EMOTIONAL BEHAVIOR FOLLOWING LESIONS OF THE VENTROMEDIAL NUCLEUS OF THE HYPOTHALAMUS IN THE RAT

by

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Abstract

Grossman (1966) formulated the hypothesis that the behavioral effects of ventromedial hypothalamic (VMH) lesions were due to an enhancement of the emotional responsiveness of the animal towards all sensory stimuli. In this study, following the placement of bilateral VMH lesions in adult, female hooded rats, behavioral measures were taken in an open-field; on resistance to handling; and in a simple one-way escape-avoidance situation, in order to assess the predictive power of Grossman's (1966) hypothesis. The variable of handling was also manipulated to determine if handling could act to attenuate primary lesion effects. It would be predicted from Grossman's hypothesis that VMH lesioned subjects would differ from control subjects by increased defecation and immobility in the open-field; increased resistance to handling; and, improved avoidance performance. No VMH lesion effect was found on open-field behavior. VMH subjects were significantly ($p < .001$) more resistant to being handled compared to control subjects. Handling was found ineffective as a means of attenuating the primary effects of VMH lesions. Finally, VMH lesions were found to impair one-way avoidance performance. These results are discussed in terms of the implications they pose for Grossman's (1966) hypothesis.

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Introduction

The research reported here is concerned with the emotional disturbances accompanying lesions of the ventromedial nucleus of the hypothalamus (VMH) in the rat. The production of obesity by VMH lesions is a well established experimental effect in the rat (Hetherington and Ranson, 1940), in the cat (Wheatley, 1944), in the dog (Heinbecker and White, 1944), in the monkey (Brooks, Lambert, and Bard, 1942), and in the mouse (Mayer, 1955). While the mechanisms involved in the production of this obesity are not perfectly understood, the evidence generally favors the theoretical view elaborated by Stellar (1954) emphasizing disturbances in appetitive, rather than metabolic, processes.

However, as Grossman (1966) has indicated, Stellar's (1954) formulation does not treat adequately the behavioral disturbances produced by VMH lesions in situations where the regulation of the bodily energy balance does not appear to be a primary factor in the animal's behavior; e.g., the improved avoidance performance and the increased resistance to handling produced by VMH lesions in the rat. To incorporate such behavioral effects, Grossman has advanced the hypothesis that the effect of VMH lesions is to increase the animal's emotional or affective responsiveness to all sensory input, whether or not this input is related to food-seeking behavior.

Throughout this paper we have adopted Grossman's (1966) usuage of the term emotional reactivity, to refer to a general, normative, level of affective responsiveness to sensory stimulation.

In the experiment reported here, data are reported which bear on the adequacy of Grossman's (1966) hypothesis by:

1. Examining the effects of VMH lesions on open-field behavior, which behavior is generally regarded as a reasonable, if controversial, indicator of the rat's emotional state (Hall, 1934).

2. Repeating Grossman's study of the effect of VMH lesions on avoidance performance with a major procedural change: viz., the substitution of a one-way avoidance procedure for the two-way procedure employed by Grossman. The introduction of this procedural change was motivated by the accumulating evidence that two-way avoidance performance is not a straightforward indicator of the rat's reactivity to punishment; e.g., in the case of septal forebrain lesions, at least, the faciliation of two-way avoidance is accompanied by the impairment of all other avoidance performance (Garber and Simmons, 1968).

In both test situations, Grossman's theoretical position would lead one to predict that VMH lesions would produce behavior reflecting increased responsiveness

to the stimulus situation; i.e., increased defecation and immobility in the open-field, and improved avoidance performance.

Finally, in the present experiment, an attempt was made to treat a small but important technical problem raised by the increased resistance to handling induced by VMH lesions in rats. Responses of VMH lesioned rats to handling frequently includes avoidance, squealing, and biting. There is the danger that what appear to be primary behavioral effects of VMH lesions may, in fact, be secondary effects mediated by increased stress due to incidental handling of the subjects during the course of the experiment. The reports of previous research in this field have not been sufficiently detailed to allow one to resolve the question on the basis of existing data.

Method

Subjects

Fifty-five Long-Evans hooded female rats, 100-120 days old at the beginning of the experiment, obtained from Simonsen Laboratories, Gilroy, California, served as subjects.

Preoperative procedure

All subjects were individually housed in wire mesh cages in an animal room controlled for temperature (23-24° C.). Throughout the experiment the animal room was lighted for 13 hours each day (8 a.m.-9 p.m.). For five days prior to surgery all subjects were adapted to eating a wet Purina rat chow mash (50% water by volume) from 8-oz. glass feeding jars. Food and water were available to the subjects ad libitum. One day prior to surgery, the subjects were weighed and were rated on their resistance to handling by two independent raters using a four-point scale; viz.:

0 - placid, no resistance to being handled,

1 - avoidance, squealing, struggling, becoming passive after initial attempts to escape.

2 - as for a rating of 1, except that the subject persists in its attempts to escape,

3 - as for a rating of 2, except that the subject bites.

Following preoperative ratings on resistance to handling, subjects were assigned to one of four groups: (1) Handled VMH, (2) Unhandled VMH, (3) Handled Control, and (4) Unhandled Control. The assignment of subjects to groups was made so as to equalize preoperative resistance to handling ratings and body weights.

Surgical Procedure

All surgery was carried out with the subjects under deep ether anesthesia. VMH lesions were produced electrolytically by passing an anodal current (discharge of a 100 mf. capacitor at 120 volts) through a stainless steel electrode (.015 in.) positioned with a Kopf model 400 stereotaxic instrument. All electrodes were fully insulated except for the electrode tip.

Two groups of operated control subjects underwent surgery. One group received burr holes in the skull while a second group received electrode placements. A third group of subjects served as unoperated control subjects.

Postoperative Procedure

Handling. Beginning on postoperative day one and continuing through day 25 all subjects in the handled groups were handled for 2 min. each day. Handling consisted of repeatedly grasping the subject, stroking, and repeatedly passing the subject back and forth from one hand to the other. Protective gloves were worn by the experimenter at all times.

Open-field. On postoperative day 21, each subject was placed in an open-field for 3 min., and the following items were recorded:

1. Latency in leaving the first square,
2. Total number of squares entered,
3. Fecal boluses left in the open-field.

The open-field consisted of a box, approximately 3 X 3 ft., painted a medium blue-gray color, with walls 14 in. high. The floor of the open-field was marked with 9-in. squares. Each trial was started with the open-field dimly illuminated. Approximately 5 sec. after placing the subject in the apparatus the open-field was flood lighted for the remainder of the 3 min. trial. Between each trial the floor area of the open-field was cleaned with a damp sponge. All observations were made from behind a cheese cloth barrier.

Cage leaving latencies. On postoperative day 22 all subjects were tested for their willingness to leave their home cages to enter the open-field. The same open-field described previously was used. Each trial consisted of placing the subject, in it's home cage with the front cage door open, adjacent to the outside wall of the open-field. A trial started when access to the open-field was made possible by raising a guillotine type door on the wall of the open-field. On each trial the guillotine door was raised simultaneously with the flood lighting of the

open-field. Latencies in leaving the home cage were recorded. A trial was terminated when either the subject placed all four feet in the open-field or when 10 min. had elapsed.

One-way escape-avoidance. On postoperative day 26, the subjects were tested in a one-way escape-avoidance situation. The apparatus was designed to eliminate the need for handling the subjects during the intertrial interval. A wooden trough, 43 (length) X 10 (width) X 12 (height) in., served as a framework. The initial 12-in. segment of the trough was painted black; the remainder, white. In this framework was placed two identical Plexiglas boxes, 11 (length) X 8 (width) X 10 (height) in., with transparent walls, a grid floor, and opague black guillotine doors at each end. With the boxes in place, the apparatus simulated an ordinary shuttle box with a black starting compartment and a white goal compartment.

To begin training the subject was transferred from its home cage to one of the boxes. About 15 sec. before the beginning of each trial, the box containing the subject was placed in the initial segment of the trough, and the other box was placed in the terminal segment. The doors separating the compartments were then raised. Five seconds later, a 0.22-ma. shock was applied to the grid floor of the starting box. When the subject left the

starting compartment, the doors were closed. About 45 sec. later, the compartments were interchanged, and another trial was run. Each subject received 20 acquisition trials before reversal training was begun. On the first reversal trial, the compartments were not interchanged; the doors were raised, and 5 sec. later shock was delivered to the terminal compartment. On nine subsequent trials, normal procedures were followed, except that the white segment of the trough housed the starting box and the black segment housed the goal compartment.

If on any trial, the subject failed to escape the shock within 60 sec., the trial was terminated, and another trial begun at the end of a 60 sec. waiting period.

Resistance to handling. On the first, tenth, and twentieth postoperative days, the subjects were again rated on their resistance to handling.

Body weights. At the time of their being rated on resistance to handling, the subjects were also weighed.

Food intake. On the tenth, eleventh, twentieth, and twenty-first postoperative days, each subject's 24-hr. food intake was measured by weighing its food dish at the beginning and end of the 24-hr. period. Obvious spillage was returned to the dish prior to the terminal weighings. A 10-Gm. allowance for water evaporation was

subtracted from each 24-hr. food intake measurement.

Anatomical procedures. At the end of the experiment, all allegedly lesioned subjects and randomly selected control subjects were sacrificed under deep ether anesthesia and perfused with physiological saline and with formalin. The brains were sectioned at 50 micra, and every other section through the area of the lesion was photographed.

Statistical analysis. Multiple group comparisons were made using the Kruskal-Wallis H test; pair-wise comparisons were accomplished using the Mann-Whitney U test. Two-tailed tests with a .05 level of significance were employed throughout the analysis. The p values reported are the minimum obtainable values using the computational procedures and tabulations available in Siegel (1956).

Results

Anatomical Findings

On the basis of their brain damage, the subjects were classified into three major groups; within these major groupings, there was, of course, an additional subdivision of subjects according to whether or not they were handled during the postoperative period. The character of these groupings is outlined below.

VMH: subjects in which bilateral destruction of more than 1/2 of VMH was accomplished, as described in the rat brain atlas of Pellegrino and Cushman (1967). A representative lesion is illustrated in Figure 1. This group consisted of 9 unhandled and 7 handled subjects.

Other brain damage: subjects not meeting the criterion for VMH but in which there was brain damage greater than that caused by the passage of the electrode. This group includes 2 subjects sustaining unilateral lesions of VMH and 12 subjects in which the damage was posterior to the center of VMH. A representative posterior lesion is illustrated in Figure 2. This group consisted of 7 unhandled and 7 handled subjects.

Control: subjects in which brain damage did not exceed that caused by the passage of the electrode. This group consisted of 12 unhandled and 12 handled subjects.

Of the 55 original subjects one was excluded from the experiment after it was accidentally placed on water

deprivation for two days midway through the experiment.

The Effects of Handling

The experimental results are summarized in Table 1 (weight gains and food intake), Table 2 (resistance to handling), Table 3 (open-field behavior), and Table 4 (one-way escape-avoidance behavior).

