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Response facilitation and suppression with electrical stimulation of the brain of the rat

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Response Facilitation and Suppression with Electrical Stimulation of the Brain of the Rat

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Introduction

Burns and Mogensen (1961) while studying the interference of cortical stimulation on performance in the rat have reported some peculiar improvement effects demonstrated by some of their animals under several experimental conditions. While studying the acquisition of a pressing response for food reward in a Skinner box when brain stimulation was administered simultaneously with food reward, they found in some of their animals a trend indicating improvement in the acquisition of the response. In order to study the effect of the cortical stimulation on the performance of this habit, animals trained up to criterion on the task were implanted with electrodes and subsequently retested. Some of these animals responded at a rate slightly higher than that of the control group. To study the effect on the retention of a habit, animals were retested in a Lashley III maze (8 choice points) following brain stimulation. Some of the animals in this experiment demonstrated a decrease in time required to run the maze even though the stimulation was administered to them no sooner than 4 to 6 hours before the maze running session

was begun. Upon histological study of the brains of all the animals demonstrating an improvement under these various conditions, it was found that the stimulating tips of the electrodes had penetrated well into the corpus callosum.

An improvement effect was also occasionally observed by Feldman (1963) while studying the effects of electrical stimulation of the hippocampus on avoidance behavior in the rat. The improvement was very marked in one animal, so this animal was selected for a systematic verification of the phenomenon (Feldman and McGowan, 1963). In this experiment a conditioned grid shock avoidance response was established in this animal, with bar pressing as the instrumental response, and a flashing light as the conditioned stimulus. The following procedure was then carried out.

First the rat was given one trial of 5/sec. electrical stimulation to the brain (ESB) applied synchronously with CS, light flashes (5/sec.), followed by two trials of the flashing light alone, and this block of three trials was repeated 10 times. This procedure consisting of 30 trials was carried out at voltage levels 1-8 volts, increasing the voltage by one volt each time. The results of this experiment, which are shown in Fig. 1, indicated that under conditions of ESB + light (ESB at 1 through

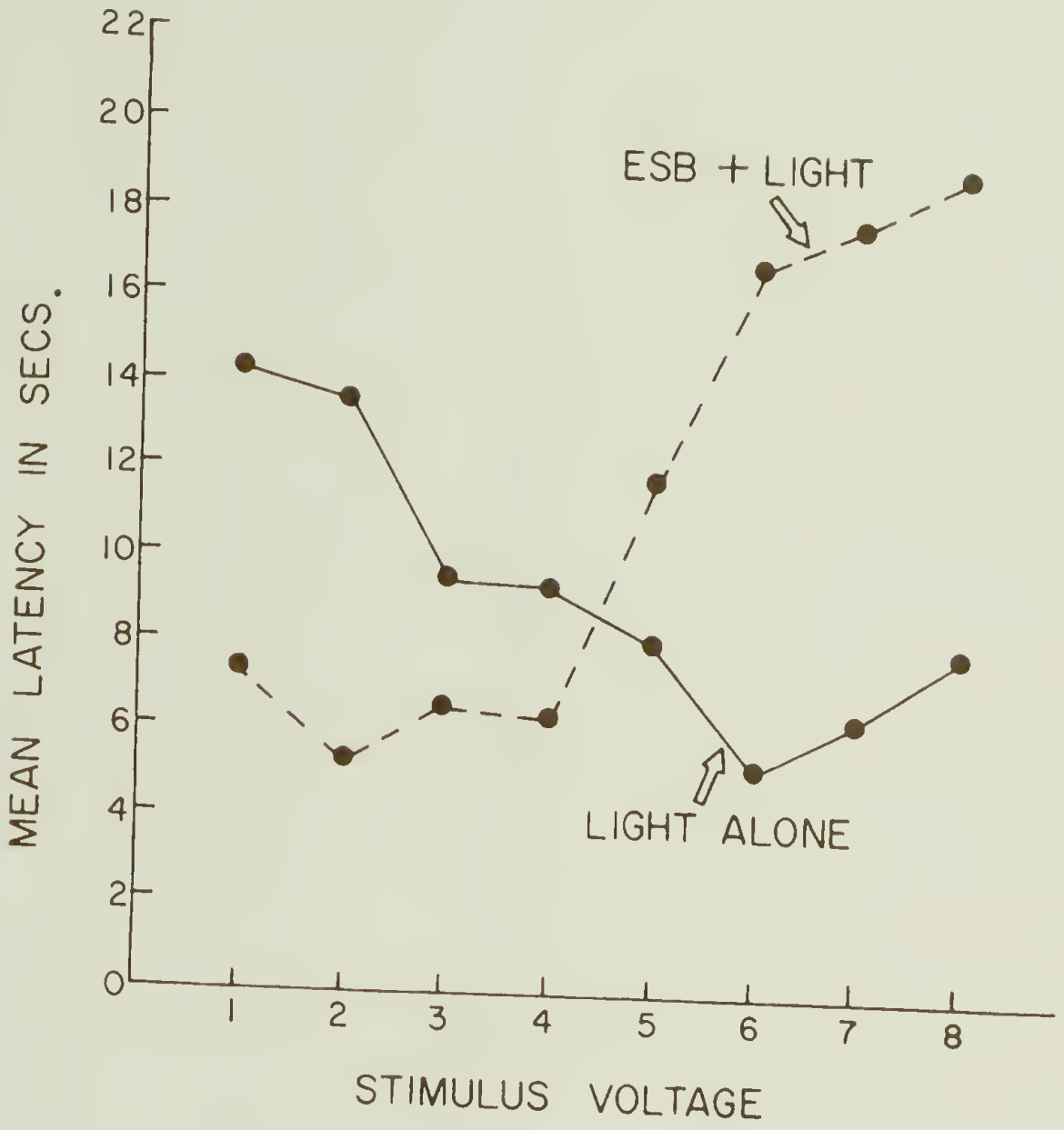


Figure 1. Comparison of response latencies for ESB + light trials with light alone trials as a function of brain stimulation voltage. (Feldman and McGowan, 1963).

4 volts), the task was performed with significantly shorter latencies. At 5 volts a suppression effect occurred which became more evident at 6 - 8 volts, and on trials at these higher voltages the rat did not respond on the majority of trials until the grid shock ensued.

