Effects of ventromedial hypothalamic lesions on passive avoidance behavior in rats

Donald Berl Irwin

Iowa State University

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Donald Berl Irwin

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INTRODUCTION

Studies 35 years ago by Hetherington and Ranson (1940), implicating the ventromedial hypothalamus (VMH) in the regulation of food intake in the rat, sparked experimental interest in this small anatomical area. Although many studies have subsequently confirmed the initial observation that VMH destruction induces overeating (hyperphagia) and obesity, there has since been amassed a bewildering, often paradoxical, array of experimental findings relating VMH function to feeding and other behaviors. It has been said that "far more functions per millimeter of tissue have been imputed to the hypothalamus than to any other portion of the nervous system" (Grossman, 1967, p. 755). That many of those functions have been assigned to the VMH attest to the complexity of this anatomical area. The VMH has classically been highlighted as an integrative center for satiety, functioning as an inhibitor of a lateral hypothalamic feeding center (Stellar, 1954). More recently this classic interpretation has undergone considerable reformulation as the VMH has been implicated in other forms of behavior. The present study focuses on one of these behaviors, passive avoidance responding, in an attempt to clarify existing data with respect to recent reinterpretations of VMH function.

Passive avoidance is defined as the inhibition of a response which leads to punishment. Passive avoidance responses (PARs) are measured in several paradigms. First, appetitive approach-avoidance tasks are used. Water and/or food deprived rats receive mild electric shock after making a previously rewarded instrumental response. The PAR is demonstrated by the subsequent inhibition of approach, i.e., withholding of
the instrumental response. A second type of PAR task involves nonappetitive approach-avoidance. Rats first acquire an active avoidance response in a one-way conditioning paradigm. The rat learns to run from a shock compartment to a safe compartment to avoid signaled electric shock. After reaching criterion, footshock is shifted to the previously safe area. The PAR is demonstrated by avoidance of the formerly safe compartment. A third type of PAR task is both nonappetitive and requires no pretraining. It is the step-down paradigm used extensively in memory consolidation studies. Rats without training naturally step down from an elevated platform. When the rat steps down, footshock is applied until the rat returns to the platform. A PAR occurs if on subsequent trials the rat does not step down.

Studies evaluating VMH function using passive avoidance paradigms have relied extensively on appetitive approach-avoidance tasks. Since changes in appetitive motivation following VMH destruction would obviously affect performance on such tasks, it is necessary to review the effects of VMH damage on appetitive motivation.

Bilateral destruction of the VMH with electrolytic lesions produces hyperphagia which results in obesity (Brobeck, Tepperman, and Long, 1943). Intuitively, it would seem plausible that the destruction disrupts central appetitive regulatory mechanisms resulting in increased hunger motivation. Paradoxically, however, Miller, Bailey, and Stevenson (1950) and Teitelbaum (1957) reported that VMH destruction decreases hunger motivation. Their lesioned rats performed more poorly than control rats on a variety of hunger motivated, food reinforced
tasks. These data suggest that VMH lesions decrease hunger motivation. The hyperphagia was interpreted as an inability to terminate feeding behavior. It was suggested that the VMH functioned as a satiety center (Miller, 1964). Since VMH destruction decreased hunger motivation, PAR deficits, failure to withhold responses, in appetitive approach-avoidance tasks could not reasonably be attributed to increased appetitive motivation.

Reynolds (1965) subsequently criticized the methodology used by Miller, et al. (1950) and Teitelbaum (1957). He first raised the issue that the rats in the Miller, et al. study were, in fact, not hyperphagic and then argued that the tests employed in Teitelbaum's study were not good measures of relative motivation. Reynolds concluded that there was reason to question whether VMH lesioned rats were hypomotivated. While citing evidence that VMH lesioned rats were hypermotivated (Falk, 1961), Reynolds, unfortunately, did not attempt to replicate Miller, et al. and Teitelbaum's work with appropriate methodological improvements. Thus two important studies remained experimentally unexamined.

Grossman (1966) provided an alternative to the satiety interpretation of VMH function that also accounted for the VMH paradox. Grossman reported that small (cannula-produced) lesions produced hyperphagia but decreased performance of instrumental, food-rewarded responses. In his "affective hypothesis" Grossman proposed that the VMH normally inhibits affective reactions. VMH lesions disrupt this inhibition resulting in exaggerated affective responses to both positive and negative stimuli. Grossman hypothesized that the motivational paradox and many other
effects resulting from VMH dysfunction could be accounted for in terms of this altered affectivity. Accordingly, VMH lesioned rats overreact to freely available, palatable diets by overeating but work less for food because of an overreaction to the negative stimuli of handling and the test situation.

It is difficult to make predictions based on the "affective hypothesis" about the performance of VMH lesioned rats in appetitive passive avoidance tasks. Are approach responses to the positive appetitive stimuli stronger than the avoidance responses to the negative shock stimuli? Post hoc observations indicate that the positive stimuli are stronger. There is, however, no way of knowing the relative strengths of the positive and negative stimuli beforehand. Grossman's "affective hypothesis" offers a parsimonious explanation of the motivational paradox but has limited applicability for predicting the behavior of VMH lesioned rats in passive avoidance paradigms.

The VMH paradox (hyperphagia accompanied by decreased hunger motivation) has been recently examined with experiments that reflect awareness of the inadequacies of the Miller, et al. and Teitelbaum studies. Kent and Peters (1973) and Peters, Sensenig, and Reich (1973) reported that VMH lesioned rats performed at higher levels than control rats on food-reinforced lever pressing and runway tasks when more appropriate testing procedures and between-group comparisons were made. These data are indicative of increased hunger motivation. The authors argue for a reformulation of the motivational effects of VMH lesions to encompass the notion that VMH lesioned rats exhibit increased rather than decreased hunger motivation.
The above findings are augmented by Porter, Allen, and Arazie's (1974) report that body weight (non-obese vs. obese) is a determinant of performance on hunger-motivated tasks. Indeed, as more evidence comes forth (Sclafani and Kluge, 1974; Singh, 1974; Wampler, 1974) for the reformulation of the role of the VMH in hunger motivation, one must conclude as do Porter, et al. that "VMH lesioned rats do not have a decreased hunger motivation, but that their performance is a complex function of the behavioral task, amount of training, the level of deprivation at the time of testing, and the body weight at the time of testing (non-obese vs. obese)" (p. 631).

While the appetitive motivational effects of VMH lesions have been reassessed, the role of the VMH per se in producing these effects has also been challenged. Early lesion studies localized the VMH region as an effective lesion site for production of hyperphagia (Brobeck, Tepperman, and Long, 1943; Brooks, 1946a, 1946b). Recently Paxinos and Bindra (1973) pinpointed the destruction of the anterior tip of the ventral medial nucleus (VMN) as the critical site. Recent chemical stimulation studies, however, have pharmacologically defined pathways that may account for the effects of VMH lesions.

Anatomical studies have identified the VMH as a bilateral area located ventral to the dorsomedial nucleus and between the anterior and posterior hypothalamic areas. It is separated from the third ventricle by the periventricular-arcuate nucleus and is medial to the lateral hypothalamic area (LH). Prominent within the area is the VMN. The VMN has been described as a parvicellular nucleus, composed mainly of small ovoid cells (Clementi and Ceccarelli, 1970).
Afferent and efferent VMH connections have been difficult to trace. The major afferent pathway terminating in the VMH is the stria terminalis, carrying amygdaloid efferents (Raisman, 1970). Chi (1970) found evidence of an afferent tract from the anterior hypothalamus to the posterior portion of the VMN. Millhouse (1973) has described VMH efferents that project to the LH (especially ventral to the plane of the fornix), to the anterior hypothalamic area, and through the zona incerta. Additional efferents project caudally with the medial forebrain bundle and into the periventricular fiber system. Other VMH efferents have been reported to project to the tegmentum through the hypothalamo-tegmental tract and also to enter the tubero-hypophyseal tract in cat and man (Haymaker, 1969; Nauta and Haymaker, 1969).

The existence of fronto-hypothalamic fibers has been suggested but also questioned (Crosby and Showers, 1969; Nauta and Haymaker, 1969). Kievit and Kuypers (1975) have demonstrated anatomical connections between the hypothalamus and the frontal and parietal cortex in rhesus monkeys. Using retrograde enzyme transport, they traced fiber terminals in the cortex to their parent cell bodies in the medial and lateral hypothalamus, the substantia innominata, and the thalamus. These findings are the first reported evidence of direct cortical afferent fibers from hypothalamic areas concerned with motivation.

