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Behavioral Changes Following VMH Lesions in Rats With Controlled Insulin Levels[1]

THOMAS R. VILBERG[2] AND WILLIAM W. BEATTY

Department of Psychology, North Dakota State University, Fargo, ND 58102

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VILBERG, T. R. AND W. W. BEATTY. *Behavioral changes following VMH lesions in rats with controlled insulin levels.* PHARMAC. BIOCHEM. BEHAV. 3(3) 377–384, 1975. – The effects of ventromedial hypothalamic (VMH) lesions were studied in female rats made diabetic with streptozotocin that were given twice daily injections of protamine zinc insulin (0.75 μ/100g/day) and in non-diabetic animals of the same sex. Hyperphagia resulted from VMH lesions in both diabetic animals whose insulin levels were controlled and in non-diabetic animals. All animals with lesions exhibited persistent increases in feeding during the light protion of the light–dark cycle. Significant increases in body weight gain were observed in both diabetic and non-diabetic lesioned animals, but the magnitude of weight gain was greater after VMH lesions in non-diabetic rats. VMH lesions also reduced wood-gnawing and increased emotionality, aversion to quinine and reactivity to electric shock. None of the behavioral changes were dependent on hyperinsulinemia, although hyperinsulinemia may contribute to the magnitude of certain of these effects.

VMH Lesions Insulin Diabetes Streptozotocin Emotionality Food intake Body weight Wood gnawing Finickiness Pain sensitivity

VENTROMEDIAL hypothalamic (VMH) lesions result in hyperphagia, obesity and hyperinsulinemia in adult animals of several species [11]. Recently, considerable attention has been devoted to examining the interrelationships among these effects. While it is clear that hyperinsulinemia develops after VMH lesions in the absence of both hyperphagia and obesity [10,12], the question of whether hyperphagia and obesity can develop in the absence of hyperinsulinemia is not yet resolved. In weanling rats, which do not usually display either hyperphagia or increased weight gain following VMH lesions, hyperinsulinemia is observed [7,9], suggesting that hyperinsulinemia and hyperphagia are dissociable, at least in immature animals. Furthermore, Friedman [6] observed hyperphagia and increased weight gain, both in non-diabetic rats with VMH lesions and in alloxan-diabetic lesioned animals given controlled doses of insulin. In contrast, York and Bray [23], who induced diabetes with streptozotocin, concluded that hyperinsulinemia was necessary in order for hyperphagia and obesity to develop after VMH lesions. Since York and Bray's findings are at variance with Friedman's work, we attempted to replicate part of York and Bray's experiment, inducing diabetes with streptozotocin as they did.

VMH lesions also cause a number of other changes in behavior including an increase in the percentage of food consumed during the light portion of the light–dark cycle [1,13], increased sensitivity to electric shock [20], increased emotionality [22], finickiness [4,19], and reduced wood gnawing [2, 5, 16]. A second purpose of the current work was to examine the dependence of these behavioral effects of VMH lesions upon hyperinsulinemia.

METHOD

Animals

Twenty-nine albino female rats of the Holtzman strain that initially weighed 261–322 g were divided at random among four treatment conditions: VMH lesion-diabetic (N = 5); VMH-non-diabetic (N = 7); Sham operation-diabetic (N = 8) or sham operation-non-diabetic (N = 9). Data from four additional lesioned animals that did not meet the histological criteria were discarded. The animals were caged singly with food (Purina Lab Chow pellets) and a pine wood block (approximately 4 × 4 × 2 cm) continuously available in an animal room maintained at 27 ± 2°C which was illuminated from 0700 to 1900. Tap water was avail-

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[2] Now at Bowling Green State University.

able ad lib except during the finickiness test when quinine or saccharin-adulterated water was provided.

Surgery and Histology

Bilateral VMH lesions were produced on Day 24 under Chloropent anesthesia (Fort Dodge Laboratories, Fort Dodge, Iowa; 2 cc/kg) supplemented by atropine sulfate (0.05 mg) to reduce mucus secretion. With the rat's head held approximately horizontal between bregma and lambda, 2.4 mA DC from a Nuclear Chicago constant current stimulator was passed between the brain anode (a O ga stainless steel insect pin insulated except for 0.5 mm at the tip with Epoxylite) and the animal's tail which was immersed in a saline bath and served as the cathode. The target coordinates in mm with respect to bregma were: 2.7 P, 0.6 L and 8.7 below the surface of the cortex. Sham operated animals received a scalp incision at the same time.

