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Behavioral perseveration: Lesions of the septal nuclear complex and ventromedial hypothalamic nucleus

by

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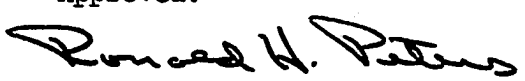

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INTRODUCTION

Recent behavioral evidence, and some neuroanatomical evidence, suggest that the functions of the septal nuclear complex (SNC) and ventromedial nucleus of the hypothalamus (VMH) may overlap and interact to a considerable extent. The SNC is located in the telencephelon between the lateral ventricles. It is a bilaterally symmetrical midline structure having massive connections with the frontal cortex, hippocampus, hypothalamus, and tegmental region. The VMH is a bilateral structure lying on either side of the third ventricle just above the median eminence. Although the SNC and VMH are widely separated anatomically, they may be linked via the large, diffuse, medial forebrain bundle.

The behavioral effects of damage to the SNC and VMH are very similar, although the behavioral similarities have been largely unrecognized. At least two factors serve to mask the recognition of possible functional overlap. A review of the terms employed by different workers to describe the behavioral effects of SNC and VMH damage provides a list of adjectives that is both bewildering and misleading in scope. Postoperative behavior has been characterized as being emotional, hyperemotional, hyperirritable, savage, or perseverative depending upon the animal specie, lesion locus, behavioral test, and, perhaps, the descriptive creativity of the author. It is often difficult to determine whether the term is intended to be purely behaviorally descriptive, or whether theoretical implications are intended.

Secondly, there is a tendency to view the functions of a structure in

a unitary sense ("behavior centers"), thus rendering comparisons between areas a difficult task. The literature concerning the behavioral effects of ventromedial hypothalamic lesions tends to emphasize the dramatic hyperphagia, obesity, and food-related behavior associated with the lesion. Other behavioral characteristics tend either to be ignored or related in some way to the food-intake characteristics of the organism. Animals with VMH damage have also been described as being "vicious" (Wheatley, 1944). "finicky" with respect to food acceptance (Teitelbaum, 1955), or simply "hyperemotional" (Smith, Salisbury, and Weinberg, 1961; Grossman, 1966).

Literature related to the effects of SNC damage has emphasized the hyperemotional and/or perseverative (repetitive) behavioral characteristics resulting from the lesion. It was not until quite recently that it was recognized that septal damage may also produce hyperphagia, polydipsia, and "finickiness" in appetitive behavior (Beatty and Schwartzbaum, 1967; Harvey and Hunt, 1965; Singh and Meyer, 1968).

While the SNC and VMH are undoubtedly not identical in function, the possibility of functional overlap cannot be ignored. Anatomical comparisons tend to strengthen the impression of functional similarity, although some of the specific anatomical information remains controversial to date. Lesions involving either the SNC or VMH may result in response disinhibition, exhibited as behavioral perseveration. In order to facilitate further discussion, the review of the literature will be divided into separate anatomical and behavioral sections.

REVIEW

Anatomical Considerations

The telencephalic region often called simply "the septum" or the "septal region" is a complex collection of nuclei and tracts. To avoid considering this region as unitary in either structure or function, the term "septal nuclear complex" (SNC) is used.

The SNC is bounded dorsally by the corpus callosum, and its ventral border is generally taken to be the line of the anterior commissure. The lateral extent of the region is well defined by the presence of the lateral ventricles, while the rostral-caudal limits are established by the genu of the corpus callosum and fornix columns, respectively. Within these boundaries there exists a complex network of morphologically definable nuclei and fiber tracts: part of the diagonal band of Broca; dorsal fornix; medial septal nucleus; lateral septal nuclei, triangular septal nucleus; and septofimbrial nucleus.

Recent anatomical investigations have indicated the existence of a precise projection between the SNC, hippocampal fields, frontal cortex, and medial forebrain bundle. Of specific interest is the observation that the medial septal nucleus receives hippocampal afferents from only cytoarchitectonic fields CA 1 anterior and posterior (Raiseman, 1966, 1969; Raiseman, Cowan, and Powell, 1966). Frontal efferents project specifically to the medial septal nucleus from the prefrontal orbital area (Johnson, Rosvold, and Mishkin, 1968), and the medial septal nucleus has reciprocal connections with the hypothalamus via the medial forebrain bundle (Raiseman, 1966). It would appear that the medial septal nucleus

plays an important role in the integration of activity between the hypothalamus (via the medial forebrain bundle), hippocampus (via the dorsal fornix and fimbria), and frontal cortex (via prefronto-orbital septal projections).

The anatomical connections of the VMH are not so clear. Amygdaloid efferents to the area of the ventromedial nucleus have been described (via the stria terminalis). It is almost certain that the VMH is invaded by dendrites from cells of the hypothalamic dorsomedial, lateral, and arcuate nuclei. Although it has been suggested that fronto-hypothalamic fibers terminate in the VMH, the existence of such fibers remains in doubt (Crosby and Showers, 1969; Nauta and Haymaker, 1969). Efferents of the VMH project to the tegmentum via the hypothalamotegmental tract, and VMH fibers probably also contribute to the dorsal longitudinal fasciculus. Ventromedial hypothalamic fibers have been reported to contribute to the tuberohypophysial tract in the cat and man, though such fibers are not observed in the rat (Haymaker, 1969; Nauta and Haymaker, 1969).

Lesions of the VMH and SNC result in behavioral changes that are similar in several respects. Analysis of behavioral information lends strength to the hypothesis that these areas comprise part of a functional system.

Behavioral Considerations: The Septal Nuclear Complex

Hyperemotionality

Early work concerned with the behavioral effects of SNC lesions gave rise to the hypothesis that such damage results in "hyperemotionality" (Brady and Nauta, 1953, 1955). The behavioral pattern sometimes called the septal syndrome is dramatic in comparison to the animal's preoperative behavior, particularly in the rat. Rats that are relatively docile preoperatively show immediate postoperative "savageness" or "wildness," in that they resist capture vigorously, show exaggerated startle responses, attack objects held close to the snout, and vocalize, defecate, and urinate with frequency when disturbed. The mere presence of laboratory personnel standing close to the cage, speaking in normal tones, may be sufficient to elicit the latter responses. The severity of the septal syndrome tends to decrease spontaneously over time, so that by the thirtieth postoperative day the exaggerated nature of the syndrome has subsided considerably. Daily handling produces an even more rapid decline in the severity of the "syndrome" (King, 1958, 1959; Singh, 1969; Yutzey, et al., 1964). Other components of the behavioral effects of the lesion, such as facilitated active avoidance responding, are unchanged by the passage of time.

The hyperemotional component of the septal syndrome appears to be specie-dependent, while other characteristics of septal behavior are consistent across species. Hyperemotionality is a common effect of septal lesions in the rat. King (1959), however, noted genetic differences in the septal syndrome. The severity of the exaggerated responsivity was

significantly greater in rats of the hooded Lashley strain than in albino Wistar rats. Septal lesions in the cat produce reports of hyperemotionality somewhat less frequently (Moore, 1964). Observations of the hamster (Sodetz, et al., 1967) and squirrel monkey (Buddington, et al., 1967) following septal damage have failed to note the hyperemotionality component of the septal syndrome.

Septal hyperemotionality appears to be a consistent symptom only when behavioral rating scales are used to measure emotionality. Brady and Nauta (1953, 1955), King (1958, 1959), Singh (1969) and Yutzey, et al. (1964) reported consistently high ratings of septal hyperemotionality when behavior such as startle respone, resistance to capture, attack toward visually presented objects, and open-field behavior were evaluated. Other purported measures of emotionality, however, do not support the hyperemotionality hypothesis. Brady and Nauta (1953, 1955) reasoned that if septal damage produced lower thresholds of emotional responsivity, then the acquisition of a conditioned emotional response should be more rapid in septal rats. Rats tend to become immobile, or "freeze," in stressful situations. The freezing response can be elicited in the presence of a conditioned stimulus (CS) previously associated with shock (the conditioned emotional response, or CER; conditioned suppression). Thus, if the CER is elicited during an operant task, the decrease in the operant rate (relative to the rate preceding the CS) provides an index of CER strength. Contrary to prediction, the development of the freezing response was impaired by septal lesions. While unoperated and sham-operated controls demonstrated response suppression, the septal group continued to respond during the

presentation of the stimulus.

King (1958) reported that septal lesions in the rat facilitated the acquisition of an active avoidance response (AAR) and also resulted in high emotionality ratings. These data are consistent with the hyperemotionality hypothesis. Enhanced AAR acquisition following septal lesions has since been demonstrated in a number of species in a wide variety of active avoidance situations (Fox, 1964; Buddington, 1967; Krieckhaus, et al., 1964; McCleary, 1961; Moore, 1964).

Avoidance Behavior and Resistance to Extinction: The Response Disinhibition Hypothesis

It is now evident that facilitated AAR acquisition is independent of hyperirritability so often associated with septal lesions. Those species that do not develop postoperative hyperirritability still exhibit enhanced AAR acquisition. Whereas large SNC lesions in the rat produce hyperirritability, small SNC lesions result in enhanced AAR acquisition in the absence of hyperemotionality (Kenyon and Krieckhaus, 1965). Others (e.g., Harrison and Lyon, 1957) have not been able to correlate postoperative hyperemotionality with any variable other than lesion size.

Kaada (1951) reported that stimulation of the subgenual-septal area produced motor inhibition, whether the motor activity was ongoing autonomic responses, peripheral reflexes, or cortically induced movements. McCleary (1961) demonstrated that septal lesions that resulted in enhanced AAR acquisition in the cat also resulted in a passive avoidance (PAR) deficit. That is, the same cats that were highly proficient in learning to actively avoid shock in a shuttlebox were dramatically deficient in avoiding shock

associated with eating from an electrified food cup. McCleary hypothesized that septal lesions result in chronic response disinhibition, exhibited as perseverative behavior in conflict situations (excessively repetitive behavior) and generally exaggerated or enhanced behavior when conflict was not involved. The passive avoidance deficit has also been demonstrated in the rat (Kasper-Pandi, et al., 1969, Van Hoesen, et al., 1969). The notion of response disinhibition has proven to be a fruitful working hypothesis.

If septal lesions result in behavioral perseveration, these lesions should increase resistance to extinction. Zucker and McCleary (1964) reported that septal lesions did not affect the extinction rate of an AAR using usual extinction procedures (i.e. elimination of shock from the situation). Punishment of the avoidance response by presenting shock in the previously "safe" compartment of the shuttlebox (punished avoidance, PUN) resulted in precipitous extinction rates in the control group, whereas the septal group continued to respond (perseveration). It is difficult to extinguish a well-established avoidance response in normal animals, presumably because the reinforcement contingencies (successful avoidance of shock) continue to operate even though the shock is no longer presented. La Vaque (1966), using a massed extinction technique, demonstrated striking response perseveration in septal rats. Massed extinction trials produced rapid extinction in the control group. The extinction criterion (30% avoidance) was usually reached during the first extinction session by control animals. Septal animals were still responding at the acquisition criterion level of 90% avoidance at the end of the sixth extinction

session, when the experiment was terminated. The high resistance to extinction in La Vaque's experiment may have been caused by the use of a photic CS. Schwartzbaum, Green, Beatty, and Thompson, (1967) found that septal animals may have been reinforced by escaping a negative stimulus, i.e., light onset. Van Hoesen, MacDougall, and Mitchell (1969), however, reported AAR perseveration in septal rats when the massed extinction technique was used in combination with an auditory CS.

Increased resistance to extinction following septal damage is not limited to active and passive avoidance. Septal damage also increased resistance to extinction of a food-reinforced operant response (Schwartzbaum, et al., 1964). The same study demonstrated, in an experiment designed specifically to test perseverative error, that a septal rat will not shift from one response lever to another when the reinforcement contingencies shift, whereas normal animals were able to shift with the demands of the reward contingencies. Increased resistance to extinction of a bar-press response following septal lesions in primates was demonstrated by Butters and Rosvold (1968a). Further analysis of lesion locus suggested that increased resistance to extinction was associated with damage to the ventral septal region which contains primarily the medial septal nucleus (Butters and Rosvold, 1968b). The anatomical data of Johnson, et al., (1968) indicate that the orbital cortex (previously associated with perseverative behavior following lesion) projects selectively to this area of the septum. Butters and Rosvold (1968a,b) suggested that the ventral sector of the septum, in association with the orbital frontal cortex, is concerned with the regulation of dominant response tendencies.