Destruction of VMH connections with knife cuts has supported the above anatomical findings. Of particular interest have been the LH-VMH connections. Cuts between the LH and VMH produce hyperphagia and obesity (Albert and Storlien, 1969; Gold, 1970; Sclafani and Grossman,
1969). Recent studies have noted that the cuts must extend rostrally to the VMH in order to produce hyperphagia (Paxinos and Bindra, 1973; Sclafani, Berner, and Maul, 1973). These data and those of others (Arees and Mayer, 1967; Oomura, Ooyama, Yamamoto, and Naka, 1967) support the feeding-satiety center, LH-VMH reciprocity view of hunger regulation.

There are, additionally, many reports of extrahypothalamic influences on hunger regulation. Lesions, for example, in the posterior amygdala produce hyperphagia (Anand and Brobeck, 1952; Grossman and Grossman, 1963). An extensive electrical stimulation study by Robinson (1964) showed a broad distribution throughout the brain of sites involved with feeding. Chemical stimulation studies have been particularly effective in identifying noradrenergic "feeding" sites throughout the limbic system. Initially, Grossman (1962a, 1962b) reported noradrenergic-sensitive sites extending from the perifornical area to the zona incerta. Coury (1967) observed feeding from adrenergic stimulation in not only the hypothalamus but also in the preoptic area, medial thalamus, medial septal area, cingulate gyrus and the hippocampus. Booth (1967) described less extensive limbic involvement with positive sites restricted to the anterior hypothalamus, ventral thalamus, lateral septal area and zona incerta.

Recent studies by Kapatos and Gold (1973) and Ahlskog and Hoebel (1973) have linked hyperphagia and obesity which were formerly associated with VMH destruction to the destruction of a noradrenergic system. Specifically, they found that destruction of the ventral noradrenergic bundle also produced overeating and obesity. The ventral noradrenergic
bundle innervates limbic areas as it ascends from brainstem nuclei. It, however, has few fibers which terminate in the VMN (Fuxe, 1965). Gold (1973), in reviewing the role of the VMN as an integrative center for satiety, reassessed the previously mentioned lesion and knife-cut studies in light of this more recent evidence. He concluded that "many of the lesioning or stimulating procedures that produce excessive eating appear to share in common damage, blockage, or stimulation to the ventral ascending noradrenergic bundle or its terminals. The VMN is merely a prominent landmark in the vicinity of effective loci" (p. 489).

Behavioral effects resulting from destruction of the VMH, presumably, could be attributed to destruction of a noradrenergic fiber system passing through the VMH. The results of passive avoidance studies using VMH lesioned rats, then, may be produced by disruption of this noradrenergic system. This is particularly likely in studies which have found PAR deficits with VMH lesioned rats using appetitive approach-avoidance tasks. With respect to the recent motivational and anatomical reformulations, such deficits could reasonably be attributed to increased appetitive motivation.

Returning now to the PAR literature, a PAR deficit with VMH lesioned rats was initially reported by Kaada, Rasmussen, and Kviem (1962). They found a PAR deficit when rats with subcallosal, septal, hypothalamic or insular lesions were compared with normal and operated controls. Of 191 lesions, three were confined to the VMH. All rats were deprived of water for 48 hours at the time of testing. Approach to a water dish was punished with mild shock in a typical appetitive approach-avoidance
task. The VMH lesioned rats received more shocks than control rats, a PAR deficit.

Kaada, et al. offered several explanations for the deficits and rejected all but one of them. They concluded that the lesions disrupted a somatomotor inhibitory system. The PAR deficits resulted from the lesioned rats' failures to inhibit their highly motivated approach responses.

There is, in addition to failure of response inhibition, another explanation for the PAR deficit. VMH lesioned rats often exhibit polydipsia, increased water intake as a consequence of the lesion (Grossman, 1967). This polydipsia may be either a primary effect of the lesion (e.g., decreased antidiuretic hormone output) or may be secondary to increased food intake. Normally, water-deprived rats decrease their food intake. It is possible that VMH lesioned rats consume more food during water deprivation and thus increase their thirst. While Kaada, et al. did not measure food intake, if their VMH lesioned rats were overeating on the dry food provided, then there would have been an increased likelihood of drinking during the test session. Not surprisingly then, thirstier animals would be less likely to inhibit approach to water.

Kaada, et al. rejected the notion of increased thirst drive on the basis of a water-intake test. Water intake following 48-hours deprivation was compared for 23 operated control rats and 14 operated rats exhibiting a PAR deficit. No difference in water intake was found. Since there was no indication that the three VMH lesioned rats were
among those used for the test, the evidence against increased thirst is insufficient. Even if the three VMH lesioned rats were among the 15 PAR-deficient rats in the test, the VMH lesioned rats' responses would have had to vary greatly from those of the other 11 rats in order to have affected the response measure.

If VMH lesioned rats have increased hunger motivation, as has been suggested, then secondary polydipsia could account for the PAR deficit. Thus there are two possible explanations of the PAR deficit: increased appetitive motivation and failure of response inhibition.

Green (1967), using similar procedures, found the same results as Kaada, et al. Under 24-hour water deprivation conditions, VMH lesioned rats were PAR deficient. Green cited Kaada's (1960) work on a somatomotor inhibitory system but failed to discuss the data in terms of relevant neural systems. While no mention was made of hyperphagia or obesity, it should be noted that increased appetitive motivation is as likely an explanation of the PAR deficit as failure of response inhibition.

Cannula-produced lesions or direct application of atropine in the VMH produced PAR deficits in a lengthy and elaborate study by Margules and Stein (1969). Rats, maintained at a body weight of 300 grams throughout the experiment, were tested for 72 minutes a day (five days a week) for approximately six months. A modified appetitive approach-avoidance task was used. Rats were first trained to lever-press for sweetened condensed milk on a VI-2 minute schedule. Four 18-minute cycles were presented. Each cycle consisted of 15 minutes of non-punished responding on the VI schedule followed by 3 minutes of tone-
signalled, punished responding where each lever-press was reinforced with milk and punished with footshock. Shock intensity was varied until responses in the tone period were almost completely suppressed. Following this initial training, cannulas were implanted. VMH damage produced by insertion of longer inner cannulas yielded PAR deficits. Direct intracranial application of methyl atropine in another group of rats also produced PAR deficits. In addition, the effects of application of atropine to the VMH were investigated in a satiation-suppressed operant responding test and in a free-feeding situation. Atropine increased lever-pressing on a VI-2 minute schedule which had been previously suppressed by satiation. Application of atropine to the VMH either before or after satiation failed to increase feeding responses which had been suppressed by satiation.

Margules and Stein interpreted these findings similarly to Kaada, et al. (1962), that is, failure to suppress punished operant responding. Their findings suggest that the system mediating these effects involves cholinergic synapses. Since cholinergic blockade failed to disinhibit feeding following satiation but increased operant responding following satiation, they suggested that the VMH contains two systems. One system, cholinergic, functions in suppression of operant behaviors. Another system, noncholinergic, functions as a feeding-suppressant, satiety mechanism.

The study by Margules and Stein is noteworthy in that: (a) PAR deficits were shown to occur not only from VMH destruction but also from cholinergic blockade, (b) evidence was presented for the presence
of two systems in the VMH for response inhibition and feeding satiety, and (c) the response inhibitory system was shown to be cholinergically mediated. These results are consistent with the recent findings of a noradrenergic-feeding system which passes through the VMH; however, increased appetitive motivation mediated by a noradrenergic mechanism does not appear to apply as an explanation of their results.

Miczek and Grossman (1972) administered atropine to the VMH of squirrel monkeys. They found, using a paradigm similar to that used by Margules and Stein (1969), that punished responding was disinhibited following applications of atropine. The animals, however, failed to consume the rewards earned during periods of disinhibited responding. Punished and unpunished consummatory behavior was inhibited by atropine. Miczek and Grossman concluded that direct application of atropine may produce several independent but interacting effects. Their findings, like those of Margules and Stein, indicate overlapping systems in the VMH.