Response latency during light alone trials was not affected by the brain stimulation at low voltage levels (one and two volts), but at brain stimulation levels of 3 - 8 volts, the animal responded with significantly decreasing latencies on the following light-alone trials. Thus, at higher voltages while ESB increased response latency during the ongoing ESB + light trials, the response latency in the immediately following light-alone trials was considerably decreased. Histological study of the brain of this animal showed that the stimulating tips of the electrodes were imbedded in the corpus callosum (See Rat 100, Fig. 2, p. 10a). It was postulated that the decrease in response latency at low voltage was due to stimulation of the corpus callosum, and the increase of the response latency at high voltage levels was due to the spread of stimulating effects to the underlying hippocampus. The decrease in response latency during the light-alone trials at higher voltages was attributed to a long lasting facilitation effect produced by stimulation during previous trials as was shown by Burns and Mogensen (1961).

This raises the question as to what behavioral function is influenced by stimulation of the corpus callosum. In the past anatomists and clinicians have ascribed great importance to the corpus callosum in motor organization, memory, and other associative functions of the brain (Smith, 1945). Anatomically, commissural pathways of the corpus callosum represent the most extensive band of nerve fibers in the nervous system. Phylogenetically they are of very recent origin. In mammals the major neopallial portions of the hemispheres interconnect through this huge commissure. In addition to these purely commissural fibers, it includes collaterals of projection and association fibers.

Sometimes in man, whole or part of the corpus callosum is missing; such persons may show no real mental deficit "unless such lack is associated with other brain damage. When (clinical) signs do appear in most corpus callosum involvements, they are usually due to inclusion of the adjoining cortex." (Crosby et al., 1962). Injury to the corpus callosum in the genu region giving "affective disturbances" appears to involve some of the singulate gyrus (Nielson, 1951). Lesions in the posterior part of the splenium have been described as being accompanied by convulsive states and mental deficits (Schlesinger, 1951).

Ebner and Myers (1964) in a recent report have summarized results of studies on interhemispheric transfer. They reported that Stamm and Sperry indicated that destruction of corpus callosum in the cat prevented transfer of touch discrimination. After further investigation however, Glickstein and Sperry indicated that although the cross-availability of "distinctive sensory knowledge" seemed deficient in corpus callosum sectioned monkeys, they readily transferred "motor pattern and testing set". Myers and Henson in 1960 reported that corpus callosum sectioned chimpanzees who had learned laboriously to solve complex latch box problems with one hand required separate learning through the second hand. Finally, Ebner and Myers (1964) have reported results indicating no cross-recognition either between the hands or feet by corpus callosum sectioned monkeys tested on 1) a simple bar press response, 2) a warm-cold discrimination response, and 3) a more complex tactual-form discrimination response. They also indicated that initial rates of learning were no different for the corpus callosum sectioned monkeys then for normal monkeys.

Smith (1945) has stated that in man any of the three commissures of the cerebral cortex (anterior commissure, corpus callosum, and the hippocampal commissure) may be divided

without major alterations in the individual's bilateral motor organization. Either the hippocampal commissure or the anterior commissure may be sectioned in conjunction with partial or complete section of the corpus callosum without modifying noticeably the previous motor ability of the patient. Although the splenium of the corpus callosum presumably forms a part of the association system of the occipital lobes, eyedness, as manifested in performance test results, was unaffected by sectioning of this structure. Also, the fibers of the callosum may be cut without any definitive loss in performance of learned motor co-ordinations. Thus Smith states that results obtained from controlled destruction of these fibers of the callosum, together with those of the fornix and anterior commissure, without involvement of surrounding cortical tissue or embarrassment of the vascular supply to the cortex to any significant extent, "apparently precludes acceptance of earlier concepts about the functions of the callosal fibers in verbal and motor association." However, Crosby et. al. (1962), states that "because section of the corpus callosum gives no recognizable mental deficit does not signify that it has no function. It seems probable that it is concerned with such highest types of correlation and human intellectual activity as are not readily measurable". On the other hand, Smith (1945) postulates the function of the corpus callosum in the following manner. "Between

the different parts of the cortex and subcortical centers there exists an integration of activity and unification of function providing for organization of postural activity and transient moment-to-moment responses, all phases of which are of significance in the normal life of an individual."

If Smith's hypothesis is accepted, it seems reasonable to postulate that the decrease in response latency under stimulation of the corpus callosum in the studies reported here, may have facilitated integration of activity with the ultimate effect of speeding up the performance of the behavioral task.

However, in the Feldman and McGowan experiment, the question of the effect of the pairing of the ESB and the conditioned stimulus is a critical one. Would the same facilitation effects be manifest if the ESB were administered independently of the conditioned stimulus? It is possible that these facilitation effects occur only under pairing of the ESB with the conditioned stimulus and that this phenomenon could best be explained as the effect of a compound stimulus. This is possible since additional experiments described in the Feldman and McGowan study showed some evidence that low voltage ESB had become conditioned to the light flashes, at least to some degree.

Also, under the conditions of that study, the aggregate amount of stimulation over trials at each voltage level was not

controlled; i.e. since ESB was administered simultaneously with the conditioned stimulus, when the animal terminated the trial by the performance of the response, he consequently terminated the ESB. Thus, at voltage levels where response latency was decreased during ESB + light trials, the aggregate amount of stimulation was quite a bit less than the aggregate amount administered at voltage levels where suppression of response was evident. The possibility exists, then, that if duration of stimulation were controlled, this facilitation effect may not change as a function of voltage, as indicated by the Feldman and McGowan results. In any event, this effect might be altered if duration of stimulation were controlled.

The following study is a modification of the Feldman and McGowan procedure, controlling both for the effects of the pairing of the ESB with the conditioned stimulus, and the duration of the ESB. The ESB and the conditioned stimulus were not paired for this study, and the duration of stimulation was held constant throughout the changing voltage conditions.

Following the completion of the controlled study, the same experimental animals were used to replicate the Feldman and McGowan procedure to try to strengthen the generality of the results of that study.

Method

Subjects

The subjects were four Sprague-Dawley white male albino rats, approximately 65 days old when chronic brain electrodes were implanted.