Reversal Learning and Alternation

Reduced inhibition of dominant response tendencies following SNC lesions may produce response perseveration when the subject is required to reverse a position habit. Thompson and Langer (1963) reported that septal lesions markedly impaired reversal learning in rats. This finding was particularly striking because the subjects had been run to a criterion of only one correct response before reversal learning was initiated. In some respects the behavioral task was not unlike the PUN task reported by Zucker and McCleary (1964). The acquisition of a correct response in a T-maze was reinforced with escape from shock, while reversal learning was initiated by punishing the previously correct response. The authors concluded that a response inhibition deficit would account for the data, since the reversal task required the inhibition of a learned response tendency to one side of the T-maze. Zucker and McCleary (1964) trained 15 cats with septal lesions, and 9 controls, to a position habit in a Wisconsin General Test Apparatus (WGTA), and then tested for habit reversal. Although there were no significant differences between the groups during the original acquisition of the position habit, the operated cats made significantly more perseverative errors during the first reversal. During the second reversal of the position habit, the group differences were eliminated. Zucker (1965) noted that Zucker and McCleary (1964) employed a simultaneous discrimination task to establish the position habit in the WGTA, which may have minimized the chances of observing an acquisition deficit. When a successive discrimination in the WGTA was used, cats with septal lesions demonstrated both acquisition and reversal deficits. Group differences were again

eliminated during the second reversal task.

Septal lesions did not impair the acquisition of a complex spatial discrimination, although the acquisition of a brightness discrimination was impaired by septal lesions (Schwartzbaum and Donovick, 1968). The discrimination task required the rats to respond on a lever in one compartment and move to another compartment to respond before another reinforcement was provided. The discrimination task was an alternation between compartments, not unlike a shuttle-box. Although the original learning was not affected by septal lesions, reversal of the spatial discrimination problem resulted in enhanced perseverative tendencies of the previously reinforced response.

Septal lesions completely blocked the acquisition of a spatial alternation problem that was basically similar to the discrimination problem. The rats were required to move between compartments from trial to trial. An additional requirement, however, was that the subjects discriminate and alternate response position within each chamber. That is, if the left lever in one compartment was positively reinforced, then the right lever in the other compartment was reinforced. Each daily session consisted of 5 warm-up trials followed by 60 test trials to a criterion of 85% correct for two consecutive sessions. Any subject that could not reach criterion within 20 sessions was eliminated from the experiment. The control subjects required a median of 12.5 sessions to reach the criterion, and no control animal failed to reach criterion. Of 6 septal subjects run, 5 failed to reach criterion within 20 sessions. The authors concluded that the results "taken together point to a septal dysfunction that is manifest

in response perseveration...."

Donovick (1968) produced lesions restricted to the anteromedial, middle, or posterior regions of the SNC. The anteromedial lesions were restricted to the medial septal nucleus and dorsal aspect of the diagonal band, and differentially impaired discrimination reversal and spatial alternation performance. Reversal and alternation deficits following anteromedial septal lesions were comparable to reversal and alternation deficits observed after complete septal lesions (Schwartzbaum and Donovick, 1968). Butters and Rosvold (1968a) reported that rhesus monkeys were impaired in the retention of a spatial delayed-alternation task run in a WGTA following septal lesions. When lesions were placed in the ventral aspect of the septum to selectively disrupt the medial septal nucleus, the acquisition of the delayed spatial alternation task was impaired due to repetitive error (perseveration). Subjects with lesions restricted to the dorsal aspect of the SNC did not differ from the unoperated controls (Butters and Rosvold, 1968b).

If left to its own devices in a T-maze, the rat demonstrates another form of alternation known as spontaneous alternation. Spontaneous alternation is said to occur when, on the second of two non-rewarded trials in a T-maze, the rat enters the alley that was not entered on the first trial (Douglas, 1966). Douglas and Raphelson (1966) demonstrated that septal lesions decreased spontaneous alternation. The sham operated group alternated on 81.7% of the trials, while septal lesions reduced alternation to a chance level of 46.7%. The data cannot be taken as support for the perseveration hypothesis, since the septal group had no tendency to repeat

responses, and behavior on each trial appeared to be independent of the preceding trial. Clody and Carlton (1969) found that lesions restricted to the medial septal nucleus disrupted spontaneous alternation when the animals were run in a T-maze. The degree of decrement appeared to be related to the ambient light level of the room in which the tests were run. The initial alternation tests were run under conditions of low ambient levels (7.5-w. red light positioned over the choice point). The experimental and control groups were not significantly different (50% vs. 67% alternation, respectively). Under conditions of higher ambient light levels, however (room illuminated by a 25-w. bulb), the septal animals alternated at a rate of 31.3% and the controls alternated at 73.3%. When trials were again run under darkened conditions, the groups were again found to differ with the medial septal animals alternating at 64.2% and the controls and 90.0%. There is, at present, no explanation for the effects of ambient light level upon spontaneous alternation in the rat, although it is known that septal damage results in exaggerated photonegativity in the rat (see below).

Appetitive Behavior and Drive Level

It is clear that the SNC is functionally related to appetitive behavior. Harvey, Lints, Jacobson, and Hunt (1965) reported that water intake in septal rats following water deprivation was significantly higher than in control animals. Donovick and Burright (1968) and Harvey and Hunt (1965) found that both ad libitum water intake and intake following water deprivation was significantly higher in septal animals. Harvey and Hunt

(1965) found that septal rats emitted a greater number of operant responses for water reward on either fixed-interval (FI) or continuous reinforcement (CRF) schedules, but differential prewatering equalized the lever-pressing response rate. The septal rats were more efficient on a DRL (differential reinforcement of low response rate) schedule for water reinforcement. Since the DRL schedule requires that the operant response be inhibited for a period of time, the increased (or at least equal) efficiency of septal animals on this task is contradictory to the response disinhibition hypothesis. On the other hand, Ellen, Wilson, and Powell (1964) reported that septal rats were impaired in DRL response acquisition when food reinforcement was used, a finding supported by the data of Burkett and Bunnell (1966), and MacDougall, Van Hoesen, and Mitchell (1969). A detailed analysis of septal behavior during DRL acquisition (MacDougall, Van Hoesen, and Mitchell, 1969) suggested that septal lesions disrupt the behavioral sequence that usually develops to fill the interval between responses.

The data of Harvey and Hunt (1965) suggest that the operated subjects tended to maximize the amount of water reward. The data raise the possibility of increased thirst drive in septal animals. If such were the case, it could be argued that some of the behavioral deficits associated with septal damage (e.g., passive avoidance and DRL deficits) derive from the fact that the experimental animals were more hungry or thirsty than the controls. Carey (1967a) compared DRL acquisition of sham operated rats at 23 1/2 hr. and 71 1/2 hr. water deprivation with that of septal rats

deprived for 23 1/2 hours. Septal damage and increased thirst had significantly different effects on the response characteristics associated with the DRL schedule. The 23 1/2 hr. septal group emitted significantly more responses than the 71 1/2 hr. sham group. The 71 1/2 hr. sham operated rats were clearly able to inhibit responding on the DRL schedule (as measured by inter-response times) whereas the septal group was markedly deficient in this regard. It was concluded that the results were "in agreement with the hypothesis that septal lesions eliminate the normal somatomotor inhibitory influences of the subcallosal region so that these animals have unusual difficulty inhibiting ongoing motor behavior."

Lesions restricted to the dorsal fornix and diagonal band increase response rates for water, but leave DRL responding unaffected, i.e., the animals do appear to be more thirsty, but are able to inhibit responding in order to obtain water (Carey, 1967b, 1968). Later evidence (Carey, 1969) indicated that lesions placed anteriorly in the SNC enhance response rates on fixed ratio (FR), whereas posteriorly placed lesions depressed FR response rates. The latter data do not differentiate between increased thirst and response perseveration, but it does stress the anatomical differences in behavioral control of structures within the SNC.

Vilar, Gentil, and Covian (1967) reported that septal rats given free access to tap water and 1.5% saline increased their saline intake over preoperative levels by a factor of six. Personal observation of this effect of septal damage indicates that the increased intake of saline is striking,

in that the septal animal drinks large volumes of 1.5% saline while simultaneously showing signs of polyurea. Vilar et al. (1967) reported that the urine volume and amount of salt excreted also increased by a factor of six over the preoperative level, indicating that salt retention was not a factor.

Anatomical evidence suggests that the SNC may exert some control over antidiuretic hormone (ADH) release via septo-supraoptic and septo-paraventricular fibers (Powell, 1966). Wayner (1967) reported increased activity in, among other regions, the septal region and ventromedial nucleus of the hypothalamus in response to systemic saline injections. Stimulation studies indicate that some related limbic components (cingulate cortex) are also involved in the control of ADH release (Yoshida, Ibayashi, Murakawa, and Nakao, 1966). The above evidence suggests that septal lesions may produce a mild form of diabetes insipidus. Evaluation of saline preference in rats suffering from diabetes insipidus produced by supraoptic nucleus lesions (Palmieri and Taleisnik, 1969) and osmotic stress tests (Lubar, Boyce, and Schaefer, 1968) indicates that diabetes insipidus cannot account for the exaggerated saline preference exhibited by septal rats. Palmieri and Taleisnik reported rejection of only 1% saline in animals with diabetes insipidus. Titlebaum, Falk, and Mayer (1960), however, reported that diabetes insipidus resulted in increased saline intake as long as the saline concentrations were in the hypotonic range. Increasing tonicity of the fluid resulted in rejection

of saline while control animals tended to prefer the hypertonic saline. While ADH dysfunction does not appear to be implicated in septal saline preference, the saline preference studies do raise some questions regarding the response of septal animals to the incentive qualities of food and water.

Increased fluid intake associated with septal damage may be related to incentive factors. Beatty and Schwartzbaum (1967) found that septal lesions increased the rate of licking for sucrose solutions at various concentrations. The response was independent of deprivation or pre-loading variables. A previous study (Beatty and Schwartzbaum, 1967) had demonstrated an increased sensitivity of septal rats to both sucrose and quinine adulteration of drinking water. While the addition of sucrose resulted in increased fluid consumption over control levels, the addition of quinine to the drinking water resulted in rejection of the solution by septal rats, but not by controls. Donovick, Burright, and Gittleson (1968) also reported that septal lesions produced exaggerated preference for sucrose solutions. While these studies implicate a form of incentive-response alteration resulting from septal damage, such exaggerated preferences may be the result of either response perseveration or altered response (affective response?) to the incentive qualities of the stimuli, or both. The data regarding the preference characteristics of septal animals are not clear. For instance, Publos (1966) reported that septal damage produced an increased operant response rate for liquid 8% sucrose, but adulteration of the sucrose solution with quinine did not alter the response rate.

Further Localization of the "Septal Effects"

As previously noted, attempts to define a locus within the SNC associated with the hyperemotional component of the septal syndrome were not successful (e.g., Harrison and Lyon, 1957). It may be that increased reactivity is a function of damage to several nuclei within the SNC, since recent evidence indicates that other components of the septal syndrome are dissociable anatomically. It has already been noted that Carey dissociated septal polydipsia from the response disinhibition component of large lesions by varying lesion locus within the SNC. Butters and Rosvold (1968a, b) reported that ventrally located lesions involving the medial septal nucleus disrupted both delayed alternation and increased resistance to extinction of an operant (bar press) response.

