimental and control groups, males and females, or high fat and ground food groups. Further, there were no significant interactions at this point.

During the period of maximum food intake, males took in more calories than females, experimentals took in more than controls, and animals on the high fat diet took in more than those on ground food. When caloric intake was expressed in kcal/100 gm body weight, females ate significantly more than males. By 63 days, these differences had disappeared, and food intake expressed either in kcal or kcal/100 gm was the same for all groups.

Water Intake

Water intake over 63 days is shown in Figure 3. Males on the GF diet consistently drank more water than animals on the HF diet during the entire 63 day experiment. The experimental males consumed larger quantities of water than experimental females, regardless of diet.

EXPERIMENT II: EFFECTS OF DIET REVERSED

Method

The subjects, feeding dishes and diets used in Experiment I were used in Experiment II.

Procedure

Diets were reversed for all animals in Experiment I, i.e., all animals that were on the HF diet before day 63 were given GF diet, and all animals on the GF diet received the HF diet. Food and water intake and body weight were recorded every 3 days for an additional 27 days.

Figure Caption

Fig. 3. Mean water intake over 3 days. Legend applies, as in Fig. 1,

to Experiment I; in Experiment II, the diets are reversed,

but the same symbols were retained.
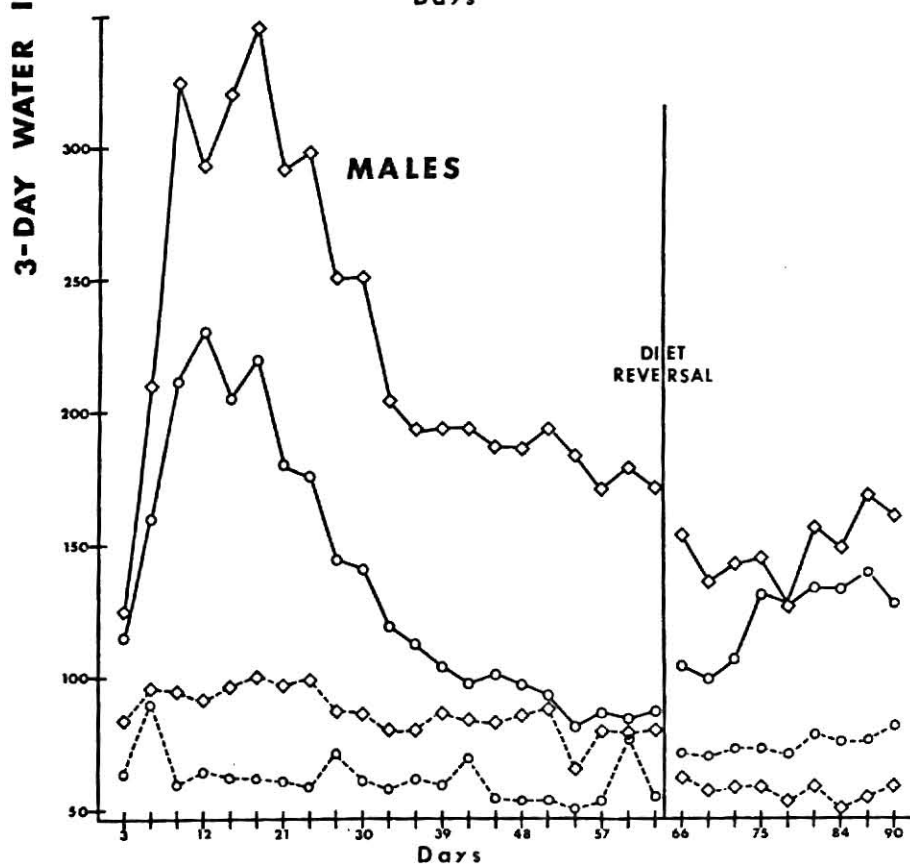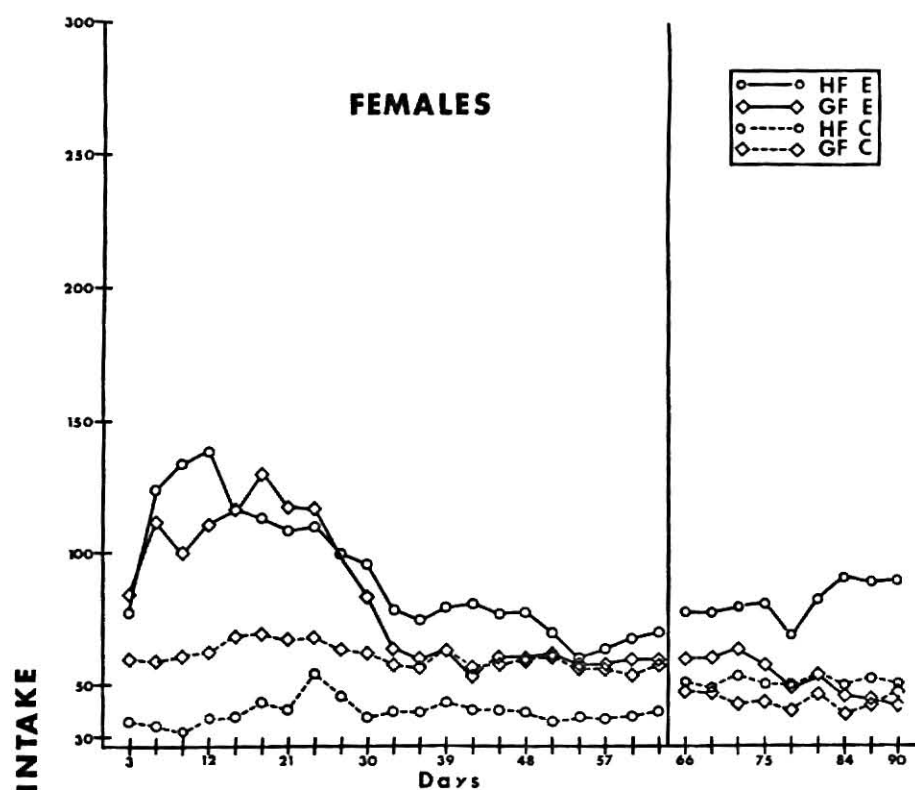
Results