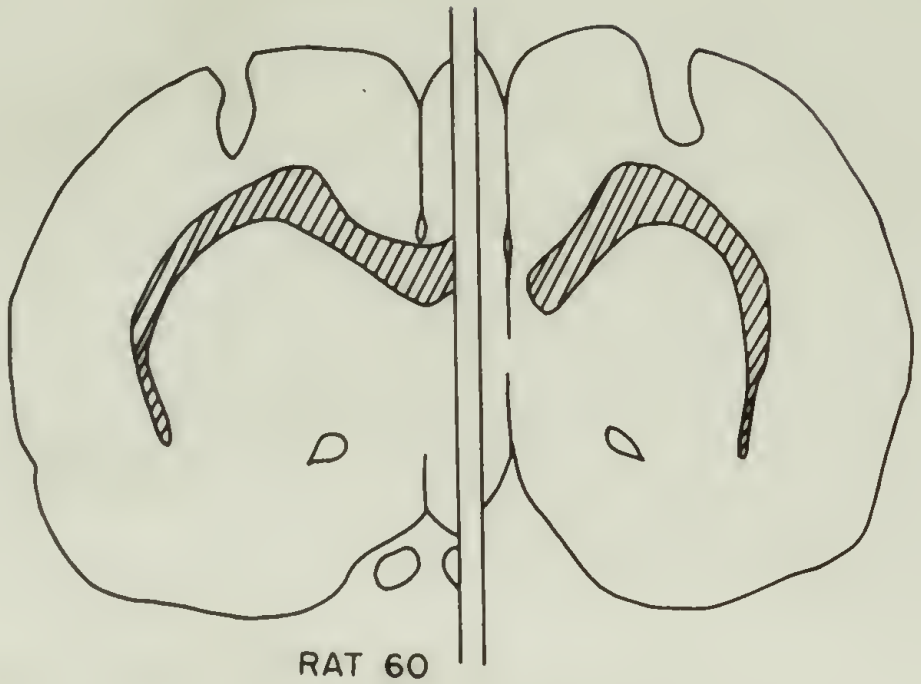
Apparatus

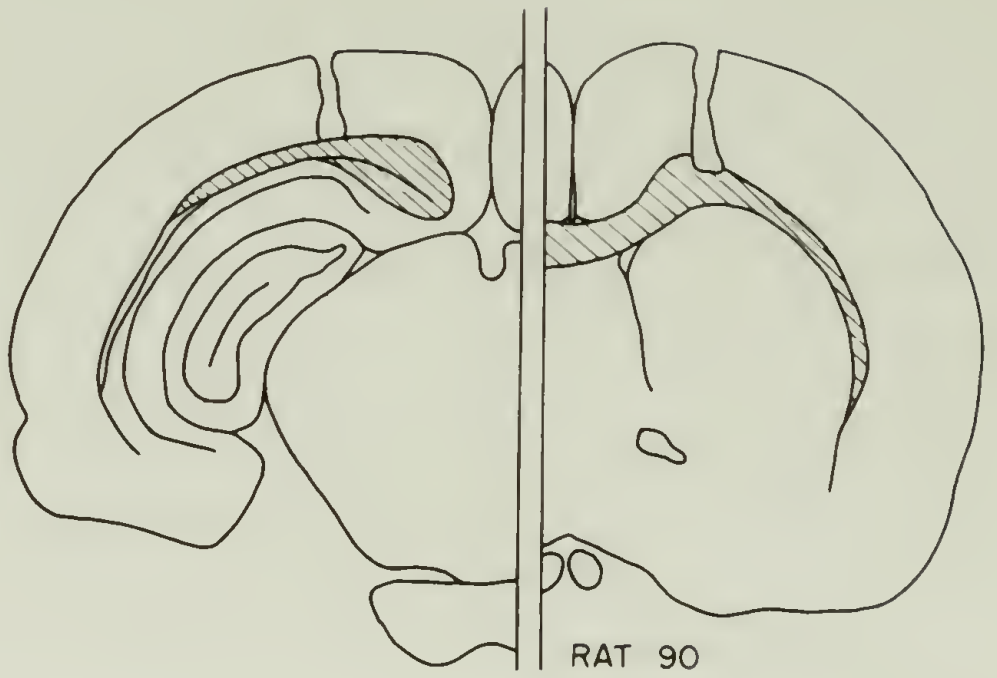
The apparatus for the behavior task was a modified Skinner box with a grid floor wired to a Grason-Stadler shock source and scrambler unit. The Skinner box was placed inside an electrically shielded sound-deadened room. A lever press during a trial interrupted a beam of light activating a photoelectrical cell which activated a circuit programmed to terminate the on-going trial. The EEG potentials were recorded from the implanted electrodes with a 5P5 Grass EEG preamplifier and a Model 5E driver amplifier which activated a Grass Model 5 oscillograph and a Tektronix Type 502 Dual Beam Oscilloscope. The flashing light source was a Grass PS-2 Photo Stimulator placed outside a window of the sound-deadened, shielded room. All brain stimulation was done with a Grass S-4 stimulator.

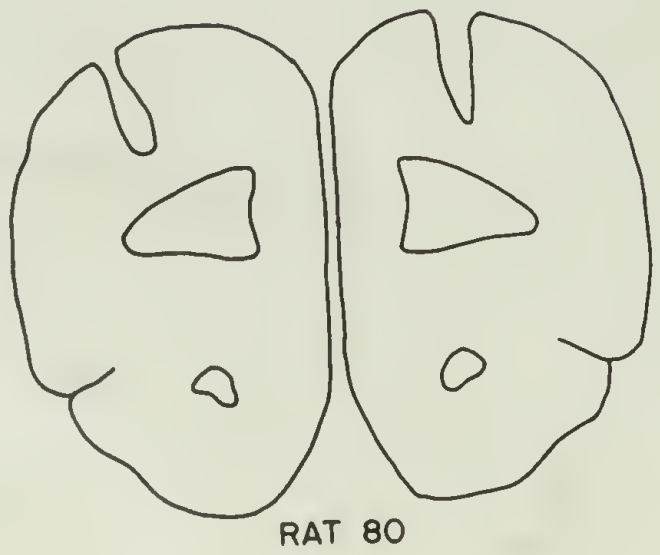
Procedure

All subjects were stereotaxically implanted with electrodes of the type described by Hodos, Valenstein, and Stein (1961) made of two stainless steel enamel-coated wires twisted together and bared at the tips. Two subjects, Rats 60 and 80, were implanted with bilateral, bipolar electrodes using the deGroot (1959) coordinates Anterior 9.0 mm, Lateral 3.0 mm at a depth of 3.0 mm from the skull aiming for the widest band of callosal fibers, 0.5 mm wide, superior to the Nucleus Caudatus/Putamen. However, histological sectioning of the brains of these animals revealed the electrode placements short of the intended corpus callosum. As shown in Fig. 2, the stimulating tips of both electrodes of Rat 60 were imbedded in Brodman's area 6, pre-motor area. The deepest penetration of the stimulating tip of the left electrode of Rat 80 was also located in Brodman's Area 6, the stimulating tip of the right electrode located more anteriorly in area 10, frontal-polar area.