Van Hoesen, MacDougall, and Mitchell (1969) noted that lesions placed within the SNC are typically not sufficiently circumscribed to allow evaluation of the lesion effects with respect to the known differential projection pathways of the various septal nuclei. Septal lesions and stria medullaris-habenular lesions disrupted performance on a food-reinforced passive avoidance task, while fornicotomy had little effect. All three forms of damage produced AAR facilitation and increased resistance to massed extinction of the AAR. MacDougall, Van Hoesen, and Mitchell (1969) found that large fornical lesions and septal lesions produced a DRL deficit, while stria-medullaris-habenular lesions had little or no effect upon DRL acquisition. Lesions restricted to the medial aspects of the fornix (no fimbrial damage) had little effect on DRL performance. This suggests that the behavioral deficit may be related to the differential

septo-hippocampal projection pathways. Specifically, the septohippocampal tracts mediating response inhibition may be those relating the septal nuclear complex to hippocampal fields CA 3 and CA 4, not the entire hippocampus.

Clody and Carlton (1969) reported that lesions restricted to the medial septal nucleus (the anatomical junction between the medial forebrain bundle, hippocampus, and orbital prefrontal cortex) produced, in addition to the decreased spontaneous alternation noted previously, perseverative responding in Y and T-maze. However, the perseverative behavior in the T-maze was characterized as perseveration of place, not response. These data may be contradictory to the response perseveration hypothesis, since perseveration of a response would have resulted in going to the opposite place in the T-maze. It should be noted that in this case the weakness of the response perseveration hypothesis becomes apparent, i.e., the difficulty in defining precisely what the response is that is "perseverated." Additional tests of this kind are needed to clarify the issue.

Hamilton, Kelsey, and Grossman (1970) found that lesions located anywhere in the SNC facilitated the acquisition of an AAR, while lesions restricted to the lateral septal nuclei impaired passive avoidance acquisition, but did not interfere with a position-reversal task in a T-maze. Lesions involving both the medial septal nucleus and the lateral septal nuclei produced perseverative behavior in the same position-reversal task. The authors suggested that the perseverative characteristics resulting from larger septal lesions may not be a unitary deficit, but

may be, in part, an artifact resulting from the involvement of several systems.

Sensory Factors

There is some evidence that septal lesions result in altered sensitivity to sensory input, although in some cases the phenomenon may not be clearly distinguished from perseverative behavior. In an excellent series of experiments Schwartzbaum, Green, Beatty, and Thompson (1967) found that septal lesions enhance reactivity of rats to photic stimuli. One of the experiments involved an attempt to habituate the septal rats to the onset of a relatively bright light, which was to serve as a conditioned stimulus in later experiments. The test was conducted in a shuttlebox, with light onset occurring only in the animal's chamber, so that the "safe" chamber was relatively dark. Septal rats did not habituate to the light onset, but demonstrated a consistent escape response in the presence of the light. In 150 trials, they escaped from the light on 88.6% of the trials, while the controls reached habituation criterion in a median 28 trials (range 10-150 trials).

The rodents' response to light is complex, but in general it is known that rats normally prefer low illumination. Hanson (reported in Lockard, 1963) found that when given a choice between darkness and bright light (80 foot-lamberts), about 98% of the time was spent in the dark. In addition, it is known that bright light onset can serve as an unconditioned stimulus for escape behavior in the rodent, although the behavior does habituate (Jerome, Moody, Conner, and Ryan, 1958). It is thus obvious

that the consistent escape behavior to light onset may have represented either increased photonegativity or response perseveration. Schwartzbaum, et al. (1967) reported that rats with septal damage may prefer to remain in a compartment with relatively low shock (.3ma) that is darkened than enter an illuminated compartment, while high shock eliminated this effect. Whether photonegativity and heightened activity levels in septal animals will continue to be a pertinent issue remains to be seen. Other investigators have noted that even restricted lesions of the SNC appear to increase reactivity to light (Donovick, 1968; Green and Schwartzbaum, 1968; Clody and Carlton, 1969).

Finally, Lints and Harvey (1969) reported that lesions of the SNC resulted in increased sensitivity to foot shock, and related this to a concomitant decrease in the seretonin level of the telencephelon. Seretonin levels in other brain areas were unaffected.

Behavioral Considerations: The Ventromedial Nucleus of the Hypothalamus

Appetitive Behavior

The vast majority of all experimental literature related to the effect of VMH lesions is concerned with the well established and dramatic post-operative development of hyperphagia, polydipsia, and adiposity. A review of that aspect of the literature would be too extensive and cumbersome, particularly since this paper is concerned with other behavioral characteristics of the VMH animal. Suffice it to say that hyperphagia, polydipsia, and excessive adiposity do develop. Recent data suggests that the obesity is particularly marked in the female rat (Cox, Kakolewski, and

Valenstein, 1969; Singh, 1969) suggesting that endocrine and metabolic factors may also be disrupted by VMH lesions. Certainly the history of endocrinological interest in hypothalamic hyperphagia cannot be ignored.

Other data regarding the behavioral effects of VMH lesions is quite sparse. Kessler (1941) and Wheatley (1944) noted that VMH lesions in cats produced extremely savage behavior. Rats are also notoriously vicious and difficult to handle following VMH lesions (Singh, 1969).

Although animals having sustained VMH lesions are notable for the amount of food they consume, they are also known to be very responsive to the taste qualities of food and water. They reject quinine adulterated food and water at much lower quinine concentrations than do controls. When the adulterant is sweet, as sucrose or saccharin, the consumption level increases over that observed when the food or water is the usual laboratory fare (Teitelbaum, 1955; Graff and Stellar, 1962; Corbit, 1965). It would be a mistake to suggest that VMH lesions increase sensitivity to taste, since Nachman (1967) demonstrated that the taste threshold of VMH hyperphagics for quinine and sucrose is essentially identical to that of unoperated controls.

Smith, Salisbury, and Weinberg (1961) noted that stomach preloading depressed the food intake of VMH animals more dramatically than in control animals. They suggested that the overconsumption of food by hyperphagic rats is the result of an "exaggerated affective reaction" to food, although the authors did not regard the increased emotional reactivity to be restricted to gustatory factors. A similar hypothesis was proposed sometime later by Grossman (1966), i.e., that VMH lesions increase

affective responsiveness to all sensory stimuli. Thus, animals with VMH lesions would be expected to overeat when the diet is palatable, and eat less when the diet is slightly noxious.

Grossman (1966) reported that cannulation-induced lesions of the dorsal VMH reliably increased food intake, while operant response levels for both food and water were depressed. This is in agreement with earlier data regarding the motivational level of hypothalamic hyperphagics (Miller, Bailey, and Stevenson, 1950; Teitelbaum, 1957). The reduced motivational component of the hypothalamic hyperphagic's food-directed activity seems to be antithetical to the clear hyperphagic effect of the lesion. Teitelbaum and Campbell (1958) noted that rats with VMH lesions did not appear to eat more frequently than controls, but once they began eating, it took much longer for them to stop. This data is compatible with the hypothesis that the VMH is a "satiety center," the absence of which results in hyperphagia because the usual "shut-off" mechanism is lacking, i.e., the organism does not meter food intake adequately (Anand and Brobeck, 1951; Anand, 1961). Although this is the classic interpretation of VMH hyperphagia, it should be noted that the response disinhibition hypothesis could be compatible with the extended bouts of eating, while endocrine imbalance resulting from the lesion could account for the exaggerated adiposity (Frohman and Bernardis, 1968a, b; Han, Lin, Chu, Mu, and Liu, 1965; Han, 1967).

Avoidance Behavior

In an attempt to evaluate the role of adrenocorticotrophic hormone

(ACTH) in the acquisition of an AAR, Levine and Soliday (1960) produced hypothalamic lesions aimed at the median eminence to block ACTH release. They hypothesized that such damage should result in a decrement in AAR acquisition. Instead, the damage resulted in enhanced AAR acquisition. Inspection of the photomicrographs provided by Levine and Soliday (1960) suggests that the median eminence lesions also invaded the medial components of the VMH.

Grossman (1966) reported that small, bilateral cannula-induced lesions of the dorsal VMH, in addition to depressing operant response levels for food and water, reliably facilitated the acquisition of a two-way AAR, and disrupted the acquisition of a black-white discrimination in a T-maze. Conversely, application of atropine to the VMH did not disrupt the performance of a previously acquired T-maze discrimination. In a group which acquired the discrimination while treated with atropine, re-testing in the absence of atropine produced a marked improvement in performance. AAR acquisition was facilitated by the application of atropine to the VMH. There was no decrement in avoidance performance when these same rats were re-tested in the absence of atropine. It is of interest that cholinergic blockade of the VMH produces many of the same behavioral changes associated with VMH lesions without affecting food and water intake.

Sepinwall (1969) found that cannula application to the VMH of carbachol, atropine, pentabarbital, and strychnine (intended as a control stimulant) all reliably enhanced the acquisition of a modified Sidman avoidance response. It was also found that atropine treatment resulted in a distinct passive avoidance deficit, as did cannulation-induced lesions. The

passive avoidance response was somewhat unique, in that shock was associated with an operant response that had previously been shaped only to food reward. When the animals were sated, atropine treatment did not increase ad libitum food intake. Of particular interest is the observation that the application of atropine did increase food-rewarded bar pressing that had previously been suppressed by satiation (from a pre-drug mean of 10 responses to 226 under atropine treatment), but feeding behavior associated with the operant response was not similarly reinstated. Closer examination of two subjects revealed that no reward was consumed during such an atropine session. Thus, the animals were bar pressing and ignoring the reinforcer! The behavior pattern described by Sepinwall certainly falls within those which, in the septal animal, are described as perseverative.

Sensory Factors

VMH lesions have been shown to reduce shock response thresholds in both the mouse and the rat. Turner, Sechzer, and Liebelt (1967) induced CNS lesions in the mouse with goldthioglucose injections, and in the rat using usual electrocoagulation techniques. While lesions produced by goldthioglucose are not restricted to the VMH, the effects in both cases were similar, i.e., a decrease in the flinch-jump threshold of 42% (mice) and 45% (rat). Data now exists which implicates septal lesions, lesions of the medial forebrain bundle, and lesions of the VMH in the reduction of pain-response thresholds.

Comparative Studies

Considering the striking behavioral similarities resulting from both SNC and VMH lesions, it is surprising that so few comparative studies are available. Those that do exist, however, only serve to enhance the impression that the behavioral similarities resulting from the two types of lesion are more than coincidental.

Damage to several brain areas were found by Kaada, Rasmussen, and Kveim (1962) to impair the acquisition of a passive avoidance response. In essence, lesions involving the frontal cortex, subgenual region, SNC, preoptic area, and VMH resulted in a passive avoidance deficit. It is worth noting that each of these areas are anatomically related primarily via the medial forebrain bundle. Cortical control lesions in no instance resulted in a passive avoidance impairment. While many of the lesions were large, resulting in damage that overlapped several areas, several rats had damage restricted to either the SNC or VMH, and a distinct passive avoidance decrement was evident in these cases. Other lesions that involved these areas as a part of larger lesions also produced passive avoidance impairment. It has been reported that stimulation of the VMH and SNC may inhibit spinal reflexes and cortically-induced movements (Kaada, 1951). The similar inhibitory characteristics of these areas may be mediated via the medial forebrain bundle. Kaada, Rasmussen, and Kveim (1962) concluded that those areas which, when lesioned, gave evidence of passive avoidance deficit may include a large system which normally functions during response inhibition.

Singh (1969) noted that the Kaada, et al. (1962) data suggest a similarity of function for both the SNC and VMH. With specific reference to the hyperemotionality associated with lesions in these areas, Singh suggested that damage to both areas may result in a release phenomenon which "disrupts an inhibitory system which modulates motor responses in an intact animal." This hypothesis seems to be identical to that initially proposed by McCleary (1961) and later by Kaada, et al. (1962) to account for the behavioral effects resulting from damage to these areas. Evaluation of the hyperemotionality resulting from lesions in these areas suggested that they differ in at least two respects. Septal hyperemotionality attenuated over time, and daily handling hastened the process (as reported earlier by King, 1958), while VMH hyperemotionality was not reduced as a function of either time or handling. The fact that VMH hyperemotionality does not seem to decrease suggests that this area may be "...a nodal point for a number of fiber systems, chiefly from the anterior 'rhinencephalic' areas, concerned with the regulation of autonomic functions and inhibitory influences on somatomotor activities" (Kaada, et al., 1962).

