THE SEPTAL SYNDROME AND THE
DIENCEPHALIC "AFFECTIVE DEFENSE"
PATHWAYS

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A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF
THE UNIVERSITY OF FLORIDA
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

August, 1965

ACKNOWLEDGMENTS

The author wishes to express his deep appreciation to Dr. Bradford N. Bunnell, Chairman of his Supervisory Committee, for his guidance and personal interest in this project. Dr. Fred A. King was also very helpful, and through his kind office technical assistance in the preparation of histological specimens was made available. The services of Drs. Wilse B. Webb, Donald Goodman, Robert L. King, and James D. Winefordner, members of his Supervisory Committee, are gratefully acknowledged. Very special thanks are due Mrs. Jerre L. Basch for her encouragement and assistance with the surgery and behavioral testing. Miss Hope Razzano prepared a number of the histological slides.

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INTRODUCTION

The early work of Bard (1928) demonstrated that cats deprived of telencephalon and diencephalon rostral to the mid-hypothalamus would exhibit a relatively well-organized rage pattern at low threshold. Further elimination of tissue in the vicinity of the posterior hypothalamus results in animals which can still respond defensively, although at high threshold and in a fragmentary manner (Bard and Macht, 1958). Thus it appears that parts of the caudal diencephalon facilitate and coordinate mechanisms of defensive behavior situated lower in the brain stem. In turn, higher regions of the brain evidently exert a net inhibitory influence upon the hypothalamic-mesencephalic defense centers, since their removal tends to release defensive behavior from normal restraint. A great amount of research has been devoted to understanding the identity and interplay of these excitatory and inhibitory systems.

One such release phenomenon may be obtained when the septal region of the forebrain is destroyed (Spiegel, Miller, and Oppenheimer, 1940). In the rat, this septal syndrome is characterized by an exaggerated reactivity to stimulation of the dorsum; a tendency to attack and bite intruding objects; a curious rabbit-like gait when fleeing; vigorous biting, struggling, and squealing while being handled; and increased susceptibility to "animal hypnosis" or cataplexy (Brady and Nauta, 1953 and 1955). With daily handling these symptoms usually subside within two weeks, often much sooner.

Other effects of septal lesions, which may or may not be related to the symptoms of irritability, are difficult to analyze. Following early reports of septal "emotionality," King (1958) found that septal rats learn active avoidance in a shuttle box more rapidly than controls, supporting the interpretation that the enhanced acquisition results from the greater fear of the operated rats. Later it was shown that septal animals exhibit severe deficits of passive avoidance (McCleary, 1961; Kaada, Rasmussen, and Kveim, 1962; Fox, Kimble, and Lickey, 1964). This finding was taken to indicate that the effects of septal ablation are a form of motor release essentially unrelated to emotionality. The septal syndrome, according to this view, consists of exaggerated skeletal and autonomic components of fear-anger reactions without the cognitive aspects and goal-directedness of true emotion. Consistent with this hypothesis are reports that septal rats perform poorly on a DRL reinforcement schedule (Ellen, Wilson, and Powell, 1964) and that they are more resistant to extinction (Schwartzbaum, Kellicutt, Spieth, and Thompson, 1964), both effects suggesting a loss of ability to suppress approach tendencies.

Quite recently this motor release interpretation has also been questioned. It has been found that septal lesions augment thirst and perhaps hunger (Harvey and Hunt, 1965), which could well account for poor performance on tasks involving approach-avoidance conflict. A "deficit" in passive avoidance can result not only from a loss of restraint but also from an increased approach tendency as seen in water-deprived septal rats (Harvey, Lints, Jacobson, and Hunt, 1965). Indeed, the willingness of an animal to accept shock to obtain a goal has long been used as the

obstruction method for measuring the strength of drives (Munn, 1950). Moreover, in contrast to the impaired DRL performance reported by Ellen et al. (1964), Harvey and Hunt (1965) found that septal rats responded more efficiently than controls on several types of schedule including DRL. The methodological or other cause of this discrepancy has not yet been determined. Changes in avoidance performance are also somewhat problematical. Although the finding of enhanced acquisition of active avoidance by King (1958) has been well substantiated (Krieckhaus, Simmons, Thomas, and Kenyon, 1964; Fox et al., 1964), it appears that preoperatively established avoidance is abolished by septal lesions (Moore, 1964; Rich and Thompson, 1965) and, further, these animals may be unable to reacquire avoidance conditioning postoperatively (Rich and Thompson, 1965). Whether the difference between these results and those of earlier workers who found improvement are due to pseudoconditioning, as Rich and Thompson (1965) suggest, or to other factors is presently uncertain. Whatever the status of these various septal effects may be, it is widely reported that the septal irritability syndrome is independent of them (Schwartzbaum, et al., 1964; Thomas, Moore, Harvey, and Hunt, 1959; Krieckhaus et al., 1964; Moore, 1964), and might well involve separate anatomical mechanisms.

It has been proposed that the septal syndrome is mediated by the hypothalamus; more specifically, that hypothalamic rage or defense centers are released from tonic inhibition when the septum is destroyed (King and Meyer, 1958; Gellhorn and Loofbourrow, 1963). Such "affective defense" centers have been mapped by Hess (1954) and his coworkers by means of

chronically implanted electrodes. In particular, stimulation of the rostral hypothalamus surrounding the fornix columns elicits well-directed escape or attack apparently indistinguishable from the responses of cats confronted with a barking dog. Hunsperger (1956) has shown that this perifornical defense system extends continuously from the amygdala, along the stria terminalis, perifornical region, intermediate hypothalamus, and into the periaqueductal gray. A number of components of agonistic behavior (aggressiveness, threat, or fear) may be obtained from this system, including such septal-like items as vocalization, urination and defecation, biting, and escape (Brown and Hunsperger, 1963). Typical feline responses, such as folding the ears down or back, protrusion of claws, arching of the back, hissing, and striking with the forepaws are also observed, the specific pattern depending upon external stimuli, location of the electrode, and stimulation intensity. Moore (1960), who has studied the septal syndrome in cats, explicitly notes the similarity between the effects of destroying the septal area and stimulating the perifornical region in these animals.

Both structural and functional considerations, then, seem to favor the possibility that septal efferents traveling with the fornix normally inhibit the hypothalamic mechanisms of defensive behavior. Nonetheless, the septal nuclei possess rich interconnections with the hippocampus, amygdala, and basal regions of the telencephalon (Valverde, 1963; Powell, 1963), any of which may be involved in the transmission of septal inhibition.

The present experiment was specifically designed to determine whether or not the known hypothalamic mechanisms of emotional expression are responsible for the excitatory phase of the septal syndrome. An experimental group (SPF) was given combined septal and perifornical hypothalamic lesions. For control purposes three additional groups were included: operated control (C), septal (S), and perifornical (PF). All animals were rated before and after the operation on a scale known to be sensitive to the septal syndrome (King, 1959). Should the septal syndrome result from a release of perifornical excitation, removal of the perifornical region may be expected to block its development. On the other hand, if under such circumstances the septal syndrome still appears, pathways other than the perifornical "affective defense" mechanisms must be involved. It was reasoned, therefore, that if the perifornical region is a crucial link in the septal syndrome, then the SPF rats should exhibit a low level of irritability comparable to that of C and PF animals; if not, then the SPFs should closely resemble the S rats.

METHOD

Subjects. Data were obtained from 46 naive male Long-Evans rats, ranging in preoperative weight from 210 to 397 grams. During the experimental period they were housed individually, with food and water constantly available.