Rat 90 was implanted with the same right electrode coordinates as Rat 60 but somewhat deeper, and the left electrode coordinates Anterior 3.0 mm, and Lateral 3.0 mm, 3.0 mm deep from the skull in the region of the corpus callosum superior to the hippocampus. As also shown in







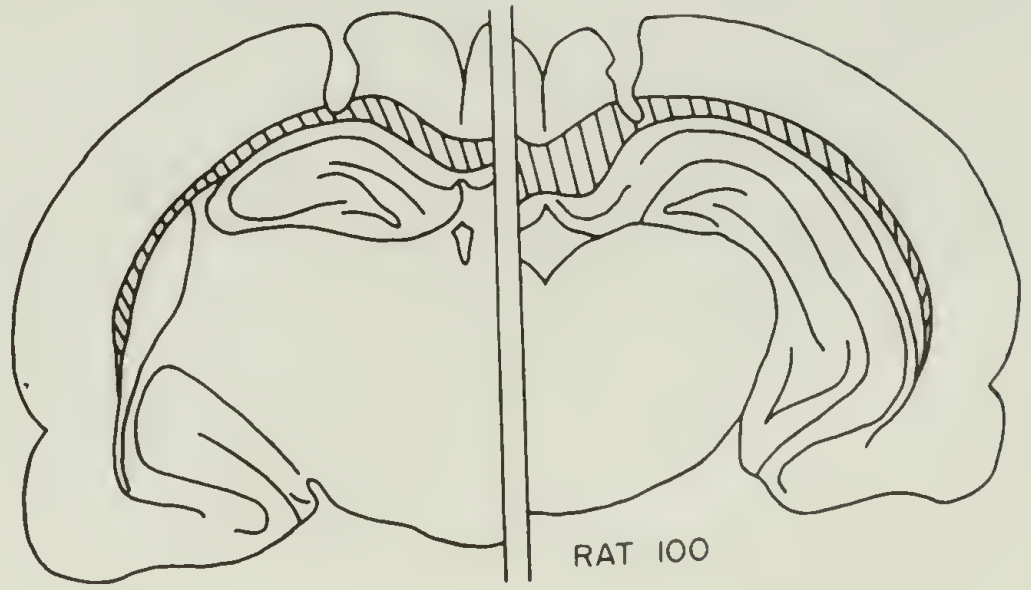


Figure 2. Representations of transverse sections of the rat brain to show the depth and placement of the electrode tips.

Fig. 2, histological sectioning of the brain of this animal revealed that the stimulating tips of both electrodes were imbedded in the intended structures; the right electrode was located in the dorsal lateral corpus callosum, and the left electrode tip was located in the upper border of the medial tip of the corpus callosum. For purposes of comparison, the electrode placements for the animal reported in the Feldman and McGowan study (Rat 100) are also shown here.

Another animal was used as a control animal and was implanted with bilateral bipolar cortical electrodes, Anterior 3.0, Lateral 3.0 mm. Both electrodes penetrated the dura in the cortical region specified as Area 17, the visual cortex.

One week following the electrode implantation, the animals were trained following the method described by Feldman and Bremner (1963) in a conditioned grid shock avoidance task with the flashing light as the conditioned stimulus, and a press and release of a lever as the conditioned response. The behavioral task consisted of the presentation of the flashing light for 20 seconds followed by the addition of grid shock. A press and release of the lever at any time during the twenty seconds terminated the trial (avoidance). A press and release of the lever after the 20 seconds terminated the grid shock and

the flashing light (escape). At least 4 sessions of four hours each were necessary for each subject to establish the training criterion of 70% avoidance.

Subsequent to training, the following experimental procedures were carried out. First, in each daily session the animal was retrained up to the response criterion of at least 70% successful avoidance on ten successive trials.

Session 1. After the initial retraining, each animal was given 20 trials at a constant intertrial interval of 50 seconds, then rested for 10 minutes. Following the 10-minute rest, the animal was retrained up to a response criterion of 70% successful avoidance on 10 successive trials, then given 20 more trials, rested 10 minutes and so on, for a total of four blocks of 20 trials.

Session 2. On each of three days, each animal was given four blocks of twenty trials with a constant intertrial interval of 50 seconds in the manner indicated in Session 1. Three of these blocks of 20 trials included conditions involving brain stimulation, the remaining block having no stimulation administered (control block). On a stimulated trial, the animal received a train of 5/sec bi-phasic pulses, duration 1 millisecond

for 10 seconds at an interval of 20, 30 or 40 seconds before the onset of the trial. There were three voltage conditions; 1, 4 and 7 volts. The interval between the ESB and the conditioned stimulus, and the voltage level remained constant throughout one block of 20 trials, but was varied between blocks. It is to be emphasized that at no time during any of the above sessions was the ESB administered simultaneously with the CS (the flashing light).

Session 3: Following the procedure of Feldman and McGowan (1963), each rat was given a series of 30 trials at varying voltage levels. On a particular day, the animal was retrained up to criterion on 10 successive trails, then tested on the series of 30 trials at a particular voltage level. Each series of 30 trials consisted of 10 blocks of three trials, one trial with ESB presented simultaneously with the light followed by two light-alone trials. Following these 30 trials, the animal was again retrained up to the criterion of 70% successful avoidance on 10 successive trials, and then tested on aother series of 30 trials at a different voltage level, and so on for a total of 4 series of 30 trials on one day. These series consisting of a total of 120 test trials were repeated three more times. On

the first day of Session 3, the animal was tested at voltage levels 1, 2, 3, and 4 volts in that order, and the succeeding day the animal was tested on voltage levels 5, 6, 7, and 8 (ascending order). On the next day of testing, the animal was tested on voltage levels 7, 5, 3, and 1 (descending order), and finally on the last day at voltage levels 2, 4, 6, and 8 (ascending order).

Special Procedures. In addition to the procedures described above, the following supplemental procedures were carried out in an attempt to obtain further information that might help in interpreting the findings.

Rat 60: Following Session 1 (control session), Session 2 was conducted with all stimulation applied to the left hemisphere. In addition, the conditions of Session 2 were repeated stimulating the right hemisphere. Then Session 3 was carried out with ESB applied to the right hemisphere.

Rat 80: Session 1 was conducted, then Session 2 with all ESB applied to the right hemisphere. In addition Session 2 was repeated with ESB applied to the left hemisphere. Further, for this animal, to determine if a lengthening of the duration of stimulation could effect a decrease in the response latency, the procedures of Session 2 were repeated with the duration of stimulation changed from the originally specified 10 seconds to 20 seconds.

