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HIPPOCAMPAL ACTIVITY DURING AVOIDANCE BEHAVIOR IN THE RAT

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Hippocampal Activity During Avoidance Behavior in the Rat

Frederick J. Bremner

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Doctorate of Philosophy Degree in Psychology at the
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Acknowledgments

Introduction

Many investigators have systematically probed the
functional significance of the hippocampus. Evidence seems
to indicate that this phylogenetically old cortex may be
the locus of integration for such complex processes as in-
stinct, memory and learning. For instance Penfield and
Milner (1958) have reported that unilateral lesions in the
dominant hippocampal formation caused a temporary memory loss
of verbal material in man. They further indicated that
bilateral destruction of the hippocampus caused a permanent
loss of memory for recent events. Furthermore, Kaada,
Rasmussen, and Kveim (1961) found that bilateral and unilat-
eral hippocampal lesions in rats produced significantly more
errors during learning and greater loss in retention of a
maze habit than either operated or non-operated controls.
In addition, it has been demonstrated by Kimura (1958) that
bilateral lesions in the posterior part of the dorsal hippo-
campus of the rat interfered with the acquisition and
retention of an avoidance response in the straight runway.
On the other hand, Isaacson, Douglas, and Moore (1961) found
that rats with extensive, but subtotal, bilateral lesions of

the hippocampus showed lower latencies in both learning and extinction trials and reached the learning criterion of an avoidance response sooner than did control animals when tested in a shuttle box. Porter, Conrad, and Brady (1959) trained monkeys to self-induce brain stimulation and found that with electrodes placed in the posterior part of the hippocampus, self-stimulation yielded seizure-like oscillographic patterns of sharply rising high amplitude waves followed by no recordable activity. However, after the termination of these patterns and a return to a normal EEG, lever-pressing continued to occur at a high rate. These investigators found, as did Feldman (1961) in the rat, that during post-ictal depression when lever-pressing could not elicit seizure activity there was a corresponding decrease in lever-pressing. This suggested that the animals experienced some reward associated with hippocampal seizures. It is worth noting here that young human patients that are subject to petit mal seizures will sometimes intentionally spread fingers apart and wave hands in front of their eyes while looking at bright lights in order to induce seizure activity.

In a paper more directly related to the present study, Adey, Dunlop, and Hendrix (1960), using an electrophysiological method, discovered a neural correlate of approach behavior in the hippocampus. By correlating EEG patterns from the hippocampus with approach behavior in the cat, they

were successful in determining that the characteristic 5-7
cps theta wave was present immediately before and during
"goal directed behavior" in a runway task. Also, Adey and
Dunlop (1960) studied the hippocampal effects of the anal-
gesic cyclohexamines, Sernyl and Cl-400, which gave rise to
psychic disturbances in man such as hallucinations and
echolalia. When injected intraperitoneally in cats these
agents abolished the 5-7 cps wave in the hippocampus and
induced seizure spiking. At the same time these cyclohex-
amines interfered with the goal-directed behavior in their
subjects in that the animals no longer traversed the runway
for a food reward. During recovery from the drug, the theta
rhythm reappeared with a return of approach behavior.
These findings support their contention that the hippo-
campal theta rhythm is a correlate of goal-directed motor
activity.

There seems little doubt that EEG frequencies of 5-7
cps of approximately sinusoidal form can be detected at the
hippocampus. These so-called theta wave patterns have been
found in the guinea pig (Green and Morin, 1952) and in the
cat, monkey and rabbit (Green and Arduini, 1954). However,
their exact relationship to any behavioral end point is not
quite clear. For, in contrast to Adey's hypothesis that
the hippocampal slow waves are a correlate of goal-directed
behavior, Green and Arduini (1954) had earlier demonstrated
that they can be produced by purely sensory input. These

latter investigators further suggested that there was a
"reciprocal or inverse relationship between the activity of
the hippocampus and the cortex ...." In particular this
relationship was characterized by synchronization of the
hippocampus and desynchronization of the cortex, and further-
more, that both of these phenomena are related to attention
or alerting of the organizm. Moreover, they stated that
these neuro-electrical phenomena could be initiated by sen-
sory stimulation of all modalities.

On the other hand some investigators (Grastyan, Lissak,
Madarász, and Donhoffer, 1959) have considered the hippo-
campal slow wave pattern as a correlate of an orienting re-
flex (OR) of the Pavlovian type. It should be noted that in
both Pavlov's work and in current Russian psychophysiology
the OR has been studied as a response to sensory stimuli.
Razran (1961) in a recent review of the Russian literature
characterized the OR as an "investigatory" attitude or as a
temporary response to novel stimuli. Razran further ex-
plained that although the stimulus need not be strange to
the animal, at least its relationship to the conditioning
situation had to be novel for the animal. Also, the OR
adapts quickly, and in classical conditioning decreases as
the conditioned response increases. Razran further pointed
out that evidence published in the Russian literature in-
dicated that the OR has electrophysiological correlates in
the cortex (characterized by desynchronization) and sub-

cortical areas, as in the hippocampal which typically shows synchronous activity.

The above discussion leads to the conclusion that the theta rhythm is related to behavior in some way, either as a correlate of a planned motor act (Adey et al, 1960), as a correlate of the Pavlovian orienting reflex (Grastyán et al, 1959) or as a correlate of arousal or attention (Green and Arduini, 1954).

To complete these introductory remarks, a brief description of the neuroanatomy of the hippocampus and related structures follows. The hippocampus is composed in part of primitive cortex (archipallium), histologically distinguishable from the cortex of most recent origin (neopallium). This primitive cortex is characterized by the absence or poor development of the supragranular layers, the ending of the afferent plexus in the superficial layers, and the relative paucity of cells of short axon, the so-called Golgi Type II cells (MacLean, 1959). Although no direct sensory afferents to the hippocampus are known, there are indirect connections to the hippocampal formation from virtually all parts of the brain stem and cortex (Adey, Dunlop, and Sunderland, 1959; Papez, 1958).