The analysis of the effects of handling, attending only to the issue raised in the Introduction, proceeded by pair-wise comparisons between the VMH and control groups and between their handled and unhandled subgroups. In only one comparison was a statistically significant ($p < .05$) effect attributable to handling found; the unhandled VMH subjects were significantly slower ($p < .02$) than the handled VMH subjects in leaving their home cages. Whether one regards this as a statistical accident or a substantive finding, this one effect cannot be allowed to obscure the more important point to be made here; viz., in no instance did the effects of handling amplify or attenuate a significant VMH lesion effect.

For informational purposes only, the distinction between the handled and unhandled subjects is preserved in the tabulations of the results. However, in the statistical tests cited in the table, the handled/unhandled distinction was ignored, and only the anatomical grouping were considered.

Weight Gains and Food Intake

See Table 1. The VMH subjects ate significantly more food and gained significantly more weight than did the control subjects or the subjects with other brain damage.

Resistance to Handling

See Table 2. Both the VMH and other brain damaged subjects showed significant increased resistance to handling on postoperative day 1. This effect persisted in the VMH subjects through postoperative day 20. The effect was more transient in the other brain damaged subjects, which were indistinguishable in their ratings from the control subjects by day 10.

One-way Escape-avoidance

See Table 4 and Figure 3. Both the VMH and other brain damaged subjects manifested significantly poorer performance during the early acquisition trials. In later trials, including the reversal trails, there was no significant difference between the performance of the three groups.

Table 1. For each subject the mean daily weight gains over the 20 day postoperative period, and mean daily food intake as sampled over postoperative days 10, 11, 20, and 21, were calculated. The medians and ranges of these means are tabulated by groups. Where 3-Group $\underline{H}$ values are significant, pair-wise significant $\underline{U}$ test comparisons include:

1. Weight gains: VMH versus Controls, $\underline{U} = 34$, $(p < .001)$
   VMH versus Others, $\underline{U} = 37$ $(p < .002)$
2. Food intake: VMH versus Controls, $\underline{U} = 97$ $(p \approx .01)$
   VMH versus Others, $\underline{U} = 55.5$ $(p < .02)$

Table 1

Mean Daily Food Intake and Weight Gains

			Mean weight gains per day (Gm.)	Mean food intake per day (Gm.)
VMH	Unhandled n = 9	median	2.83	67.75
		range	(1.00-8.00)	(43.00-93.25)
	Handled n = 7	median	2.00	63.50
		range	(1.90-3.75)	(52.25-71.25)
Other Damage	Unhandled n = 7	median	1.00	55.00
		range	(-0.50-4.20)	(41.00-69.00)
	Handled n = 7	median	0.20	51.75
		range	(-0.60-3.55)	(46.75-94.00)
Controls	Unhandled n = 12	median	1.00	50.50
		range	(-0.10-2.25)	(36.50-72.00)*
	Handled n = 12	median	1.10	57.25
		range	(0.55-1.55)	(34.75-67.50)
			$\underline{H}$=19.58 $p < .001$	$\underline{H}$=7.62 $p < .05$

*one subject deleted from analysis as food measure not secured.

Table 2. Resistance to handling ratings. Each subject was rated for resistance to handling preoperatively, and on postoperative days 1, 10, and 20 (see Method section for details of the 4-point rating scale used). For each subject the two rating scores awarded by the raters were summed to yield a single score for each subject for each of the four days that ratings were taken. The medians and ranges of these single scores are tabulated by groups. Where 3-Group $\underline{H}$ values are significant, pair-wise significant $\underline{U}$ test comparisons include:

Postoperative days:

1 - VMH versus Controls, $\underline{U} = 78$ ($p < .001$)

- Others versus Controls, $\underline{U} = 103$ ($p < .05$)

10 - VMH versus Controls, $\underline{U} = 106.5$ ($p < .02$)

20 - VMH versus Controls, $\underline{U} = 111$ ($p < .03$)

Table 2

Resistance to Handling Ratings

			Preoperative	Postoperative		
				Day 1	Day 10	Day 20
VMH	Unhandled n = 9	median range	2 (0-4)	4 (0-6)	2 (0-6)	1 (0-6)
	Handled n = 7	median range	2 (0-4)	4 (0-6)	0 (0-6)	0 (0-6)
Other Damage	Unhandled n = 7	median range	0 (0-2)	0 (0-4)	0 (0-3)	0 (0-2)
	Handled n = 7	median range	2 (0-4)	4 (0-4)	0 (0)	0 (0-2)
Controls	Unhandled n = 12	median range	2 (0-4)	0 (0-4)	0 (0-3)	0 (0-3)
	Handled n = 12	median range	2 (0-4)	0 (0-2)	0 (0)	0 (0)
			$\underline{H}$=2.37 N.S.	$\underline{H}$=12.82 $p < .01$	$\underline{H}$=11.13 $p < .01$	$\underline{H}$=10.10 $p < .01$

Table 3. Group comparisons on open-field behavior. All subjects were tested for latencies in leaving the first square following their being placed in the open-field; total squares entered; and boluses left in the open-field at the end of the 3-min. test period. All subjects were also tested for their willingness to leave their home cage to enter the open-field. The medians and ranges of these open-field measures of behavior are tabulated by groups. 3-Group $\underline{H}$ values are shown.

Table 3

Open-field Behavior

			Latencies in first square (sec.)	Total Squares entered	Boluses	Cage Leaving latencies (min.)
VMH	Unhandled n = 9	median	13	28	1	2.39
		range	(7-23)	(11-39)	(0-2)	(1.38-4.25)
	Handled n = 7	median	15	36	0	1.36
		range	(6-35)	(29-52)	(0-5)	(0.54-2.15)
Other Damage	Unhandled n = 7	median	3	44	0	1.55
		range	(1-11)	(24-78)	(0-3)	(0.46-10.00)
	Handled n = 7	median	17	35	0	2.39
		range	(9-30)	(22-65)	(0-6)	(0.37-7.43)
Controls	Unhandled n = 12	median	10.5	42.5	0.5	1.80
		range	(2-25)	(33-54)	(0-6)	(0.35-10.00)
	Handled n = 12	median	11.5	35.5	0	1.29
		range	(5-20)	(18-64)	(0-6)	(0.41-8.54)
			$\underline{H}$=2.14 N.S.	$\underline{H}$=5.12 N.S.	$\underline{H}$=0.81 N.S.	$\underline{H}$=0.35 N.S.

Table 4. One-way escape-avoidance performance. All subjects were run in 20 acquisition trials followed immediately by 10 reversal trials. Medians and ranges descriptive of avoidance responses are tabulated over blocks of acquisition trials, 1-5, 1-10, 1-20, and over reversal trial blocks, 1-5, and 1-10. Where 3-Group $\underline{H}$ values are significant, pair-wise significant $\underline{U}$ test comparisons include:

Acquisition Trials:

1-5 - VMH versus Controls, $\underline{U} = 114$ ($p < .03$)

1-10 - VMH versus Controls, $\underline{U} = 107$ ($p < .02$)

Others versus Controls, $\underline{U} = 101.5$ ($p < .05$)

Table 4

One-way Escape-avoidance Performance

			Acquisition Trials			Reversal Trials	
			1-5	1-10	1-20	1-5	1-10
VMH	Unhandled n = 9	median	0	2	12	2	6
		range	(0-2)	(1-5)	(9-15)	(0-3)	(2-8)
	Handled n = 7	median	0	3	13	2	6
		range	(0-2)	(0-7)	(8-16)	(0-2)	(2-7)
Other Damage	Unhandled n = 7	median	1	4	14	1	5
		range	(0-2)	(1-6)	(9-15)	(1-3)	(3-7)
	Handled n = 7	median	1	3	13	2	5
		range	(0-1)	(0-6)	(8-16)	(0-2)	(3-8)
Controls	Unhandled n = 12	median	1	4.5	13	2	7
		range	(0-3)	(1-7)	(9-17)	(0-4)	(0-9)
	Handled n = 12	median	0.5	5	15	2	6.5
		range	(0-3)	(2-8)	(8-18)	(0-3)	(4-8)
			$\underline{H}$=6.81 $p<.05$	$\underline{H}$=7.19 $p<.05$	$\underline{H}$=5.35 N.S.	$\underline{H}$=5.23 N.S.	$\underline{H}$=5.13 N.S.

Figure 1: A typical ventromedial hypothalamic lesion.

1.1 - Anterior extent of lesion.

1.2 - midway portion of lesion.

1.3 - Posterior extent of lesion.

Lesions are shown as cross hatching on coronal sections of the brain from the atlas of Pellegrino and Cushman (1967). The scales on the margins are stereotaxic coordinates. The numbers in the upper portion are anterior--posterior distances in mm.: upper left, distance from bregma; upper right, distance from ear bar zero.

Relevant abbreviations: (given only for structures proximal to VMH).