Singh and Meyer (1968) indicate that both SNC and VMH lesions result in hyperphagia. The hyperphagia was exaggerated in the VMH group however, and, in both forms of damage, female rats were more hyperphagic and obese than males, again suggesting endocrine involvement. Electrophysiological evidence (Wayner, 1967) demonstrated that both the SNC and VMH responded with increased activity in response to intravenous injection of hypertonic saline. The significance of that report remains to be evaluated.

Summary

It is clear that damage to both the SNC and VMH result in similar behavioral effects. Briefly, both forms of damage produce hyperemotionality, facilitate the acquisition of an active avoidance response, impair passive avoidance acquisition, produce appetitive "finickiness," disrupt maze learning, and increase sensitivity to foot shock. The theoretical views regarding the function of these areas have always been somewhat divergent and, therefore, the behavioral tests are not always comparable.

It would appear that these areas overlap functionally along at least two theoretical dimensions: response inhibition and incentive motivation (affective reactions to sensory quality). It is not possible to clearly distinguish between the two on a behavioral level, and so the distinction may be meaningless. An organism may over-respond to the presence of quinine or sucrose either because its affective response to the taste quality is exaggerated, or because of a disrupted capacity to inhibit a dominant response tendency once the behavior is initiated (perseverative responding).

The affectivity hypothesis, with respect to the effect of VMH lesions, suffers from the same weakness as it did when applied to the behavioral effects of SNC lesions. The weakness is best illustrated in the passive avoidance experiments. An animal that is hyperemotional would not ordinarily return to the source of shock. At least, as usually defined,

such behavior would not be labeled as being "hyperemotional."

It is recognized that it would be a critical error to assume that both the SNC and VMH are functionally identical. It would also be an error to assume that either is unitary in its function. It is clear that the two areas may not be totally dissimilar in function. Whereas VMH lesions result in hyperphagia, septal lesions produce less dramatic hyperphagia. Septal lesions produce a clear form of response disinhibition. The same characteristic has not been shown to be a component of the VMH syndrome. (For exceptions, see Kaada, et al. 1962 and Kaada, 1951). There is, however, sufficient evidence to suggest that a large component of the VMH-lesioned animals' response pattern may result from just such an inhibitory dysfunction.

The concept of the VMH involvement with response inhibition is not new. Kaada (1951) suggested it may function as an integrative inhibitory mechanism:

> These most important and interesting results open the question whether the inhibitory influence of "rhinencephalic" structures on savage behavior are channeled through this hypothalamic area. It will be recalled that electrical stimulation of the ventro-medial nucleus quite recently has been demonstrated to inhibit spinal reflexes and cortically evoked movements and, further, that this hypothalamic area appears to be a nodal point for a number of fiber systems, chiefly from the anterior "rhinencephalic" areas, concerned with the regulation of autonomic functions and with inhibitory influence on somato-motor activities. Thus, chiefly through the medial forebrain bundle it appears to receive important contributions from the posterior orbital surface of the frontal lobe, the olfacory tubercle, the septal areas and the amygdala (by way of the stria terminalis). It is possible that the ventromedial nucleus contains an integrative mechanism for the restraining influence on savage behavior. (Kaada, 1951, p. 254)

It is postulated that lesions involving either the SNC or VMH will result in response disinhibition, as measured by perseverative response patterns. The following section describes a series of behavioral tests intended to evaluate the response inhibitory capabilities of both VMH and SNC lesioned rats.

The tests are intended to allow the comparison of response patterns following SNC or VMH lesion in order to determine:

a.) whether response perseveration results from both SNC and VMH damage

b.) whether the degree and character of the perseverative deficit is similar following both SNC and VMH damage, and,

c.) whether the perseveration following SNC and VMH damage is differentially task specific.

Specifically, active avoidance extinction, passive avoidance, and response reversal have been chosen as the comparative behavioral tasks to be used.

METHOD

Surgery and Histology

Surgery

All subjects (Ss) were adult male Long-Evans hooded rats. Anesthesia consisted of intraperitoneal injections of sodium pentobarbital (40mg/kg) and ether supplementation during surgery if necessary. Atropine sulfate (.04mg) was given in combination with the sodium pentabarbital to reduce respiratory complications.

Four groups were formed for each behavioral test. These included an unoperated control group (C), operated control group (OC), septal lesion group (SNC), and a hypothalamic ventromedial nucleus lesion group (VMH). The SNC coordinates, using the de Groot (1959) coordinate system, were 7.8mm AP, 0.5mm L, and 1.5mm H, and the VMH coordinates were 5.8mm AP, 1.0mm L, and -3.0mm H. The lesions were produced electrolytically, using 2ma. anodal current for 20 seconds at each placement via 32 S.W.G. stainless steel electrodes insulated with diamel. Approximately 0.5mm at the electrode tip was not insulated. All lesions were bilateral. The electrodes were lowered to the target coordinates in the operated controls and removed without passing current.

Each operated S was allowed a minimum 5 day postoperative recovery period before behavioral testing was begun. Each experiment had 30 operated animals (10 SNC, 10 VMH, 5 OC-SNC and 5 OC-VMH) and 10 unoperated control animals (independent groups).

Histology

When the behavioral tests were completed, each operated S was sacrificed using a lethal dose of sodium pentobarbital. Intracardial perfusion was accomplished using 0.9% saline followed by 10% formalin. Prior to sectioning, brains were stored in a 30% sucrose and 10% formalin solution. Fifty micron frozen sections through the lesion site were taken. Every fourth section was stained using a modified Klüver-Berrara technique (Wolf and Yen, 1968).

Experiment 1: Active Avoidance Conditioning

This experiment used a two-chambered plexiglas shuttlebox. The dimensions for each chamber were 9"w x 9"h x 12"l. The chambers were separated by a hurdle made of independently rotating bearings that prohibited balancing on the barrier to escape shock. Avoidance conditioning was accomplished in three phases: habituation; acquisition; and massed extinction.

Habituation consisted of placing S in the shuttlebox for 15 minutes on each of two days prior to the start of avoidance training. Acquisition consisted of 50-trial sessions given 24 hours apart. The conditioned stimulus (CS) was provided by a 12 volt buzzer. The voltage was reduced and the buzzer housing was packed with soft material to provide a muted buzz. The unconditioned stimulus (UCS) was a constant-current device modified from the design of Brown, Reus, and Webb (1961). The shock level was empirically adjusted to the minimum value required to elicit escape behavior from all Ss.

Each trial consisted of a 60 second intertrial interval (ITI) and a 10 second CS-UCS interval. If S jumped into the opposite chamber during the CS but before the UCS onset, an avoidance response was automatically recorded. An escape response was recorded when the S responded following the onset of the UCS. An escape or avoidance response terminated the trial and initiated the next ITI. Once the CS and/or UCS were presented they remained on until a shuttling response occurred. The avoidance criterion was set at 90% avoidance (18 out of 20) on each of two days. Any S which failed to reach criterion within 6 sessions (300 trials) was eliminated from further testing.

The massed extinction sessions were each 50 trials in length. A total of 6 massed extinction sessions were given to each S that reached the avoidance criterion. Each extinction trial consisted of a 10 second ITI and 10 second CS period. Failure to respond during the 10 second CS period resulted in automatic termination of the CS without UCS presentation. As during acquisition, any shuttling response during the CS terminated the CS and initiated the ITI.

Histology

The data from only one S, VMH-6, were discarded from analysis because of an inadequately placed lesion. The damage in this animal was ventral and lateral to the VMH unilaterally and the contralateral side was spared completely.

The most extensive hypothalamic damage extended from the caudal aspect of the anterior hypothalamus to the rostral components of the premammillary

nuclei. The lateral aspect of the lesion ranged just beyond the fornix, while dorsally the dorsomedial nucleus was almost completely destroyed. The lesion included damage to the caudal part of the anterior hypothalamus, paraventricular nucleus, arcuate nucleus, ventromedial nucleus, dorsomedial nucleus, fornix, and premammillary nuclei.

The least extensive hypothalamic lesion ranged from some unilateral damage to the anterior hypothalamus, unilateral ventromedial nucleus damage in the middle of the rostro-caudal extent of the lesion with bilateral VMH damage in the most caudal extent of the lesion. The caudal 1/2 of the VMH was spared bilaterally. Parts of the arcuate nucleus were incorporated in the lesion area.

The SNC lesions were all very similar in morphology. They generally extended from just posterior to the genu of the corpus callosum posteriorly to include the region of the precommissural fornix. Only occasionally did the lesion invade the nucleus accumbens, anterior commissure, or extend laterally far enough to damage the medial wall of the caudate nucleus. Damage to these structures, when it occurred, was minimal and was not used as grounds for rejection due to lack of lesion restrictiveness.

The most extensive lesion in the SNC extended from the most anterior aspect of the septal region (just posterior to the genu of the corpus callosum) posteriorly to include the ventral aspect of the septofimbrial nucleus, parts of the columns of the fornix and the medial portion of the lateral septal nucleus. The far lateral walls of the lateral septal nucleus were intact in this instance. In other instances the lesion may have been more restricted in the anterior to posterior dimension, but

some damage to the medial walls of the caudate nucleus was sometimes seen. The least extensive SNC lesion extended from rostral parts of the lateral septal nucleus just below the genu of the corpus callosum to about the middle of the SNC posteriorly. The posterior half of the SNC was spared, and the lesion was very restricted medially, not involving the lateral septal nuclei to any great extent. Lesions in the SNC usually included damage to the hippocampus pars anterior, lateral septal nuclei, medial septal nucleus, fornix superior, diagonal band, and medial aspects of the nucleus accumbens, and precommissural fornix.

In no instance was anything of a remarkable nature noted in the control placements. In most instances, only faint traces of the electrode track could be identified.

Results

Not all Ss reached the acquisition criterion. The number of animals rejected in each group and the reasons for their elimination from the experiment are shown in Table 1. Of those that failed to reach the acquisition criterion, only one was rejected for histological reasons.

The average number of trials each group required to reach the extinction criterion is presented in Figure 1, and the standard deviation above and below the mean is also represented. Analysis of variance indicated that the avoidance acquisition differences were not statistically significant ($F = .61$, $df = 4/30$, $p > .25$). Unexpected differences appeared during extinction. The summary table for the repeated measures analysis of the extinction sessions appears in Table 2. Four a priori comparisons

between the treatment groups were performed. The comparisons were between all lesioned and all unlesioned animals (A_1), between group SNC and group VMH (A_2), between the normal controls and the operated controls (A_3), and between the two operated control groups (A_4). The overall treatments effect (A) was significant ($F=4.26$, $df=4/29$, $p<.01$). The comparison between lesion groups SNC and VMH (A_2) suggests that the overall treatment effect was due primarily to the extinction characteristics of the SNC lesion group ($F=14.73$, $df=1/29$, $p<.001$). Reference to Figure 2 supports the conclusion that the VMH group did not differ in extinction characteristics from the non-lesioned groups, as does the observation that only comparison (A_2) produced a sum of squares of any appreciable magnitude.

The significant sessions effect (B) ($F=70.80$, $df=5/20$, $p<.001$) indicates that the massed extinction technique was effective. The

Table 1. Subject rejection from avoidance data analysis

Group	Starting	Reaching Criterion	Rejected
SNC	10	9	1 (CRC)[a]
VMH	10	7	2 (CRC)+1H[b]
C	10	9	1 (CRC)
OC-SNC	5	4	1 (CRC)
OC-VMH	5	5	0

[a](CRC) indicates rejection for failing to reach criterion.
[b](H) indicates rejection because of lesion inadequacies.