At the conclusion of the experiment all rats with lesions were sacrificed with an overdose of Chloropent and perfused with saline and Formalin. Frozen sections were cut at 40 μ on a cryostat, stained with cresyl violet [18] and reconstructed with the aid of the König and Klippel [14] atlas. Damage was quantified as described in detail elsewhere [21]. In brief the VMH was defined as the region ventral to a line connecting the fornices, medial to a line perpendicular to the first line, extending from plates 31 to 37 of the atlas [14]. This region was subdivided into 62 blocks each 0.5 X 0.5 X 0.25 mm and destruction of more than 50% of a block was scored as 1 unit of damage. Extra-VMH damage was scored in the same way. The non-diabetic group incurred damage to a mean of 34.3 blocks within the VMH (SD = 8.0) and 8.3 blocks outside the VMH (SD = 7.7), while the VMH-diabetic group sustained damage to a mean of 33.4 blocks within the VMH (SD = 5.7) and 10.2 blocks outside the VMH (SD = 6.1). Nearly all damage outside the VMH was anterior to the VMH nuclei as shown in the representative lesion depicted in Fig. 1.

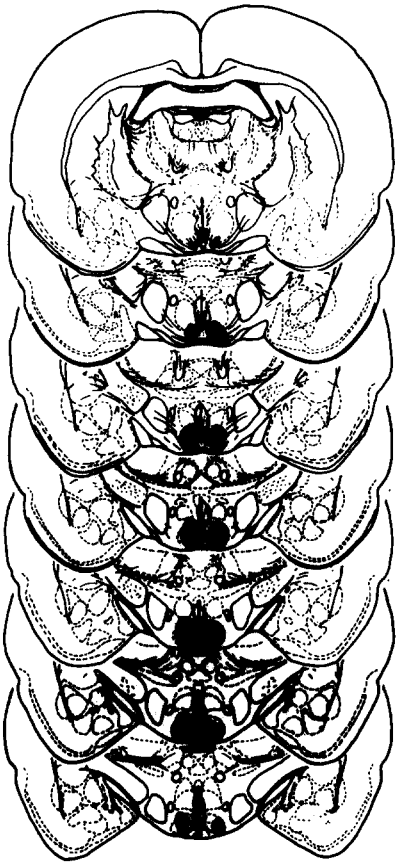

FIG. 1. A typical VMH lesion reconstructed on consecutive plates from the König and Klippel [14] atlas. The top plate is Plate Number 29; the bottom plate is Number 35.

Procedure

Table 1 summarizes the order of treatments and measurements. Following a 3 day period (P) of pretreatment measures of food intake, body weight and wood gnawing, diabetes mellitus was induced in 16 animals by injecting freshly prepared Streptozotocin (Upjohn U9889, 65 mg/kg in citrate buffer, pH = 4.5) into the tail vein. Non-diabetic controls received equivolume (0.10 cc/100g) injections of the citrate buffer.

Glycosuria was measured 3 days later (Day 7) using Tes-Tape (Eli Lilly and Co., Indianapolis) which had been checked against glucose standards. On this test all streptozotocin-injected rats passed urine which contained at least 2% glucose while all buffer-injected animals passed urine containing 0% glucose. After 13 days of insulin treatments two streptozotocin treated rats passed urine containing 0.1% glucose while two passed urine containing 0.25% glucose; the remaining rats in both groups exhibited 0% glucose in the urine on the second test.