In his comprehensive discussion of the mammalian hippocampus Green (1960) draws attention to the connections between the hippocampus and the ascending reticular activating system (ARAS). These connecting fibers reach the hippo-

campus via the tegmentum and hypothalamus. In addition to these connections from reticular formation and hypothalamus there are afferents from the amygdala, septum, and entorhinal cortex. Besides these extrahippocampal afferents, the hippocampal commissure serves to conduct impulses from one hippocampus to that of the opposite side.

The major efferent projections of the hippocampus have been described for the rat by Nauta (1956). He reported that the fibers leaving the hippocampus via the fornix terminated in the septum, the nucleus of the diagonal band, the preoptic nucleus of the hypothalamus, and the mammillary body. Moreover, he described direct pathways to the hypothalamus and the thalamus. Nauta further described an indirect pathway from the hippocampus to the midbrain via the mammillotegmental tract and medial forebrain bundle.

In particular, the present study was an attempt to discover if in the dorsal hippocampus of the rat there were characteristic theta EEG patterns which correlated with responding in the nondiscriminative Sidman Avoidance Task (SAT). The task typically consists of the subject avoiding short grid shock (ca. 0.5 sec) through a floor grid in a Skinner-box by making a periodic lever-press-and-release. Sidman (1953a, 1953b, 1954, 1955) has reported that when this response has stabilized, the response rate (number of responses per minute) does not vary from session to session more than 0.1 responses per minute. Specifically, although

the animals respond in a random fashion within each day's
session, the response rate is virtually the same from day to
day. The SAT is designated as nondiscriminative because
there is no specific exteroceptive warning signal which
serves as a cue to elicit the response; that is, there is no
"proper" time to respond, as for example within 5 seconds
after a warning signal. Now then, if one considers that the
hippocampal slow wave is an accompaniment of the Pavlovian
orienting reflex or even a correlate of mere sensory input,
then if there were no external warning signal, the EEG
records should be devoid of the 5-7 cps theta rhythm. It
was the major hypothesis of the present study that hippo-
campal theta rhythm would appear in rats trained in a Sidman
avoidance task in which no warning signal was used. A re-
sult such as this would seem to favor an arousal explanation
of the hippocampal theta rhythm. Furthermore, if the theta
rhythm indeed occurred, it was planned to establish whether
or not it was necessary for the performance of an avoidance
task by altering it by means of electrical brain stimulation.
This was done by simultaneously stimulating the hippocampus
and recording the electrical change by means of a contra-
lateral electrode. The advantage of this technique over
previous attempts was the greater control over electrical
brain stimulation than was possible with a drug or lesion
technique. Also, effects of electrical brain stimulation on
the EEG can be immediately and accurately recorded in con-

trast to drug or lesion effects. Previous evidence (Adey et al., 1960) led to the prediction that there would be shifts from the normally asynchronous EEG pattern between lever presses to a 5-7 cps pattern correlated with presses, and further, that changes in the EEG pattern due to electrical brain stimulation would correlate with changes in lever-press responding.

Method

Subjects

Fourteen mature male Sprague Dawley rats ranging in
age from 120-180 days were used as subjects. Six of these
were unoperated and used to standardize training procedures
in the Sidman avoidance task and to obtain estimations of
response rates. The remaining 8 animals each had 2 bipolar
electrodes stereotaxically implanted in deep brain structures.
The experimental group consisted of 6 of these implanted
animals all of which had at least one electrode in the dor-
sal hippocampus. Two other animals designated as operated
controls had bipolar electrodes stereotaxically placed in
brain areas other than the hippocampus; one animal had one
electrode in the lateral ventricle and the other in the cor-
pus callosum. The other operated control animal had one
electrode in the amygdala and a second electrode in the
putamen.

Apparatus

The apparatus for the behavioral task consisted of a
Skinner-box with a grid floor wired to a Grason-Stadler
shock source and scrambler unit (#E1106J4GS). The Skinner

box was placed in an electrically shielded, sound-deadened
room. To further reduce possible electrical interference
which would contaminate EEG recording, a lever-press inter-
rupted a beam of light activating a photoelectrical cell.
This photoelectrical cell activated a circuit which was
programmed to delay a 0.5 sec 2 ma ac shock for 30 seconds
only after the last lever-press and release. With this
program the delays were not cumulative. Also, the apparatus
provided records of lever-pressing behavior.

The EEG potentials were recorded with a 5P5 Grass EEG
pre-amplifier and a Model 5D driver amplifier which attenu-
ated a Grass Model 5 oscillograph. The bipolar electrodes
were made of two stainless steel enamel-coated wires twisted
together and bared at the tips and set in a miniature socket
as described by Valenstein, Hodos, and Stein (1961). The
greatest distance across both wires of these bipolar elec-
trodes was .026 inches. Special cable which reduces wire
flexion artifacts was used within the Skinner-box to connect
the brain electrodes to the recording and stimulating sys-
tem.

These cables leading from the brain electrodes were
connected to a slip ring (Lehigh Valley Electronics # 1373)
fastened to the ceiling of the rat chamber and from there
the leads passed to a pair of relay contacts. This relay
permitted the experimenter to switch from the recorder to
the stimulator or from the stimulator to the recorder from

outside the experimental chamber. All brain stimulation was done with a Grass Model S4 stimulator.

Procedure

The 6 unoperated control animals were used to develop a rapid and efficient training technique for the SAT. This technique consisted of using a hand-operated switch to deliver short duration (110 V. ac, 0.5 sec, 2 ma) grid shocks to the feet of the animal to train the animals by successive approximation. At first shocks were given to goad the animal to move until it was in the vicinity of the lever. Next the short shocks were delivered until the animal pressed the lever. After a lever-press and release the animal was given a 30 second delay at which time another automatically programmed shock occurred unless lever-pressing intervened. Occasionally, the animals had to be goaded by using the hand-operated switch to induce more lever-pressing, but eventually the use of this switch was discontinued as the animals' performance improved. The subjects were trained in this fashion until they avoided at least 70% of the due grid shocks without the use of the hand-operated switch. All sessions were 5 hours in duration and all animals reached the avoidance criterion within 2 sessions.

