EFFECTS OF KINDLING OR SUB-THRESHOLD STIMULATION ON AGGRESSION

THE EFFECTS OF BILATERAL KINDLING OR BILATERAL SUB-THRESHOLD STIMULATION OF THE AMYGDALA OR SEPTUM ON MURICIDE, RANACIDE INTRASPECIFIC AGGRESSION AND PASSIVE AVOIDANCE IN THE RAT

By

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A Thesis

Submitted to the School of Graduate Studies

in Partial Fulfilment of the Requirements

for the Degree

Master of Arts

McMaster University

May, 1978

MASTER OF ARTS (1978) McMASTER UNIVERSITY
(Psychology) Hamilton, Ontario

TITLE: The Effects of Bilateral Kindling or Bilateral Sub-threshold Stimulation of the Amygdala or Septum on Muricide, Ranacide, Intraspecific Aggression and Passive Avoidance in the Rat

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NUMBER OF PAGES: v, 45

Abstract

No differences were found between muricidal and non-muricidal or between ranacidal and non-ranacidal hooded rats in septal or amygdaloid after-discharge thresholds. Bilateral kindling or bilateral sub-threshold stimulation of the amygdala or septum did not induce or inhibit muricide or ranacide or facilitate intraspecific aggression. Bilateral kindling of the amygdala or septum tended to impair performance on a passive avoidance task but sub-threshold stimulation of these regions did not.

Acknowledgements

I wish to thank Dr. Ron Racine for his encouragement and critical reading of the thesis, and Drs. B.G. Galef and A.H. Black for reviewing the thesis.

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General Introduction

The Kindling Phenomenon

Repeated electrical stimulation of discrete brain sites can result in the progressive development of behavioral convulsions. This phenomenon has been termed kindling by Goddard, McIntyre and Leech (1969). Initially, low intensity stimulation may have little effect, but after several applications distributed over time, a number of electrographic and behavioral changes occur. On subsequent trials, stimulation consistently evokes an after-discharge (AD), reflecting a local reduction in the AD threshold (Racine, 1972a; Tress and Herberg, 1972). Increases in the frequency, duration and amplitude of the AD develop with further stimulation, and the AD propagates to additional brain structures (Racine, 1972b). As a result of triggering ADs, motor seizures progressively develop through a number of stages culminating in a generalized convulsion characterized by bilateral forelimb clonus, rearing and falling (Racine, 1972b). If the stimulation regimen is continued, it eventually results in the production of spontaneously recurrent seizures (Pinel, Mucha and Phillips, 1975; Pinel and Rovner, 1978; Wada, Sato and Corcoran, 1974). Goddard, McIntyre and Leech (1969) have shown that the kindling effect is not due to tissue destruction, edema, gliosis or the deposition of toxic metallic ions but results from the electrical activation of neurons.

Goddard, McIntyre and Leech (1969) examined the effects of varying the interstimulation interval on the number of stimulations required to

produce a generalized convulsion. They found that the duration of the intertrial interval was inversely related to the number of stimulations required to kindle the amygdala. Unfortunately, Goddard, McIntyre and Leech (1969) did not record AD activity and some of their stimulations may not have triggered ADs. Racine et al. (1973) also found that more stimulations were required to fully kindle rats when short interstimulation intervals (less than one hour) were used. But Racine et al. (1973) reported no significant differences in the rate of motor seizure development with intertrial intervals of one hour, two hours or 24 hours.

Evidence from several experiments suggests that kindling produces widespread neural changes. Repeated stimulation of one brain site increases the seizure susceptibility of other brain sites (Goddard, McIntyre and Leech, 1969). For example, if repeated unilateral stimulation is applied to the amygdala until convulsions are elicited, then fewer ADs are needed to elicit motor seizures in the contralateral amygdala (Goddard, McIntyre and Leech, 1969; Racine, 1972b). This positive transfer effect occurs even after removal of the primary site of stimulation (Racine, 1972b).

Racine, Gartner and Burnham (1972) have shown that these transsynaptic changes are not restricted to seizure activity per se. They reported an increase, following convulsion development, in the amplitude of potentials evoked in the hippocampus, preoptic area and the ventromedial nucleus of the hypothalamus by brief pulses presented to the amygdala. Goddard and Douglas (1975) and Racine, Tuff and Zaide (1975) have obtained similar results in monosynaptic model systems. These results suggest that the kindling effect is at least partly due to an increase in

synaptic connectivity.

Kindling produces neural changes which are not only widespread but very long-lasting. Goddard, McIntyre and Leech (1969) found a considerable reduction in the number of stimulations required to elicit a convulsion after allowing their kindled animals a 12-week stimulation-free rest period. In fact, convulsions were usually elicited on the first trial. The reduction in AD threshold is also permanent (Racine, 1972a; Tress and Herberg, 1972).

Goddard, McIntyre and Leech (1969) were the first to point out the relevance of kindling to learning. The kindling model has many properties which are consistent with the hypothesis that kindling and engram formation are related phenomena (see Goddard and Douglas, 1975; Racine and Zaide, 1978). Although kindling may be a useful model of learning, there have been few attempts to demonstrate changes in behavior resulting from the kindling treatment.

Kindled animals do not exhibit any obvious behavioral disturbances. Thus, the long-term changes in behavior that have been detected were evident only when the appropriate tests were used. McIntyre and Molino (1972) found that rats with either bilateral lesions of the amygdala or a unilateral lesion and a contralateral kindled focus were severely retarded in acquiring a conditioned emotional response (CER). Also, the establishment of bilateral, but not unilateral, kindled foci in the amygdala impaired performance on a one-trial passive avoidance task (Boast and McIntyre, 1977).

Convulsion development and long-lasting behavioral alterations can

also be produced by chemical stimulation of the brain. Grossman (1963) found that a single bilateral administration of a minute quantity of carbachol (0.1 to 2.0 µg) to the seizure-prone basolateral amygdala of cats produced pronounced affective changes and spontaneously recurrent seizures. The cats became hyperreactive and they attacked the experimenter and other cats without provocation. These behavioral changes and the concomitant abnormal electrical activity persisted throughout the five month observation period. In addition, repeated application of carbachol to the amygdala, hippocampus or caudate nucleus in rats elicited a pattern of seizure development similar to the one produced by repeated electrical stimulation of these structures (Vosu and Wise, 1975).

Belluzzi and Grossman (1969) and Goddard (1969) have shown that bilateral injections of carbachol into the amygdala of rats produced seizures, but the overt behavioral and electrographic effects disappeared within a few hours. However, the impairments in active avoidance, passive avoidance and CER learning lasted for several weeks after the convulsions had subsided.

Although the treatments described above all produced some form of motor seizure, Adamec (1975) has shown that the elicitation of convulsions is not necessary for the production of behavioral changes. Adamec examined the defensive and predatory behavior of partially kindled cats; convulsions were not developed in these animals although some after-discharges were elicited. Rat-killing cats had higher AD thresholds in the basolateral nucleus of the amygdala than non-rat-killing cats. These differences in threshold do not reflect a general difference in brain excitability, since

no differences were found in the white matter, lateral to the amygdala, or in the ventral hippocampus.

