Sex differences in obesity and food-directed activity in normal and hyperphagic rats

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Age-matched male and female rats with lesions in the ventromedial hypothalamic area were compared for food consumption as a function of fixed-ratio schedule and palatability of food. Results show marked sex differences in obesity; female lesioned rats gained significantly more body weight than did male lesioned rats. However, sex differences in hyperphagia were evident only when regular food was available and could be obtained at lower ratio schedules. Finally, unlike normal rats, no sex differences were evident for sucrose consumption in lesioned rats.

In a previous study, Singh & Meyer (1968) reported that electrolytic lesions in the ventromedial hypothalamic area (VMH) cause excessive food consumption and body weight gains in female rats in comparison to their male counterparts. Recently, Valenstein, Cox, & Kakolewski (1969) have confirmed this finding. However, it remains to be shown whether male VMH-lesioned rats show similar "finickiness" (i.e., overreaction to taste and caloric content of food) and motivational deficits (e.g., reduction in food intake when required to make greater effort or to tolerate electric shock) as exhibited by female lesioned rats (Teitelbaum, 1961). The question of sex differences in finickiness after VMH damage becomes extremely pertinent in light of the fact that special mechanisms have been invoked to explain finickiness (Graff & Stellar, 1962; Jacobs, 1966).

The present experiment was conducted to ascertain if both male and female VMH-lesioned rats will work as much as normal for food under an increasing fixed-ratio schedule. The experimental situation used was identical to the one used by Teitelbaum (1957), to ensure comparability between the present study and that study.

SUBJECTS AND APPARATUS

The Ss were 40 (20 male and 20 female) 120-day-old Holtzman albino rats. All rats were housed in individual cages throughout the experiment. Four identical Skinner boxes were used for training and testing. Each box contained a graduated water bottle and was placed inside a soundproof chamber.

SURGICAL PROCEDURE

After initial barpress training on CRF

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(100 reinforcements), 14 male and 14 female rats received bilateral electrolytic lesions in the VMH area, while 6 male and 6 female Ss served as sham-operated (insertion of electrode) controls. Surgery was carried out using Chloropent (Fort Dodge Laboratories) anesthesia (males—3.15 cc/kg, females—2.35 cc/kg).

The VMH-area lesions were produced using an anodal current of 3 mA passed for 20 sec on each side through the uninsulated tip (.5 mm) of a stainless steel electrode (.031-in. diam). All Ss were given intramuscular injections of 25,000 units of procaine penicillin. Three female and two male Ss were lost in surgery; therefore, the results are based on 11 female and 12 male lesioned rats.

period, each S was trained (CRF) to obtain food pellets (45-mg Noyes) in a Skinner box for a 12-h period, after which S was removed and placed in the living cage without food for 12 h. Water was available at all times in both situations. This cycle of 12 h in the Skinner box followed by 12 h of food deprivation was maintained throughout the entire experiment.

After 4 days of this initial training, each S worked under a fixed-ratio (FR) schedule of 1, 16, and 64, in ascending order, to obtain three kinds of Noyes (45-mg) food pellets: (1) regular, (2) 50% cellulose mixed by weight in regular pellets, or (3) 100% sucrose. Each schedule was maintained for 9 consecutive days before the S was shifted to the next-higher schedule. Within each schedule, each type of food was used for 3 consecutive days before the S was given another type of food. All Ss were started on regular food followed by 50% cellulose and then 100% sucrose within each schedule. Daily records of number of pellets consumed, water intake, and body weight were maintained. After this experimental period, all Ss were maintained in their living cages on ad lib food and water until the 104th postoperative day, when the final body weight was obtained.

At the end of the experiment, all Ss were perfused; their brains were removed and embedded in paraffin. Brain sections were cut at 6-micron thickness and stained in Hemotoxylin and Eosin (H & E). Brains were reconstructed to determine the locus and extent of lesions.

TRAINING PROCEDURE

After a 7-day postoperative recovery

Fig. 1. Mean food/body weight ratio for control males (N = 6), control females (N = 6), VMH males (N = 12), and VMH females (N = 11) as a function of type of food and ratio schedule.

Table 1
Mean Body Weights for Normal and Lesioned Groups as Measured During the Successive Major Phases

			Postoperative Days Weight (Grams)				
		Initial					
Condition		Weight (Grams)	2	7	34	74	104
Male Ss							
Normal (N = 6)	Mean	372.8	371.5	380.8	343.5	441.5	468.8
	SD	5.7	3.2	4.4	5.0	14.24	15.7
VMH (N = 12)	Mean	373.5	350.5	362.8	260.0	443.8	513.5
	SD	5.0	4.7	7.8	13.4	13.6	15.7
Female Ss							
Normal (N = 6)	Mean	284.0	285.5	289.8	249.3	309.5	323.3
	SD	5.5	6.1	7.5	5.5	8.5	5.6
VMH (N = 11)	Mean	283.2	256.8	283.7	200.3	484.3	550.3
	SD	5.6	6.4	7.2	13.9	38.6	48.7

RESULTS

Histology

All VMH lesions were extensive and quite comparable for male and female Ss. In all the Ss the VMH lesions bilaterally destroyed the ventromedial and arcuate nuclei. All lesions formed a continuous cavity involving the third ventricle and extended to the base of the brain. In quite a few Ss dorsomedialis was destroyed, and in a few there was damage to the fornix. The anterior-posterior extent of lesions was large and extended from just behind the optic chiasma to the mammillary body.

