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ELECTRICAL ACTIVITY OF THE HIPPOCAMPUS DURING DELAYED RESPONSES AND HYPOTHALAMIC STIMULATION IN THE CAT

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Abstract. Electrical activity of hippocampus was investigated in cats in the delayed response situation by comparing spectral analysis and integration of electrohippocampogram rhythms in different stages of delayed response performance. In addition, electrical stimulation of lateral and ventromedial hypothalamic nuclei was used to observe changes in the hippocampal theta rhythm, as well as the behavioral effect during the delayed response performance. It is concluded that changes in the hippocampal theta rhythm are related to the changes in the drive level: high drive results in increasing the theta rhythm, whereas drive reduction results in its suppression. The activating role of hypothalamus in the dynamic changes occurring in the limbic circuit and their function in solving the delayed response problem are widely discussed.

INTRODUCTION

Recently a great deal of attention has been devoted to the study of dynamics of hippocampal electrical activity during the performance of both unconditioned and conditioned motivational behavior. It has been established that the hippocampal electrical activity undergoes regular shifts in various phases of elaboration of defensive (14, 36) or food (9, 14, 22, 30, 45) conditioned reflexes. Yoshi (45, 46) as well as Elazar and Adey (9) maintain that the dynamics of electrohippocampogram may reflect the correct or incorrect responses in the animal's performance during discrimination learning. In particular, only during correct responses but not during an error the theta rhythm of hippocampus becomes larger. There is considerable discrepancy on this point (22, 29). The majority of authors maintain that the dynamics of the hippocampal theta rhythm indicates the drive level and pattern of motivation (11, 12, 18, 23, 31).

On the other hand, it has been established that the occurrence and alteration of the theta frequency in the hippocampus is not accounted for by intrahippocampal nervous mechanisms. This is supported by the finding that the theta rhythm is neither observed after septal and hypothalamic lesions (5, 15, 35), nor in response to any peripheral or central stimulation. Obviously, the hippocampal theta rhythm develops due to the hypothalamic impulses spreading via the septum. Such impulsation from the hypothalamus evokes not only synchronization in the hippocampal electrical activity (theta rhytm) but also the general desynchronization (29, 31, 38, 40). We have demonstrated that the increase in the hippocampal theta rhythm is produced by electrical or chemical activation of the hypothalamic regions which contribute to the formation of alimentary and defensive reactions; stimulation of other areas eliciting inhibition of these reactions tends to suppress the theta rhythm (31).

In this paper the data are presented on the dynamics of the electrohippocampogram during delayed responses. The effects of stimulation of various parts of the hypothalamus on the hippocampal electrical activity and on delayed responses are also discussed.

METHODS

Experiments were carried out on 22 cats. Stainless steel electrodes insulated with glass except for an exposed tip of 100 - 200 μ were implanted in different areas of the neocortex, the hippocampus and hypothalamus with the aid of a stereotaxic instrument, using coordinates of Jasper and Ajmone-Marsan (19). The electrodes in a socket were fastened to the skull with steracryl.

Experiments were performed in an experimental cage with two chambers. The smaller one (0.3 m^2) was the starting place, where the animal was kept in the intervals between trials. The larger chamber (1 m^2) had windows on the right and left side-walls, beyond which feeders were placed, hidden from the animal's view. In order to get food the cat had to open the window with a forepaw and take a piece of meat from the feeder. In response to a tone of 500 Hz presented from a loudspeaker placed inside the cage above the feeders, the cat had to approach the right feeder, and the left one to a click. A conditioned signal was followed by opening of the door after 10-15 sec. The cat approached the feeder, took a piece of meat and returned back.

After the cat had reached a criterion of 100% of correct responses on each daily session consisting of 20-25 trials with 2-3 min intertrial intervals, experiments with estimation of the maximal length of delay were begun.

In these experiments a preparatory conditioned signal (tone or click) was delivered for 10 to 15 sec and the door was opened not during the delivery of the signal but at a certain time after its cessation. The delay period after which the cat was able to solve the task correctly in 90-95% of trials was regarded as the maximum of delay. Recordings of the electroencephalogram were made on 13-channel ink-writing "San'Ei" electroencephalograph. Spectral analysis of the EEG was made according to Gray–Walter on a 2-channel analyzer-integrator of the same firm. Integrative values were qualitatively processed and validity of the changes observed was verified by Student's t-test (25).

Hypothalamic structures were stimulated with bipolar electrodes. Rectangular pulses from a generator with high-frequency output were used. Stimulation parameters could be altered within a large range (0.5-10 v, 1-300/sec, 0.1-2 msec). After termination of the experiments the cats were sacrificed, brains fixed in 10% formalin solution and the exact placement of the electrode tips verified.

RESULTS

Changes in hippocampal electrical activity to conditioned signals during alimentary behavior

In our experiments the cats were trained to approach the feeders in response to a complex of conditioned signals. For the right feeder the complex consisted of a tone and the opening of the door, for the left feeder of a click plus the opening of the door. In each case according to Ławicka and Konorski (26) these components may be classified as preparatory (tone or click) and triggering (opening of the door) signals. As may be noted, the preparatory signals for running to the feeders are different, the triggering being the same. Thus, it is evident that the animal was responding on the basis of discrimination between two preparatory signals. In the preliminary stage the orientation reaction to tone and click was extinguished and the electroneocorticogram and electrohippocampogram showed no appreciable changes. After a few food reinforcements from the appropriate feeders the two conditioned signals began to evoke orientation reaction with alertness. During that period the electroneocorticogram showed the desynchronization and there was a remarkable increase of the hippocampal theta rhythm. After the formation of a stable conditioned reflex and discrimination of conditioned signals the dynamics of the hippocampal electrical activity regained a regular pattern. This was expressed in the increase of synchronization of slow waves in the hippocampus, produced by a preparatory signal and desynchronization in the neocortex (Fig. 1*A*). As to the slover hippocampal waves (delta rhythm) they were depressed in some cats by a conditioned signal, and considerably increased in others, as compared with the background activity (Fig. 1*A*). It has to be pointed out that the dynamics of delta rhythm depends on the background activity. If before the onset of a preparatory signal the animal sits quietly and the delta rhythm prevails in the electrohipocampogram, the conditioned signal causes a