As the studies just cited indicate, experiments assessing VMH function with passive avoidance tasks need to be examined carefully. Disruption of either a noradrenergically-mediated appetitive motivational mechanism or a cholinergically-mediated response inhibitory system may produce the same result (PAR deficits). VMH lesions may selectively damage one or both systems. Additionally, the PAR paradigm selected may obscure the nature of the VMH damage. In appetitive passive avoidance tasks increased appetitive motivation as a result of VMH lesions is an appealing explanation of PAR deficits. The PAR deficit, however, may result from the independent action of response disinhibition. In
nonappetitive tasks there is less likelihood of confounding the two processes, assuming that increased appetitive motivation has little effect in nonappetitive tasks. Data are lacking concerning the role of appetitive motivation in nonappetitive PAR paradigms.

Sclafani and Grossman (1971) recognized that the action of two systems was possible but emphasized increased appetitive motivation as an explanation of their results. VMH lesions in rats produced hyperphagia, obesity and a PAR deficit. The PAR task involved 20-minute drinking sessions. On test days contact with the drinking tube resulted in a mild shock (0.20 ma). When 22.6-hours water-deprived and given free access to food, VMH lesioned rats received significantly more shocks, a PAR deficit. No deficits were reported when rats were 22.6-hours water-deprived and placed on a restricted diet. The latter condition reduced VMH lesioned rats' water intake to levels comparable to those of controls. Sclafani and Grossman contended that this procedure equated thirst between lesion and control groups. Restricting food intake, presumably, reduced secondary polydipsia in VMH lesioned rats by eliminating overeating. If reduced water intake were indicative of reduced thirst, then approach to the drinking tube would decrease. Only in the condition where rats were given free access to food, and water intake was not adjusted, were PAR deficits found.

Sclafani and Grossman suggested that their data indicate that increased appetitive motivation is a relevant factor in the PAR deficit, a factor which may work in conjunction with other disinhibitory influences. While equating water consumption by restricting access to
food does not necessarily equate thirst or hunger as Sclafani and Grossman contend, nonetheless, increased appetive motivation provides a better explanation of their PAR deficits than disinhibition of responding. The "failure to inhibit responding" explanation would apply if PAR deficits had occurred on all the tasks used. On the tasks where secondary polydipsia was reduced, no PAR deficits were found.

In a recent report of PAR deficits from VMH lesions (Singh, 1973) one could not clearly attribute the PAR deficit to either increased thirst or disinhibition of responding. Water intake was restricted to 30 minutes daily in the test apparatus. On test days (when footshock was introduced) an additional 30 minutes of access to water in the home cage was provided following testing. Obviously, the previously presented argument of increased food intake resulting in secondary polydipsia applies to this experiment as well. Singh, however, conducted two other tests which suggest that failure to inhibit responding was also involved.

One of the tests involved reversal learning in a T-maze with vanilla-flavored Metrecal for reward. Singh used two response measures: days to criterion and number of errors before achieving criterion. On the original learning which preceded the reversal, VMH lesioned rats were significantly better than controls on both measures. During reversal learning, VMH lesioned rats made significantly more errors in reaching criterion than controls but took significantly fewer days to reach criterion. The greater number of errors was attributed
to response perseveration or failure of response inhibition as was the fewer days to criterion.

It is difficult to reconcile how response perseveration first hinders then facilitates reversal learning as Singh suggests. However, it is possible to explain the data in terms of response disinhibition and increased appetitive motivation. Response disinhibition or response perseveration would favor the making of reversal errors. Increased appetitive motivation, on the other hand, would favor the learning of the reversal. It would be possible then that the interaction of the two opposing tendencies would be reflected in more errors to criterion but fewer days to criterion. The control group's continued errors over more days than the lesioned group could be attributed to their lower level of motivation.

The natural motor tendency of rats to spontaneously alternate between arms of a T-maze was also disrupted by VMH lesions. As Singh concluded, this suggests that VMH damage disrupts an inhibitory system which leads to response perseveration. It does not, however, when placed with his other findings, suggest that inhibitory loss is the best available explanation of the effects of VMH damage. Neither inhibitory loss nor increased appetitive motivation can fully account for all of Singh's results.

Singh did make an interesting application of McCleary's (1966) work on limbic inhibitory mechanisms to the general body of VMH data. He interpreted the variety of anomalous data resulting from VMH damage as loss of inhibition of the highest habit-strength response in each task.
VMH lesioned rats, responding on tasks with high approach habit-strength (e.g., PAR appetitive tasks) when in competition with lesser habit-strength avoidance responses, would exhibit disinhibition. The utility of this explanation does not preclude the interaction of motivational effects which influence habit-strength and approach-avoidance tendencies. It may be that the interaction between motivational and inhibitory systems is precisely what makes the VMH lesion data so enigmatic.

A final PAR study (McNew and Thompson, 1966) should be mentioned because a nonappetitive approach-avoidance task was used. Rats with medial hypothalamic (but not VMH) lesions were PAR deficient in a one-way avoidance apparatus. In view of the fact that the effects of VMH lesions now appear to result from damage to fibers of passage, the data from studies with medial hypothalamic damage and PAR deficits may be relevant to the data from studies with VMH damage.

McNew and Thompson's choice of tasks would appear to exclude the possibility of explaining the data in terms of increased appetitive motivation. A PAR deficit in a nonappetitive situation could be accounted for by disinhibition of the previously acquired avoidance response. VMH lesioned rats would be unable to inhibit the avoidance response, thereby demonstrating a PAR deficit. Performance on appetitive PAR tasks may be, however, a function of deprivation conditions or level of appetitive motivation. Relevant data are lacking on this important point.

Two main interpretations have thus emerged from reviewing the VMH-PAR literature. Both increased appetitive motivation and
disinhibition of responding have been used as explanatory concepts. Neither view can fully account for the data; yet, taken together they present a complex picture of interacting systems.

This complexity can be further illustrated by considering the data from studies evaluating VMH function using two-way active-avoidance paradigms. In this situation subjects alternate between two compartments. Shock avoidance in the first compartment is accomplished by running to the second compartment. Shock avoidance in the second compartment occurs by returning to the first compartment. Two-way active avoidance then contains a strong passive avoidance component (Bolles, 1967). A rat must return to the compartment where it was previously shocked in order to avoid being shocked in its present compartment. If VMH lesioned rats are PAR deficient, such deficiencies should facilitate two-way avoidance responding through an increased tendency to return to the previously shocked compartment.

Facilitated two-way avoidance responding has been reported by several investigators (Green, 1967; Grossman, 1966, 1972; Levine and Soliday, 1960; Weisman and Hamilton, 1972). While similar procedures were used in each study, there were notable differences. Green studied prepuberal and postpuberal lesioned rats and reported that both groups exhibited facilitation. The facilitation, however, fell short of statistical significance. Grossman was able to produce facilitation with small cannula-produced lesions (1966) as well as with electrolytic lesions (1972). Weisman and Hamilton reported facilitation in VMH lesioned rats at a variety of shock levels from 0.15 to 0.90 ma.
Of greater interest than the procedural differences are the various interpretations of the facilitory effects of VMH lesions. Grossman's (1966) "affective hypothesis" proposes that VMH lesioned rats exhibit an increased reactivity to aversive stimulation. Facilitated two-way avoidance responding was one outcome that VMH lesioned rats exhibited as the result of heightened affective reactivity to the negative shock stimuli. In his later study (1972) Grossman offered an alternative explanation. In a reversal of his earlier position, he suggested that VMH lesioned rats were, in fact, less fearful than normal rats. Weisman and Hamilton also reject the original Grossman "affective hypothesis" and his later fear reduction explanation as well. They explained their results in terms of an inhibitory deficit. Recognizing that returning to the previously shocked compartment is like drinking at an electrified tube, they suggested that VMH lesions produce disinhibition of the PAR component. The resulting increased tendency to return to the previously shocked compartment would then produce facilitation of two-way avoidance responding.

Studies employing cholinergic blockade of the VMH have indicated that facilitation of two-way avoidance responding is a general finding. Grossman (1965) reported that direct application of atropine facilitated two-way avoidance responding. He used these data to support his contention that the VMH was a regulatory center for affective reactions. Sepinwall (1969) found facilitation using atropine and a modified Sidman schedule in which shock onset is unsignaled. Interestingly, cholinergic stimulation (carbachol) also facilitated responding on the
task. Sepinwall attributed this to nonspecific stimulation effects of the carbachol rather than specifically to a cholinergic action.