AHA - anterior hypothalamic area

ARH - arcuate nucleus

DMH - dorsomedial nucleus

FX - fornicis

LHA - lateral hypothalamic area

MFB - medial forebrain bundle

PH - posterior nucleus of hypothalamus

PMV - praemamillaris ventralis

PVH - paraventricularis hypothalami

RE - reuniens thalami

V - ventricle

ZI - Zona incerta

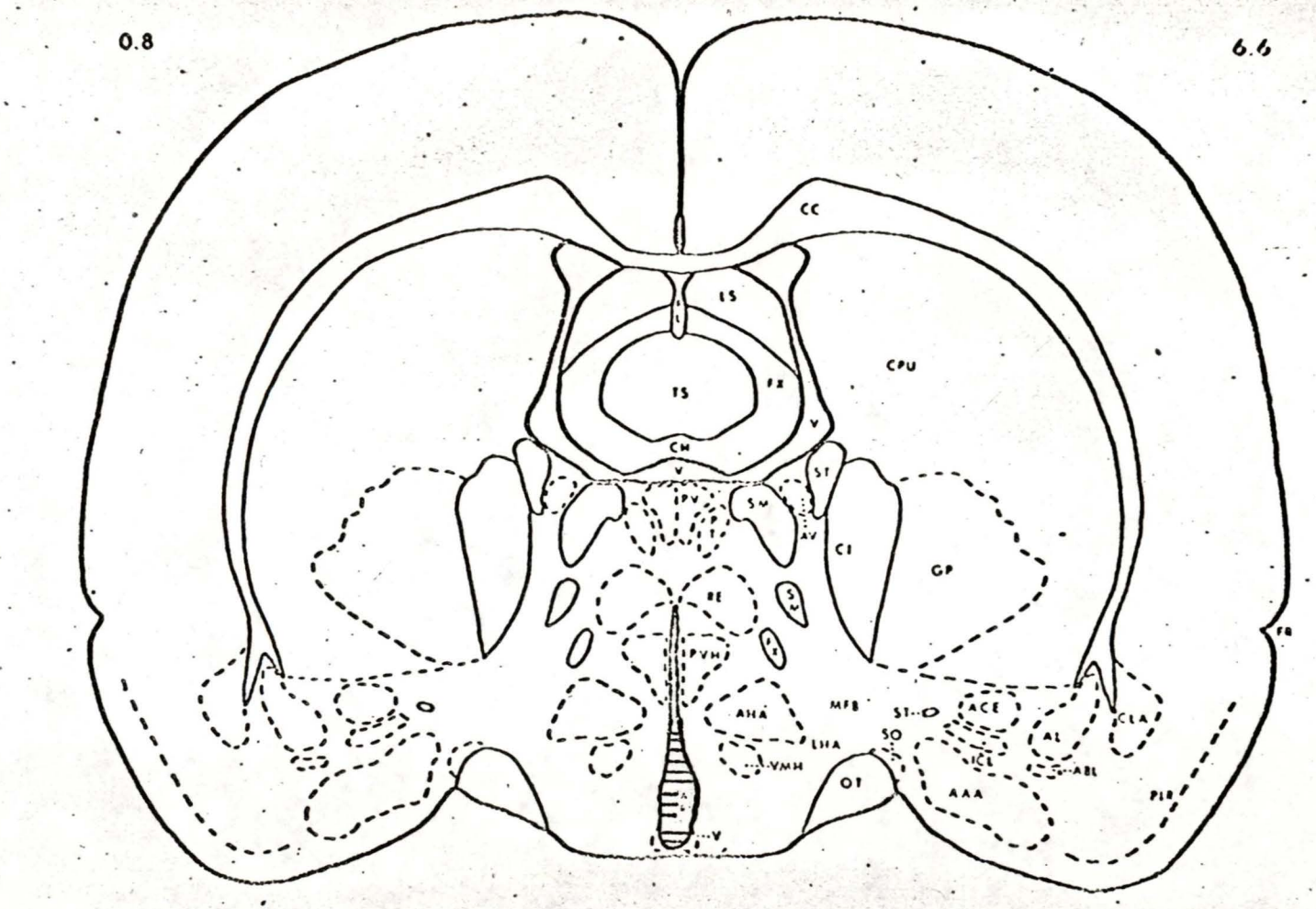
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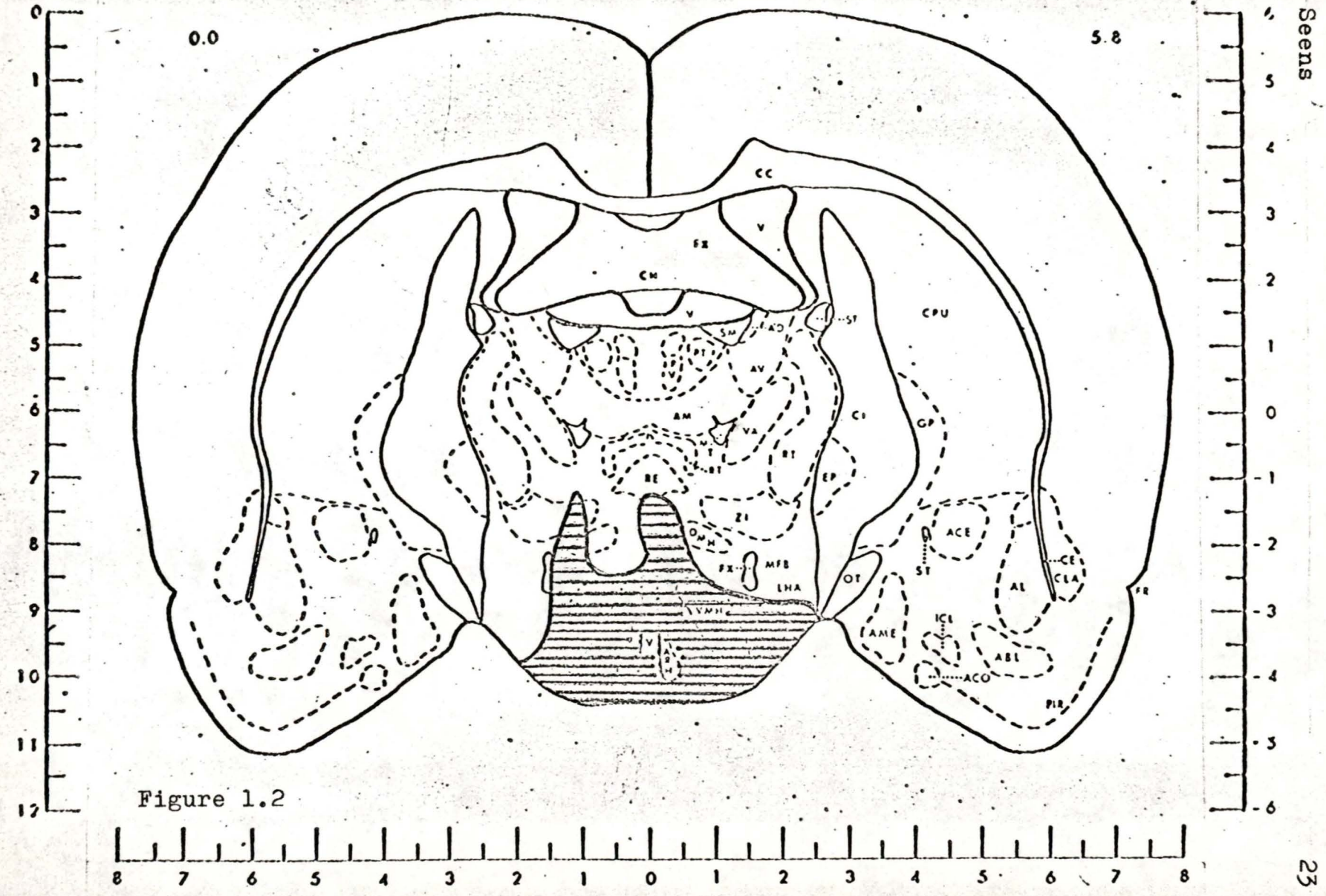
Figure 1.1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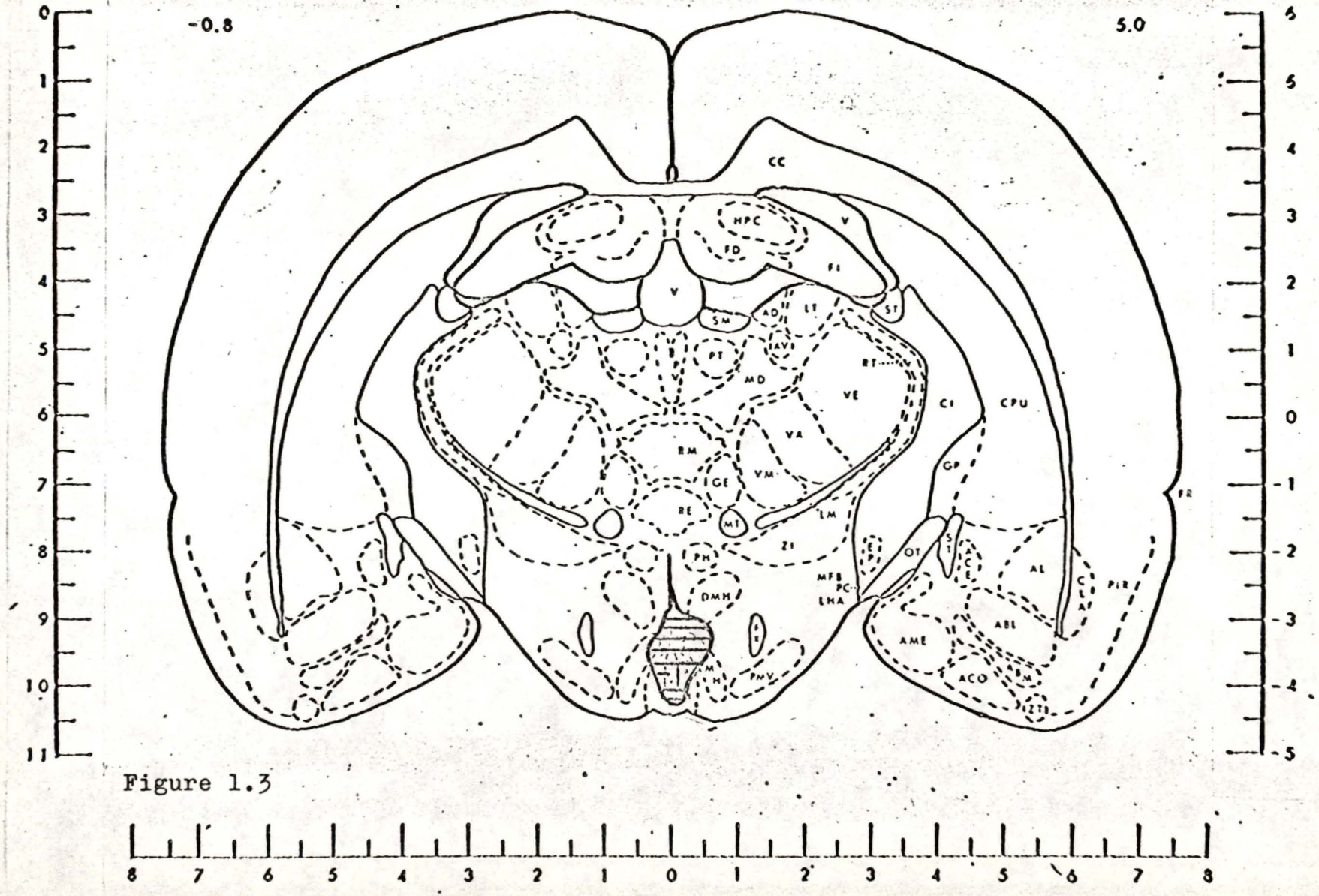
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Figure 1.3

Figure 2: Lesion typical of the category, Other brain damage.

2.1 - Anterior extent of lesion.

2.2 - Midway portion of lesion.

2.3 - Posterior extent of lesion.

Lesions are shown as cross hatching on coronal sections of the brain from the atlas of Pellegrino and Cushman (1967). For an explanation of scale markings appearing on these plates refer to explanatory comments on Figure 1.

Relevant abbreviations: (given only for structures proximal to VMH).