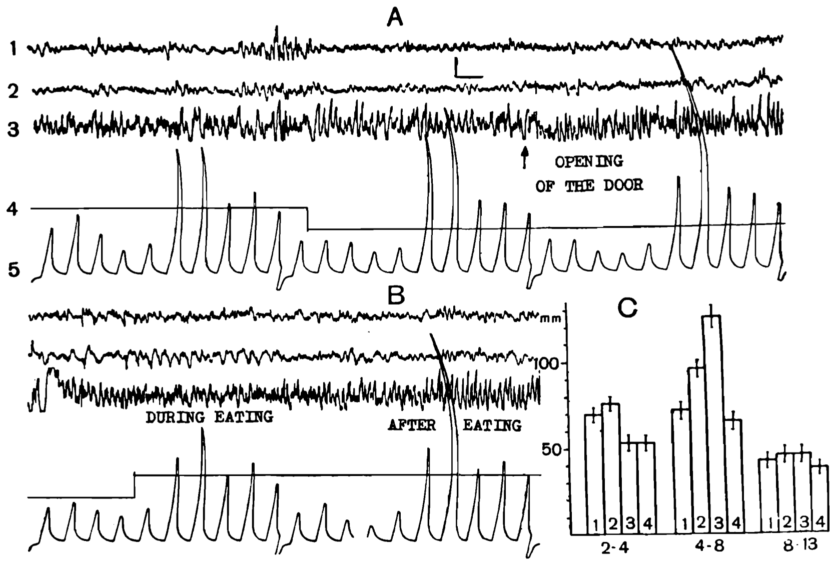

Fig. 1. Changes in the electrical activity of the neocortex and the hippocampus during conditioned signals (*A*) and during performance of conditioned alimentary reflex (*B*). Leads: *1*, auditory cortex; *2*, visual cortex; *3*, dorsal hippocampus; *4*, signal line marks the onset (downward) and cessation (upward) of the preparatory conditioned signal (tone 500 Hz); *5*, integrated values of separate delta (2-4 Hz), theta (4-8 Hz), alfa (8-13 Hz), beta (13-20 Hz) and beta (20-30 Hz) rhythms; epoch of integration is equal to 10 sec. The first five deflections show the integrated rhythms of the auditory cortex; other five deflections, the hippocampal rhythms. *C*, statistical data of delta, theta, alpha rhythms during different phases of performance of the conditioned alimentary reflex. The first column for each rhythm shows the values before the onset of the conditioned signal; the second column, during the preparatory conditioned signal; the third, after the opening of the door; the fourth, during eating. Arrow upward on *A* indicates the opening of the start chamber door. Calibration 100μv; time 1 sec.

decrease of this rhythm. During the wakefulness of the animal the delta rhythm is not always altered, as compared with the prestimulation state. Activation of the hippocampal theta rhythm is observed throughout the approaching behavior, but not at the moment of receiving food and its consumption. During eating the hippocampal theta rhythm is suppressed (Fig. 1*B*), but as may be seen from the integrated data, it is not associated with the slowing of the electrohippocampogram in which no increase in the delta rhythm can be observed. After receiving a piece of meat, the hungry animal is either searching the same feeder or turns to the other, which results again in an increase of the theta rhythm.

The results of statistical evaluation of the data on the changes of delta, theta and alpha rhythms in different periods of performance of alimentary conditioned reflexes, i.e., approaching the appropriate feeders to signals are presented in Fig. 1*C*. The first column for each rhythm shows their values before the onset of the conditioned signal, the second column — during the preparatory conditioned signal, the third column — after the opening of the door during the animal's movement toward the feeders and in the process of getting food, the fourth — during eating. The most striking changes occur in the hippocampal theta rhythm, the alpha remaining unchanged.

Changes in the hippocampal electrical activity during delayed responses

It may be suggested that a great increase in the hippocampal theta rhythm produced by the triggering stimulus is accounted for by summation of the two effects (the preparatory and triggering stimuli). However, this supposition is contradicted by the pattern of hippocampal activity during delayed conditioned response. The hippocampal theta rhythm is augmented more considerably after the cessation of the preparatory signal. Changes in the hippocampal theta rhythm to a preparatory and triggering stimulus during performance of delayed reaction are illustrated in Fig. 2. In a hungry cat the predominance of the theta rhythm in the hippocampus and desynchronization in the neocortex can be seen (Fig. 2*A*), whereas a preparatory signal significantly augments the hippocampal theta rhytm (Fig. 2*A*). this augmentation maintaining for a certain time, lasting after the cessation of a conditioned signal too (Fig. 2*B*). Some time later following the cessation of the preparatory signal the hippocampal theta rhythm begins to decrease to the initial background level (Fig. 2*B*). Against this background, the cat leaves the start chamber as soon as its door is opened and approaches the feeder. In response to the triggering conditioned signal during approaching behavior the hippocampal theta rhythm is remarkably increased (Fig. 2*C*), the extent of its increase prevailing over that observed to the preparatory conditioned signal. In this case too, after getting the reinforcing portion of meat and during the cat's eating there is depression of hippocampal theta rhythm.