Active avoidance facilitation was reported by Sechzer, Turner, and Liebelt (1966) in mice after goldthioglucose-induced VMH lesions. Injections of goldthioglucose have been shown to produce lesions in the VMH of mice resulting in hyperphagia and obesity. Sechzer, et al. used a one-way active avoidance task. Their findings conflict with those of McNew and Thompson (1966) who reported impairment of one-way avoidance responding in rats with electrolytically-induced lesions in the medial hypothalamus.

Sechzer, et al. suggested that altered emotionality could account for the facilitation. The goldthioglucose lesioned mice exhibited lower shock thresholds and less "freezing" behavior than control mice. It should be noted that less "freezing" could be the result of the lowered shock thresholds. The lowered shock threshold could result from reasons other than altered emotionality. Several obvious explanations of the discrepancy between McNew and Thompson's data and those of Sechzer, et al. exist. First, species differences could account for the differences in active avoidance acquisition reported. Second, McNew and Thompson's sites were outside of the VMH. Third, different lesioning techniques were used in the two studies.

A two-way active avoidance response deficit has been reported in VMH lesioned cats (McAdam and Kaelber, 1966) and attributed to an increased tendency to "freeze" in the experimental situation. A more recent study by Colpaert and Callens (1974) found two-way active
avoidance responding to be a function of shock intensity in cats. This contrasts with the previously cited findings of Weisman and Hamilton (1972) in rats in which facilitation occurred at all levels of shock used. Colpaert and Callens reported that high intensity shock (2.0 ma) produced "freezing" while moderate shock intensity (1.2 ma) did not. They rejected Weisman and Hamilton's suggestion of a "PAR deficit" in favor of Grossman's "reduced fear" explanation. Undoubtedly, there are species differences involved; yet, if disinhibition of passive responding occurs, it is unclear why the effects are not noticeable at the high shock intensity.

Two-way active avoidance response deficits have also been reported following hypothalamic knife cuts (Grossman, 1970; Grossman and Grossman, 1970). These data are of interest because of the recently reported evidence that fiber tracts and not the VMN are responsible for the observed effects of VMH lesions. Grossman reported that transecting the lateral connections of the medial hypothalamus in rats reliably depressed acquisition in a two-way active avoidance task. Cuts just anterior to the level of the VMN produced little or no change in two-way avoidance behavior. Cuts just posterior to the level of the VMN disrupted acquisition of a two-way active avoidance response. The posterior cuts were not as disruptive as the lateral cuts. These results are surprising in view of the previously mentioned studies which have reported facilitated active avoidance behavior. Grossman's data do not contradict the lesion studies but, instead, suggest that the cuts did not disrupt the same inhibitory system as did the lesions.
This review of the studies using two-way active avoidance paradigms to evaluate VMH function shows strongest support for the position that VMH lesions disrupt an inhibitory fiber system. The resulting disinhibitory effects produce PAR deficits which in turn facilitate two-way active avoidance responding. The disinhibitory position, however, is not consistently supported by the data, a fact which gives added emphasis to the complexity of the systems involved.

A third area of VMH research serves further to highlight this complexity. An aversion conditioning paradigm has recently been used to evaluate the effects of VMH lesions. If a rat is allowed to consume a substance and is subsequently made sick by injections of toxic compounds such as lithium chloride or apomorphine, the animal will associate the taste of the substance with the postingestional stress and exhibit a conditioned aversion to the substance after recovery (Revusky and Gracia, 1970; Rozin and Kalat, 1971).

Aversion conditioning is conceptually similar to passive avoidance tasks in that the subject learns to inhibit a response (approach to the appetitive substance). Three studies have been published which have used variations of the basic paradigm to evaluate the effects of VMH destruction on the strength of aversion conditioning. The results of these studies are no less equivocal than those of the passive and active avoidance studies.

Gold and Proulx (1972) reported a conditioned aversion deficit in VMH lesioned rats. Lesioned rats were deficient in their ability to learn an aversion to saccharin-sweetened water associated with
apomorphine. They consumed more of the saccharin water which had been paired with apomorphine than control rats. The lesioned rats also exhibited more rapid extinction of the aversion than the controls. The authors attributed their results to impaired ability of lesioned rats to form gustatory-visceral associations since rats lesioned after aversion conditioning continued to avoid the saccharin water.

A study by Peters and Reich (1973) strongly suggests that increased appetitive motivation resulting from VMH lesions can account for the aversion deficit reported by Gold and Proulx. Rats maintained at 95 percent of their free-feeding weight and allowed to bar-press for food on a continuous reinforcement schedule exhibited strong aversion to sucrose pellets associated with lithium chloride toxicosis. Rats maintained at 80 percent of their free-feeding weight exhibited significantly less aversion when compared to the 95 percent group. Likewise, VMH lesioned rats at 95 percent body weight performed similarly to the 80 percent group and exhibited an aversion response deficit. These lesioned rats reacted like control rats with increased hunger motivation and consumed more of the sucrose pellets.

A third study (Weisman, Hamilton, and Carlton, 1972) presents data contradictory to the two previously mentioned studies. Weisman, et al. reported facilitated aversion conditioning in rats with VMH lesions. Lesioned rats consumed less of a sweetened-condensed milk solution associated with sickness induced by methyl atropine and exhibited greater resistance to extinction of the aversion than did control rats. Weisman, et al. attributed their results to increased responsivity to
both extero- and interoceptive stimuli following VMH lesions. Their interpretation is in line with Grossman's "affective hypothesis". They concluded that either VMH-PAR studies were not comparable to the aversion conditioning paradigm or VMH-PAR deficits were due to other factors. Procedural differences between the three studies could account for the different results: deprivation schedules, test substances and toxic compounds were different in each study.

Again a situation arises where no one explanation can account for all the data. Increased appetitive motivation appears to be a likely explanation in view of Peters and Reich's work. Such a view can easily account for Gold and Proulx's findings. It is difficult, however, to account for the decreased consumption in the Weisman study in terms of increased hunger. A disinhibitory explanation can account for Gold and Proulx's data but is difficult to reconcile with either of the other two studies. One might argue that the VMH lesioned rats in the Peters and Reich study exhibited disinhibition and coincidentally similar responses to the control group maintained at 80 percent of their free-feeding body weights. This, however, ignores the growing body of data which indicates that VMH lesioned rats have increased appetitive motivation. Weisman, et al. reported heightened, not lessened, inhibition of approach. The "affective hypothesis" provides the least effective explanation of these results. As Peters and Reich have noted, unless one has a priori information about the relative contributions of the positive and negative properties of stimuli, hyperreactivity is equivocal in its predictions. Weisman, et al. base their conclusions on
increased responsivity to the aversive stimuli, ignoring the effects of increased responsivity to the rewarding stimuli present in their task (e.g. sweetened-condensed milk).

Clearly the data from VMH aversion conditioning studies indicate the complexity that arises when appetitive, inhibitory and possibly affective mechanisms are confounded. Further studies are needed where the various factors are isolated in order to delineate the role of each mechanism.

The present experiments were designed to investigate the role of appetitive mechanisms in passive avoidance conditioning and further detail VMH aversion conditioning effects. The performance of VMH lesioned rats and unoperated control rats maintained at preoperation free-feeding body weights was compared in a nonappetitive approach-avoidance task (one-way paradigm), in a step-down task and in the aversion conditioning paradigm. The nonappetitive tasks were chosen because they had not been utilized in previous VMH studies and they presented the opportunity to sort out the confounded appetitive and disinhibitory effects of VMH lesions. Use of the aversion paradigm provided the opportunity to test the same rats on two tasks, one non-appetitive and the other appetitive.

Therefore, two experiments were conducted. In Experiment I the one-way and aversion tasks were used. In Experiment II rats were trained in both the step-down and aversion paradigms. Various outcomes on these tasks would be predicted by the different explanations previously noted. Specifically, if the previously-reported appetitive
PAR deficits are due to increased appetitive motivation one would predict no impairment on the nonappetitive passive tasks and a conditioned aversion response deficit. However, if the effects are due to disruption of inhibitory mechanisms causing disinhibition, then performance should be impaired by VMH lesions on both appetitive and nonappetitive tasks. If the two mechanisms interact, then predictions may be like those from the "affective hypothesis", i.e., equivocal.
EXPERIMENT I

Method

Subjects

The subjects were 39 Long-Evans female hooded rats (Blue Spruce Farms, Inc., Altamont, N.Y.) approximately 100 days old and weighing 234-288 gm at the beginning of the experiment. All rats were housed in individual cages under constant illumination. Twenty-five rats were anesthetized with sodium pentobarbital (40 mg/kg). Bilateral electrolytic lesions, aimed at the VMH, were produced by passing 2.0-ma anodal current for 20 sec between a 30-gauge nichrome-steel electrode, insulated except at its conical tip, and a rectal cathode. Stereotaxic coordinates for the electrode placements were: A=5.6, H=-3.5, L=0.7 (de Groot, 1959). Three rats died following surgery. The remaining 14 unoperated rats served as controls.