Beginning on Day 8 and continuing for the duration of the experiment animals that received streptozotocin injections on Day 4 were injected twice daily immediately after weighing with 0.325 U/100g Protamine Zinc Insulin (Eli Lilly, U-100) subcutaneously; animals in the non-diabetic groups received an equivalent volume of the distilled water vehicle (0.10 cc/100 g). Body weight, food intake and wood gnawing were measured twice daily at 0700 and 1900 during the P, S, I, L, and E periods as indicated in Table 1. Additional procedural details are reported elsewhere [21]. Emotionality was assessed by determining whether or not the animal bit the experimenter during evening injections on the first 5 days after the lesions were produced (Days 25–29). Shock thresholds were determined on Day 49 using a modified method of limits. The rat was placed in a Plexiglas chamber (30.48 X 20.32 X 30.48 cm) with a grid floor made of 0.32 cm bronze rods spaced 1.27 cm apart. Two observers located in an adjacent rooms classified the rat's motor behavior into four mutually exclusive categories: No Response; Flinch – the animal made a brief motor response, usually at shock onset; Shuffle – the animal moved all four feet; or Jump – the animal removed all four feet from the grid. The incidence of vocalization was also noted. Shocks of 0.5 sec duration were delivered with an intershock interval of 5–20 sec from a Grason Stadler E700 source. Intensities of 0.05, 0.06, 0.08, 0.10, 0.13, 0.16, 0.20, 0.25, 0.30, 0.40, 0.50, 0.60, 0.80, 1.0, 1.3, 1.6 and 2.0 mA could be delivered. The first ascending series began with 0.05 mA and continued until both raters agreed that the rat had made three consecutive jump responses. This current value served as the initial value for the first descending series. Shock intensity was lowered in steps

TABLE 1

SEQUENCE OF EXPERIMENTAL TREATMENTS AND OBSERVATIONS

Day	Treatment	Period	Observation
1–3		Pretreatment (P)	12 hr body weight, food intake, wood gnawing
4	Streptozotocin/buffer injected		
5–7		Strepto (S)	12 hr body weight, food intake, wood gnawing
7	Streptozotocin efficacy verification		Glycosuria
8	Insulin injections initiated		
9–23		Insulin Replacement (I)	12 hr body weight, food intake, wood gnawing
20	Insulin efficacy verification		Glycosuria
24	VMH/Sham lesions produced		
25–39		Lesion Period (L)	12 hr body weight, food intake, wood gnawing
25–29	Emotionality		Frequency of attacking experimenter
50	Reactivity to shock		Flinch, shuffle, jump and vocalize thresholds obtained
55–79	Finickiness Test		One bottle fluid consumption
55–59			Water intake
60–63			Saccharin intake
64–69			Water intake
70–73			Quinine intake
74–79			Water intake
91–93		End Period (E)	12 hr body weight, food intake, wood gnawing

until both raters agreed the rat had not responded on 3 consecutive trials. Each animal received three ascending and descending series. Thresholds for each response category were taken as the arithmetic mean of the highest value clearly above threshold and the lowest value clearly below threshold. Interrater reliability ranged from 0.74 for the shuffle threshold to 0.88 for the flinch threshold and differences between raters did not affect conclusions about treatment effects.

Reactivity to saccharin (0.13% sodium saccharin dihydrate, Matheson Coleman and Bell) and quinine (0.013% quinine hydrochloride, Sigma) was assessed on the days indicated in Table 1. Fluid intake was measured every 12 hr at the onset of the light and dark periods and the calibrated drinking tubes were refilled with fresh solutions at the time of measurement. Tap water was available except when saccharin or quinine were tested; only one fluid was available at any one time. One rat from the VMH-diabetic group failed to consume the quinine fluid and died, apparently in an insulin coma. It's data from the quinine period were discarded.

RESULTS

Body Weight

Mean body weights are shown in Fig. 2. During the streptozotocin block (S) animals injected with streptozotocin showed a greater decrease in weight than buffer-injected controls, $F(1,25) = 22.07$, $p<0.001$. During insulin replacement (I) all animals exhibited increased weight gain