ARH - arcuate nucleus

DMH - dorsomedial nucleus

FX - fornicis

LHA - lateral hypothalamic area

MFB - medial forebrain bundle

ML - lateral mamillary nucleus

MM - medial mamillary nucleus

MP - posterior mamillary nucleus

MT - Mamillothalamic tract

PH - posterior nucleus of hypothalamus

PM - pedunculus mamillaris

PMD - dorsal premamillary nucleus

RE - reuniens thalami

SUM - area supramamillaris

V - ventricle

ZI - Zona incerta

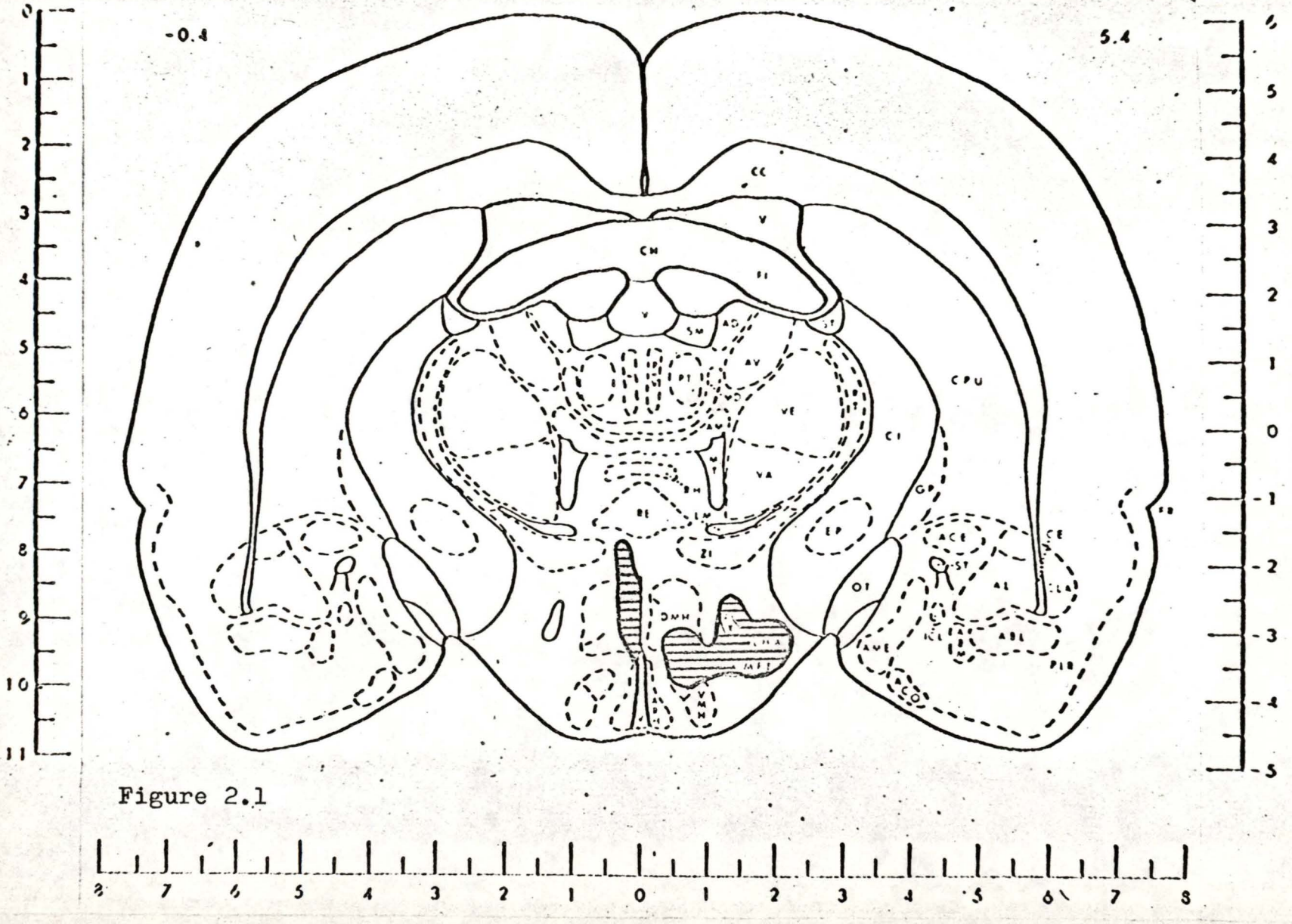
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Figure 2.1

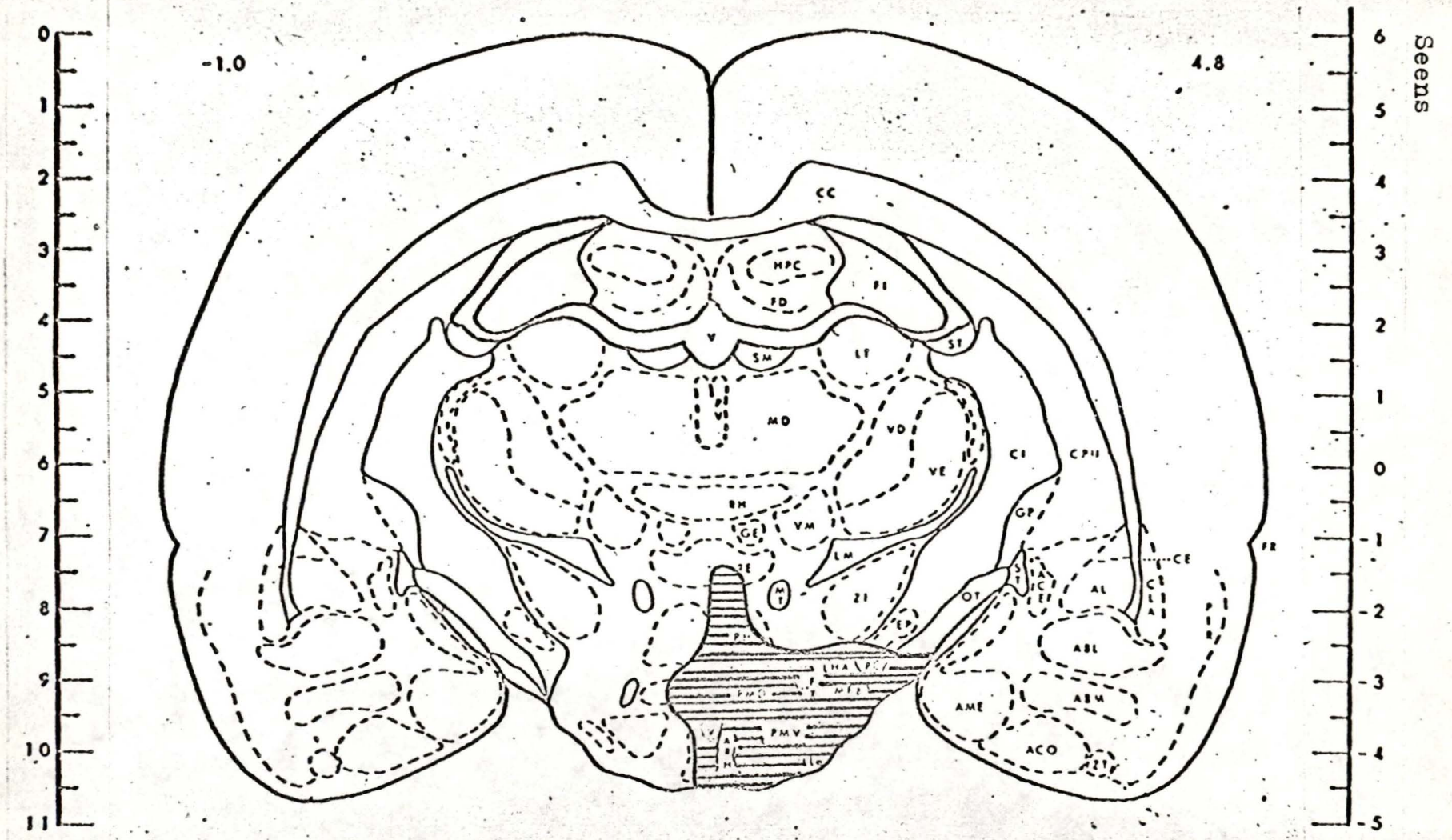
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Figure 2.2

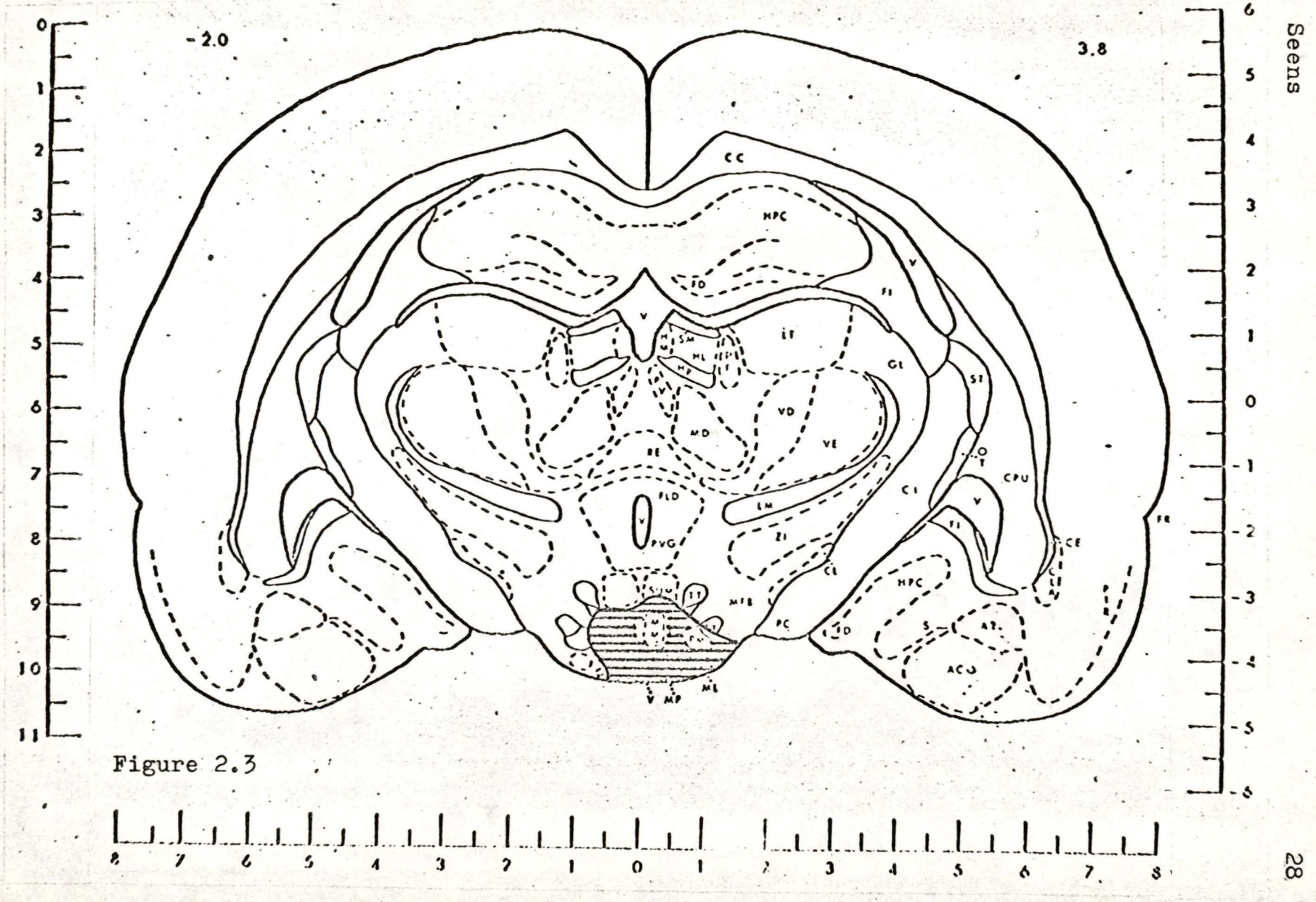
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Figure 2.3

Figure 3: One-way escape-avoidance performance. All subjects were tested over 20 acquisition trials followed immediately by 10 reversal trials. (see Table 4 for tabulation of group performances). This Figure compares VMH, and control subjects over single trials and plots performance as percentage of subjects avoiding on each trial.