Apparatus

A one-way avoidance box (63x20x26 cm) was constructed of sanded plexiglas. The box consisted of two 31x20 cm compartments, separated by a wall with a 13x10 cm opening. The opening could be closed by dropping a sanded plexiglas guillotine door. The grid floor was made of 3.2 mm stainless steel rods, positioned 5 cm above the floor and 2 cm apart. Grid-shock was obtained from a high voltage source in series with sufficient resistance to maintain constant current through the rat as long as the rat touched any two bars of the grid floor (Brown, Reus, and Webb, 1961). Grid-shock could be applied to either compartment. During active avoidance conditioning, raising the door activated a timer which
after a 5-sec delay turned on 0.3 ma grid-shock in the first compartment. During passive avoidance conditioning, grid-shock was always on in the second compartment.

The rats' home cages were used for the LiCl aversion conditioning. During testing the rats' regular water bottles were replaced with similar bottles containing a 0.1 percent solution of sodium saccharin.

Procedure

The rats were housed in individual cages upon arrival from the supplier and were allowed free access to food (Wayne Lab Blox) and water for 21 days to establish preoperation baseline weights. Daily body weight measurement for all rats began 4 days prior to surgery and continued throughout the testing phase of the experiment. Food intake was measured for all rats for the 4 days prior to surgery and the 4 days following surgery. Beginning on the fifth days after surgery, all rats were reduced to their body weights on the day of surgery and were maintained at that weight for the remainder of the testing phase. Body weights were maintained by weighing the rats before each daily test session and on nondeprived days placing a variable amount of food directly into the home cages immediately following testing. On the day of surgery food was removed from all rats for 24 hrs and 25 rats were randomly selected for lesion operations. The 22 rats which recovered from surgery were designated Group VMH. Group C consisted of 14 control rats. Since each rat was to be tested with two tasks, order effects were controlled by randomly dividing the VMH and C rats between two orders. Order AP-AC rats were presented the one-way active-passive task first followed by aversion conditioning. The tasks were reversed in order AC-AP.
On day 1 of behavioral testing, order AC-AP rats were deprived of food and water. Twenty-four hours later consumption of the saccharin solution was measured in a 15-min test, followed by the return of food and water. On day 5 rats were again deprived of food and water and 24 hrs later consumption of the saccharin solution was measured during a 15-min period. Amount of deprivation and length of the consumption test period were increased to increase the amount of saccharin solution consumed. On day 9, following 24-hrs deprivation, consumption of the saccharin solution was measured for 30 min. On day 15, following 48-hrs deprivation, a 30-min consumption test was conducted. Immediately following this test session, all rats were given intraperitoneal injections of a 2% body weight dose of 0.15M LiCl. On day 20 all rats were again tested for consumption of the saccharin solution after 48-hrs deprivation with a 30-min session. This procedure was repeated on days 25 and 30. Thus a conditioned aversion to the saccharin solution was established and three subsequent tests of the strength of the aversion without further reinforcement were made.

One-way active avoidance conditioning was begun on day 31. Three squads of 6 rats each were formed for this task. A trial consisted of placing a rat in the first or shock compartment, raising the door and recording whether the rat avoided or escaped to the safe compartment. When the rat entered the safe compartment, the door was lowered. The rat was removed from the safe compartment after a 20-sec delay. Each rat received 10 daily trials in rotation within a squad. When a criterion of 10 consecutive avoidances was reached, a second phase of
passive avoidance conditioning was begun. Grid-shock in this phase was always on in the previously safe second compartment and was never applied in the first compartment. A rat was placed in the first compartment and the door was raised. If after 5 sec the rat had not entered the second compartment, the door was promptly lowered. If the rat had entered the second compartment, then the door was lowered only after the rat had returned to the first compartment to escape the shock. After a 20-sec delay in the first compartment, the rat was removed and returned to its home cage. During this phase, one trial per day was given. The number of passive avoidances (remaining in the first compartment) was recorded. When a criterion of four successive passive avoidances was reached, testing was stopped. On day 37 all rats were given free access to food.

The rats in order AP-AC began with the one-way active-passive task. The procedures were identical to those just described for order AC-AP. On day 10 the last day of the passive testing, food and water deprivation began for aversion conditioning. On day 12 consumption of the saccharin solution following 48-hrs deprivation was measured in a 30-min test. On day 17 a second 30-min consumption test was conducted with the 48-hr deprived rats. Immediately following this test session, all rats were given intraperitoneal injections of a 2% body weight dose of 0.15 LiCl. The strength of this conditioned aversion to the saccharin solution was tested as in order AC-AP with three 30-min consumption tests on days 22, 27, and 32. Following the end of testing on day 32, all rats were given free access to food.
Following the behavioral testing phase, all rats in both orders were maintained with free access to food and water for a period of 70 days. Body weights were obtained at the end of this period to determine weight gains.

**Histology**

The lesioned rats were given a lethal dose of sodium pentobarbital. Intracardial perfusion was accomplished using physiological saline followed by 10% formalin. The brains were removed and prior to sectioning were stored in 10% formalin. Frozen sections were taken at 150 μ in the coronal plane described by König and Klippel (1963). Photographic enlargements of the unstained sections were used to assess the extent and location of lesion damage.

**Results**

Five measures were recorded for each rat: body weight, food intake, saccharin consumption, trials to one-way active avoidance criterion and trials to one-way passive avoidance criterion. These data were analyzed with several analyses of variance. One control rat died following the LiCl injection and the data from two lesioned rats were discarded when histological examination revealed that their lesions were outside of the VMH. Data were analyzed from 20 rats in Group VMH and 13 rats in Group C.

At the end of the 70 day weight-gain period, it was noted that a number of lesioned rats (7 in order AC-AP and 6 in order AP-AC) had failed to become obese, contrary to earlier indications of elevated food intake and rapid weight gains. Tissue from each rat was histologically examined and revealed no systematic differences between obese and
nonobese lesioned rats other than the two cases previously mentioned. The range of VMH lesion placements according to Konig and Klippel (1963) coordinates was: AP = 4.0 to 4.4; H = -3.2 to -3.8; and L = 0.2 to 1.0. In four rats the lesions were primarily unilateral. The lesions generally were large and extended laterally and posteriorly beyond the boundaries of the VMH. Because of the discrepancies between the behavioral data and the histological examination, the data from the lesioned rats were divided into obese lesioned and nonobese lesioned categories. All analyses were made on the basis of three lesion conditions: obese, nonobese, and control.

Figures 1 and 2 present, by orders, mean body weights for the three lesion conditions on three selected days. These data were analyzed according to the mixed design of Table 1 (all tables are located in Appendix). Since there were unequal numbers of subjects in cells and the frequencies were not proportional, an unweighted means analysis was used in this and all subsequent analyses of variance. There was an overall effect due to lesion conditions ($F = 30.83, df = 2/27, p < .001$) and due to days ($F = 74.67, df = 2/54, p < .001$). The interaction between lesion conditions and days was also significant ($F = 25.92, df = 4/54, p < .001$), indicating that the increase in body weight resulting from lesion conditions was not the same across the three days.

Selected pairwise comparisons among body weight means using Tukey's test (Kirk, 1968) were made to analyze further the body weight differences. Body weights on the day of surgery were not significantly different among the lesion conditions. Five days after surgery the obese
EXPERIMENT I - ORDER AC-AP

O = Obese lesioned
N = Nonobese lesioned
C = Control

Figure 1. Mean body weight on three selected days during the experiment for Group VMH (obese & nonobese) and Group C
Figure 2. Mean body weight on three selected days during the experiment for Group VMH (obese & nonobese) and Group C
Lesioned rats weighed significantly more than the control rats ($q = 4.38$, $p < .01$), while the nonobese lesioned rats were not significantly different from either of the other two conditions. The nonobese rats, however, did increase their body weight significantly from the day of surgery ($q = 3.92$, $p < .01$) as did the obese rats ($q = 4.70$, $p < .01$) while the control group did not. On the final weight day the obese group differed significantly from both the nonobese ($q = 15.10$, $p < .01$) and the control groups ($q = 15.62$, $p < .01$). The obese and control groups showed a significant increase in weight from the fifth to the final day ($q = 16.05$, $p < .01$ and $q = 3.88$, $p < .01$, respectively). The nonobese rats, as noted earlier, failed to show a significant weight gain from day five to the final day.