Also, to determine if ESB was aversive for this rat, the animal was tested on trials where ESB was presented for 20 seconds instead of the light. The animal was presented with a series of 30 trials at each of 3 voltage levels - 1, 4, and 7 volts. The apparatus was programmed so that the animal could shut off the ESB by pressing and releasing the lever. As on all experimental days, the animal was first trained up to criterion on 10 successive light-alone trials.

Following these experiments, Session 3, the session pairing ESB and light, was conducted with all stimulation being applied to the left hemisphere.

Rat 90: Following the completion of Sessions 1 - 3 with ESB applied to the right hemisphere, the entire series of experiments was carried out with ESB applied to the left hemisphere.

Finally, to determine if ESB could be rewarding to this animal, the rat was presented with a situation where it could stimulate itself by pressing the lever. The release of the lever terminated the ESB. After the animal made the first press, it was given one hour under one of the specified voltage conditions. During this time the rat could stimulate itself for as long and as often as it wanted. The number of presses and the duration of

stimulation were recorded automatically. The ESB parameters were identical to those presented during all experimentation, biphasic pulses, duration 1.0 ms., 5 cps; the voltage levels used were one, four and seven volts. All ESB was administered to the left side. Following this experimentation, the animal was tested with the frequency changed to 100 cps, the pulse duration remaining the same, 1.0 ms.

Rat 5 (Control): The animal was run under conditions specified as Sessions 1 and 2. Additionally, the procedures indicated for Session 2 were followed with the three voltage conditions changed to 12, 16, and 20 volts. Following this, the first two days of experimental Session 3 were carried out, all ESB being applied to the left hemisphere.

Following the completion of the experiment, the four subjects were sacrificed. The animals were first anesthetized with nembutal and then were perfused with saline and 10% Formalin. Successive microtome sections of the brain were made to locate the deepest point of electrode penetration.

Results

All amimals were conditioned within the four training sessions up to the response criterion of 70% successful avoidance. During Session 1 (control session) it was found that stable response latencies for each animal were clearly established.

Response Facilitation and Suppression: With respect to response facilitation resulting from prior brain stimulation as shown in Fig. 3, a comparison of response latency as a function of ESB voltage level at three ESB - trial intervals showed no consistent trends. That is, the group as a whole did not exhibit any consistent facilitation at a specific voltage level or intertrial interval, nor did any one animal exhibit consistent trends toward a facilitation of the response.

Results with the experiments pairing ESB with the conditioned stimulus are shown in Fig. 4. As indicated in the graphs, when ESB was applied simultaneously with the light at low voltage levels, the expected facilitation of response did not occur -- the response times of the animals being relatively unaffected by the ESB. However, in Rats 60, 80 and 90, as voltage was increased,

Fig. 3. Response latency as a function of ESB voltage and the ESB-test interval.

ESB-test interval: ——— = 20 secs
------ = 30 "
..... = 40 "

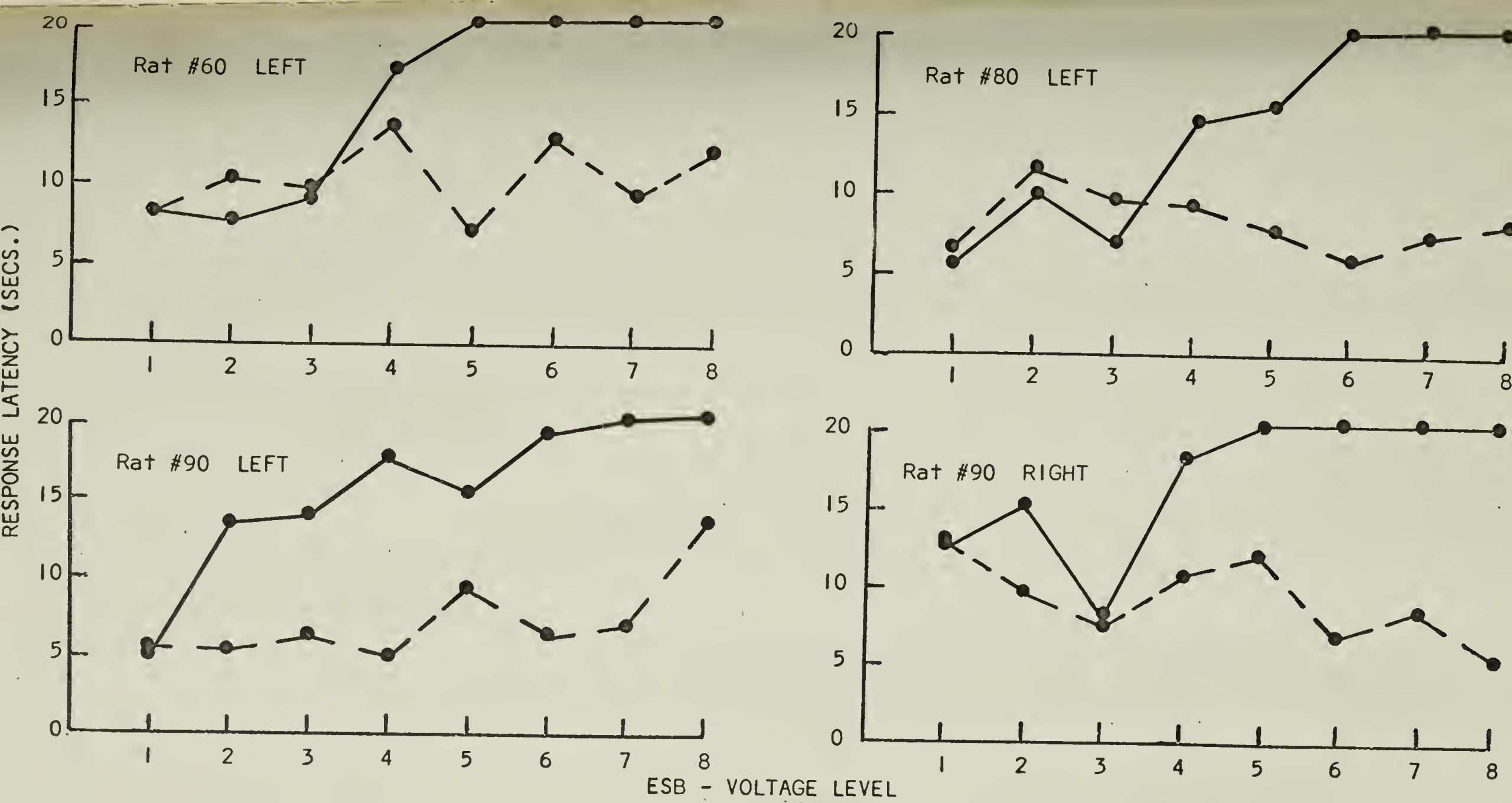
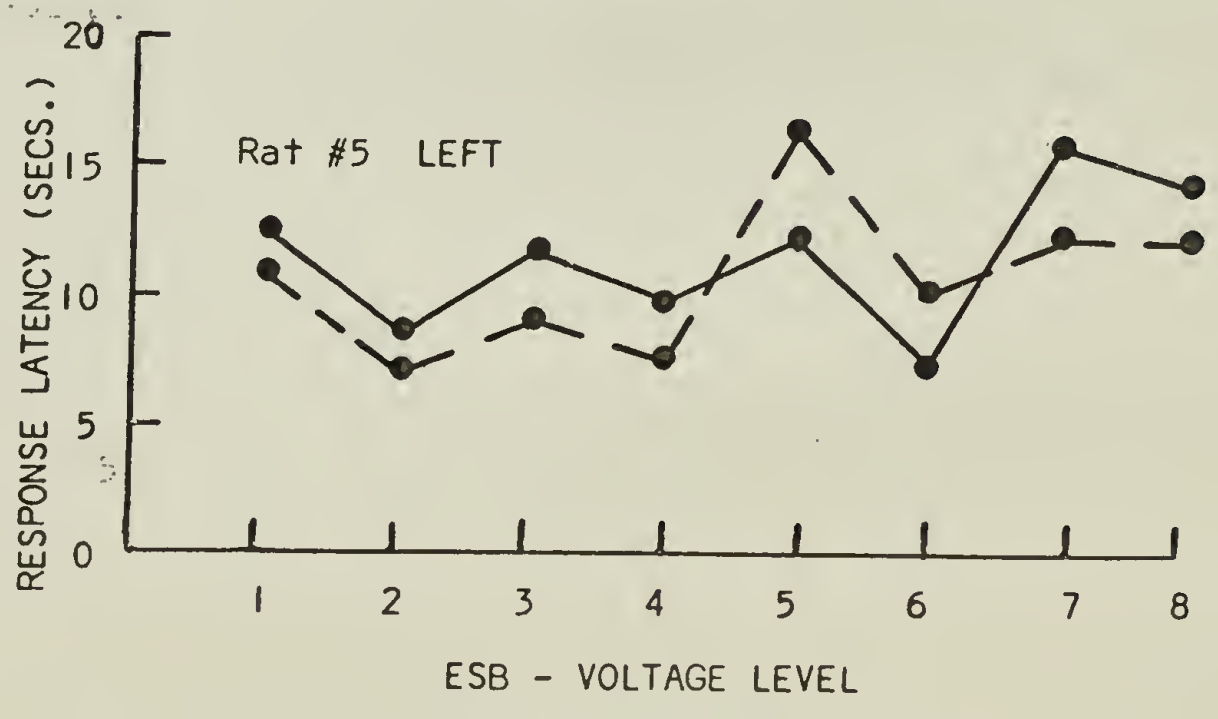