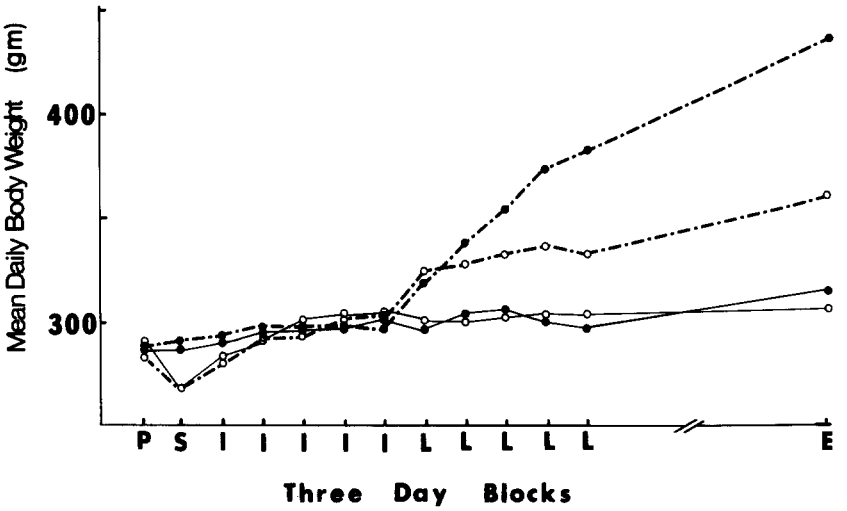

FIG. 2. Mean body weight during various stages of the experiment. Each data point is the mean value for three consecutive days. Legend: Open circles = diabetic; Filled circles = non-diabetic; Broken lines = VMH lesions; Solid lines = sham operates. Streptozotocin was injected immediately prior to S. Insulin replacement began just before I and continued for the remainder of the experiment. Lesions were produced prior to L.

but the diabetic groups that were now receiving insulin gained weight more rapidly (Streptozotocin X Blocks: $F(1,25) = 17.84$, $p<0.001$), recovering the weight lost during stage S.

VMH lesions produced significant increases in weight gain, regardless of whether or not the animals had controlled levels of insulin (see Stage I on Fig. 2). Prevention of hyperinsulinemia did influence the amount of weight gained; the non-diabetic rats with VMH lesions gained more weight than diabetic lesioned animals. Analysis of the data during Stage L revealed significant effects of Lesion, $F(1,25) = 65.04$, $p<0.001$; Streptozotocin, $F(1,25) = 4.72$, $p<0.05$ and Blocks, $F(4,100) = 22.69$, $p<0.001$. In addition, all of the two-way and the three-way interactions among these variables were significant beyond the 0.05 level. Subsequent analyses revealed that by the fifth block of the L period, animals in the non-diabetic VMH group were heavier than animals in any other group. Diabetic rats with VMH lesions were also heavier than animals in either of the non-lesioned groups; there was no difference in body weight between the diabetic and non-diabetic controls. These group differences in body weight persisted to the end of the experiment (E).

Food Intake

Food intake data throughout the experiment are presented in Fig. 3. Because animals destined to receive streptozotocin ate less than the buffer-treated animals ($p<0.05$) prior to any experimental treatment, analyses were conducted on both the absolute food intake data and upon difference scores computed by subtracting food intake during Stage S from that in Stage P. Neither analysis revealed any significant effect of streptozotocin. During the insulin replacement phase (I), the diabetic groups exhibited marked increases in food intake $F(1,25) = 181.60$, $p<0.001$, especially during the first 3 blocks (Streptozotocin X Blocks: $F(4,100) = 5.31$, $p<0.001$).

VMH lesions caused hyperphagia regardless of whether or not the animals were diabetic and receiving maintenance doses of insulin (see Phase L of Fig. 3). The effects of Lesion $F(1,25) = 116.85$, $p<0.001$, and Streptozotocin, $F(1,25) = 16.79$, $p<0.001$, were significant and essentially additive over the 15-day measurement period Lesion X Streptozotocin: $F(1,25) = 1.16$. There was some difference in the time course of hyperphagia in the two lesioned groups, as evidenced by a significant Lesion X Streptozotocin X Blocks interaction, $F(4,100) = 6.33$, $p<0.001$. By the end of the study (E) hyperphagia had diminished, but non-diabetic lesioned animals ate more than their controls ($p<0.05$).