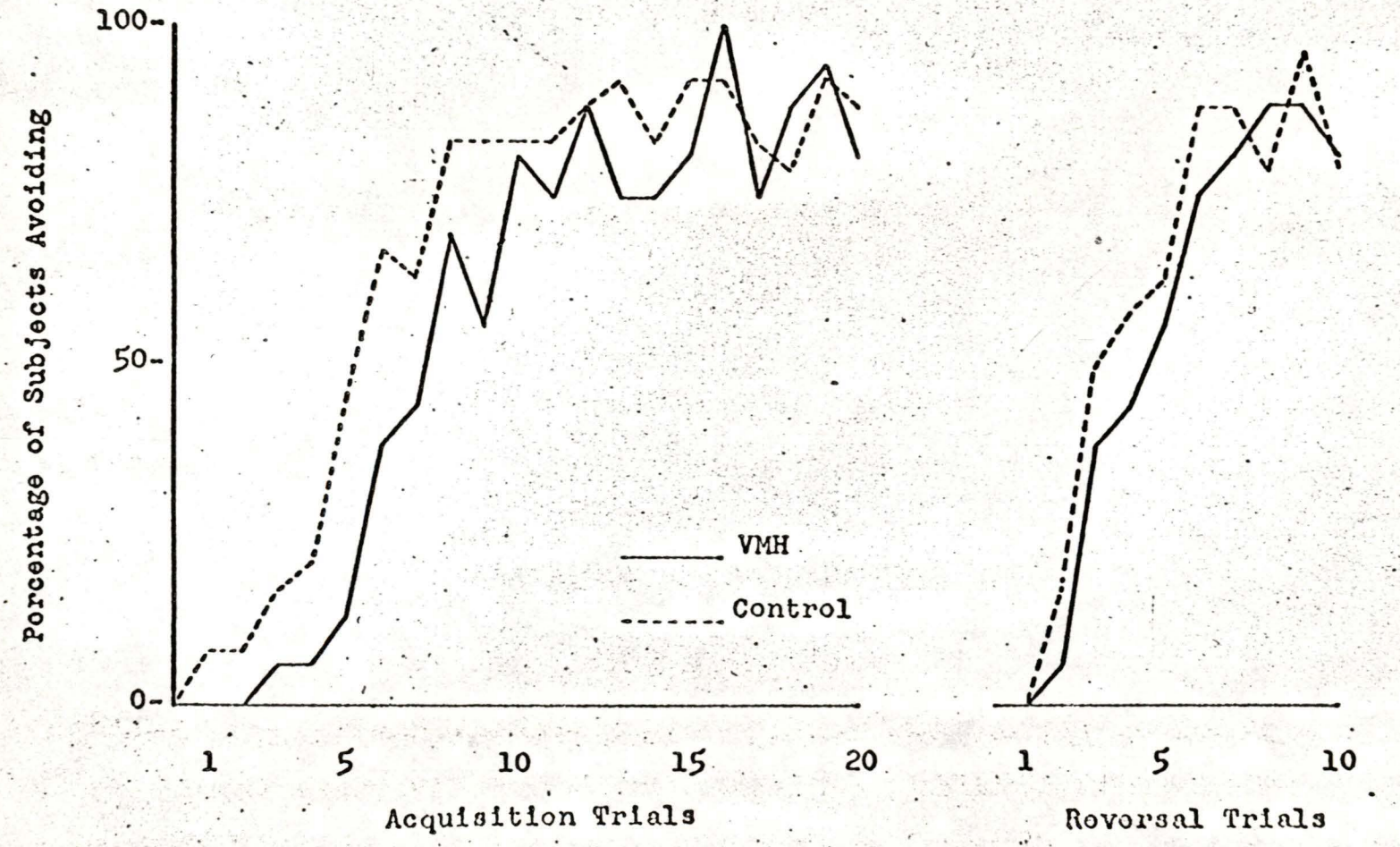

Figure 3. One-way escape-avoidance performance.

Discussion

On the basis of both anatomical and behavioral evidence the VMH lesions were effective, that is, the VMH animals showed increased food comsumption, abnormal body weight increases, and heightened emotional reactivity to being handled. In the other brain damaged subjects the locus and extent of damage was more variable, as was the behavioral data, however, for the issues to be raised here the comparisons of interest are between the VMH and control subjects.

The data gives no indication that handling has a differential effect on VMH lesions that would influence either food intake or body weight gains in rats. There is also no indication that handling can differentially influence performance in the open-field, or in one-way escape-avoidance. In fact, the handling manipulations even failed to influence the ratings on resistance to handling over the 20 day experimental period. This complete absence of an effect of handling suggests two possibilities: (1) the subjects were not handled for a long enough period of time, or (2) handling *per se*, is an ineffectual means of reducing the heightened emotional reactivity which is a concomitant of VMH lesions. This latter supposition would appear to be the most probable reason for this lack of an effect attributable to handling. Singh (1969) reports

that handling is effective in reducing the hyperemotionality of septal, but not VMH lesioned rats. While firm conclusions are not yet justified on the basis of the evidence available, it seems most unlikely that the incidental handling of VMH lesioned rats during the course of conducting an experiment, can contribute in any substantial manner to a masking of the primary lesion effects.

The fact that VMH lesioned rats are significantly more resistant to being handled than control subjects ($p < .001$), does not in itself provide evidence of a lesion effect acting to enhance the emotional reactivity of these animals towards all stimuli, as is required by Grossman's (1966) hypothesis. The data reported here suggests that the greater resistance of the VMH subjects to being handled is a response specific to being picked up, otherwise, it should be expected that a nonspecific enhancement of emotional responsiveness would generalize to the open-field situation. The fact that handling manipulations fail to attenuate this response in VMH lesioned rats, in contrast with septal lesioned rats, raises an interesting question for further study.

The fact that no differences appeared between VMH and control subjects on measures taken in the open-field, contradicts what would be predicted from

Grossman's hypothesis. If VMH lesions do in fact increase the animal's general emotional reactivity to sensory stimulation, this enhancement of emotional reactivity should lead to greater immobility and more frequent defecation in the open-field.

The most substantial contradiction this study poses for Grossman's hypothesis concerns the one-way escape-avoidance data. From Grossman's hypothesis one would predict a facilitation effect of VMH lesions in the one-way escape-avoidance task, attributable to an enhancement of the emotional reactivity of the VMH lesioned subjects. This in fact, is the observation Grossman made when he tested his subjects in a two-way shuttle apparatus. The present experimental results clearly demonstrate that no such facilitation effect is present in VMH lesioned rats tested in a simple one-way escape-avoidance apparatus. In fact, not only the VMH, but also the other brain damaged subjects, showed an impaired ability to avoid in the one-way situation.

The magnitude of the impairment observed in one-way avoidance performance attributable to VMH lesions varies with the mode of statistical analysis, but holds over any form of analysis in its direction. An $\underline{H}$ test calculated on the original 6-Group design does not reach statistical significance. A 3-Group

comparison, which drops the distinction between handled and unhandled subjects, yields the significant H values that are tabulated in Table 4. Of interest also, are post hoc t tests between independent groups which were calculated for greater comparability to the results reported by Grossman. When applied to the data of this experiment the t statistic functions to accentuate the impairment of the VMH subjects to an order of magnitude comparable to the magnitude of the facilitation effect reported by Grossman. For the information they provide, the t test comparisons made between VMH and control subjects were:

1. Acquisition trials, 1-5, ($t = 2.14$) $p < .05$
2. Acquisition trials, 1-10, ($t = 2.59$) $p < .02$
3. Acquisition trials, 1-20, ($t = 2.26$) $p < .05$

It is interesting to speculate on why the results of the one-way avoidance tests run in this experiment are in complete contradiction of the facilitation effect Grossman observed in VMH lesioned rats tested in a two-way shuttle box apparatus.

The conflict of the results reported here with what would be predicted from Grossman's (1966) hypothesis may be due to procedural differences. For example, more research will be required before we can safely assume comparability of electrolytic lesions (used in this study), and atropine produced lesions (used by Grossman).

Precautions have also not been taken in studies of this type to ensure that conflicts in results do not, at least in part, arise from a lesion effect acting to disrupt the normal diurnal cyclical responsiveness of rats in the test situations. This failure to control for, and report, testing times may be crucial, especially when we consider the almost exclusive use that has been made of female rats in studies of hypothalamic obesity (Cox, Kakolewski, and Valenstein, 1969; Singh and Meyer, 1968). Grossman (1966) has been one of the few investigators who used male rats.

A further consideration which possibly underlies the contradiction of the results reported here and those of Grossman (1966), invòlves the apparatus used in these two experiments. We can note that a facilitation of performance in a two-way shuttle box apparatus has been reported following lesions in the median eminence of the tuber cinereum (Levine and Soliday, 1960); and following lesions of the septum (King, 1958; Krieckhaus, Simmons, Thomas, and Kenyon, 1964). Garber and Simmons (1968) have demonstrated that, in the case of septal lesions, the apparent facilitation effect in two-way avoidance, is an effect peculiar only to the two-way shuttle box apparatus, rather than a true facilitation of adaptive behavior. Impaired one-way avoidance following septal lesions has previously been demonstrated

by Vanderwolf (1964). This impairment of one-way avoidance, following septal lesions, has recently been confirmed in this laboratory (Liedtke, 1969).

What the foregoing suggests to this author is that the apparent facilitation effect of VMH lesions on escape-avoidance performance reported by Grossman (1966) may arise, as in the case of septal lesions, as an artifact of the two-way shuttle box apparatus. If correct, this may also explain the apparent facilitation in avoidance responding that follows lesions in the median eminence of the tuber cinereum (Levine and Soliday, 1960).

In summary, no evidence was found in this study which lends to an interpretation supporting Grossman's (1966) hypothesis that the effect of VMH lesions is to enhance the emotional responsiveness of the animal towards all sensory stimuli. The increased resistance to being handled which regularily follows VMH lesions apparently is not an emotional enhancement of reactivity which generalizes to the animal's behavior across different test situations. With specific regard to escape-avoidance performance, one reasonable line of speculation appears to be that a facilitation of performance in a two-way shuttle box apparatus it not a simple indicator of a facilitation of adaptive behavior.

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Appendix A

A Survey of Research on the Ventromedial Hypothalamus

The following review is limited specifically to lesions studies of the ventromedial hypothalamus (VMH) in the rat. For a more general, and comphrensive review of hypothalamic regulation of feeding behavior, reference can be made to Herrero (1967).

The involvement of the hypothalamus in the regulation of food intake, independent of the hypophysis, was established by Hetherington and Ranson (1940). It was later demonstrated that the most effective lesions for producing the two phenomena of hyperphagia and obesity were lesions which were bilateral and in the area of the ventromedial nuclei of the hypothalamus (Brobeck, Tepperman, and Long, 1943; Hetherington, 1943).