Fig. 4. Comparisons of response latency when avoidance trials were or were not accompanied by brain stimulation.

———— = With ESB

- - - - - - = Without ESB



the suppression effects of the ESB become manifest. At 4 volts the suppression of response is evident, becoming complete at higher voltage levels where the animals failed to make any response on the majority of trials. For all 3 subjects during trials in which the animal failed to respond within the allotted time (20 seconds), clonic motor movements of the paws were often observed. However, the animal usually performed the conditioned bar pressing response within a second or two following the cessation of the ESB. It should be emphasized that grid shock was applied only on those trials in which the response did not occur within approximately 5 seconds of termination of ESB. Thus, it appears that ESB did not evoke seizures that are usually followed by post-ictal depression, but rather caused a temporary motor arrest, with the conditioned lever press response occurring upon termination of ESB. It is also to be noted that no effects of the ESB, even at these higher voltage levels, were manifest in the control animal (Rat 5). Indeed, the curve representing light-alone trials and the curve representing light plus simultaneous administration of ESB seemed to parallel each other.

The supplemental procedures showed the following results. For Rat 80, the duration of brain stimulation was lengthened from the originally specified 10 seconds to 20 seconds because it was

thought that this increase in duration might lead to a decrease in response latency as compared with the original experiment. However, the results did not support this hope; the mean response latency under conditions of 20 second ESB duration (8.13 seconds) was actually greater than the mean latency under conditions of 10 second duration (7.72 seconds).

The additional experiment to determine if ESB had been aversive for this animal showed conclusively that it was not. Rather, of the total responses the animal could have made to terminate the ESB, it terminated the ESB at one volt on only 16.6% of the trials, and at four volts only on 40% of the trials. At 7 volts the animal did not terminate the ESB at all, but rather seemed to pay no attention to the stimulation. It is to be noted that before the experimenter began the test trials, the animal had made two or three responses to the ESB alone so that it was known that the subject was able to perform the task.

For Rat 90, additional procedures were employed to determine if stimulation through the left electrode could produce rewarding effects. The animal was presented with the conditions permitting it to stimulate itself by pressing the lever. Results indicated that the parameters of stimulation used in this experiment were not rewarding for the animal. The most responses

occurred at one volt where the animal pressed 49 times and held the lever down for a total duration of 89.3 seconds out of the available 3600, only 2.5% of the time available. When frequency was changed to 100 cps at this same voltage level, the total time was increased to 359 seconds, approximately 9.9% of the available time. This implies that stimulation to this area might have had some weak rewarding properties depending upon the parameters of stimulation.

For Rat 5, in order to determine if higher voltage ESB could elicit some observable effects on behavior, Session 2 was rerun with ESB voltage level changed to 12, 16, and 20 volts. The results indicated that under these conditions of stimulation the median response latency was 9.13 seconds while the mean of the control blocks was 9.17 seconds. Therefore, there was essentially no difference between conditions of non-stimulation and stimulation even though the voltage level was high.

Neuroelectric Phenomena: Samples of electroencephalograms recorded from bipolar electrodes in the respective locations for each subject are shown in Fig. 5. After the training period, electroencephalograms (EEGs) were recorded each day during experimentation to determine if post-stimulation seizure spiking was effecting the suppression of the behavioral response.

