STIMULATION OF THE RAT BRAIN:

EVOKED BEHAVIOR AND REWARD

ELECTRICAL STIMULATION OF THE BRAIN STEM OF THE HOODED RAT:

EVOKED BEHAVIOR AND REWARDING EFFECTS

By

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SCOPE AND CONTENTS: This thesis is concerned with the functional organization of motor patterns as indicated by electrical stimulation of the rat brain stem. The thesis also examines the relationship between the evoked behavior and the rewarding effects produced by stimulation of the same sites. The results showed that stimulation of the midbrain, diencephalon and striatum elicited a variety of behavior patterns including components of grooming and digging behavior as well as walking, running, exploratory behavior, escape and vocalization which have been demonstrated previously in other species. The majority of sites that yielded evoked behavior were neutral in self-stimulation tests in the sense that they supported neither self-stimulation nor escape behavior.

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INTRODUCTION

As early as 1863, Sechenov (1965) expressed the view that "all external manifestations of the functioning of the brain can be reduced to muscular movement."

In the same vein, Sherrington (1933) states:

> "I may seem to stress the preoccupation of the brain with muscle. Can we stress too much that preoccupation when any path we trace in the brain leads directly or indirectly to muscle? The brain seems a thoroughfare for nerve action passing on its way to the motor animal. It has been remarked that life's aim is an act not a thought." (p.10)

In response to what he viewed as an increasing trend to the study of the sensory side of brain function, Sperry (1964) asserted that "the primary function (of the brain) is essentially the transforming of sensory patterns into patterns of motor coordination."

To each of these authors, an analysis of motor activity was central to an understanding of the physiological basis of behaviour.

Theories of Motor Organization

The theory of the reflex was one of the earliest mechanistic explanations of animal and human behaviour. Rene Descartes is usually given credit for the essential idea of the reflex (Boring, 1950), but it was not until the time of Marshall Hall, by way of his studies of the spinal cord, that the reflex concept became established in biology (Fearing, 1964). Modern conceptions of the reflex are based largely on the work of Sherrington (1906) who defined a reflexive response as one dependent on the operation of a reflex arc. Anatomically, he described the reflex arc as consisting "of at least three separable structures, - an _effector_ organ, e.g., gland cells or muscle cells; a conducting nervous path or _conductor_ leading to that organ; and an initiating organ or _receptor_". Early authors contrasted reflexive acts with voluntary behaviour which was assumed to be intrinsically different from reflexive behaviour and dependent on the activity of a special agent, the psyche.

However, the reflex arc gradually began to be used by some theorists as an explanation for all behaviour. Workers such as Bekhterev (1932) and Pavlov (1960) were very explicit in their belief that all behaviour could be explained in terms of reflex action. Bekhterev (1932), using quasi-neurological diagrams, illustrated how complex activities such as human speech depended on cerebral reflex arcs or transcortical reflexes. Pavlov (1960, p.10) assumed that long sequences of motor activity were chain reflexes in which each component response acted as the stimulus for the next response in the chain.

Theories that all behaviour is essentially reflex in nature never gained general acceptance and have been criticised by a number of authors (Hebb, 1949; Lashley, 1951; Pribram, 1960; Skinner, 1938). The criticisms of reflex theory take several forms: (a) Since no stimulus is known for many movements, the fundamental postulate of reflex action is an assumption.
(b) Since the stimulus should always have immediate effects, how can the theories explain cases where a single stimulus leads to a response only after a long delay? (c) With chain reflexes, how is it possible for the same stimulus to initiate two different responses, as in a double alternation experiment? More generally,

how can any one movement be part of more than one chain? In addition, experimental studies of the role of peripheral feedback in movement have shown that many actions can be performed in a more or less normal fashion after widespread destruction of sensory input. Von Holst (cited in Tinbergen, 1951) has shown that teleost fish "in which all dorsal roots except the two innervating the pectoral fin were severed" showed complete swimming movements. Gray and Lissman (1940) have found that the toad is capable of coordinated locomotion with afferent input from only one limb, the dorsal roots of the other three limbs being cut. Doty and Bosma (1956) demonstrated that even with removal of some of the muscles involved in the swallowing reflex, the order and temporal sequence of the contractions of the remaining muscles was normal.

As an alternative to explaining all behaviour in terms of reflex action, some theorists maintain that some behaviours are reflexive while others are not. Skinner (1938), for example, supposes that control of movements is of two types: (1) respondent or reflex where the response is dependent on antecedent stimuli and, (2) operant or voluntary where the occurrence of the response is controlled by subsequent stimuli. A somewhat analogous distinction between reflexive and voluntary acts is made in neurology. Neurological findings suggest that reflex and voluntary movements probably depend on different mechanisms. For example, some brain damaged patients are able to laugh in response to sensory stimuli, or engage in involuntary licking, but are not able to grimace or lick using the same muscles when asked to, even though they understand what is wanted of them (Taylor, 1958).

Another type of classification of motor activities has been suggested by Hess (Koella, 1962). He distinguished between "ereismatic" and "telokinetic" motor activity. "Ereismatic" movements include all motor activity involved in support and preparation for the second type of motor activity. "Telokinetic" movements include all directed and skillful movements. Taking jumping in the cat as an example, raising the head and flexing the hind limbs are the "ereismatic" components and the action of jumping itself is the "telokinetic" component of the response.

Any complex sequence of acts is generally assumed to be dependent on the operation of mechanisms in the forebrain, but no generally accepted theory of their organization exists. However, Hughlings Jackson (Taylor, 1958) suggested one of the fundamental organizing principles in the central nervous system. He believed that motor organization occurred in at least three different levels related in a hierarchical fashion. At the lowest or bulbo-spinal level simple reflexes were represented. A second or middle level, the motor cortex, re-represented the lower level with a more complex organization that made possible the occurrence of complex motor sequences. The highest level, localized in the frontal lobes, was the final representation of the most complex and "finest" movements. At each level the elements of a lower level are combined to form a larger functional unity. Activity in the lower elements is governed by the higher levels and if the higher level is destroyed, the lower elements may appear less excitable, more excitable, or simply disorganized. This general type of concept has found wide acceptance in neurology. Considerable experimental evidence also supports this idea. For example, a cat with a high spinal transection is unable to stand or walk, although nearly all the elementary movements such as the positive supporting reaction, leg flexion and contralateral extension are present (Denny-Brown, 1960; Gardner, 1963). With transection of the brain stem rostral to Deiter's nucleus the circuitry necessary for reflex standing is present. If the brain is transected at a still higher level, just rostral to the red nucleus and posterior portion of the hypothalamus, spontaneous walking occurs in cats (Hinsey and Ranson, 1928). In a similar vein, thalamic cats (section just rostral to the thalamus and hypothalamus) possess patterns of reflex biting, chewing and swallowing but do not eat spontaneously. If the section is made just rostral to the striatum (destroying all cortex) spontaneous eating will occur and the animals do not require the tube feeding necessary for a thalamic cat's survival.

An important recent illustration of Jackson's principles is provided by a study by Woods (1964). Woods decerebrated rats at the level of the superior colliculi with clear separation of the posterior hypothalamus and mesencephalon. An "island" of hypothalamic tissue was left intact to maintain normal water and mineral balance. Normal temperature was maintained by artificial heating. Within a week following the operation a drop or two of water anywhere on the body initiated a vigorous bout of grooming. This involves sitting up, washing the face and licking the fur. After two or three weeks the grooming was good enough that manual care of cleaning by the experimenter was no longer necessary. The basic motor components of feeding, chewing, licking and swallowing were initiated by contact of the lips with a solid object or drinking spout. However, the rats never engaged in spontaneous feeding behaviour and they had to be fed by stomach tube. They were spontaneously active and responded appropriately to noxious stimuli by struggling, pushing with forepaws and vocalizing. Thus, many of the motor patterns seen in normal rat behaviour are dependent on levels of the neuraxis no higher than the midbrain. However, these fundamental "bits" of behaviour are no longer fully integrated into adaptive patterns when the forebrain is destroyed.

Inherent in jacksonian neurology is the principle of the dependence of lower mechanisms on influences from higher levels. It has often been supposed that the highest level of control is the neocortex. This view seems to have been suggested primarily by the fact that man, presumed to have a "higher" type of mind than other animals, has a very well developed neocortex. That the cortex represents the highest level of motor function is not a proven fact and recently Penfield (1954; Penfield and Roberts, 1959) proposed a theory of motor organization in which the diencephalon, midbrain and pons (higher brain stem) are regarded as the "highest level of integration". According to Penfield, this "centrencephalic integrating system" initiates the neural activity that produces voluntary behaviour. The role of the motor cortex is one of transmitting or transmuting the patterned activity originating in the centrencephalic system to the voluntary motor pathways. Complex innate mechanisms such as those responsible for chewing, swallowing, vocalization and running are located in the midbrain and below and may be activated by the motor cortex. With the exception of the relocation of the highest level of integration to the higher brain stem, this theory conforms closely to Jackson's original formulations.

The theory that the motor system consists of a hierarchical organization of action patterns is also consistent with the results of studies utilizing localized electrical stimulation of the brain in freely moving animals. Such work appears to demonstrate an anatomical basis for the centers controlling various motor patterns. The first systematic studies of this sort were undertaken by W. R. Hess (Hess, 1957; Gloor, 1954). He found that stimulation of the cat diencephalon and midbrain elicited complex autonomic and somatic motor activity (changes in blood pressure, rage, locomotion etc.) that was in many cases highly integrated and well coordinated. Subsequently others have elaborated these findings in the cat (Hunter and Jasper, 1949; Skultety, 1962) and extended them to the chicken (von Holst and von Saint Paul, 1962, 1963), rabbit (White and Himwich, 1957) and monkey (Delgado, 1952, 1964, 1965).

Fernandez de Molina and Hunsperger (1962) using the combined techniques of stimulation and coagulation demonstrated the hierarchical nature of the subcortical system governing defensive behaviour in the cat. They showed that a defensive pattern consisting mainly of growling and growling-hissing could be evoked by stimulation of the amygdala, hypothalamus and central grey matter of the midbrain. Lesions in the hypothalamus or midbrain ipsilateral to a stimulating electrode in the amygdaloid nucleus abolished defensive behaviour elicited at that site. However, even bilateral coagulation of the amygdala did not affect the pattern obtained from the hypothalamus and midbrain. "The hissing pattern obtained from the hypothalamus is only suppressed by a bilateral coagulation in the midbrain field" (Fernandez de Molina and Hunsperger, p.208). They concluded that the amygdala, hypothalamus, and central grey matter of the midbrain were of "progressively increasing importance" in defensive behaviour. It is presumed that the basic behaviour patterns exist largely in the midbrain but that higher mechanisms can coordinate or modify their activity. "The brain stem mechanisms represent executive mechanisms modifiable from various places" (Bard and Macht, 1958).

These findings led Delgado (1964) to propose a "theory of the fragmental organization of behaviour" stating that "behavioral performance may be considered as a pattern of motor fragments organized in time and space, with each fragment having anatomical and functional reality inside the brain, which can be triggered by electrical or physiological stimulation" (Delgado, 1965). An interesting postulate of this theory is that the same behavior fragment can form part of a number of different behavioral sequences. For example, Bolwig (1964) found that all the manipulative abilities of a captive baboon were based on a very small repertoire of arm and hand movements. Delgado (1964) further illustrates that essentially the same behavior fragment can be part of one of several behavior patterns. Licking, for example, may be part of alimentary reactions, body cleaning, maternal and sexual behavior.

The finding of Kennedy, Evoy and Hanawalt (1966) that a single cell can trigger a complex stereotyped motor pattern involving one hundred or more efferent units is suggestive of how multiple use of a given fragment could occur. They found that stimulation of a single interneuron produced flexion of several abdominal segments in the crayfish. In Delgado's framework, a particular behavior fragment could be triggered by the action of a single cell located in the anatomical representation of a larger behavior pattern. This implies that the highest "centers" would only need a few cells to elicit and control a relatively complex but stereotyped behavior pattern that could be called into action much as a subroutine is used in a computer program. Delgado also postulates that different fragments of behavior "may have a functional affinity and form a sequence." The fragments of behavior may also be linked by learning and the linkages are reinforced by usage.

Ethology is a third broad area of research which has emphasized the hierarchical nature of the motor system. Tinbergen (1951) has proposed that motor organization consists of succesive levels of motor centers ranging from the organization of an entire instinct down to terminal components (fixed action patterns) consisting of individual, or of a small group, of muscle contractions. An important feature of this theory is that the various levels are continually primed and require only the proper releasing stimuli for a given behavior to occur. As an illustration, the reproductive behavior of the male three-spined stickleback is at the level of a major instinct where an instinct is defined "as a hierarchically organized nervous mechanism which is susceptible to certain priming, releasing and directing impulses of internal as well as external origin, and which responds to these impulses by coordinated movements that contribute to the maintenance of the individual and the species." The second level organizes the activities of fighting, nest building, mating, and care of offspring in separate centers. The third level is the level of the consummatory act. For fighting this includes the centers organizing chasing, biting, and threatening motor patterns. Still lower levels comprise the fixed action pattern such as specific fin movements and individual muscle movements.

Covariation Between Evoked Motor Activity and Reinforcement

Experimental psychology has developed the view that much of the spontaneous behavior of animals is operant behavior. That is, the occurrence of a movement at a given time is determined by a history of rewards and punishments which followed that movement in the past. The process by which a particular response is strengthened in this way is referred to as "reinforcement." Traditionally, there has been little contact between this line of work and other biological studies of motor performance in animals.

However, recent developments suggest that neurological studies of motor performance may provide a clue to the physiological nature of reinforcement.

According to Tinbergen (1951) reinforcement consists essentially of the performance of a consummatory motor pattern. The performance of these simple responses "satisfies" the animal by using up the neural activity responsible for their activation. To illustrate, a rat learns to run a maze because the run is followed by the release of the reservoir of activity in the motor centers responsible for eating behavior. Taste and post-ingestional factors are presumed irrelevant. As it stands, this idea is clearly incorrect. Miller and Kessen (1952) have shown that reinforcement occurs with direct injection of food into the stomach. Chambers (1956) showed a reinforcing effect of intravenous injection of glucose. However, in such studies it is possible that the effects of food in the stomach or glucose in the blood could produce low-level activation of the motor system. Sheffield et al. (1951) and Premack (1959, 1962) have also proposed response theories of reinforcement.

Ideas of this sort have been related to neurophysiological studies by Glickman and Schiff (1966). These authors propose that "in the intact animal, motor control involves the sequential facilitation of motor sequences already <u>preformed</u> in the brain stem and conducted caudally through the extrapyramidal rather than the corticospinal pathways." These preformed motor sequences include simple head turning, locomotion, and complex approach or withdrawal behavior such as eating or flight and escape. A major feature of this theory is the identification of approach and withdrawal behavior with positive and negative reinforcement respectively. Facilitation of the motor activity in the pathways involved in these behaviors is considered the sufficient condition for reinforcement. It should be pointed out that facilitation of neural activity in these pathways can occur without an overt response. However, the neural activity and the occurrence of a response would normally be related and the degree of reinforcement would be positively correlated with the vigor of an overt response. This would appear to be a possibility in the Miller and Kessen (1952) study where the learning was best when the consummatory responses were actually made.

According to these views there should be a consistent relationship between reinforcement and approach and withdrawal behavior (classification of Schnierla, 1959) evoked by electrical stimulation of the brain. Specifically, elicitation of approach behaviors should be positively reinforcing and elicitation of withdrawal behaviors should be negatively reinforcing. The theory, then, predicts that self-stimulation behavior occurs because of direct activation of or facilatation of motor activity directing various behavior patterns.

Two basic experimental designs have been used to study the covariation of evoked behavior and reinforcement. The first design relates evoked behavior and self-stimulation of the same site. The second type of study examines the reinforcing effects of performance of the evoked response.

The covariation between evoked effects and self-stimulation is best demonstrated in the hypothalamic control of eating. Margules and Olds (1962) and Hoebel and Teitelbaum (1962) have shown that both feeding and self-stimulation obtained from the same hypothalamic sites are sensitive to artificial and physiological manipulations of hunger. These authors concluded that the rewarding effects produced by electrical stimulation are similar to the effects produced by eating. Herberg (1963) observed seminal ejaculation (but without penile erection or other sign of sexual arousal) in rats following self-stimulation in the ventromedial hypothalamus. Administration of androgen enhanced self-stimulation rates. Plutchik, McFarland, and Robinson (1966) found that certain types of self-stimulation of the diencephalon and septum were clearly related to the type of evoked behavior (lip-licking, food and object intake, penile erections) obtained by stimulation.