Adamec then lowered the AD thresholds in the basolateral amygdala of rat-killing cats by repeatedly applying sub-threshold electrical stimulation. This procedure inhibited rat killing and increased the cats' defensive responses to rats and to tape recorded 'threat howls' of an adult male cat. These changes lasted for as long as the cats were kept alive, which, in some cases, was three months.

The purpose of this thesis is to extend the findings of Adamec (1975) by investigating the effects of kindling selected limbic sites on aggressive behavior and passive avoidance in the rat. A limited review of the neurological substrates of aggressive behavior is provided below.

Role of the Amygdala and Septum in Aggression

Amygdala

Aggressive behavior and defensive reactions to noxious stimulation are facilitated by the amygdala. The cortical nucleus and piriform cortex facilitate intraspecific aggression, the central and lateral nuclei facilitate pain-elicited defensive reactions, and the centromedial region facilitates muricide. The activity of this latter region may be modulated by the medial amygdaloid nucleus which apparently plays a role in the inhibition of muricide.

Lesion-Induced Changes in Emotionality

Several experiments, using a variety of species, have shown that bilateral lesions of the amygdaloid nuclei result in placidity (see Clemente

and Chase, 1973; Goddard, 1964; and Richardson, 1973 for reviews). These studies have usually found that the placidity is evident immediately after the operation and is long-lasting. Amygdalectomized animals show reduced fear reactions to threatening stimuli. Normally, rats freeze when exposed to an immobile cat, even on their first exposure (Blanchard and Blanchard, 1971). But rats with bilateral lesions of the amygdala approached and even climbed onto the back of an immobile cat (Blanchard and Blanchard, 1972).

Shock-Elicited Defensive Behavior

Rats with lesions of the amygdala are less likely than normal rats to exhibit pain-elicited defensive reactions. Normal rats subjected to footshock reliably exhibit stereotyped upright postures and lunging movements with the forelimbs. This behavior is often characterized as pain-elicited aggression or reflexive fighting (e.g. Ulrich and Azrin, 1962). However, it appears that this behavior may be more accurately described as defensive, rather than aggressive. Scott (1966) suggested that the shocked rats exhibit defensive reactions towards the perceived source of pain, the other rat. Blanchard et al. (1977b) have shown that the boxing posture is a defensive strategy and have postulated that the forepaw blows are pain-elicited reflexive jerks (Blanchard and Blanchard, 1977). In fact, they have been able to elicit these forepaw movements in the absence of other rats (Blanchard et al., 1977a).

Removal of the piriform cortex or cortical nucleus of the amygdala had little effect on shock-elicited defensive reactions (Miczek et al., 1974; Vergnes, 1976), but damage to the central or lateral nuclei reduced

shock-elicited defensive responding (Miczek et al., 1974; Vergnes, 1976). It has also been reported that complete amygdalectomy inhibited pain-elicited defensive responding (Allikmets and Ditrikh, 1965; Eichelman, 1971), although there has been one negative report (Finch et al., 1968). Destruction of the amygdala did not alter the rats' sensitivity to foot-shock (Eichelman, 1971).

Intraspecific Aggression

The effects of amygdala lesions on intraspecific aggression have been studied with the use of the tube paradigm. Briefly, food-deprived rats are trained to run through a narrow tube for food reinforcement until their running speeds are stabilized. Two rats matched for weight and running speed are then placed at opposite ends of the apparatus and eventually one animal will be forced back into the compartment in which it started. Vicious fighting then occurs that is similar in form to that seen in feral rats and dominance can be assessed from these aggressive interactions.

Miczek et al. (1974) found that removal of the central or lateral nuclei did not alter the frequency of aggressive behavior or the dominance/submission relationships. But bilateral removal of the piriform cortex, the adjacent transitional zone and the cortical nucleus completely abolished aggressive behavior. Previously dominant rats suffered defeats and exhibited on-the-back postures during post-operative testing.

These results suggest that the piriform cortex and the cortical nucleus are part of a neural circuit that facilitates intraspecific aggression in the rat (Miczek et al., 1974). However, these structures do

not appear to be involved in the regulation of pain-elicited defensive reactions.

Muricide

Total destruction of the amygdala (Galef, 1970; Karli, 1956) or less extensive lesions confined to the central nucleus, the dorsal part of the medial nucleus and the basomedial nucleus inhibited muricide (Horovitz et al., 1966; Karli and Vergnes, 1965) in wild and domesticated rats. Karli et al. (1972) have suggested that the amount of destruction of the central nucleus is the critical factor in determining the effectiveness of the lesion. Miczek et al. (1974) have reported, however, that lesions of the central nucleus did not alter mouse-killing behavior. Removal of the lateral nucleus had no effect on muricidal behavior (Karli et al., 1972; Miczek et al., 1974; Vergnes, 1976). Therefore, it appears that the amygdala facilitates muricide.

But the amygdala is also involved in the inhibition of muricide. Bilateral lesions of the medial nucleus did not induce muricide unless they were preceded by a period of food deprivation (Vergnes, 1975). Eighty-eight percent of the lesioned rats started to kill mice following food deprivation, whereas only 16 percent of the control animals did so. In addition, the percentage of rats that started to kill mice as a result of septal lesions was significantly increased by prior lesions of the medial amygdaloid nucleus (Penot and Vergnes, 1976). Thus, it appears that the medial nucleus plays a role in the inhibition of muricide, possibly by modulating the facilitatory centromedial region (Karli et al., 1972).

Electrical stimulation of the amygdala never results in the facilitation of mouse-killing. Stimulation of the amygdala either had no effect or resulted in a stimulus-bound inhibition of killing (Karli et al., 1972). Vergnes and Karli (1969) found that stimulation which interfered with the release of the killing response also produced paroxysmal activity in the ipsilateral hypothalamus. Electrical stimulation of the amygdala may disrupt normal patterned activity and thus inhibit muricide (Karli et al., 1972).

In summary, destruction of the amygdala produces a tame and placid animal. Removal of the centromedial region inhibits muricide, destruction of the cortical nucleus and the piriform cortex reduces intraspecific aggressive behavior and removal of the central or lateral nuclei inhibits pain-elicited defensive responding. But the amygdala is only part of an anatomically complex system which controls emotional and aggressive behavior.

Septum

The septum also facilitates the expression of intraspecific aggression but inhibits pain-elicited defensive reactions. It has been reported that removal of the septum induces muricide but there are also negative reports in the literature.

Lesion-Induced Changes in Emotionality

Lesions of the septum produced 'rage' reactions and hyperemotionality in rats (e.g. Brady and Nauta, 1953; 1955; for a review see Fried, 1973). Septal rats were hyperreactive; they attacked objects thrust towards them, vigorously resisted handling and exhibited exaggerated startle reactions.