Following the electrode implanting surgery the 8 animals implanted were rested for one week. The 6 animals that were supposed to have one or more hippocampal electrodes were then given a 5 sec biphasic electrical stimulation in

the hippocampal lead (100 cps, 1.0 msec pulses) increasing
the voltage stepwise from 2 to 10 volts to try to elicit
hippocampal seizure discharges. All hippocampus implanted
rats showed the typical seizure patterns described by Liber-
son and Akert (1955); thus, it was assumed that the electrodes
were accurately placed. The 8 implanted animals were then
trained in the SAT as described above without lead wires
attached to the animals. On the day after the avoidance
criterion was reached the contacts of the implanted elec-
trodes were connected to the lead wires leading to the re-
cording or stimulating apparatus. After the subjects had
reached the 70% criterion, EEG recordings were made periodi-
cally during the last 2 hours of the next session. On
the following 2 sessions in addition to EEG recording,
trains of biphasic electrical pulses were delivered to the
hippocampus on one side while recordings were made from
the other side. Brain stimulation (biphasic 3 and 6 cps
at 1.0 msec duration) was used in an attempt to alter the
hippocampal activity and disrupt the animal's avoidance
behavior. The experimenter began these stimulations when
he perceived a transition from irregular hippocampogram
to the regular theta pattern. Since it was possible that
errors in judgment and timing might be responsible for a
lack of effects, a second series of stimulations was given
in which the stimulation was initiated without regard to
appearance of the theta rhythm. In the second series the

3 best performing animals (numbers 9, 10, and 15 which averaged over 80% avoidance) were stimulated with 1.0 min trains of 1.0 msec pulses at 3 and 6 cps. In either series the voltage was gradually increased from 1.5 volts to the subseizure tolerance level of the individual subject - - usually below 6 volts. These trains were initiated when the subject appeared quiet but were terminated if either seizure-like behavior or seizure spiking was observed on an oscilloscope monitor prior to the end of the one minute period of stimulation.

Following the completion of the experiment all 8 implanted subjects were sacrificed. The animals were first anesthetized with nembutal and then were perfused with 10% formalin. The whole brain was then removed and stained with thionin using a technique reported by Chang (1936). Microtome sections were made at 15 u to find the deepest point of electrode penetration.

Results

SAT performance

All 14 animals were successfully trained to avoid 70%
of the grid shock. The mean percent avoidance for the 6
unoperated control animals during the fourth and fifth hours
of the last 4 sessions was 76.6% while that for the animals
with hippocampal electrodes including sessions with brain
stimulation was 80%. A t-test showed no significant differ-
ence between the 2 groups (P>.10). The 2 operated control
animals had a mean percent avoidance of 71.4%.

Histology

Figure 1 shows the results of histological examinations
of the recovered electrode implanted brains, and shows that
the electrode implacements were situated as intended. It
shows that animals 7, 10, 12 had bilateral (bipolar) elec-
trodes located in the dorsal hippocampal arch (plane 54;
Krieg, 1946). Animal 8 had the right electrode in the
hippocampus and the left in the lateral nucleus of the thal-
amus; animal 9 had the left electrode in the hippocampus
with the right being in the corpus callosum; and number 15
had a left hippocampal electrode while the right was in the

Fig. 1. Representations of transverse sections of the
rat brain after Krieg (1946) to show the depth and placement
of the electrode tips. The black or open circles represent
the position of the electrode tips. AM, amygdala; HIPP,
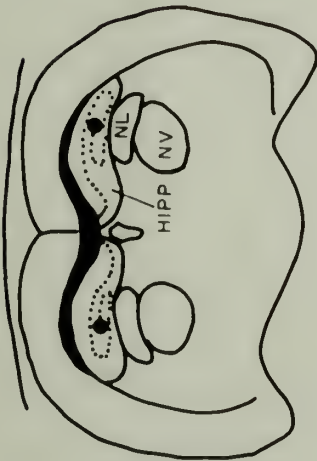hippocampus; LV, lateral ventricle; NL, lateral nucleus of
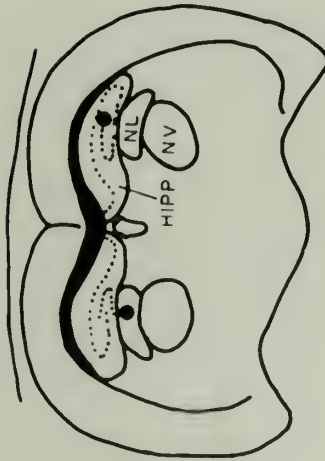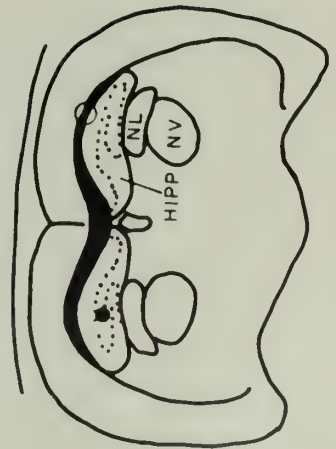thalamus; PUT, putamen.
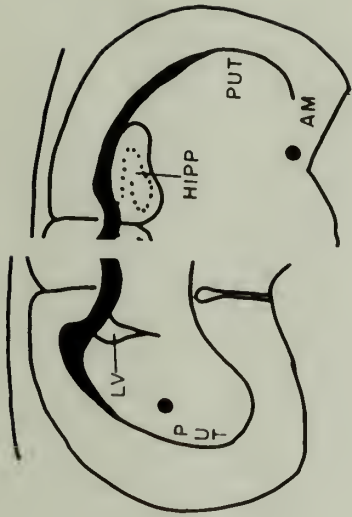
RAT 13
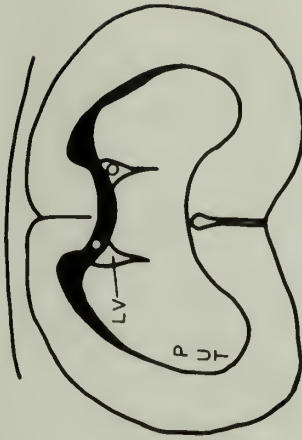
RAT 14
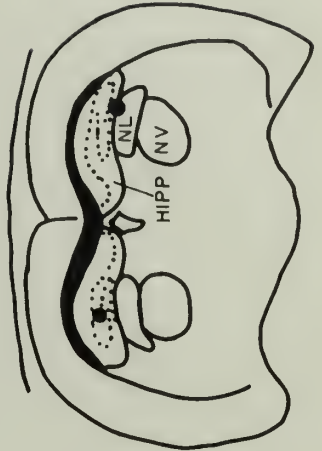
RAT 15

RAT 7, 10, 12

RAT 8

RAT 9

lateral nucleus of the thalamus. The Figure also shows the electrode placement for the 2 operated controls; rat 13 had the left electrode in the putamen and the right in the amygdala. Rat 14 had the right electrode in the lateral ventricle and the left in the corpus callosum.