Though there was some variation in the extent of damage among Ss, there was no significant relationship between the extent of damage and food intake and weight gain. A similar lack of relationship between extent of VMH lesion and obesity or hyperphagia is reported by other investigators (Valenstein et al, 1969).

Food Consumption

Since initial body-weight differences for male and female Ss were large, the ratio of number of food pellets/body weight (g) was computed for each S for each day. Figure 1 presents mean food/weight ratios for all groups, based on 3 days of testing for each type of food under each schedule. Under FR-1 schedule both male ($t = 2.41$, $df = 16$, $p < .05$) and female ($t = 3.31$, $df = 15$, $p < .01$) lesioned rats ate significantly more than their respective controls. Furthermore, under the same conditions, lesioned females ate significantly more than lesioned males ($t = 2.43$, $df = 21$, $p < .05$). When the ratio was increased to 16, both male and female lesioned rats drastically reduced food intake. Under FR-64, both lesioned male and female Ss further reduced their food intake and did not significantly differ from each other, though they ate significantly less than their respective controls.

Under 50% cellulose food, no sex differences were evident for any ratio schedule. Both lesioned groups sharply reduced food intake as the ratio was increased.

When 100% sucrose was available, the control females ate significantly more than the control males ($t = 2.67$, $df = 10$, $p < .05$) under the CRF schedule. No significant differences were evident for FR-16 or FR-64. The sex differences for sucrose consumption in normal rats has been reported previously (Valenstein, Cox, & Kakolewski, 1967; Zucker, 1969). The low consumption of sucrose by lesioned rats is quite surprising: On the basis of the hyperreactivity-to-taste hypothesis (Corbit & Stellar, 1964), it was expected that VMH lesioned Ss would eat more sucrose than their controls; however, both lesioned male ($t = 4.65$, $df = 16$, $p < .01$) and female ($t = 3.81$, $df = 15$, $p < .01$) Ss ate significantly less than their respective controls under the FR-1 schedule. Lesioned Ss ate significantly less than controls under all ratio schedules. Furthermore, no sex differences were evident for lesioned male and female Ss for any ratio schedule. However, it should be pointed out that low sucrose consumption could be due to an interaction of lesion with the effect of the preceding 3 days of exposure to the cellulose diet. Nonetheless, within the confines of the present experimental design, both lesions and an increase in the ratio schedule obliterate sex differences in sucrose consumption.

In summary, ratio schedules caused all groups to eat less under all three types of food, with the most marked decline in the lesioned groups. This finding, that VMH-lesioned rats work less for their food as ratio schedule increases, is consistent with previous reports (Teitelbaum, 1961). Finally, also consistent with previous reports (Singh & Meyer, 1968), the water/food ratios were approximately the same for all Ss under all types of food and ratio schedules.

Body Weight

Table 1 presents mean initial, 2nd, 7th, 34th, 74th, and 104th postoperative-day body weight for all groups. All Ss were on ad lib food and water from the 1st through the 7th postoperative day (postoperative

recovery period), under 12-h food-deprivation cycle from the 8th through the 34th postoperative day (testing period), and had ad lib access to food and water from the 35th through the 104th postoperative day.

The weight loss evident in Ss on the second postoperative day could be attributed to the anesthetic agent and surgery; surprisingly, VMH-lesioned Ss ate very little during the first 2 postoperative days. At the end of the 7-day recovery period, all control Ss weighed slightly more than their initial body weight, while lesioned Ss did not. The weight losses appearing for all groups on the 34th postoperative day could be attributed both to a reduction in food consumption from the ratio schedules and to the 12-h deprivation cycle maintained during testing. The maximum weight loss was shown by lesioned Ss in this period. However, during subsequent ad lib feeding (35th through 104th postoperative day), all Ss gained in body weight. By the 74th postoperative day, the lesioned females surpassed their controls in body weight, while the lesioned males did not. The role of sex differences becomes striking at the end of the ad lib period: the female lesioned group gained a mean of 223 g, while the lesioned males gained only 43 g, compared to their respective control groups.