The increased reactivity appeared immediately after the operation but disappeared within two to four weeks. But time was not the only factor which diminished the effects of the lesions; daily post-operative handling also attenuated septal hyperreactivity (Brady and Nauta, 1953). In addition, Fried (1969) and Harrison and Lyon (1957) have reported that extensive pre-operative handling considerably reduced the percentage of rats that exhibited septal irritability.

Although the increase in reactivity has been attributed to damage in the dorsal anterior septal nuclei (Schnurr, 1972), the bed nucleus of the stria terminalis (Turner, 1970) and additional structures such as the diagonal band of Broca and the nucleus accumbens lying ventral to the septal nuclei (Thomas and Van Atta, 1972), a thorough study by Albert and Richmond (1975) confirmed reports of increased reactivity following lesions in or ventral to the septum. Lesions which destroyed the septal nuclei bilaterally or the stria terminalis as well as the septal nucleus produced a significant increase in reactivity. Lesions confined to the bed nucleus of the stria terminalis also caused a significant increase in reactivity but this increase was not as great as that produced by damage ventral to the anterior septum. Removal of the septum and the area ventral to the anterior septum produced the most hyperreactive rats. These results suggest that damage to areas in and around the septum can result in hyperreactivity.

Shock-Elicited Defensive Behavior

It appears that the septum inhibits pain-elicited defensive reactions. Shock-elicited defensive reactions occurred more frequently in

rats with septal lesions than in normals, even after the irritability had subsided (Ahmad and Harvey, 1968; Miczek and Grossman, 1972; Wetzel et al., 1967). Since shock-elicited defensive responding was more intense when the rats were irritable, septal irritability could have altered the qualitative nature of the behavior without altering the probability of its occurrence (Ahmad and Harvey, 1968).

Septal lesions also increased the rats' sensitivity to footshock, as measured by the flinch-jump technique (Lints and Harvey, 1969). This increase in sensitivity to electric shock could still be demonstrated 48 days post-operatively and therefore may not be related to the expression of septal irritability. Also, the increased frequency of responding exhibited by septal rats is probably not related to the shock being a more painful stimulus, since lesions of the dorsomedial tegmentum or the hippocampus, which also increased the rats' sensitivity to footshock, did not alter the level of shock-elicited defensive behavior (Ahmad and Harvey, 1968; Eichelman, 1971).

Intraspecific Aggression

Several experiments have examined the effects of septal lesions on intraspecific fighting. Using food competition tasks, Miczek and Grossman (1972) and Lau and Miczek (1977) found that pre-operatively dominant rats became submissive and showed a temporary reduction in the number of physical attacks following removal of the septum. These changes were reversible; rats which did not fight five days after surgery showed pre-operative levels of aggression and dominance when retested 15 days after surgery. Septal destruction did not alter the frequency or duration of

lateral attacks, defensive upright postures or mutual upright postures in either experienced dominant or subordinate animals. Blanchard et al. (1977) reported that septal damage produced a significant decrease in attack behaviors, including lateral attack, in dominant colony males. These results suggest that septal animals are less aggressive than normal rats towards members of their own species.

Muricide

Destruction of the septal nuclei did not inhibit attacks directed towards mice; mouse-killing rats continued to kill after septal ablation (Miley and Baenninger, 1972). In fact, the opposite may be true. Miczek and Grossman (1972) found that septal lesions induced muricide if the first post-operative test was given within ten days. But extensive pre-operative experience with mice reduced the percentage of rats that started to kill as a consequence of septal ablation (Miley and Baenninger, 1972; Penot and Vergnes, 1976). In addition, there is a strain-lesion interaction. Long-Evans rats showed a greater propensity to kill mice than Sprague-Dawley rats following removal of the septum (Latham and Thorne, 1974).

The topography of the muricidal behavior of animals with septal lesions was different from the stereotyped behavior of normal mouse-killers. Normal killer rats held the mouse down with their forepaws and delivered a bite to the nape of the neck severing the spinal cord. Septal rats indiscriminately bit any region of the mouse and continued to attack following the death of the mouse (Latham and Thorne, 1974; Miczek and Grossman, 1972; Miley and Baenninger, 1972). Since the

topography of the killing response was drastically altered by removal of the septum, septal lesions may produce an increase in septal irritability rather than predatory aggression.

Karli et al. (1969), Malick (1970) and Yamamoto and Ueki (1977), on the other hand, reported that septal lesions did not induce muricide. In fact, Malick tested his naive (with respect to mice) Long-Evans rats well within the time limits suggested by Miczek and Grossman (1972). However, Malick used a relatively short (5 min) test period and different results might have been obtained if a longer test period was used.

In summary, septal damage temporarily produces hyperreactive rats that readily exhibit pain-elicited defensive reactions. But removal of the septum reduces the number of attacks on other adult rats and possibly induces muricide.

Introduction

In the cat, the basolateral nucleus of the amygdala tonically inhibits predatory behavior (Egger and Flynn, 1967) and facilitates defensive behavior (Kaada, 1972; Zbrozyna, 1972). Adamec (1975) found that AD threshold reduction in the basolateral nucleus inhibited rat killing and increased cats' defensiveness towards threatening stimuli. Adamec suggested that modification of epileptic excitability by repeated stimulation is a useful model of neurobehavioral plasticity.

Evidence reviewed in the General Introduction suggests that, in the rat, the amygdala and septum facilitate intraspecific aggression, that the centromedial region of the amygdala facilitates muricide and that the

septum possibly inhibits muricide. The purpose of this thesis, then, is to extend the findings of Adamec (1975) by examining the effects of kindling or repeated sub-threshold stimulation of the amygdala or septum on inter-specific aggression, intraspecific aggression and passive avoidance in the rat.

Method

Subjects

One hundred and eleven male hooded rats and 84 male albino Wistar rats were obtained from Canadian Breeding Farms, St. Constant, Quebec. The hooded rats served as the experimental subjects and the albino rats were used as opponents in the intraspecific aggression test. The hooded rats weighed 325 to 425 g at the time of surgery. The animals were housed individually in standard wire cages, with Purina rat chow and water continuously available.

Male CF1 (Outbred Albino) mice, weighing approximately 20 g, and leopard frogs (Rana pipiens) were used as prey. The mice were obtained from Canadian Breeding Farms. Groups of 5 mice were housed in plastic cages in a room isolated from the rat colony. All mice were allowed free access to food and water. The frogs were purchased from a commercial bait dealer and were communally housed in an aquarium.

Surgical and Histological Techniques

Subjects were anesthetized with sodium pentobarbital (50 mg/kg). Two bipolar electrodes, made with 0.25 mm nichrome wires insulated with isonel, were implanted bilaterally in either the amygdala or septum. The

electrodes were positioned using the following co-ordinates obtained from Pellegrino and Cushman (1967): amygdala: A.P. 1.0 mm posterior to Bregma, M.L. 5.0 mm lateral to midline, D.V. 8.5 mm below the surface of the skull; septal: A.P. 2.0 mm anterior to Bregma, M.L. 0.5 mm lateral to midline, D.V. 5.5 mm below the surface of the skull. A stainless steel jeweller's screw, attached to a male Amphenol pin, was inserted into the skull and used as the ground electrode. At the conclusion of the operation, each subject was injected intramuscularly with 15,000 units of penicillin.