Body Weight

The body weight data for Experiment II are plotted on the right side of Figure 1. Two animals died during Experiment II, one experimental male originally on the GF diet and one control from the same group. Data from these animals were not included in Experiment II, although their data were included in Experiment I. An ANOVA on the percent change in body weight from day 63 through 90 yielded the following results: there was no significant effect of the lesion by control variable and no effect of sex. There was, however, a significant effect of the diet (F = 74.60, df = 1/36, p < .01). Animals of both sexes, whether experimental or control, increased their caloric intake tremendously when switched to the HF diet. There was no significant lesion by sex interaction, but the lesion by diet and the sex by diet interactions were both significant (F = 18.60, df = 1/36, p < .01; F = 7.65, df = 1/36, p< .01, respectively). In individual comparisons, the only significant difference was between the males and females on the HF diet (F = 4.26, df = 1/36, p < .05) i.e., lesioned males gained more weight than lesioned females.

Food Intake

The right side of Figure 2 shows the food intake during Experiment II. Experimental animals of both sexes who were previously on the GF diet initially ate large quantities of the HF diet after the switch. These animals reduced their food intake to about their previous caloric intake level. Controls on HF also showed a marked increase in caloric intake to about their previous level. Changes in food intake are reflected in body weight (Fig. 1). Experimental animals of both sexes previously on the HF diet

initially exhibited a decrease in caloric intake. Throughout the 27 days
of Experiment II, experimental male animals switched to GF exhibited a
caloric intake slightly less than their controls, while the intake of the
experimental females was slightly higher than their controls. Both exper-
imental groups on GF showed a marked, prolonged decrease in food intake.

