CORRELATION OF THE HIPPOCAMPAL THETA RHYTHM WITH CHANGES IN CUTANEOUS TEMPERATURE[1]

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RUNNING HEAD: THE THETA RHYTHM AND CUTANEOUS TEMPERATURE

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ABSTRACT

In the present study, a possible role for the hippocampus in alerting an animal to changes in cutaneous temperature was examined. Following local warming or cooling of the ears of unanesthetized, loosely restrained rabbits, theta waves (4-7 Hz EEG waves) were recorded from electrodes straddling the hippocampus. The onset of the hippocampal theta rhythm was correlated with changes in cutaneous temperature, an observation consistent with studies indicating that the theta rhythm is a nonspecific response evoked by stimulation of several sensory modalities. Additional data from cats and rabbits were correlated with specific neurons within the hippocampus, namely pyramidal cells. Post-stimulus time histograms obtained by excitation of the dorsal fornix were interpreted in terms of excitatory and inhibitory inputs to pyramidal cells. Thus, the theta rhythm, which appears to be evoked by changes in cutaneous temperature, can be related to a specific type of hippocampal neuron which is in turn connected with other areas of the brain involved in temperature regulation.

EEG correlates with alterness, temperature pathways, neural networks.

Conditions tending to arouse an animal evoke a particular pattern of neural activity in the hippocampus, the theta rhythm. Even though there is still debate as to the detailed function of the hippocampus and the remainder of the limbic system (5, 19-21), Green and Arduni (11) have shown that these theta waves (4-7 Hz in the rabbit) can be evoked by the following types of stimuli: auditory, olfactory, optic, tactile, and direct brain stem stimulation. However, it has not been determined whether changes in cutaneous temperatures alone could elicit the theta rhythm and the involvement of rhythms in thermoregulatory behavior has not been extensively studied.

On the one hand, temperature regulation in mammals has been shown to be a complex process involving both hypothalamic and extrahypothalamic components (cf. 1, 8, 12, 14). Based primarily on physiological studies, several models for a temperature controller, centered in the posterior hypothalamus, have been proposed (6, 12, 14). None has stressed the possible relationship of the hippocampus to the hypothalamus and midbrain, the latter being the principal areas presently included in thermoregulatory models.

On the other hand, neural networks within the hippocampus have been subjects of extensive study, and the theta rhythm has been associated with pyramidal cells in these networks (cf. 4). Unlike the complex anatomical arrangement of neurons within the hypothalamus, the hippocampus is comprised of ordered arrays of neurons; therefore unit activity can be correlated with particular neurons with some certainty as to the connections of neurons within neural networks. For example, Kandel et al. (18) obtained long-lasting inhibitory potentials (IPSPs) which they attributed to pyramidal cells. These IPSPs were later related to a neural network with pyramidal cells forming a forward branch and basket cells a recurrent inhibitory pathway (2,3). This particular neural network has been further characterized by the presence of damped oscillatory waveforms following fornix stimulation; and the electric fields of these neurons have been mapped (16). A number of studies have

centered on the inhibition of pyramidal cells by basket cells, yet the effectiveness of basket cells in inhibiting the pyramidal cells as fornix stimulation is increased has not been extensively studied. Pyramidal cells are involved not only in hippocampal networks but also send their axons to the hypothalamus (27).

The observations that the hippocampus is anatomically connected with the hypothalamus and midbrain, and that changes in at least some sensory modalities serve to elict the theta rhythm, has led to the examination of the possibility that the hippocampus may be involved in temperature regulation. To this end, the present study centers on the following questions: (a) can the hippocampal theta rhythm be evoked by changing cutaneous temperature; and (b) can additional data be obtained consistent with the hypothesis that arrangement of pyramidal cells in specific networks does not rule out a role for these cells in the generation of theta waves. Rabbits were used to answer question (a) and cats to answer question (b).

METHODS

Seven New Zealand white rabbits (3–4 kg) were tranquilized with chloropromazine (0.4–0.5 mg IM), anesthetized with sodium pentobarbital injected into the marginal vein of the ear, and maintained on pentobarbital anesthesia throughout the course of electrode implantation. Atropine sulfate was injected IM to reduce secretions. Electrodes were made from stainless-steel wire with a nominal diameter of 0.25 mm and with a 0.5 mm uninsulated tip. After placing the rabbit in a stereotaxic head holder, burr holes were drilled in the skull approximately 1 mm anterior to the coronal suture and 0.5 and 1.5 mm lateral to the saggital suture. Two electrodes (used to stimulate a fiber tract, the fornix) were held by a carrier and lowered together to a position two millimeters above the fornix [a vertical height V7 by the rabbit atlas (24)] and temporarily left at that position. Then a second pair of electrodes (used to record hippocampal waveforms) was lowered on another carrier through burr holes (approximately 4 mm from the saggital suture in a coronal plane 3 mm posterior to the coronal suture) to straddle the hippocampal pyramidal cell layer (one electrode at V9, the other at V7). Final

positioning of the electrodes was aided by recording characteristic evoked potentials. To search for these waveforms, the electrodes above the fornix were slowly lowered while repetitive shocks (with an amplitude of 6 volts and a duration of 1.0 msec) were applied across them. At the same time, potentials from each of the two hippocampal electrodes with respect to a reference clip were amplified with Grass P511 preamplifiers and displayed on a 565 Tektronix oscilloscope. When the stimulating electrodes pierced the fornix and excited action potentials over this fiber tract, inverted waveforms were usually observed across the hippocampus. If necessary, the vertical position of the hippocampal electrodes were adjusted to obtain characteristic waveforms (Fig. 1C), and then all electrodes were cemented in place at the burr holes and the electrode carriers removed. The threshold for the characteristic waveforms was a 3 to 4 volt, 1.0 msec shock delivered to the dorsal fornix. Four stainless steel screws were fixed in burr holes over the cortex for anchoring a small, rectangular, 9-pin Cannon connector (MDl-9SL1) on the skull of the rabbit. Hippocampal leads, fornix leads and wires connected to the cortical screws were soldered to the connector. NuWeld dental cement was placed over the screws and exposed wires, and built up to secure the base of the connector.