When the experiment was completed, the rats were administered an overdose of sodium pentobarbital and then perfused with physiological saline followed by 10% formalin in physiological saline. After three days of storage in formol-saline, the brains were frozen and sectioned. Sections (50 µm) in the region of the electrode tract were stained with thionin.

Experimental Design

All hooded rats were given one 15 min test for muricide in their home cages prior to electrode implantation. Forty-two killers and 42 non-killers were randomly selected for the experiment.

The rats were randomly assigned to one of six groups: septal kindled (N = 16), amygdala kindled (N = 16), spetal sub-threshold stimulation (N = 16), amygdala sub-threshold stimulation (N = 16), septal control (N = 10) and amygdala control (N = 10). An equal number of killers and non-killers were assigned to each of the groups.

Apparatus

The rats were tested for ranacide and intraspecific aggression in

33 x 33 x 45.5 cm plywood boxes with wire mesh fronts. The fronts were covered with cardboard during the ranacide tests in order to keep the frogs from escaping through the wire mesh. However, the cardboard was removed for the intraspecific aggression tests.

The apparatus for the passive avoidance task consisted of a plywood box (34 x 34 x 29 cm) with a wooden platform (15.5 x 11 x 5.5 cm) positioned in a corner. The floor was made of stainless steel rods (0.5 cm dia.) separated by 1 cm.

After-discharge Threshold Testing

AD thresholds were measured one week after surgery in the kindled and sub-threshold stimulation groups. For half of the animals, AD thresholds were measured in the right amygdala or septum on the first day (Site 1). The remainder of the animals had their left amygdaloid or septal AD thresholds measured first (Site 1). Both groups then had AD thresholds in the homologous sites in the contralateral hemisphere measured on the following day (Site 2).

One sec of 20 μA stimulation was applied and the intensity was increased in discrete steps every two min until an AD of at least 4 sec duration was triggered. The stimulation consisted of 1 msec biphasic square-wave pulses delivered at a rate of 60 Hz. The current intensity was initially raised in 20 μA steps until an intensity of 100 μA was reached. At this point, the current was increased in 50 μA increments until the 300 μA level. Thereafter, 100 μA steps were used. No animal was stimulated at a current intensity greater than 1000 μA.

After the rats in the kindled and sub-threshold stimulation groups

had completed all of the behavioral tests, AD thresholds were remeasured.

Stimulation Regimen

After the AD thresholds were measured, the rats were put on a schedule of daily (five days per week) unilateral stimulation. Sites in the right and left hemispheres were stimulated on alternate days. All stimulation parameters except current intensity were the same as those used in threshold testing. Electrographic responses were recorded on all sessions for the four stimulated groups. The control subjects were handled for 20 days but not stimulated.

The current intensity was kept at the original threshold value for the kindled groups. Each site was stimulated until two generalized seizures were elicited. If this criterion had not been met after 20 days of stimulation then the alternation procedure was terminated and daily unilateral stimulation was applied to one site until the criterion was reached. Stimulation was then applied to the other site.

For the sub-threshold stimulation groups, the current intensity was initially set at approximately 50% of each animal's lowest threshold value and after 10 days of stimulation the intensity was reduced by half. If the stimulation elicited an AD, on any of the 18 trials, then the current intensity was reduced by half.

ADs were elicited in all subjects in the subthreshold stimulation groups during the initial AD threshold testing period, and a few ADs were elicited during the subsequent stimulation regimen. Animals in the sub-threshold stimulation groups, then, experienced two to five ADs prior to behavioral testing but convulsive behavior was not exhibited by any of

these animals.

After completion of the stimulation or handling regimen every animal was given a rest period of one week. The rest period allowed for the disappearance of interictal spiking.

Behavioral Testing

After the rest period, all rats were given one 15 min home-cage muricide test per day for two successive days. The latencies for each rat to physically contact and to attack the mouse were recorded. Mice that were killed were removed immediately.

On the day following the last muricide test, each rat was given 30 min to adapt to one of the test boxes. A leopard frog was then introduced into the apparatus and the behavior of the animals was observed through the open tops of the boxes for 30 min.

The next day all rats were tested on a step-down passive avoidance task. All rats were placed on the platform so that they were facing the corner of the box in which the platform was situated and a timer was then activated. When the rat placed all four paws on the grid floor 3 sec of 1.6 mA DC scrambled footshock was delivered and the latency to step down was recorded. The rats could escape the footshock by jumping back onto the platform. Fourteen hr later, the retention test was given and each rat was allowed up to 300 sec to step down.

The animals were then tested, during the dark segment of the light cycle, for intraspecific aggression. All tests were conducted in a 2 hr period starting 1 hr after light offset at 2200. Each rat was allowed 1 hr to adapt to one of the test boxes. The test box was then carried

from the darkened 'adaptation room' to the testing room which was illuminated by a 25 W red light situated 55 cm above the middle of the floor of the test box. A naive albino rat was then introduced into the apparatus and the behavior of the animals was videotaped. The fight trials lasted 20 min and, at the end of the test periods, the number of wounds inflicted on the albino rats were noted. This procedure took 28 days to complete and animals from all groups were tested throughout this period.

The videotapes were subsequently analyzed by an experienced rater. The duration of lateral blocks, mutual upright postures, allogrooming and on-the-back postures exhibited by the experimental rats and the duration of on-the-back postures shown by the albino rats were timed on an Esterline-Angus event recorder. In addition, the number of lateral blocks, attacks and on-the-back postures exhibited by the experimental rats and the number of on-the-back postures exhibited by their opponents were noted. The descriptions of these behaviors as basically outlined by Grant and Mackintosh (1963) are as follows:

a) Allogroom. Nibbling and pulling the fur of the other rat. Sniffing and licking the genital region are not included.

b) Attack. A bite or leap directed at the other animal.

c) Lateral Block. The rat orients broadside to its opponent and rotates its body so that the legs closest to the other animal are off the ground. The back is arched and the legs are extended.

d) Mutual Upright. Both animals are upright and facing each other.

e) On-the-back. The rat lies flat on its back with all feet in the air or leans back against a wall with all feet off the floor. The

ventral surface is exposed in both cases.

After-discharge Threshold Reduction

Both sub-threshold stimulation groups were subjected to an additional eight-day period of stimulation after completion of all behavioral tests and after AD thresholds were measured for the second time. This was done in an attempt to produce further AD threshold reductions, as the AD threshold reductions resulting from the initial procedure were rather small. The current intensity was set at one step below the level needed to evoke an AD (determined by the second AD threshold test). If an AD was elicited then the current was reduced by one step. Daily unilateral stimulation was applied to one site for four days and then to the homologous site in the contralateral hemisphere for the remainder of the period.