Three experiments have shown that the performance of behavior evoked by electrical stimulation of the brain is positively reinforcing. In behavioral tests, Roberts and Kiess (1964) evoked attack behavior in cats by stimulation of the lateral hypothalamus. They found that during stimulation these cats would learn to run a Y-maze to obtain a rat which could be attacked and killed. No attempt was made to eat the dead rat. Attack did not occur in the absence of stimulation. Roberts and Carey (1965) evoked gnawing without hunger effects by stimulating the rat hypothalamus. These rats learned a Y-maze and a black-white discrimination to obtain a piece of wood suitable for gnawing. Caggiula and Hoebel (1966), in the only study that used the two types of experimental designs, found a point in the posterior hypothalamus where self-stimulation was increased in rate following testerone administration, constant stimulation evoked copulation with receptive females, and the rats would press a bar during constant stimulation to obtain access to a female rat. While it is not certain that these two sets of experiments involve the same type of mechanism, Glickman and Schiff's theory would predict that each condition would result in facilitation of activity in the motor systems organizing the response sequences and consequently would be reinforcing. It should be noted that they regard "the conventional primary reinforcing agents as stimuli which, during proper drive states, possess unusual ability to control such motor path facilitation" (Glickman and Schiff, p.34).

Although several studies (Brown and Cohen, 1959; Delgado, Roberts and Miller, 1954) have shown escape or avoidance learning with brain stimulation, none have analysed or related evoked escape behavior with self-stimulation. There is, however, a crude overlap between certain "fear" sites (Ursin and Kaada, 1960) and sites eliciting escape self-stimulation (Wurtz and Olds, 1963) in the amygdala. All but one of the studies demonstrating a covariation of evoked and reinforcing effects have stimulated only regions in the hypothalamus. In addition, the evoked effects were very complex approach kinds of behavior. It is still not established whether or not covariations will appear with any regularity with extra-hypothalamic sites and/or simple motor behavior such as head movements or locomotion. Some points that yield evoked behavior may be neutral in the sense that they will support neither self-stimulation nor escape behavior. Penfield (1954) and Delgado (1952, 1964) have indicated that stimulation does not always have a "**concomitant** emotional component".

Purposes of the Research

The purposes of the present research were two-fold. The functional organization of behavior patterns in the rat hypothalamus has received considerable attention from many workers as indicated in the Introduction (see also Brobeck, 1960). The same can also be said of the study of "hypothalamic substrates of reward" (Olds, 1962). Since there is little information on the functional organization of behavior patterns outside the hypothalamus, an exploration of the brain stem, particularly extra-hypothalamic sites, using electrical stimulation was undertaken. The first experiment investigated evoked behavior with reference to that peculiar to the rat and to comparative data on behavior similar to that evoked in the chicken, cat and monkey. The second experiment examines the relationship between evoked behavior and self-stimulation also with particular emphasis on extra-hypothalamic structures.

CHAPTER TWO

EXPERIMENT ONE: Behavior Testing

METHOD

Subjects

The subjects were 50 male hooded rats weighing from 200 to 425 grams.

Surgical and Histological Procedures

Using a stereotaxic technique, from one to five, usually two, bipolar steel electrodes were implanted while the subject was anesthetized with Nembutal. Atropine sulphate was injected intramuscularly at the start of the operation to inhibit mucous secretion in the respiratory pathway. The electrodes were embedded in a mound of dental cement moulded over stainless steel screws mounted in the skull. At the conclusion of the operation, penicillin was administered intramuscularly. At least two weeks were allowed for recovery. Over periods of up to eight months, the subjects did not show any side effects attributable to the operation or presence of the electrodes. A total of 110 points in the striatum, diencephalon, midbrain and a few points in the hippocampal formation were explored.

At the conclusion of the experiments, the subjects were perfused with 10% formalin solution while under deep barbiturate anesthesia. The brain was removed and stored in formalin for at least one week. Frozen sections of the brain were cut at a thickness of 40 microns. Every second or third section through the electrode tract was kept. The majority of sections were stained with cresyl violet. A few were stained with thionin. The location of the stimulating tips of the electrodes was verified independently on two occasions without knowledge of the behavioral or self-stimulation effects of specific electrodes.

Electrodes and Stimulation Parameters

The electrodes were made from twisted Nichrome wire 0.010 in. in diameter and were completely insulated except for the cross-sectional area of the tips. The tips were separated from 0.5 to 1.0 mm. The electrodes were constructed by soldering male Amphenol connectors (17-766-02) to the ends of a four inch length of Nichrome wire with the insulation removed for about 3 mm. at each end. Placing the connectors side by side, the wire was twisted from the center. Dental cement was moulded around the base of the connectors forming a rigid assembly for mounting in the stereotaxic instrument. Each electrode was checked with a voltmeter and a saline solution to make certain there were no breaks in the insulation. If any leaks were found the electrode was coated with epoxylite and baked in an oven. This process was repeated if necessary.

The stimulator was a Grass Model S4 set for biphasic square wave pulses of 0.1 msec. duration. Frequencies of 5, 20, and 200 pulses per second were used. At each frequency voltages of 1.5, 3, 5, 7, and 9 volts were used. Occasionally other voltages were also used. Leads to the animal were attached to the male connectors by means of Amphenol female connectors (17-763-02).

Apparatus

The behavior testing platform measured 20 x 30 in. and had a wall 4 in. high around the perimeter. The floor was covered with sawdust. A plywood insert was used to cover the sawdust in some tests. The behavior testing situation is shown in Figure 1.

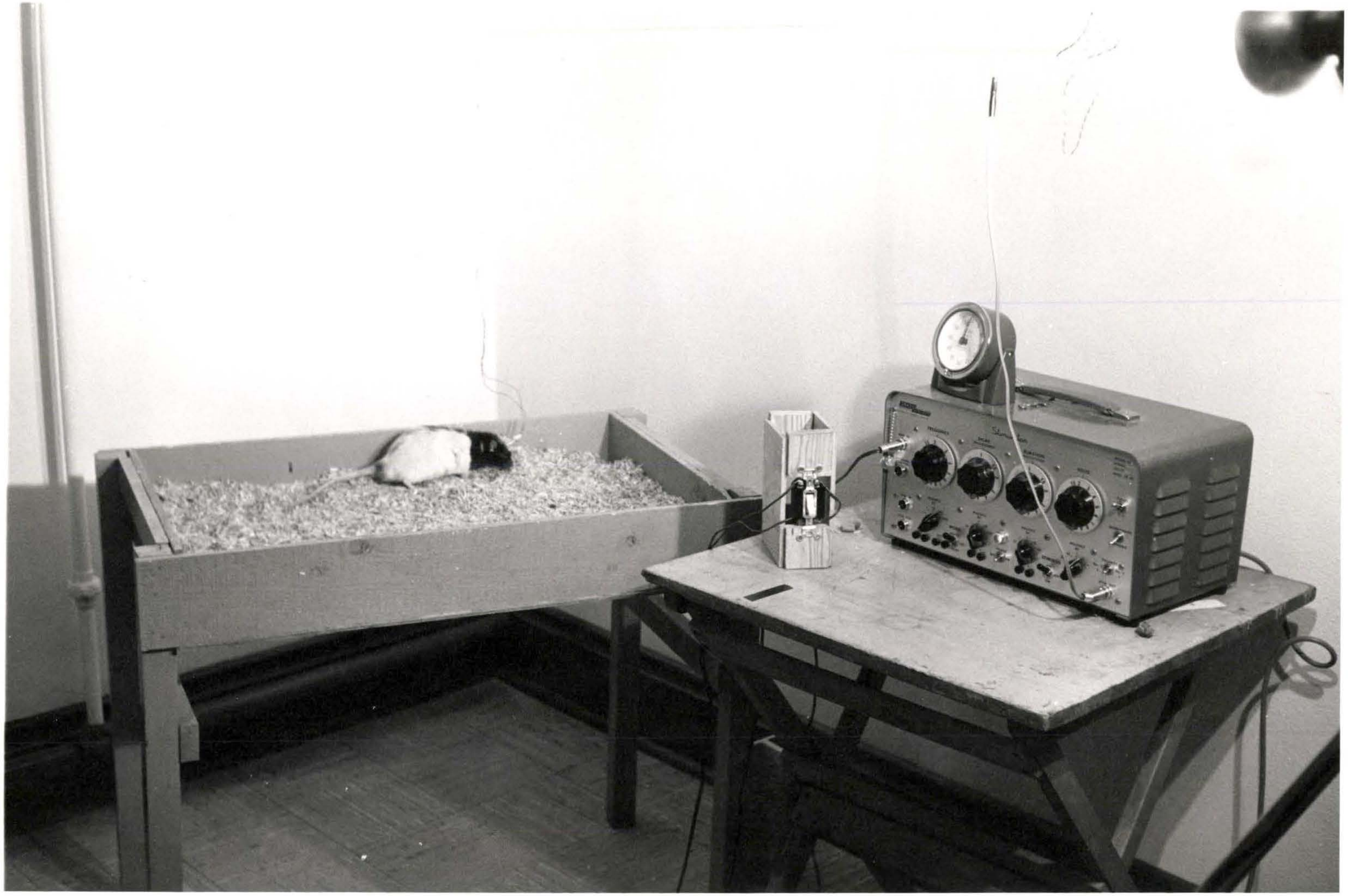


FIGURE 1

Experimental arrangement for behavior testing.

Procedure

The subject was placed on the test platform for 10 minutes before stimulation was started. Each site was stimulated at least twice at each frequency (5, 20, 200) and voltage (1.5, 3, 5, and 9) combination that evoked behaviour. Pulse trains were of 15 or 30 sec. durations. There was an interval of at least one min. between pulse trains. Many animals were re-tested on later occasions, some after intervals of several weeks. On occasion, stimuli such as other rats, food, paper strips, and obstacles were presented during a test. Detailed written records were made of the evoked behavior and in some cases motion pictures were taken.

RESULTS

Observation of behavior evoked by electrical stimulation of the brain is facilitated by a sound knowledge of behavior in the normal animal. Some of the following descriptions of evoked behavior are supported by descriptions and observations made on rat behavior as it occurs under normal physiological conditions. Comparison and contrast of evoked and normal behavior also gives a clearer picture of the degree to which electrical stimulation does or does not evoke behavior like that occuring normally.

Electrical stimulation of the brain stem produced motor responses of some sort in all but one of the 110 loci tested. The site not yielding a motor response when stimulated was infected at the time of perfusion and it was not possible to identify the neural tissue in the region of the tips. Although infection may have been the reason for the lack of an effect, a few other sites showing evidence of infection, but to a lesser degree, did not exhibit any apparent differences in their evoked effects. Since experimental animals usually survived for long periods, it is probable that the infections developed after behavioral testing was complete. Because there were no differences in the thresholds and general characteristics of the behavior evoked by stimulation of these sites, they are included in the histological composites.

The results will be presented primarily in terms of functional or behavioral categories. Each of the responses to be reported was evoked several times from a given animal. Re-testing on subsequent days and weeks showed that the evoked response remained stable over time, as has been noted by others (Delgado, 1964). However, slight changes in stimulus intensity required to evoke a response and in details of the response were evident in some animals re-tested after several weeks.

Circling

Electrical stimulation of wide areas of the striatum, diencephalon and midbrain produced a class of responses which were called circling. In the majority of subjects circling consisted of walking or running in a circle to the side opposite the brain electrode (contraversive circling). Some subjects were found that circled toward the side of stimulation (ipsiversive circling). The directional component of circling behavior will be discussed below.

Circling behavior ranged from exploratory-like behavior at one extreme to forced plodding, quite unlike natural walking at the other extreme. In between these two extremes, a virtually continuous range of intermediate forms was observed. It was possible, however, to take a few basic features of circling behavior, form categories on the basis of those features, and still cover the class quite well. The categories of circling behavior used were: exploratory, simple, intermittent, and backwards circling.

With changes in stimulation parameters, stimulation of a given neural site frequently evoked more than one category of behavior. In the appendix, several instances of this can be seen in A and B summary tables. For this reason, the categories are not differentiated in the composite diagrams of the electrode sites. Usually, however, increasing the intensity of stimulation in the steps used resulted in a gradual development of the response without a great change in the form of the response. For example, the latency of the appearance of the response could shorten, duration lengthen, or speed of circling could increase with increases in stimulus intensity.

The exploratory-like circling was a response in which the animal walked around the test platform sniffing, rearing, looking around, peering over the edge of the test platform, and approaching objects placed on the test platform. A common pattern consisted of forward walking with frequent "bursts" or peaks of exploratory activity. One particularly good example was observed in a rat that walked the length of a side of the test platform, peered over the edge, walked on to the next corner, peered over the edge, and so on, as long as stimulation was continued. These exploratory circling responses were determined in part by external stimuli as indicated by the approach to objects presented in the test field and by peaks of activity occurring in the corners of the platform.

The responses comprising the simple circling category consisted of continuous, well-coordinated walking or running in circles. These subjects did not approach objects placed in the test field. The circles were generally large with diameters from 1.5 ft. to the limits of the test platform. This response was in most respects very difficult to distinguish from normal locomotion.

The distinguishing feature of the third category of responses was that circling occurred in an intermittent or stepwise manner with pauses up to several seconds between movements. While the rat was pausing, a static position was maintained with curvature of the trunk and with the head turned in the direction of the circling. The circles were generally small and usually the hind legs were located as a pivot or center around which the animal turned. Most of the turning was brought about by the front legs and by trunk curvature. The hind legs followed turning with a short delay giving the appearance of being a postural adjustment. Animals falling in this group were less able to avoid obstacles placed in their paths and turning was either delayed or prevented if the side to which they were turning was close to the walls of the test platform.

The circling responses in the above three categories were basically forward locomotion with turning in one direction only. The fourth category consists of backward locomotion with pronounced circling. The response consisted of rapid backward running in circles away from the side being stimulated, that is, in the contraversive direction. Flexion of the neck and trunk similar to that sometimes observed when rats are shocked on the feet (on a grid) or on the snout was characteristic of this response. Urination, defecation, and vocalization were often associated with backward circling. This backward circling is clearly related to the escape behavior discussed below.

The large majority of circling responses were in the contraversive direction. However, stimulation of about twenty sites evoked turning or circling in the ipsiversive direction. Several of the electrode placements from which ipsiversive circling was obtained were ventral placements near the midline. The rest were ventral placements located more laterally. Four of these were located in the region of the medial lemniscus and substantia nigra. No dorsal lateral or dorsal medial placements yielded ipsiversive circling.

Most responses tended to fatigue, that is, to die out or decrease in strength, both as a function of train duration and rate of train repetition. All the circling responses were "forced" in the sense that they were highly stimulus dependent. That is, circling started shortly after stimulus onset and ceased virtually simultaneously with stimulus offset.

The neural sites from which forward circling was evoked are illustrated in Figures 2* and 3. Figure 4 shows sites from which backward circling was evoked.

Table A of the appendix summarizes circling behavior and the anatomical sites associated with each evoked effect. There does not appear to be any simple relation between the categories and anatomical locus that would allow anatomical generalizations to be made.

A variety of postural reactions, probably both primary and secondary effects of stimulation, and turning phenomena involving rotation of the head and trunk, extension or flexion of the neck and limbs, and unusual limb positions often were associated with circling behavior. These features have been included under the heading "superimpositions" in Table A of the appendix.

* abbreviations for all brain diagrams are on the following page

Circling did not occur at a frequency of 5 pps in the range of voltages tested. Each category of the circling behavior was obtained with frequencies of 20 and 200 pps. The voltage required to evoke a circling response at a frequency of 200 pps was approximately half that required at a frequency of 20 pps. There was no substantial difference in thresholds for the four categories as is shown in Table 1.

* ABBREVIATIONS FOR BRAIN DIAGRAMS

Diagrams after Konig and Klippel (1963). Anterior-posterior levels in mm. with reference to interaural line are given above each diagram,

A = Anterior
P = Posterior

A = amygdala
BCI = brachium of inferior colliculus
CC = crus cerebri
CI = inferior colliculus
CP = caudate putamen nucleus
CS = superior cerebellar penduncles
DG = dentate gyrus
F = fornix
FF = Forel's Fields H_1 and H_2
FL = fasiculus longitudinalis
FPT = fibrae pontis traversae
FR = fasiculus retroflexus
FT = fasiculus mammillo-tegmentalis
G = medial geniculate body
GP = globus pallidus
H = hypothalamus

HI = hippocampal formation

HV = ventral hippocampal commissure

IC = internal capsule

IP = interpeduncular nucleus

L = lateral nucleus

LL = lateral lemniscus

LP = lateral posterior nucleus

M = medial thalamus

MB = mammillary body

MFB = medial forebrain bundle

ML = medial lemniscus

P = posterior nucleus

PF = parafasicular nucleus

R = reuniens nucleus

RF = lateral reticular formation

RH = rhomboid nucleus

RU = red nucleus

S = septum

SC = superior colliculus

SM = stria medullaris

SN = substantia nigra

T = mammillothalamic tract

TS = tractus tectospinalis

V = ventral nucleus

VM = ventromedial nucleus

ZI = zona incerta

Escape Behavior

It is possible to relate a number of responses in a class of escape-like behavior. The dominant components of escape behavior were running, jumping, and vocalization. One important difference between escape running and the running of circling was that the escape running was not direction specific, that is, the rat could run in any direction. Freezing and attempts to leave the platform often occurred

FIGURE 2

Composite frontal diagrams showing sites from which stimulation evoked forward circling. Anterior placements. Sites are indicated by triangles. Abbreviations for all diagrams are given on page .