Although no post-stimulation spiking was found in connection with performance or non-performance of the avoidance task, some other important electrical phenomena were evident. Recording from Area 6 in Rat 60, and from Areas 6 and 10 in Rat 80, there seemed to be a distinct electrical correlate to the performance of the avoidance task. In Rat 90 with electrodes in the corpus callosum, and Rat 5, with electrodes in the dura superior to the visual cortex, similar patterns were identified although they were not as distinct as those of Rats 60 and 80. As can be seen from the record samples in Fig. 5, there is a characteristic high voltage low frequency present before the onset of the trial. This rhythm was most evident during resting periods especially in the latter part of the daily session. During a trial, this high voltage activity was seen to change to low voltage fast activity just before the avoidance task was performed by the animal. The animal never responded unless this latter rhythm was evident, although occasionally this rhythm appeared but the animal did not respond. However, in general, the neuroelectric response was consistent enough so that the behavior of the animal could be predicted solely by watching the emerging electroencephalogram.

Specifically, for Rat 60, two samples of EEGs are shown. Sample A is a typical EEG where the animal made the correct response of pressing the lever and avoiding the grid shock. Sample B is a sample typical of a trial in which the animal did not avoid the grid shock. The illustrated electrical patterns in Sample A seem most closely allied with electrical patterns generally described as "desynchronization" of the cortical response (Wells, 1963). In example B where the animal did not make the correct response, the high voltage slow activity is seen to persist throughout the 20 seconds of the trial, and the desynchronization pattern never appeared. In Rats 80 and 90, a DC or base-line shift is illustrated which often occurred in conjunction with the desynchronization for these subjects.

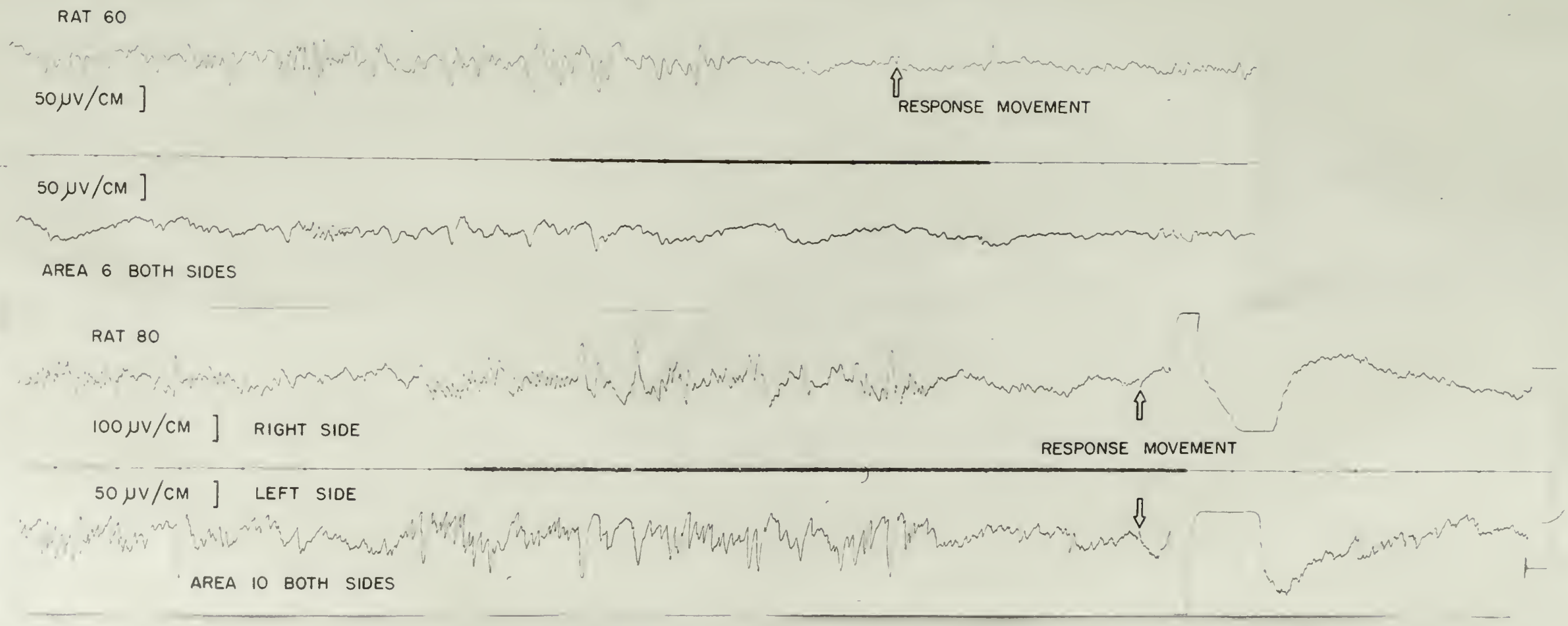


Figure 5. Electrical tracings from rats 60 and 80 showing voltage suppression preceding an avoidance response. The start and the duration of a trial is indicated by the heavy black line in the middle tracing.

Discussion

Response Facilitation and Suppression: The results of procedures on Rats 60, 80, and 90, indicated no decrease in response latency on trials following ESB in Session 2 nor in the light-alone trials of Session 3. The results also indicated that intervals between administration of ESB and the light-alone trials employed in this study, 20, 30, and 40 seconds, were not a significant factor. The failure to find these effects could be due to a number of factors.

First, it is to be recalled that electrode tip placements for Rats 60 and 80 were short of the intended corpus callosum. However, in Rat 90 the electrodes of both hemispheres were in the corpus callosum, the left electrode duplicating the placement of the animal reported in the Feldman and McGowan study. But, even in this animal facilitative effects were not observed. It is now suggested that the behavioral task in general was probably not conducive to an exhibition of this facilitation phenomenon. Most rats responded with a latency less than 10 seconds, and the minimum possible time for execution of this task is at least 4 seconds. This difference (6 seconds)

obviously does not leave enough margin to illustrate a decisive improvement in performance time unless the animal is a slow responder. (It is to be noted here that the animal in the Feldman and McGowan study was a slow responder -- it responded at an average latency of over 13 seconds.)

It is further suggested that some of the facilitative effects of stimulation could have been masked by presentation of the test trial too soon after the stimulation to the brain. Often after presentation of the ESB, especially at higher voltage levels, the animal seemed "disoriented" and this was still in evidence upon presentation of the trial which occurred 20, 30 or 40 seconds following the ESB. Perhaps a longer interval between presentation of the ESB and the test trial would have brought out an improvement in performance. This view is supported by Burns and Mogensen's 1961 report that an increase in performance upon stimulation of the corpus callosum occurred even though the animal was stimulated no less than 6 hours previous to the test situation. Thus, it is possible that the difference in the three intervals between ESB and the trials were not large enough to indicate any significant changes in behavior patterns of the animals as a function of the ESB.