Augmentation of the hippocampal theta rhythm during a preparatory conditioned signal and after its cessation is well correlated with the alert state of animal. In the first days of experimentation with responses after delay, the cats placed in the start chamber are restless; upon cessation of the preparatory conditioned signal they attempt to open the door of the start chamber and run to the feeder. During this time the hippocampal theta rhythm shows a remarkably strong increase, this state lasting for more than a minute. The animals then gradually subside and the electrohippocampogram also recovers to norm. In the subsequent days the cats responded to preparatory signals only by orientation reaction and alertness. In this stage the after-effect of the preparatory conditioned

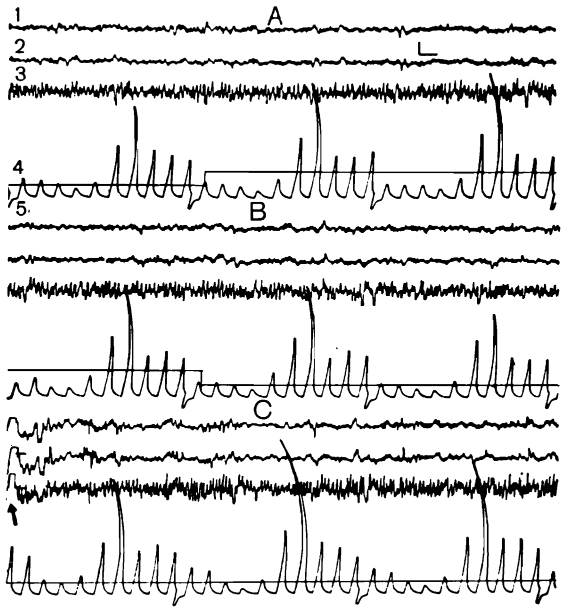

Fig. 2. Changes in the electrical activity of the neocortex and hippocampus during conditioned delayed reactions. Leads and calibration are the same as in Fig. 1. The signal line upward indicates the onset of the conditioned signal (tone 500 Hz). Arrow indicates the opening of the door of the start chamber. For *A*, *B* and *C* see explanations in text.

signal manifested in alertness and augmentation of the hippocampal theta rhythm lasts for a short time (10-20 sec, see Fig. *2B*) but nevertheless it does not affect the duration of delay. On the contrary, the animal reacts correctly even after the maximal delay period. The maximal length of delay periods in different subjects shows considerable variability within the range of 1-15 min.

The length of a delay period is likely to be defined by the duration of traces of the preparatory conditioned signal. It has to be assumed that the traces of different preparatory conditioned signals are dissimilar and therefore the same triggering stimulus may activate the more recent trace. After the extinction of the trace, the cats respond to the triggering stimulus by approaching, but commit errors and the percentage of correct responses does not exceed chance level. However, even on such occasions opening of the door evokes changes in the electrohippocampogram identical to those observed during delay. Differentiation between the frequency of hippocampal theta rhythm during correct and incorrect choices, as reported in the literature (9, 45), was not observed in our experiments (29). In this respect our findings are consistent with those of Konorski, Santibañez-H. and Beck (22).

Changes in hippocampal electrical activity during drinking and feeding behavior

Analysis of the electrohippocampogram throughout the performance of conditioned or delayed responses showed an occurrence of depression of the theta rhythm during eating (Fig. 1*B*). Depression of the theta rhythm during unconditioned eating was described by Routtenberg (37). This is not associated with enhancement of the motor activity, with chewing, in particular. This is supported, in the first place, by the finding

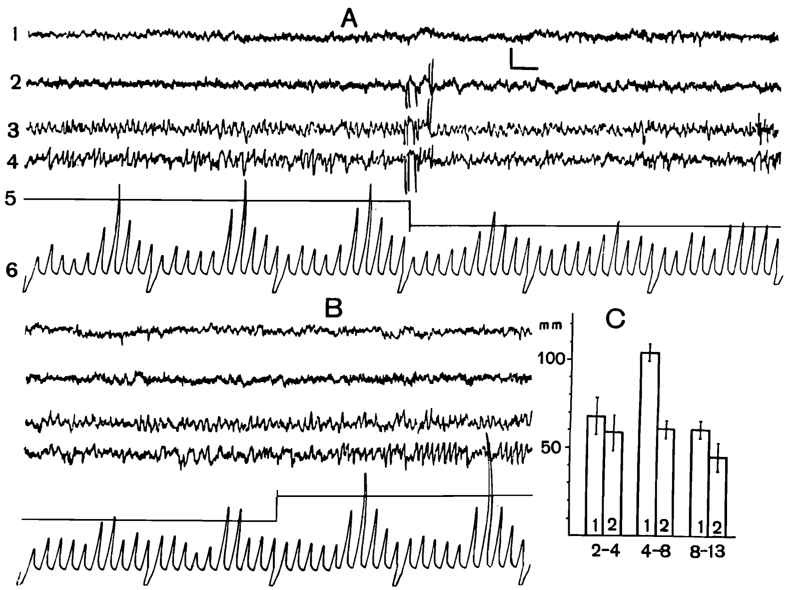

Fig. 3. Changes in the electrical activity of the neo- and paleocortex during drinking behavior. Leads: *1*, auditory cortex; *2*, pyriform cortex; *3* and *4*, symmetrical points of the right and left hippocampus; *5*, signal line downward, beginning of drinking; signal line upward, cessation of drinking; *6*, integrated values of delta, theta, alpha, $beta_1$ and $beta_2$ rhythms of the auditory cortex (first five deflections) and the hippocampus (other five deflections) during 5 sec epoch. *A*, before and during drinking; *B*, during and after cessation of drinking; *C*, statistical evaluation of changes in delta, theta and alpha rhythms before (column 1) and during (column 2) drinking behavior. Calibration 100μv; time 1 sec.