Circadian Pattern of Food Intake

Table 2 presents the mean percentage of food consumed during the dark portion of the light–dark cycle during different stages of the experiment. During stage S diabetic animals ate a greater percentage of their food during the dark than non-diabetic animals, $F(1,25) = 5.21$, $p<0.05$. Insulin treatment twice daily (Stage I) reversed this difference, $F(1,25) = 5.19$, $p<0.05$. This effect persisted throughout the experiment.

VMH lesions reduced the percentage of food consumed during the dark; this effect was observed during Stage L, $F(1,25) = 62.30$, $p<0.001$, and at the end of the experiment, $F(1,23) = 19.19$, $p<0.001$, when the lesioned animals were only slightly hyperphagic. Moreover the shift in feeding toward the day caused by VMH lesions was observed in both diabetic and non-diabetic groups.

Wood Gnawing

Figure 4 presents the mean amount of wood gnawed during three-day periods throughout the experiment. No differences were observed during the P and S stages of the study. During the insulin phase (I), wood gnawing declined

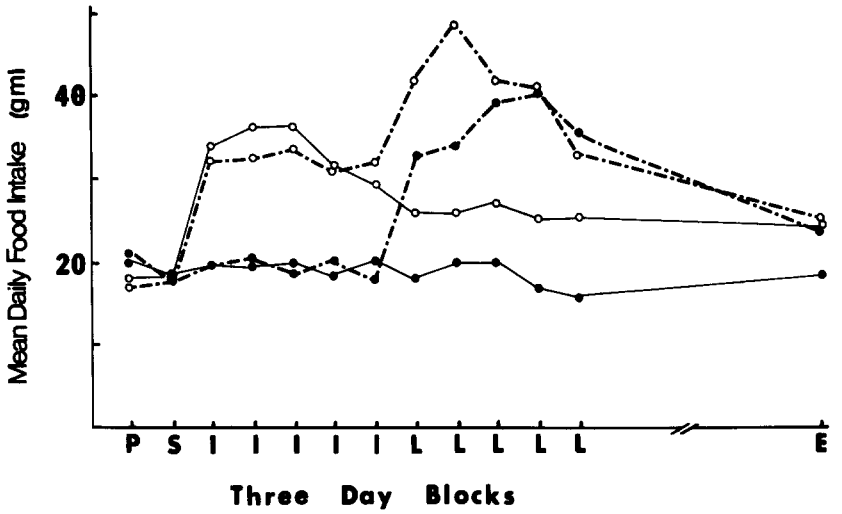

FIG. 3. Mean food intake during various stages of the experiment. Each data point is the mean value for three consecutive days. Legend: Open circles = diabetic; Filled circles = non-diabetic; Broken lines = VMH lesions; Solid lines = sham operates. Streptozotocin was injected immediately prior to S. Insulin replacement began just before I and continued for the remainder of the experiment. Lesions were produced prior to L.

TABLE 2

MEAN PERCENT FOOD CONSUMED DURING THE NIGHT

Experimental Stage	Nondiabetic		Diabetic	
	Control	VMH	Control	VMH
P	73.8	71.7	70.9	77.3
S	67.4	64.9	74.9	72.9
I	71.0	70.0	66.4	65.2
L	69.6	55.6	64.9	56.6
E	73.7	59.3	61.7	54.2

in all groups and the diabetic animals receiving insulin gnawed less than the non-diabetic groups, $F(1,25) = 21.94$, $p<0.001$. This effect did not persist in later phases of the study.

VMH lesions significantly depressed gnawing, both during Stage L, $F(1,25) = 16.99$, $p<0.001$, and in Stage E, $F(1,23) = 11.63$, $p<0.01$, regardless of whether or not the animals had controlled levels of insulin.

Reactivity to Electric Shock

Mean thresholds for each of the behavioral responses are presented in Table 3. VMH lesions significantly reduced the current required to elicit flinch, shuffle and jump responses, $F(1,24) = 4.71$, 11.07, and 9.45 respectively, $ps<0.05$, 0.005, 0.01 respectively, but did not affect the vocalization threshold ($p>0.20$). Streptozotocin did not affect performance on any measure, nor was there evidence of a significant Streptozotocin X Lesion interaction on any measure.