Procedure. Each subject was rated on successive afternoons, utilizing a scale slightly modified from that devised by King (1959) to quantify the septal syndrome. The ratings were made simultaneously but independently by two experimenters, one of whom handled the rats while the other recorded the data. Beginning with the rat in his home cage, the following items were scored: 1) Object presentation (OP). Animal is presented with a pencil-shaped probe in front of the snout and observed for escape or attack; 2) Response to tap on the back (TR). Scored according to the magnitude of startle response; 3) Resistance to capture (RC). Rat is gently picked up and observed for biting and attempts to escape; 4) Resistance to handling (RH). Rat is shifted from hand to hand, noting tendency to bite and struggle; 5) Vocalization (VOC). Amount of squealing during the rating sequence; 6) Urination-defecation (UD). Amount and kind of excretion during rating; 7) An additional measure for cataplexy was added to the scale, since it had been observed that septal rats appear to be unusually susceptible to this symptom. This item (CAT) was rated by holding the posterior end of the rat in the left hand and pinning the animal in a supine position with the right

hand for 5-10 seconds. Delays in righting after removal of the right hand were taken to indicate cataplexy. The entire rating scale is included in Appendix A.

Ratings were taken on five preoperative and one or more postoperative days, until the animal died or the score dropped to a low level. Prior to the first postoperative rating, the rats and their cages were scrambled by one rater (JLB) to minimize experimenter bias on the part of the other (JES).

In addition, it had been planned to obtain a measure of performance on a passive avoidance task; however, the rapid deterioration of the animals receiving hypothalamic lesions precluded this testing.

Surgery. Upon completing the fifth preoperative rating, the subjects were divided randomly into four groups: operated control (C), septal (S), perifornical (PF), and combined septal-perifornical (SPF), according to the lesions they were to receive. Anesthesia was induced by a standard intraperitoneal injection of .2 cc of 50 mg/cc Nembutal and .2 cc of 300 mg/cc chloral hydrate. Further injections of chloral hydrate maintained, as necessary, the proper depth of anesthesia. Also, .3 cc of .4 mg/cc atropine and 100,000 units of penicillin were administered to each rat at the time of operation.

Following standard surgical procedures, the appropriate bilateral lesions were produced stereotaxically through a stainless steel electrode made from a #0 insect pin, insulated except at the tip with GE formvar enamel. The coagulating current was generated by a Grass LM-3 radio frequency lesion maker, and the circuit was completed through a stainless steel anal electrode.

The electrode was inserted six times in each animal, including the controls. However, the control punctures were performed to make an electrode track similar to that in the true lesions, but without encroaching upon the area which would have been occupied by a lesion. Orientation of the electrode was in accordance with the coordinate system of de Groot (1959), referring the anterior plane to the interaural line, depth to the surface of the brain, and lateral to the midsagittal sinus. The specific coordinates are given in Table 1. It should be noted that both sets of septal coordinates were applied to each rat, so that the lesions would conform better with the shape and extent of the septum.

Table 1

Stereotaxic Coordinates for Septal and Perifornical Lesions

Type Lesion	Anterior	Lateral	Deep	
			Lesion	Control
Septal #1	8.0	.4	5.4	3.3
#2	7.7	.4	5.1	3.3
Perifornical	6.0	1.2	7.4	6.4

For all lesions the current was passed for ten seconds. Initially, an intensity of 63 was used for septal lesions and 58 or 57 for perifornicals. As early histological results indicated that these intensities were too great, smaller lesions were made in subsequent operations with lower values of 62 and 55, respectively. These adjustments did not

seem to have any noticeable behavioral effect, and therefore data from rats receiving larger and smaller lesions were combined.

RESULTS

Behavioral. Mean irritability ratings for the days immediately before and after surgery are given in Table 2 and depicted graphically in Fig. 1. After the operation Group C exhibited no change in score, while S and SPF animals underwent a sharp increase. Likewise the PF group showed a rise, although somewhat less than the S and SPF rats.

Table 2

Mean King Scale Ratings of Rats Receiving No Lesions (C), Septal Lesions (S), Perifornical Lesions (PF), and Combined Septal-Perifornical Lesions (SPF)

Group	N	Rater	Preop 4	Preop 5	Postop 1
C	6	JES	4.6	3.8	3.8
		JLB	4.8	3.5	3.8
PF	11	JES	3.4	3.9	8.9
		JLB	3.1	3.7	9.4
SPF	15	JES	3.1	3.0	13.2
		JLB	3.2	2.8	13.8
S	14	JES	3.8	3.2	14.2
		JLB	3.8	3.3	14.6

Fig. 1. Postoperative changes in irritability rating.

Table 3

Postoperative Day 1 Differences and Significance of Differences between Groups

Comparison	Difference	Significance
S vs C	10.4	.002
SPF vs C	9.4	.002
PF vs C	5.1	.002
S vs SPF	1.0	n.s.
SPF vs PF	4.3	.02

As can be noted in Table 3, all three lesioned groups differed significantly from the controls (Mann-Whitney U, 2-tailed). It is also apparent that perifornical destruction does not preclude the rise in irritability which typically follows septal lesions, since the SPFs are significantly higher in rating than the PFs ($p < .01$, 1-tailed). On the other hand, the difference between groups S and SPF is small and not significant.

Usually before the second postoperative day, both groups of rats with PF lesions began to exhibit a progressive deterioration symptomized by somnolence, poor grooming, nasal discharge, and ultimately death. In most instances this debility did not seriously affect the first postoperative rating; however, the small difference between the S and SPF groups seems in part attributable to a slight somnolence in the latter animals.

Although ratings beyond the first postoperative day were recorded, meaningful comparisons between groups which received PF lesions and those that did not are impossible, since the debility of the former animals caused the ratings to drop sharply. Also, PF and SPF groups began to be depleted by death of the animals soon after the operation. Therefore, data beyond postoperative day 1 are excluded from the text of this report (see Appendix B). Scores for the Ss dropped quite rapidly after the first day, as did those for the albino septals of King (1959) and the Long-Evans hooded rats of Yutzey, Meyer, and Meyer (1964).

Analysis of individual items of the rating scale (Table 4) reveals some interesting effects. To facilitate presentation of these data, statistical results will be given in parentheses. The score treated will be indicated first, followed by the groups compared, and finally by the highest level of significance. The Mann-Whitney U-test, 2-tailed, is used throughout.

Table 4

Postoperative Day 1 Comparisons on Items of the Rating Scale

Group	OP	TR	RC	RH	VOC	UD	CAT
C	.1	.4	.8	1.2	.6	.7	.0
PF	2.5	1.6	1.0	.9	.6	.4	1.8
SPF	3.1	1.6	1.8	1.9	1.5	.6	2.6
S	2.2	1.8	2.1	2.9	1.6	1.1	2.4

In confirmation of the overall results, the SPFs scored higher than the Ss on all items except response to a tap on the back (TR), on which these two groups were equal. It is also noteworthy that virtually all of the increase of the PFs was on three items: OP, TR, and CAT. On object presentation the PFs exhibited a marked tendency to attack the probe, often with considerable vigor (OP: PF vs C, .02). SPFs attacked even more vigorously, significantly more so than Ss (OP: SPF vs S, .05) but not the PFs.

All three lesioned groups increased in responsiveness to the tap on the back (TR: PF vs C, .002; SPF vs C, .02; S vs C, .05), but differences between these groups were insignificant. Resistance to capture was enhanced in both groups receiving septal lesions, but not by perifornical ablation (RC: S vs C, .05; SPF vs PF, .05).