Water Intake

The right side of Figure 3 shows water intake during Experiment II.
Experimental animals of both sexes which were previously on the HF diet
exhibited an increase in water intake when switched to GF diet. This in-
crease was greater than that exhibited by the corresponding control animals.
Throughout Experiment II, experimental animals on GF maintained higher
absolute levels of water intake than did their controls. Male experimental
animals shifted to the HF diet at the reversal maintained a high level of
water intake, whereas the experimental females shifted to the HF diet did
not. Controls of both sexes showed a reversal of water intake levels at
the diet reversal, i.e., control animals previously on the GF diet reduced
their water intake to the level manifested by the HF controls in Experiment
I, while controls on the HF diet, when switched, increased their water
intake to the pre-reversal level of the controls in Experiment I.

The results of these experiments clearly indicate that there are no
sex differences in body weight gain following VMH lesions when either rela-
tive or absolute gain is considered. Females and males gain weight rapidly
and at the same rate on a high fat diet. On ground food, females and males
do become obese, if given enough time. The males on either diet had a
very large water intake during the first 40 days. A high level of water

intake is maintained by males on GF throughout the experiment (greater than any other experimental group). Compared to control females on either diet, lesioned females show an increase of water intake at first but return to control levels.

The diet has a great effect on the development of obesity. Lesioned males and females given a highly palatable diet gain weight rapidly and eventually stabilize at a much higher level than lesioned animals on the ground food diet. Lesioned males and females also consume more food (in calories) when given a palatable, calorically dense food. In contrast, lesioned animals given the GF diet ingest fewer calories and stabilize at a significantly lower weight than animals given a more palatable diet. Lesioned animals on GF do gain significantly more weight than their controls.

All groups of lesioned animals show a marked reduction of food and water intake between 30 and 40 days. At this point, the animals begin to stabilize in body weight. When the diets are reversed, animals previously on the GF diet consume a large quantity of the HF diet. Animals previously on the HF diet reduce their intake markedly. If intake is expressed in kcal/100 gm, lesioned animals switched to the GF diet eat less than their controls.

Lesioned animals appear to begin regulating their food and water in- take somewhere between 30 and 40 days. By day 63 they are controlling their food and water intake within a narrow range; however, when the diet is switched from a highly palatable to a less palatable food, lesioned animals show a marked reduction in food intake. In contrast, lesioned animals which were on a less palatable diet and given a highly palatable diet, show a huge

increase in food intake, and rapidly increase their body weight. Lesioned animals switched to the GF diet regulate their body weight at the level reached on the HF diet. Lesioned animals switched to the HF diet increase their body weight and stabilize at or near the level of the animals switched to the GF diet. Lesioned animals given the GF diet at day 63 maintain their weight at the previous level. This regulation is clearly seen in the females, but is somewhat confounded in males because of the normal steady body weight increase. Both males and females increase their water intake when they are given the GF diet at day 63, and maintain a higher level of water intake. Females reduce their water intake when switched to the HF diet, while males on HF show a decrease and then an increase to about the previous level of water intake on GF.

In summary, lesioned males do become as obese as lesioned females on either a highly palatable or ground food diet. Males on either diet show a marked water intake increase after lesioning, which is not as pronounced in females on the same diets. After the diet reversal, lesioned animals switched to the less palatable diet attempt to maintain their previous high weight; lesioned animals switched to a more palatable diet increase weight rapidly and stabilize near the weight of groups which were previously more obese. The animals switched to ground food attempt to regulate their weight by some means other than a high food intake, perhaps a reduction of activity.

DISCUSSION

The report by Cox et al. (1969) that there are sex differences in weight gain following VMH lesions is not supported by the present experiments. The duration of observation in the previous study was too short:

at 21 days, the animals in the present experiment on the GF diet were at maximum intake, and not at a point of regulation. In the present experiment, the animals were starved postoperatively to avoid inhalation of food particles. This could account for the fact that the females on the GF diet were not significantly different from their controls at 21 days. By day 27, the GF females were significantly different from their controls, but the GF males were not. In addition, experimental males on GF did not begin to surpass their controls until day 15.