Emotionality

The number of days each animal bit the experimenter during weighing was recorded on Days 2–6 after production of the lesions. All 5 animals in the diabetic-VMH group and 5 of 7 animals in the non-diabetic VMH group exhibited biting behavior, while only one non-lesioned animal (in the diabetic group) bit the experimenter.

Separate Fisher Exact Probability tests confirmed differences in the incidence of biting between lesioned and non-lesioned subjects for both diabetic and non-diabetic conditions (both $p<0.01$). Differences between lesioned diabetics and non-diabetics were not significant.

Finickiness Test

Average daily fluid intake during the various phases of the finickiness test is shown in Fig. 5. Diabetic animals receiving insulin drank significantly greater amounts of fluids at every stage of the test except when saccharin was present (all $p<0.001$ except during saccharin. These effects were not dependent on the integrity of the VMH and except for the quinine phase, interactions between Streptozotocin and Days were not significant. When quinine-adulterated water was the sole source of fluid, the diabetic-insulin treated animals exhibited greatly reduced intake on the first day followed by substantial recovery on subsequent days. Fluid intake was depressed throughout the quinine test in the non-diabetic groups and consequently the Streptozotocin X Days interaction was significant, $F(3,69) = 7.71$, $p<0.001$. VMH lesions depressed fluid intake during the quinine phase, $F(1,23) = 4.90$, $p<0.05$, but did not cause reliable changes in consumption of unadulterated water or saccharin.

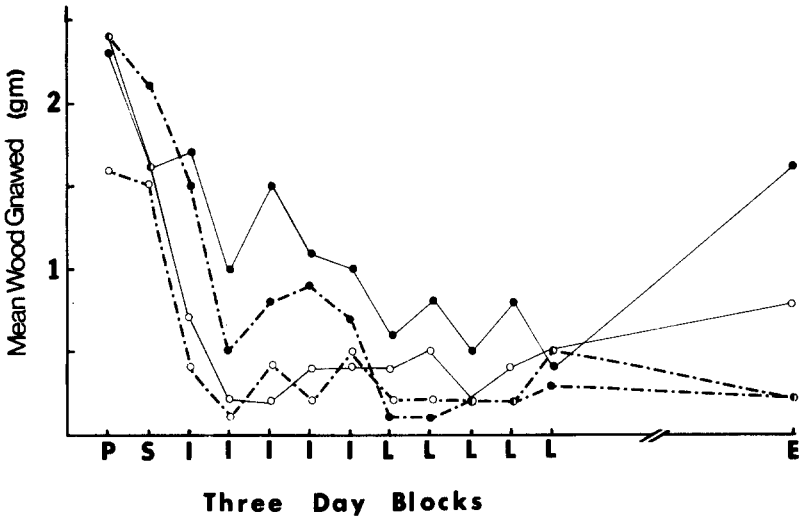

FIG. 4. Mean wood gnawing during various stages of the experiment. Each data point is the mean grams of wood gnawed during consecutive three day periods. Legend: Open circles = diabetic; Filled circles = non-diabetic; Broken lines = VMH lesions; Solid lines = sham operates. Streptozotocin was injected immediately prior to S. Insulin replacement began just before I and continued for the remainder of the experiment. Lesions were produced prior to L.

TABLE 3

MEAN SHOCK THRESHOLDS (mA)

Group	N	Flinch	Shuffle	Jump	Vocalize
Non-diabetic Control	9	0.132	0.300	0.596	0.288
Non-diabetic VMH	6	0.110	0.240	0.444	0.211
Diabetic Control	8	0.121	0.284	0.546	0.184
Diabetic VMH	5	0.086	0.200	0.408	0.194

DISCUSSION

In the present experiment VMH lesions resulted in hyperphagia and increased weight gain, both in animals which were not diabetic and presumably developed hyperinsulinemia as well as in animals which were diabetic and receiving controlled amounts of insulin designed to maintain their insulin at the same level as that of non-lesioned controls. These findings are quite similar to those of Friedman [6] who produced diabetes with alloxan. Friedman also observed that the degree of hyperphagia was somewhat greater in insulin-treated diabetic rats with VMH lesions than in lesioned animals that were not diabetic, but the non-diabetic lesioned animals gained more weight than the insulin-treated diabetic animals with VMH lesions. As in the present study, Friedman reported that diabetic insulin-treated rats with VMH lesions gained more weight than either non-diabetic or diabetic-insulin-treated controls.