The results on resistance to handling would indicate that PF lesions diminish the struggling and biting associated with this score. However, the PF and SPF rats were observed to cease their struggles soon after being picked up, and become quite limp. The somewhat lowered scores on RH reflect this general fatigue effect as much as a specific reduction in struggling and biting.

Vocalization, like resistance to capture, was increased by septal lesions and not by perifornical damage (VOC: S vs C, .05; SPF vs PF, .02). Scores on urination-defecation were slightly, but not significantly, depressed by PF lesions.

Interpretation of the cataplexy ratings is complicated by the somnolence and fatigability of the rats that received PF lesions. This item was very satisfactory when applied to septal rats, and the Ss manifested a strong and characteristic tendency to bob up and down as they breathed. Limp, somnolent PFs, on the other hand, did not make these movements. It was often impossible to determine how much of the immobility in PFs and SPFs was due to cataplexy and how much was due to other factors. For this reason no specific meaning can be attached to the numerical increase in this case. Nonetheless it did appear to the raters that the PFs and SPFs exhibited a genuine increase in proneness to cataplexy.

Neuroanatomical. Histological sections of the brains were stained for Nissl substance (cresyl violet or neutral red), and in a number of cases for Myelin as well (Weil or luxol fast blue). In general, the lesions were appropriate in size and extent, although some of the earlier PF lesions were rather large. The septal lesions destroyed nearly all of the septum above and rostral to the anterior commissure, often extending far enough caudally to interrupt the fornix (Fig. 2). Damage to the perifornical region was observed lateral to the upper part of the third ventricle, and immediately rostradorsal to the ventromedial

Fig. 2. Representative septal and perifornical lesions. Sections correspond approximately with anterior planes 7.8 and 6.8, respectively, of de Groot (1959).

hypothalamic nucleus. Anteriorly the PF lesions terminated close to the boundary between the preoptic region and the rostral hypothalamus. In every case the fornix and surrounding gray matter was severely damaged. However, the lesions in one PF rat (D60B) were exceptionally

far posterior, occupying a position immediately dorsal to the ventromedial nucleus. This animal failed to exhibit the debility and irritability that typically occurred in PFs. When this animal was perfused it was noted that its stomach was much distended with air or water, a condition which did not appear in other members of this group.

Additional data. Prior to undertaking the main experiment, a number of exploratory operations were performed with the object of examining various regions of the brain that for one reason or another might participate in the septal syndrome. Essentially the same procedure was followed as above, except that the rats had been handled during previous behavioral experiments, and control procedures were minimal. Hence these data (Table 5) can be no more than suggestive. Some of the histological results are shown in Figs. 3-6.

These observations, however tentatively, are consistent with the view that the septal syndrome is not dependent on the dorsomedial or anterior thalamic nuclei, periaqueductal gray, amygdala, or frontal polar region. Damage to the rostral hypothalamus seemed to produce irritability and to augment the septal syndrome. Amygdaloid lesions also tended to produce irritability, but only after a lapse of three weeks or more. In the absence of septal destruction, irritability was not produced in the few rats that received lesions in the ventral midline metencephalic tegmentum or caudal medial forebrain bundle.

Table 5

Effects of Single and Combined Lesions on King Scale Ratings

Lesion	N	Effect ^a	Histology ^b	Comments
Anterior thalamic nuclei plus septal (Fig. 3)	2	1	2	
Dorsomedial thalamic nuclei plus septal (Fig. 4)	2	1	2	
Periaqueductal gray plus septal	2	1	1 and 2	
Anterior polar region plus septal	2	1	3	Well-developed hop Somnolent and aphagic
Amygdala-pyriform (Fig. 5) plus septal	2	2	3	
Amygdala (Fig. 6) plus septal	2	2	2	Irritable after three weeks
Anterior hypothalamus plus septal	2	3	0	
Amygdala-pyriform (Fig. 5)	2	2	3	Irritable after several months
Amygdala (Fig. 6)	2	0	2	Very slight irritability after three weeks, increased by addition of septal lesions
Medial forebrain bundle (caudal hypothalamus)	1	0	0	Aphagia, ataxia, ptosis
Anterior hypothalamus	1	3	0	
Ventromedial pontine tegmentum	1	0	2	Destroyed fibers direct from septum to this region

Note: For Effect, 0 means no syndrome; 1, syndrome apparently normal; 2, slowly developing syndrome; 3, long lasting, well-developed irritability.

^a0 denotes no irritability; 1, syndrome apparently normal; 2, slowly developing syndrome; 3, long lasting, well-developed irritability.

^b0 denotes no histological data; 1, RF lesions properly placed, but somewhat small; 2, large RF lesion destroying whole structure; 3, radical lesion produced by stereotaxic cutting and suction (septal by coagulation).

Fig. 3. Rat D55A, showing septal and anterior thalamic lesions. Anterior planes 7.3 and 5.6. This rat increased 6.5 points on the rating scale.

Fig. 4. Brain sections from rat D57A, which received combined lesions in the septum and dorsomedial thalamic nuclei. Anterior planes 7.5 and 4.2 (de Groot, 1959). King scale rating increased 8.5 points postoperatively.

Fig. 5. Example of a radical amygdala-pyriform lesion produced by stereotactically guided cutting, followed by aspiration of the severed structures.

Fig. 6. Amygdalectomy produced by RF coagulation by means of five electrode placements per side.

DISCUSSION

Since the perifornical region of the hypothalamus is associated with the facilitation of defensive behavior (Hess, 1954), it would seem plausible to expect that its destruction would raise the threshold for such responses. Paradoxically, the rats with perifornical lesions became irritable. They showed a strong tendency to attack intruding objects and to overreact to a tap on the back; they did not, however, demonstrate an increased tendency to bite, struggle, or squeal during handling. Quite probably these behavioral changes resulted from damage near the medial preoptic area, since it has been reported that lesions in this vicinity result in a "septal-like" syndrome (Larsson and Heimer, 1964). Maire and Patton (1956) similarly obtained, from rats with anterior hypothalamic-preoptic lesions, states in which "gentle blowing on the hair of the back often provoked wild jumping and squealing. When prodded lightly with a metal bar, operated animals attacked it viciously with teeth and claws." The likeness between this syndrome and the behavior of the present series of PFs is unmistakable, although exaggerated squealing was not observed in the latter rats. Also, Maire and Patton (1956) found that their rats became quite hyperactive, a characteristic that was not clearly present in the PF group. No doubt differences in the method of production, size, and shape of the lesions account for these discrepancies.

The more or less rapid deterioration of the PF and SPF rats, at times accompanied by copious nasal discharge, closely resembles other effects obtained by Maire and Patton (1956) following rostral hypothalamic-preoptic lesions. These experimenters found that lesions immediately above the optic chiasm, close to the midline, cause rapidly fatal pulmonary edema. Other rats, with lesions in the same general area, died without developing lung congestion, presumably because of hyperthermia. Although the PF lesions were somewhat dorsal and lateral to the ones placed by Maire and Patton, closely related anatomical systems were evidently disturbed in the two studies.

Despite the fact that perifornical lesions alone served to produce a definite change in behavior mimicking the septal syndrome, it is clear that additional septal lesions caused irritability significantly greater than that attributable to hypothalamic damage. On two items that were not appreciably affected by perifornical lesions - resistance to capture and vocalization - the added septal lesions of the SPFs yielded increases quite comparable to those of septal lesions alone. These comparisons are especially valid because SPFs and PFs were equally somnolent, and differences between these groups cannot be ascribed to this factor. All indications, then, are that the septal syndrome is not dependent upon the perifornical "affective defense" centers of the hypothalamus. The septal syndrome must therefore be expressed via a descending pathway other than that destroyed in the present experiment, and apart from the septohabenular connections previously eliminated by Brady and Nauta (1955). It is also clear that the neocortex is not involved crucially in this

relay (Yutzey et al., 1964). Before attempting to interpret these results more fully, it is well to take cognizance of some of the difficulties involved in any attempt to unify the general mass of experimental evidence regarding defensive behavior into a reasonably parsimonious, internally consistent theory. Accordingly, several of the major factors will be touched upon before proceeding with a discussion of the various possible anatomical mechanisms whereby the septal syndrome may be mediated.