Five days were allowed for recovery. The rabbit was then placed in an acoustically and electrically shielded environmental chamber and only very loosely restrained (primarily by leads attached to the Cannon connector and threaded through the top of a cage to a Beckman R411 pen writer). For some trials a resistor was taped to the inner surface of the ear. Heat generated by current through the resistor raised the local temperature which was measured by a thermocouple (as described below). In the remaining trials, water was continuously circulated at a constant flow first through a metal coil (outside the environmental chamber) and then through a single skin thermode consisting of an M shaped 16 gage stainless steel tube soldered to a 2 x 2 cm copper sheet. The metal coil was placed in a Blue M Microtrol water bath adjusted so that the temperature at the skin thermode was the

same as the ear temperature in the absence of the thermode. Temperature was measured by a constantan-copper thermocouple placed between the thermode and the ear. The temperature of the water flowing through the skin thermode could then be rapidly and quietly altered by immersing the metal coil into a Thelco water bath. A constantan-copper reference junction was maintained at constant temperature by an Omega ice point cell, and voltage changes across the two junctions, connected in series, were recorded on the Beckman R411 pen writer.

Twenty adult cats were injected with sodium pentobarbital (35 mg/kg, i.p.) and given sustaining intraperitoneal injections of sodium pentobarbital during the course of the experiment. Rectal temperature was maintained between 36 and 38 C. Tungsten microelectrodes were used to record data for post-stimulus time (PST) histograms (16). The potentials from electrodes were amplified by Grass P5C pre-amplifiers. Averaged evoked potentials (AEPs) and PST histograms were constructed using a Mnemotron 400A computer of average transients. Typically 100 transients were averaged for each record and the Mnemotron was gated so that the start of each transient waveform sampled preceded a shock to the fornix by a fixed period of time. Methods on cats are more fully described in a previous study (16). The placement of electrodes in the cat varied depending on experimental protocol as described in the results section.

RESULTS

Potential fields measured adjacent to the hippocampal pyramidal cell layer following stimulation of fiber tracts. The averaged evoked potentials (AEPs) shown in Fig. 1 indicate that electrical fields in the brain from both distant and nearby sources can be recorded by electrodes placed across the cat hippocampus. Column A shows recordings (with respect to a reference screw over the nasal sinus) from two electrodes, J and K, separated by 2 mm (see insert in Fig. 1) and held in place on either side of the hippocampal pyramidal cell layer. When stimulating electrodes

were lowered vertically from the surface of the brain toward the dorsal fornix, they pierced two major fiber tracts -- first the corpus callosum and then the fornix. Once excited, the corpus callosum, in turn, synaptically excites cells in the neocortex. Hence, when the stimulating electrodes were first lowered to a vertical position V9.5 [by the coordinates of Snider and Niemer (29)] the AEPs shown at the top of column A were attributed to spreading fields in a volume conductor (16) whose source was the neocortex. The AEP recorded from J, the electrode closer to the neocortex, has a larger amplitude than does the AEP from K, the electrode farther from the neocortex. Yet both have similar waveforms. As the stimulating electrodes were lowered to a vertical position of V5.8 (shown at the conclusion of the experiment by marking deposits to coincide with the fornix), single shock stimulation elicited inverted waveforms (the lowest pairs of AEPs in column A). The inversion indicates that a population of neurons on a plane between the electrodes J and K is the source of the potential field. Moreover, when the stimulating electrodes were lowered to V5.8, the amplitude of the AEPs recorded on a screw lateral to the stimulating electrodes and over the neocortex was decreased, indicating that the neocortex below the screw was no longer directly excited.

A second set of AEPs through the cat brain is shown in column B. In this case, the stimulating electrodes were positioned in the fornix and held in place while a recording electrode was lowered through the brain. The vertical height of the electrode at each site on the tract is shown at the left of each AEP. With fornix stimulation, evoked activity decreases as the electrode is displaced from the pyramidal cell layer in the hippocampus. The location of the pyramidal cells is indicated by the inversion of waveforms between V8.0 and V7.5. Thus for fornix stimulation, the potential field measured at a sequence of sites along a vertical track cutting through the layer of pyramidal cells has the following characteristics: (a) it is localized to the hippocampus; (b) it inverts across the pyramidal cell layer; and (c) it differs from other potential fields (e.g., the field generated by

the neocortex with stimulating electrodes in the corpus callosum as shown in column A).

Single transients from electrodes placed across the pyramidal cell layer in the rabbit also shown inverted waveforms (column C). These inverted transients, A and B, were not observed when the stimulating electrodes were above the fornix. The waveforms shown in column C were taken to indicate that the electrodes were precisely positioned to record activity across the pyramidal cell layer. The transients are very similar to evoked potentials recorded in the rabbit (2,3) after the brain above and lateral to the hippocampus had been removed.