York and Bray [23] induced diabetes with streptozotocin either before or after they produced lesions of the VMH. When induction of diabetes preceded VMH lesions hyperphagia and weight gain were prevented; replacement therapy with controlled doses of insulin maintained eating and body weight or increased food intake and weight gain depending on the dose of insulin. With insulin levels controlled the rats with VMH lesions gained weight no more rapidly than their appropriate controls. When diabetes was produced after destruction of the VMH, hyperphagia and the development of obesity were interrupted; replacement therapy with insulin led to a similar pattern of recovery of eating and weight gain in both lesioned and control animals. York and Bray [23] concluded: "The hyperphagia which follows ventromedial lesions is secondary to increased insulin secretion." (page 892).

Obviously the findings of York and Bray [23] are not in agreement with the results of Friedman [6] or those of the

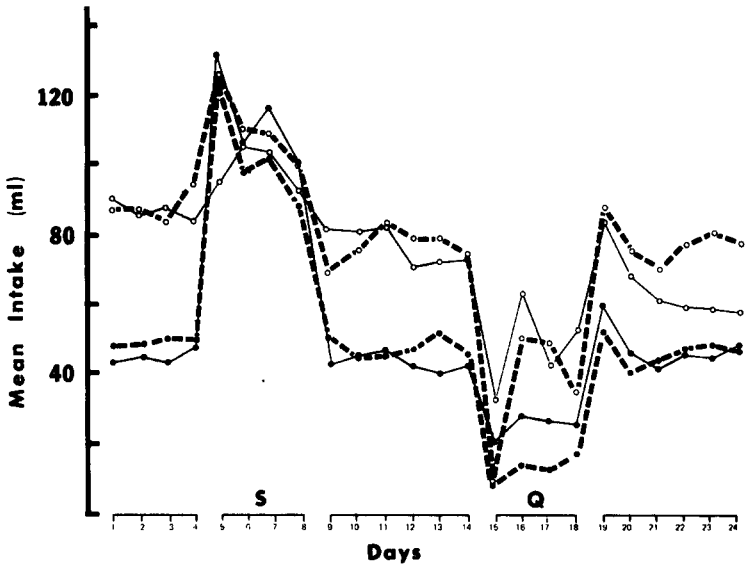

FIG. 5. Mean daily fluid intake during the finickiness tests. Legend: Open circles = diabetic; Filled circles = non-diabetic; Broken lines = VMH lesions; Solid lines = sham-operates. During the period labelled S saccharine was the only source of fluid. During Q only quinine was available. At other times tap water was the fluid source.

present study, but the reasons for this discrepancy are not clear. In most respects the procedures used by York and Bray seem to be very similar to the ones employed in the present work. We employed twice daily insulin injections while York and Bray injected insulin only once a day but this procedural difference is probably not crucial since Friedman also used a single daily insulin injection. Differences in size or location of the VMH lesions might account for the discrepancies in the results, but the possibility is difficult to evaluate since York and Bray did not present histological results.

Finally, differences in the degree of destruction of the pancreatic β cells could explain the discrepancies in the results of the Friedman [6], the York and Bray [23] studies and the current work.

Although all of the animals in our diabetic groups exhibited clear signs of glycosuria three days after streptozotocin treatment, the possibility that some recovery of pancreatic function occurred subsequently cannot be ruled out. If such recovery did occur, then the diabetic-lesioned animals could have developed a mild degree of hyperinsulinemia. This possibility seems slight in view of the fact that the diabetic control group displayed chronic elevation of both food and water intake, symptoms which are associated with the diabetic state.