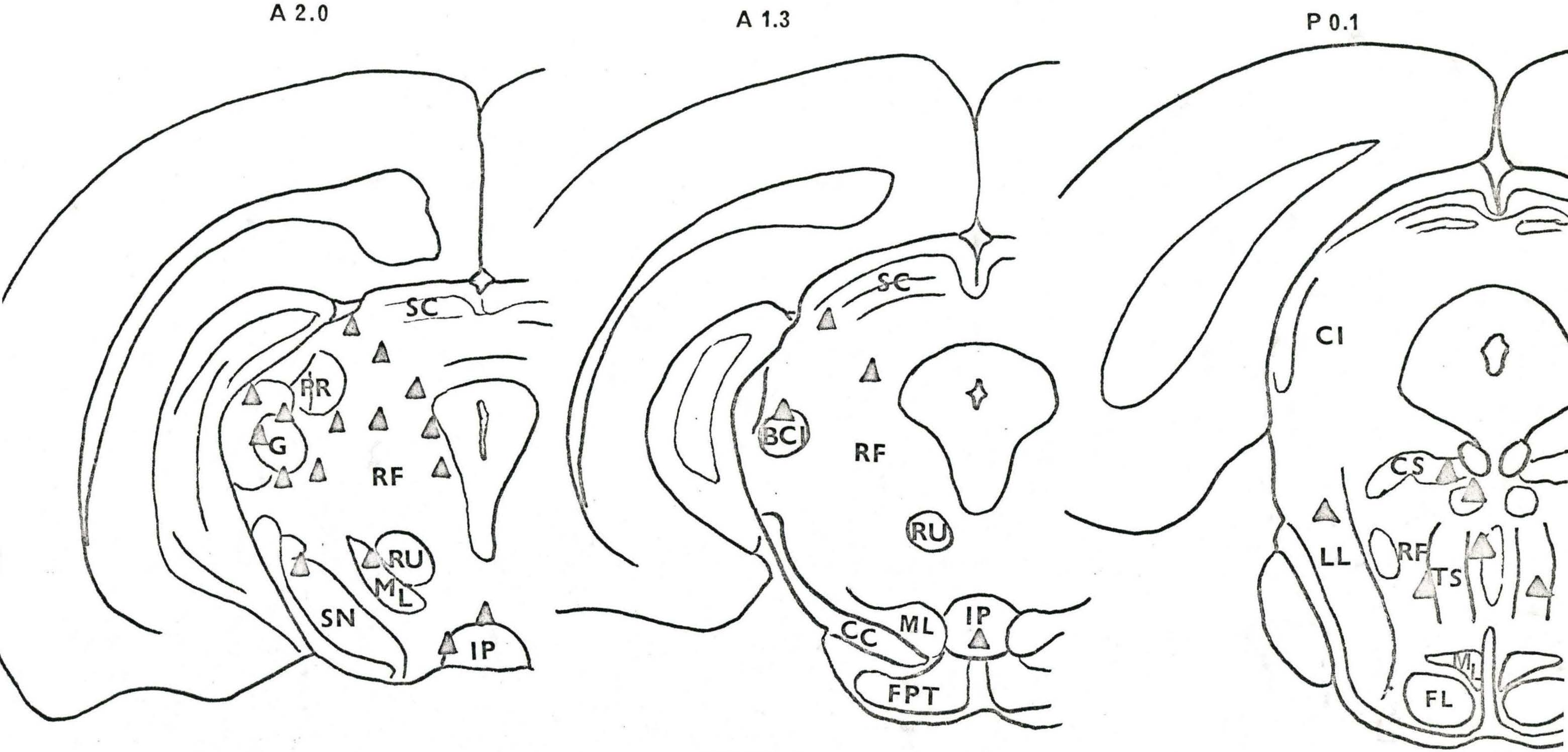


FIGURE 3

Composite frontal diagrams showing sites from which stimulation evoked forward circling.

Posterior placements.

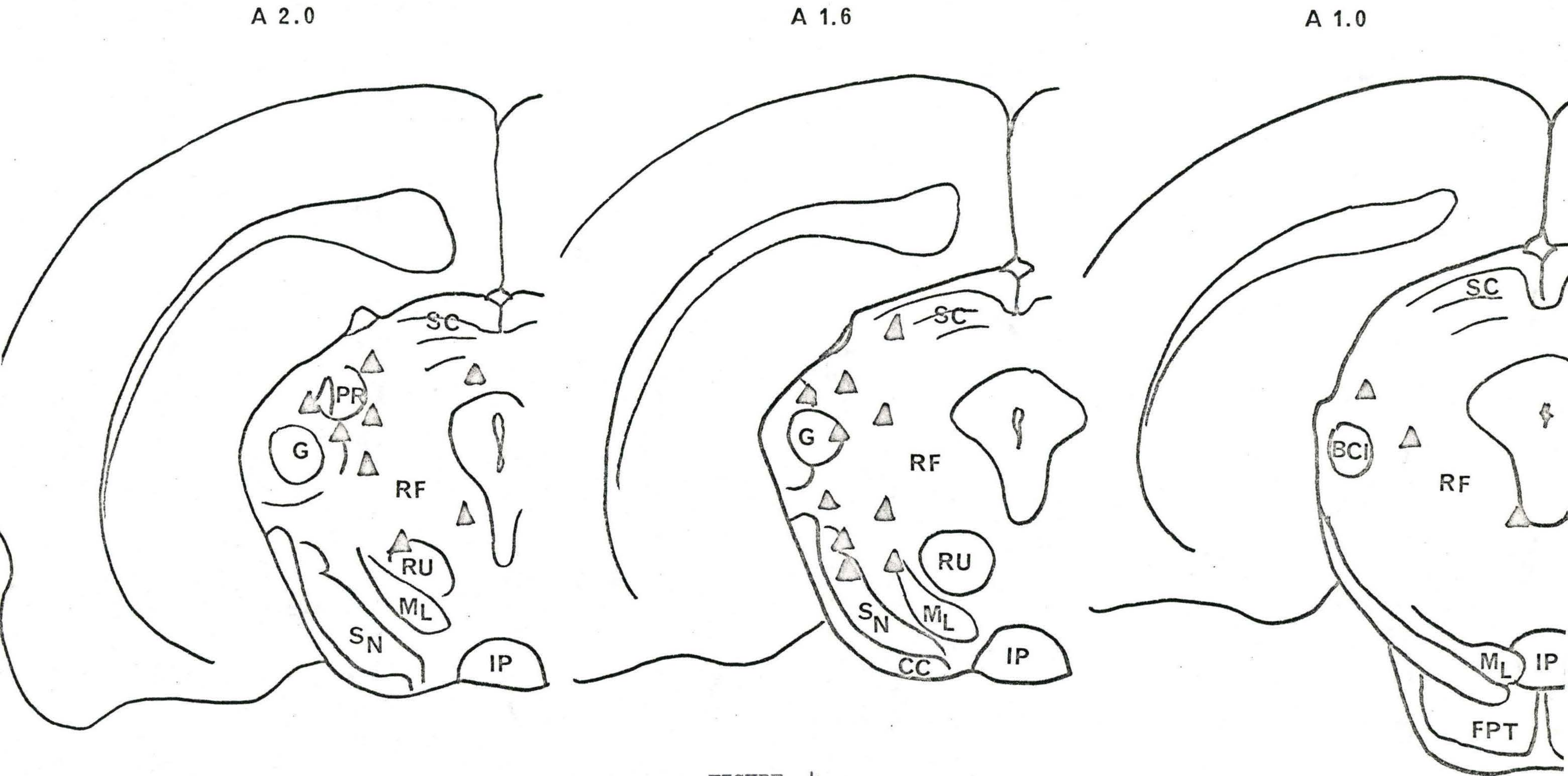


FIGURE 4

Composite frontal diagrams showing sites from which stimulation evoked backing.

TABLE I

Average Voltages for Appearance of First Circling Responses

Category	Exploratory		Simple		Intermittent		Backwards	
N	4	8	28	35	16	18	8	9
Frequency	20	200	20	200	20	200	20	200
Mean	7.3	3.8	7.4	3.0	5.5	2.7	7.0	2.7
Range	5-10	1.5-9	3-15	1.5-7	3-10	1.5-7	3-9	1.5-7

when stimulation ceased unless, of course, the rat had already escaped by a jump off the platform. Other responses indicative of aversive stimulation such as widening of the palpebral fissure, urination and defecation usually occurred.

A stimulation aftereffect, lasting several seconds much like a "running fit" occurred in some animals which jumped off the test platform. In a "running fit" the animals ran rapidly around on the floor banging into table legs and walls only to stop abruptly after several seconds and remain crouched in a corner. This running had an additional characteristic typical of seizures. The attack could not be re-elicited for a considerable period of time, often for several hours.

Backwards running in circles also is related to escape behavior in that the above indices of aversiveness, including vocalization, but not jumping, are associated with this response.

Five animals exhibited both backward and forward movements during the same stimulation train. This appeared to be an interaction with evoked running and evoked backing alternately gaining dominance. Higher intensities of stimulation evoked a strong escape response from three of the subjects and backing from the other two of these five subjects. Here it appears that one response gained dominance entirely over the other. Four of the sites from which this effect was evoked were very caudal in the brain stem in the lateral reticular formation at the level of the pons. The electrode in the fifth rat was in the periaqueductal grey and nucleus interstitialis adjacent to the lateral reticular formation.

Jumping occurred frequently and was always associated with behavior suggesting aversive stimulation. The jumping response was often very explosive and was not directed toward a particular landing area. Since animals were tested on an elevated platform, the possibility that jumping was in part due to the elevation cannot be overlooked. One subject who jumped from the platform did not exhibit jumping when tested on a large open area of floor. However, there were animals who exhibited escape behavior but did not jump off the platform.

Vocalization was evoked only as a component of escape reactions. Vocalization ranged from barely audible "peeping" to loud continuous squealing. It varied both with anatomical location of the stimulating tips and intensity of stimulation. Vocalization also occurred as an aftereffect of stimulation eliciting escape behavior.

Table B of the appendix summarizes escape behavior. Escape behavior was evoked by stimulation of structures throughout the midbrain including the superior colliculus, medial geniculate body, lateral reticular formation, red nucleus, medial lemniscus, and substantia nigra. Figure 5 is a composite of the neural sites from which stimulation elicited escape behavior.

Grooming Behavior

Stimulation of several brain stem areas elicited components of grooming or self-care behavior. Two of the evoked behaviors, grooming of the back, and face washing are part of the normal, stereotyped grooming behavior of the rat which includes grooming of the fur by licking and brushing the fur with the front paws, face washing, and scratching with a hind leg. Normally, each of these components will occur in a sequence of grooming. The third self-care-behavior is the "shaking response" which consists of a series of rapid side to side movements of the head and trunk plus (probably) lateral movements of the skin.

Stimulation of the superior colliculus and pretectal area produced grooming of the back in four subjects. In the normal animal, the basic posture for grooming of the back is with trunk erect, support from the hind legs, and turning of the head and shoulders to the side being groomed. From this position,

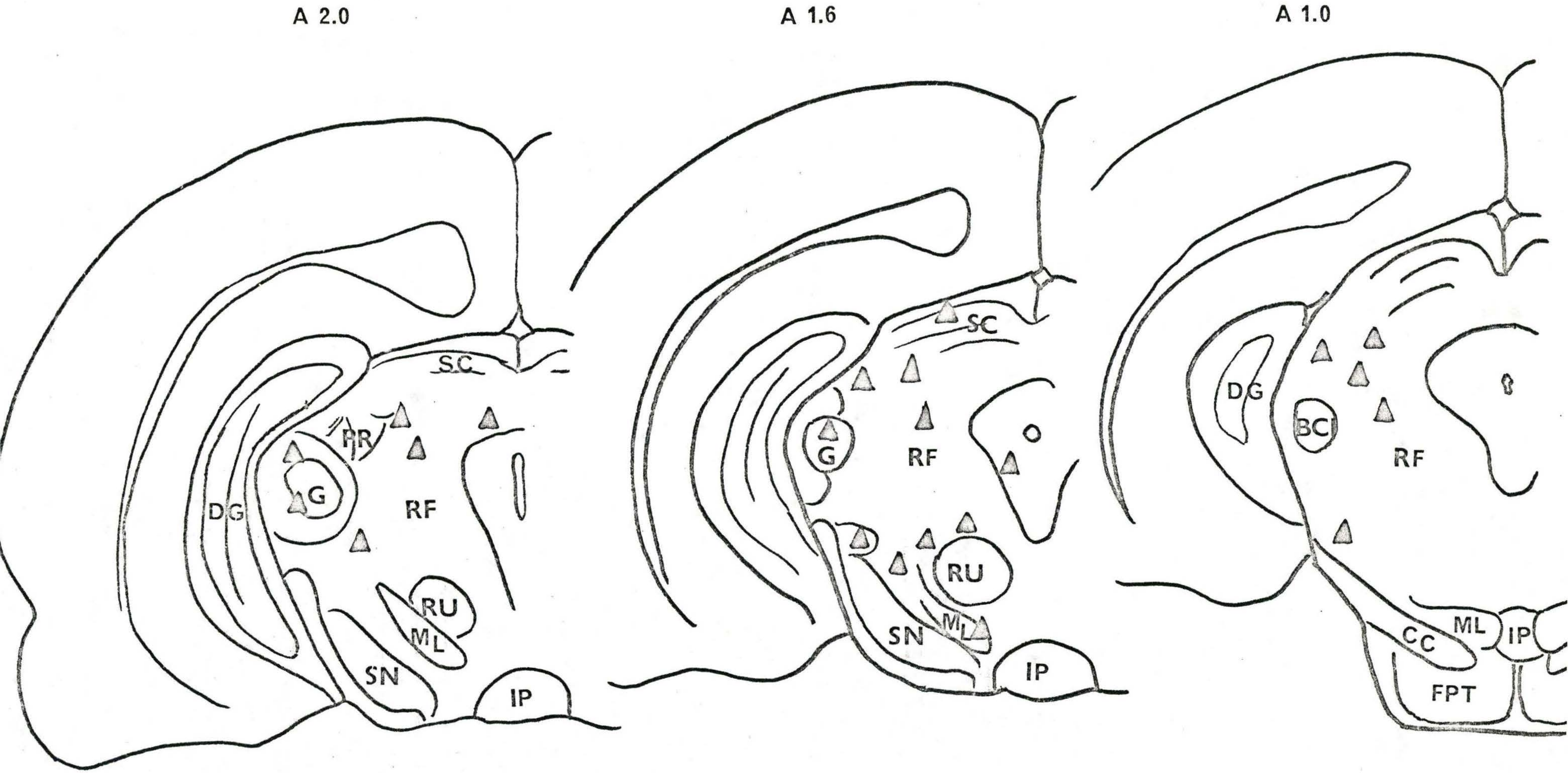


FIGURE 5

Composite frontal diagrams showing sites from which stimulation evoked escape behavior.

the rat licks and brushes the fur of the back for several seconds. The evoked response was virtually the same in all four subjects. Jaw movements and phasic head and limb movements occurred directed toward the region of the back opposite the side of stimulation. Initially, the foreleg on the side being groomed was extended while the paw of the other leg grasped the fur of the extended leg as can be seen in Figure 6. Next, both forelegs usually brushed the fur of the back while the rat made chewing and licking movements. The evoked response differed from the normal in that the grooming was directed to only the upper part of the back and the phasic movements were not as rapid or of as long duration as in the normal response. An interesting feature of this response was that if the animal was in the act of face washing and the stimulation was turned on, there was a more or less perfect transition to grooming of the back. This was in contrast to stimulation applied while other behavior was occurring. Usually when stimulation was applied the animal had difficulty assuming the adequate posture on its hind legs and often lost its balance. At levels of stimulation below those which evoked grooming, head turning and circling to the side opposite the stimulating electrode were obtained. Figure 7 shows the superior colliculus-pretectal area from which grooming was evoked.

FIGURE 6

Photographs of evoked grooming of the back.