Following fornix stimulation, the AEPs of both cats and rabbits contain alternating peaks and valleys. The first peak corresponds primarily to the antidromic excitation of a layer of pyramidal cells, neurons whose axons form part of the fornix. Other pathways in the fornix are also excited by the electrical shock so that the first peak in the AEP may be modified by secondary signals; e.g., a signal over a multisynaptic path connecting the septal area to the pyramidal cell layer. The valley following the peak in the AEPs corresponds to inhibition of pyramidal cells as a result of a feedback signal from interneurons (2,3,16). The stainless steel electrodes, having a diameter of 0.25 mm, record an average of the dendritic responses of hundreds of hippocampal pyramidal cells. Unlike the hypothalamus, where neurons are oriented in all directions, the hippocampal pyramidal cells are neatly arranged with their apical dendrites pointed away from a surface. Hence the fields of individual pyramidal cells synchronously driven will sum to give a potential field of several hundred microvolts.

The theta rhythm in unanesthetized, loosely restrained rabbits. When a pair of electrodes was positioned as described in the preceding section, differential recording in awake, unrestrained animals showed rhythmic slow wave activity following novel sensory stimuli (Fig. 2). The waveforms in Fig. 2 indicate that a variety of stimuli can evoke the theta rhythm (see also reference 10). Comparison of the EEG activity for changes in temperature show waveforms that are similar to those obtained by other changes in sensory stimuli in that the theta rhythm is evoked.

Changing the temperature of the rabbit ear required more time than changing stimulus parameters of sensory modalities; e.g., the intensity of a light or the sound level of an audio amplifier. Figure 2 shows that during the continual increase or decrease in temperature which occurrred over several seconds the hippocampal activity in the rabbit shifts abruptly from an irregular, rapid waveform to the more regular, slower, high amplitude 4-7 Hz theta rhythm denoted by arrows in Fig. 2. As with other types of sensory stimulation, there is variability in the response to temperature changes. (Light and sound stimuli also served to evoke the theta rhythm in all rabbits considered here). When the theta rhythm was observed there was always a sharp, rapidly-occurring shift to the 4-7 Hz waveform; i.e., this response was not graded in that it did not increase in amplitude with greater temperature changes.

Changes of approximately 2 C occurring over a 2-4 second interval were sufficient to evoke the theta rhythm. For example, an increase in cutaneous temperature from 36 to 38 C and a decrease from 36 to 34 C were enough to evoke the rhythm as shown in Figs. 2B and 2C. In 6 out of 7 rabbits an increase between 2 and 4 C was sufficient to increase the theta activity and in all 7 rabbits a decrease from 2 to 4 C also served to increase theta activity (see table 1). EEG waves were recorded with high frequency filters set at 30 Hz and low frequency filters set at .53 Hz.

The theta rhythm (4), as well as fast components of EEG activity (30), appear to be the summed dendritic potentials of individual pyramidal cells within the hippocampus. That is, this EEG rhythm is evoked by extrahippocampal signals, possibly from the septum (26), while the AEPs result from excitation to the fornix, yet both the theta rhythm and AEPs reflect activity of pyramidal cells. The data in Fig. 2 are consistent with this hypothesis in that the electrodes were placed to record AEPs from pyramidal cells and the bipolar recordings also display hippocampal theta rhythms. The relation of the septum and fornix to the hippocampus is diagrammed in Fig. 3.

Correlation of the theta rhythm with a neural network in the hippocampus. The electrical activity of single neurons can be correlated with particular cell types. PST histograms were recorded at a depth of approximately 0.35 mm below the surface of the lateral ventricle (corresponding to the layer of pyramidal cells) and AEPs recorded at the same site had a maximal positive wave (2,3). The cells fire, are inhibited, and then fire again to give a series of peaks on PST histograms. Following initial excitation, a pyramidal cell is inhibited indicating that the position of a cell in a feedback network will constrain its activity (Fig. 3B). The period of suppressed activity (labeled D_1 in Fig. 4) is lengthened by increasing the amplitude of fornix stimulation from 2.5 to 5.0 volts (the threshold for driving the pyramidal cell was close to 2.5 volts). For fornix stimulation at 5.0 volts the pyramidal cell does not fire for some 30 msec following initial excitation, an indication of the potent inhibitory drive from the interneuron population. The increase in inhibition parallels an increase in the amplitude of the first peak P_1 with increasing stimulus voltage. This is consistent with the network in that the more intensely the pyramidal cells are driven the more intensely they will drive the interneurons. PST histograms like that in Fig. 4 were recorded from 25 neurons.

Associated with PST histograms were matching AEPs recorded at the same site. Such pairs are shown in Fig. 4. The record of the action potentials over a single pyramidal cell fiber (the PST histogram) is related to the dendritic activity of a population of cells (the matching AEP) in that the peaks in the histograms coincide with the portions of the AEPs having a negative slope. All of the records in this study thus reflect different aspects of the pyramidal cell population within the hippocampus. The oscillatory activity of the AEPs and PST histograms are consistent with the inhibitory hippocampal network diagrammed in Fig. 3B (16).