DISCUSSION

The obtained results show that, within the limits of the experimental period, lesioned female rats gain more body weight than do lesioned male rats. The sex differences among VMH-lesioned rats are consistent with previous findings (Singh & Meyer, 1968; Cox et al, 1969; Valenstein et al, 1969). However, in a recent study, Gold (1970) has shown that if female lesioned rats are equated for body weight with male lesioned rats and both are maintained on high-fat diets, there are no sex differences in body weight gain. Thus, it will appear that under certain dietary conditions marked sex differences in weight gain after VMH lesioning may not be evident.

Sex differences in hyperphagia were evident only when food was regular and could be obtained on lower ratio; when the quality of the food was changed or effort to obtain food was increased, there were no sex differences. Surprisingly, VMH damage obliterates the differences for sucrose consumption that are otherwise obtained between normal male and female rats. It should be pointed out, however, that in the present study different types of food were not counterbalanced, and hence, there is a possibility that the findings may be confounded. This possibility of

confounding is ruled out in our later research, where the quality of food was counterbalanced, and essentially the same results were obtained (unpublished study). The lack of sex differences is also observed when VMH-lesioned male and females are tested for reaction to electrical shock on a passive avoidance test or on a timing behavior test (unpublished study).

The basis for the presence of sex differences after VMH damage in obesity and absence of it in "finickiness" is not clear. It is possible, as suggested by Cox et al. (1969), that sex differences in obesity after VMH damage reflect some differential endocrinological and metabolic effects in males and females. The role of some metabolic factor contributing to the body weight can be inferred from those studies which have shown that VMH-lesioned rats gain more weight than do control animals of the same caloric intake (Brooks & Lambert, 1946). The endocrinological factor can be inferred from those studies which report that gonadectomy results in greater weight gains in females but decreased weight gains in males (Kakolewski, Cox, & Valenstein, 1968). Furthermore, Cox et al. (1969) report that male rats castrated and lesioned at the same time exhibit greater weight gains following VMH damage than do noncastrated VMH-lesioned males.

On the basis of these reports, if it is accepted that resultant obesity from VMH damage is at least partly governed by sex-related endocrinological factors, the lack of sex differences in finickiness would imply that finickiness was governed by some separate neural mechanism that is relatively insensitive to sex-related endocrinological factors. The existence of such separate, but overlapping, neural mechanisms for obesity and finickiness within the VMH area has been hypothesized by Graff & Stellar (1962). If further experimental data sustain their hypothesis, the present finding can be explained within that context, adding that while the neural mechanism for obesity is affected by sex differences, the mechanism for finickiness is not.

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Reversal learning in birds as a function of amount of overtraining*

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Bobwhite quail were given 80, 240, 400, 640, or 2,000 overtraining trials after learning a simultaneous visual-pattern discrimination and were then reversed. Reversal performance after all levels of overtraining either did not differ from or was significantly inferior to that of nonovertrained birds. Failure to obtain an ORE was attributed to the fact that overtraining did not reduce responding to an irrelevant position dimension.

Mackintosh (1969) has recently demonstrated that the presence of both a difficult simultaneous visual discrimination and a large reward are sufficient (if not necessary) conditions for the occurrence of the overtraining reversal effect (ORE) in rats. However, using a difficult pattern task and a large magnitude of reward, Matyniak (1970) failed to find any evidence of an ORE in pigeons, indicating that other factors may be important in obtaining the ORE in birds.

A review of avian ORE studies suggests that number of overtraining trials may be a relevant variable. Mackintosh (1965) obtained an ORE in young chicks given 100 overtraining trials, but both Schade & Bitterman (1965) and Matyniak (1970) found that 200 overtraining trials did not facilitate reversal learning in pigeons. Williams (1967) obtained an ORE in pigeons receiving 500 overlearning trials, but in another experiment with pigeons the same number of trials produced no ORE

(Marsh & Johnson, 1968). Finally, Eimas (1967) and Birnbaum (1967) have obtained results suggesting that number of overtraining trials is related to the occurrence of an ORE in rats. Birnbaum, for example, found that 400 overtraining trials facilitated reversal learning, but 200 did not.

The present experiment was designed to determine if the variability of the ORE data in birds could be partially accounted for by differential effects of amount of postcriterion training on speed of reversal learning. Since no single experiment with birds has systematically investigated the effects of varied amounts of overtraining, it was decided to include a number of different levels of overtraining that extended over a wide range.

METHOD

The Ss were 48 male adult bobwhite quail, *Colinus virginianus*, approximately 4-6 months old. Upon arrival at the laboratory, Ss were quartered in individual wire cages in which both food and water were continuously available for 1 month prior to the beginning of the experiment.

The apparatus consisted of a rectangular discrimination chamber, 21 x 11 x 17 in., constructed of ¼-in. Masonite. Three Gerbands transparent circular-response keys, ¾ in. in diam, were mounted on the rear wall of the chamber and were 1½ in.