Thus both lesioned groups exhibited rapid weight gains immediately following surgery, while the unoperated control group did not. This pattern changed following a final weight-gain period with the obese rats continuing to show significant weight gains while the nonobese rats did not.

Mean food intake for lesion conditions across selected days is presented in Figures 3 and 4. As shown in Table 2, the food intake effects are similar to the body weight findings. Lesion conditions produced a significant effect ($F = 16.40$, $df = 2/27$, $p < .001$) as did days ($F = 86.31$, $df = 2/54$, $p < .001$) and the interaction of days with lesion conditions ($F = 9.90$, $df = 4/54$, $p < .01$). Pairwise comparisons among selected means using Tukey's test were made. Before surgery the three groups did not differ significantly. Immediately after surgery the obese group consumed significantly more food than either the nonobese
Figure 3. Mean food intake on three test days for Group VSH (obese & nonobese) and Group C
EXPERIMENT I - ORDER AP-AC

O = Obese lesioned
N = Nonobese lesioned
C = Control

FOOD INTAKE (GRAMS)

DAY BEFORE SURGERY
O 18
N 18
C 19

DAY AFTER SURGERY
O 38
N 33
C 26

5TH DAY AFTER SURGERY
O 40
N 36
C 23

Figure 4. Mean food intake on three test days for Group VMH (obese & nonobese) and Group C
(q = 3.32, p < .05) or the control groups (q = 6.81, p < .01). The non-obese group also ate significantly more than the control group (q = 3.49, p < .05). On the fifth day after surgery both the obese and the nonobese groups ate significantly more food than the control group (q = 10.20, p < .01 and q = 7.78, p < .01, respectively) but did not differ from each other.

The obese rats showed a significant increase in food intake from before surgery to immediately after surgery (q = 13.20, p < .01) but showed no further increase. The nonobese exhibited a similar pattern (q = 9.59, p < .01). As would be expected following deprivation, the control rats showed a similar significant increase (q = 5.33, p < .01). By the fifth day their intake declined significantly (q = 3.02, p < .05), returning to a level that did not differ significantly from the amount consumed before surgery. Thus the lesioned rats displayed sustained hyperphagia following surgery. Both the obese and the nonobese rats following lesioning exhibited typical VMH lesion patterns of hyperphagia accompanied by rapid weight gains.

Figures 5 and 6 present mean amounts of saccharin solution consumed by the lesion conditions across days. The number of subjects for this analysis was reduced by six, the number of rats failing to drink at least 7 ml of solution on the aversion day. The only significant effect (see Table 3) was that for days (F = 43.68, df = 3/63, p < .001). Pairwise comparisons among Day means (Tukey's test) indicated that the observed aversion was significant across all groups (q = 16.16 p < .01) and that there was a significant day to day increase after the initial
Figure 5. Mean amount of saccharin solution consumed on the day of aversion conditioning and on three subsequent test days for Group VMH (obese & nonobese) and Group C.
Figure 6. Mean amount of saccharin solution consumed on the day of aversion conditioning and on three subsequent test days for Group VMH (obese & nonobese) and Group C
drop ($q = 5.10\ p < .01$ and $q = 4.35\ p < .01$, respectively). The amount consumed on test day 3, however, was still significantly depressed below that consumed on the aversion conditioning day ($q = 6.71,\ p < .01$). Thus, while strong aversions occurred in all three groups, there were no significant between group differences.

Mean trials to criterion for one-way active avoidance are shown in Figure 7. As shown in Table 4, there were no significant differences between lesion conditions. An effect due to orders, however, did occur ($F = 39.01,\ df = 1/27,\ p < .001$). Rats which began behavioral testing with the one-way task took significantly more trials to reach criterion than rats which began the one-way task after experiencing aversion conditioning. After the active avoidance criterion was reached, passive avoidance training began. Analysis of the data from the passive avoidance task yielded no significant differences (see Figure 8 and Table 5).
Figure 7. Mean trials to the active avoidance criterion
EXPERIMENT I

O = Obese lesioned
N = Nonobese lesioned
C = Control

Figure 8. Mean trials to the passive avoidance criterion
EXPERIMENT II

Method

Subjects

The subjects were 39 Long-Evans female hooded rats (Blue Spruce Farms, Inc., Altamont, N.Y.) weighing 237-296 gm and approximately 100 days old at the beginning of the experiment. The rats were maintained and surgery was accomplished under the same procedures as in Experiment I. Group VMH contained 22 lesioned rats and Group C contained 14 unoperated control rats.

Apparatus

A 31x23x38 cm step-down box was constructed of sanded plexiglas. The grid floor was made of 3.2 mm stainless steel rods positioned 5 cm above the floor and 2 cm apart. A 23x13 cm sanded-plexiglas platform was located 5 cm above the grid floor in one end of the box. Grid-shock was obtained from a high-voltage source in series with sufficient resistance to maintain a constant current through the rat as long as it touched any two bars on the grid (Brown, Reus, and Webb, 1961). A manually-operated electronic timer was used to measure step-down latencies. Stopping the timer electrified the grid floor. The apparatus for aversion conditioning was the same as that described in Experiment I.

Procedure

The initial procedures before actual behavioral testing was begun on day 1 were the same as in Experiment I. Baseline weights were established; daily body weight was measured; and pre- and post-surgery food intake was recorded. Groups were formed (VMH and C); following
surgery a baseline weight was maintained; and orders were arranged. In order SD-AC rats were given the step-down task first followed by aversion conditioning. The tasks were reversed in order AC-SD.

On day 1 of behavioral testing order SD-AC rats began the step-down task. This consisted of placing a rat on the raised platform and starting the timer. When the rat stepped down onto the grid floor with four feet, the timer was stopped which automatically presented 1.0-ma grid-shock. When the animal returned to the safety of the platform, it was removed after a 20-sec delay and was returned to its home cage. The latency to step-down as measured by the timer was recorded. A single trial per day was given. On the following day and all subsequent daily test trials, the rat was again placed on the platform and latency to step-down recorded, but no grid-shock was given. If a rat did not step down after a maximum latency of 300 sec, it was then removed to its home cage. Testing was completed on day 8.

Following testing on day 8, all rats were deprived of food and water for 24 hrs. On day 9 consumption of the saccharin solution was measured in a 30-min session. Following the session, the rats were given access to food and water. On day 12 a 48-hr deprivation period began. On day 14 consumption of the saccharin solution was recorded in a 30-min session. Immediately following this session, all rats were given intraperitoneal injections of a 2% body weight dose of 0.15M LiCl. As in Experiment I, the strength of this conditioned aversion to the saccharin solution was measured on three subsequent test trials without further reinforcement. The test trials were conducted following 48-hrs
deprivation on days 19, 24, and 29. On day 31 all rats were given free access to food.

The rats in order AC-SD began with the aversion conditioning task. On day 1 all rats were deprived of food and water for 24 hrs. On day 2 a 15-min consumption test was conducted after which food and water were restored. On day 6 a second 15-min consumption test was given following 24-hrs deprivation. On day 11 a 30-min consumption test was given following 48-hrs deprivation. Immediately after the 30-min test of saccharin solution consumption on day 16 (following 48-hrs deprivation) all rats received intraperitoneal injections of a 2% body weight dose of 0.15M LiCl. Three tests of the strength of this conditioned aversion to the saccharin solution were made without further reinforcement. The tests were conducted following 48-hrs deprivation on days 21, 26, and 31.

Step-down conditioning was begun on day 32 and ended on day 37. The procedures were the same as those for order SD-AC. Following the end of testing on day 37 rats in order AC-SD were given free access to food.

Following the behavioral testing phase, all rats in both orders were maintained with free access to food and water for a period of 70 days. Body weights were obtained at the end of this period to determine weight gains.