DISCUSSION

The hippocampal theta rhythm and cutaneous temperature. The onset of theta activity in the electroencephalogram recorded from the hippocampus was correlated

with "arousal" by Green and Arduini (11) in 1954. However, even though this early study has stimulated much addtional work by neurophysiologists as well as psychologists, there is at the present time no general agreement on the detailed relationship between hippocampal theta activity and behavior. For example, Klemm (19) argues that the theta rhythm is a non-specific, reflex response to sensory excitation of the brain stem reticular formation that induces an over-all "readiness response" so that the animal may react to biologically signigicant stimuli. He interprets EEG and EMG activity recorded concurrently in the rat as consistent with his proposal. On the other hand, Landfield et al. (21), based on analysis of experimental data obtained from rats tested for retention in one-trial training, propose that the theta rhythm may be a temporal correlate of memory storage. That these alternative interpretations are not easily reconciled is shown by the exchange of letters between Klemm and Landfield (20). While these studies indicate that the rhythm can be associated with different factors depending on the experimental paradigm, they illustrate only one aspect of current proposals on the role of the theta rhythm as it relates to behavior.

An example of studies directed to the interpretation of particular frequency components or shifts in the frequency spectrum of EEG activity as behavior is altered is the study by Gray (10). He suggests that a septo-hippocampal system operates so that a theta rhythm in the 7.5 to 8.5 Hz band is responsible for processing of information and suppression of ongoing behavior upon receipt of signals of novelty, punishment, or omission of anticipated reward. Bennett (5), who has critically reviewed the electrical activity of the hippocampus as interpreted by a wide range of investigators, had concluded that the evidence best supports the view that the theta rhythm is related to "orienting or attention." Nevertheless, recent studies still associate theta waves with arousal, memory, learning, or motor activity (10, 19, 21, 25, 28).

Although there are still many interpretations of the behavioral significance of theta rhythms, it is generally agreed that this rhythm is evoked when unanesthetized

animals are presented with a novel sensory stimulus (5, 11, 20). Moreover, the onset of theta activity appears to be a nonspecific response in that it is evoked by a variety of sensory inputs; and, to the list of previously known stimuli, the data in Fig. 2 indicate that alteration of cutaneous temperature can be added.

In this regard, the theta rhythm was evoked by changes in cutaneous temperature at "normal" (e.g., 37-39 C) as well as at higher temperatures (40-42.5 C) (Fig. 2). However, although the behavioral responses of the rabbit did not appear to differ at the various cutaneous temperatures, and although skin temperatures used fall within the range of thermal receptor sensitivity (15), theta waves evoked at the higher temperatures may reflect the interaction of several sensory modalities (e.g., a noxious component).

Electrodes were positioned on either side of area CA_3 in the hippocampus so that differential recording would display activity from hippocampal networks. Monopolar records from relatively large electrodes, such as used in the chronically implanted rabbits, may pick up electrical fields established by distant sources, such as fields generated by the neocortex (as demonstrated by the AEPs in column A, Fig. 1, for anesthetized cats). However, characteristic electrical fields which are localized in the hippocampus can be measured as shown by AEPs recorded along vertical paths through the hippocampus (column B, Fig. 1). Moreover, the oscillations in evoked potentials can be correlated with the activity of individual cells recorded with microelectrodes at a precisely known depth below the surface of the brain, a depth corresponding to the layer of pyramidal cells (Fig. 4). These records, together with more extensive maps of the fields (2,3,16) indicate that once the variations of the evoked potentials are identified (column C, Fig. 1), AEPs can be used to precisely place recording electrodes on either side of the pyramidal cell layer (thus obviating the need to rely on a brain atlas except for the initial positioning of the electrodes). The importance of precise orientation of electrodes to detect hippocampal rhythms has been stressed by Whishaw and Vanderwolf (32).

Neural networks and the theta rhythm. The hippocampus is linked anatomically with areas of the central nervous system which are postulated to play an important role in temperature regulation, particularly the brain stem and the hypothalamus. On one hand, signals appear to travel from the reticular formation to the septum and then to the hippocampus (Fig. 3B). The reticular formation in turn receives signals from a variety of sensory inputs. It is likely that temperature receptors located on the skin (15), within the anterior hypothalamus (13,14) and within the spinal cord (6,17,31) encode signals which are relayed to the reticular formation. On the other hand, one of the major fiber tracts leaving the hippocampus, the fornix, makes synaptic connections with neurons in the hypothalamus, an area of the brain which has been associated with temperature regulation on the basis of extensive thermode studies as well as studies of single unit activity (8,13,14). Thus the hippocampus is connected by a pathway from the reticular formation and by a pathway to the hypothalamus.

The hypothesis that EEG waves including the theta rhythm can be related to the electrical activity of a particular cell type has been advanced in several studies (4, 10). The same population of cells generating EEG waves can be driven by fornix stimulation (2,3,16) so that AEPs also reflect the activity of the pyramidal cells aligned in a dense pallisade over a curved surface (22,27). The activity of a population of cells has been shown to be correlated with the activity of a single neuron in several areas of the brain (7,9). The matching AEPs and PST histograms (Fig. 4) provide additional data showing that the action potentials of single pyramidal cells are correlated with hippocampal population activity (2,4). Thus, in addition to evidence that the theta rhythm is evoked by changes in cutaneous temperature, there are a variety of studies which relate the rhythm to a particular hippocampal neuron, the pyramidal cell.