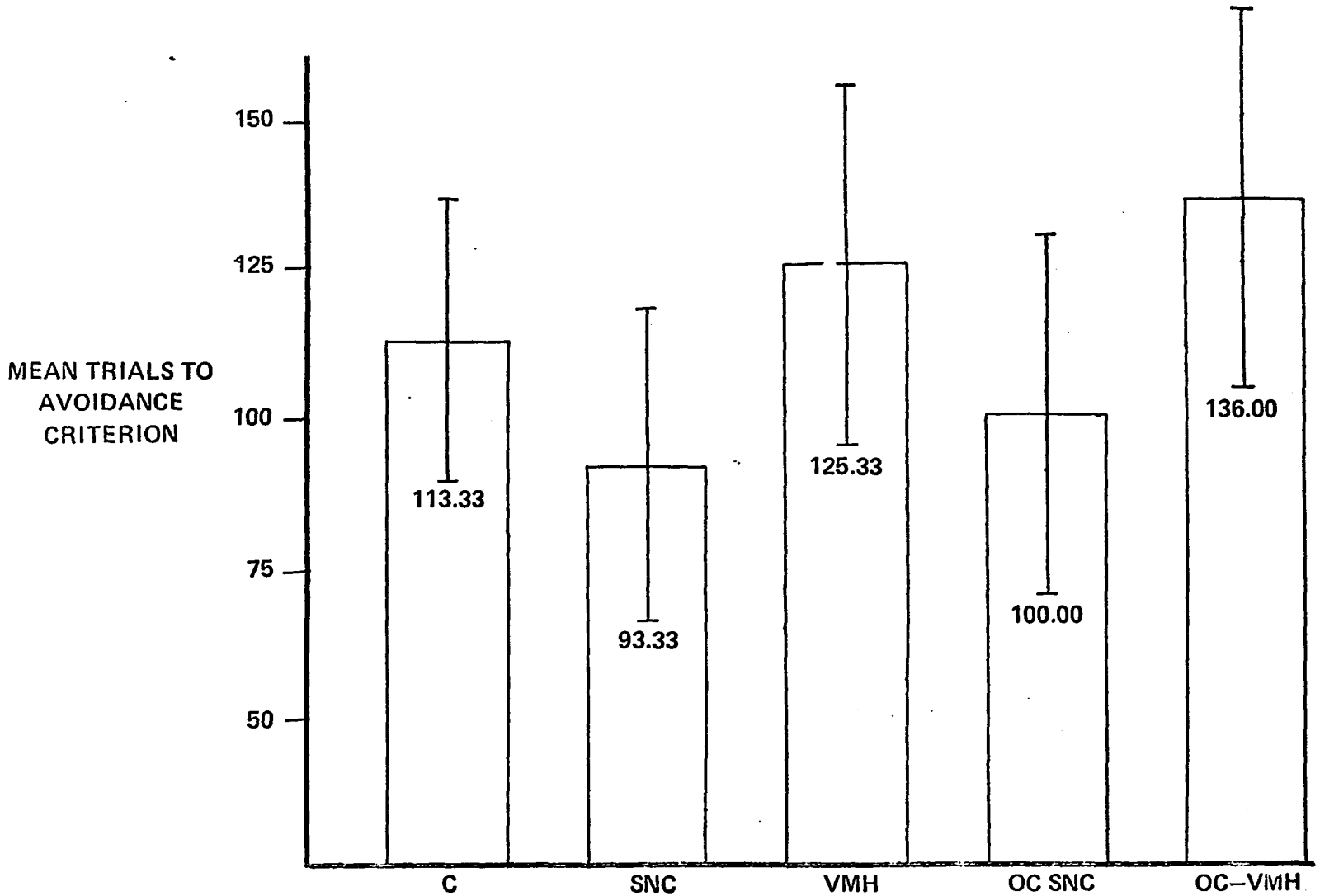

FIGURE 1. MEAN TRIALS TO AVOIDANCE CRITERION BY TREATMENT GROUP. ONE STANDARD DEVIATION ABOVE AND BELOW THE MEAN INDICATED.

Table 2. Summary table for the analysis of variance of active avoidance extinction in experiment 1

Source	df	SS	MS	F	P
(A) Treatments[a]	4	966.26	241.5659	4.2629	.01[b]
A_1	(1)	123.16	123.16	2.17	
A_2	(1)	834.82	834.82	14.73	.001
A_3	(1)	3.34	3.34	---	---
A_4	(1)	4.93	4.93	---	---
S/A	29	1643.32	56.67		
(B) Sessions	5	6354.39	1270.88	70.80	.001
AxB	20	668.26	33.41	1.86	.025
A_1xB	(5)	244.49	48.90	2.72	.025
A_2xB	(5)	86.01	17.20	---	---
A_3xB	(5)	70.37	14.07	---	---
A_4xB	(5)	267.36	53.47	2.97	.025
S/AxB	145	2602.69	17.95		
Total	203	12234.92			

[a]See text for an explanation of treatment and comparisons.
[b]All p values are less than the indicated value.

differences in the extinction trend (AxB interaction) were significant ($F=1.86$, $df=20/145$, $p<.025$). There was a significant A_1xB (all operated vs. all control groups) interaction ($F=2.72$, $df=5/145$, $p<.025$) which again appears to be attributable to the performance of the SNC group during extinction. Reference to Figure 2 suggests that the significant A_4xB interaction ($F=2.97$, $df=5/145$, $p<.025$) derives from the variability of the operated control groups performance during extinction. That variability may simply be a reflection of the small sizes of those groups.

Discussion

This experiment failed to support the major hypothesis that both the SNC and VMH comprise parts of a single system related to behavioral inhibition. Although the septal animals did demonstrate increased resistance to extinction (perseveration) during the massed extinction sessions, animals with VMH damage did not. The hypothesis required that increased resistance to extinction be exhibited by both operated groups.

The behavior of the rats with septal damage in this situation was reasonably consistent with behavior reported by others. Although two-way AAR acquisition is most often reported to be facilitated by septal lesions (Kenyon and Krieckhaus, 1965; McCleary, 1961; Schwartzbaum, et al., 1967; Van Hoesen, et al., 1969) others have reported no differences in AAR acquisition (La Vaque, 1966; Kasper-Pandi, et al.,

1969) or retarded AAR acquisition (Dalby, 1970) following septal lesions. Increased resistance to extinction following septal damage has been reported previously (La Vaque, 1966; Van Hoesen, et al., 1969) and is consistent with the response disinhibition hypothesis.

Previous investigators (Grossman, 1966) reported that VMH damage resulted in facilitated AAR acquisition. Facilitated AAR acquisition following VMH damage was not observed in this experiment. In fact, the tendency was in the opposite direction, i.e., VMH rats tended to acquire the avoidance response more slowly. The fact that the rate of extinction did not appear to differ from that of control rates argues against the hypothesis that the VMH may normally function as part of a system involved with behavioral inhibition.

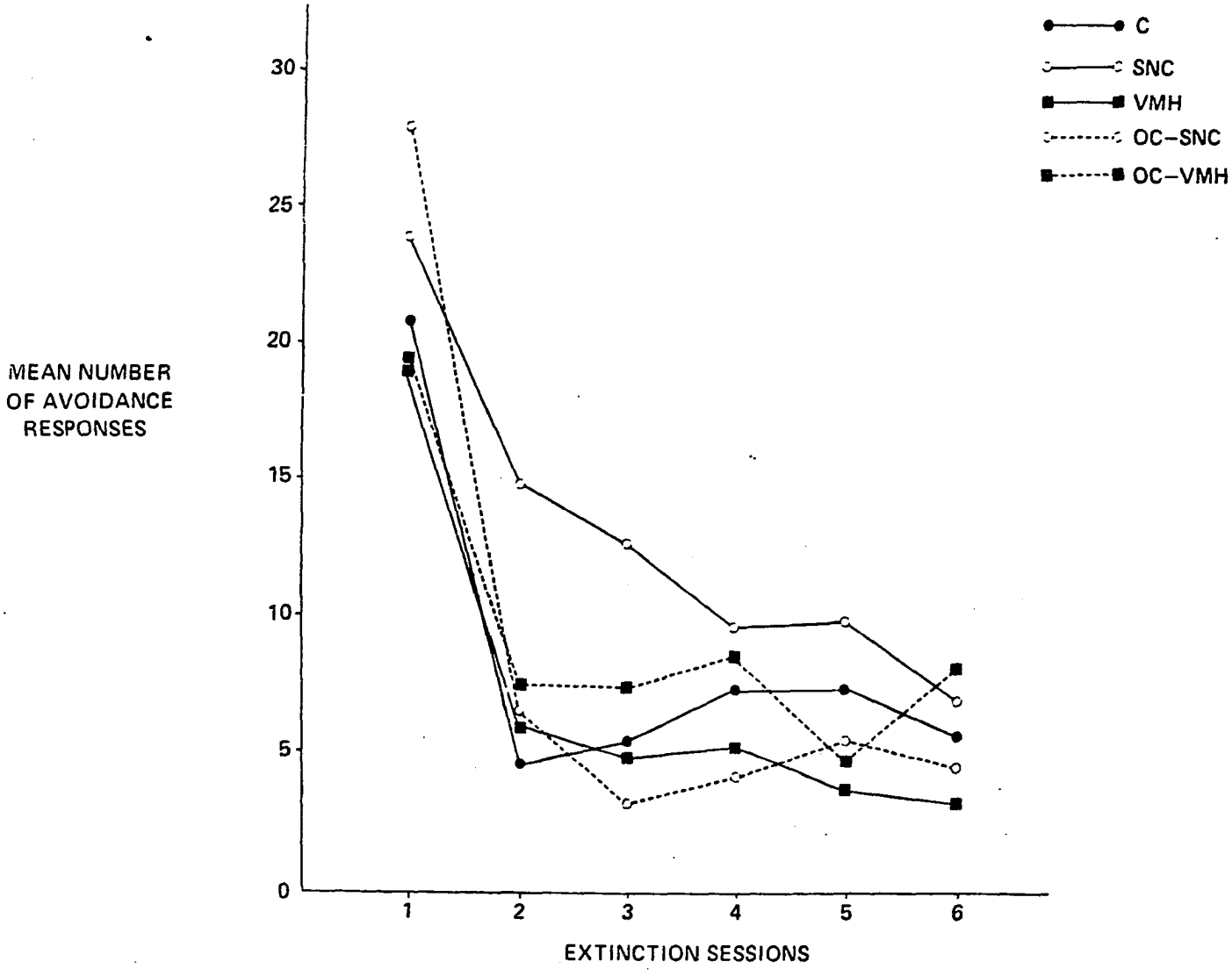

FIGURE 2. MEAN AVOIDANCE RESPONSES BY EXTINCTION TREATMENT GROUP.

Experiment 2: Passive Avoidance

This task provided a situation in which S either approach a goal chamber previously associated with both food and shock (perseveration), approach a goal associated only with non-reward (active avoidance), or not respond at all (passive avoidance). The apparatus, modeled after that described by Ursin, Linck, and McCleary (1969), consisted of a start chamber that opened to two alleys extending in opposite directions. Each alley terminated in a goal chamber containing a food cup and water source.

The dimensions of the apparatus are shown in Figure 3. Each alley was marked off in three inch segments to permit scoring of the approach or avoidance responses during the latter part of this experiment. One alley and its associated goal chamber were painted flat black, the other alley and chamber were painted flat white, and the start chamber was painted gray. The start chamber was separated from the alleys by two removable gates made of clear plexiglas. The floor of the entire apparatus was a grid through which shock could be administered.

Prior to discrimination training, each S was given a 30 minute habituation session on each of two days. Due to the hyperreactive nature of some of the Ss in the SNC group, extensive overnight habituation was necessary in some cases. Rats having sustained septal lesions tended to be combatively resistant to removal from the apparatus. No similar tendencies were noted in any of the VMH-operated animals. On the habituation days, Ss were fed 45 mg. Noyes pellets in their home cage to habituate them to the novel food. A 22-hour food deprivation schedule was maintained

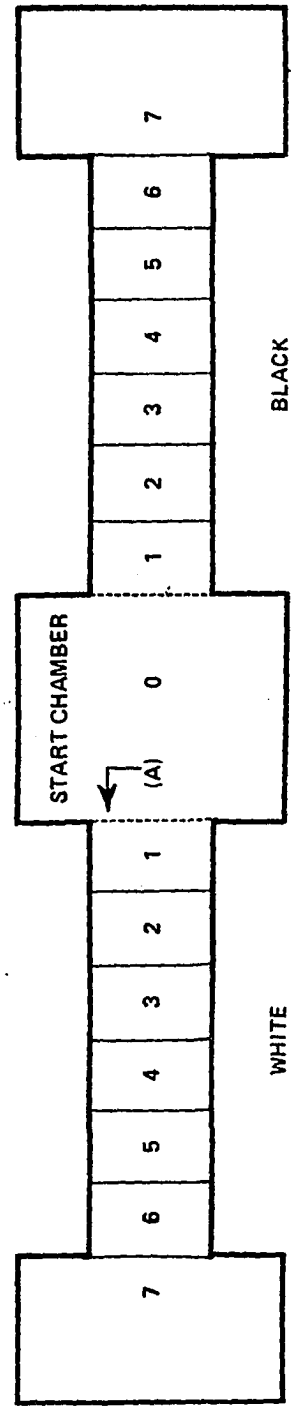

FIGURE 3 DIAGRAMMATIC REPRESENTATION OF THE PASSIVE AVOIDANCE CHAMBER "A" INDICATES ALLEY ACCESS DOORS

throughout the experiment, including the habituation period. Water was available ad libitum throughout the experiment. The animals were given one hour access to food in their home cages following each discrimination session.