Results presented on Rats 60, 80 and 90 indicated a decisive suppression effect due to presentation of ESB at higher voltage levels. As was suggested earlier, this suppression of response was probably due to a motor involvement evoked by the ESB. It is to be noted that in Rats 60 and 80, Area 6 was being stimulated. In primates, Area 6 supplements the motor function of Area 4, and electrical stimulation of this area has been shown to elicit involuntary motor movements (Crosby, 1962).

The suppression of ongoing response under conditions of high voltage stimulation to the corpus callosum found by Feldman and McGowan was confirmed in this study. (See Fig. 4, Rat 90). Their explanation for this phenomenon was that there was a spread of electrical effects to the underlying hippocampus, a structure which is known to suppress behavior when stimulated. However, since this suppression was found also in Rats 60 and 80, with electrode positions far rostral to the hippocampus, there is the question of whether or not the suppression of response was due to a spread of electric current to the underlying structures, such as nucleus caudatus/putamen or hippocampus, or whether a more encompassing explanation needs to be found. Response interference has been reported by several authors. Akert (1961) reported that electrically induced hippocampal after-discharges

interfered with the cat's capability to respond with defense behavior to complex "danger and distress" signals and Adey and Dunlop (1960) found that induced seizure spiking in the hippocampus interfered with goal-directed behavior. Flynn and Wasman (1960) offered an explanation for this response interference. They suggested that disruption of previously learned behavior by stimulation to the hippocampus might be explained by motor deficiency due to the effects of the induced hippocampal seizure on the motor cortex. They also suggested that seizures might depress learned responses by affecting motor mechanisms.

Since practically identical results were obtained with rats whose electrodes were placed in motor area (Rats 60 and 80) and rats whose electrodes were placed in corpus callosum superior to the hippocampus (Rat 90, and original animal reported in the Feldman and McGowan study), it is possible to conclude that the suppression of response may have been a direct or indirect consequence of involvement of the motor cortex.

This view is supported by results reported by Bremner (1963) which showed that no disruption of conditioned non-discriminated (Sidman) avoidance behavior occurred under stimulation of the hippocampus unless motor effects were noted, even

though the normal neural activity of the hippocampus was disrupted as indicated by evoked discharges recorded from the contralateral hippocampus. However, Bremner's results lead to the question of whether or not the suppression as reported in the present and other studies may be effected only when dealing with a discriminated instead of a non-discriminated avoidance response. Future studies will attempt to rule on these possibilities.

Neuroelectric Phenomena: It was definitely established that the neuroelectric changes that were described were not simple correlates of the conditioned stimulus, the flashing light, nor a correlate of response movement of the animal. First, the change in the pattern of the electroencephalogram occurred after the onset of the conditioned stimulus; second, during trials where the animal did not respond there was no change in the EEG pattern even though the flashing light was present; and third, the response movement of the animal always occurred after the change in the EEG pattern as can be seen by the movement artifacts in the EEG records.

Desynchronization has been recently discussed in relationship with hippocampal theta rhythm (Green 1964). Green and Arduini (1954) previously have shown that under conditions

in which the neocortex becomes "desynchronized" the hippocampus shows "synchronization"; that is, regular, rhythmic, sinusoidal waves of 4 to 7 cycles per second which are referred to as "theta" waves. When the neocortical and hippocampal records were examined simultaneously they were seen to alternate in almost reciprocal fashion, but without exact time correlates (Green, 1964). Shumilina (1960) studying conditioned defensive reflexes in rabbits found a synchronized rhythm at 4 - 6 cps that arose in brain stem reticular formation and in the medial nucleus of the thalamus at the moment when cortical desynchronization appeared in response to the conditioned stimulus.

Grastyan et al. (1959) in his experimentation with cats observed that the first presentation of a new stimulus produced a startle response, associated with desynchronization in both hippocampus and cortical areas. This was distinguished from the orienting reflex which appeared after a stimulus had been presented several times and was associated with searching or turning toward the source of stimulation. When the stimulus caused an orienting reflex rather than a startle response, slow 4 - 7 cps high amplitude waves appeared in the hippocampal region, associated with desynchronization in the cortical areas.

In the development of conditioned reflexes, the first presentation of the conditioned stimulus usually produced a startle response with desynchronization in both hippocamal and cortical regions. With further pairing of the conditioned and unconditioned stimuli, however, the CS began to effect an orienting reflex, associated with 4 - 7 cps rhythm in the hippocampus region and desynchronization in the cortical region. When the animal developed a stable conditioned reflex, both the hippocampal and cortical responses disappeared.

On the other hand, Adey et al. (1960) has failed to confirm Grastyan's results. In cats with chronically implanted electrodes, simultaneous photographic records and EEGs were made to correlate electroencephalographic and behavioral activities. They found that these theta waves were not associated with an orienting response but were associated with the animal's approach to a goal.

The results reported in this study show desynchronization of cortical EEGs with every performance of the avoidance task, and in a Sidman, non-discriminated avoidance conditioning situation, Bremner (1963) has demonstrated the appearance of theta rhythm with every performance of the avoidance response. These results would certainly be inconsistent with the results presented

by Grastyan, i.e. that desynchronization in cortical areas and theta rhythm from the hippocampus appears only with an orienting reflex, and drops out or "habituates" after the animal has learned the response.

However, if there is a consistent reciprocal relationship between hippocampal theta rhythm and cortical desynchronization, our results do support those reported by Adey where the theta rhythm occurred with every presentation of the trial. On the other hand, Adey also stated that this rhythm was associated with approach to a goal. In the animals reported here, the desynchronization appeared before the response movement of the animal, and occasionally the desynchronization appeared although the animal did not approach the lever and make the avoidance response, two facts which militate against desynchronization being directly associated with approach to a goal. It is understood, of course, that since there was no simultaneous measure of hippocampal activity in our animals, this argument can only be suggestive.

Also, it is reasonable to assume that some differences might be found solely as a function of the different tasks conditioned. Thus, the possibility still exists that one might find theta rhythm occurring <u>simultaneously</u> with approach to a positive incentive as Adey did, and <u>before</u> responding to a negative incentive as we

and Bremner did. Future studies will attempt to broaden our understanding of the relationships between approach and avoidance conditioning and the electrical rhythms and changes coincident with the learning and performance of these tasks.

Summary

Four rats with chronically implanted electrodes were trained in a conditioned grid shock avoidance task. The effects of stimulation to the brain both prior to and simultaneous with the conditioned stimulus, a flashing light, were ascertained. A suppression of the ongoing response was noted at high voltage levels when electrodes were placed in motor cortex and in two placements in corpus callosum superior to the hippocampus and superior to the nucleus caudatus/putamen.

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