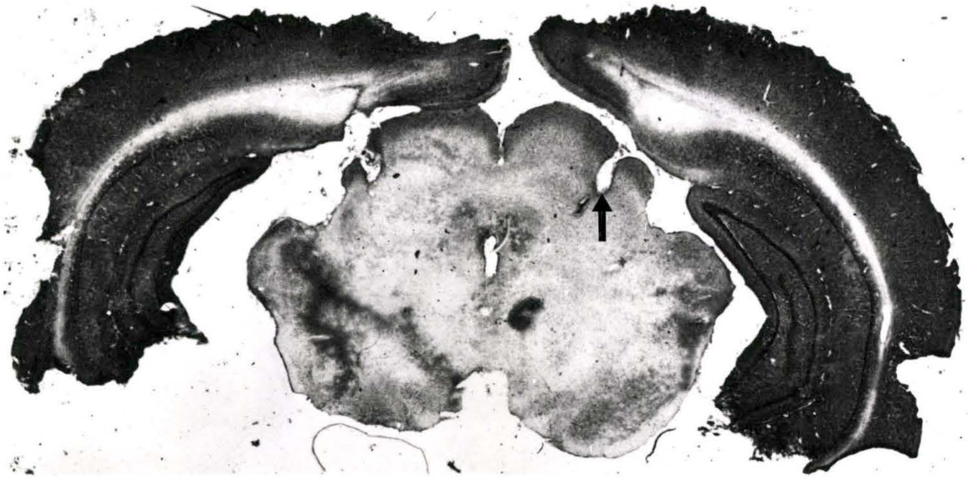


FIGURE 7: Photomicrograph of a frontal section showing the superior colliculus - pretectal area from which grooming of the back was evoked (top).

FIGURE 8: Photomicrograph of a frontal section showing a similar locus from which grooming was not evoked (bottom).

Figure 8 shows a similar locus from which grooming was not evoked.

Components of the above grooming response were evoked by stimulation of different areas in three other animals. These areas were the caudate/putamen nucleus, the region of the amygdala and cerebral peduncle, and the lateral reticular formation. The basic posture with trunk erect, support from the hind legs and contraversive turning of the head and shoulders was present in each of these animals during stimulation. However, the direct head and limb movements were lacking in these responses.

A second class of evoked grooming response was face washing. In the four animals from which this response was obtained there was not as high a degree of organization or precision of movement as was observed in some of the animals who groomed their backs. The face washing response consisted of rapid bilateral, repetitive, but not synchronous, movements of the front legs with the paws near the mouth. Chewing and licking movements accompanied the foreleg response and the animals supported themselves on their hind legs. The paws were not placed in the mouth or actually licked except by one animal. This exceptional animal put one paw briefly in its mouth a few times during stimulation. When examined after stimulation the paw was wet with saliva. An unusual feature of this animal's response was that before making the response the animal would sometimes pick up sawdust in its mouth or gnaw on the wood of the test platform. This rat did not eat when given access to food during and after stimulation indicating that the chewing was not food motivated. The electrodes producing face washing were located (in different animals) in the posterior hypothalamus, the pretectal group of nuclei, substantia nigra, and the lateral reticular formation bordering the periaqueductal grey at the level of the inferior colliculus.

A third class of grooming response which was obtained, has been called shaking. Although shaking responses have not been studied previously and are not well-known, they appear to occur very frequently during normal behavior. The response can be produced physiologically by sprinkling water or sawdust on the head and back of a rat. The response consists of rapid cyclic movements of the head or entire body from side to side. Shaking of the head alone occurs more often than shaking of the entire body in the normal animal. In contrast, the shaking evoked by electrical stimulation was predominantly shaking of the entire body.

The variables responsible for eliciting shaking are not fully known, but under some conditions it occurs at a high rate. In normal rats the response removes dust from the fur after digging or nest building. However, the response also occurs spontaneously. In a naive female and a male, shaking occurred at the rate of 50 and 74 per hour respectively (observed for a one half hour period). It is possible that the rate could be related to other behavior or to endocrinological changes. Observations of a post-partum female indicated that shaking occurs at a very high rate even when the female was not nest building. The rate of 128 per hour, mainly head shaking, was the same with or without the presence of the pups in tests conducted one week after birth of the pups. Five weeks after the birth of the pups, shaking in this female occurred at the rate of 66 responses per hour. The above observations are summarized in Table II.

Shaking evoked by electrical stimulation of the brain differs from physiological shaking in two quantitative respects. The evoked shaking almost always involved the entire body rather than mainly the head only as was the case in the normal response. The evoked shaking was also much more vigorous. Once initiated by an electrical stimulus, shaking responses would continue intermittently for as long as eight minutes in some cases. The shaking responses elicited by stimulation of the brain occurred during stimulation but were most often an aftereffect occurring

TABLE II

Shaking Response per Hour in Normal Rats

	Post-Partum Female		Naive Female	Naive Male
	1 week	5 weeks		
Pups present	128			
Pups absent	128	66	50	74

first at stimulus offset. "Bursts" of shaking become less and less frequent as a function of time from stimulus offset, but the character of individual "bursts" did not change.

Frame by frame analysis of 8mm film exposed at 16 frames per second showed that the evoked shaking response had a duration of less than half a second. The shaking occurred at a rate of about five cycles per second where one cycle was defined as movement of the body to the right, back to the starting position, movement to the left and finally back to the starting position. There were no pauses in these movements.

Tests with one animal showed that even with frequent stimulation, the response could be evoked reliably and repeatedly. Stimulation for ten seconds every minute for 30 minutes on two successive days evoked body shaking following 90% of stimulus applications on day one and 80% of the applications on day two. In half hour pretest periods, shaking occurred 12 and 14 times respectively but these were virtually all head shaking responses. In the test periods the head shaking tended not to occur. The intensity of electrical stimulation used in these tests was just above threshold for the appearance of the response and most stimulations at higher intensities are followed by a series of shaking responses.

Anatomically, shaking was evoked by stimulation of limbic system structures including the hippocampus, dentate gyrus, subiculum, fornix, septal nuclei, diagonal tract of Broca, and the pyriform cortex. The ten sites from which shaking was evoked are shown in Figure 9.

Exploratory Behavior

Exploratory behavior has been discussed above in relation to circling behavior. The exploratory behavior evoked by stimulation of the brain stem consisted of rearing, increased general activity, sniffing, approach to objects placed in the test field, and visual searching. The specific sequence of response elements was variable and readily responsive to environmental stimuli. Circling bias was always present but could be overcome to the degree that objects presented on either side during a test were approached without difficulty. With increased intensity of stimulation, the exploratory behavior became more "agitated" and circling tendencies became more pronounced.

One response component of exploratory behavior under greater stimulus control was rearing, shown in Figure 10. This response occurred only in association with exploratory behavior but was not inevitably associated with it. The rearing response was observed in only 6 of 16 rats that exhibited exploration.

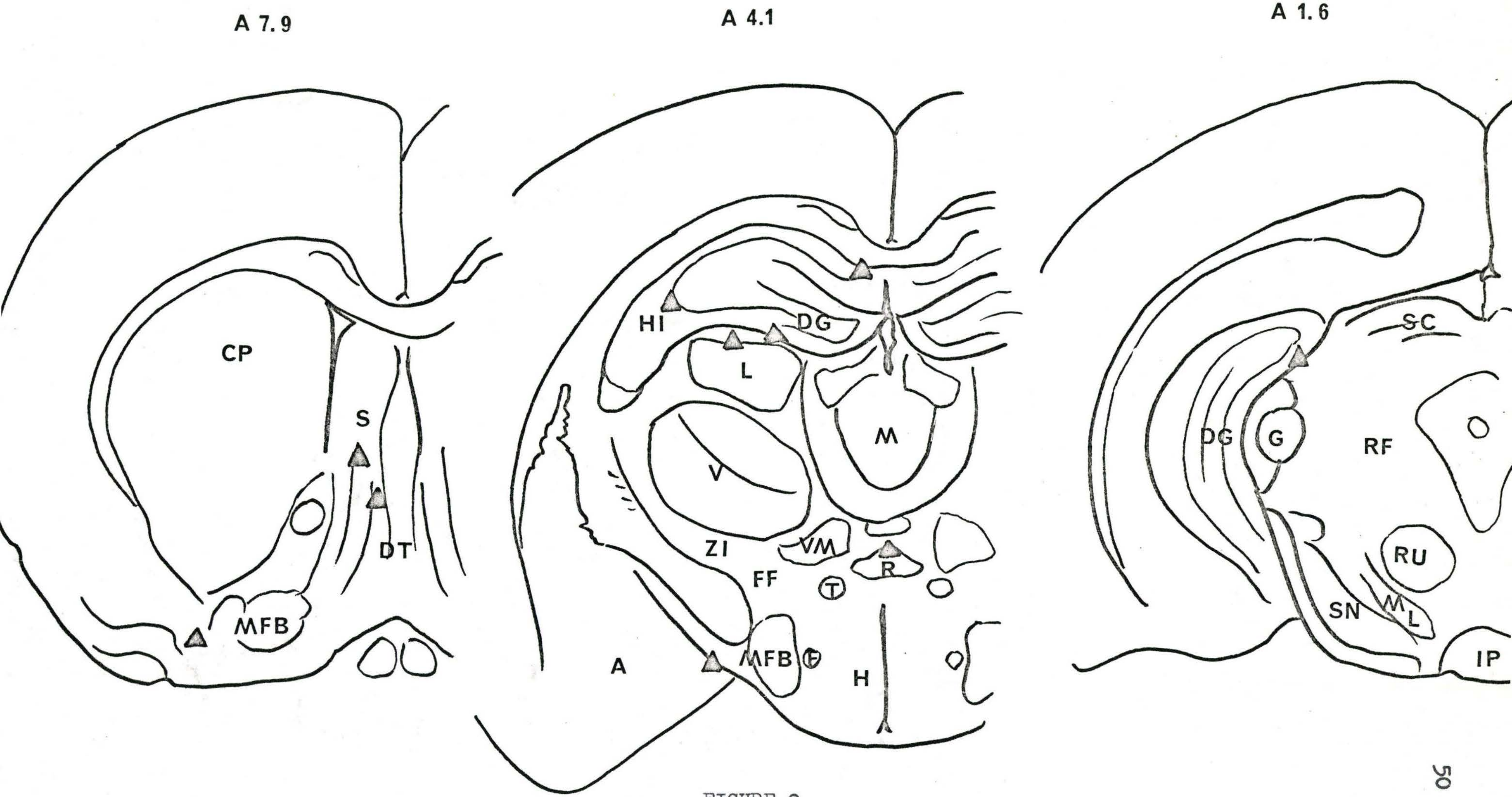


FIGURE 9

Composite frontal diagrams showing sites from which stimulation evoked shaking.

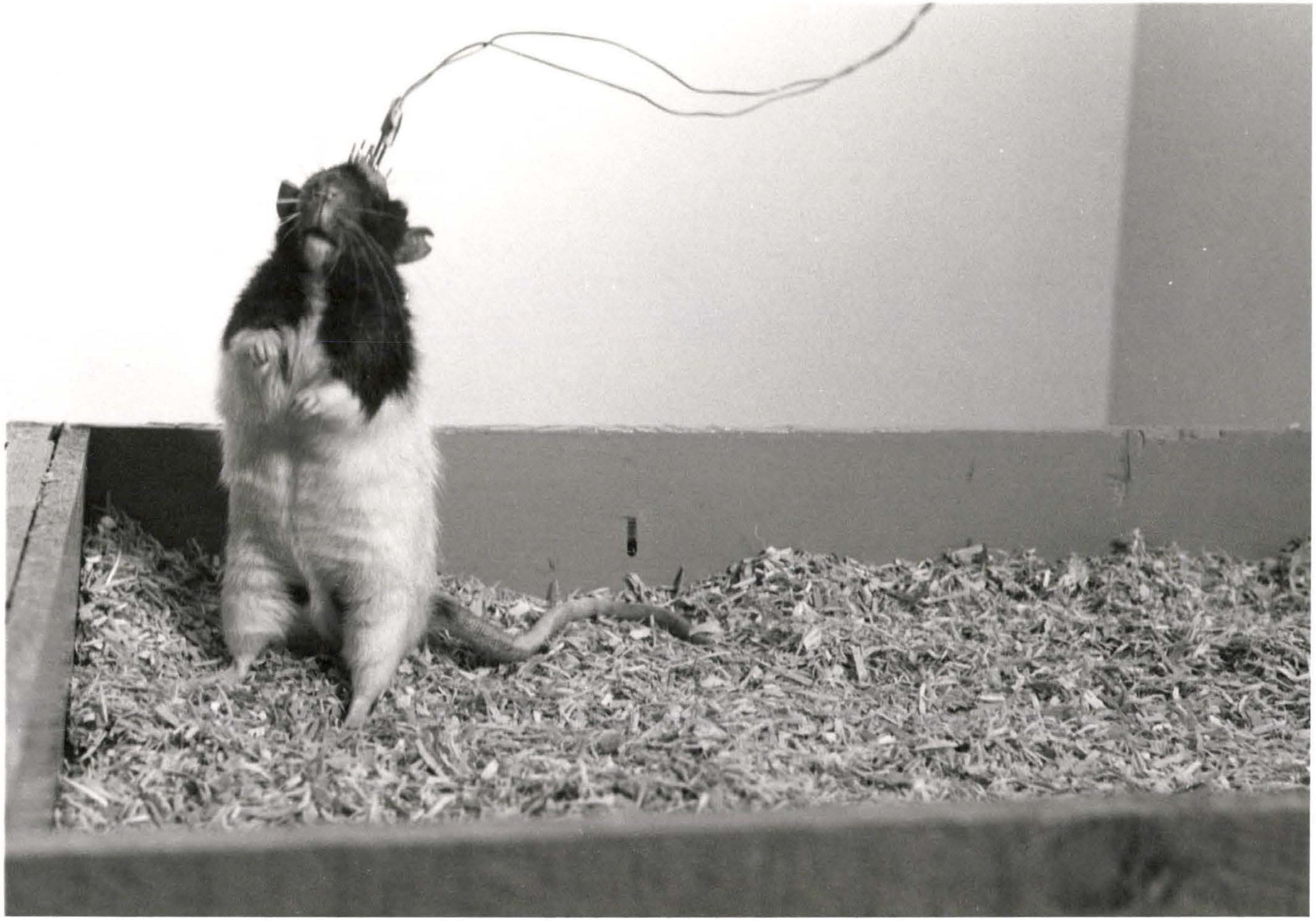


FIGURE 10

Photograph of the rearing component of evoked exploratory behavior

Rearing consisted of standing erect on the hind legs and holding the forelegs slightly flexed in front. The trunk and neck were noticeably extended with the snout held high in the air. Sniffing frequently occurred. Rearing occurred at stimulus onset with a latency of one second but was of short duration (1-2 sec.) and did not occur again during that stimulus train. Walking and sniffing occurred during the remainder of the stimulus train. With intervals of about one minute between stimulus trains rearing always occurred at the onset of each new train. At higher intensities of stimulation, the responses took on a more forced appearance, trunk and hind leg extension were exaggerated, and the erect position was held for several seconds.

Rearing was elicited by stimulation of the subthalamus and dorsal hypothalamus. Structures in the region of the tips included the reuniens, gelatinosus, and periventricular nuclei, and the zona incerta, medial forebrain bundle, and the fasiculus retroflexus (Figure 11).