With these considerations we conclude that hyperinsulinemia is necessary neither for the hyperphagia nor for the greater than normal weight gain that develop following VMH lesions in adult female rats, although hyperinsulinemia may contribute to the magnitude or the time course of these effects. If hyperinsulinemia contributes to weight gain in rats with VMH lesions it does so only if hyperphagia is permitted to develop. Mature rats with VMH lesions, pair-fed to controls, develop a modest degree of hyperinsulinemia, but gain less weight than non-lesioned controls [8]. Moreover other data question the view that VMH lesions cause hyperphagia by inducing hyperinsulinemia. Non-diabetic animals with VMH lesions do not eat as much as controls in response to high doses of exogenous insulin [15] and hyperinsulinemia does not occur in weanling animals with VMH lesions if they are restricted to four hour daily access to food [8]. Further direct injections of glucose or glucose and insulin into the VMH inhibit feeding after a latent period of at least four hours [15]. These observations suggest that VMH lesions probably do not remove a tonic source of inhibition over insulin secretion, but instead disturb a portion of the system which adjusts feeding to changes in endogenous glucose and insulin levels.

Regardless of whether or not they were diabetic and receiving insulin injections, rats with VMH lesions increased the percentage of food they consumed during the daylight hours, although the magnitude of the lesion-induced shift in feeding rhythms was somewhat altered in the diabetic animals. Although the present data indicate that hyperinsulinemia is not essential to the shift toward daylight feeding, it is not possible to conclude that hyperinsulinemia is of no importance in this effect. The fact that insulin injections increased the percentage of food consumed during the day and in fact reversed the initial effect of streptozotocin treatment, may indicate an involvement of insulin in controlling feeding patterns during the day or it may merely be an artifact of the twice daily injection regimen employed in the current work.

It is also interesting to note that increases in the percentage of food consumed during the day by rats with VMH lesions persisted until the end of the present study (68 days after the lesions were produced). At this time food intake had returned to nearly normal levels. Similar findings have been reported by Kakolweski *et al.* [13]. It should be noted that incidental damage to the dorsomedial hypo-

thalamus may have contributed to the shift toward daylight feeding. Lesions of the dorsomedial hypothalamic nuclei have been reported to increase the percentage of food consumed during the day in weanling male rats [3].

In agreement with earlier studies [2, 5, 16] VMH lesions depressed wood gnawing. This effect was observed in both diabetic and non-diabetic animals, eliminating the possibility that hyperinsulinemia is necessary to the reduced wood gnawing that accompanies VMH lesions. Although insulin treatment did temporarily reduce gnawing, streptozotocin did not affect gnawing. Thus, hyperinsulinemia probably does not contribute to the effect of VMH lesions on wood gnawing.

VMH lesions also reduced thresholds for eliciting flinch, shuffle and jump responses but did not affect vocalization thresholds. Except for the vocalization measure, these results replicate the findings of Turner *et al.* [20]. Here the data indicate that hyperinsulinemia is not involved in the lesion-induced increases in reactivity to electric shock. Diabetic animals, regardless of whether or not they received lesions, always exhibited slightly lower thresholds than non-diabetic animals. Thus, if hyperinsulinemia has any influence at all on reactivity to shock it must be to reduce rather than enhance sensitivity. A similar conclusion seems to apply to the increased emotionality following VMH lesions. Like the increased reactivity to electric shock this behavioral change seems unrelated to changes in insulin level.

VMH lesions increased rejection of quinine but failed to alter consumption of saccharin, replicating previous findings [17]. The finding that diabetic rats with VMH lesions resumed drinking of appreciable amounts of quinine much earlier than non-diabetic animals with lesions does not necessarily mean that hyperinsulinemia contributes to the quinine aversion induced by VMH lesions, although it may. The fact that the diabetic animals with VMH lesions resumed drinking quinine on the second day of the test more likely reflects their greater need for water, a possibility that is supported by the greatly increased water intake of both diabetic groups and the observation that the only animal in the diabetic-VMH group that did not resume drinking on the second day of the quinine test died in a coma on the following day. It is also important to note that on the first day of the quinine test animals in the diabetic-VMH group drank no more than non-diabetic animals with lesions. This low level of consumption represented a much greater reduction in fluid intake for the diabetic lesioned animals than for the non-diabetic VMH group. In short, there is no reason to assume that hyperinsulinemia is a necessary condition for the increased quinine aversion displayed by animals with VMH lesions; a subtle contribution of hyperinsulinemia to the magnitude of the finickiness phenomenon cannot be ruled out at present.

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