Neuro-electric correlates of non-discriminated avoidance

Samples of the hippocampal recordings are presented in Figure 2 and 3. In Figure 2 animals 7, 10, and 12 had bipolar electrodes in both hippocampi and, except possibly for rat 7 on the left side, the theta rhythm appeared on both sides prior and during a lever-press. Figure 3 shows samples of the records of animals 8, 9, and 15 which had one bipolar electrode in the hippocampus and the second more superficially, in the corpus callosum, or in a deeper structure, the lateral nucleus of dorsal thalamus. It is quite apparent that as these rats were about to make a response the recordings from the hippocampal electrodes showed a shift from the irregular hippocampogram to one of almost sinusoidal regularity, but this shift did not occur in the other structures. The only other noticable change was a reduction of amplitude in the record from the lateral nucleus of the thalamus in rat 15.

An analysis of the hippocampograms of these 6 experimental animals was done in an effort to establish whether or not there were any consistent differences between wave forms that occurred independently of a lever-press and those

Fig. 2. Records from the 3 bilateral hippocampal
animals. Paper speed 30 mm per second. A stimulus marker
is shown in the center channel making the small pips 1.0
sec apart and the heavy black marks on the far right of
each record indicate a lever-press.
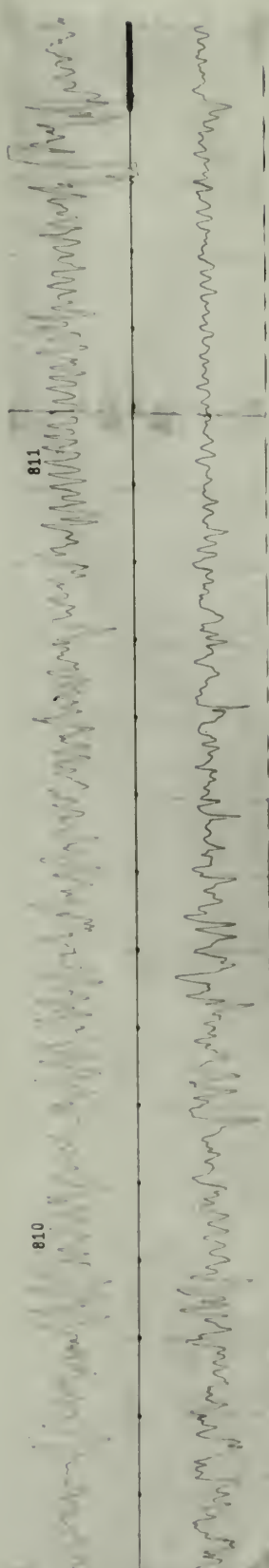
RAT 7
R.HIPP.
30μV/CM.
L.HIPP.
30μV/CM.

810   811
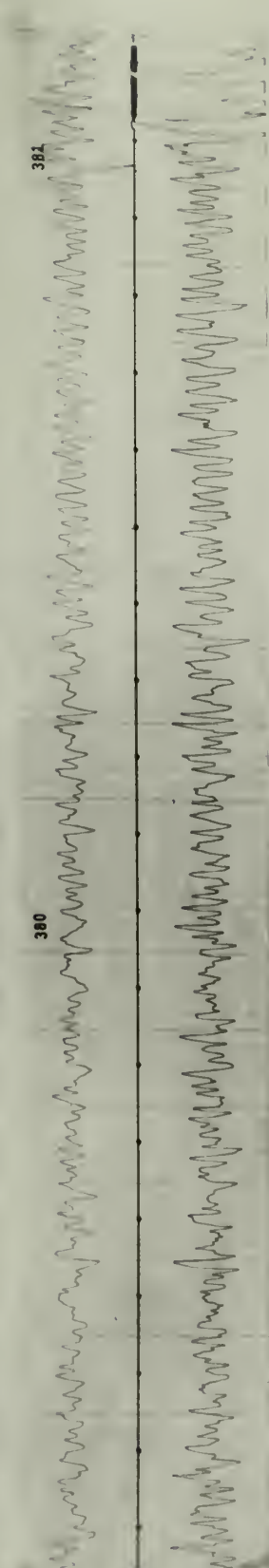
RAT 10
L.HIPP.
75μV/CM
R.HIPP.
30μV/CM

380   381
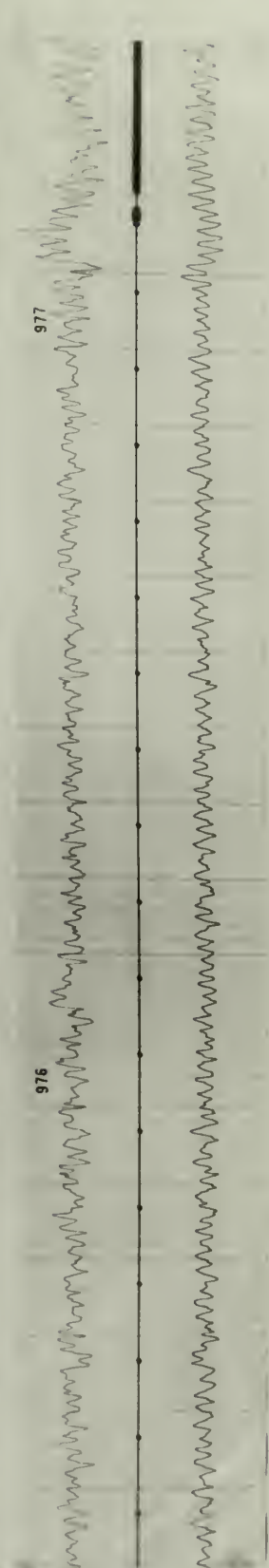
RAT 12
R.HIPP.
150μV/CM
L.HIPP.
150μV/CM

976   977

Fig. 3. Records for the 3 animals with one hippocampal
electrode and a second electrode in adjacent structures.
Paper speed 30 mm per second. Stimulus marker programmed
as in Figure 2.