Histology

Tissue examination for lesion damage was carried out under the same procedures as in Experiment I.
Results

Four measures were recorded for each rat: body weight, food intake, saccharin consumption, and step-down latency. The data from the first three measures were analyzed with analyses of variance similar to those used in Experiment I. The step-down data were analyzed using Kruskal-Wallace's H-test (Kirk, 1968). One lesioned rat died following the LiCl injection and the data from one other lesioned rat were discarded when histological examination revealed that the lesion site was posterior to the VMH. Data were analyzed from 20 rats in Group VMH and 14 rats in Group C.

As in Experiment I, a discrepancy between initial weight gain and food intake and final weight gain was noted among a number of the lesioned rats (4 in order AC-SD and 7 in order SD-AC). Histological examinations of tissue from each rat were made and no systematic differences were observed that would account for the differential final weights. The lesions were similar to those observed in Experiment I (generally large and extending laterally and posteriorly beyond the boundaries of the VMH) and fell within the same ranges as those reported in Experiment I. In four rats there was only apparent unilateral damage to the VMH. Because of the above findings, the lesioned rats were divided into obese and nonobese categories and the data analyses were made with the three resulting lesion conditions.

Figures 9 and 10 display the mean body weights for the lesion conditions in orders SD-AC and AC-SD. Significant effects noted were lesion conditions ($F = 14.65$, df = 2/28, $p < .001$), days ($F = 236.27$, ...
EXPERIMENT II - ORDER SD-AC

O = Obese lesioned
N = Nonobese lesioned
C = Control

Figure 9. Mean body weight on three selected days during the experiment for Group VMH (obese & nonobese) and Group C
EXPERIMENT II - ORDER AC-SD

O = Obese lesioned
N = Nonobese lesioned
C = Control

Figure 10. Mean body weight on three selected days during the experiment for Group VMH (obese & nonobese) and Group C
df = 2/25, p < .001), and the lesion x day interaction (F = 43.55, df = 4/56, p < .001). A summary of the analysis is found in Table 6 (all tables are located in Appendix). Selected pairwise comparisons (Tukey's test) were made to assess further the main effects. The body weights initially did not differ significantly. By the fifth day after surgery the obese and nonobese rats' body weights had increased significantly (q = 9.18, p < .01 and q = 6.26, p < .01) and were not significantly different from one another. In contrast, the control rats' body weights did not increase significantly and were significantly less than either the obese (q = 5.29, p < .01) or the nonobese rats' (q = 3.68, p < .05). Comparing day 5 with the final day, all groups showed a significant increase in body weight (obese, q = 23.19, p < .01; nonobese, q = 3.38, p < .05; control, q = 4.92, p < .01). The obese group on the final day had gained significantly more than either the nonobese (q = 14.54, p < .01) or the control groups (q = 13.95, p < .01). The final weights of the nonobese and the control groups did not differ significantly. As in Experiment I there were rapid weight gains among lesioned rats immediately following surgery and none among the control rats. At the end of the experiment the nonobese rats weighed no more than the control rats while the obese rats had increased their body weights substantially beyond those of the control rats.

Mean food intake for lesion conditions across days is presented in Figures 11 and 12. As displayed in Table 7, the significant effects were similar to those for the body weight data (lesion, F = 14.96, df = 2/28, p < .001; day, F = 126.75, df = 2/56, p < .001; lesion x day,
Figure 11. Mean food intake on three test days for Group VMH (obese & nonobese) and Group C.
Figure 12. Mean food intake on three test days for Group VMH (obese & nonobese) and Group C.
F = 18.81, df = 4/56, p < .001; lesion x order x day, F = 3.56, df = 4/56, p < .02). The amount of food consumed increased across days. The lesion groups differed in the amount of food consumed but the pattern of group difference varied across orders and across days. Pairwise comparisons (Tukey's test) with selected means were made to evaluate further the main effects. Before surgery the groups did not differ significantly in food intake. While all three conditions exhibited significant increases following surgery (obese, q = 15.96, p < .01; nonobese, q = 9.25, p < .01; control, q = 7.93, p < .01), only the lesioned rats continued to increase significantly from the first day after surgery to the fifth day after surgery (obese, q = 3.51, p < .05; nonobese, q = 4.27, p < .01). In contrast the control group's intake declined from that of the first day after surgery (q = 4.76, p < .01). The hyperphagia displayed by the lesioned rats was similar to that observed in Experiment I and was accompanied by rapid weight gains.

Figures 13 and 14 present means for saccharin consumption among lesion conditions across days. The number of rats contributing data to the analysis was reduced by one rat which failed to drink more than 7 ml on the aversion conditioning day. A summary of the analysis is presented in Table 8. There was a significant day effect (F = 90.07, df = 3/81, p < .001) and unlike the data from Experiment I, a significant order x day interaction was found (F = 3.41, df = 3/81, p < .025) and an interaction between lesion conditions and days which approached significance was present (F = 2.17, df = 6/81, p = .054). This indicates that there was a change across days in saccharin consumption that did
Figure 13. Mean amount of saccharin solution consumed on the day of aversion conditioning and on three subsequent test days for Group VOIH (obese & nonobese) and Group C.
Figure 14. Mean amount of saccharin solution consumed on the day of aversion conditioning and on three subsequent test days for Group VMH (obese & nonobese) and Group C.
not show the same pattern among lesion conditions or across orders. Pairwise comparisons (Tukey's test) were made with selected means. The observed aversion was significant across groups and orders \((q = 23.36, p < .01)\). There was a significant day to day increase after the initial drop \((q = 8.82, p < .01 \text{ and } q = 4.23, p < .01, \text{ respectively})\). The amount consumed on test day 3, however, still represented a significant aversion \((q = 8.26, p < .01)\). Within orders the pattern of recovery from the aversion varied. In order AC-SD there was a significant increase in consumption from test day 1 to test day 2 \((q = 4.11, p < .01)\). A similar increase did not occur in order SD-AC until test day 3 \((q = 4.08, p < .01)\). Comparisons between lesion conditions across orders showed that the control group's recovery from the aversion began on test day 2 \((q = 5.88, p < .01)\). Recovery from the aversion in the lesioned groups began on test day 3 (obese, \(q = 3.59, p < .05 \text{ and nonobese, } q = 5.10, p < .01\)).

While these interactions occurred, it is important to note that strong aversions occurred in all conditions in both orders.

Figure 15 presents median step-down latencies for lesion conditions across days. Inspection of Figure 15 reveals a strong passive avoidance response for all conditions in both orders which on the last three test days decreased for the control group. There was also an order effect, as the decrease in the control group's responses occurred two days after conditioning in order AC-SD and after five days in order SD-AC. Because of the highly skewed distribution of the data, Kruskal-Wallis's H-test was used to analyze by orders the data from the last four test trials.
Figure 15. Median step-down latencies on the day of conditioning and on subsequent test days for Orders SD-AC and AC-SD and Groups VMH (obese & nonobese) and C.
For order SD-AC the following effects were noted: T4—no difference among conditions; T5—a significant difference, $H' = 9.15$, $p < .025$; T6—a significant difference, $H' = 8.18$, $p < .05$; T7—no difference among lesion conditions, $H' = 2.71$, $p < .30$. For order AC-SD the effects were: T2—no difference; T3—no difference; T4—a significant difference, $H' = 21.14$, $p < .01$; T5—a significant difference, $H' = 8.43$, $p < .02$. When compared with the control group, the lesioned rats exhibited facilitated passive avoidance responding, remaining on the platform more test days than the control group.
DISCUSSION

The results of these experiments have implications for three aspects of VMH functioning. First, the response disinhibition interpretation of the effects of VMH destruction was not supported. Several researchers (Kaada, Rasmussen, and Kviem, 1962; Margules and Stein, 1969; Singh, 1973) have suggested that the VMH functions as a response inhibitory center. Destruction of the VMH would result in general response disinhibition. McCleary (1966) has proposed that the deficit in response inhibition would occur with the response which had the highest habit strength. VMH lesioned rats should exhibit PAR deficits because the now punished highly dominant response is disinhibited.

Passive avoidance deficits were not observed in the VMH lesioned rats used in this study. This outcome contrasts with the findings cited above and those of Green (1967) and Sclafani and Grossman (1971). The five previous studies all used appetitive passive avoidance tasks. As noted in the introduction, performance on such tasks is confounded with changes in appetitive motivation. Sclafani and Grossman have suggested that increased appetitive motivation offers a better explanation of VMH-PAR deficits than response disinhibition.