that during the running toward the feeder the hippocampal theta rhythm is increased and not decreased; secondly, during incorrect responses, when the cat attempts in vain to get a piece of meat from the feeder, it naturally develops a stronger motor activity causing an increase in the theta rhythm rather than its decrease. Only during eating is the suppression of hippocampal theta rhythm observed which seems to be connected with the satisfaction of the animal's need. This may be also seen in the electrohippocampogram during drinking behavior. Generally, in hungry and thirsty cats a prominent hippocampal theta rhythm occurs with no accessory stimulation (Fig. 3*A*). During drinking of milk the hippocampal theta rhythm is strongly suppressed. In case of the insufficient amount of milk to satisfy the animal's thirst, after drinking performance the theta rhythm reincreases (Fig. 3*B*). Characteristically, suppression of the hippocampal theta rhythm during eating or drinking behavior is not associated with the development of slower rhythms in the electrohippocampogram, i.e., this time delta rhythm is not increased, but even diminished (Fig. 1*B*). Suppression of the hippocampal theta rhythm is not associated with an increase of higher frequency rhythms either. Results of statistical analysis of the data show that during drinking behavior, as compared with the state of thirst, a suppression of the hippocampal theta and alpha rhythms occurs, which is statistically significant (Fig. 3C). Delta rhythm also tends to be suppressed. As far as beta I and beta II rhythms are concerned no appreciable changes are observed.

Influence of electrical stimulation of lateral hypothalamus on deldyed responses and hippocampal electrical activity

The character and degree of changes of the hippocampal theta rhythm in response to a conditioned signal depends on the satiety of the animal. In hungry and thirsty animals the background electrical activity of the hippocampus shows predominance of the theta activity, which is strongly augmented by conditioned signals (Fig. 2). After multiple reinforcements of conditioned signals with food, the animals are eventually satiated and the conditioned signal evokes negligible increase of the theta rhythm. Finally, when the animals do not leave the start chamber, theta rhythm is appreciably decreased in amplitude instead of being augmented. Figure 4 illustrates changes of the hippocampal theta rhythm procuded by conditioned signals at two different levels of satiation. In the half-satiated animals (after having consumed 150 g of meat) the conditioned signal still causes a marked increase in the hippocampal theta rhythm (Fig. 4*A*). However, in the satiated animal (after consumption of 250 g of meat) a conditioned signal not only fails to augment the hippocampal theta rhythm, but even suppresses it considerably (Fig. 4*B*). In this latter case the animal does not leave the start chamber after opening of the door and remains quietly sitting there.

After satiation with a reinforcing portion of meat the animal frequently does not leave the start chamber, i.e., does not perform alimentary reaction, though the preparatory as well as the triggering stimulus still produce a marked increase in the hippocampal theta rhythm (Fig. 5*A*). However, if at this moment the lateral hypothalamus is electrically stimulated, causing alimentary behavior in satiated animals and augmentation of the theta rhythm (Fig. 5*B*), the animal will perform alimentary reaction. It is of particular interest that on such occasions the animal performs the correct response, i.e., runs to the signalled feeder. Similar behavior may also be observed when lateral hypothalamic stimulation is applied 20-40 sec after the cessation of the auditory signal.

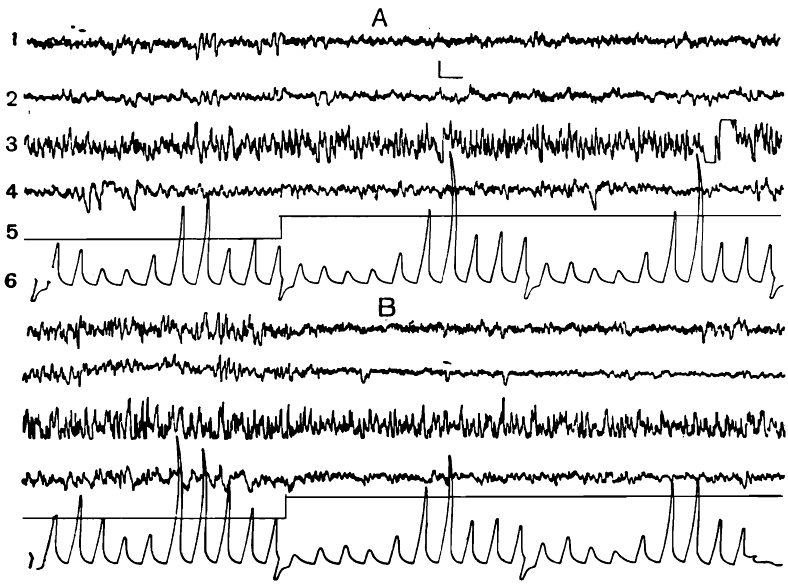

Fig. 4. Changes in the electrical activity of different structures of the brain evoked by conditioned signal during different states of satiety. Leads: *1*, auditory cortex; *2*, visual cortex; *3*, dorsal hippocampus; *4*, reticular formation; *5*, signal line upward shows the onset of the conditioned signal; *6*, the integrated values of delta, theta, alpha, $beta_1$ and $beta_2$ rhythms of the auditory cortex (the first five deflections) and hippocampus (other five deflections) during 10 sec epoch. *A*, semi-satiated; *B*, satiated states. Calibration 100 μv; time 1 sec.