On the day following the last stimulation, these rats were given another 15 min test for muricide.

Statistical Comparisons

Nonparametric procedures were used to analyze the threshold data. The Wilcoxon Matched-Pairs Signed-Ranks test was used to examine the effects of kindling and sub-threshold stimulation on AD thresholds except when the number of rats in a group was less than 6, in which case the Sign test was used. The Mann-Whitney U test was used to assess AD threshold differences between killer and non-killer rats.

The Kruskal-Wallis analysis of variance by ranks was used to analyze the retention test step-down latencies because of the imposition of an arbitrary time limit to step down. Analyses of variance were used to compare the initial step-down latencies and the intraspecific aggression

data. The proportion of mouse-killing and frog-killing rats in the control and experimental groups were compared with the use of the Fisher exact probability test.

Results

Animals in the kindled or sub-threshold stimulation groups which had one or both electrodes misplaced were eliminated from the experiment. The electrode placements as verified by histological examination are presented in Fig 1. Septal placements were located in the lateral septal nucleus except for one electrode which was situated in the medial septum. Most of the amygdala placements were in the dorsal half of the anterior two-thirds of the amygdala, with the majority of the placements in the lateral, basal or central nuclei.

Seven out of ten amygdala controls and five out of ten septal controls had bilateral placements in the intended sites. The remaining control rats had one electrode in the amygdala or septum and the contralateral placement was dorsal or dorsolateral to the intended site. All control rats were retained in the experiment after an analysis of the data revealed that there were no differences on any of the behavioral measures between animals with bilateral and unilateral placements in the intended sites.

During the course of the stimulation regimen, three rats pulled their headcaps and one other rat did not develop convulsions after 67 stimulations. Two other rats lost their headcaps after they had completed all of the behavioral tests but before the final AD thresholds were measured. The initial AD threshold data for all of these animals and the behavioral

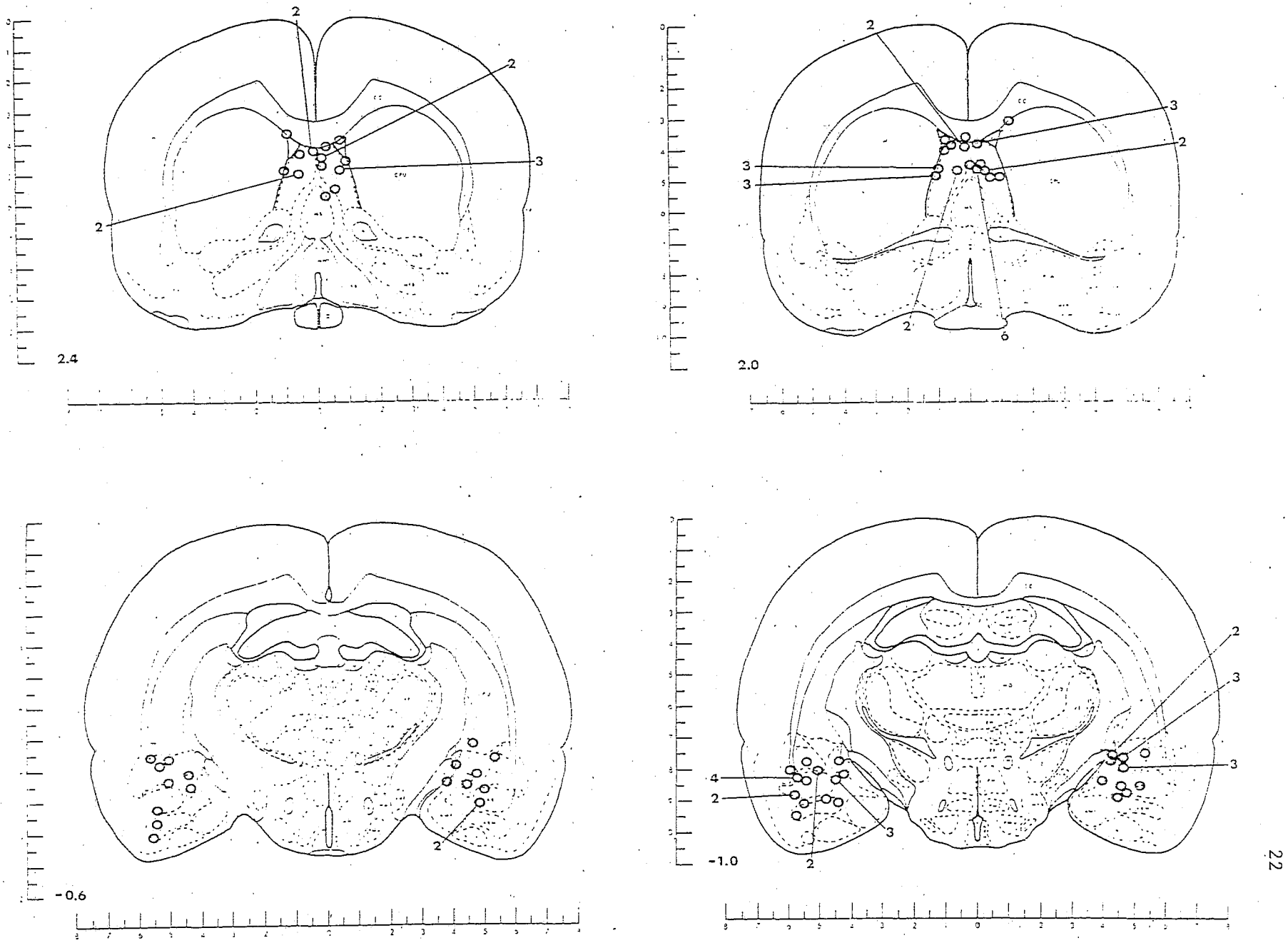

Figure 1. The histologically verified placements are shown in these atlas diagrams. Numbers refer to the number of electrodes ending at that site. A circle without an accompanying number indicates that only one electrode ended at that site. The A-P coordinates in mm from Bregma are shown in the bottom left corner of each diagram.

data for the latter group of animals were included in the statistical analyses.

Initial AD Thresholds and Muricide

The initial and final AD threshold data for muricidal and non-muricidal rats are presented in Table IB. Since the kindled and sub-threshold stimulation groups received identical treatment until completion of the initial AD threshold testing procedure, the data for these groups were combined. There were no significant differences between muricidal and non-muricidal rats in initial amygdaloid or septal AD thresholds (see Table IB).

Effects of Kindling and Sub-threshold Stimulation on AD Thresholds

Contrary to expectation, many animals in the sub-threshold stimulation groups did not show AD threshold reductions and the final AD thresholds for the amygdala (Sites 1 or 2) or septal (Site 2) sub-threshold stimulation groups were not significantly different from the initial AD thresholds. However, final AD thresholds for Site 1 in the septum were lower than initial AD thresholds in five out of eight rats. The AD thresholds for the other three rats were unchanged. These data and the results of the statistical analyses are presented in Table IA.