Behavioral nomenclature. This problem has been noted by Green, Clemente, and de Groot (1957), who observe that "rage is readily confused with fear, aggressiveness or, perhaps, frustration and even types of playfulness, while placidity might be confused with indifference, catalepsy, catatonia, stupor, and idiocy." Compounding this difficulty is the plethora of terms applied to essentially the same phenomenon, or the use of the same term for several distinct emotional-behavioral states. Thus, a marked tendency of an animal to defend himself is variously referred to as "rage," "savageness," "affective defense," "irritability," "anger," "emotionality," "pseudoaffective behavior," "wildness," and, perhaps most inappropriately, "aggressiveness." It is felt that the last designation should be restricted to those forms of behavior in which the subject actively seeks out another animal to attack. Another word which presents some difficulty here is "emotionality" which, owing to its broad connotations in the sphere of human discourse in addition to its narrow ones in the study of rat behavior (Hall, 1934), should perhaps be avoided. Of the remaining expressions,

"rage," "affective defense," and "irritability" have appeared frequently and have been rather consistently applied to behavior which resembles the septal syndrome. These three terms or the abbreviation DR (defense reaction) will be used more or less interchangeably. In general, the word preferred by the author of a paper will be applied when discussing his work.

Type of lesion. In studies in which lesions are produced in the central nervous system it is sometimes difficult to determine whether the results are due to a primary loss of tissue or to irritation of the surrounding, more or less intact regions. The finding of clearly incompatible, opposite results from lesions of the amygdala by Bard and Mountcastle (1947) and Schreiner and Kling (1953) may exemplify this source of confusion. Green, Clemente, and de Groot (1957) suggest that the slowly developing rage of Bard and Mountcastle's (1947) cats resulted from incidental damage to the hippocampus and the resulting seizure discharge.

A more carefully documented nuance of lesion production was reported by Reynolds (1963), who compared the effects of anodal DC and radio frequency (RF) methods of coagulating brain tissue. Rats receiving DC lesions in the ventromedial hypothalamic nucleus, and in which the electrolytic deposition of iron was demonstrated, manifested the usual symptoms of irritability and hyperphagia (Wheatley, 1944). On the other hand, RF lesions otherwise comparable did not yield the behavioral effects nor was iron deposited from the electrode. Reynolds proposes that the metal causes discharging foci and that this activity, not release, is

the source of hyperphagia and irritability. In assessing the literature on brain lesions and emotional behavior, it may be noted that Hunsperger (1956) is one of the few investigators who used RF current to coagulate brain tissue.

As far as the septal syndrome is concerned, the method of lesion production is not critical. Brady and Nauta (1953) made septal lesions with a cutting device; Moore (1964) with a suction pipette; Zeman and King (1958) with implanted tumors; and in the present experiment RF was used. All of these techniques were effective in causing the septal syndrome.

Another point that bears mention is the possibility that studies in which lesions are produced serially (e.g. Bard and Mountcastle, 1947; Rothfield and Harman, 1954) may involve readjustments of the "spontaneous reorganization" type (Stewart and Ades, 1951) which could mask certain effects of tissue destruction. Such an effect might explain why total neocortical and paleocortical ablation reportedly produces rage (Bard and Mountcastle, 1947), while bilateral spreading depression evidently does not, at least not without subcortical lesions (Teitelbaum and Cytawa, 1965). Some work critically comparing the effects of spreading depression and decortication, and of simultaneous and serial lesions, seems indicated.

Adjacent or overlapping reciprocal networks. Finally, a complexity that may contribute heavily to the problem of septal inhibitory outlet is the fact that in the immediate vicinity of the septal nuclei - indeed, within the septum itself - lie points which produce irritability when

stimulated. Fernandez de Molina and Hunsperger (1959) have evoked DRs from points in the stria terminalis throughout its course, part of which abuts the ventrolateral septum near the anterior commissure. Similarly, Hernandez-Peon et al. (1963) elicited rage from the ventrolateral septum, medial preoptic area, and points along the borders separating septal, caudate, and accumbens nuclei. This was done by means of precise cholinergic stimulation. Incidental observations of Forman and Ward (1957) and Galeano et al. (1964) confirm the presence of defense facilitatory sites in the septum, especially the lateral portion.

Before leaving the topic of septal stimulation, a remarkable observation of Olds (1955) should be mentioned. In conducting his studies on self-stimulation he noted that septal stimulation causes an immediate arrest of all ongoing activity. Most interestingly, when the stimulation ceased these rats exhibited "rebound" behavior strongly reminiscent of the syndrome resulting from septal lesions. Unfortunately, Olds did not report the exact location of the electrodes which produced this effect.

In addition to these sources of excitation, other structures lying beneath the septum and intimately interconnected with it appear to be inhibitory. Damage in the vicinity of the olfactory tubercle (Fulton and Ingraham, 1929; Spiegel, Miller, and Oppenheimer, 1940) and preoptic region (Nauta, 1946; Maire and Patton, 1956; Larsson and Heimer, 1964) will produce a long lasting septal-like syndrome. It may be that these structures comprise, with the septum, a more or less unitary rage inhibitory

region, having a common discharge pathway. Such a system could correspond with the motor inhibitory area described by Kaada (1962) in certain aspects.

However tempting a scheme of this type may be, there are indications that throughout the brain separate or even opposing functions can occupy the same general location. It is especially relevant that Hernandez-Peon et al. (1963) have shown that cholinergic stimulation of the upper medial preoptic area produces sleep, while noradrenalin applied through the same cannula yields alertness or rage. No doubt more extensive pharmacological investigations will continue to reveal effects of this type.

A completely satisfactory integration of these facts is not possible at the present time; however, it does seem that the septum and surrounding structures consist of opposing, juxtaposed, and perhaps partly overlapping circuits with respect to defensive behavior. At least part of the failure to identify the precise anatomical locus responsible for the septal syndrome (Harrison and Lyon, 1957) may be explainable in terms of such intertwining neural systems. With these suggestions, precautions, and hazards in mind, the remaining septal efferents may be considered. These will be categorized, for purposes of discussion, into hypothalamic, thalamic, and telencephalic.

Hypothalamic. Since the hypothalamic connections of the septal nuclei which travel with the fornix columns have already been eliminated from further consideration, this section will be confined to the other major septohypothalamic tract, the medial forebrain bundle. Anatomically

the medial forebrain bundle is well situated to conduct from the septum, olfactory tubercle, and preoptic area to modify activity in the DR centers of the hypothalamus and periaqueductal gray (Powell, 1963). It would be expected that if DR inhibition occurred by this means, interruption of the medial forebrain bundle between the basal telencephalon and hypothalamus would mimic the effect of septal lesions. While damage to the medial preoptic area above the chiasm does produce a septal type syndrome, similar lesions in the lateral preoptic which would sever the medial forebrain bundle do not affect the DR threshold (Larsson and Heimer, 1964). Teitelbaum and Cytawa (1965) have destroyed the lateral hypothalamic hunger center, which also lies along the course of the medial forebrain bundle, but obtain irritability only if spreading depression is applied. These workers used anodal current to produce the lesions, however, and in view of Reynolds' data (1963) it may be suspected that discharging foci rather than simple release are responsible for the behavioral change. In neither case did the effect of interrupting the medial forebrain bundle alone resemble the septal syndrome, and it would seem, therefore, that most or all DR inhibition from the septum must be exerted by way of other connections.