A discrimination trial was initiated by simultaneously opening the plexiglas gates, providing access to either alley. If a response was not made within 60 seconds, the gates were closed for 30 seconds. If the rat failed to enter either alley within five "trials," it was removed, fed in the home cage, and run again on the following day. This procedure was necessary for only one animal in the SNC group, and that S began responding on the second day. Half of the animals in each group were reinforced for entering the white, and half for entering the black goal. The reinforcement consisted of three 45 mg. Noyes pellets. When S entered the non-rewarded alley, the gates were closed for 30 seconds, then opened again to allow entry into the correct alley. This procedure resulted in immediate entry into the correct alley from the start chamber as training progressed. After each trial S was placed in its home cage in the experimental room for at least 5 minutes before being placed in the start chamber for the next trial. Each S was given one 10 trial session per day. The acquisition criterion was 18 correct responses out of twenty trials.

The avoidance session was given on the day following the final acquisition criterion session. The first five trials of this session were run in the same manner as all previous trials. On trials 6 and 7, the S was allowed to enter the goal and begin eating before a 3 second shock was

presented. The shock level was the same as that empirically determined in experiment 1. The final three trials provided the measure of the approach or avoidance tendency. Failure to move from the start chamber within the 60 second start interval represented passive avoidance, and was given a score of zero. Entry into the previously non-reinforced alley was given a negative score indicative of active avoidance, and entry into the rewarded and punished alley was given a positive score, indicating response perseveration. The responses were scored according to the values assigned to the alley segments. Thus, entry into the previously correct goal was given a score of +7, while entry into the previously non-rewarded goal was given a score of -7. Fractional responses, i.e., entry into an alley and return to the start chamber or alley entry and "freezing" in the alley was scored according to the closest approach made to the particular goal.

Histology

With one exception, the lesion characteristics in both the VMH and SNC groups were not distinguishable from those reported for the first experiment, and therefore need not be detailed again. The data of one VMH animal (VMH-20) was discarded since no VMH damage was apparent. The lesion on both sides lay lateral to the extreme ventromedial nucleus and involved the fornix, mammillothalimic tract, and the extreme medial part of the laterial hypothalamus.

Results

All rats that began this experiment completed the passive avoidance sequence with the data of one animal (VMH-20) eliminated for histological reasons. Analysis of response acquisition (Table 3) indicates that the VMH group required fewer trials to acquire the discrimination ($F=4.53$, $df=4/34$, $p<.01$). Although start latencies were not recorded in this experiment, it was observed that the start latencies of rats in the VMH group were very short, while the start latencies of rats in the SNC group were quite long. The apparent differential start latencies are not reflected in the mean trials to acquisition in this experiment (Figure 4).

The overall treatment effect was significant during the passive avoidance trials ($F=4.69$, $df=4/34$, $p<.005$). Four *a priori* comparisons were performed (Table 4). As in experiment 1, the comparisons were between all lesioned and all control groups (A_1), between group SNC and group VMH (A_2), between the operated control groups and the unoperated control group (A_3), and between the two operated control groups (A_4). Only contrast A_1 (all lesioned groups vs. all control groups) was statistically significant ($F=14.72$, $df=1/34$, $p<.005$). Reference to Figure 5 indicates that both SNC and VMH animals approached the food cup more closely and earlier over trials than did animals in the other treatment groups. The SNC-VMH comparison (A_2) was not statistically significant.

The trials effect (B) was significant ($F=27.05$, $df=2/8$, $p<.005$) indicating an increased tendency to approach the food chamber in which shock had been experienced. Although the overall approach trend (AxB interaction) was not significant, comparison A_1xB was significant

($F=3.84$, $df=2/68$, $p<.05$) indicating that the post-shock approach behavior of the lesioned animals was significantly different from that of the non-lesioned rats. Reference to Figure 5 illustrates that the differential approach behavior was most apparent on the first post-shock trial. Both the SNC and VMH groups displayed a distinct passive avoidance deficit relative to the early post-shock approach behavior of the control groups.

Table 3. Summary table for the analysis of variance of the number of trials to acquisition in experiment 2

Source	SS	df	MS	F	P
Between	35.32	4	8.83	4.53	.01[a]
Within	66.42	34	1.95		
Total	101.74	38			

[a]All p values are less than the indicated value.

Discussion

The results of this experiment provide some support for the hypothesis that the SNC and VMH both contribute to a more general response inhibition system. Both operated groups in this experiment demonstrated a clear passive avoidance deficit. Although there have been previous reports of passive avoidance deficits following SNC lesions (McCleary, 1961; Kasper-Pandi, et al., 1969; Zucker and McCleary, 1964) and VMH lesions (Kaada, et al., 1962), the lesions reported in the latter study were typically

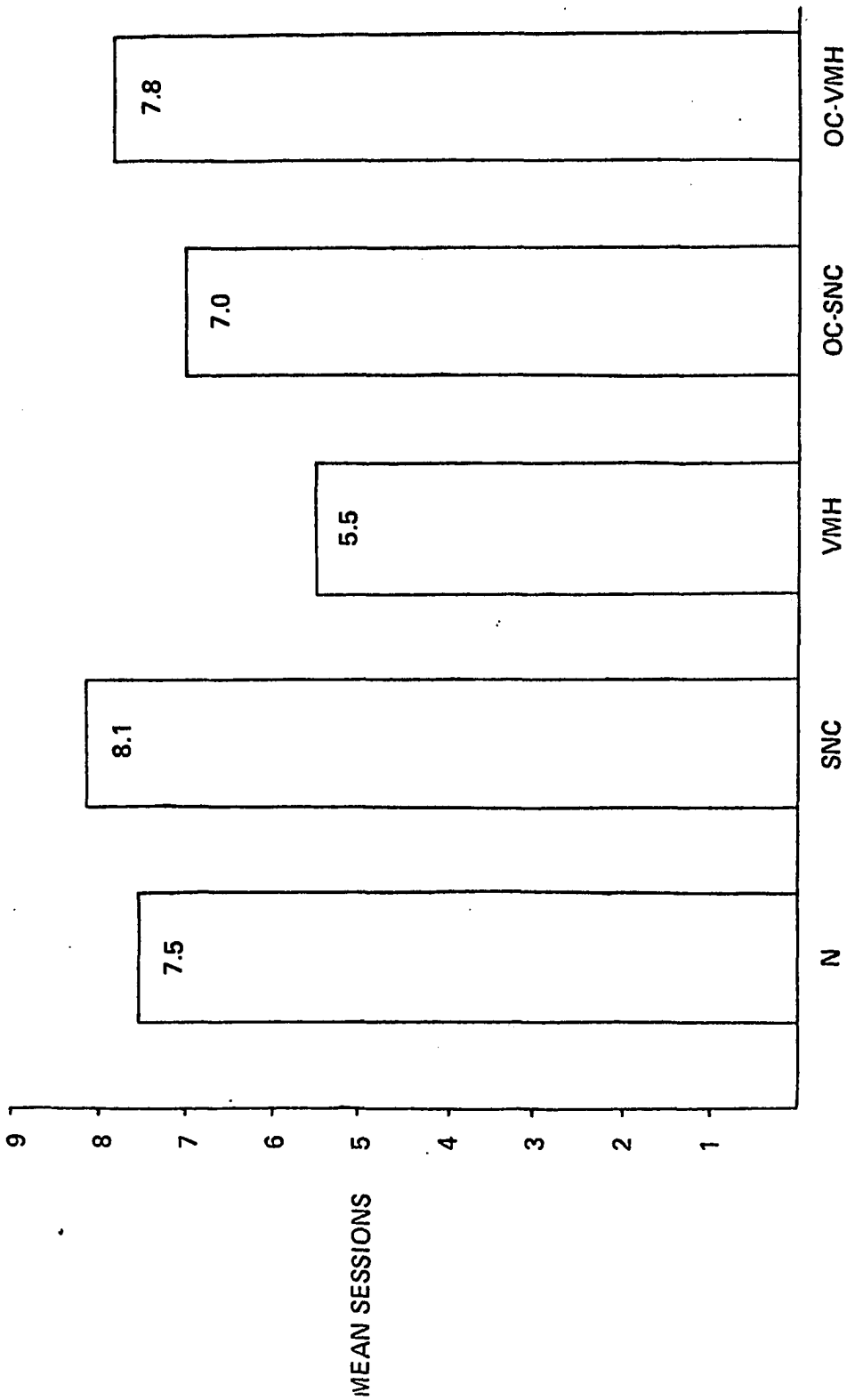

FIGURE 4. MEAN SESSIONS TO THE ACQUISITION CRITERION PRIOR TO PASSIVE AVOIDANCE TRAINING.

large and incorporated structures beyond the VMH. The present experiment suggests that both operations produce similar behavioral effects during early post-shock passive-avoidance test trials.

It was observed that animals in the SNC group were particularly reticent to leave the start chamber during the early training trials, while rats of the VMH group exited the start chamber quite readily. It is unfortunate that start latencies were not quantified in this experiment, since the operated groups exhibited clear differences in this regard. Such behavioral differences may reflect the fact that any SNC-VMH function is not completely redundant. Although both structures may function in response inhibition, they also participate differentially in other functions. One evident functional distinction is that of neuroendocrine regulation (Frohman and Bernardis, 1968; Steffens, 1970).

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Table 4. Summary table for the analysis of variance of post-shock approach behavior in experiment 2

Source	df	SS	MS	F	P
(A) Treatments[a]	4	168.71	42.18	4.69	.005[b]
A_1	(1)	132.38	132.38	14.72	.005
A_2	(1)	22.40	22.40	2.49	
A_3	(1)	5.40	5.40	0.60	
A_4	(1)	8.53	8.53	0.95	
S/A	34	305.77	8.99		
(B) Sessions	2	157.45	78.72	27.05	.005
AxB	8	27.77	3.47	1.19	
A_1xB	(2)	22.37	11.18	3.84	.05
A_2xB	(2)	0.03	0.01	---	
A_3xB	(2)	2.50	1.25	---	
A_4xB	(2)	2.86	1.43	---	
S/AxB	68	198.11	2.91		
Total	116	857.81			

[a]See text for an explanation of treatment and comparisons.
[b]All p values are less than the indicated value.