Table IA also shows that following kindling, significant AD threshold reductions were found in the septum but not in the amygdala. This latter result is also not consistent with our previous experience.

Failure to reduce AD thresholds in the sub-threshold stimulation groups and the amygdala kindled group may be related to the reported interference effects (Goddard, McIntyre and Leech, 1969; McIntyre and

TABLE I

INITIAL AND FINAL AFTER-DISCHARGE THRESHOLDS OF MURICIDAL AND NON-MURICIDAL RATS

	A								B							
	SUB-THRESHOLD STIMULATION				KINDLED				INITIAL				FINAL			
	Site 1		Site 2		Site 1		Site 2		Site 1		Site 2		Site 1		Site 2	
	I	F	I	F	I	F	I	F	M	NM	M	NM	M	NM	M	NM
AMYGDALA N	9	9	9	9	10	10	10	10	12	13	12	13	12	7	12	7
ADTs MEDIAN	80	80	98.7	101.9	65	50	113.3	70	66	77.5	125	95.8	83.3	47.5	107.5	80
RANGE	40-300	40-250	60-400	80-300	40-200	40-150	60-400	40-600	40-250	40-300	40-400	60-400	40-250	40-80	40-300	40-600
SEPTAL N	8	8	8	8	9	9	9	9	12	5	12	5	16	1	16	1
ADTs MEDIAN	425	350	150	250	475	162.5	331.2	181.2	325	566.7	200	375	187.5	500	187.5	400
RANGE	200-1000	100-1000	40-600	40-500	20-600	40-400	80-600	60-250	20-1000	250-600	40-600	80-600	40-1000	500	40-500	400

Sub-Threshold Stimulation Groups:

Site 1: initial amyg. ADTs VS final amyg. ADTs
N = 5 X = 2 NS

initial sept. ADTs VS final sept. ADTs
N = 5 X = 0 p = 0.06

Cont. . . .

Site 2: initial amyg. ADTs VS final amyg. ADTs
N = 8 T = 14.5 NS

initial sept. ADTs VS final sept. ADTs
N = 7 T = 11 NS

Kindled Groups:

Site 1 initial amyg. ADTs VS final amyg. ADTs
N = 7 T = 6 NS

initial sept. ADTs VS final sept. ADTs
N = 9 T = 1 $p < 0.01$

Site 2: initial amyg. ADTs VS final amyg. ADTs
N = 9 T = 19 NS

initial sept. ADTs VS final sept. ADTs
N = 9 T = 3 $p < 0.02$

MURICIDE:

Site 1: initial amyg. ADTs of NK VS initial amyg. ADTs of K
U = 66.5 N_K/N_{NK} = 12/13 NS

initial sept. ADTs of K VS initial sept. ADTs of NK
U = 22 N_{NK}/N_K = 5/12 NS

final amyg. ADTs of NK VS final amyg. ADTs of K
U = 18 N_{NK}/N_K = 7/12 NS

Site 2: initial amyg. ADTs of NK VS initial amyg. ADTs of K
U = 77 N_K/N_{NK} = 12/13 NS

initial sept. ADTs of NK VS initial sept. ADTs of K
U = 23 N_{NK}/N_K = 5/12 NS

final amy. ADTs of NK VS final amyg. ADTs of K
U = 36.5 N_{NK}/N_K = 7/12 NS

Cont. . . . .

TABLE I (Cont.)

RANACIDE:	Site 1:	final amyg. ADTs of NK	VS final amyg. ADTs of K	
		U = 19	N_{NK}/N_K = 6/9	NS
		final sept. ADTs of STS NK	VS final sept. ADTs of STS K	
		U = 6.5	N_{NK}/N_K = 3/5	NS
		final sept. ADTs of kindled NK	VS final sept. ADTs of kindled K	
		U = 3.5	N_{NK}/N_K = 3/6	NS
	Site 2:	final amyg. ADTs of NK	VS final amyg. ADTs of K	
		U = 21	N_{NK}/N_K = 6/9	NS
		final sept. ADTs of STS NK	VS final sept. ADTs of STS K	
		U = 3	N_{NK}/N_K = 3/5	NS
		final sept. ADTs of kindled K	VS final sept. ADTs of kindled NK	
		U = 2	N_{NK}/N_K = 3/6	NS

a) Effects of sub-threshold stimulation or kindling on AD thresholds (in μA). Note that following kindling of the septum, final (F) AD thresholds were significantly lower than initial (I) AD thresholds.

b) AD thresholds of muricidal (M) and non-muricidal (NM) rats. Note that the post-treatment muricide tests were used to determine each rat's killing status for the final AD threshold test. Four septal rats and six amygdala rats started to kill mice, one amygdala rat stopped killing mice and final AD thresholds were not measured in six amygdala rats.

Goddard, 1973). McIntyre and Goddard (1973) found that, following secondary site kindling, stimulation of the previously kindled primary site sometimes failed to elicit an AD on the first trial, suggesting an increase in the AD threshold. However, a systematic investigation into the effects of a series of alternating unilateral stimulations on AD thresholds has not been carried out. Also, it is not clear why AD thresholds were reduced following kindling of the septum but not after amygdaloid kindling.

Final AD Thresholds and Interspecific Aggression

Since neither kindling nor sub-threshold stimulation of the amygdala lowered AD thresholds, the final AD threshold data for killer rats in the kindled and sub-threshold stimulation groups and for non-killer rats in the same groups were combined. The results of the post-treatment muricide tests were used to determine each rat's killing status. There were no significant differences between mouse-killing and non-mouse-killing rats in final amygdaloid AD thresholds (see Table IB). Final septal AD threshold differences between muricidal and non-muricidal rats could not be assessed because, like control non-killer rats, most of the initial non-killer rats in the septal kindled and sub-threshold stimulation groups killed mice on the post-treatment tests. In addition, there were no significant differences between frog-killing and non-frog-killing rats in final amygdaloid or septal AD thresholds. See Table I for the results of the statistical analyses.