Thalamic. The septum is strongly connected with the anterior, dorsomedial, and reticular nuclei of the thalamus (Powell, 1963). For various reasons these nuclei, particularly the first two, have been held to participate in emotion. The anterior nuclei are part of the classical Papez (1937) circuit, although their absence does not produce obvious behavioral changes (Brierly and Beck, 1958). A somewhat

stronger case can be made for the involvement of the dorsomedial nucleus in emotion. Ablation of this part of the thalamus has been performed in man as a substitute for prefrontal lobotomy, and in addition to relieving anxiety dorsomedial thalamotomy is said to calm "aggressive, assaultive, screaming patients" (Spiegel and Wycis, 1962). Stimulation of the dorsomedial nucleus yields responses indicative of fear or pain and cats will learn to avoid such stimulation. Roberts (1962), for these reasons, concludes that this structure is part of the neural mechanism of fear. Lesions of the dorsomedial nucleus, as might be expected from this theory, virtually abolish fear-motivated active avoidance responses (Vanderwolf, 1963). Thus it is anatomically and behaviorally feasible that the septal syndrome results from a release of thalamus-mediated fear. Evidence from a small number of rats with combined septal-anterior or septal-dorsomedial thalamic lesions is inconsistent with this hypothesis, however, since the septal syndrome appeared unabated by the thalamic destruction (Table 5).

Telencephalic. In addition to the diencephalic connections, the septal nuclei distribute efferents to the hippocampus, amygdala, and basal telencephalon (Valverde, 1963; Powell, 1963). These three structures will now be considered in turn. The hippocampus, like the anterior thalamic nuclei, was assigned by Papez (1937) to a prominent place in his theory of emotion. Bard and Mountcastle (1947) extirpated the hippocampus in two cats, which were reported to display enhanced pleasure reactions. Hippocampal stimulation, in some instances at least, lowers the rage threshold (MacLean, 1952; Kaada et al., 1962), and Green, Clemente,

and de Groot (1957) attribute the rage that developed in some of their amygdalectomized cats to irritative damage to the hippocampus. There is some indication, then, that the hippocampus facilitates DRs, and that its absence results in a sort of taming. Rothfield and Harman (1954) report that while fornixectomy or neodecortication alone do not lower the rage threshold, together they do. The fornix was divided between the septum and the hippocampus, and since slight damage to the anterior hippocampus was produced the possibility of irritation cannot be ruled out. In any case, Rothfield and Harman conclude that in the absence of neocortex inhibitory influences pass from the rhinencephalon to the hypothalamus via the fornix. Taking their data at face value, however, it seems equally possible that the septum might inhibit the hippocampus.

Bearing directly on this point is the incidental finding of Moore (1964) that while several of his septal lesioned cats developed the syndrome, prior hippocampal ablation appeared to block the development of irritability. To date this is the most positive evidence that a structure is of crucial importance in the transmission of septal release, and systematic testing should be undertaken to demonstrate conclusively the role of the hippocampus in the septal syndrome and other forms of emotional expression.

Results obtained by stimulating and ablating the amygdala are among the most difficult to interpret (Goddard, 1964). With respect to DRs, it seems that the amygdala sends excitation to the hypothalamus by way of the stria terminalis, since destruction of the perifornical

region abolished responsiveness to amygdaloid stimulation (Hunsperger, 1956). However, the evidence of Zbrozyna (1960), who severed the stria terminalis and then stimulated both ends, indicates transmission in the opposite direction. Whatever means are involved in conducting DR facilitation from the amygdala, this activity could be suppressed by the septum. These two structures are connected by multisynaptic relays through the diagonal band and anterior amygdaloid area (Valverde, 1963). Behaviorally, it has been reported that lesions of the amygdala markedly attenuate the septal syndrome. In their interpretation of this finding, King and Meyer (1958) consider the possibility that both septal and amygdaloid efferents, although having opposite effects, impose them directly on the hypothalamus. Alternatively, the two could be connected in series so that the septal nuclei normally restrain the amygdala, but this seems unlikely. King and Meyer (1958) observed that the effect of amygdalectomy diminished with time, possibly indicating that the taming is not sufficiently permanent to warrant any conclusion that the amygdala is a necessary link in the expression of the septal syndrome. However, their lesions were subtotal and some degree of recovery might be attributable to the remaining intact portions of the amygdala. It would appear from the exploratory studies reported above (Table 5), in which rats with radical amygdaloid lesions were allowed to recover before placing the septal lesions, that the amygdala is in fact nonessential. The dispensability of the amygdala for other forms of rage is shown by the fact that its removal does not seriously or permanently reduce DRs obtained by making DC lesions in the ventromedial hypothalamus (Kling

and Hutt, 1958) or by stimulating the perifornical region (Hunsperger, 1956).

Finally, attention passes to the excitatory networks in and around the septum itself (Hernandez-Peon et al., 1963). It has been noted above that both excitatory and inhibitory effects on DRs have been obtained in the septum and basal telencephalon. Unfortunately, the precise distribution and especially the modes and degrees of interaction between these systems have not been determined physiologically, and it is therefore quite difficult to assess the possibility that lesions in the more inhibitory regions release excitation in nearby DR centers. Contributing further to this problem is the fact that the descending pathways whereby the telencephalon communicates with the lower rage facilitatory effectors are not known. It might be expected that a simple course is followed by the perifornical system through the intermediate hypothalamus into the mesencephalon. On the contrary, Hunsperger (1956) found that interruption of this system in the caudal hypothalamus resulted in an isolated rostral component which continued to yield DRs at low threshold. Until these uncertainties are resolved, an experimental analysis of the possibility that septal release is achieved locally will be problematical.

In sum, it is evident that septal inhibition of defensive behavior is not mediated by the fornix columns and surrounding gray matter, by the habenula, or by the neocortex. There is, furthermore, some reason to doubt that any of the direct septal efferents to the diencephalon are involved. The amygdala, while it may exert a general facilitatory effect on defensive behavior and the mechanisms responsible for the

septal syndrome, does not seem crucial. On the other hand, preliminary evidence is available which indicates that the hippocampus might be the site of septal inhibition. It also seems possible that septal inhibition of defensive behavior may be achieved locally within the septum itself and in subjacent regions.

Cataplexy. The marked cataplexy associated with septal damage has been little studied, and no attempt seems to have been made to determine what relationship may obtain between this phenomenon and others such as "animal hypnosis," "playing 'possum," human catatonia, and bulbocapnine catalepsy. One interesting lead is the finding that in "hypnotized" rabbits the hippocampal theta rhythm is reduced (Silva et al., 1959). It has been reported that this rhythm is paced by cells in the septum, and that it is abolished by septal destruction (Green and Arduini, 1954; Brugge, 1965). Perhaps reduction of the theta activity by septal ablation lowers the threshold for "hypnosis." Recordings from opossums in their characteristic death feint are not significantly different from typical waking activity (Norton et al., 1964). Unfortunately, no electrodes were placed in the hippocampus and theta rhythms were apparently absent from the neocortex. It remains uncertain whether the electrical manifestations of "animal hypnosis" and "playing 'possum" are similar.