RAT 8
L.LAT.NUC.THAL.
75μV/CM

R.HIPP.
150μV/CM

RAT 9
L.HIPP.
50μV/CM

R.CORPUS CALL.
100μV/CM

RAT 15
R.LAT.NUC.THAL.
30μV/CM

L.HIPP.
30μV/CM

that occurred just prior to a lever-press. Therefore, for
each rat, comparisons were made between a set of 25 samples
related to lever-presses and a set of 25 samples lying half-
way between 2 lever-presses which were at least 14 seconds
apart. An analysis of variance was performed on von Neu-
mann's Mean square of Successive Difference (MSSD) as des-
cribed by Leiderman and Shapiro (1962). They reported
that the MSSD is a quantitative way of describing the varia-
bility of a time-series of observations which is applicable
to an analysis of wave data of the type observed in this
study. They further pointed out that the MSSD is a more
sensitive measure than either the mean or the variance alone.

To obtain the MSSD a transparent grid of vertical lines
2mm apart was placed over each of the one-second samples
chosen (recorded at 30 mm/sec) and an amplitude reading
made where each vertical grid line first crossed the EEG
wave. Sixteen such readings were entered on an IBM card
for each second. These data were then processed by an IBM
1620 computer according to the formula for the MSSD,
$$\frac{\sum_{i=1}^{n-1} (X_i - X_{i+1})^2}{n-1},$$ yielding one MSSD score for each second
of data sampled. Fifty such scores were obtained in the
same way for each animal, 25 scores related to lever-presses
and 25 not related to lever presses. A subjects by treat-
ments by treatments analysis of variance was then done on
these scores. The results are shown in Table 1.

Table 1

Results of Analysis of Variance of MSSD Values

Source of Variance	df	SSq	MS	F	p
SS(Subjects)	5	1.2193110	.24386220		
A(Type of score)	1	1.746030	1.746030	8.4855686	.05
M(Measure)	24	1.2044630	5.018588E-02	1.0864960	
SS x A	5	1.090430	.20580860		
M x SS	120	5.5428780	4.6190650E-02		
M x A	24	1.8754120	7.8142166E-02	2.4920	.001
SS x A x M	120	3.7622810	.03135230		
Total	299	16.379791			

21

As can be seen from Table 1, there is a significant dif-
ference between the two types of scores, related and non-
related, (A, $P < .05$). There was also a significant inter-
action of "measures by type of score" (M x A, $P < .001$).
This latter effect is illustrated by Figure 4. It shows
that the related samples are of lower value and cluster
closer together while the non-related samples have a higher
mean value and are more diffuse. The results of the anal-
ysis indicated one more important fact, namely that even
though the samples were selected serially, there were no
serial effects (P for measures = .50). This analysis thus
supports the contention that the hippocampogram became
organized in those samples related to a lever-press.

Referring again to Figure 2 it is apparent that the
hippocampogram not only became organized but the frequency
consistently falls within the theta range (5-7 cps) as
revealed by a simple frequency count. Table 2 shows the
result of this frequency count which was made on the same
25 samples that were used to obtain the MSSD values. The
operated control animals on the other hand did not show
this organizing trend and the frequencies just prior to
lever-presses remained irregular and difficult to count.
Electrical brain stimulation

In neither the first nor the second series was there
any evidence for response suppression due to brain stimula-
tion as long as seizures did not occur. In the second series

Table 2

EEG Frequencies for Related Samples

	Rat 7	Rat 8	Rat 9	Rat 10	Rat 12	Rat 15
Mean	6.65	7.00	7.08	7.64	6.96	6.92
SD	.757	.707	.837	.491	.456	.400