Research directed towards gaining a greater understanding of the neural mechanisms acting to regulate food intake can be divided into two areas of major emphasis. The first of these involves attempts to discover an effect of these lesions acting to alter the normal metabolic processes of the animal. The second area of research emphasis has arisen out of the failure of investigations to uncover any basic alteration in the metabolism of VMH lesioned animals, and has attended primarily to behavioral manifestations which have been observed to regularily accompany VMH lesions.

Herrero (1967) has in summary form, referred to the effects of VMH lesions in terms of a syndrome of disturbances, the various factors of which may or may not be interdependent, sufficient or necessary conditions, for the obesity which follows as a consequence of these lesions. Portrayed in this manner, the various phenomena of hyperphagia; obesity; hyperreactivity; finickiness to dietary adulterations of food or water; and changes in behavior subsumed as motivational, may reflect a disturbance of one or more neural mechanisms located in the area of the ventromedial hypothalamus.

One consequence which has followed from this separation in research emphasis has been the development of a number of explanatory hypotheses which are suitable only to singular aspects of this total VMH syndrome. As presently formulated no one of these hypotheses can account for all of the research evidence available. Such being the case, our present knowledge of the effects of VMH lesions is more a collection of observations, than a systematic, integrated theoretical view of the disruption of neural mechanisms by VMH lesions.

Brooks and Lambert (1946) divided the time course in the development of hypothalamic obesity into two phases, a 'dynamic phase' and a 'static phase'. The dynamic phase is descriptive of the postoperative period in which the lesioned rat increases its daily food intake

over normal by two or three times, and during which body weight gains reach as high as 8-10 grmas per day. This dynamic phase persists for approximately one month or until the rat reaches a physiological limit. The static phase which follows is characterized by the animal maintaining it's asymptote of body weight while daily food consumption declines to a level slightly above or twice the normal consumption. The permanency of the effect of VMH lesions has been demonstrated experimentally. If the VMH animal has reached the static phase and is then starved back to it's preoperative body weight, these phases will then repeat if the animal is given access to ad libitum food (Brobeck, et al., 1943).

After extensive investigations failed to disclose an effect of VMH lesions acting to alter the metabolism of the VMH animal, Brobeck, et al., (1943) concluded that the most important factor contributing to the obesity of the VMH animal was the increase in food consumption. VMH lesioned rats commonly display ravenous eating post-operatively even before the effects of the surgical anesthesia have worn off (Brobeck, et al., 1943). As noted above VMH lesioned rats increase their daily food consumption by as much as two or three times normal (Brobeck, et al., 1943) and manifest weight gains as high as 8-10 grmas per day (Brooks and Lambert, 1946). The immediate 24-hr. postoperative food consumption of these

animals may be three times the intake during any other comparable 24-hr. postoperative period (Brobeck, 1946).

Measures taken on respiratory quotients, indicative of metabolic processes, have failed to disclose any significant differences between control and obese VMH lesioned rats (Brobeck, et al., 1943; Brooks, 1946). Brooks, Marine, and Lambert (1946) found essentially the same food-feces ratios in VMH and normal rats which discounts a possible lesion effect acting in some unknown manner to increase the efficiency of the digestive system of the lesioned animals. These same investigators did find a somewhat lowered level of oxygen consumption in their lesioned subjects which may have contributed in part, to the obesity observed. This reduction in oxygen consumption was however, of an order of magnitude that fell far short of accounting for more than a fraction of the total accumulation of adipose tissue.

Hetherington and Ranson (1942) suggested that the obesity which follows VMH lesions could be due to a lesion effect acting to interfer with the animal's ability to utilize body stores of fat as a source of energy. Studies in which VMH rats have been allowed to become obese and then placed on food deprivation, have served to discount this possibility. Obese VMH rats show no impairment of their ability to metabolize their stores of body fat when placed on a starvation diet (Brobeck, et al., 1943).

The general conclusion which follows from these physiologically oriented investigations is that the obesity which follows VMH lesions is primarily attributable to the increased food consumption of the VMH animal (Brobeck, et al., 1943). This appetitive hypothesis has been incorporated into the theoretical formulations of Stellar (1954) which stresses the recriprocal roles of the VMH and lateral hypothalamic centers in the regulation of the organism's energy balance. Within this theoretical framework the destruction of the VMH removes the mechanism of satiety, which would normally function to inhibit the excitatory, or eating centers of the lateral hypothalamus.

A considerable body of experimental evidence has accumulated which demonstrates some very substantial behavioral differences between normal and VMH lesioned animals, which cannot be readily accounted for in terms of the above appetitive hypothesis.

In an attempt to account for the obesity of VMH lesioned rats, Hetherington (1941), and Hetherington and Ransom (1942) hypothesized that the decreased activity of VMH rats was responsible for the obesity of these animals. Measures of the activity of VMH lesioned rats dislosed a significant decrease in the total running of these animals in activity wheels. More recently, similar observations have been made with VMH lesioned mice (Mayer, French, Zighera, and Barnett, 1955). These observations

stand in contradiction of the observations of Brooks (1946), who found that the suppression of activity following VMH lesions was temporary, and independent of both the hyperphagia and obesity when measures of activity were secured using tambour cages. This conflict of results involving these two methods of measuring activity suggests that perhaps the recovery of a normal level of activity is not observable in an activity wheel, due to the developing obesity acting to make this particular response impossible.

Regardless of the above, this hypoactivity hypothesis must be considered inadequate because it fails to take into account the increased food consumption of the VMH animal. It seems most probable, that if lessened activity does contribute to the obesity, the lessened activity is itself secondary to the increased weight of the VMH animal.

A further behavioral disturbance attributable to VMH lesions involves changes in the animal's feeding habits. Brooks, Lockwood, and Wiggins (1946) observed a disruption in the rat's normal nocturnal eating habits. Whereas rats normally hoard their food during the day and eat it at night, VMH lesioned rats devour their food immediately. This change in frequency of meals eaten is also accompanied by an increase in the size of the meals eaten.

The increased food consumption of VMH lesioned rats suggests that a possible effect of these lesions may have been to increase the hunger drive of the animal. Drive

reduction theory would predict that VMH animals should show a greater willingness to work for food rewards in an instrumental reward situation. Miller, Bailey, and Stevenson, (1950); and Teitelbaum, (1957), have shown that VMH lesioned rats are indeed less willing to bar press, or lift weighted covers from food bins, than are control animals.

VMH lesioned rats have also been demonstrated to be abnormally sensitive to the sensory aspects of their diet (Miller, et al., 1950: Teitelbaum, 1957). The lesioned animal shows an impaired ability to compensate, and thus maintain a constant calorie intake, when the food supply is adulterated with cellulose roughage. Whereas normal rats will maintain a normal level of caloric intake by increasing their volume of consumption, the VMH lesioned rat appears to be more sensitive towards the positive or negative aspects of it's food (Teitelbaum, 1955). VMH rats reject cellulose or quinine adulterations of their food at concentrations that normal rats will tolerate. Conversely, VMH rats will gorge themselves on food sweetened with dextrose in contrast with the normal animal who tends generally to maintain a constant caloric intake (Grossman, 1967). Krasne (1962) has observed similar exaggerated rejection responses by VMH rats to quinine dilutions of their water supply (cited in Grossman, 1967). Corbit and Stellar (1964) have shown that when the caloric density

of the diet is held constant, the VMH rat is more reactive to changes in the texture of their diet than are normal rats. This apparent hypersensitivity to the stimulus aspects of food has also been shown not to be dependent upon obesity developing following VMH lesions (Graff and Stellar, 1962).

Grossman (1966) hypothesized that the finickiness of VMH animals to adulterations of their food or water supply may be reflecting an altered affective reaction to taste, rather than a change in the quality or intensity of the sensation itself. The notion that the primary effect of VMH lesions is to lower thresholds for both the positive and negative aspects of the stimulus, allows Grossman to develop a logical explanation for both the overeating and behavioral disturbances that are characteristic of VMH lesions. Within this schema VMH animals over eat as a result of their enhanced reactivity to the positive sensory aspects of their food, and reject adulterations because of their enhanced reactivity to the negative aspects of the adulterated food. In support of this hypothesis Grossman has shown that atropine produced lesions of the VMH in rats results in an impairment of instrumental responding for food and water rewards. VMH rats were also found by Grossman (1966) to be superior to normal animals in escape-avoidance performance when tested in a two-way

shuttle apparatus. Both of these experimental outcomes would be predicted from Grossman's hypothesis. In the first case the poorer performance of the VMH animals is attributed to the enhanced reactivity of the VMH animal to the negative aspects of having to perform the instrumental responses in order to obtain the food or water rewards. In the second test the improved avoidance is attributed to the enhanced reactivity of the VMH animal to the conditioned stimulus cues.

While Grossman's (1966) affective hypothesis may have logical appeal the experimental evidence necessary to substantiate it is missing. Mook and Blass (1968) found that while VMH rats are more reactive than normal rats to quinine adulterations of their water supply, this hyperreactiveness is not attributable to a lowering of aversion thresholds in the VMH animals.

In the experimental section of this thesis evidence has been presented which stands in contradiction to what would be predicted from Grossman's hypothesis. VMH rats do not show an enhancement of their affective responses when tested in an open-field situation. The reactivity of VMH rats to being handled was found to be a response specific to being picked up, with no indication that this heightened reactiveness generalized to other test situations as would be predicted from Grossman's hypothesis. VMH rats were found to be impaired in their performance when

tested in a one-way escape-avoidance apparatus. One possible explanation of why Grossman observed an apparent facilitation of avoidance performance in the two-way shuttle box apparatus is put foward in the discussion section of the research paper in this thesis.

To conclude this review, it seems reasonable to state that the major contribution of the research carried out up to this time, has been to eliminate a number of logically possible explanations for the effects which are characteristic of VMH lesions. The more generally accepted appetitive hypothesis finds it's greatest support in research with a physiological emphasis, but this hypothesis must still be considered an incomplete explanation since it does not emcompass the behavioral disturbances which are attributable to lesions of the ventromedial nuclei of the hypothalamus.

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Appendix B - Notes on Procedure

Standard procedures were used throughout this study, with one exception; photographs were used in histology in place of standard staining procedures.

35 mm. photographs were taken of the mounted brain on the microtome stage following every second section taken through the extent of the lesions. Sections of 50 micra thickness were taken commencing immediately posterior of the crossing of the anterior commissure. Photographs were taken with a Honeywell Pentax model H3V camera, using Kodak Plus X Pan, B & W film. All exposures were taken through a Honeywell Pentax Bellows 11 attachment, at a shutter speed of 1/60, with an aperature opening of F 16. The initial focusing was accomplished with the maximum aperature opening, F 11. The camera was mounted in a stationary position so that approximately four inches separated the front of the bellows attachment from the blade edge of the rotary, Spencer model 820 microtome. Lighting conditions were controlled by mounting a standard desk model florescent lamp directly above the camera, directed onto the cutting surface of the brain mount. A black, flat surfaced paper, provided a surround for the brain mount which acted to eliminate extraneous light reflections from the microtome surfaces.

All film was developed by a professional photographer* for maximum contrast of brain structures.