The activity of pyramidal cells is constrained by their location in neural networks within the hippocampus. The network shown in Fig. 3B, a network proposed by Andersen et al. (2,3), is embedded within other networks (23), yet the

interconnected neurons appear to allow the pyramidal cells to be repetitively excited 4 to 7 times per second. Following activation of a pyramidal cell (indicated by peaks P in Fig. 4), the pyramidal cell is suppressed only for a limited time by the interneurons within the feedback path. The data show that the pyramidal cells are completely suppressed for a short period following excitation, a factor not documented in previous PST histograms (16). These averaged traces are consistent with the single traces of the intracellular potential recorded from pyramidal cells (2,3) where the short periods correspond to intervals where cells have large IPSPs. Thus, as in indicated in Fig. 4, pyramidal cells can be repetitively excited by action potentials arriving from extrahippocampal areas at the rate of four to seven impulses per second. Moreover, the inhibition is not sufficient to block periodic pulse trains below approximately 40 Hz (16). As in numerous other studies (7,9,16), the properties of neural networks and the relation of single units to neural populations was based on data from anesthetized cats; yet since the hippocampal network in Fig. 3B (2,3) is the same for both rabbits and cats, and since the theta rhythm is more easily detected in rabbits (5), in this study data on the theta rhythm were obtained from chronically implanted rabbits.

In conclusion, different areas of the brain appear to have specific functions with regard to temperature detection and regulation. The hippocampal theta rhythm appears to be evoked by novel changes in cutaneous temperature and this rhythm has been associated with arousal or alertness. The anterior hypothalamus and septal area are involved in thermodetection as shown by the fact that the appropriate physiological response is evoked by local warming and cooling with chronically implanted thermodes. The posterior hypothalamus may serve as one part of a neurocontroller for the integration of effector signals. Sensory signals are transmitted to the thalamus, cortex, and other areas of the central nervous system for delineation of topographic localization and intensity of cutaneous temperature.

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FIGURE LEGENDS

Figure 1. Potentials evoked in the anesthetized cat (columns A and B) and the rabbit (column C). Column A shows averaged evoked potentials (AEPs) from recording electrodes J and K at fixed sites above and below the hippocampus. The recording electrodes remained in one position while stimulating electrodes were lowered. The numbers adjacent to the AEPs in column A indicate the vertical height of the pair of stimulating electrodes lowered toward the fornix from V9.5 to V5.8 [using vertical (V), anterior (A), and lateral (L) coordinates of cat atlas by Snider and Niemer (29)]. Column B shows AEPs recorded on a recording electrode advanced through the hippocampus with the stimulating electrodes held fixed in the fornix at A9, V5.8, L1 and A9, V5.8, L2. The numbers next to the AEPs in column B denote the vertical height of the recording electrode at successive sites as it was lowered through the hippocampus. For each AEP in columns A and B, 100 transients were averaged following a shock of 5 volts and duration 0.01 msec. The inserts show the location of stimulating and recording electrodes with respect to the hippocampus and fornix. In column C are shown single transients recorded across the pyramidal cell layer in the rabbit. Transient A was recorded from an electrode placed just lateral to the pyramidal cell layer. In all AEPs and transients negative potentials are plotted upward.

Figure 2. EEG records from electrodes on each side of area CA_3 of the hippocampus (labeled H) and across two cortical electrodes (C) in the unanesthetized rabbit. In A, theta waves are present following either the onset of a tone or a light, or an increase in cutaneous (ear) temperature (T). The theta wave was evoked at a temperature of 42.5 C (indicated by arrow) as the ear was warmed. In B, the rabbit's ear was cooled by circulating cold water through a small coil taped to the ear and a theta wave was evoked at 37 C. In C the rabbit's ear was warmed by circulating warm water through a small coil taped to the ear and a theta wave was evoked at 38.5 C. All temperatures were measured by a thermocouple between the rabbit ear and thermode.

Figure 3. Sketch of hippocampal neural circuits with respect to other areas of the central nervous system. A. Orientation of the hippocampus to the septum and hypothalamus showing some of the linking fiber tracts. An afferent pathway to the hippocampus via the septum is labeled 1 and 2. An efferent pathway from the hippocampus to the hypothalamus is labeled 3. B. A simplified outline showing one neural circuit involving extrahypothalamic elements as well as a neural network within the hippocampus. The pyramidal cells (2 cells drawn with triangular shaped cell bodies) send fibers out of the hippocampus via the fornix and in addition send collaterals to excite (+) interneurons. The interneurons (drawn with a circular cell body labeled I) in turn form a feedback branch and inhibit (–) the pyramidal cells.

Figure 4. PST histograms and matching AEPs all recorded at the same site in the cat. In each pair the PST histogram is drawn as a sequence of dots and the AEP as a line. The stimulus voltage was increased from 2.5 volts for pair A to 5.0 volts for pair D. For the PST histograms the number of times a unit fired in each 3.75 msec interval divided by the number of transients averaged was taken as the firing probability of the neuron. A probability of 0.04 is marked off on a vertical scale. [Thus for the histogram in A the probability that a unit will fire during the first 3.75 msec interval is close to 0.03 and hence in 100 transients one would expect to record a total of 3 action potentials during the first 3.75 msec of the transients]. The first 20 msec of each PST histogram show the mean spontaneous firing level. SA is the shock aritifact due to the fields associated with fornix stimulation. Following an initial peak P_1 in firing probability, there is a decrease below the background level (region D_1). For the last 20 msec interval on each trace no unit activity was averaged thus providing a baseline of zero firing probability, and trace D shows that the pyramidal cell was completely inhibited for a period following the first peak P_1.