Figure 5 illustrates an experiment in which the lateral hypothalamus is stimulated 20 sec after the cessation of the preparatory conditioned signal and the animal performs the correct response. Stimulation of the lateral hypothalamus has a significant effect on the maximal length of

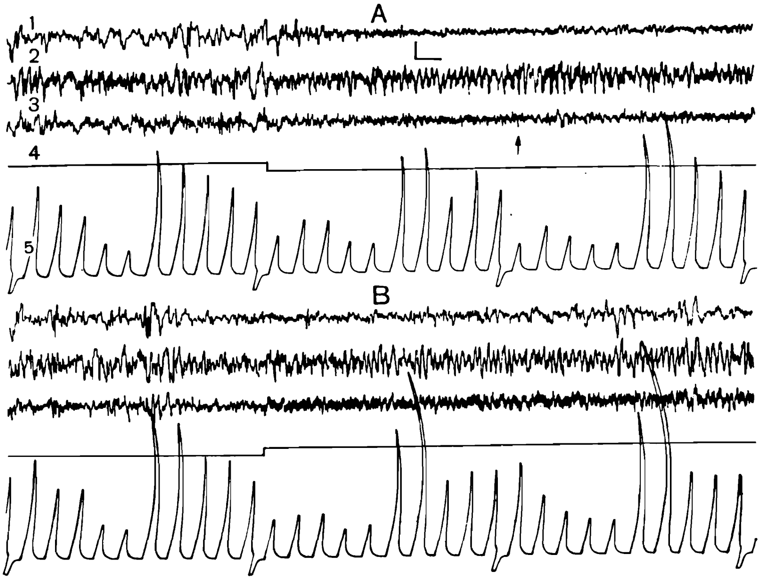

Fig. 5. Changes in the electrical activity of the neocortex and the hippocampus evoked by the conditioned signal (*A*) and by the electrical stimulation of the lateral hypothalamus (*B*). Leads: *1*, sensori-motor cortex; *2*, dorsal hippocampus; *3*, ventral hippocampus; *4*, signal line downward (*A*) marks the onset of the conditioned signal and signal line upward (*B*) shows electrical stimulation of the hypothalamus; *5*, integrated values of delta, theta, alpha, $beta_1$ and $beta_2$ rhythms of the sensori-motor cortex first five deflections) and dorsal hippocampus (other five deflections) during 10 sec epoch. Arrow indicates the opening of the door. Calibration 100μv; time 1 sec.

delay in delayed conditioned responses in hungry animals. The effect, however, is more or less dependent on the period of stimulation. Thus, for instance, if the lateral hypothalamus is stimulated either during the preparatory conditioned signal or immediately before it, the increase of the maximal length of delay appears negligible. However, if similar stimulation is delivered after the first half of the delay period, its maximal duration will increase by 50-80%. This suggests that under the influence of impulsation from the "center of hunger" the trace of the preparatory conditioned signal may be strengthened and maintained for a longer time.

Influence electrical stimulation of ventromedial hypothalamic nucleus on delayed response and hippocampal electrical activity

Electrical stimulation of the ventromedial hypothalamic nucleus appeared to have an opposite effect on the length of delay in delayed responses. In our experiments the stimulation of the ventromedial hypothalamic nucleus, inhibiting alimentary behavior in hungry animals, resulted in shortening of the delay duration. Such a stimulation proved to be most effective when delivered either during the preparatory signal or after its cessation. On such occasions neither delayed response nor response to actual stimuli were executed. If stimulation of the ventromedial hypothalamic nucleus was delivered during the approach response, the cat would stop responding. After cessation of stimulation the animal continued to approach the feeders, but committed errors. Likewise,

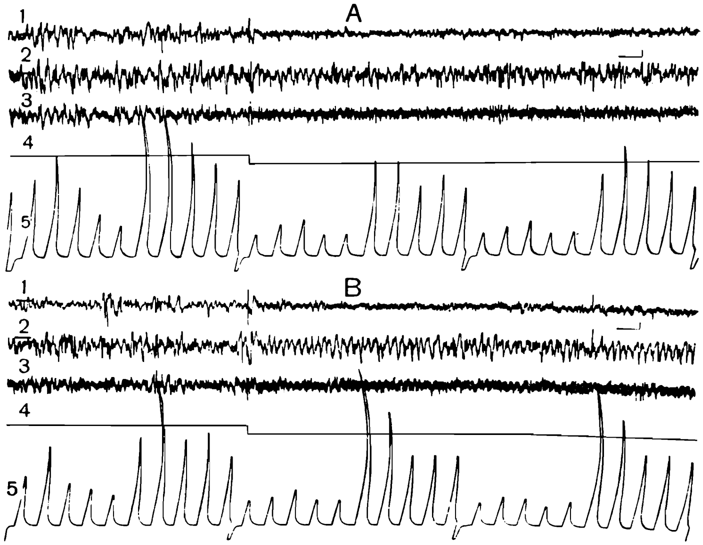

Fig. 6. Changes in the electrical activity of the neocortex and hippocampus induced by electrical stimulation of the ventromedial hypothalamus with different intensities. The parameters of stimulation: *A*, 1.5 v; 100 cycles/sec, 0.1 msec; *B*, 3 v, 100 cycles/sec, 0.1 msec. The signal downward marks the onset of stimulation. Leads and calibration are the same as in Fig. 5.

if stimulation of the ventromedial hypothalamus was produced after the cessation of a preparatory conditioned signal and the door was opened at different intervals after electrical stimulation had been ceased, the cat would leave the chamber, but would make errors. During inhibition of alimentary behavior produced by electrical stimulation of the hypothalamic ventromedial nucleus, depression of all rhythms in the electroneocorticogram and elecetrohippocampogram is observed (Fig. 6*A*). In some cases an increase of the hippocampal delta rhythm in parallel with the depression of theta rhythm and general desynchronization of the neocortical electrical activity occurs (Fig. 6*B*). Characteristically, an inhibition of feeding behavior during such a stimulation sets in with no accessory behavioral or somato-motor reactions. During stimulation the cats subsided and quietly sat in the cage. Following cessation of electrical stimulation very frequently intensified alimentary behavior was observed: the cats approached the feeders vigorously, but the responses were incorrect.