The lesioned males on the GF diet dropped in weight at first, perhaps due to an uncompensated polyuria. The lesioned males on the GF diet were polyuric and, therefore, polydipsic. These animals may have been attempting to gain weight, but were losing body salts, body water and nitrogen very rapidly through the urine. If it were not for the polyuria, the males might have been different from their controls by day 21. Cox et al. (1969) do not report water intake for their animals. A consistent difference between the sexes is found only in the comparison of the water intake data.

Gold (1970) reported that VMH males get just as fat as females, but males do not begin gaining weight until second or third postoperative week. Gold's finding of no sex difference is supported by the present study, however, males were hyperphagic and showed a weight gain as soon as females (six days after surgery was begun). If the two body weight curves are superimposed on one another, males and females gained weight at the same rate on the high fat diet.

Gold (1970) also reported that males and females reach the same absolute weight and suggested that VMH lesions produce the same setpoint for

weight regulation. This result was not obtained in the present experiment. Rather, lesioned males remained relatively heavier than lesioned females. The difference in the results may be attributable to Gold's use of a random-bred strain of animals. In a random-bred strain, the variance in body weight and size is much greater in males than females. The site and extent of destruction would necessarily fluctuate as body weight fluctuates. Thus, lesions aimed at the VMH in females would be expected to produce more consistent effects, while similar lesions in males would be more variable in placement and, thus, in effect on weight. Essentially, Gold's animals all reach the same weight because more females than males show strong effects. The use of a highly inbred strain in the present experiment facilitated the observation that the relative and absolute weight gains are not controlled by sex, but that the terminal absolute weights are determined by sex.

The present experiments demonstrate that there is a sex difference in the water intake following VMH lesions; however, no persistent difference between the sexes exists in food intake or body weight gain. By using the animals' finickiness to increase the rate of weight gain (high fat diet), over the slow weight gain seen in animals on a GF diet, it is possible to show a rapid and equal gain in males and females. The finickiness will have an influence on the level at which the weight of the animal becomes relatively stable. It is known that diet composition has a great influence on the quantity of food intake in the static phase of the syndrome (Teitelbaum, 1955, 1957, 1961); therefore, it would be expected to have a great influence on the weight at which the animal stabilizes. Although all groups of animals appear to be regulating their weight and food

intake at 63 days, there must be other factors involved. For example, the body weights of the lesioned animals on the GF diet in Experiment I were in the process of stabilizing, but the body weight drastically increased when a more palatable food was given. This would suggest that some limiting factor, such as a maximal distension of the stomach and intestines, or the developing finickiness of the animals for ground food, is keeping the weight low.

The use of a strain of animals with a small variance in body size within each sex allowed for the demonstration of consistent relative gains between sexes and of different final weights.

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THE INFLUENCE OF DIET AND
SEX ON THE DEVELOPMENT OF OBESITY
FOLLOWING VENTROMEDIAL HYPOTHALAMIC LESIONS

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AN ABSTRACT OF A MASTER'S THESIS

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Male and female rats of an inbred strain were given either high fat or ground food diet following ventromedial hypothalamic lesions (16 of each sex) or sham lesions (8 of each sex). Twelve animals of each sex were given each diet. After 63 days on one of the diets, diets were reversed for 27 days. Over 63 days, lesioned animals of both sexes showed a significant increase in weight over their controls, and there was no difference in the sexes in weight gain. Lesioned animals given high fat diet were significantly heavier than those given ground food. When diets were reversed, lesioned animals now on ground food maintained about the same weight as on the high fat diet, while animals switched to the high fat diet increased their body weight to a point near that of the animals originally on the high fat diet.