If VMH destruction results in response disinhibition, PAR deficits should have been observed in the nonappetitive tasks. Deficits were not observed in either the one-way passive avoidance task or the step-down task. It is possible that some other response had a higher habit strength than the passive response and, therefore, was disinhibited. This is impossible to determine a priori but appears unlikely in the tasks involved.
Increased appetitive motivation resulting from VMH destruction should have no direct effect on performance in the nonappetitive tasks. However, an indirect effect may occur. If increased appetitive motivation contributes to an increased general drive state, then the increased drive should further energize the dominant response tendency. If this occurs, then facilitation of nonappetitive passive responding would be predicted. There was facilitation present in the step-down task used in Experiment II. VMH lesioned rats, when compared with control rats, remained on the platform (the passive response) significantly longer. Such facilitation would be difficult to detect with the trials-to-criterion acquisition measure used in the one-way task, where learning of the passive response occurred very rapidly. A measure more analogous to the one used in the step-down task would be the number of trials necessary for a rat to return to the shock compartment after reaching the acquisition criterion.

The present results are also in direct contrast with those of the one previous study which used nonappetitive one-way passive avoidance (McNew and Thompson, 1966). McNew and Thompson reported a PAR deficit; however, their lesions were located outside of the VMH in the medial hypothalamus. Because the area is neuro-anatomically complex and fiber tracts may be involved (Gold, 1973), such differences are not surprising.

The results from the one-way active avoidance task which preceded the passive task also differed from previously reported findings. Weisman and Hamilton (1972), for example, found active avoidance facilitation following VMH lesions in rats. They, like the other researchers who have reported active avoidance facilitation, used a two-way task.
They proposed that the facilitation resulted from disinhibition of the passive component in the two-way paradigm. The passive component is not present in one-way active avoidance. Because the disinhibitory position was not supported in the present study, the results of these two-way active avoidance studies should undergo reinterpretation.

Rats which received the nonappetitive tasks after first experiencing the aversion conditioning procedures acquired the nonappetitive tasks more quickly. These order effects, present in both the one-way active avoidance task and the step-down task, were undoubtedly due to increased docility and familiarity with the general testing situation. The order effects, however, do not obscure the major finding that disinhibition of passive avoidance responding did not occur.

The second implication for VMH functioning is that the use of aversion conditioning paradigms to evaluate VMH function needs further investigation. Data from the present study are in accord with those reported by Weisman, Hamilton and Carlson (1972), showing no aversion deficit. Unlike Weisman, et al., there was no facilitation of the aversion. The data from this study conflict with those reported by Gold and Proulx (1972) and Peters and Reich (1973), who found aversion deficits. There are enough procedural variations among the four studies to account easily for the differences. It may be that the aversion conditioning paradigm is an extremely sensitive design. In such a design small procedural differences would result in differential aversion effects. Peters and Reich have shown this sensitivity to be the case with levels of deprivation. Undoubtedly the test stimulus (i.e., sucrose, saccharin, sweetened-condensed milk) associated with the
aversive toxicosis is of great importance. Gold and Proulx's interpretation of impaired associative mechanisms may be partially correct. Some test stimuli may be more quickly or effectively associated with the sickness. Presumably, the interpretation of aversion effects is further complicated by the interaction of these various factors.

While the results from nonappetitive tasks cast doubt on the disinhibitory interpretation of VMH function, the increased appetitive motivation position was not supported by the results of the aversion conditioning task. Aversion response deficits are predicted by the increased appetitive motivation position. There were not any deficits.

The major finding of the aversion conditioning task is that more investigation of variations in procedures is needed. Whether PAR tasks are, in fact, comparable to aversion conditioning tasks needs further study.

A third implication for studies of VMH function is reflected in the data for body weight and food intake. Three behavioral criteria were used to evaluate the effectiveness of the lesions in destroying the VMH. The first of these was a significant increase in food intake. Reviewing Figures 3, 4, 11, and 12, sustained hyperphagia among the lesioned rats was clearly present. While the control rats' intake declined across post-surgery test days, the intake of lesioned rats remained elevated above the pre-surgery test day. The lesioned rats in this study, therefore, fulfilled the first criterion.

The second criterion was rapid weight gain, accompanying the increase in food intake. Again the lesioned rats met this criterion (see
Lesioned rats rapidly gained weight following surgery, while control rats did not.

A third criterion for evaluation of the effectiveness of VMH lesions was the attainment of a static obese weight. In this study, rats were maintained at their presurgery body weights a maximum of 37 days during the behavioral testing phase and then allowed a period of 70 days with free access to food and water to attain a static obese weight. Seven out of 20 lesioned rats in Experiment I and 9 out of 20 lesioned rats in Experiment II were judged to have reached the criterion. Obviously there was strong indication of VMH destruction from the post-surgery food intake and body weight data (confirmed by subsequent histological examinations), but there was a perplexing lack of obesity in over half of the lesioned rats. While more sophisticated histological techniques may have revealed anatomical differences, division of the lesioned rats into obese and nonobese categories for data analysis revealed no consistent differences between the groups. The only measure on which the obese and nonobese rats consistently differed was final body weight.

Such a discrepancy indicates that the lesions produced complex effects and implies that the criteria used for assessing the effectiveness of such lesions should be carefully considered. Had a single criterion, attainment of a static obese weight, been used in the present study and had the post-surgery food intake and body weight data not been collected, the useful data from over half the lesioned rats would have been discarded from analysis.

Beginning with the early studies of Hetherington and Ranson (1940) production of obesity became sine qua non for indicating VMH
destruction. It now appears to be neither an essential nor sufficient condition for describing the complex effects of VMH lesions. The data from this study indicate that maintenance at presurgery body weight may either alter the effects of the lesions or allow time for compensatory action by other parts of a larger neural hunger circuit. The fact that VMH lesioned static obese rats, when reduced to their normal body weights, quickly regain their obese weights (Brobeck, Tepperman and Long, 1943), does not bear directly on the first explanation, as there may be anatomical differences between the lesions of the obese and non-obese rats. The recent work by Gold and others (Alskog and Hoebel, 1973; Gold, 1973; Kapatos and Gold, 1973) does favor the latter interpretation. If the effects of VMH lesions are due to destruction of fiber systems passing through the VMH, then the failure of many lesioned rats in the present study to become obese is more easily understood. Within the typical range of VMH lesion placements, the fibers of passage might be completely disrupted, partially disrupted, or not affected at all. Complete disruption could result in a rat meeting all three of the above mentioned criteria. Partial disruption could result in the data observed in this study. Lack of disruption could result in a rat meeting none of the criteria. Such factors indicate the need for refined techniques when dealing with such basic VMH effects as weight gains.

In summary, the results of this study indicate: failure to support the disinhibition interpretation of the effects of VMH lesions; the need to further evaluate aversion conditioning as a useful paradigm.
for assessing the effects of VMH lesions; and that basic VMH lesion effects such as increased body weight must be given as careful scrutiny as seemingly more complex effects such as PAR deficits.
REFERENCES


Brooks, C. McC. Activity and the development of obesity. *Federation Proceedings*, 1946, **5**, 12. (a)

Brooks, C. McC. A study of the respiratory quotient in experimental hypothalamic obesity. *American Journal of Physiology*, 1946, **147**, 727-734. (b)


Falk, J. L. Comments on Dr. Teitelbaum's paper. *Nebraska symposium on motivation*, 1961, 9, 65-68.


Grossman, S. P. The ventromedial hypothalamus and aggressive behaviors. Physiology and Behavior, 1972, 9, 721-725. (b)


Hetherington, A. W. and Ranson, S. W. Hypothalamic lesions and adiposity in the rat. Anatomical Record, 1940, 78, 149-172.


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I am particularly thankful for Dr. Peters' assistance in the design and completion of this dissertation and for the contributions of the other members of my graduate committee, Drs. Lloyd Avant, David Edwards, Frederick Hembrough, George Karas, and Robert Strahan.

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Finally, I wish to thank the several relatives and good friends who, by their continued interest in my work, have helped me complete this dissertation.
APPENDIX
Table 1. Summary of the analysis of variance (unweighted means) of body weight data for Experiment I

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Table 2. Summary of the analysis of variance (unweighted means) of food intake data for Experiment I

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Table 3. Summary of the analysis of variance (unweighted means) for the aversion conditioning data of Experiment I

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Table 4. Summary of the analysis of variance (unweighted means) for the one-way active avoidance data of Experiment I

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Table 6. Summary of the analysis of variance (unweighted means) for the body weight data of Experiment II

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