Grand Mean - - - - 7.04

Overall Standard Deviation .755

Fig. 4. Distribution of mean MSSD values for non-related and related measures.
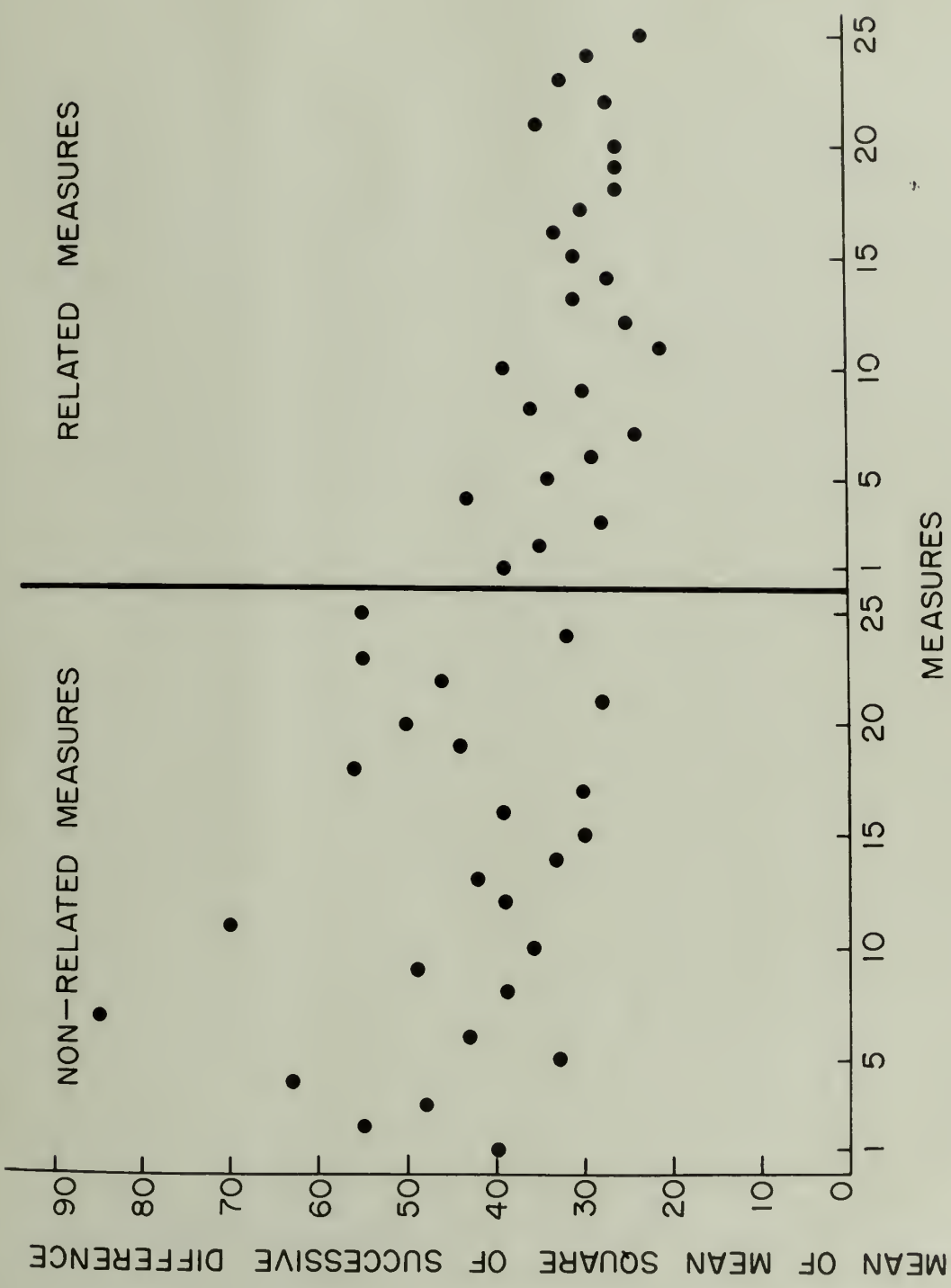
with stimulation over longer intervals (one minute), similar
lack of effects was noted and this was substantiated by the
analysis made possible by this method. Table 3 shows results
of the more systematically investigated second series using
trains of 3 and 6 cps pulses. The tabulation shows the num-
ber of lever-presses during 10 one-minute brain stimulations
periods and 10 randomly picked one-minute samples for each
subject, chosen by using a table of random numbers. Since
neither 3 nor 6 cps stimulations yielded any difference in
responding, the brain stimulation samples were picked re-
gardless of stimulus frequency. It can be seen that there
is virtually no difference in response rate under conditions
of stimulation or non-stimulation. Only in the case of rat
10 was there any appreciable difference but a t-test showed
that this difference was not significant (P>.10).

Figure 5 shows records taken during contralateral brain
stimulation at 6 cps, 2 volts, for rat 10 with bilateral
hippocampal electrodes, and for rat 15 which had one thalamic
and one hippocampal electrode. Rat 15 was stimulated (3.0
volts) at the thalamic electrode and recordings taken from
the hippocampal electrode. It can be seen that theta activ-
ity occurred prior to and during lever-pressing, and no driv-
ing of the hippocampal record appeared. At the highest
voltages driving did occur but seizures quickly ensued and
the stimulation was halted.

However, Figure 6 shows recordings at the hippocampus dur-

Table 3

The Effect of Electrical Brain Stimulation (EBS)
on Conditioned Response Rate

| | Rat #10 | | Rat #8 | | Rat #15 | |
| | CR's/min during EBS | CR's/min with no EBS | CR's/min during EBS | CR's/min with no EBS | Cr's/min during EBS | CR's/min with no EBS |
Sample						
1	3	4	7	5	3	3
2	3	4	6	6	2	2
3	5	4	5	6	2	6
4	5	4	7	6	3	4
5	6	6	7	5	4	4
6	6	6	5	9	4	2
7	11	5	2	7	5	5
8	13	7	6	6	4	2
9	5	5	5	7	1	4
10	7	6	5	5	3	2
Mean	6.4	5.1	6.1	6.2	3.1	3.4

Fig. 5. Hippocampograms recorded from the left hippo-
campi of rats 10 and 15 during 6 cps electrical brain stim-
ulation. Rat 10 was stimulated in the right hippocampus,
whereas rat 15 was stimulated in the right lateral nucleus of
the thalamus. The electrical brain stimulation was already
on and continued throughout the period shown.