Digging

Digging was evoked in two animals. Normal digging consists of three response patterns: alternating movements of the front legs which push sawdust under the belly, thrusting

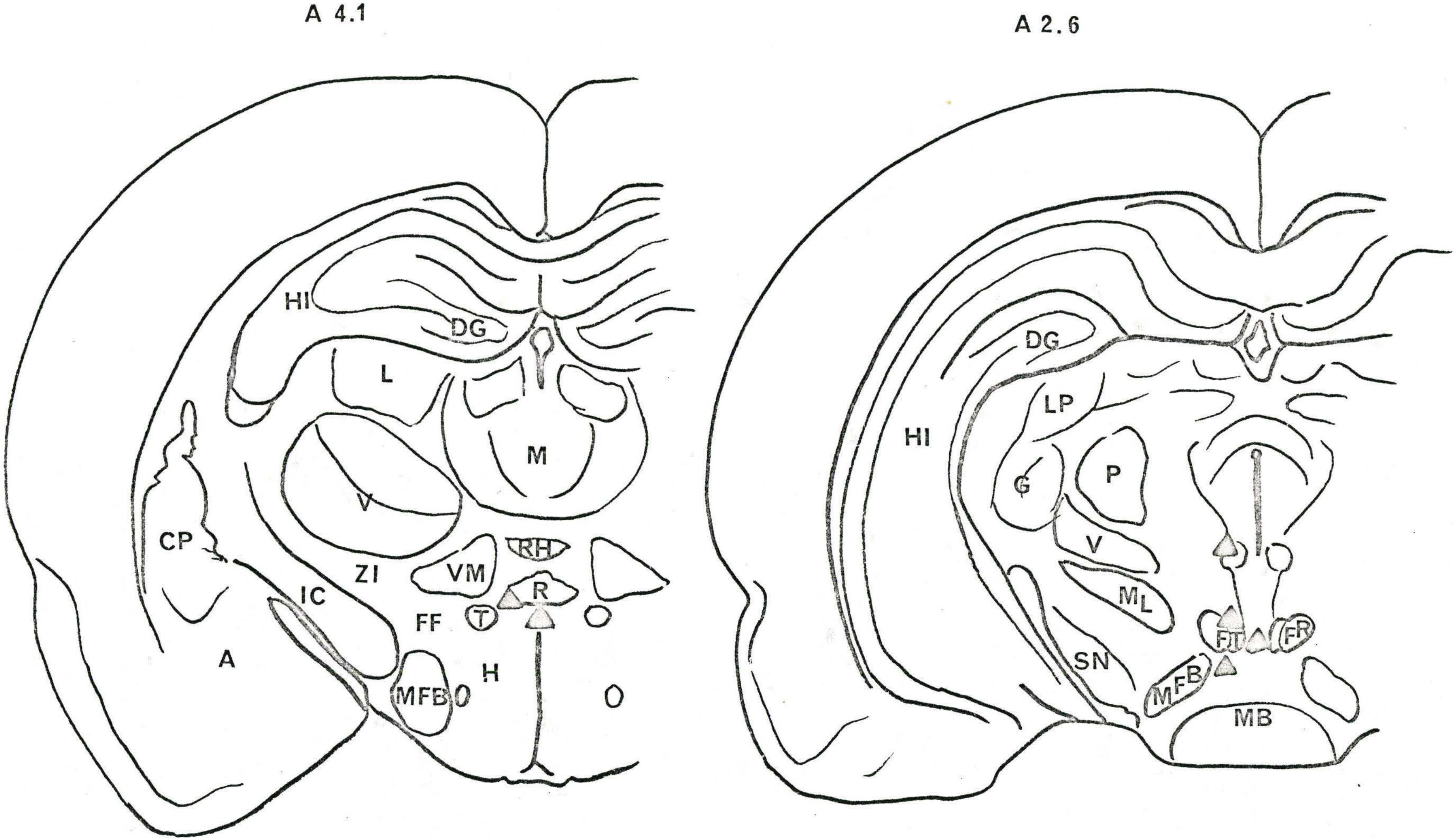


FIGURE 11

Composite frontal diagrams showing sites from which stimulation evoked rearing.

movements of the hind legs which move sawdust from under the belly to a point behind the rat, and alternating forward pushing movements of the front legs (Eibl-Eibesfeldt, 1961). The digging behavior evoked in the two animals consisted only of the first component of digging described. Figures 12 and 13 show the start of the evoked digging response and the maximum backward movement of the fore legs in the evoked response respectively. The response in the first case consisted of nearly continuous digging in the sawdust, while moving forward, for the duration of the stimulus. The maximum train duration applied was seven minutes. The first digging occurred 15 to 30 seconds after stimulus onset. If stimulation was continued the rat always stepped over the small pile of sawdust accumulated by the digging, walked several steps forward, and began digging a new hole. If the stimulation was terminated just when a pile of sawdust from digging was under the rat's belly, the second component of digging, the hind leg thrust, sometimes occurred.

This rat walked around or over obstacles during stimulation and did not respond selectively to paper strips, young pups, or other rats. When tested on a plain board floor no digging at all occurred but if small objects, such as

FIGURE 12

Beginning of digging movement produced by stimulation

FIGURE 13

Maximum backward movement of the front legs in the evoked digging response. The shallow depression (shadow) in the sawdust is the result of the evoked digging.

food pellets, were placed on the floor the rat approached them, pushed them backward with its front paws, and continued the exploratory behavior which was dominant in the absence of digging. The animal always turned in a contraversive direction near the edge of the test platform.

The second animal in which digging was evoked exhibited a somewhat different and less striking pattern of behavior. After a few seconds of stimulation, rapid, backward, alternating, digging movements with the front paws occurred. This was followed by a short burst of running and jumping such as was seen in escape behavior. Digging did not occur again in a given pulse train after the initial response. At lower intensities of stimulation, exploratory behavior occurred. Electrodes in both rats were located in the area of the reuniens nucleus, zona incerta and the dorsal hypothalamus as shown in Figure 14.

Seizure Activity

The final class of evoked behavior to be discussed did not have a counterpart in normal behavior. Seizure activity was evoked by stimulation of eleven sites. The seizures were

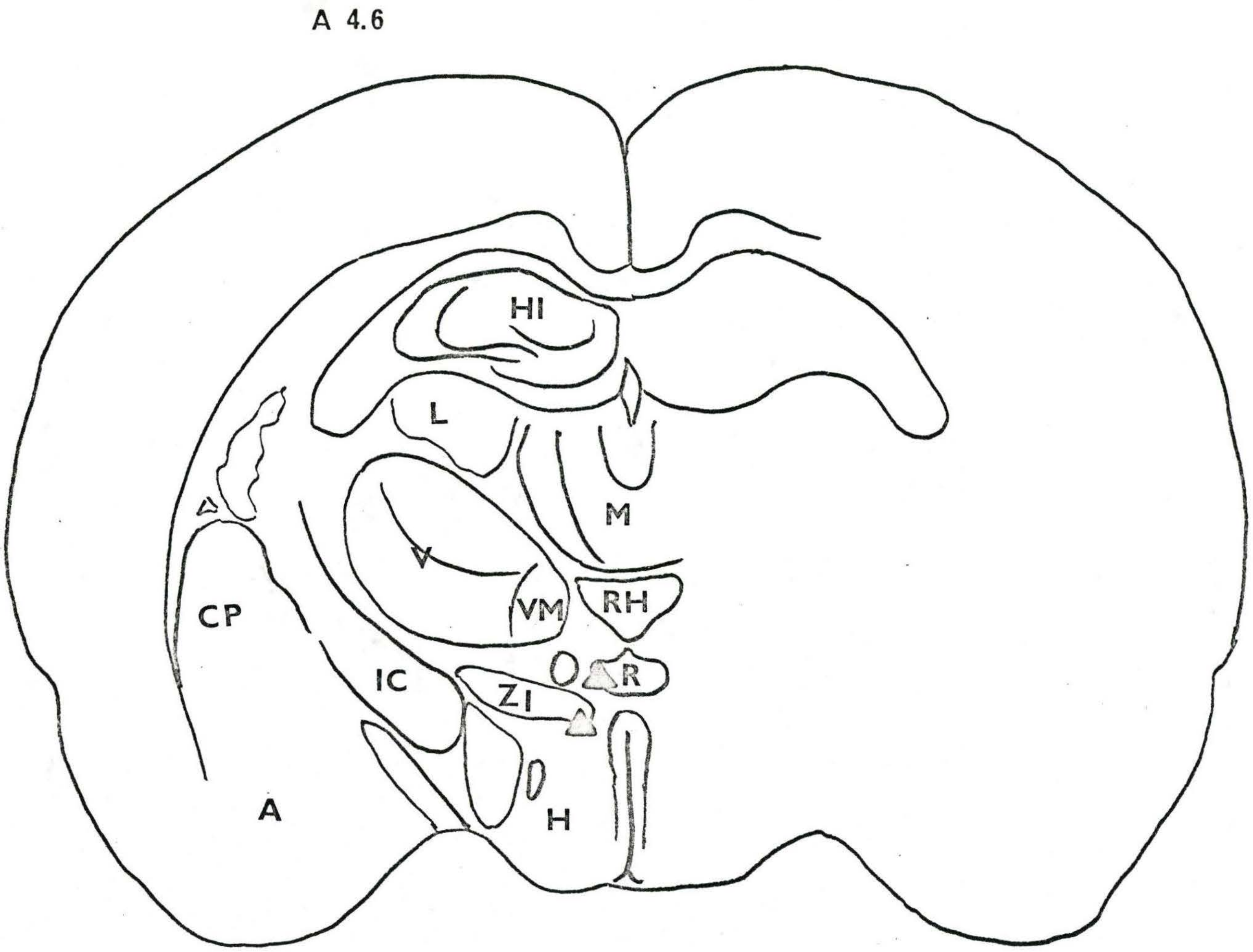


FIGURE 14

Frontal diagram of the sites from which stimulation evoked digging.

surprisingly uniform responses even though they were evoked from several different areas. The main characteristics of seizures were a gradual development and building up of motor activity, motor aftereffects, and an after effect lasting up to several hours during which it was not usually possible to evoke another full seizure.

The initial stages of a seizure consisted of head nodding and phasic movements of the front limbs. As these movements became more vigorous, the trunk was raised and chewing and facial movements developed. The head and trunk would continue to elevate until the animal lost its balance and fell over on its back or side. The animal would then right itself. If the stimulation was kept on after this response, seizure activity of less strength which was different from the original pattern sometimes occurred. When stimulation was terminated, the animal assumed a sitting position during which an after effect of head nodding occurred.

Many of the motor components of the seizure such as head nodding, chewing, and foreleg movements could be evoked from the same sites at parameters other than those which produced the seizures. Seizures were more likely to be evoked by stimulation of the caudate-putamen nucleus, septal nuclei, and globus pallidus than by stimulation of more caudal structures (Figure 15). Seizures were evoked by stimulation of 7 of 15 striatal sites, 3 of 19 diencephalic sites, and 1 of 76 midbrain sites. The midbrain site was in the medial gemiculate body and adjacent to the dentate gyrus and therefore the seizure may have resulted from stimulation of this gyrus rather than the brain stem. The threshold stimulation parameters were similar in all three areas.

Summary of Behavior Testing

The behavior testing showed that stimulation of wide areas of the brain stem can evoke a variety of the components of normal behavior of the rat. Generally, the evoked behavior was in the form of a large pattern that could be reliably evoked on every stimulus application. There was some variability in the details of the performance of the response from stimulus to stimulus due to environmental factors such as was the case in forward and backward locomotion, escape behavior, and

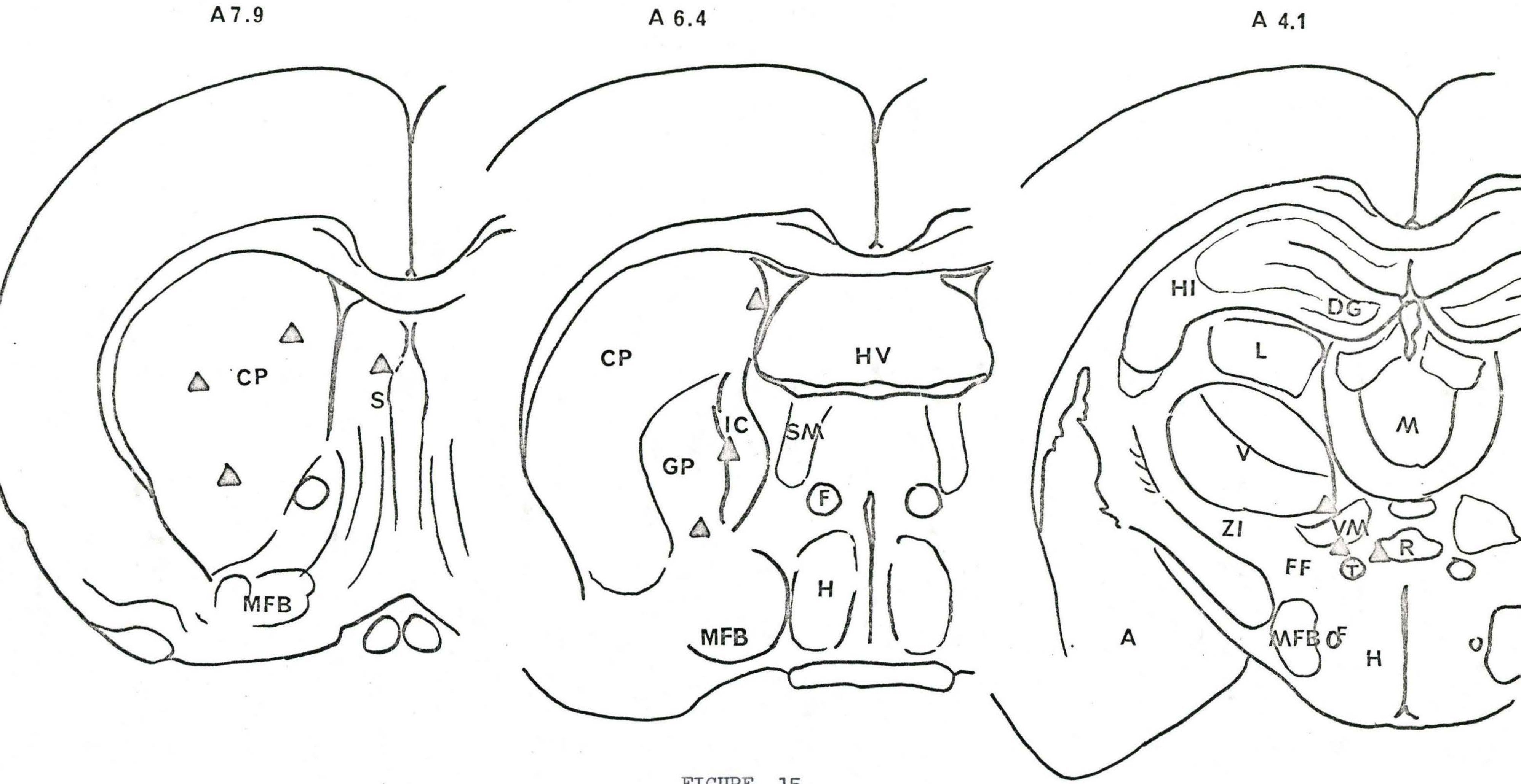


FIGURE 15

Composite frontal diagrams of sites from which stimulation evoked seizures exploratory behavior. Many responses such as vocalization, grooming of the back, shaking, rearing, and digging, could be identified as components of a larger pattern of behavior.

The final expression of the evoked behavior was a synthesis of the interaction of the effects of the electrical stimulus with the ongoing behavior and the environment. Nonetheless, the electrical stimulus was compeling enough that differences in the ongoing behavior or changes in the environment did not result in significant changes in the majority of the evoked behaviors. Two interesting exceptions were grooming of the back and digging. There was a more or less perfect transition to grooming of the back, the evoked effect, if the animal was face washing, but grooming of the back was elicited with difficulty (i.e., some time was required, 5 sec.) if the rat was engaged in some other activity when the stimulus was applied. Digging behavior did not occur if environmental support in the form of a surface suitable for digging was not present.

Not all the responses had counterparts in normal behavior. Among these abnormal responses were unusual head and limb positions and seizures.

CHAPTER THREE

EXPERIMENT TWO: Self-stimulation Tests

METHOD

Subjects

The subjects were 25 male hooded rats selected from the behavior testing experiment.

Surgical and Histological Procedures

This procedure was the same as in Experiment 1.

Stimulation Parameters

The stimulator was a Grass Model S4 set for biphasic square wave pulses of a .1 millisecond duration. Frequencies of 5, 20 and 200 pulses per second were used. Voltages from 1.5 to 9 were used.

Apparatus

Self-stimulation tests were conducted in a simple Skinner box or in a two compartment shuttle-box. The Skinner box measured 10 x 12 x 9 in. and was equipped with a plexiglass door and roof and a wire mesh floor. The walls were grey. The bar, 3.5 in. from the floor, was 2.0 x 0.75 in. and required 40 gms. to operate it. After preliminary tests the Skinner box was modified to produce higher operant rates of bar pressing. A hood was built to cover a 40 watt light bulb mounted behind the bar assembly. A 2.25 x 3.75 in. piece of paper-board was attached to the bar. The modified bar required 28 gms. of pressure to operate it. The light behind the bar provided the only source of light.

Other self-stimulation tests were carried out in an apparatus similar to that of Valenstein and Myers (1964). Basically a shuttlebox measuring 8 x 21.5 in. with a tent-like roof 12 in. high in the center, it was divided into two identical compartments by a 1.0 in. hurdle. The front was made of plexiglass and the walls were black plastic. The floors of both compartment were pivoted at the center of the box and the ends were supported by springs outside the box. A subject's weight on either side of the hurdle operated microswitches with output to Grason Stadler programming equipment and an event marker.

Procedure

Twenty-five subjects from the behavior testing experiment were selected for the self-stimulation experiments. The parameters selected for self-stimulation tests were ones that evoked clear, easily recognizable behavior in the behavior tests. The stimulus frequency and voltage were selected individually for each subject.

In the first experiment, three subjects were tested in a well-lighted room for self-stimulation in the Skinner box with the small bar. Daily sessions of one-half hour duration were given in the Skinner box. Operant levels of bar pressing (i.e. without stimulation) were recorded for two or three sessions. Then, shaping of bar pressing for electrical stimulation of the brain was attempted for two or three sessions. If bar pressing was established on the first day, shaping was discontinued. An external control operated by the experimenter was used to provide reinforcements during shaping. Train duration of each reinforcement was 0.50 sec.

Using the procedure described by Valenstein and Myers (1964), 22 subjects were tested in the shuttlebox. At the beginning of a test a subject, with stimulating leads attached, was placed in the box with free access to both compartments. A test consisted of 21 one-minute periods. In the first minute of the test, brain stimulation was not available on either side. On succeeding minutes, a random sequence assured that during the remaining 20 periods, the probability of either side being positive was equal. The only cues as to which side was positive were the brain stimulation and the clicking of a counter during stimulation. Testing was conducted in a dark room with the only source of light being a 40 watt light bulb outside the center of the shuttlebox and below the level of the floor of the box. Brain stimulation was delivered for 0.25 sec. every sec. in most cases (in some cases 0.5 sec. every sec.) while the subject was in the positive (stimulation) compartment. The experimenter was in the test room during testing to ensure that the leads remained secure. Tests were conducted daily for five days or until the shuttlebox behavior remained relatively stable for three days.