TABLE 1

THETA ACTIVITY BEFORE AND AFTER A CHANGE IN CUTANEOUS TEMPERATURE

RABBIT NUMBER	HEATING			COOLING		
	No. trials averaged	Theta in Interval A[1]	Theta in Interval B[2]	No. trials averaged	Theta in Interval A	Theta in Interval B
1[3]	1	7.5	12.5	4	6.8	11.4
2[4]	4	3.9	7.2	4	2.8	6.6
3	3	5.3	4.0	3	6.5	11.7
4	4	0.5	5.2	5	2.2	5.2
5	1	0.0	15.0	3	2.8	9.2
6	2	2.0	7.2	8	4.9	6.4
7	3	6.8	8.2	4	6.2	11.9

Notes:

1. When the skin temperature changed 2 C, the time was noted as T_1 on the records. The 15 second interval just prior to T_1, denoted interval A, was scanned to determine what portion of that interval had a theta rhythm. That is, each second of the interval for which 4 or more peaks were present at a 4 to 7 Hz rhythm was scored as having theta activity.

2. A 15 second interval just after time T_1, denoted interval B, was scanned to determine what portion of that interval had a theta rhythm. Thus in rabbit 3, the average theta in 3 trials was 4.0 sec.

3. In rabbit 1 current was passed through a resistor to heat the ear. The initial temperature was as shown in Fig. 2.

4. In rabbits 2-7 skin thermodes were used to heat and cool the rabbit's ear. Prior to heating or cooling, the temperature of the skin thermode was adjusted to equal the temperature of the ear in the absence of the thermode.

Figure 1

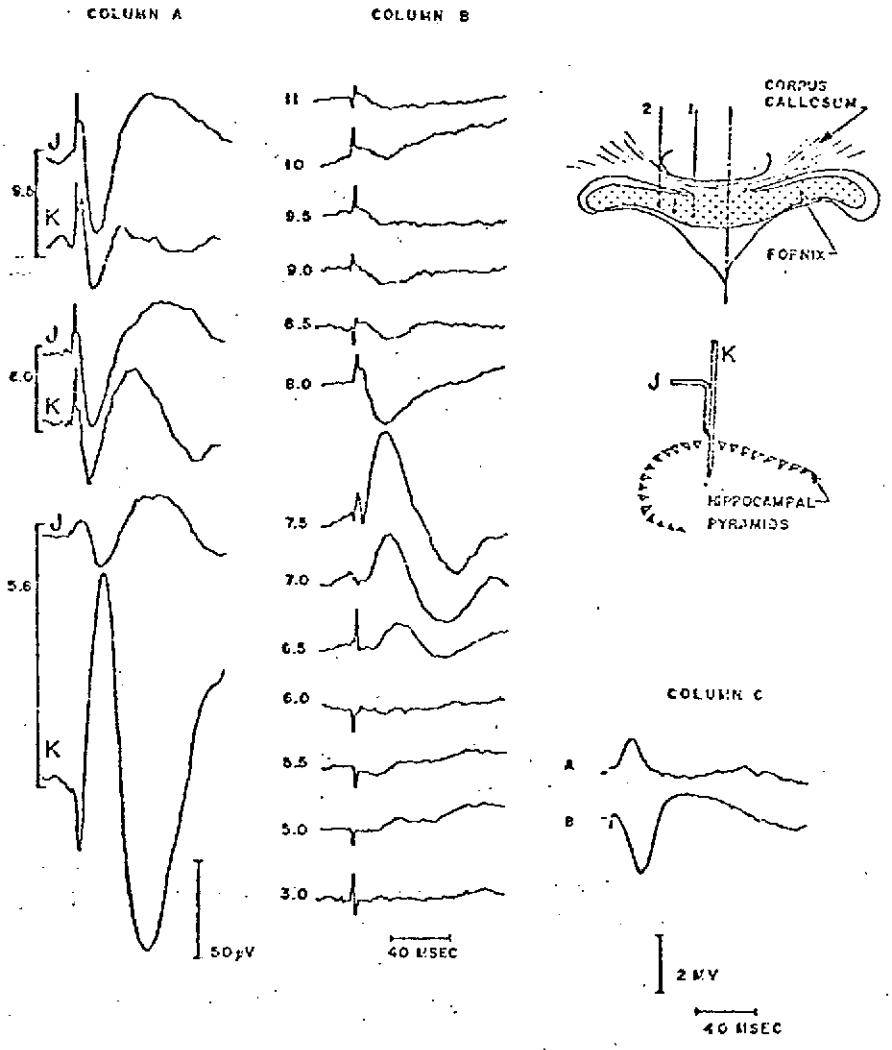

COLUMN A
COLUMN B
COLUMN C
J
K
9.6
6.0
5.6
50μV
11
10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
3.0
40 MSEC
CORPUS CALLOSUM
2
1
FORNIX
HIPPOCAMPAL PYRAMIDS
A
B
2 MV
40 MSEC