RAT IO
L.HIPP.
75µV/CM

R.HIPP.
STIM. 6cps
2 VOLTS

703

704

RAT I5
L.HIPP.
30µV/CM

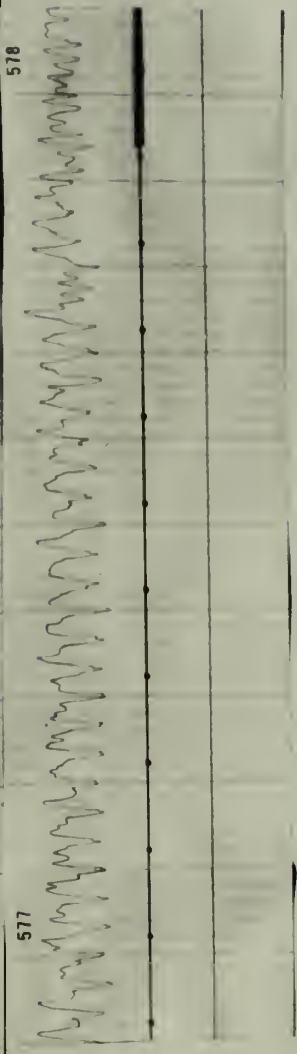R.LAT.NUC.THAL.
STIM. 6cps
3 VOLTS

168

169

Fig. 6. Hippocampograms recorded from the left hippo-
campi of rats 10 and 15 during 3 cps electrical brain stim-
ulation. Rat 10 was stimulated in the right hippocampus
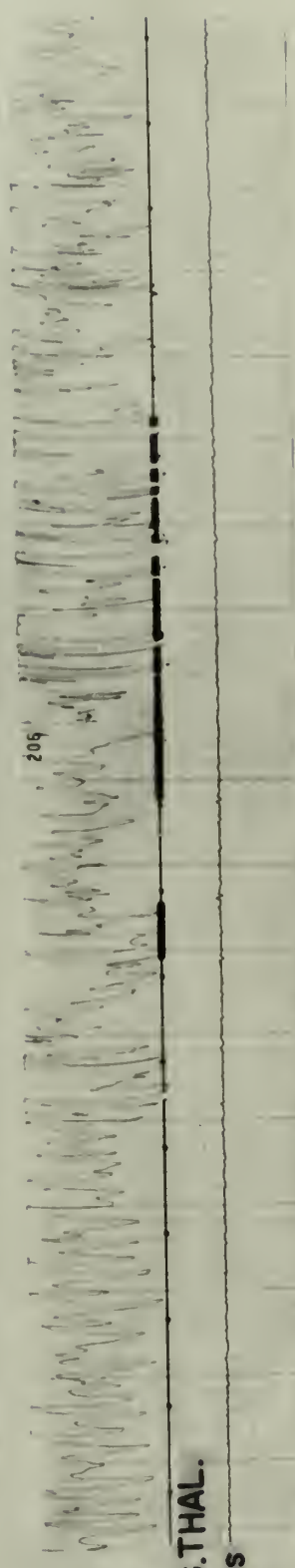while rat 15 was stimulated in the right lateral nucleus of
the thalamus.
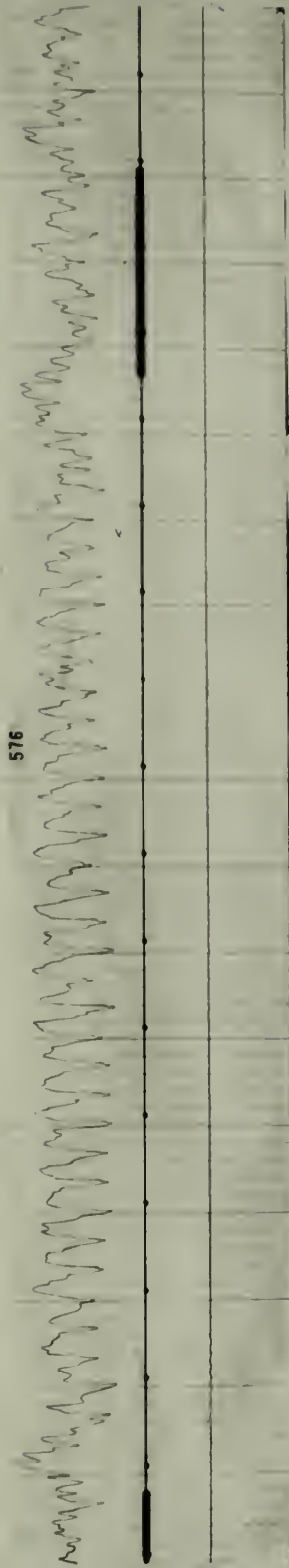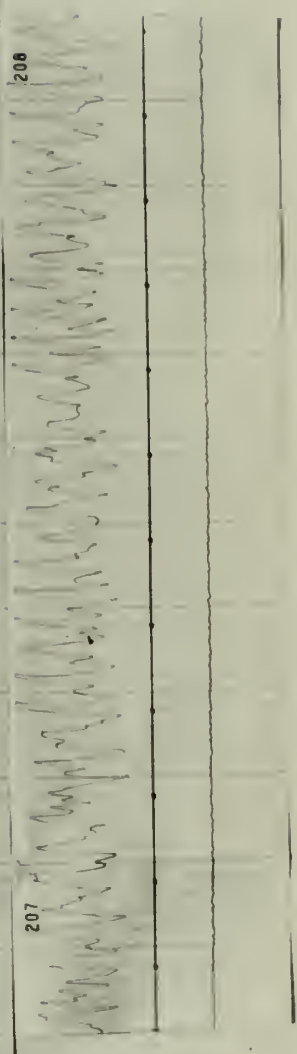
RAT IO
L.HIPP.
75μV/CM

R.HIPP.
STIM. 3cps
3 VOLTS

RAT I5
L.HIPP.
30μV/CM

R.LAT.NUC.THAL.
STIM. 3cps
4 VOLTS

ing contralateral 3 cps stimulation for both of these rats in which it can readily be seen that hippocampal areas under the recording electrode were being driven by the impressing stimulation with a most predictable wave pattern occurring when the contralateral hippocampus was stimulated in rat 10. This Figure also shows an unexpected phenomenon for rat 10 that occurred when stimulated at 3 cps; the impressed 3 cps rhythms were replaced by the theta rhythm just prior to a lever-press. It is felt that a similar phenomenon occurred for rat 15 although the evoked pattern was more complex (probably due to the stimulus site being the thalamus) and it was somewhat obscured by a movement artifact. Also, when the site of stimulation for rat 15 was reversed -- stimulating the hippocampus and recording from the thalamus -- no theta rhythm was ever seen from the thalamic electrode nor was there evidence of suppression or an impressed 3 cps rhythm. This was also true of rat 8 which had electrodes placed similarly to those of rat 15.

Discussion

With respect to the demonstration that hippocampal theta
rhythms are correlated with overt behavior in the rat, the
results of the present study support the findings obtained
on the rabbit, cat and monkey (Green and Arduini, 1954; Adey
et al, 1960; and Grastyan et al, 1959). However, the re-
sults reported here do not support the hypothesis of Grastyan
et al (1959) that the theta rhythm is a correlate of the
orienting reflex. This is so because they assumed that an
exteroceptive warning stimulus is a necessary antecedent for
the OR. The present study demonstrated that the theta rhythm
was present even when no warning stimulus was used. Further-
more, the theta rhythm did not show adaptation or extinction
as the OR does (Razran, 1961). In the present study the
theta rhythm continued to be present during hundreds of
avoidance conditioning trials. Also, Adey et al (1960) show-
ed that the theta rhythm correlated with responding even
after "many thousands of trials" during approach responding
conditioning trials in their animals, and this further mili-
tates against an OR hypothesis. Rather, they attributed the
theta rhythm to the effect of "goal-directed behavior." This

does not appear to be far different from the statement of
Green and Arduini (1954) that the hippocampal theta rhythm
is a correlate of attention or arousal. In the studies of
Adey and others (Adey and Dunlop, 1960; Adey et al, 1960)
the animals were placed in the start chamber of a "T-box"
1.5 meters long and had to determine the correct side by lo-
cating an illuminated rectangle. The animals certainly had
to be attentive to the cues in order to respond correctly in
this 2-choice situation; therefore, in this case the differ-
ence between the arousal concept and the goal-directed be-
havior concept seems to be a semantic one.