Other problems. Although the present experiment was not specifically planned to deal with them, it may be profitable to consider two major issues concerning the septal syndrome. The first of these is the question of "septalness": whether it is destruction of the septal nuclei

proper, or incidental damage to surrounding structures that is responsible for the irritable behavior. Brady and Nauta (1955) weighed the possibility that interruption of the fornix was critical, but Harrison and Lyon (1957) showed that this is not the case. The latter experimenters went on to report that there is no consistent relationship between lesion size and position, and the magnitude of the septal syndrome. Their conclusion was that some unspecified structure outside the septum must be held responsible for the syndrome. The poor relationship between lesions and irritability has also been noted by Thomas et al. (1959). The presence of widespread and probably overlapping facilitatory and inhibitory regions in the telencephalon suggests the slightly different interpretation that for reasons of congenital individual or species differences, and possibly "functional" determinants, parts of the inhibitory system are differentially relied upon in the intact animal. One rat, for example, might develop strong septal inhibition, to the expense of medial preoptic area or olfactory tubercle; conversely, those animals which normally depend on the medial preoptic would exhibit a relatively slight degree of septal irritability. Any formulation of this type must be highly tentative at the present time, but might provide an explanation of how identical appearing lesions produce in some instances quite different degrees of the septal syndrome. The fact that the syndrome can be produced by restricted lesions rather far apart is consistent with the hypothesis of a single, fairly large inhibitory system. Recovery of the syndrome would then be a matter of the remaining parts of the system assuming, partly through a type of learning, the function of the lost

parts. If this is true, then it is predictable that destruction of a large portion of the inhibitory region should result in a septal syndrome which is refractory to habituation. Another factor which may help to account for the results of Harrison and Lyon (1957) is that since the septum includes both excitatory and inhibitory points, both are usually destroyed simultaneously and some degree of balance may be retained by the remaining parts of the septum and basal telencephalon.

The other major question to be discussed is whether the septal syndrome is a manifestation of true emotion, in the full motivational sense, or whether, instead, it is simply a matter of motor release. The latter interpretation is based primarily on the findings of McCleary (1961) and Kaada et al. (1962) concerning passive avoidance deficits. It has already been mentioned that these results may be due to increased approach tendencies (Harvey et al., 1965), and this negative evidence therefore loses much of its force. Several attempts have been made to demonstrate fear enhancement by means of active avoidance training. King (1958), for example, reported that septal rats learn to perform in a shuttle box more rapidly than controls, and concludes that they did so because of greater fear motivation. Krieckhaus et al. (1964) confirmed this finding, but feel that an adequate explanation can be found in the reduction of competing unconditioned responses. Also, animals trained preoperatively to avoid shock lose the response following septal lesions; furthermore, they reacquire active avoidance only with difficulty (Rich and Thompson, 1965). Roberts (1962), in support of his theory that the dorsomedial nucleus of the thalamus is part of the fear mechanism, also

employed active avoidance. In this case, it was stimulation of the dorsomedial nucleus that the animals learned to avoid. However, this demonstration fails to distinguish between the aversive properties of fear and simple pain, and is thus inconclusive.

A straightforward alternative to active avoidance as a measure of increased fear is suggested by the observation that septal rats, if they escape during rating, show a notable tendency to seek a place to hide. Septal rats, if indeed more fearful, might be expected to learn and run a maze with a dark hole as the incentive. While irritable and nonirritable septal rats both learn avoidance more quickly than controls, the latency is significantly less in the animals exhibiting the septal syndrome (Kriekhaus et al., 1964). This difference could be related to the enhanced tendency of the irritable rats to flee. It is somewhat difficult to reconcile observations of this kind with the increased "boldness" of irritable septal rats in leaving their cage to enter an open field, however (Thomas et al., 1959).

At the present time it seems impossible to produce firm answers to questions relating to the nature of the septal syndrome. It is beginning to appear that septal function cannot be so easily characterized in terms of one or a few simple behavioral categories such as thirst, fear, or motor inhibition. With the complex interconnections of the septal region and other structures implicated in the interpretation and responsiveness to threatening situations, allowing for almost unlimited degrees and kinds of interaction, this is perhaps not so surprising.

SUMMARY

Rats with septal, perifornical hypothalamic, and combined septal-perifornical lesions were compared with control animals on a rating scale designed to quantify the septal syndrome. Destruction of the perifornical "affective defense" zone failed to block development of the septal syndrome. Analysis of scores reveals that either septal or perifornical lesions enhanced the rat's tendency to attack an intruding object and to jump when struck on the back. Septal lesions, alone or in the presence of perifornical destruction, increased scores on struggling, biting, and vocalizing in response to capture and handling; perifornical lesions did not have these effects. Also, septal and possibly perifornical lesions heightened susceptibility to cataplexy. It is concluded that the septal syndrome is not mediated by connections with the perifornical region. Other aspects of septal and perifornical function are also considered.

BIBLIOGRAPHY

- Bard, P. A diencephalic mechanism for the expression of rage with special reference to the sympathetic nervous system. Amer. J. Physiol., 1928, 84, 490-515.
- Bard, P., and Macht, M. B. The behavior of chronically decerebrate cats. In Wolstenholme, G. E. W., and O'Connor, C. M. (Eds.), CIBA Foundation symposium on the neurological basis of behavior. Boston: Little, Brown, 1958.
- Bard, P., and Mountcastle, V. B. Some forebrain mechanisms involved in the expression of rage with special reference to suppression of angry behavior. Res. Publ. Assoc. Nerv. Ment. Dis., 1947, 27, 362-404.
- Brady, J. V., and Nauta, W. J. H. Subcortical mechanisms in emotional behavior: affective changes following septal forebrain lesions in the albino rat. J. comp. physiol. Psychol., 1953, 46, 339-346.
- Brady, J. V., and Nauta, W. J. H. Subcortical mechanisms in emotional behavior: the duration of affective changes following septal and habenular lesions in the albino rat. J. comp. physiol. Psychol., 1955, 48, 412-420.
- Brierley, J. B., and Beck, E. The effects upon behavior of lesions in the dorsomedial and anterior thalamic nuclei of cat and monkey. In Wolstenholme, G. E. W., and O'Connor, C. M. (Eds.), CIBA Foundation symposium on the neurological basis of behavior. Boston: Little, Brown, 1958.
- Brown, J. L., and Hunsperger, R. W. Neurothology and the motivation of agonistic behavior. Animal Behav., 1963, 11, 439-448.
- Brugge, J. F. An electrographic study of the hippocampus and neocortex in unrestrained rats following septal lesions. EEG clin. Neurophysiol., 1965, 18, 36-44.
- De Groot, J. The rat forebrain in stereotaxic coordinates. N. V. Noord-Hollandsche Uitgevers Maatschappij, Amsterdam, 1959.
- Ellen, P., Wilson, A. S., and Powell, E. W. Septal inhibition and timing behavior in the rat. Exp. Neurol., 1964, 10, 120-132.