Six subjects from the shuttlebox experiment were tested subsequently for self-stimulation in the modified Skinner box. Testing was conducted in a dark room with a 40 watt bulb mounted behind the bar assembly. Sessions were half an hour long. Operant levels of bar pressing were recorded for two sessions. On subsequent days, brain stimulation was delivered for each bar press for two sessions and shaping was attempted for two further sessions. Brain stimulation was delivered in 0.5 sec. trains for each bar press.

RESULTS

Of the 25 sites tested, electrical stimulation of one site was positively reinforcing, stimulation of five sites was negatively reinforcing, and stimulation of the other 19 sites was without a reinforcing effect.

The first self-stimulation experiment involved three subjects. Stimulation of the subthalamus and the dorsal posterior hypothalamus of Rat A2 evoked digging and exploratory behavior at a frequency of 20 and a voltage of 7 (F 20 V 7) and rearing and exploratory behavior at F 200 V 2. Stimulation of this site in 0.5 sec. pulse trains at both frequencies was positively reinforcing, as shown in Figure 16.

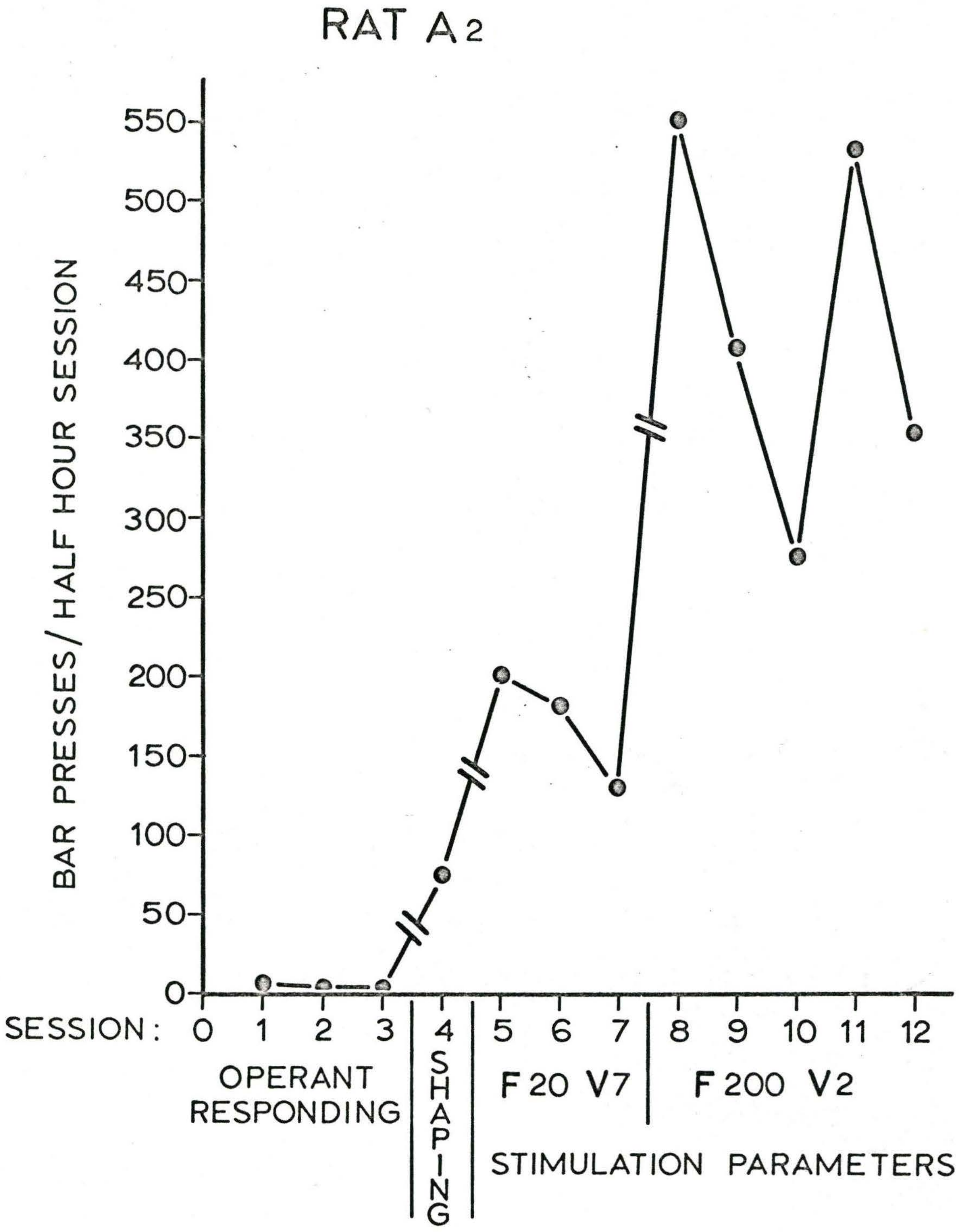


FIGURE 16

Bar presses per half hour session of Rat A2 with two sets of stimulation parameters.

The other two subjects in this experiment could not be shaped to bar press for stimulation and their operant levels of responding were so low that it was not possible to determine whether or not the stimulation was neutral or not in its reinforcing effect. The stimulation each of these subjects received in the Skinner box produced brief motor effects like those observed in the behavior testing. Stimulation of Rat A7 at F 5 V9 during behavior testing evoked face washing and chewing movements with turning to one side, and stimulation of Rat A10 evoked rearing, rapid walking, and escape behavior at F20 V9 during behavior testing. Table III presents the raw data of this experiment and Table IV summarizes the results.

Since the above experiment did not yield information that allowed differentiation of negative and neutral stimulation effects, a procedure developed by Valenstein and Myers (1964) for testing reinforcing effects of electrical stimulation of the brain was used. The apparatus was a two compartment box in which the animal received brain stimulation 50% of the time if it did not orient toward or away from the electrical stimulation. There may have been a slight bias in the apparatus since five normal animals tested in the apparatus spent an average of 47%

TABLE III

Raw data of self-stimulation experiment one. Bar presses per half-hour and stimulation parameters

DAY	RAT					
	Rat A2		Rat A7		Rat A10	
Operant Responding						
1	4		4		4	
2	0		2		1	
3	0		1		-	
Self-stimulation						
1	74*	F20 V7	0*	F5 V9	1*	F20 V9
2	200	F20 V7	0*	F5 V9	0*	F20 V9
3	181	F20 V7				
4	131	F20 V7				
5	551	F200 V2				
6	412	F200 V2				
7	274	F200 V2				
8	532	F200 V2				
9	357	F200 V2				

* Shaping Session

TABLE IV

Summary of Self-Stimulation Experiment One

RAT	BEHAVIOR		SITE
	Evoked	Self-Stimulation	
Rat A2	digging, exploration	positive	n. reuniens, n. gelatinosus, dorsal posterior hypothalamus
	rearing, exploration	positive	
Rat A7	face washing and chewing movements, turning	neutral or negative	lateral reticular formation bordering the periaqueductal grey at the level of the inferior colliculus
Rat A10	rearing, exploration, rapid walking, escape	neutral or negative	n. reuniens, zona incerta, dorsal hypothalamus, mammilothalamic tract

of their time in the positive compartment.

Twenty-two subjects were tested in this apparatus. The results are summarized in Table V and Figure 17. The motor effects evoked by stimulation of these animals during behavior testing were quite varied. Stimulation during behavior testing evoked shaking in 2 subjects, rearing and exploratory behavior in 3, circling in 4, turning to left or right of head and trunk in 3, components of grooming in 3, backwards walking in 2, escape responses in 3, and forward extension of the trunk without hind leg movement and walking in 1 subject. Again it was noted that brief motor effects were produced during the self-stimulation testing each time a stimulus was delivered. Stimulation of 17 of the sites was without reinforcing effect and stimulation of 5 sites was negatively reinforcing. Four of these 5 showed escape during behavior testing; the 5th showed forward trunk extension and walking. None of the 22 animals behaved in a manner consistent with positive reinforcement.

To demonstrate that the above procedure gives results comparable to those obtained with a bar pressing task, six subjects from the above experiment were tested in the Skinner box modified

TABLE V

Summary of the Results of Self-stimulation

Experiment Two

Rat	Behavior		Parameter	Site
	Evoked	Self-stimulation		
MI	Shaking	neutral	F20 V5	lateral septum, diagonal tract
C5	Shaking	neutral	F20 V9	septal nuclei
E15	rearing, exploration	neutral	F20 V7	mammillothalamic and mammillotegmental tracts, supramammillary decussation, medial forebrain bundle.
E21	rearing, looking	neutral	F200 V1.5	mammillotegmental and retroflexus tracts, supramammillary decussation.
E24	rearing, exploration	neutral	F20 V7	mammillotegmental and retroflexus tracts, tegmental decussation.
E20	alerting, looking, running	neutral	F20 V9	lateral reticular formation, tectospinal tract.
E6	alerting, circling to right	neutral	F20 V9	lateral reticular formation, superior cerebellar peduncle.
E18	circling to right	neutral	F200 V1.5	globus pallidus, internal capsule.
E12	circling to left	neutral	F200 V1.5	Forel's Field H_1, zona incerta, medial lemmiscus.
E10	circling right	neutral	F20 V7	lateral recticular formation, tectospinal tract.
E16	turns to left, trunk raised	neutral	F20 V7	medial forebrain bundle, pyriform cortex, preoptic nucleus.
E5	turns to left, head near back	neutral	F200 V2	lateral reticular formation.
E13	chewing, paw movements, turns to right	neutral	F20 V7	lateral reticular formation, substantia nigra.

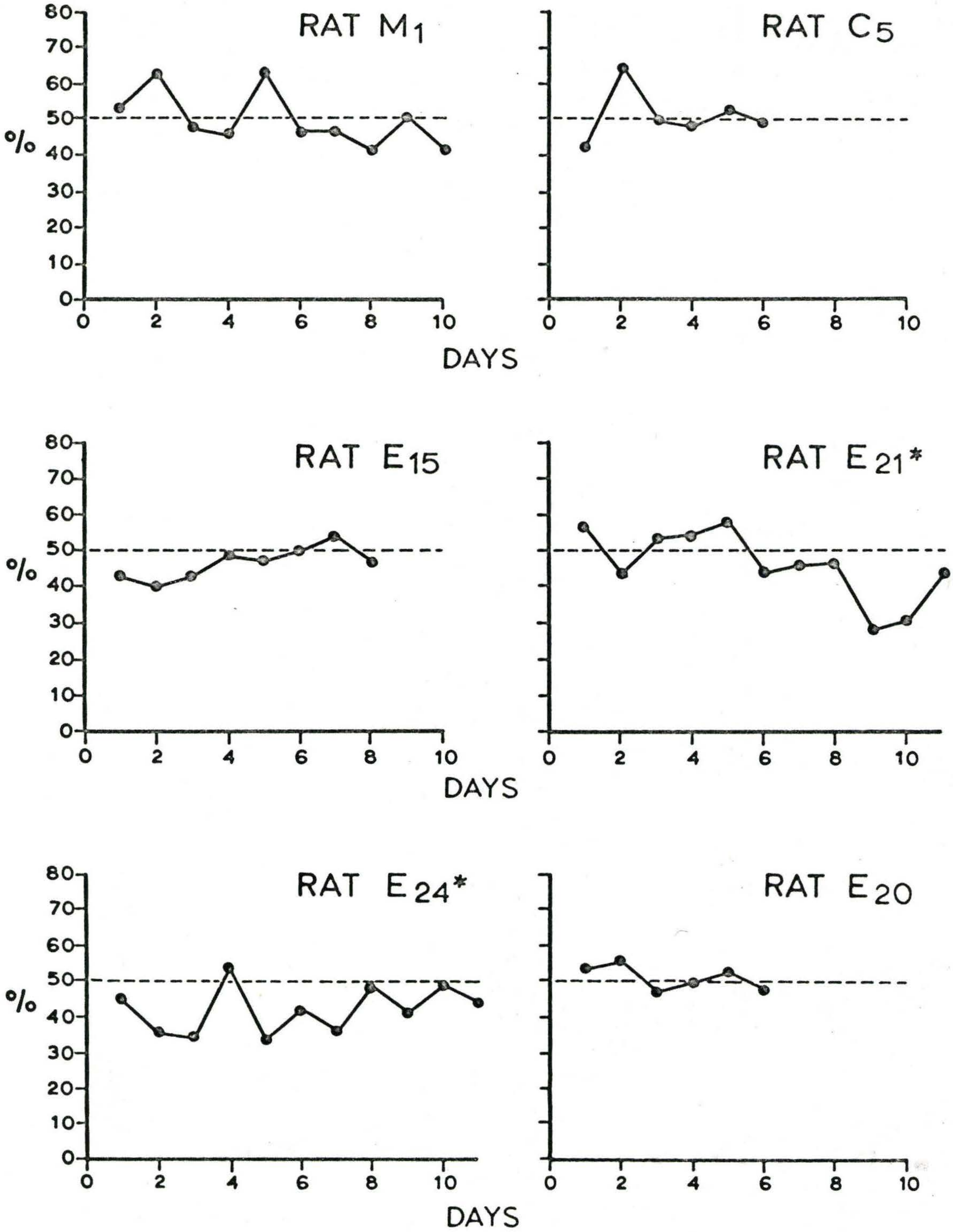
continued ...

Rat	Behavior		Parameter	Site
	Evoked	Self-stimulation		
E7	components of grooming back	neutral	F200 V3	caudate putamen nucleus
E17	components of grooming back	neutral	F20 V9	cerebral peduncle, amygdala
E9	components of grooming back	neutral	F20 V9	medial lemniscus, zona incerta
M4	backwards circling, forward movements	neutral	F20 V7	ventral and ventromedial nuclei of thalamus.
E19	backwards walking	negative	F200 V1.5	periaqueductal grey.
E3	stretching, trunk raised, circling to right	negative	F200 V5	medial lemniscus, transverse pons
E14	running, jumping, freezing	negative	F200 V1.5	ventral tegmental decussation, interpreduncular nucleus.
E2	running, jumping, escape	negative	F200 V3	Forel's Field H_1, posterior hypothalamus.
E1	vocalization, jumping, escape	negative	F20 V7	periaqueductal grey.

FIGURE 17

Self-stimulation behavior of 22 rats tested in shuttlebox showing per cent of time spent on positive (brain stimulation) platform.