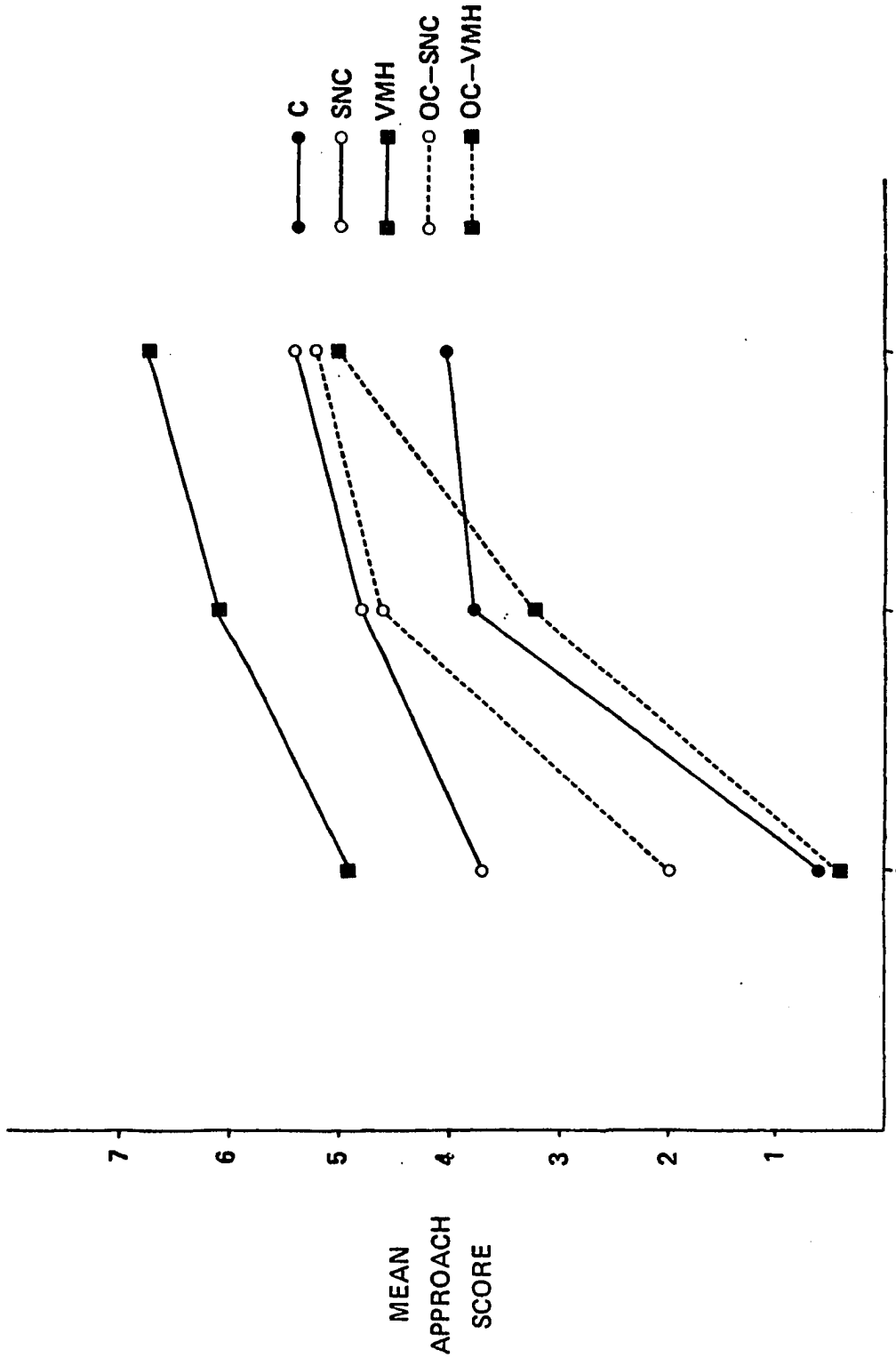

FIGURE 5. MEAN APPROACH TO THE FOOD CHAMBER ON THREE POST–SHOCK TRIALS.

Experiment 3: Position Reversal

The apparatus for this experiment was designed with a two-fold purpose. First, it was intended to serve as a relatively simple modified T-maze in which a simple right-turn or left-turn response could be easily conditioned. Second, the apparatus was designed to eliminate handling between trials, since rats with either SNC or VMH lesions are often extremely reactive to handling. In essence, the apparatus was a continuous plexiglas maze in which one of two goals could be entered by negotiating two consecutive turns in a single direction once the start chamber had been exited. The dimensions of the apparatus are given in Figure 6.

All Ss were maintained at 85% of their pre-operative body weight. After they had stabilized at the 85% level, they were fed 10g. of 45mg. pellets in the home cage. They were then fed pellets in the maze for 30 minutes of each of two days. Each goal chamber contained 5g. of the pellets. Free entry to the goal chambers from the start chamber was allowed by removing the entry doors during the 30 minute habituation sessions. On the third day each S was given 5 response preference trials. A preferred response was defined as that goal entered most frequently. During these tests, the start chamber exit door and the lateral alley doors remained open, and the S was removed from the goal by hand. Each goal contained three 45mg. pellets during this test. During subsequent conditioning of the position habit, S was run to the non-preferred side.

Each S received two 10-trial sessions per day. Sessions within a day were at least 30 minutes apart, during which time S was returned

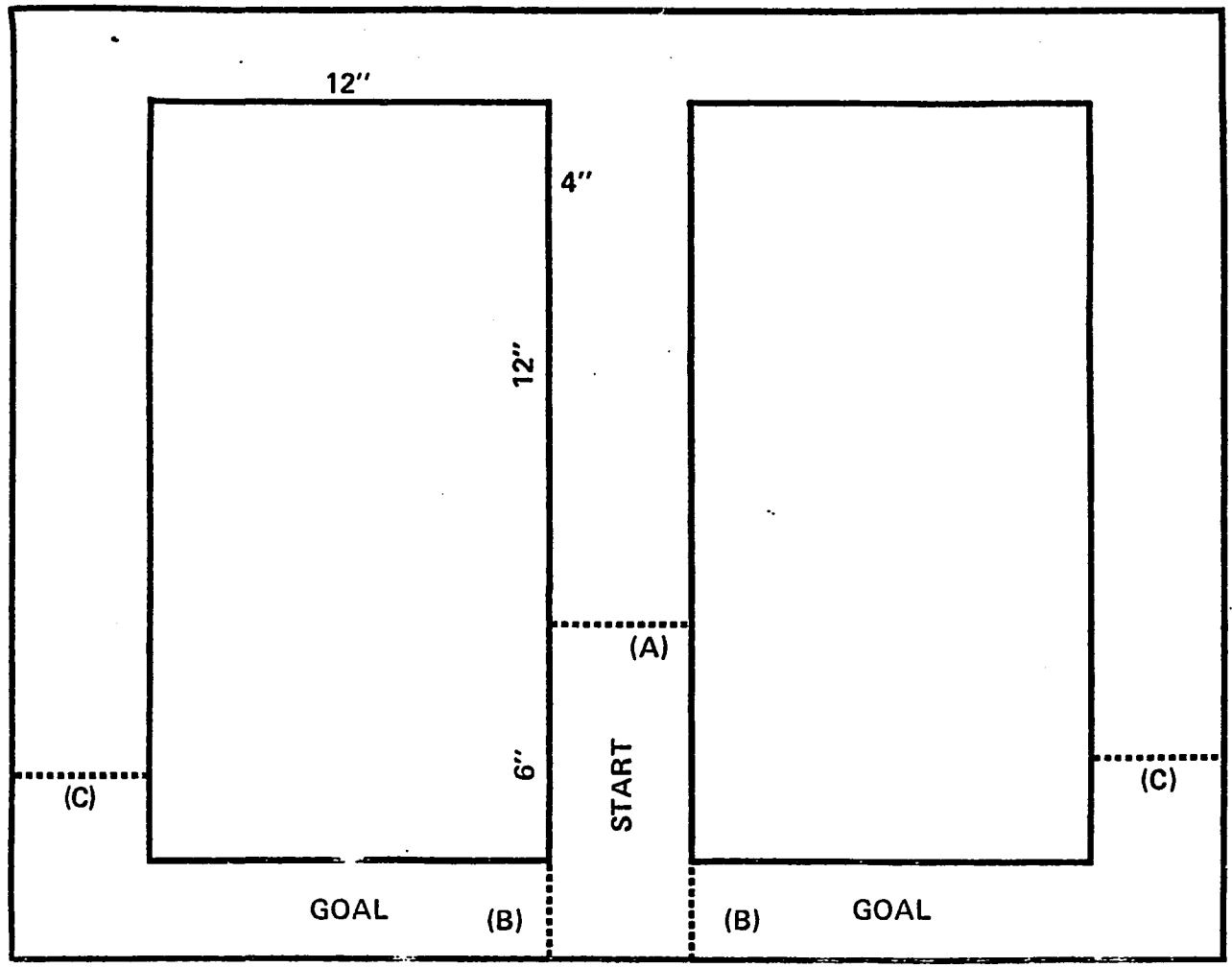

FIGURE 6. MAZE USED IN EXPERIMENT 3. THE START DOOR IS INDICATED AT "A", THE GOAL EXIT (OR START CHAMBER ENTRY) DOORS ARE INDICATED AT "B", AND THE LATERAL ALLEY DOORS ARE AT POINT "C".

to the home cage but remained in the experimental room. During the 15 second intertrial interval within sessions, the animal was retained in the start chamber. At the end of the intertrial period, the lateral goal access doors were raised, then the start chamber door was raised. As training progressed, the sound of the lateral doors being raised served as a cue signaling the start of another trial, and S oriented toward the start door as it was raised.

Once a goal was entered, the three alley doors were lowered to prevent retracing, and the start chamber access door for that goal was opened, providing access to the start chamber directly from the goal. Retracing could occur any time before the lateral alley doors were lowered. Entry into the correct goal was rewarded with three 45mg. pellets. The acquisition criterion was set at 18 correct responses in two consecutive sessions (20 trials).

If S "froze" in the maze, it was allowed to remain in the maze for at least 5 minutes before being returned to the start chamber by hand. If freezing occurred on 5 consecutive trials, S was removed and run in the next session as usual. If the freezing behavior was not eliminated within 4 such sessions, S was eliminated from the experiment. The session following the final acquisition trial was the first reversal session, where the reinforcement contingencies were reversed so that the previously non-reinforced goal was now reinforced. All other procedures remained the same. The reversal criterion was set at 8 correct reversals within one 10-trial session.

Histology

The lesion morphology in this experiment was again similar to that seen in the first two experiments. None of the operated animals were rejected on the basis of lesion inadequacy. One VMH lesion was marginal, in that the lesion was distinctly asymmetrical, probably because the electrode penetrated the floor of the hypothalamus on one side. Thus, at one locus the lesion was complete, extending laterally to invade the medial border of the fornix and medially to invade the arcuate nucleus. The contralateral lesion primarily involved the inferior portion of the VMH and arcuate nucleus, and extended posteriorly to invade the anterior component of the premammillary nuclei. Although approximately 40% of the VMH nucleus was intact unilaterally, the animal data were not discarded.

The SNC lesion morphology was also similar to that seen in the first experiments, except that in no instance was the caudate nucleus involved in the lesion site. Again, the lesions extended from the subgenual region of the SNC, and in some cases extended posteriorly far enough to invade the fornix columns. There were no observable differences in lesion morphology for those animals that failed to reach the acquisition criterion in either lesion group.

Results

Not all animals reached the acquisition criterion. Groups C and VMH both contained 3 Ss that failed to acquire the response, while 2 Ss in the SNC group did not reach the criterion performance. One S in each

operated control group failed to reach the acquisition criterion.

Analysis of variance (Table 5) of the number of sessions to acquisition indicated no significant difference between groups ($F=2.348$, $df=4/25$, $p>.05$). The same result (Table 6) was true of the reversal data ($F=0.867$, $df=4/25$, $p>.05$). The number of sessions required to reach the reversal criterion was extremely consistent between groups indicating that the response reversal measure in this instance was not at all sensitive to the lesion effects.

Although both the normal and VMH groups contained an equal number of animals that failed to reach the acquisition criterion, the behavior of the VMH animals was quite different from that of Ss in the other groups. VMH animals generally entered the alley readily, but then froze for extended periods of time at one of the far corners of the maze. This was true of VMH animals that successfully acquired the position response as well as those that failed to reach the acquisition criterion.

The response characteristic of the VMH animals was somewhat stereotyped. After exiting from the start chamber, a VMH rat would traverse one alley as far as the lateral alley door, then retrace to the opposite goal door. The pattern was often repeated several times before goal entry occurred. Although Ss of other groups exhibited retracing behavior, it was not as persistent as in the VMH group.

The difference between those VMH rats that reached the acquisition criterion and those that did not was primarily that the latter animals exhibited freezing behavior to the extent that further testing proved

Table 5. Summary table of the analysis of variance of trials to acquisition in experiment 3

Source	SS	df	MS	F	p
Between	15.513	4	3.878	2.3489	n.s.[a]
Within	41.287	25	1.651		
Total	56.800	29			

[a]Not statistically significant.