Verification of extent and locus of lesions was accomplished by reading the developed film through a standard photographic enlarger. Representative drawings of typical lesions were made by transcribing the enlargements of these films to the appropriate plates in the atlas of the rat brain prepared by Pellegrino and Cushman (1967).

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Appendix C

Speculations for further research on VMH Lesion Effects

In appendix A of this thesis I stated that the research which has been carried out to-date on the effects of VMH lesions, is divisible into two categories of emphasis--that which is primarily physiological, and that which emphasizes behavioral changes. It is my intention in this section to suggest a method of research which will attend to both physiological and behavioral variables simultaneously, and thus generate a body of research data that will be compatible to both the viewpoints of the physiologist, and physiological psychologist.

The concept of "metabolic scope" has been used by comparative physiologists to determine the range of metabolic capability an organism has for meeting increased energy requirements placed upon it by environmental pressures. The ongoing metabolism of the freely moving animal is measured in an open system respirometer, during which time, varying degrees of stressful stimuli can be introduced. This technique has made it possible to quantify the capability of an organism to increase its metabolism to release energy over and above the amount needed for basic physiological maintenance. This measure of metabolic scope has also provided useful information on the extent to which particular species have evolved in their metabolically regulated adaptiveness to stress

situations arising from the environment.

Whereas comparative physiologists have employed this measure of metabolic scope as outlined above, it is proposed here to use this technique to assess the effect of VMH lesions on the metabolism of rats where the environmental factors are held constant. I submit that this technique will clearly demonstrate that a fundamental effect of these lesions is to sustain a level of metabolism in VMH animals that is abnormally high relative to control animals under identical environmental conditions. This effect on metabolic rate has not been demonstrated before simply because measures taken on the metabolic rates of VMH animals have been taken only for relatively short periods of time. It is intended here to monitor metabolism over a 24-hr. period. The effect of VMH lesions to enhance the ongoing metabolic rate should be evident in one or the other of the following ways:

(1) The ongoing (24-hr.) level of metabolic rate may be sustained at an above normal level which will act to eliminate the normal ongoing cyclical variation of the unoperated animal, or,

(2) The enhanced metabolic activity may "override" without disrupting the normal circadian rhythm.

Regardless of which of the above alternatives proves to be the case, it will be possible to quantify the effects of VMH lesions on metabolism in terms of caloric units of energy.

The implications for the behavioral changes attributable to VMH lesions become clear if we conceive of the enhancement of metabloic rate as indicative of the organism's state of "energy-mobilization". By employing the quantified measure of metabolic rate being suggested, it should be possible to more objectively describe the effects of VMH lesions, rather than having to resort to such descriptive terms as, "hyper-reactivity", "hyper-sensitivity", or "hyper-agitation", which now appear with monotonous frequency in the research literature. It may also be possible, on the basis of these measures, to develop a scale which will relate metabolic rate to degrees of behavioral responsiveness which we now attempt to describe with the terms noted above. A logical extension of this idea would be to compare the effects of prescribed lesions in different areas of the brain to the ongoing metabolic rate.

The initial objective of this proposed research should be to secure normative data on the ongoing metabolic rate of both male and female rats over a 24-hr. period. A comparison can then be made between VMH and normal rats on their total metabolism. This technique of open system respirometry allows for an accumulative measurement of oxygen consumption, from which the total energy expenditure of the animal can be calculated. This measure will allow for a comparison of energy expenditure against

a known daily caloric intake. In addition total volume of food ingested, water consumption, and body weight gains can be recorded.

These measures should yield a definite pattern over a 24-hr. period relating metabolic rate (quantified) to the behaviorally significant factor of diurnal physiological responsiveness to external stimulation. Given this pattern we then have a reference against which we can compare differences which are inherent in the variables of sex, age, or subspecies, and differences in responsiveness to environmental factors such as food contamination or adulteration. This latter category would include the addition of cellulose or other roughage to the food supply which can serve as an indicator of the animal's caloric compensatory capabilities. The addition of adulterative substances such as quinine or sucrose would serve as indicators of a lesion effect operating to alter motivational determinants of food preferences. Similarily, this technique will allow for a detailed assessment of lesion effects peculiar to high fat, high protein, or high carbohydrate diets.

To extend my speculations ever further, I would suggest that VMH lesions may function to disrupt only one aspect of the energetics system which is reflected in our measures of metabolic rate. Two distinct processes can be conceived to be involved in the total metabolism

of an organism: (1) the conversion processing of food stuffs into body stores of energy (including adipose tissue), and (2) the reconversion or utilization of existing energy reserves to meet the ongoing energy requirements of the organism. If one postulates that the primary effect of VMH lesions is to disrupt only the first of these metabolic processes, we have a theoretical basis for incorporating much of the physiological and behavioral data currently available. With in this schema the effect of VMH lesions is to "release" the ongoing conversion mechanism so that the conversion processing of food stuffs proceeds "non-stop" in the operated animal. This pathological abundance of energy far exceeds the ongoing energy requirements of the organism and thus accumulates in the form of excessive adipose tissue.

It can be pointed out that there is no conflict between the above notion and the data of other physiological studies of VMH lesion effects. For example, Brooks (1946) found that in a pair-feeding situation there was no evidence that VMH lesions functioned to increase the digestive "efficiency" of the lesioned animals when they were limited to the same food-intake volumes as their paired control partners. Further, the above speculation does not conflict with the demonstrated ability of obese VMH animals to metabolize their body stores of adipose tissue in a normal manner when placed on a starvation

diet (Brobeck, et al., 1943). Conceived of in this manner the excessive food-intake of VMH lesioned animals can perhaps be accounted for in terms of an internally stimulated "hunger", or need state which arises from the pathology of the mechanism responsible for the regulation of food conversion processes.

The above speculation does not in any way conflict with the generally held notion that the VMH acts as a satiety center for the regulation of food-intake. There is not however, any concensus on what the adequate stimulus is for this satiety center. It is being suggested here that the VMH satiety center may be responsive to caloric intake. If this is correct then the proposed research method should clearly demonstrate this dependency for satiety upon caloric intake.

If an empirical basis for the above speculation can be established, it should be a relatively simple matter to account for many of the behavioral alterations which have been found to regularily accompany VMH lesions. If we assume for the moment that it is possible to develop a scale relating metabolic rate to the reactivity of the animal to sensory stimulation, we should then be able to account for the behavior of VMH lesioned animals in terms of a heightened state of energy mobilization. I am suggesting that it is this state of heightened energy mobilization that VMH lesioned animals are constantly

maintained in, that accounts for the behavioral impairments that are observed when these animals are placed in threatening or stressful test situations.

To elaborate further, if it is possible to demonstrate an enhancement effect of VMH lesions on metabolism it should be possible to equate behavioral differences to differences in metabolic rates. Re-stated, it should be possible to equate the enhanced behavioral reactivity of the VMH animal to an enhanced state of energy mobilization.

The advantage of what is being suggested here over Grossman's (1966) hypothesis, is that this suggestion avoids the "dead-end" of appealing to an explanation based on a concept of emotion. There is also no need to postulate a lowering of thresholds for sensory stimulation as must follow from Grossman's hypothesis. The emphasis within the hypothesis proposed here is placed solely upon the 'vigor, or 'magnitude', of the response attributable to an enhancement of the energization of the response. It should be emphasized that the responses of the VMH animal are not different in 'kind' from the responses of the normal animal. The difference in the VMH animal is only in the 'magnitude' of the response.

In conclusion, I believe that the foregoing represents a viable method for an objective assessment of the effects of VMH lesions, and perhaps for the assessment

of all brain lesions. I have argued for a method which I believe will provide an objective assessment of the effect of VMH lesions as they function to alter the animal's state of energy mobilization, an effect which I believe to underlie the behavioral manifestations characteristic of VMH animals.

Appendix D

Original Data

Table 1: Individual data on body weights and food consumption.

Table 2: Individual data on resistance to handling ratings.

Table 3: Individual data on open-field behavior.

Table 4: Individual data on one-way escape-avoidance performance.

Relevant abbreviations: (appearing in column of Tables headed Treatment)

UH - unhandled

H - handled

VMH - ventromedial hypothalamic lesions

OBD - other brain damage caused by lesions not satisfying criteria of VMH lesions

C - control

(B) - burr holes, operated control

(E) - electrode placement, operated control

(NO) - unoperated control

Table 1

Individual Data on Body Weights and Food Consumption

Subject	Treatment	Body Weights (Gms.) Operative wt.	10 Days post-op.	20 Days post-op.	Food Consumption (Gms.) Day 10	Day 11	Day 20	Day 21
92	UH-VMH	239	293	312	81	102	74	66
98	"	234	274	264	89	80	38	45
105	"	245	341	405	71	90	133	119
106	"	245	284	305	55	68	73	79
109	"	240	282	317	72	78	84	77
122	"	239	271	271	103	91	64	67
129	"	253	293	353	88	90	96	86
144	"	259	298	312	68	78	71	56
145	"	250	264	270	60	71	43	38
112	H-VMH	231	276	283	53	103	65	77
113	"	240	283	281	88	97	57	56
116	"	262	296	302	78	80	61	45
119	"	255	294	296	81	75	85	84
123	"	249	291	289	72	71	53	53
127	"	263	294	338	85	96	68	45
142	"	253	301	291	77	78	64	54
91	UH-OBD	248	254	262	63	71	68	72
93	"	235	270	278	70	79	52	59
99	"	258	245	248	48	60	67	53
101	"	261	288	345	87	88	84	57
137	"	266	283	286	66	72	44	93
143	"	237	251	274	55	62	53	37
146	"	236	252	250	53	54	64	33

Table 1 (cont'd)

Individual Data on Body Weights and Food Consumption

Subject	Treatment	Body Weights (Gms.) Operative wt.	10 Days post-op.	20 Days post-op.	Food Consumption (Gms.) Day 10	Day 11	Day 20	Day 21
95	H-OBD	232	225	230	53	61	70	72
115	"	257	261	271	46	56	58	73
132	"	247	294	318	110	103	93	110
135	"	238	236	258	58	65	51	53
139	"	250	241	245	52	75	68	78
140	"	259	245	247	56	64	63	50
141	"	244	240	248	55	63	74	55
90	UH-C-(B)	261	259	272	43	49	58	36
96	" -(B)	246	257	266	39	48	54	57
100	" -(B)	247	264	269	50	62	63	67
107	" -(E)	254	271	274	68	54	85	69
111	" -(NO)	234	256	257	110	64	51	56
117	" -(E)	227	242	247	97	107	56	68
118	" -(NO)	251	263	282	43	53	55	48
121	" -(NO)	242	254	267	84	55	68	65
125	" -(NO)	251	260	270	Not secured-deleted from analysis			
126	" -(B)	234	244	246	83	87	42	59
131	" -(E)	247	263	271	49	62	51	60
133	" -(E)	235	250	248	61	55	59	56
94	H-C-(E)	233	246	239	50	46	43	40
97	"-(E)	249	258	260	73	76	71	67
102	"-(NO)	241	268	276	60	58	65	73
103	"-(NO)	238	266	282	73	72	60	60
104	"-(E)	260	266	296	61	77	78	74
108	"-(NO)	260	289	305	79	93	72	66