Figure 2

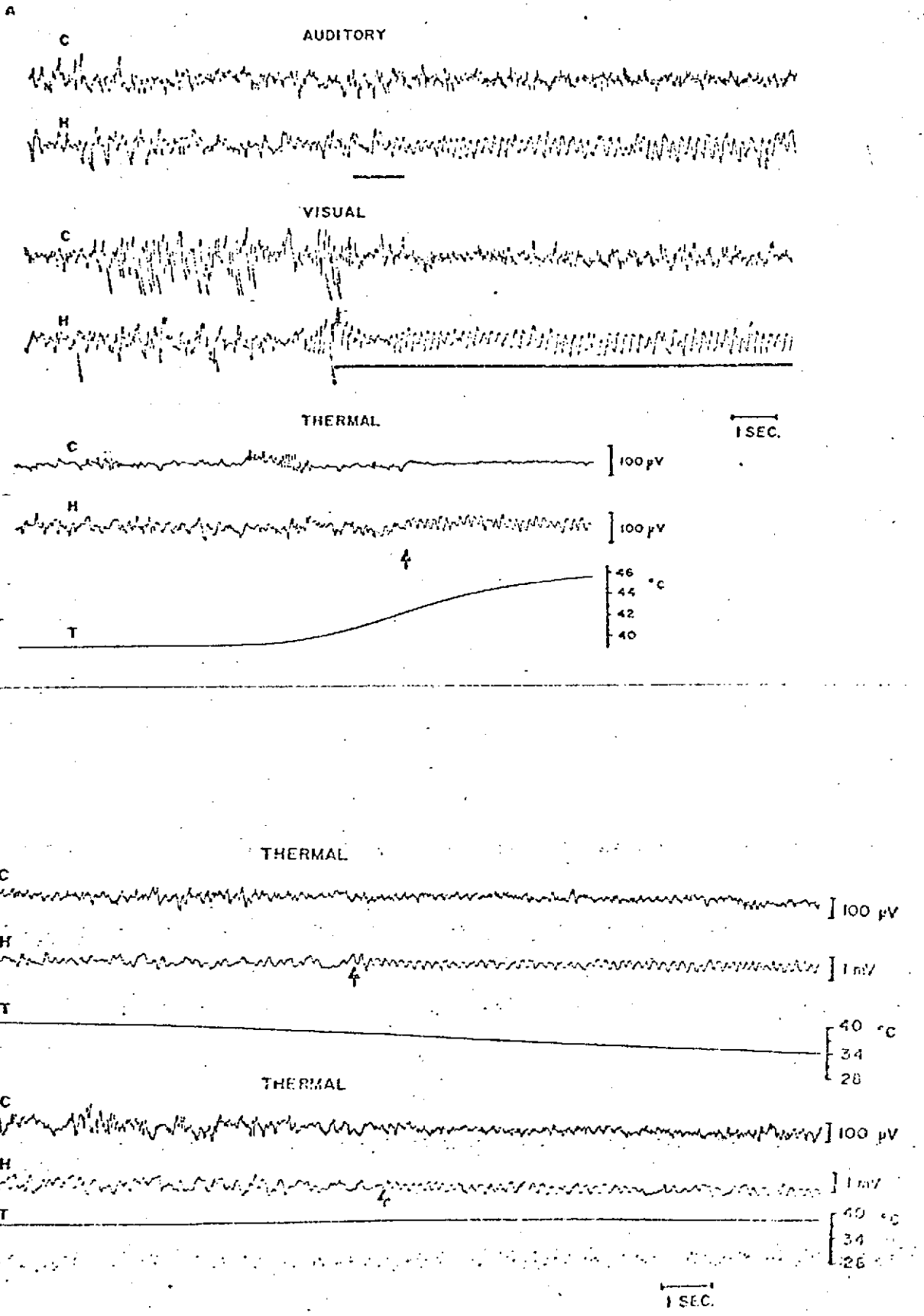
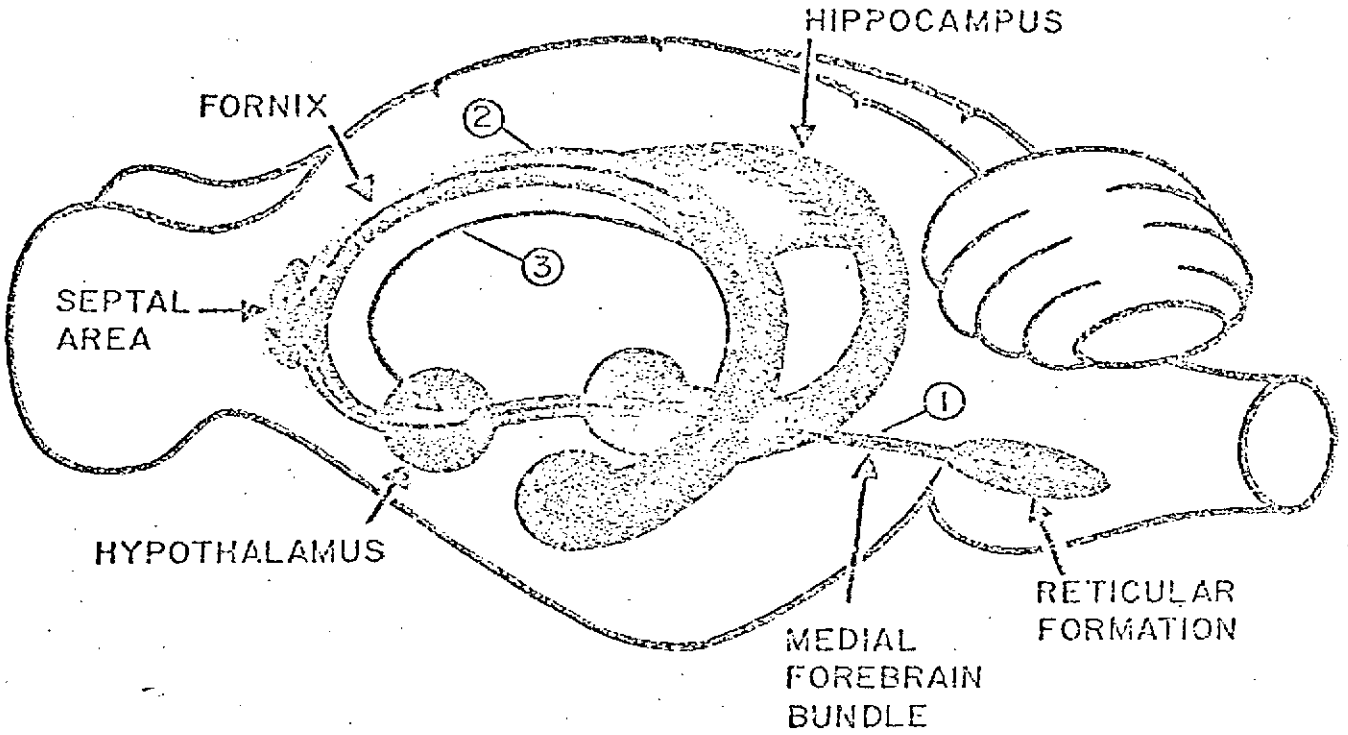