- Fernandez de Molina, A., and Hunsperger, R. W. Central representation of affective reactions in forebrain and brain stem: electrical stimulation of amygdala, stria terminalis, and adjacent structures. J. Physiol., 1959, 145, 251-265.
- Forman, D., and Ward, J. W. Responses to electrical stimulation of caudate nucleus in cats in chronic experiments. J. Neurophysiol., 1957, 20, 230-244.
- Fox, S. S., Kimble, D. P., and Lickey, M. E. Comparison of caudate nucleus and septal-area lesions on two types of avoidance behavior. J. comp. physiol. Psychol., 1964, 58, 380-386.
- Fulton, J. F., and Ingraham, F. O. Emotional disturbances following experimental lesions of the base of the brain (pre-chiasmal). Amer. J. Physiol., 1929, 90, 353.
- Galeano, C., Roig, J. A., and Sommer-Smith, J. A. Conditioning of subcortical telencephalic stimulation effects. EEG clin. Neurophysiol., 1964, 17, 281-293.
- Gellhorn, E., and Loofbourrow, G. N. Emotions and emotional disorders. New York: Hoeber, 1963.
- Goddard, G. V. Functions of the amygdala. Psychol. Bull., 1964, 62, 89-109.
- Green, J. D., and Arduini, A. Hippocampal electrical activity in arousal. J. Neurophysiol., 1954, 17, 533-557.
- Green, J. D., Clemente, C. D., and de Groot, J. Rhinencephalic lesions and behavior in cats. J. comp. Neurol., 1957, 108, 505-536.
- Hall, C. S. Emotional behavior in the rat. I. Defecation and urination as measures of individual differences in emotionality. J. comp. Psychol., 1934, 18, 385-403.
- Harrison, J. M., and Lyon, M. The role of the septal nuclei and components of the fornix in the behavior of the rat. J. comp. Neurol., 1957, 108, 121-137.
- Harvey, J. A., Jacobsen, L. E., and Hunt, H. F. Long-term effects of lesions in the septal forebrain on acquisition and retention of conditioned fear. Amer. Psychologist, 1961, 16, 449.
- Harvey, J. A., and Hunt, H. F. Effect of septal lesions on thirst in the rat as indicated by water consumption and operant responding for water reward. J. comp. physiol. Psychol., 1965, 59, 49-56.

- Harvey, J. A., Lints, C. E., Jacobson, L. E., and Hunt, H. F. Effects of lesions in the septal area on conditioned fear and discriminated instrumental punishment in the albino rat. J. comp. physiol. Psychol., 1965, 59, 37-48.
- Hernandez-Peon, R., Chavez-Ibarra, G., Morgane, P. J., and Timo-Iaria, C. Limbic cholinergic pathways involved in sleep and emotional behavior. Exp. Neurol., 1963, 8, 93-111.
- Hess, W. R. Diencephalon: autonomic and extrapyramidal functions. New York: Grune and Stratton, 1954.
- Hunsperger, R. W. Affektreaktionen auf elektrische Reizung im Hirnstamm der Katze. Helv. Physiol. Acta., 1956, 14, 70-92.
- Kaada, B. R., Rasmussen, E. W., and Kveim, O. Impaired acquisition of passive avoidance behavior by subcallosal, septal, hypothalamic, and insular lesions in rats. J. comp. physiol. Psychol., 1962, 55, 661-670.
- King, F. A. Effects of septal and amygdaloid lesions on emotional behavior and conditioned avoidance responses in the rat. J. nerv. ment. Dis., 1958, 126, 57-63.
- King, F. A. Relationship of the "septal syndrome" to genetic differences in emotionality in the rat. Psychol. Rep., 1959, 5, 11-17.
- King, F. A., and Meyer, Patricia M. Effects of amygdaloid lesions upon septal hyperemotionality in the rat. Science, 1958, 128, 655-656.
- Kling, A., and Hutt, P. J. Effect of hypothalamic lesions on the amygdala syndrome in the cat. Arch. Neurol. Psychiat., 1958, 79, 511-517.
- Krieckhaus, E. E., Simmons, H. J., Thomas, G. J., and Kenyon, J. Septal lesions enhance shock avoidance behavior in the rat. Exp. Neurol., 1964, 2, 107-113.
- Larsson, K., and Heimer, L. Mating behavior of male rats after lesions in the preoptic area. Nature, 1964, 202, 413-414.
- Maire, F. W., and Patton, H. D. Neural structures involved in the genesis of "preoptic pulmonary edema," gastric erosions and behavior changes. Amer. J. Physiol., 1956, 184, 345-350.
- McCleary, R. A. Response specificity in the behavioral effects of limbic system lesions in the cat. J. comp. physiol. Psychol., 1961, 54, 605-613.

- MacLean, P. D. Some psychiatric implications of physiological studies on fronto-temporal portion of limbic system (visceral brain). EEG clin. Neurophysiol., 1952, 4, 407-418.
- Moore, R. Y. "Rage" as a consequence of ablation of the septal nuclei in cats. Amer. Psychologist, 1960, 15, 483 (Abstract).
- Moore, R. Y. Effects of some rhinencephalic lesions on retention of conditioned avoidance behavior in cats. J. comp. physiol. Psychol., 1964, 57, 65-71.
- Munn, N. L. Handbook of psychological research on the rat. Boston: Houghton Mifflin, 1950.
- Nauta, W. J. H. Hypothalamic regulation of sleep in rats. An experimental study. J. Neurophysiol., 1946, 9, 285-316.
- Nauta, W. J. H. An experimental study of the fornix system in the rat. J. comp. Neurol., 1956, 104, 247-271.
- Norton, A. C., Beran, A. V., and Misrahy, G. A. Electroencephalograph during "feigned" sleep in the opossum. Nature, 1964, 204, 162-163.
- Olds, J. Physiological mechanisms of reward. In Jones, M. R. (Ed.), Nebraska symposium on motivation, III, 1955.
- Papez, J. W. A proposed mechanism of emotion. Arch. Neurol. Psychiat., 1937, 38, 725-743.
- Powell, E. W. Septal efferents revealed by axonal degeneration in the rat. Exp. Neurol., 1963, 8, 406-422.
- Reynolds, R. W. Ventromedial hypothalamic lesions without hyperphagia. Amer. J. Physiol., 1963, 204, 60-62.
- Rich, Irene, and Thompson, R. Role of the hippocampo-septal system, thalamus, and hypothalamus in avoidance conditioning. J. comp. physiol. Psychol., 1965, 59, 66-72.
- Roberts, W. W. Fear-like behavior elicited from dorsomedial nucleus of cat. J. comp. physiol. Psychol., 1962, 55, 191-197.
- Rothfield, L., and Harman, P. J. On the relation of the hippocampal-fornix system to the control of rage responses in cats. J. comp. Neurol., 1954, 101, 265-282.
- Schreiner, L., and Kling, A. Behavioral changes following rhinencephalic injury in the cat. J. Neurophysiol., 1953, 16, 643-659.

- Schwartzbaum, J. S., Kellicutt, M. H., Spieth, T. M., and Thompson, J. B. Effects of septal lesions in rats on response inhibition associated with food-reinforced behavior. J. comp. physiol. Psychol., 1964, 58, 217-224.
- Silva, E. E., Estable, C., and Segundo, J. P. Further observations on animal hypnosis. Arch. Ital. Biol., 1959, 97, 167-177.
- Spiegel, E. A., Miller, H. R., and Oppenheimer, M. J. Forebrain and rage reactions. J. Neurophysiol., 1940, 3, 538-548.
- Spiegel, E. A., and Wycis, H. T. Stereoccephalotomy. II. clinical and physiological applications. New York: Grune and Stratton, 1962.
- Stewart, Jean W., and Ades, H. W. The time factor in reintegration of a learned habit lost after temporal lobe lesions in the monkey (*Macaca mulatta*). J. comp. physiol. Psychol., 1951, 44, 479-486.
- Teitelbaum, P., and Cyta, J. Spreading depression and recovery from lateral hypothalamic damage. Science, 1965, 147, 61-63.
- Thomas, G. J., Moore, R. Y., Harvey, J. A., and Hunt, H. F. Relations between the behavioral syndrome produced by lesions in the septal region of the forebrain and maze learning in the rat. J. comp. physiol. Psychol., 1959, 52, 527-532.
- Valverde, F. Studies on the forebrain of the mouse. Golgi observations. J. Anat., Lond., 1963, 97, 157-180.
- Vanderwolf, C. H. The effect of medial thalamic lesions on previously established fear-motivated behaviour. Canad. J. Psychol., 1963, 17, 183-187.
- Wheatley, M. D. The hypothalamus and affective behavior in cats. Arch. Neurol. Psychiat., 1944, 52, 296-316.
- Yutzy, D. A., Meyer, Patricia M., and Meyer, D. R. Emotionality changes following septal and neocortical ablations in rats. J. comp. physiol. Psychol., 1964, 58, 463-465.
- Zbrozyna, A. W. Defense reactions from the amygdala and stria terminalis. J. Physiol., 1960, 153, 27-28P.
- Zeman, W., and King, F. A. Tumors of the septum pellucidum and adjacent structures with abnormal affective behavior: an anterior midline structure syndrome. J. nerv. ment. Dis., 1958, 127, 490-502.