However, there is additional evidence to support the
arousal concept. The present study demonstrated that elec-
trical stimulation of the hippocampus that was below seizure
threshold did not disrupt the animals' behavior. This
supports the results presented by Holmes and Adey (1960) who
applied electrical stimulation at 6 and 100 cps to the entor-
hinal cortex, which has a direct anatomical relationship
with the hippocampus and found that 2-choice runway behavior
was not disturbed. This suggests that the theta rhythm
which can be monitored in the hippocampus is initiated by
arousal but is not itself a necessary concommitant of arous-
al or responding, at least with respect to well established
habits. It is recalled, however, that the cyclohexamines did
depress the hippocampal theta rhythm, elicited seizure dis-
charges and depressed runway behavior (Adey and Dunlop,

1960). This apparent contradiction can be explained by the
suggestion that excessive stimulation or seizure activity can
effect adjacent structures that are more directly related to
arousal. Also, since it is known that analgesics and psycho-
tropic drugs affect the thalamus, hypothalamus and brain
stem reticular formation (Berger, 1960) it is very possible
that cyclohexamines primarily affected the ARAS and this in
turn altered the hippocampal theta rhythm and responsivity.
This arousal hypothesis becomes even more inviting when one
considers the neural connections of the hippocampus. As was
previously mentioned Nauta (1956) demonstrated that there
are direct thalamic and hypothalamic connections to the hippo-
campus, and also, that there are indirect midbrain-reticular
connections to this structure. This anatomical evidence
that is well supported by the studies of Green and Arduini
(1954) and Adey et al (1958) is certainly consistent with an
arousal explanation of the theta rhythm mediated by the ARAS.
Moreover, Eidelberg, White, and Brazier (1959) have demon-
strated a direct relationship between the ARAS and the hippo-
campus. They found that when stimulating various ARAS struc-
tures the hippocampogram showed a theta pattern, and that if
the neural connections from these structures to the hippo-
campus were cut, the hippocampogram no longer showed the
theta rhythm. In the present study it can be emphasized that
the displacement of driven 3 cps hippocampal rhythms by theta
activity just prior to a conditioned response (Figure 6)

strongly supports the contention that theta activity in
the hippocampus is evoked by other proactive mechanisms.
This finding also suggests that there is a strong tendency
for hippocampal theta activity to occur during arousal but
is not necessary for arousal.

The major hypothesis of the present study was that the
hippocampal theta rhythm in the rat could be correlated with
responding in a nondiscriminative avoidance task and this
was supported by the results. However, the prediction that
brain stimulation which disrupted the theta activity would
also disrupt responding in an avoidance task was not support-
ed. However, an _ad_ _hoc_ hypothesis would hold that this re-
sult is what one would expect if the hippocampal theta rhy-
thm is merely correlated with arousal but not a necessary
correlate for on-going learned behavior.

Returning to the behavioral studies mentioned in the
Introduction in which lesions were placed in the hippocampus
(Kimura, 1958; Kaada et al, 1961; Isaacson et al, 1961; and
Isaacson and Wickelgren, 1962) evidence was presented that
led to the conclusion that the hippocampus _does_ play an im-
portant role in performing a variety of learned responses.
While it is not unusual for the results of lesion studies and
the results of electro-physiological studies to suggest some-
what different interpretations of the function of any given
brain structure, Flynn and Wasman (1960) presented evidence
which suggests a reconciliation of these views. They demon-

strated that cats could learn a classically conditioned leg
withdrawal during the after-discharge of hippocampal seiz-
ures even though they were not capable of performing it dur-
ing the seizure. They further reported that disruption of
previously learned behavior by brain stimulation might be
explained by motor deficiency due to the effects of the in-
duced hippocampal seizure on the motor cortex. In particular
they found that hippocampal seizures increase the latency of
cortically evoked movement: thus, lesions, like seizures might
depress learned responses by affecting motor mechanisms.
The fact that only bilateral hippocampal seizures disrupt
learned responses (Flynn et al, 1961) and that the effect may
well be on the motor side (Flynn and Wasman, 1960) of the
conditioned relationship agrees with the results of the pres-
ent study. In the present study stimulating the hippocampus
with 6 cps at 2 and 3 volts showed no evoked discharges in
the hippocampus on the opposite side although it was quite
likely that the stimulated structures were being affected.
However, no disruption of conditioned behavior occurred.
But, applying 3 cps electrical stimulation of subseizural
intensity to the hippocampus disrupted normal neural activ-
ity on both sides as shown by the driven hippocampogram
(Figure 6), but it did not prevent the subject from making
the conditioned response, presumably since the motor centers
were not effected. Further, the displacement of the driven
rhythm by theta rhythm indicates that the arousal mechanisms
were still intact.

In short, when one considers the evidence of the present
study with respect to neuroanatomy, electrophysiology, and
behavior correlates, the arousal hypothesis of the origins
of the theta rhythm seems to integrate more facts than any
other single hypothesis.

Summary

In a Sidman avoidance task, rats with bipolar hippo-
campal electrodes showed that irregular hippocampal EEG ac-
tivity changed to regular 5-7 cps theta activity just preced-
ing and during an avoidance lever-press. The appearance of
these theta rhythms during the Sidman avoidance task sug-
gested that the theta rhythm was not dependent upon extero-
ceptive stimuli, but rather was a correlate of centrally in-
itiated attention or arousal. Simultaneous stimulation and
recording showed that altering the hippocampal rhythms did
not disrupt avoidance behavior if stimulating voltage was
below seizure inducing levels; this suggested that hippo-
campal theta activity, though correlated, is not causally
related to arousal.

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