A
AUDITORY
C
H
VISUAL
C
H
THERMAL
1 SEC.
C
100 µV
H
100 µV
46
44
42
40
°C
T
B
THERMAL
C
100 µV
H
1 mV
T
40
34
28
°C
C
THERMAL
C
100 µV
H
1 mV
T
40
34
26
°C
1 SEC.

Figure 3

A


HIPPOCAMPUS
FORNIX
2
3
SEPTAL AREA
1
HYPOTHALAMUS
RETICULAR FORMATION
MEDIAL FOREBRAIN BUNDLE

B

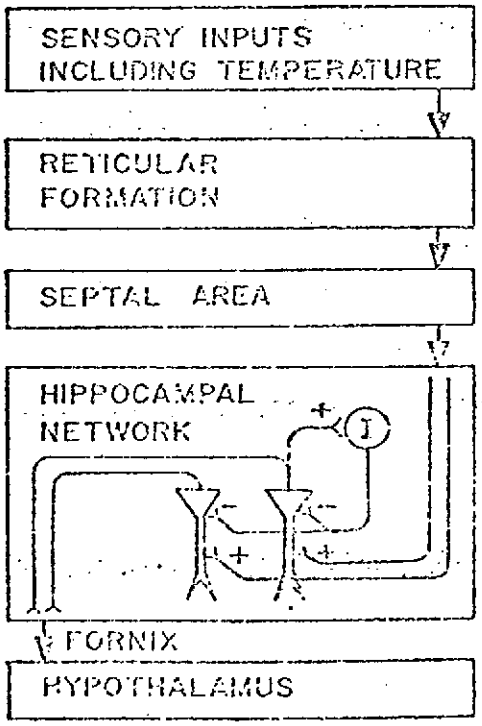
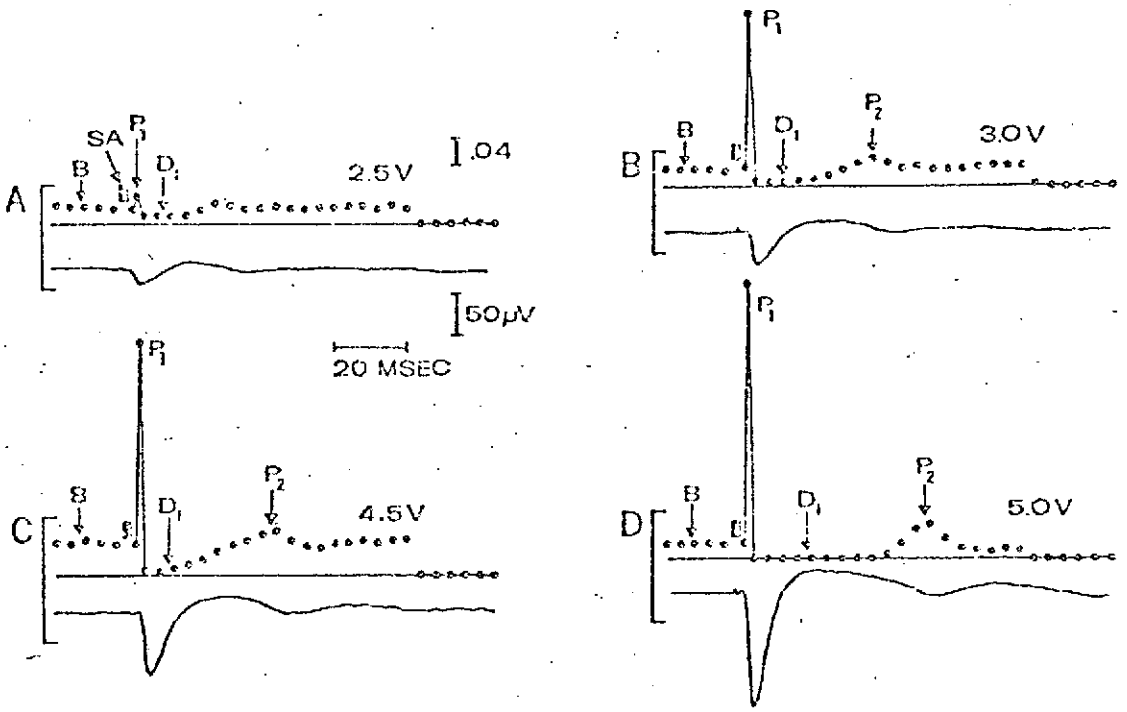

SENSORY INPUTS INCLUDING TEMPERATURE
RETICULAR FORMATION
SEPTAL AREA
HIPPOCAMPAL NETWORK
1
FORNIX
HYPOTHALAMUS

Figure 4


A
SA
B
D1
P1
2.5V
1.04
50μV
20 MSEC
B
P1
D1
P2
3.0V
C
B
D1
P2
4.5V
D
B
P1
D1
P2
5.0V