Table 1 (cont'd)

Individual Data on Body Weights and Food Consumption

Subject	Treatment	Body Weights (Gms.) Operative wt.	10 Days post-op.	20 Days post-op.	Food Consumption (Gms.) Day 10	Day 11	Day 20	Day 21
114	H-C-(NO)	258	269	295	74	77	86	67
120	"-(B)	241	249	255	47	47	67	64
124	"-(B)	233	252	263	59	97	71	74
128	"-(E)	229	238	236	64	71	68	70
134	"-(B)	257	248	255	51	58	58	50
138	"-(B)	248	254	257	37	50	53	51
110	H-VMH	258	225	245	67	66	85	86

(Due to accidental water deprivation subject 110 was dropped from experiment)

Table 2

Individual Data on Resistance to Handling Ratings

Subject	Treatment	Pre-op Rater 1	Pre-op Rater 2	Post-op Day 1 Rater 1	Post-op Day 1 Rater 2	Post-op Day 10 Rater 1	Post-op Day 10 Rater 2	Post-op Day 20 Rater 1	Post-op Day 20 Rater 2
92	UH-VMH	1	1	0	0	1	1	0	0
98	"	1	2	3	3	2	2	0	0
105	"	1	1	2	2	3	3	3	3
106	"	2	2	1	1	1	1	1	1
109	"	0	0	0	0	0	0	0	0
122	"	1	1	3	3	1	1	1	1
129	"	1	1	2	2	1	1	1	1
144	"	0	0	1	0	0	0	0	1
145	"	1	1	2	2	1	1	0	0
112	H-VMH	0	0	0	0	0	0	0	0
113	"	1	1	1	1	0	0	0	0
116	"	0	0	3	3	0	0	0	0
119	"	1	1	2	2	0	0	1	0
123	"	1	1	2	2	1	1	1	1
127	"	2	2	3	3	3	3	3	3
142	"	0	1	0	0	0	0	0	0
91	UH-OBD	0	1	0	0	0	0	0	0
93	"	0	0	0	0	0	0	0	0
99	"	0	0	0	0	0	0	0	0
101	"	1	1	1	1	0	0	0	0
137	"	0	0	0	0	0	0	0	0
143	"	0	0	2	2	0	1	0	0
146	"	0	0	2	2	2	1	1	1

Table 2 (cont'd)

Individual Data on Resistance to Handling Ratings

Subject	Treatment	Pre-op		Post-op Day 1		Post-op Day 10		Post-op Day 20	
		Rater 1	Rater 2	Rater 1	Rater 2	Rater 1	Rater 2	Rater 1	Rater 2
95	H-OBD	2	2	2	2	0	0	1	1
115	"	1	1	1	1	0	0	0	0
132	"	1	1	2	2	0	0	0	0
135	"	2	1	2	2	0	0	0	0
139	"	0	0	2	2	0	0	0	0
140	"	0	1	0	0	0	0	0	0
141	"	0	0	0	0	0	0	0	0
90	UH-C-(B)	0	0	1	0	0	0	0	0
96	" -(B)	1	1	0	0	1	1	0	1
100	" -(B)	1	1	0	0	0	0	0	0
107	" -(E)	0	0	0	0	0	0	0	0
111	" -(NO)	1	1	0	0	0	0	0	0
117	" -(E)	2	2	1	1	1	1	0	0
118	" -(NO)	0	0	0	0	0	0	0	0
121	" -(NO)	0	0	0	0	0	0	0	0
125	" -(NO)	1	1	1	1	0	0	0	0
126	" -(B)	1	1	0	0	0	0	0	0
131	" -(E)	1	0	0	0	0	0	0	0
133	" -(E)	2	2	2	2	2	1	2	1
94	H-C-(E)	1	1	0	0	0	0	0	0
97	"-(E)	1	2	0	0	0	0	0	0
102	"-(NO)	2	2	1	1	0	0	0	0
103	"-(NO)	1	1	0	0	0	0	0	0
104	"-(E)	1	1	0	0	0	0	0	0
108	"-(NO)	0	0	0	0	0	0	0	0

Table 2 (cont'd)

Individual Data on Resistance to Handling Ratings

Subject	Treatment	Pre-op Rater 1	Pre-op Rater 2	Post-op Day 1 Rater 1	Post-op Day 1 Rater 2	Post-op Day 10 Rater 1	Post-op Day 10 Rater 2	Post-op Day 20 Rater 1	Post-op Day 20 Rater 2
114	H-C-(NO)	0	0	0	0	0	0	0	0
120	"-(B)	1	1	1	1	0	0	0	0
124	"-(B)	2	2	1	1	0	0	0	0
128	"-(E)	0	0	0	0	0	0	0	0
134	"-(B)	0	0	0	0	0	0	0	0
138	"-(B)	1	1	0	0	0	0	0	0
110	H-VMH	1	0	0	0	0	0	0	0

(Due to accidental water deprivation subject 110 was dropped from experiment.)

Table 3

Individual Data on Open-field Behavior

Subject	Treatment	Lat. in First Sq. (sec.)	Total Squares Entered	Boluses	Cage leaving latencies (min.)
92	UH-VMH	12	26	2	4:25
98	"	14	18	1	1:38
105	"	23	25	1	1:49
106	"	20	39	1	4:18
109	"	13	39	0	2:33
122	"	7	11	1	2:39
129	"	7	39	0	4:06
144	"	15	28	0	3:35
145	"	12	39	1	1:52
112	H-VMH	29	29	0	0:54
113	"	15	34	0	1:36
116	"	7	36	0	1:16
119	"	8	38	0	2:15
123	"	16	39	5	1:12
127	"	6	35	1	1:41
142	"	35	52	2	2:03
91	UH-OBD	3	43	3	1:55
93	"	2	44	2	4:32
99	"	11	45	0	0:46
101	"	1	54	0	0:58
137	"	3	42	0	1:49
143	"	6	78	0	2:58
146	"	1	24	0	No Response

Table 3 (cont'd)

Individual Data on Open-field Behavior

Subject	Treatment	Lat. In First Sq. (sec.)	Total Squares Entered	Boluses	Cage leaving latencies (min.)
95	H-OBD	9	22	6	3:27
115	"	17	39	0	0:37
132	"	23	24	2	5:56
135	"	16	35	0	7:43
139	"	11	65	0	0:43
140	"	30	30	0	2:39
141	"	25	37	0	1:26
90	UH-C-(B)	5	43	6	2:53
96	" -(B)	8	42	1	No Response
100	" -(B)	8	54	1	0:49
107	" -(E)	21	46	0	0:35
111	" -(NO)	4	33	3	3:29
117	" -(E)	25	48	0	0:48
118	" -(NO)	2	42	0	2:13
121	" -(NO)	14	38	0	1:42
125	" -(NO)	13	36	0	0:59
126	" -(B)	17	42	5	3:23
131	" -(E)	8	46	0	1:47
133	" -(E)	15	54	2	3:29
94	H-C-(E)	5	45	0	3:32
97	"-(E)	7	39	1	1:01
102	"-(NO)	18	30	3	1:11
103	"-(NO)	8	18	0	5:01
104	"-(E)	12	64	6	1:09
108	"-(NO)	11	38	0	1:38

Table 3 (cont'd)

Individual Data on Open-field Behavior

Subject	Treatment	Lat. in First Sq. (sec.)	Total Squares Entered	Boluses	Cage leaving latencies (min.)
114	H-C-(NO)	7	53	1	1:21
120	"-(B)	12	61	0	0:59
124	"-(B)	7	30	1	3:46
128	"-(E)	20	33	0	3:43
134	"-(B)	14	30	0	0:41
138	"-(B)	14	22	0	8:54
110	H-VMH	17	35	0	0:55

(Due to accidental water deprivation subject 110 was dropped from experiment)

Table 4

Individual Data on One-way Escape-avoidance Performance

		Avoidance Responses					
		Acquisition Trial Blocks				Reversal Trial Blocks	
Subject	Treatment	1-5	6-10	11-15	16-20	1-5	6-10
92	UH-VMH	0	2	4	4	3	5
98	"	0	2	5	5	2	5
105	"	0	4	1	5	0	2
106	"	0	3	5	4	2	4
109	"	0	2	4	4	2	5
122	"	2	3	5	5	2	5
129	"	0	1	0	3	0	2
144	"	0	5	4	3	2	4
145	"	0	1	5	3	1	5
112	H-VMH	0	5	4	5	0	5
113	"	0	0	3	5	2	4
116	"	2	5	5	4	2	5
119	"	0	3	4	5	0	2
123	"	0	4	4	5	2	5
127	"	0	3	5	5	1	5
142	"	0	3	5	5	2	3
91	UH-OBD	2	3	5	5	1	5
93	"	1	4	5	5	2	5
99	"	0	1	4	4	2	4
101	"	2	4	3	5	0	4
137	"	1	2	4	4	1	4
143	"	0	1	3	5	1	2
146	"	0	4	5	5	1	3

Table 4 (cont'd)

Individual Data on One-way Escape-avoidance Performance

		Avoidance Responses					
		Acquisition Trial Blocks				Reversal Trial Blocks	
Subject	Treatment	1-5	6-10	11-15	16-20	1-5	6-10
95	H-OBD	1	3	5	5	3	5
115	"	1	2	5	4	2	4
132	"	1	3	5	5	1	2
135	"	0	0	3	5	2	2
139	"	1	5	5	5	2	5
140	"	0	1	5	4	2	2
141	"	0	3	5	5	1	4
90	UH-C-(B)	2	5	5	5	3	5
96	" -(B)	1	3	5	5	4	5
100	" -(B)	2	5	5	5	2	5
107	" -(E)	0	1	0	2	3	4
111	" -(NO)	0	2	4	5	1	4
117	" -(E)	1	2	4	5	1	5
118	" -(NO)	1	4	4	3	1	3
121	" -(NO)	0	3	5	3	0	0
125	" -(NO)	0	2	3	4	2	5
126	" -(B)	0	5	5	4	2	3
131	" -(E)	1	4	5	5	2	5
133	" -(E)	3	4	4	5	3	4
94	H-C-(E)	0	5	5	5	2	4
97	"-(E)	3	4	5	5	3	5
102	"-(NO)	3	5	5	5	3	4
103	"-(NO)	1	5	5	4	2	5
104	"-(E)	0	5	5	4	1	5
108	"-(NO)	2	5	5	4	2	5

Table 4 (cont'd)

Individual Data on One-way Escape-avoidance Performance

		Avoidance Responses					
		Acquisition Trial Blocks				Reversal Trial Blocks	
Subject	Treatment	1-5	6-10	11-15	16-20	1-5	6-10
114	H-C-(NO)	0	4	5	3	2	5
120	"-(B)	0	2	2	4	0	4
124	"-(B)	1	4	5	5	0	5
128	"-(E)	0	5	5	5	2	4
134	"-(B)	3	5	5	5	2	5
138	"-(B)	0	2	4	4	2	4
110	H-VMH	0	4	5	4	2	5

(Due to accidental water deprivation subject 110 was dropped from experiment)

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