*These rats were also tested for self-stimulation in a Skinner box.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RAT E_{24}*
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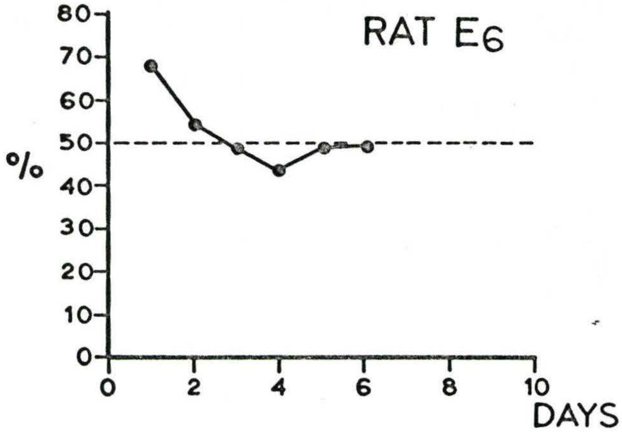
DAYS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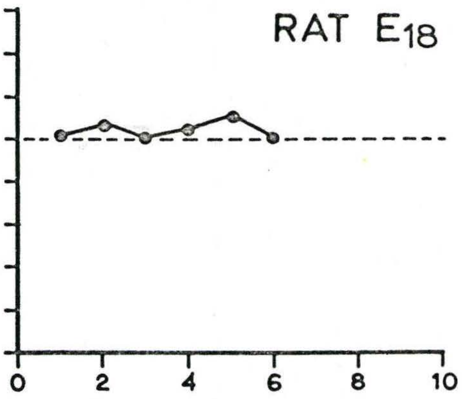
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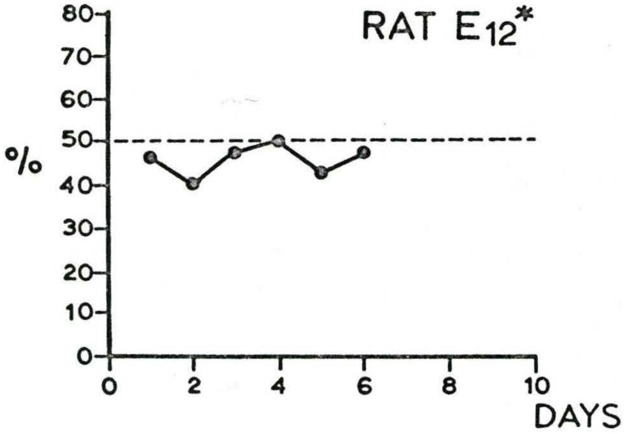
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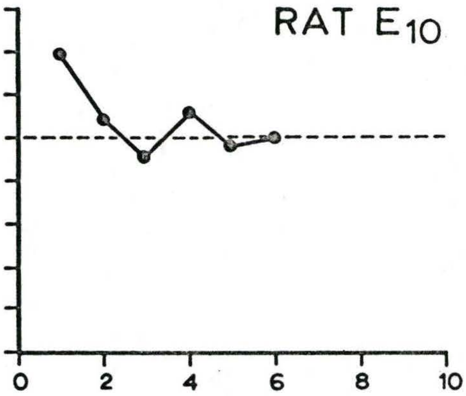
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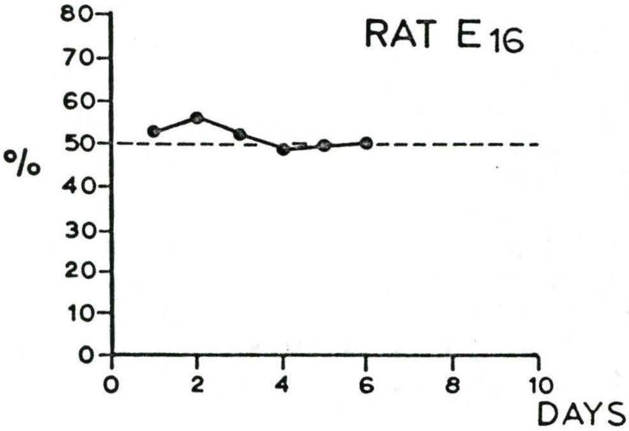
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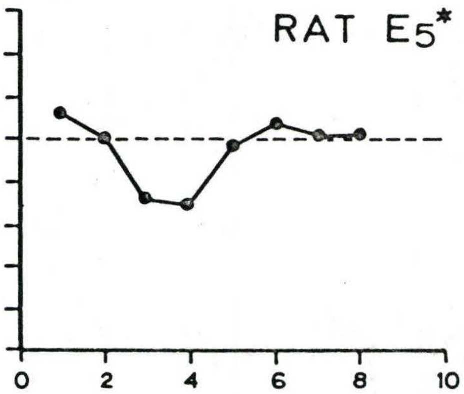
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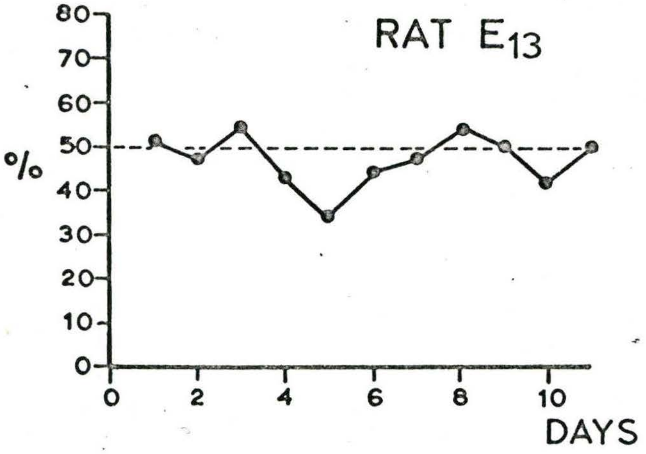
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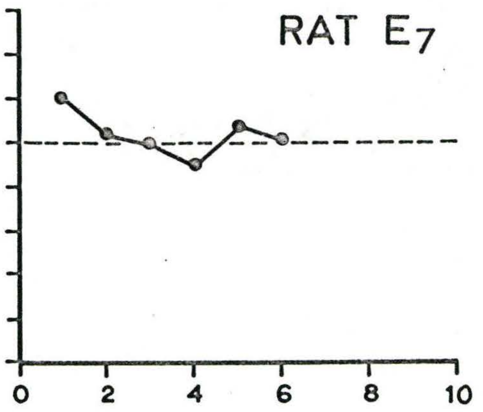
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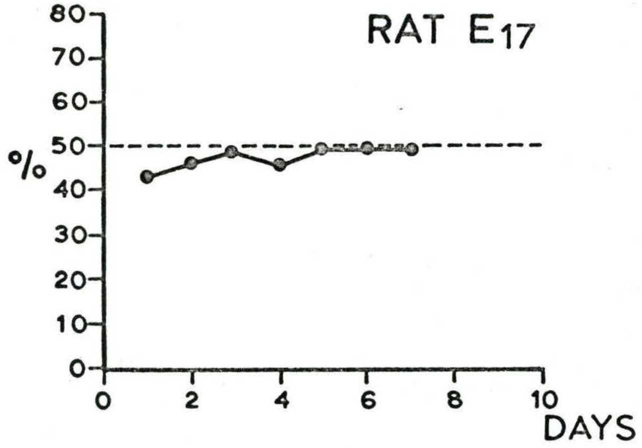
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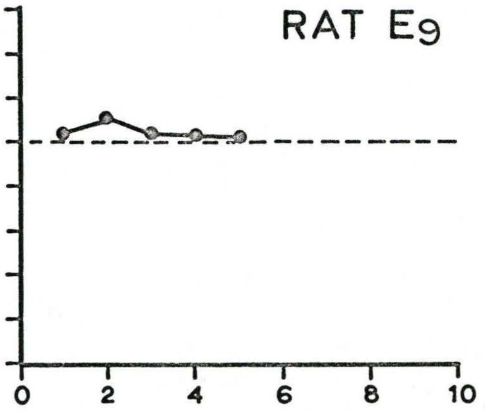
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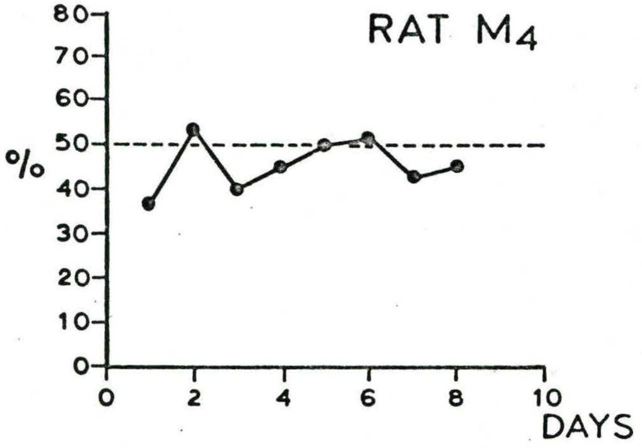
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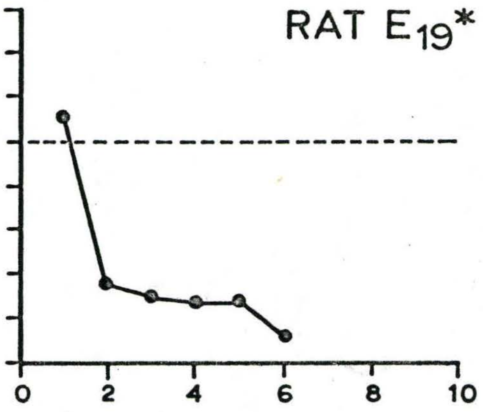
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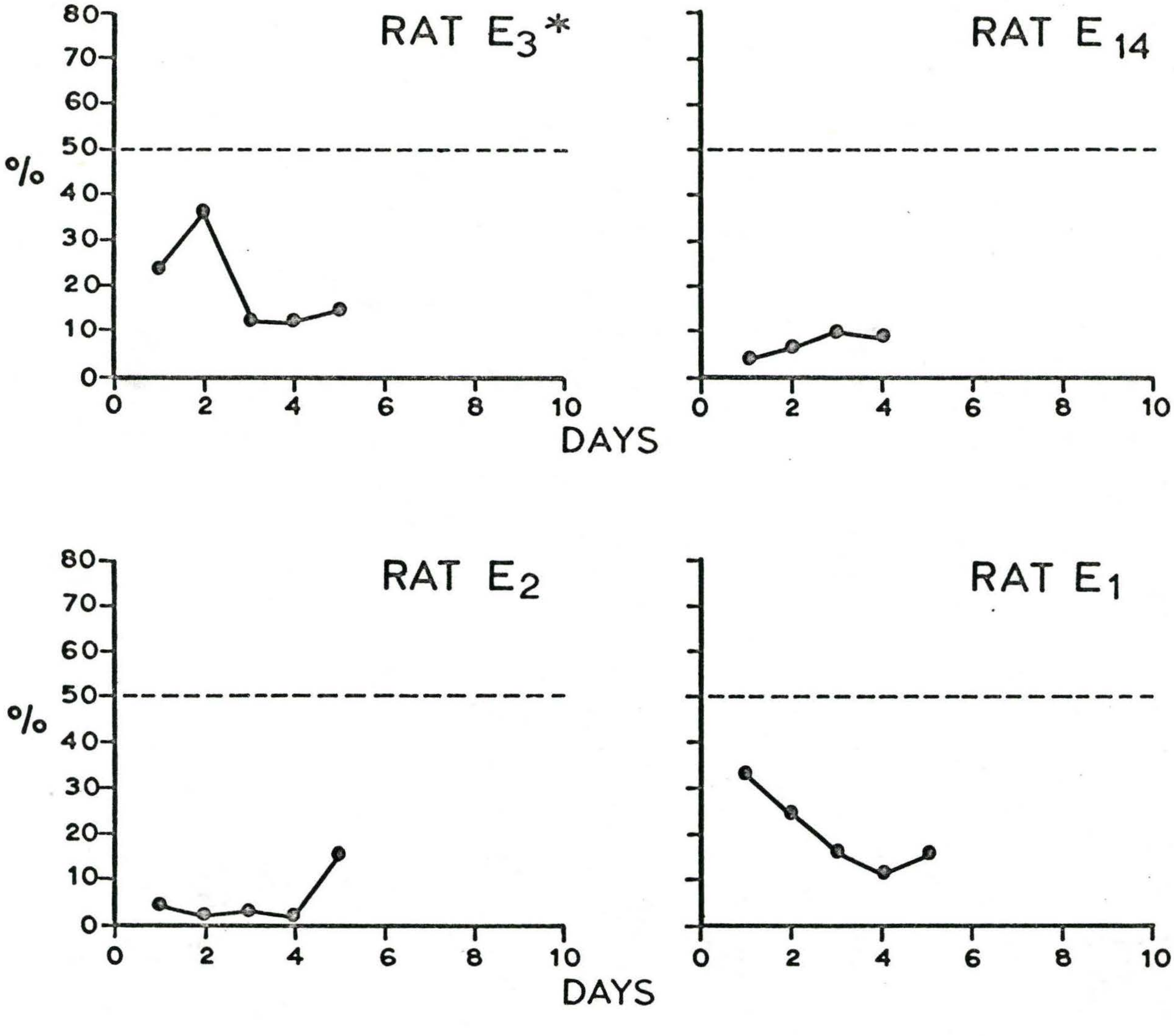
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RAT E2
RAT E1
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from the first experiment. The modifications introduced to enhance the operant levels of responding raised the rate per half hour from an average of 2.1 (N=3) to an average rate of 18.0 (N=6).

Two of the six subjects selected oriented away from the stimulation in the shuttlebox experiment and four were near chance expectancy of 50%. Two of these latter four subjects exhibited evoked behavior of rearing and exploratory behavior. It had been expected that these two subjects would show positive self-stimulation behavior in the shuttlebox since exploratory behavior often occurs with stimulation of rewarding sites (Roberts and Kiess, 1964). Testing the animals in the Skinner box provided an additional check on the shuttlebox measure since their shuttlebox behavior was contrary to expectation. Table VI shows that none of the animals self-stimulated even with two sessions of attempted shaping. Thus, these results are consistent with those obtained using the shuttlebox.

Summary of Self-Stimulation Experiments

In summary, for the majority of the evoked behaviors of this research, there was no positive or negative effect associated with stimulation of the same sites under the conditions

TABLE VI

Raw data of self-stimulation experiment three.
Bar presses in half-hour sessions in Skinner box.

	Bar Pressing					
	Operant		Self-stimulation		Shaping	
Rat Session	1	2	3	4	5	6
E21	41	9	87	19	5	2
E24	10	7	12	17	8	13
E12	3	2	5	1	1	0
E5	6	1	0	0	3	0
E19	6	1	3	8	1	1
E3	57	23	22	9	6	6

of the self-stimulation experiments. Specific motor effects and general locomotory patterns were not associated with rewarding effects. However, negatively rewarding effects were obtained from animals showing escape during behavior testing.

CHAPTER FOUR

DISCUSSION

Behavior Testing

Electrical stimulation of the rat brain stem produced a variety of behavior patterns including components of grooming and digging behavior as well as walking, running, exploratory behavior, escape and vocalization which have been demonstrated previously in other species.

Even though considerable stress has been placed on the motor functions of the brain, it is remarkable that stimulation evoked some sort of motor response from all sites except one exhibiting infection produced damage. A similar result was obtained by Lilly (1958) who stimulated the cerebral cortex of unanesthetized monkeys. In a monkey with 610 electrodes implanted on the surface of one hemisphere he failed to find even one electrode that did not evoke a motor response. It would be tempting to suggest that there are no sites in the brain from which motor activity cannot be evoked. However, several studies have demonstrated inhibition of motor behavior from brain stem stimulation (Hodes, Peacock and Heath, 1951; Hunter and Jasper, 1949; Sheer, 1961). A number of reasons suggest why there was such a dominance of excitatory effects. Because of the relatively large size of the electrodes compared with the size of the rat brain, the tips of the electrodes often entered two or more structures one of which could have been "silent" or even inhibitory in its effect if it had been stimulated singly. In addition, in a small brain such as the rat has, the spread of current to other structures is always a possibility. The results (see Table A of the Appendix) indicate a substantial incidence of mixed effects, some combinations of which do not have their counterpart in normal behavior. An example of this is forward locomotion with a marked tilt of the head to one side. Such an effect is probably due to stimulation of neural pathways which are not normally active simultaneously. Finally, if a particular electrical stimulus did not result in an evoked effect, no tests were conducted to establish whether or not an inhibitory response, such as arrest, was present.

Most of the results confirm the comparative findings in other species and suggest some interesting parallels. The shaking response evoked by stimulation of the rat limbic system is most likely of similar origin as the intensive body scratching and grooming in cats and shaking and grooming in rats following hippocampal stimulation (MacLean, 1957). MacLean (1957) has suggested "that a neural system involving the hippocampus, cingulate gyrus, and septum is implicated in the pleasure and grooming reactions" that he observed following stimulation.

In a study analysing the directional component of the circling response in rats, Skultety (1962) observed forward circling and one case of backward circling. On the basis of his results, he postulated a lateral tegmental area from which contraversive turning can be elicited and a ventromedial tegmental area from which ipsiversive responses can be elicited. This differentiation of areas has some support from this study and suggests that the neural organization of locomotion may be similar in the cat and rat. Contraversive circling in the rat was obtained from the dorsal lateral tegmentum and ipsiversive responses were obtained from ventral medial areas. However, some contraversive circling responses were obtained by stimulation of ventral medial areas in the rat. Since both the Skultety study and the present research examined relatively few points, it is possible that the generalization made by Skultety is too broad.

The present findings are relevant to Delgado's (1964) conception that electrical stimulation acts as a trigger of physiological mechanisms having "anatomical and functional reality inside of the brain." Evidence that the stimulation activates pathways involved in normal behavior is found in the results showing interactions between the evoked behavior and either ongoing behavior or environmental factors. The clearest example of and interaction between an evoked behavior and ongoing behavior was found with the evoked grooming. Here it was observed that the ongoing component (face-washing) facilitated the performance of the evoked component (grooming of the back).

The most striking example of interaction with environment in the present research was seen in the evoked digging. In the two subjects observed, a suitable environment, most likely some yielding surface such as sawdust or dirt, was required before the animal performed the response. In the absence of the suitable environment, exploratory behavior occurred. Similar interactions have been reported by other authors (Levison and Flynn, 1965; Roberts and Carey, 1965; von Holst and von Saint Paul, 1963). These interactions are indications of the importance of providing a variety of environmental stimuli in a test for evoked behavior.

It is known that both ongoing behavior and the external environment can interact with evoked behavior and the results of Olds (1958) and Herberg (1963) indicate that the internal environment can also influence the expression of evoked behaviors. It is possible that both shaking, which appears to be more frequent in post partum female rats, and digging might be affected by internal factors. How these and other motor patterns might be affected is a question that could be answered by further research.

Although postural adjustments must have been frequent, it is not clear whether they were primary or secondary effects of stimulation. Abnormal postures were infrequent and in several cases of phasic turning it appeared that the hind legs were involved only after a certain point in turning had been reached. Considered with the longer latency of the hind leg response, this suggested a secondary postural compensation. Delgado (1952) has provided direct evidence on the question of postural adjustment. He found that postural adaptation upon stimulation varied with the position of the animal at stimulus onset.