At higher intensities of electrical stimulation of the ventromedial hypothalamic nucleus behavioral reaction as well as hippocampal electrical activity were qualitatively different. Depending on the intensity and duration of high-frequency electrical stimulation of the ventromedial nucleus the cat developed reaction of aggression with hissing, stretching of claws, dilatation of pupils, piloerection and attack. All these behavioral reactions were accompanied by a strong augmentation of the hippocampal theta rhythm. It is obvious that such a stimulation also brought about disturbances in the actual responses both after and without delay. The results of these experiments have not been included in the present paper.

DISCUSSION

The foregoing material may be considered in several aspects.

1. According to the data of Grastyán's group (12, 14), augmentation of the hippocampal theta rhythm by a conditioned signal occurs only at the beginning of acquisition of conditioned alimentary reaction and is determined mainly by the development of orientation reaction. During consolidation of conditioned reaction, conditioned signals cause desynchronization of the electrohippocampogram instead of increasing the theta rhythm. Adey and his co-workers (1, 9), in the experiments dealing with dynamics of the hippocampal activity in the process of discriminative learning have not corroborated the findings of Grastyán and his associates (14). They have associated an increase of the hippocampal theta rhythm with a preferential goal-directed approach movement. Discussing these results Grastyán and co-workers (11) have maintained that in the experiments of Elazar and Adey (9), due to the complexity of their experimental set-up, there was no decrease of orientation reaction after the conditioned reflex had been consolidated. This resulted in lack of suppression of the hippocampal theta rhythm to conditioned signal and during performance of alimentary conditioned reflex. However, in a recent paper of Holmes and Beckman (18) an increase of the hippocampal theta rhythm is again considered as a manifestation of a goal-directed reaction.

In our experiments as well as in those of Elazar and Adey (9) the hippocampal electrical activity was studied during discriminative learning. The reflex was elaborated to different auditory conditioned signals in the presence of the two feeders. After discrimination of conditioned signals had been attained, the animals were directly approaching the appropriate feeders. Under these conditions the increase of the hippocampal theta rhythm was also observed. In some animals following prolonged tests on delayed reactions the preliminary conditioned signal was found to have no effect on the hippocampal theta rhythm, while the triggering signal evoked augmentation of this rhythm. Observations on the behavior of such animals showed that the preparatory conditioned signal caused only a weak orientation reaction. The animals responded to the triggering signal more readily and went straightforward to the feeders. The absence of appreciable behavioral and electroencephalographic effects in the interval between the preparatory and triggering signals may be explained by its analogy with the Pavlovian trace reflex (33), where in the interval between conditioned and unconditioned signals two phases are observable, i.e., the inhibitory and the excitatory one.

Predominant increase of the hippocampal theta rhythm in response to the triggering conditioned signal and during the approaching behavior may be explained by the strengthened feeding motivation; alternatively this increase might be determined by an increase of motor activity. The first assumption may be supported by the finding that increase of the hippocampal theta activity may be observed in curarized animals in response to the hypothalamic electrical stimulation which evokes neither motor reactions nor changes in the heart rate (39, 40). This shows that impulsation from the hypothalamus is sufficient to increase the hippocampal theta rhythm. Moreover, it has been established that after hypothalamic lesions the hippocampal theta rhythm is no more evoked during the direct stimulation of the reticular formation (15) or the peripheral nerve (5, 32). Since the hypothalamus is considered to be the substrate for the coordination of motivation, it may be suggested that the increase of motivation enhances also the hippocampal theta activity in unrestrained animals. However, one must not ignore the significance of the motor activity in augmentation of the hippocampal theta rhythm in the course of motivational behavior. Electrical or chemical stimulation of the hypothalamus with chronically implanted electrodes shows a distinct correlation between the motor reactions and the hippocampal theta waves (31).

Vanderwolf (41) and Paxinos and Bindra (34) have shown that during voluntary movements augmentation of theta rhythm is observed while the theta rhythm is suppressed in the case of local movements. This fact also suggests the significant role of motivation in regulating the hippocampal electrical activity, since it is a voluntary movement that must be triggered by motivational processes.

Thus, it may be assumed that during approaching the increase of the hippocampal theta activity is determined not by the unspecific diffuse motivation (11), but by the specific feeding motivation. This does not imply that the dynamics of the hippocampal theta rhythm concerns the changes of the feeding motivation only, since the theta rhythm develops also during conditioned and unconditioned defensive reactions (10, 15, 31). It is worth mentioning that the dynamics of the hippocampal theta rhythm properly reflects the motivational level, whenever it concerns orientation reactions with alertness, fear reactions, aggression or alimentary behavior.

2. Alterations in the hippocampal electrical activity during delayed responses evoke particular interest. The hippocampus, as one of the most significant structures of the limbic system, is considered to play an important role in the organization of motivational behavior. In particular the hippocampus is thought to be responsible for recent memory (28). Our experiments show that the increase of the hippocampal theta rhythm which develops in the presence of the preparatory conditioned signal persists also after its cessation. Duration of this after-effect depends on the level of animals' satiation. In a state of hunger the conditioned signal causes a stronger reaction of alertness, overlasting the conditioned stimulation during which the hippocampal theta activity is increased. In semi-satiated animals the after-effects become shorter, while in a state of full satiation the conditioned signals no more evoke the increase of the hippocampal theta waves.