Effects of Kindling or Sub-threshold Stimulation on Interspecific Aggression

Table II shows that kindling or sub-threshold stimulation of the amygdala or septum did not inhibit muricide. AD thresholds were reduced

TABLE II

EFFECTS OF KINDLING OR SUB-THRESHOLD STIMULATION ON INTERSPECIFIC AGGRESSION

	CONTROL	KINDLED	SUB-THRESHOLD STIMULATION
Initial Mouse-Killers:			
Amyg.	5/5	5/6	3/3
Sept.	5/5	7/7	5/5
Initial Non-Mouse-Killers:			
Amyg.	4/5	1/6	5/6
Sept.	4/5	2/2	2/3
Frog-Killers:			
Amyg.	7/10	8/11	2/5
Sept.	7/10	6/9	6/8

Numbers refer to the number of initial mouse-killing rats and initial non-mouse-killing rats that killed mice and the number of rats that killed frogs. None of the pairwise comparisons between a control group and an experimental group in the proportion of rats that stopped killing mice, in the proportion of rats that started to kill mice or in the proportion of rats that killed frogs were significant.

bilaterally in five initial killers in the septal kindled group and in one initial killer in each of the sub-threshold stimulation groups (see Table III). None of these rats stopped killing mice. No qualitative changes in the stereotyped killing response were noted in any of the initial killers. In addition, there were no significant differences among the six groups of initial killers, on either of the post-treatment tests, in their latency to physically contact mice ($F = 0.88$, $df = 5, 22$; $F = 1.23$, $df = 5, 22$) or to attack mice ($F = 0.99$, $df = 5, 22$; $F = 0.82$, $df = 5, 22$).

Since there were no significant differences in these latencies among the six groups of initial killers, the post-treatment data for all groups of initial killers was combined so that the effects of the repeated experience of killing mice could be assessed. The mean latencies in sec for killers to physically contact mice for the screening test and the two post-treatment tests were 65.1, 7.2 and 8.5, respectively. In order, the mean latencies in sec for killers to attack mice were 189.6, 30.7 and 28.1. The repeated experience of killing mice caused a significant reduction in the latency to physically contact mice ($F = 8.24$, $df = 2, 54$, $p < .001$) and in the latency to attack mice ($F = 13.46$, $df = 2, 54$, $p < .001$).

Table II also shows that most of the initial non-killers killed mice in the post-treatment tests except for the rats in the amygdala kindled group in which only one out of six killed mice. However, there was not a significant difference between the amygdala control group and the amygdala kindled group in the proportion of initial non-killers that killed mice in the post-treatment tests. No other differences between a control group and an experimental group in the proportion of initial non-killers that

	Pre-Treatment Muricidal Status		Post-Treatment Muricidal Status		AD Thresholds
AMYG. KINDLED	M	6	M	5*	++, E-, + -
			NM	1	E+
	NM	6	M	1	- -
			NM	5	3- -, EE, + -
AMYG. SUB-THRESHOLD STIMULATION	M	3	M	3	- -, ++, E+
			NM	0	
	NM	6	M	5	2E-, 2+ -, E+
			NM	1	E+
SEPT. KINDLED	M	7	M	7	5- -, 2- +
			NM	0	
	NM	2	M	2	2- -
			NM	0	
SEPT. SUB-THRESHOLD STIMULATION	M	5	M	5	2-E, - -, E+, + -
			NM	0	
	NM	3	M	2	E-, + -
			NM	1	- -

*2 rats pulled headcaps before AD thresholds were remeasured.

Cont. . . . .

TABLE III (Cont.)

+	Final AD theshold was greater than initial AD threshold
-	Final AD threshold was lower than initial AD theshold
E	Initial and final AD thesholds were equal

became killers were significant (see Table II).

The behavior, towards mice, of the amygdala kindled rats that did not become killers was not different from their pre-treatment behavior. They bit and pulled on the fur of the mice, but did not inflict any wounds, and often carried the mice to the back of the cage. All rats which killed mice displayed the normal killing pattern.

Table III shows that there was not a consistent relationship between AD threshold reduction and the induction of muricide. For example, four initial non-muricidal rats had AD thresholds reduced bilaterally as a consequence of amygdaloid kindling. Only one of these rats started to kill mice. Two initial non-killer rats in the septal kindled group had AD thresholds reduced bilaterally and both started to kill mice. A comparable reduction in AD thresholds was produced in one initial non-muricidal rat in the septal sub-threshold stimulation group and this rat did not start to kill mice. Finally, one rat in the amygdala sub-threshold stimulation group started to kill mice even though one AD threshold was raised and the other was unchanged.

There were also no significant differences between the amygdala control group and the amygdala kindled or amygdala sub-threshold stimulation groups or between the septal control group and the septal kindled or septal sub-threshold groups in the proportion of rats that killed frogs. There were no obvious differences in the qualitative nature of the killing response among the rats in the six groups. The frogs were killed by a bite delivered to the cervical region of the spinal cord.

Following measurement of the final AD thresholds, rats in both sub-threshold stimulation groups were given an additional eight day period of

stimulation. In comparison with the final AD threshold values, AD thresholds were reduced bilaterally in seven out of eight septal rats and AD thresholds were reduced unilaterally in the remaining septal animal and in all eight rats in the amygdala sub-threshold stimulation group. This additional period of stimulation did not induce or inhibit muricide.

Passive Avoidance

The mean initial step-down latencies in sec for the control (C), sub-threshold stimulation (S) and kindled (K) groups were: AMYG (C): 8.7, SEPT (C): 11.3, AMYG (S): 11.7, SEPT (S): 13.3, AMYG (K): 5.3, SEPT (K): 4.0, respectively. The groups were not significantly different on this measure ($F = 1.66$, $df = 5, 51$).

The median latencies in sec to step down from the platform on the retention test for the control, sub-threshold stimulation and kindled groups were: AMYG (C): 38.6, SEPT (C): 76.8, AMYG (S): 76.1, SEPT (S): 77.3, AMYG (K): 25.8, SEPT (K): 29.6, respectively. Although the median latencies to step down for the kindled groups were lower than those for the other four groups, there was not a significant difference among the groups on this measure ($H = 5.04$, $df = 5$).

Intraspecific Aggression

Six dependent measures taken during the intraspecific aggression test occurred very infrequently and the data were eliminated from further analysis. The remaining data and the results of the statistical analyses are summarized in Table IV.

There were no significant differences among the groups in the frequency of attacks or lateral blocks or in the frequency of on-the-back

EFFECTS OF KINDLING OR SUB-THRESHOLD STIMULATION
ON INTRASPECIFIC AGGRESSION

		ATTACK		LATERAL BLOCK		ON-THE-BACK POSTURE		MUTUAL UPRIGHT POSTURE		ALLO-GROOMING	
		$\bar{x}$	Range	$\bar{x}$	Range	$\bar{x}$	Range	$\bar{x}$	Range	$\bar{x}$	Range
AMYG.	CONTROL N = 10	0.9	0-3	0.8	0-3	1.3	0-7	0.4	0-2.5	27.5	0-56.5
	SUB-THRESHOLD STIMULATION N = 9	0.3	0-2	1.1	0-6	0.9	0-4	1.7	0-13.5	17.8	1-47.5
	KINDLED N = 12	0.4	0-2	0.8	0-5	0.4	0-2	0.9	0-8.5	7.0	0-23
SEPT.	CONTROL N = 10	0.9	0-3	2.0	0-9	2.0	0-8	13.2	0-79	24.6	0-147
	SUB-THRESHOLD STIMULATION N = 8	0.6	0-2	2.4	0-14	0.5	0-2	4.5	0-24.5	31.1	4-74
	KINDLED N = 9	0.6	0-2	3.4	0-20	1.0	0-6	1.0	0- 3.5	30.2	1.5-163.5

Attacks	F = 0.63	df = 5, 52
Lateral Blocks	F = 0.74	df = 5, 52
On-The-Back Postures	F = 0.88	df = 5, 52
Mutual Upright Postures	F = 1.75	df = 5, 52
Allogrooming	F = 0.94	df = 5, 52

There were no significant between-group differences in the frequency of On-The-Back postures, Lateral Blocks or Attacks or in the duration (in sec.) of Mutual Upright Postures or Allogrooming.

postures displayed by their opponents. There were also no significant differences among the groups in the duration of mutual upright postures or allogrooming.