Table 6. Summary table of the analysis of variance of the reversal scores in experiment 3

Source	SS	df	MS	F	p
Between	5.760	4	1.44	0.867	n.s.[a]
Within	41.607	25	1.66		
Total	47.367	29			

[a]Not statistically significant.

impossible. If left in the maze for an extended period of time (longer than 5 minutes), the VMH Ss exhibited a persistent grooming behavior that alternated with immobility. This behavior was not observed in any other treatment group in this experiment. Review of the histological material failed to give evidence of differences in lesion morphology that might account for the behavioral differences within the VMH group.

It is of interest to note that Ss in the SNC group responded well in this alley situation, unlike the initial behavior of the SNC Ss in the passive avoidance experiment, when extensive habituation was sometimes required. On the other hand, rats in the VMH group responded without difficulty in the passive avoidance alley, but required extensive habituation in the modified T-maze.

Discussion

The reversal learning task has been reported to provide a sensitive index of behavioral perseveration following septal lesions (Thompson and Langer, 1963; Zucker and McCleary, 1964; Zucker, 1965). The operated animals in this experiment did not demonstrate any tendency to maintain the originally conditioned response in the face of reversed reinforcement contingencies. Since response perseveration in this type of task has been reported so frequently in animals with SNC lesions, it is of considerable interest to determine the reason that the phenomenon did not occur in this experiment.

The use of a clear plexiglas maze undoubtedly resulted in visual cues from the experimental room. It had been decided at the outset of this experiment that the particular cues used by the Ss in establishing

the response was irrelevant to the question of perseveration during the reversal task. However, the absence of perseveration in a task which is otherwise a sensitive indicator of a perseverative defect suggests that the existence of relatively strong exteroceptive cues may have served to ameliorate the effect of the lesion. The question can only be answered empirically. Certainly the results of such a study could provide some important insights into those stimulus factors which contribute to or mitigate against behavioral perseveration.

It is also possible that response perseveration did not occur in this experiment because considerable retracing could, and often did, occur before the S was prevented from retracing upon entering the goal chamber. All Ss demonstrated such "choice vacillation" during the early conditioning trials, and the Ss of the VMH group were, as noted above, somewhat outstanding in this regard.

Those studies which reported behavioral perseveration on a position habit differed in several respects from the present study. First, the experiment which reported position perseveration in a T-maze (Thompson and Langer, 1963) used shock avoidance as the reinforcement contingency, and secondly, perseveration on the position reversal task was demonstrated following only one correct response in the T-maze. Thus, the Ss could gain relatively little experience in the maze before reversal behavior was tested. Other studies reporting position perseveration also used tasks in which any sort of "retracing behavior" was not possible. Zucker and McCleary (1964) reported a reversal deficit in cats following septal lesions. The position habit, however, was established in a Wisconsin

General Test Apparatus (WGTA). Since self-correction was not allowed a response would occur rapidly with no chance of "retracing" in the situation. The same situations would exist in a relatively short T-maze.

The apparatus used in the present experiment contained comparatively long alleys, and at least two right turns or two left turns had to be negotiated before the goal was entered and retracing became impossible. Thus, the Ss could gain considerable reversal experience in the alleys before a "choice" was defined by actual entry into a goal. There will be further discussion of these points in the next section of the paper, since they raise questions that may be important to an understanding of perseverative behavior.

General Discussion

It was hypothesized that both the septal nuclear complex and the hypothalamic ventromedial nucleus are functionally related to a general response inhibition system. Thus, lesions in both areas should result in a form of behavioral dysfunction usually described as response perseveration. The results of many previous experiments suggest that such a behavioral deficit may occur following SNC or VMH lesions. There exist, however, only a few direct comparisons of behavior resulting from both types of brain damage (Singh and Meyer, 1968; Kaada, Rasmussen, and Kveim, 1962).

The three behavioral tasks employed in this study all represented situations in which response perseveration had been demonstrated on previous occasions. Of these, only the passive avoidance experiment provided any evidence that both SNC and VMH damage produce similar

behavioral deficits. Both the active avoidance experiment and position reversal experiment failed to support the hypothesis. While rats with septal lesions exhibited increased resistance to extinction during massed extinction trials on a two-way avoidance task, rats with VMH damage extinguished the avoidance response at a rate comparable to control animals. The position reversal experiment did not produce any indices of response perseveration on the reversal task in either operated group.

The fact that the passive avoidance task was the only one in which response perseveration occurred merits special attention. It is possible that rather than reflecting a response inhibition dysfunction, the passive avoidance deficit might be attributable to heightened appetitive motivational states which have been reported following both types of lesions. It is well known that VMH lesions produce obesity and hyperphagia. It has been questioned whether the marked postoperative hyperphagia results from actual increased hunger motivation (Grossman, 1966). Rats with VMH lesions, in addition to becoming hyperphagic and obese on an ad libitum feeding schedule, show exaggerated reactivity to the stimulus qualities of food, rejecting food that is even slightly adulterated with quinine and, in addition do not exert effort to obtain food. Unoperated rats that have been food deprived will accept quinine adulterated food and will exert effort to obtain food (Miller, Bailey, and Stevenson, 1950). Such evidence suggests that the hunger motivation of VMH rats is not necessarily higher than normal, and may even be lower than normal, even though the ad libitum intake increases dramatically.

Recent evidence suggests that the reduced hunger motivation in VMH rats may be seen only when they are allowed to remain obese. If VMH rats are maintained at a weight level below or equal to their preoperative weight, they will exhibit heightened hunger motivation in alley performance and lever pressing to obtain food (Kent, 1970). That observation is particularly important, since the operated rats in the passive avoidance experiment in the present study were also maintained at a weight level below that of the pre-operative body weight.

Septal lesions have been reported to produce both polydipsia (Kasper-Pandi, et al., 1969) and mild hyperphagia (Singh and Meyer, 1968). Harvey and Hunt (1965) suggested that the postoperative polydipsia reflects a true thirst motivation, since rats with SNC damage tend to maximize water reinforcements on a DRL schedule, while differential water pre-loading of the septal rats equalized their response rates to normal controls. Hyperphagia following SNC lesions is not a consistent finding, since Kasper-Pandi and her co-workers did not observe hyperphagia. The same study demonstrated that the passive avoidance deficit following SNC damage is independent of altered appetitive motivational states. A passive avoidance deficit was seen in a non-appetitive passive avoidance task which utilized punishment of a previously established active avoidance response, similar to the punished avoidance task described by Zucker and McCleary (1964).

In contrast to the data of Harvey and Hunt, Carey (1967a) demonstrated that polydipsia and response perseveration on a DRL schedule are anatomically dissociable effects of SNC damage. Based upon the evidence presently

available, it seems reasonable to conclude that the passive avoidance deficit seen in the septal animals in this study did not derive from a possible altered appetitive motivational state, especially since there is no conclusive evidence for heightened hunger motivation following septal damage, and food reward was used in the present study.

The possibility that the VMH rats were operating under a heightened hunger drive cannot be disregarded. It may be argued, however, that if passive avoidance behavior operates independently of thirst drive, there is no compelling reason to assume that hunger motivation in and of itself will produce a passive avoidance deficit. The issue can best be resolved by testing both SNC and VMH animals in a non-appetitive passive avoidance task of the kind described by Kasper-Pandi, et al. (1969) and Zucker and McCleary (1964). The present study suggests that both VMH and SNC lesions produce a passive avoidance deficit that derives from response disinhibition rather than from altered motivational states.

The fact that only rats with SNC lesions exhibited response perseveration during extinction of the active avoidance response represents a clear instance in which the hypothesis was not supported. As noted previously, the hypothesis demands that both operated groups exhibit similar deficits on the same task, and that was not the case in this experiment. At present there exists no clear reason for the failure of the VMH group to exhibit response perseveration in this task, and so the hypothesis was not supported by this experiment.

The response reversal experiment requires careful consideration, since response perseveration in this task has been reported several times

following SNC lesions. In this study neither the SNC nor the VMH animals exhibited response perseveration during position reversal. It is thus possible that the same factors which mitigated against response perseveration for the septal animals may have been operating to eliminate that behavior in the VMH rats as well.

There were two unusual aspects to the position reversal experiment reported in the present study. First, the experiment was run in a clear plexiglas maze, and second, the maze was constructed in a manner that allowed considerable retracing behavior to occur before a response was defined by goal entry, thus eliminating any possibility for retracing to occur.

It was noted previously that the use of a clear plexiglas maze resulted in the presence of a considerable number of directional cues from the experimental room itself. Response perseveration may depend upon the absence of such external directional cues, and occur when such brain-damaged animals are dependent primarily upon proprioceptive cues. Indeed, McCleary (1966) suggested that dependence upon proprioceptive cues may contribute to response perseveration in septal animals. A second possibility is that the opportunity for considerable retracing in the maze may have mitigated against the occurrence of response perseveration. Several studies (Schwartzbaum and Donovick, 1968; Zucker, 1965; Zucker and McCleary, 1964) suggest that the extent of postoperative experience in a given task may serve to attenuate behavioral effects of the lesion.

Certainly repeated trials on the same task have been shown in several instances to either reduce or abolish perseverative errors. Zucker and

McCleary (1964) reported that septal cats exhibited no deficits on the acquisition of a position habit in a WGTA, but they made significantly more perseverative errors when they were required to reverse the position habit. It is important to note, however, that there were no differences between groups during the second reversal of the position habit. Similar results were reported by Zucker (1965). The results of three of five of his experiments of them are particularly instructive with respect to the question presently under discussion. Cats with septal lesions were all run in three WGTA experiments. Experiment 1 consisted of training on a successive discrimination problem followed by two reversals, and experiment 2 was the establishment of a simple instrumental response which was reinforced, on the average, every other trial (VR-2 schedule), followed by the extinction of that response. Experiment 3 consisted of training in a simultaneous discrimination problem followed by two reversals of the habit. Half of the cats were tested in Order A (Experiments 1, 2, 3) and half in Order B (the reverse order). Those operated cats tested in Order A required significantly more trials to learn the original successive-discrimination than did the unoperated controls, and were impaired on the first reversal of the problem. It is significant that the same cats exhibited no impairment on the second reversal, a finding that is consistent with the report of Zucker and McCleary (1964). It is perhaps more significant that those septal cats given prior experience on the reversal of the simultaneous discrimination problem (Order B) exhibited no impairment on either the acquisition or reversal of the successive discrimination problem.

Schwartzbaum and Donovick (1968) reported that septal lesions produced a deficit in the reversal of a complex spatial discrimination problem in which response to a right or left lever were differentially reinforced depending upon which chamber of a shuttlebox the levers were located in. Following each reinforcement, the rat was required to enter the opposite chamber and respond to the lever located in the opposite position of the one that produced a reinforcement in the other chamber. Thus, if the right lever was correct in one chamber, the left lever was correct in the other compartment. There was extensive preliminary training in the situation. The septal rats exhibited no deficit in the acquisition of the spacial discrimination, and the reversal deficit declined markedly across repeated reversal sessions, although the septal performance remained inferior to the control performance.

Taken together, these experiments all indicate that repeated experience in the same or similar problems will attenuate the behavioral effects of septal lesions in later tests. The absence of a reversal deficit in the present study may have resulted from the fact that relatively free retracing behavior served to provide postoperative reversal experience in the situation. It would be of interest to determine whether simple postoperative exploratory experience in a maze situation (prior to position and reversal training) will effect reversal learning in lesioned rats. Considering the between-test results reported by Zucker (1965), it is also possible that inhibitory experience in one situation will generalize to a novel task. Such a result would suggest that inhibitory deficits resulting

from brain damage are not necessarily permanent, but can be ameliorated by extensive inhibitory training.

The results of this study are inconclusive. Since only one of three experiments supported the main hypothesis, the hypothesis cannot be clearly accepted or rejected. It is hoped that the result of some of the experiments suggested above will provide a clearer interpretation of the contribution of the SNC and VMH to response inhibition.

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