It may be suggested that the increase of the hippocampal theta rhythm caused by conditioned signals manifests reverberating electrographic changes within the limbic system (29, 30). After cessation of the preparatory conditioned signal, while the hippocampal theta rhythm has been increased, the animal approaches the signalled feeder. If duration of these [illegible] the conditioned signal is reinforced by electrical stimulation of the lateral hypothalamus, the animal performs approaching movement. The animal's choice appears to be correct if electrical stimulation of the lateral hypothalamus is delivered not during the conditioned signal but after its cessation. This finding is interesting in two respects. First, it indicates that stimulation of the lateral hypothalamus activates the elaborated conditioned reflex; secondly, this stimulation may trigger excitation in the previously potentiated nervous circuits which are responsible for feeding motivation and discrimination capacity. This capacity persists for some time after cessation of the conditioned signal.

Activation of conditioned alimentary reflexes by electrical stimulation of different mesencephalic structures has been described by a number of authors (4, 6, 13, 24). This phenomenon has been reported by Grastyán and co-workers (13) to result from electrical stimulation of the hypothalamus. However, in these experiments no increment of the hippocampal theta rhythm was observed, but only general desynchronization. In our experiments general desynchronization in the electrohippocampogram was observed also during electrical stimulation of the ventromedial nucleus of the hypothalamus causing inhibition of alimentary behavior. This finding indicates that enhancement of the hippocampal theta rhythm is associated with the development of motivation, while inhibition of motivation is followed by theta rhythm depression.

The findings that electrical stimulation of the lateral hypothalamus results not only in the activation of conditioned alimentary reflex, but also enables correct responding after prolongation of delay in the delayed response test, indicate the important role of the hypothalamus in the formation of conditioned reflexes and in the establishment of temporary connections, as it was previously pointed out by several investigators (2, 27, 42-44).

REFERENCES

1. ADEY, W. R., DUNLOP, C. W. and HENDRIX, C. E. 1960. Hippocampal slow waves. Arch. Neurol. 3 : 74-90.
2. ANOKHIN, P. K. 1968. Biologia i neïrofiziologia uslovnogo reflexa. Izdat. Meditsina, Moscow. 547 p.
3. BERITASHVILI (BERITOFF), I. S. 1971. Vertebrate memory. Characteristics and origin. Plenum Publ. Corporation, New York. 125 p.
4. COHEN, B. D., BROWN, G. W. and BROWN, M. L. 1957. Avoidance learning motivated by hypothalamic stimulation. J. Exp. Psychol. 53 : 228-233.
5. CORAZZA, R. and PARMEGGIANI, P. L. 1963. Central course of the afferent system eliciting the theta rhythm in the cat's hippocampus upon ischiatic stimulation. Helv. Physiol. Pharmacol. Acta 21 : C10-C12.
6. DELGADO, J. M. R., ROBERTS, W. W. and MILLER, N. E. 1954. Learning

motivated by electrical stimulation of the brain. Amer. J. Physiol. 179 : 587-593.

7. ECCLES, J. C. 1953. The neurophysiological basis of mind. Clareton Press, Oxford. 314 p.
8. ECCLES, J. C. 1964. The physiology of synapses. Springer-Verlag, Berlin, 316 p.
9. ELAZAR, Z. and ADEY, W. R. 1967. Electroencephalographic correlates of learning in subcortical and cortical structures. Electroenceph. Clin. Neurophysiol. 23 : 306-319.
10. GRASTYÁN, E. 1959. The hippocampus and higher nervous activity. *In* M. A. Brazier (ed.), The central nervous system and behavior. J. Macy, Jr. Found., New York, p. 119-205.
11. GRASTYÁN, E., KARMOŠ, G., VERECZKEY, L., and KELLENYI, L. 1966. The hippocampal electrical correlates of the homeostatic regulation of motivation. Electroenceph. Clin. Neurophysiol. 21 : 34-53.
12. GRASTYÁN, E., KARMOŠ, G., VERECZKEY, L., MARTIN, J. and KELLENYI, L. 1965. Hypothalamic motivational processes as reflected by their hippocampal electrical correlates. Science 149 : 91-93.
13. GRASTYÁN, E., LISSÁK, K. and KÉKESI, F. 1956. Facilitation and inhibition of conditioned alimentary and defensive reflexes by stimulation of the hypothalamus and reticular formation. Acta Physiol. Hung. 9 : 133-151.
14. GRASTYÁN, E., LISSÁK, K., MADARÁSZ, I. and DONHOFFER, H. 1959. Hippocampal electrical activity during the development of conditioned reflex. Electroenceph. Clin. Neurophysiol., 11 : 409-430.
15. GREEN, J. D. and ADEY, W. R. 1956. Electrophysiological studies of hippocampal connections and excitability. Electroenceph. Clin. Neurophysiol. 8 : 245-262.
16. HEBB, C. O. 1949. The organization of behavior. J. Wiley and Sons, New York.
17. HEBB, C. O. 1954. The problem of consciousness and introspection. *In* E. D. Adrian (ed.), Brain mechanisms and consciousness. Blackwell Sci. Publ., Oxford, p. 402-422.
18. HOLMES, J. E. and BECKMAN, J. 1969. Hippocampal theta rhythm used in predicting feline behavior. Physiol. Behav. 4 : 563-565.
19. JASPER, H. and AJMONE-MARSAN, C. 1954. A stereotaxic atlas of the cat. Nat. Res. Council of Canada, Ottawa, 126 p.
20. KONORSKI, J. 1961. The physiological approaches to the problem of recent memory, *In* J. E. Delafresnaye (ed.), Brain mechanisms and learning. Blackwell Sci. Publ., Oxford, p. 115-132.
21. KONORSKI, J. 1967. Integrative activity of brain. An interdisciplinary approach. Univ. Chicago Press, Chicago. 531 p.
22. KONORSKI, J., SANTIBAÑEZ-H., G. and BECK, J. 1968. Electrical hippocampal activity and heart rate in classical and instrumental conditioning. Acta Biol. Exp. 28 : 169-185.
23. KRAMIS, R. C. and ROUTENBERG, A. 1969. Rewarding brain stimulation, hippocampal activity and foodstomping in the gerbil. Physiol. Behav. 4 : 7-11.
24. LAGUTINA, N. I. and ROZHANSKII, N. A. 1949. On the localization of the subcortical alimentary centers (in Russian), Fiziol. Zh. SSSR 35 : 587-593.
25. LAKIN, G. F. 1968. Biometria. Izdat. Vysshaya Shkola, Moscow.
26. ŁAWICKA, W. and KONORSKI, J. 1959. Physiological mechanism of delayed reactions. III. The effects of prefrontal ablations on delayed reactions in dogs. Acta Biol. Exp. 19 : 221-231.
27. LYUBIMOV, N. N. 1958. Electrical changes in the structures of the cortex and