APPENDIX A

SEVEN RATING SCALES FOR THE STUDY OF EMOTIONALITY

I. REACTION TO OBJECT PRESENTATION: Pencil is presented close to animal's snout.

- 0 - Rat ignores pencil
- 1 - Rat alert and attentive, some body tenseness
- 2 - Legs and body tense and immobile, vibrissae point forward
- 3 - Scurries away or makes an occasional mild biting attack on pencil
- 4 - Intermediate
- 5 - Very aggressive attack, disorganized panic, or violent flight

II. RESPONSE TO TAP ON BACK

- 0 - No reaction
- 1 - Twitching or restlessness
- 2 - Twitching or scurrying away
- 3 - Jumps or hops up a bit, but then settles down
- 4 - Leaps in air and runs about in fright. Big hop and movement after
- 5 - Leaps violently, dashes off in panic, frantic rebounding from side to side of cage

III. RESISTANCE TO CAPTURE: Glove is extended forward to animal slowly and rat is grasped firmly but not roughly.

- 0 - Remains calm, does not move when approached, does not struggle when grasped
- 1 - Remains calm when approached, but scurries away and tugs a bit when grasped
- 2 - Retreat and moderate struggle
- 3 - Retreats when approached, struggles vigorously when grasped
- 4 - Strong attempt to escape when approached, struggles strongly and is disorganized. Some biting
- 5 - Leaps violently when grasped, bites frantically, exceedingly difficult to catch

APPENDIX A (CONTINUED)

IV. RESISTANCE TO HANDLING: Animal passed from hand to hand for about 30 seconds.

- 0 - Relaxes in hand, does not attempt to escape
- 1 - Restless with some feeble squirming
- 2 - Sporadic attempts to pull out of hand
- 3 - Struggles pretty continuously and quite vigorous in attempt to escape
- 4 - Bites also
- 5 - Frantic biting, powerful tugging and disorganized twisting

V. VOCALIZATION TO CAPTURE AND HANDLING

- 0 - None
- 1 - Few squeaks
- 2 - Frequent squeaking
- 3 - Frequent squealing-squawking
- 4 - Squealing continuous
- 5 - Frantic and loud screeching continued

VI. URINATION AND DEFECATION IN REACTION TO HANDLING

- 0 - None
- 1 - Slight urination
- 2 - Few stools

VII. CATAPLEXY: Animal is held in the left hand by the hindquarters. With the right hand the rat is restrained in a supine position for about 5-10 seconds, then released.

- 0 - Animal sits up or struggles as soon as released
- 1 - Rights or struggles after release, but with a brief latency
- 2 - Longer latency
- 3 - Remains supine indefinitely (at least 30 seconds) and exhibits a marked tendency to bob up and down with respiratory movements.

APPENDIX B

Total Scores for Individual Rats throughout Period of Testing

Rat	Day												
	Preop		Postop										
	4	5	1	2	3	4	5	6	7	8	9	10	11
<u>Control</u>													
D38B	5½	3½	2½	3½	4	T							
D39B	3½	5½	2½	1	1½	T							
D42B	2	½	1	0	T								
D62B	8½	8	5	4	4½	T							
D68B	4½	2	5½	1½	T								
D75B	3½	3	6	4	T								
<u>Perifornical</u>													
D24B	5½	5½	9 ^b	7 ^{ab}	1½ ^{ab}	X							
D28B	3½	2	9	17	6½	P							
D32B	1½	1½	7 ^b	6 ^{ab}	X								
D33B	5	4½	7½	X									
D43B	3	6½	12½	16	X								
D53B	4½	5	8½	6	X								
D59B	3½	4½	7 ^a	2 ^{ab}	X								
D60B	4	3	4½	2½	3½	P							
D67B	1½	2	11 ^a	9 ^e	7	8½	8½	11½	8	P			
D71B	2½	2½	8	6	P								
D78B	2½	6	13½	13½ ^f	5½	X							

APPENDIX B (CONTINUED)

Rat	Preop		Postop		Day								
	4	5	1	2	3	4	5	6	7	8	9	10	11
<u>Septal-perifornical</u>													
D23B	2	2½	10	9	6	P							
D34B	4	0	21	9	13½	6½	P						
D34B	2½	1½	13	X									
D44B	1½	2	5½ ^a	X									
D45B	4	5	18½	8 ^a									
D49B	1	1	8	X									
D52B	6	5	19½	17									
D56B	2½	4	14½	11									
D57B	4	2	14	16½ ^a	P								
D58B	2	3	19 ^{ac}	16½ ^{ac}	14½ ^{ac}	9 ^{ac}	13½ ^{ac}	10 ^{ac}	X				
D61B	4½	5½	16½	12	13	13	14	11	11½	9	8		
D65B	2	2	4½ ^a										
D69B	2	5½	12½	I	12½	8½	X						
D72B	3½	2½	11	X									
D73B	5	3½	10	X									
<u>Septal</u>													
D62B	4	4	16½	3	1								
D31B	5½	3½	13	6½	1½								
D37B	3	3	10	1	1½								
D40B	3	1	21½	15	9½								

APPENDIX B (CONTINUED)

Rat	Preop		Postop		Day								
	4	5	1	2	3	4	5	6	7	8	9	10	11
<u>Septal</u> (Continued)													
D47B	0	1	19½	10									
D48B	3	5	18½	15½									
D50B	6	5	6½	7									
D51B	4½	1½	10	8									
D55B	3	3½	8½	5½									
D63B	3½	3½	4	1½	1								
D64B	8	6	11½	3	2½	1½							
D66B	4½	1½	21	15½	11½	12½	7	4½	1	1			
D70B	2½	2	18	15	15	11½	13½	9	4½	5			
D74B	2	4½	20	16½	14½ ^d	P							

Note: X signifies death of rat; T, termination of rating; P, rat perfused; I, rat immobile, could not be rated.

^aSomnolent

^dWeakness and respiratory infection

^bNasal discharge

^eMore alert

^cAtaxic

^fNo somnolence

BIOGRAPHICAL SKETCH

John Edward Swisher was born January 8, 1932, at Jacksonville, Florida. In June, 1949, he was graduated from Landon High School. From September, 1949, to October, 1952, he attended Vanderbilt and Stetson Universities. He served as an aviator with the United States Navy from 1953 through 1956. In the spring of 1957 he reentered Stetson University and there received the degree Bachelor of Science in June, 1958. From September of that year through 1962 he was enrolled in the Graduate School of the University of Florida, where he received the degree Master of Science in June, 1961. Mr. Swisher was employed as an Assistant Professor of Psychology at the University of Miami from February, 1963, to June, 1965.

This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of that committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council, and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August 14, 1965

Ernest H. Cox
Dean, College of Arts and Sciences

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