The results appear to support two other of Delgado's (1964) postulates. He theorized that fragments of behavior are organized into more complex patterns of behavior. Several of the behaviors evoked in this experiment appear to be components or fragments of larger behavior patterns. For example, the evoked grooming of the back and shaking are only component parts of the total grooming behavior of the rat. The evoked digging was only one component of the three components that normally occur in digging behavior. In addition, the finding of Fernandez de Molina and Hunsperger (1962) that lesions abolished defensive behavior but not the concommitant turning phenomena indicates that the two components of behavior have independent anatomical organization.

Some of the results also support the suggestion that behavioral fragments may have a functional affinity for one another and a tendency to form linkages. In the results, both escape and exploratory behavior are described as clusters of symptoms. With escape behavior, running, jumping, vocalization and autonomic effects all tend to occur in association with one another. Neither jumping or vocalization occurred in the absence of the strong affective response associated with escape behavior. Exploratory behavior also exhibited this sort of clustering. Rearing was not seen at any time during stimulation of any site except at the onset of stimulation evoking exploratory behavior.

This is suggestive that control of this element of exploratory behavior was in some respects different from the control over the remainder of the pattern. This is consistent with the concept of a fragmental organization of behavior. However, it is also possible that the other components of exploratory behavior inhibited the rearing. The results provide a piece of evidence that an evoked behavior could inhibit the occurrence of another behavior component (in this example a pattern of behavior not evoked by stimulation). In the evoked digging, the response usually resulted in a pile of sawdust being accumulated under the rat's belly. The rat always stepped over this pile during stimulation. Occasionally, however, if stimulation was terminated when this pile of sawdust was under the rat's belly, the normal complementary response, the hind leg thrust clearing the pile away, occurred.

The question always arises as to whether these evoked behaviors are primarily the result of stimulation of sensory or motor pathways. There does not seem to be any rule whereby one can separate the two components of a response evoked in this way and "to the best of our knowledge there is only a gradual merging and transformation of the one into the other, with nothing to suggest where perception might end and motor process begin"

(Sperry, 1964). Undoubtedly there are many sensory and motor effects taking place in the brain in the period between onset of stimulation and appearance of and during the response. The usual implication of a question such as that posed is that the electrical stimulus is merely activating sensory pathways and that most of the motor organization is a result of control exerted by the stimulus. This assumption may often be unfounded. In the present study, the grooming responses are obtained by stimulation far from classical spinocortical pathways and stimulation in or near the medial lemniscus (8 electrodes) did not evoke grooming. Similarly, many escape sites were not in the primary sensory tracts and not all sites near these areas yielded escape behavior. However, escape behavior was evoked by stimulation of areas receiving input from pain pathways terminating in the reticular formation and tectum (Crosby, Humphrey, and Lauer, 1962).

The question of the nature of the escape response is very interesting. It is well established that escape behavior consists of a cluster of symptoms but the present investigation also showed that two distinct categories of escape behavior could be evoked. These were backwards escape and escape that generally resulted in forward locomotion. A few subjects exhibited a combination of these two directions of response. In these cases, both backward and forward locomotion occurred during the same stimulus train. At higher intensities of stimulation one or the other of the responses became dominant. The question that is not answered at all conclusively for escape behavior is what determines the nature or direction of the escape response. The large overlap of areas from which escape of each type was evoked does not allow a generalization with respect to anatomical regions. There are at least three plausible explanations for these two kinds of escape behavior. (1) There may be a direct triggering of a specific escape behavior. (2) There may be a topographic representation of cutaneous pain sensation and the "perceived" direction or body surface from which noxious stimulation arises could determine the direction of the escape response. (3) There may be unlocalized "painful" stimulation and the animals may be predisposed to escape in a given way, perhaps as a result of individual experience. The first possibility is in keeping with the general theme of this thesis that the separate motor components (of the escape response) have independent fragmental organization. Skultety's (1962) report that the cat exhibiting backward circling did not display "any evidence of discomfort during the periods of stimulation" is consistent with this type of interpretation. It should be noted that the escape behavior elicited from the reticular formation and pretectal areas are regions which Olds and Peretz (1960) found to be negative reinforcement sites in self-stimulation tests.

The question of anatomical localization has not received much attention in this discussion. The concept of levels of organization as phrased by Jackson (Taylor, 1958) was very specific with respect to localization of function. Penfield (1954) also was fairly specific in assigning levels of organization to anatomical regions. Even though there is a crude hierarchical arrangement of function from spinal cord to cortex there is no real evidence for specific hierarchical anatomical organization of motor patterns of the type we have been considering. On the other hand, this research and that of others has demonstrated considerable functional organization but at the same time these stimulation studies have not demonstrated a hierarchical organization of specific motor patterns in the brain stem. Neither Tinbergen (1951) or Delgado (1964) speculate about the basic anatomical localization of function. Von Holst and von Saint Paul (1963) argue strongly against premature attempts at localization.

The results show that there is specificity of function in circumscribed areas of the brain but the great degree of overlap of evoked effects and mixed effects argue against any suggestion of small centers of localization. Anatomical organization of motor patterns is most likely along the lines suggested by Lashley (1931). The best that can be said is that brain stem structures contain neural circuits incorporating simple movements or fragments of behavior which can be co-ordinated into more complex adaptive patterns.

Self-Stimulation

The results of the self-stimulation experiments showed that for the majority of sites tested a rewarding effect was not associated with stimulation of the same sites from which motor behavior was evoked. Four of the five negative reinforcement sites yielded escape behavior during behavior testing. The single positive site was in the subthalamus and dorsal hypothalamus at the midline. The associated evoked behavior for this site was digging and exploratory behavior. It is important to note that for many of the sites tested, a brief motor effect was evoked even though the stimulation train did not exceed 0.5 sec. during self-stimulation. An unexpected result was that the animals showing evoked exploratory behavior did not self-stimulate. This is especially surprising since it is known that opportunity to explore is reinforcing (Butler, 1953; Montgomery, 1954) and exploratory behavior evoked from the hypothalamus is often associated with positively reinforcing brain stimulation (Roberts and Kiess, 1964). It seems possible that since the tips were in more than one structure, a negative effect from one region could cancel out a positive effect from another region. Also, Deutsch et al. (1962) found that the threshold for reward effects was slightly higher than for behavioral effects at the same site.

While Glickman and Schiff's theory predicts substantially more reinforcing effects, the results of these experiments were not entirely unexpected. Several studies of evoked behavior contain comments on the affective responses of their subjects during stimulation evoking motor behavior (Delgado, 1959; Penfield, 1954; Skultety, 1962). They point out that repeated stimulation of an area that resulted in a motor effect did not disturb their subjects. Also, studies considering only self-stimulation have fouhd a lack of positively reinforcing effects from midbrain areas tested in this study (Olds and Peretz, 1960).

Two points appear to be of major significance in the interpretation of these results. First, the behavior evoked from most of the sites tested was relatively simple when compared with complex behavior such as eating, agression, or sexual activity. Secondly, the majority of the sites were located in midbrain regions. These results taken together with the studies reviewed in the Introduction with respect to covariation of evoked behavior and reinforcement suggest interesting generalizations. A relationship is suggested such that behaviors evoked by stimulation of the hypothalamus tend to be complex and positively reinforcing. Behaviors elicited from the midbrain tend to be simple and neutral unless the evoked behavior is escape behavior. The majority of the hypothalamic behaviors have clear motivational aspects and exhibit greater responsiveness to the environment. The Glickman and Schiff hypothesis appears to encompass the results obtained from experiments in which the hypothalmus was stimulated, but it is not consistent with the results of the present study regarding the covariation of evoked behavior and rewarding effects from stimulation of extra-hypothalamic sites.

Summary

Bipolar electrodes were implanted in 110 points in the midbrain, diencephalon and striatum as well as a few points in the hippocampal formation in 50 rats. After at least two weeks, stimulation of each site was carried out and the evoked behavior was recorded in a written protocol and in some cases 8 mm moving pictures were taken of the evoked behaviors (Experiment One).

In a second series of experiments, 25 rats from experiment one were selected on the basis of the evoked behavior elicited by stimulation. Using parameters evoking reliable behavior patterns during behavior testing, these rats were tested for self-stimulation at the same sites (Experiment Two).

The major findings and conclusions were as follows:

(1) Electrical stimulation evoked a behavioral effect from all but one of the 110 sites tested.

(2) Generally, the evoked behavior was in the form of a consistent pattern that could be reliably evoked on every stimulus application.

(3) Many evoked responses such as vocalization, grooming of the back, shaking, rearing, and digging could be identified as components of a larger pattern of normal rat behavior.

(4) For the majority of the evoked behaviors tested, there was no positive or negative effect associated with stimulation of the same sites under the conditions of the self-stimulation experiments.

(5) Negatively rewarding effects were obtained from animals showing escape during behavior testing.

(6) The results of behavior testing support the idea that the electrical stimulation triggers physiological mechanisms having "anatomical and functional reality inside of the brain" (Delgado, 1964).

(7) The results of the self-stimulation experiment suggest that the relationship between evoked behavior and rewarding effects is different with respect to extra-hypothalamic sites as compared with hypothalmic sites.

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APPENDIX

TABLE A

Summary of Circling Behavior and Anatomical Sites*

Rat	Elec	Ex	S1	IN	BA	S	**	SITE
91	31		X					n. caudate putamen, corpus callosum
91	32		X					n. caudate putamen
M1	66		X					lateral septum, diagonal tract
72	27		X					corpus callosum, n. caudate putamen
A2	35		X			X		n. caudate putamen
E16	96		X					pyriform cortex, n. preopticus, medial forebrain bundle
E17	98		X					medial forebrain bundle, n. preopticus
62	24			X				n. caudate putamen, internal capsule
A8	49			X		X		internal capsule, globus pallidus
E18	100		X			X		globus pallidus, internal capsule
51	19		X					mammillothalamic tract, n. ventralis posterioris
52	21		X					mammillothalamic tract, n. reuniens, n. ventralis posterioris
E16	97			X		X		n. medialis lateralis, n. ventralis dorsalis
91	34				X			dentate gyrus, n. lateralis thalami
11	8			X				n. ventralis dorsalis
31	14		X			X		n. ventralis dorsalis, n. medialis lateralis
C12	65	X	X			X		n. reuniens, zona incerta, dorsal hypothalamus
6	3		X			X		n. ventralis, mammillothalamic tract, zona incerta

Rat	Elec	Ex	S1	IN	BA	S	**	SITE
A5	40	X	X	X		X		Forel's H_1, zona incerta, n. ventralis, n. ventralis medialis
A2	36	X				X		n. reuniens, n. gelatinosus, dorsal hypothalamus
A7	46		X	X				dentate gyrus, hippocampus, pretectal area
E2	75	X				X		Forel's H_1, posterior hypothalamus
E12	88		X			X		medial lemniscus, zona incerta, Forel's H_1
E3	76	X						medial forebrain bundle, supramammillary decussation
5	2				X			pretectal area, n. posterioris thalami
E18	101		X					medial geniculate body, lateral reticular formation
Y	5			X				pretectal area
52	22		X	X		X		n. posterioris thalami pretectal area, reticular formation
52	23				X			lateral reticular formation, pretectal area
A2	38			X		X		pretectal area, superior colliculus
11	9			X				superior colliculus, pretectal area
Bi	7		X			X		pretectal area, superior colliculus
51	20				X			pretectal area, superior colliculus
E19	102				X	X		periaqueductal grey, n. interstitialis lateral reticular formation
Bi	6		X	X				periaqueductal grey, lateral reticular formation, posterior commissure
N1	57			X		X		lateral reticular formation
N1	58				X			lateral reticular formation

Rat	Elec	Ex	S1	IN	BA	S	**	SITE
21	12		X					pretectal area, superior colliculus
M1	68				X	X		pretectalarea, superior colliculus, lateral reticular formation
N8	63		X	X	X			lateral reticular formation, n. red, medial lemniscus
E1	72	X				X		medial lemniscus, substantia nigra
32	16		X					subiculum, dentate gyrus, medial geniculate body
32	17			X				superior colliculus
N4	62		X		X			superior colliculus
E12	89		X					medial geniculate body, lateral reticular formation
N4	61				X			lateral reticular formation, medial geniculate body
4	1				X			medial geniculate body, lateral reticular formation
E21	107		X			X		lateral reticular formation, medial geniculate body
N8	64		X	X				substantia nigra, cerebral peduncle
91	33					X		substantia nigra, reticular formation, cerebral peduncle
E6	80			X		X		substantia nigra, cerebral peduncle
A7	47		X		X			n. red, lateral reticular formation
A10	55		X			X		n. red, n. interpeducular, tegmental decussation
E10	86	X	X			X		n. interpeduncular, medial lemniscus
U	4		X			X		periaqueductal grey, n. interstitialis

Rat	Elec	Ex	S1	IN	BA	S	**	SITE
A2	39		X					superior colliculus, brachium inferior colliculus
E19	103			X				periaqueductal grey
72	29	X						brachii of superior and inferior colliculi
A8	52		X					inferior colliculus
E9	85		X			X		lateral reticular formation, lateral lemniscus
E6	81		X			X		superior cerebellar peduncle, n. medianus raphes
E3	77			X		X		medial lemniscus, cerebral peduncle, fibrae pontis traversae
A7	48			X		X		inferior colliculus, periaqueductal grey
E13	91		X	X		X		superior cerebellar peduncle, periaqueductal grey
E10	87		X					lateral reticular formation, tectospinal tract
E24	109		X			X		n. medianus raphes, tectospinal tract
E14	93		X			X		--- a very caudal electrode
E15	95		X		X			lateral reticular formation
M4	71		X		X	X		fasiculus longitudinalis medialis, n. tegmenti ventralis

* sites arranged in an anterior to posterior order

** EX = Exploratory, S1 = Simple, IN = Intermittent, BA = Backward

S = Superimpositions

TABLE B

Summary of Escape Behavior and Anatomical Sites *

Rat	Elec	RUN	JUMP	BACKW	VOC **	SITE
C12	65	X	X			n. reuniens, zona incerta, dorsal hypothalmus
11	8	X	X			n. ventralis dorsalis thalami
91	34			X		n. lateralis thalami, dentate gyrus
A2	37	X	X			n. lateralis, n. lateralis posterioris thalami
A8	50	X			X	prectal area, brachium superior colliculus
A7	46	X				dentate gyrus, hippocampus, pretectal area
E2	75	X	X			Forel's H_1, posterior hypothalamus
62	25	X	X			dentate gyrus
5	2			X	X	pretectal area, n. posterioris thalami
E18	101	X	X		X	medial geniculate body, lateral reticular formation (FOR)
M4	70		X	X		superior colliculus
52	22			X	X	pretectal area, n. posterioris thalami, FOR
52	23			X	X	pretectal area, n. posterioris thalami, FOR
51	20			X		pretectal area, medial geniculate body, FOR
N1	58			X		lateral reticular formation
E19	102			X		periaqueductal grey, n. interstitialis, FOR

Rat	Elec	RUN	JUMP	BACKW	VOC	**	SITE
41	18		X		X		superior colliculus, pretectal area, FOR
M1	68	X	X	X	X		superior colliculus, pretectal area, FOR
N8	63			X			FOR, n. red, medial lemniscus
32	17		X		X		superior colliculus
N4	62			X	X		superior colliculus
32	16	X	X				subiculum, dentate gyrus, superior colliculus, medial geniculate body
4	1	X		X			medial geniculate body, FOR, dentate gyrus
E12	89	X	X	X	X		medial geniculate body, FOR
N4	61		X	X			FOR, medial geniculate body
A7	47	X					n. red, FOR
E21	107	X	X				FOR, medial geniculate body, brachium inferior colliculus
91	33	X		X	X		substantia nigra, cerebral peduncle, FOR
E13	90			X	X		substantia nigra, FOR, medial geniculate body.
A5	42	X					substantia nigra, FOR, medial lemniscus
E14	92	X	X				n. interpeduncular, ventral tegmental decussation
62	26	X	X				medial geniculate body, dentate gyrus
A2	39	X					superior colliculus, brachium inferior colliculus

Rat	Elec	RUN	JUMP	BACKW	VOC **	SITE
E1	73	X	X		X	periaqueductal grey, fasiculus longitudinalis
72	29	X				brachii of superior and inferior colliculi
A5	43	X				superior colliculus, brachium inferior colliculus
N2	60	X	X	X	X	FOR, brachium inferior colliculus, superior colliculus
N2	59	X	X			FOR, brachium inferior colliculus
E19	103			X		periaqueductal grey fasiculus longitudinalis
A8	52	X			X	inferior colliculus, brachium inferior colliculus
E9	85	X	X			FOR, lateral lemniscus
E15	95	X	X	X	X	lateral reticular formation
M4	71			X		fasiculus longitudinalis medialis, n. tegmenti ventralis
E20	105	X	X			FOR, tectospinal tract

** RUN = Running, JUMP = Jumping, BACKW = Backing
VOC = Vocalization