the hypothalamus in the process of formation of a conditioned food reflex (in Russian, English summary). Zh. Vyssh. Nerv. Deyat. 8 : 560-569.

28. MILNER, B. 1966. Amnesia following operation on the temporal lobes. *In* C. W. M. Whitty and O. L. Zangwill (ed.), Amnesia. Butterworths, New York, p. 109-133.
29. ONIANI, T. N. 1971. On neurophysiological mechanisms of short-term memory. *In* G. Adam (ed.), Biology of memory. Akademiai Kiado, Budapest, p. 287-298.
30. ONIANI, T. N., NANEISHVILI, T. L., KORIDZE, M. G. and ABZIANIDZE, E. V. 1969. On neurophysiological mechanisms of delayed reactions (in Russian, English summary). Fiziol. Zh. SSSR 15 : 657-663.
31. ONIANI, T. N., UNGIADZE, A. A. and ABZIANIDZE, H. V. 1970. On the hypothalamo-hippocampal relations (in Russian, English summary). Neïrofiziologia 2 : 497-506.
32. PARMEGGIANI, P. L. 1967. On functional significance of the hippocampal theta rhythm. Progr. Brain Res. 27 : 413-441.
33. PAVLOV, I. P. 1923. A natural-scientific study of the so-called soul activity of the animal (in Russian). *In* Dvadtsatiletniï opyt ob"ektivnogo izucheniya vyssheï nervnoï deyatel'nosti zhivotnykh. Vol. 3. Gosudarstvennoe Izdat., Moscow, p. 64-81.
34. PAXINOS, G. and BINDRA, D. 1970. Rewarding intracranial stimulation, movement and the hippocampal theta rhythm. Physiol. Behav. 5 : 227-231.
35. PETSCHE, H., STUMPF, Ch. and GOGOLAK, G. 1962. The significance of the rabbit's septum as a relay station between the midbrain and the hippocampus. I. The control of hippocampal arousal activity of the septum cells. Electroenceph. Clin. Neurophysiol. 14 : 202-211.
36. PICKENHAIN, L. and KLINBERG, F. 1965. Behavioral and electrophysiological changes during avoidance conditioning to light flashes in the rat. Electroenceph. Clin. Neurophysiol. 18 : 464-476.
37. ROUTTENBERG, A. 1968. Hippocampal correlates of consummatory and observed behavior. Physiol. Behav. 3 : 533-535.
38. TOKIZANE, T. 1965. Hypothalamic control of cortical activity and some observation during the different states of sleep. *In* M. Jouvet (ed.), Aspect anatomo-fonctionnel de la physiologie du sommeil. C.N.R.S., Paris. p. 151-184.
39. TOKIZANE, T., KAWAMURA, H. and IWAMURA, G. 1960. Hypothalamic activation upon electrical activities of paleo- and archicortices. Neurology 2 : 63-76.
40. TORII, S. 1961. Two types of pattern of hippocampal electrical activity induced by stimulation of hypothalamus and surrounding parts of rabbit's brain. Jap. J. Physiol. 11 : 147-157.
41. VANDERWOLF, C. H. 1969. Hippocampal electrical activity and voluntary movement in the rat. Electroenceph. Clin. Neurophysiol. 26 : 407-418.
42. VORONIN, L. G., KALYUZHNYĬ. L. V. and ZAKHAROVA, I. N. 1965. Electroencephalographic data on the role of lateral and ventro-medial nuclei of the hypothalamus in closing food temporary connections (in Russian, English summary). Zh. Vyssh. Nerv. Deyat. 15 : 364-373.
43. VORONIN, L. G. and KOTLYAR, B. I. 1962. Bioelectrical activity of some parts of the brain during elaboration and extinction of alimentary conditioned reflex (in Russian, English summary). Zh. Vyssh. Nerv. Deyat. 12 : 547-554.
44. WYRWICKA, W. 1964. Electrical activity of the hypothalamus during alimentary conditioning. Electroenceph. Clin. Neurophysiol. 17 : 164-176.

45. YOSHII, N. 1965. Background activities controlling conditioned reflex and behavior. Proc. XXIII Int. Congr. Physiol. Sci., Symp. VI. Neuronal mechanisms of conditioned reflex and behavior (Tokyo), p. 354-358.
46. YOSHII, N., SHIMAKOCHI, M., MIOYAMOTO, K. and ITO, M. 1966. Studies on the neuronal basis of behavior by continuous frequency analysis of EEG. Progr. Brain Res. 21 : 217-250.

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