Discussion

The establishment of bilateral kindled foci in the amygdala or septum tended to disrupt one-trial inhibitory avoidance behavior. The mean latency to step down for the amygdala kindled group was 30.1 sec lower than that for the amygdala control group and the average latency for the septal kindled group was 56.5 sec lower than that for the septal control group. Sub-threshold stimulation of the amygdala or septum, on the other hand, did not impair performance on the passive avoidance task. Although there were no significant differences among the groups due to the variability in the data, the results are generally in agreement with the findings of Boast and McIntyre (1977).

One animal in the septal kindled group failed to step down from the platform on the 300 sec retention test. The electrode tips for this rat were located near the anterior border of the septum. The next highest step-down latency for a septal kindled animal was 56.1 sec lower than the mean for the septal control group. The cause of the variability in performance exhibited by the other groups was not apparent.

Boast and McIntyre (1977) reported that, in most animals, the development of bilateral kindled foci in the amygdala impaired performance on a one-trial inhibitory avoidance task. Their data showed considerable variability as well: 12 out of 51 (23.5%) rats in the bilateral convulsion

group successfully avoided the chamber in which they had previously been shocked.

Because the centromedial region of the rat amygdala facilitates muricide (Karli and Vergnes, 1965; Horovitz et al., 1966), we expected findings opposite to those of Adamec (1975). That is, we expected that non-killers would have higher amygdaloid AD thresholds than killers. But muricidal and non-muricidal rats did not differ in initial or final amygdaloid AD thresholds. Recently, McIntyre (personal communication) has obtained the same results.

We also found that there were no significant differences between muricidal and non-muricidal rats in initial AD thresholds in the septum, a region possibly inhibiting muricide (Miczek and Grossman, 1972; Miley and Baenninger, 1972; Latham and Thorne, 1974; but see also Malick, 1970; Yamamoto and Ueki, 1977). In addition, ranacidal and non-ranacidal rats did not differ in final amygdaloid or septal AD thresholds.

Bilateral kindling or bilateral sub-threshold stimulation of the amygdala or septum did not inhibit or induce muricide or ranacide.

Most initial non-killers, except for those in the amygdala kindled group, killed mice in the post-treatment tests regardless of the treatment. All groups received extensive handling and this factor may have been responsible for the induction of muricide. It is unlikely that the single screening test was inadequate in determining the rats' killing status since 40.5% of the hooded rats killed mice on this test. This figure is higher than our previous results with this strain and it is also higher than the percentage of muricidal hooded rats obtained by

other investigators (e.g. Bandler and Moyer, 1970; Karli et al., 1969).

McIntyre (personal communication) found that bilateral AD threshold reduction in the amygdala did not affect muricide. Kindling the amygdala also did not inhibit or induce muricide but it did reduce Wistar muricidal rats' latency to kill in their home cages. Amygdaloid kindling, however, did not decrease hooded rats' latency to kill mice in a larger predatory arena. Unfortunately, McIntyre was unable to determine if the repeated experience of killing was responsible for this facilitation of the predatory response in the Wistar rats because only two control rats were used in the experiment.

We found that the development of bilateral kindled foci in the amygdala did not facilitate the onset of predatory attack. There were no significant differences between the amygdala control and kindled groups in latencies to physically contact or to attack mice. However, all killers exhibited a significant reduction in these measures as a result of the repeated experience of killing. Since those rats which attack and kill mice do so quickly and efficiently, it is likely that there is a high correlation between the latency to attack mice and the latency to kill mice. Our results, then, extend the results of McIntyre. We have demonstrated that home-cage attack is not facilitated in muricidal hooded rats by amygdaloid kindling.

Kindling or sub-threshold stimulation of the amygdala or septum did not increase the number of attacks or lateral blocks or increase the number of on-the-back postures exhibited by the experimental rats' opponents. Thus, the development of bilateral kindled foci in the amygdala

or septum, regions apparently facilitating intraspecific aggression (Miczek et al., 1974; Miczek and Grossman, 1972; Lau and Miczek, 1977; Blanchard et al., 1977), did not facilitate intraspecific aggression.

Pinel et al. (1977) have suggested that the development of a unilateral kindled focus in the temporal lobe increases aggressive behavior in the rat. They found that rats kindled in the amygdala or hippocampus were more difficult to handle and exhibited an increased reactivity to a tail tap. But it is not clear whether these emotionality tests measure aggressive behavior, as opposed to defensive behavior.

We found that bilateral kindling of the amygdala or septum did not induce interspecific or intraspecific aggression. It appears, then, that the findings of Pinel et al. (1977) have only a limited generality. However, Pinel et al. used more kindling trials than we did, and it is possible that a predisposition to hyperreactivity develops only after longer kindling sessions.

It appears that partial kindling of the basolateral amygdala in the cat results in changes in predatory aggression that are secondary to the increases in defensive behavior (Adamec, 1975). Adamec found that this procedure inhibited rat killing and increased the defensiveness of cats towards rats. In cats, the basolateral amygdala inhibits predatory aggression (Egger and Flynn, 1967) and facilitates defensive behavior (Kaada, 1972; Zbrozyna, 1972).

Adamec's cats exhibited defensive behavioral changes such as increases in paw striking attacks and increases in withdrawal from rats as well as an increase in autonomic responsiveness to tape recorded 'threat

howls' of an adult male conspecific. But AD threshold reduction in the basolateral amygdala did not inhibit muricide (Adamec, 1974), which probably reflects the limited ability of mice to elicit defensive behavior in attacking cats.

Spontaneous seizures are developed with significantly fewer stimulations of the amygdala in cats (Wada et al., 1974) than in rats (Pinel et al., 1975; Pinel and Rovner, 1978). It is possible that a tendency to exhibit defensive behavior develops only after a minimal number of stimulations have been applied or after a certain stage has been reached in the development of spontaneous seizures. The cat amygdala is relatively more seizure prone than the rat amygdala, and this stage is reached in cats before generalized convulsions are elicited. However, from Pinel's work, it appears that much longer kindling sessions are needed to produce changes in reactivity in the rat. Given the nature of the tests that Pinel used, it is possible that this hyperreactivity reflects an increase in defensive behavior. In any case, tests which clearly differentiate aggressive behavior from defensive behavior should be used in future work.

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