

Influence of Brain Neurochemical Systems on Frequency Spectra of Hippocampal Theta Rhythm

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Abstract: Chronic experiments with rabbits have shown that electrical destruction of dorsal amygdalofugal pathways leads to complete and persisted blockade of hippocampal theta rhythm in contrast to ventral one. In intact animals, electro- and chemostimulation of amygdala nuclei, hypothalamus, reticular formation and medial septum nucleus lead to the formation of well pronounced theta rhythm in hippocampus, but after destruction of the amygdalofugal pathway any theta-rhythm in this structure is not observed. Restoration of hippocampal EEG took place under intrahippocampal application of carbocholine and strychnine. It is proposed that one of the necessary conditions for the regulation of excitability of hippocampal neurons is the integrity of dorsal amygdalofugal pathways by means of which regulatory influence of amygdale on the hippocampal neurosecretory cells is realized.

Key words: Hippocampal theta rhythm, dorsal and ventral amygdalofugal pathway, electrical and chemostimulation, destruction.

I. Introduction

Over the years, one of the most controversial problems in the electrophysiology is the study of the hippocampal theta rhythm. Medial nucleus of the septum, which stands at the entrance to the hippocampus, demonstrates the importance of this education [1, 2]. In addition to the data indicative of the pacemaker role of the septum, there are works which demonstrated a definite role of stem-diencephalic structures in mechanisms of formation of hippocampal theta rhythm: great importance is given to the reticular formation [3], the hypothalamus [4], the thalamus [5], locus cereleus [6], nucleus raphe [1], etc. As the latest experimental studies have shown, the medial septum nucleus already received phasic encoded information from the rising system, the frequency of which determines the frequency septal discharges and frequency of hippocampal theta rhythm. There is evidence that this information comes from supramamillary nucleus of

the hypothalamus [7].

In our previous investigations it has been shown that electrical destruction of dorsal amygdalofugal leads to full and persisted blockade of hippocampal theta-rhythm in contrast to ventral one [8]. To elucidate the reasons for such profound changes, we carried out electrical and chemostimulation of limbic structures of the brain (amygdala, hypothalamus, reticular formation, medial nucleus of the septum, hippocampus) before and after the destruction of the dorsal amygdalofugal ways.

2. Methods

Experiments were carried out on 16 mature rabbits weighing 2.5-3.0 kg. The EHipG was recorded from the dorsal hippocampus (the CA₁ field: P3.0, L2.0, H8.0, and the CA₃ field: P3.0, L6.0, H7.5) and from the medial nucleus of the septum (A-3.0; L0.5; H10.5) on a Medikor electroencephalograph-16E encephalograph with the use of needle electrodes insulated except the tip. Spectral EHipG analysis was performed using standard electroencephalographic approaches. Test substances were strychnine (1%),

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carbachol (0.5-1.5 mcg), serotonin (5-50 mcg), and noradrenaline (15-20 mcg) applied in volumes of 5-6 mL via a chemotrode implanted in field CA₃.

Electrocoagulation of the dorsal amygdalofugal pathway was performed using electrodes implanted in the precommissural area (A-1, L5, H18) with currents of up to 1.0 mA for 15-25 sec. Electrical stimulation of extrahippocampal structures (reticular formation: P9, L2.5, H18.2; basolateral nucleus of the amygdala: A-1, L5, H18; central nucleus of the amygdala: A-1, L5, H16; supraoptic nucleus of the hypothalamus: A-3, L2.2, H15.8; ventromedial nucleus of the hypothalamus: AP0, L0.5, H17; medial mammillary nucleus of the hypothalamus: P2, L0.5, H18.5), medial nucleus of the septum and field CA₃ was performed using an universal electrical stimulator with square-wave impulses at frequencies of 5-100 per sec, amplitude 2-4 V, and duration 0.15 msec, for 15-30 sec; a histogram method was used for amplitude-frequency analysis of the EEG, as described by Fujimori et al. [9].

3. Results and Discussion

The results of these experiments showed that the baseline hippocampal and septal EEG demonstrated irregular activity dominated by oscillations in the range 4-6 Hz. Comparison of the electrical activity of the hippocampus and different fragments of conditioned reflex reactions supported the presence of a marked correlation of the theta rhythm with forms of behaviour such as resting, voluntary locomotion, jumps and runs, and licking, which was in agreement with results obtained in previous studies [8]. Application of test substances to the dorsal hippocampus before lesioning of the stria terminalis led to ambiguous results. In particular, the effects of biogenic monoamines ultimately led to a redistribution of the peak of the EEG amplitude-frequency characteristics in the hippocampus. Thus, while serotonin increased the EEG in the region 5-6 Hz, noradrenaline displaced the

peak of the frequency characteristic to the region 4-5 Hz. The effects of strychnine and carbachol were rather different. In this experimental situation, carbachol (like strychnine) resulted in generation of high-amplitude, regular theta waves of frequency 6-7.5 Hz at different time points, which with time could transform into epidischarges (Figs. 1c-1e). The EEG changes seen after carbachol and strychnine started in all leads simultaneously and were seen for prolonged periods of time (the maximum observation period was 3 h).

Destruction of dorsal amigdalofugal ways unlike ventral leads to a complete and irreversible blockade of hippocampal theta rhythm (Figs. 2b and 2c). Dynamic observations of the EEG after unilateral lesioning of the stria terminalis showed that the onset of EEG depression often started before the transition period, which showed transient epileptiform activity which subsequently disappeared, leaving only super slow oscillations. On this background we were unable to record neuron spike activity from field CA₃ of the hippocampus, though continuing insertion of the recording electrode resulted in the appearance of occasional neuron action potentials in the cerebral cortex.

Administration of biogenic monoamines into the hippocampus after lesioning of the stria terminalis did not induce any changes at all. Recovery of the electrical activity of the hippocampus due to electrical stimulation of various extrahippocampal structures (hypothalamus, amygdale, reticular formation, medial nucleus of the septum) did not occur, while stimulation of the hippocampus itself produced only epidischarges when the maximum stimulation current was used. The effects of application of carbachol and strychnine were identical. In this situation, there was a tendency to recovery of the overall activity of the hippocampus and septum, with some features consisting of short-lived (20-30 sec) periodically repeated generation of regular rhythmic activity in the range 0.6-7.5 Hz (Fig. 1f). Attention is drawn to the

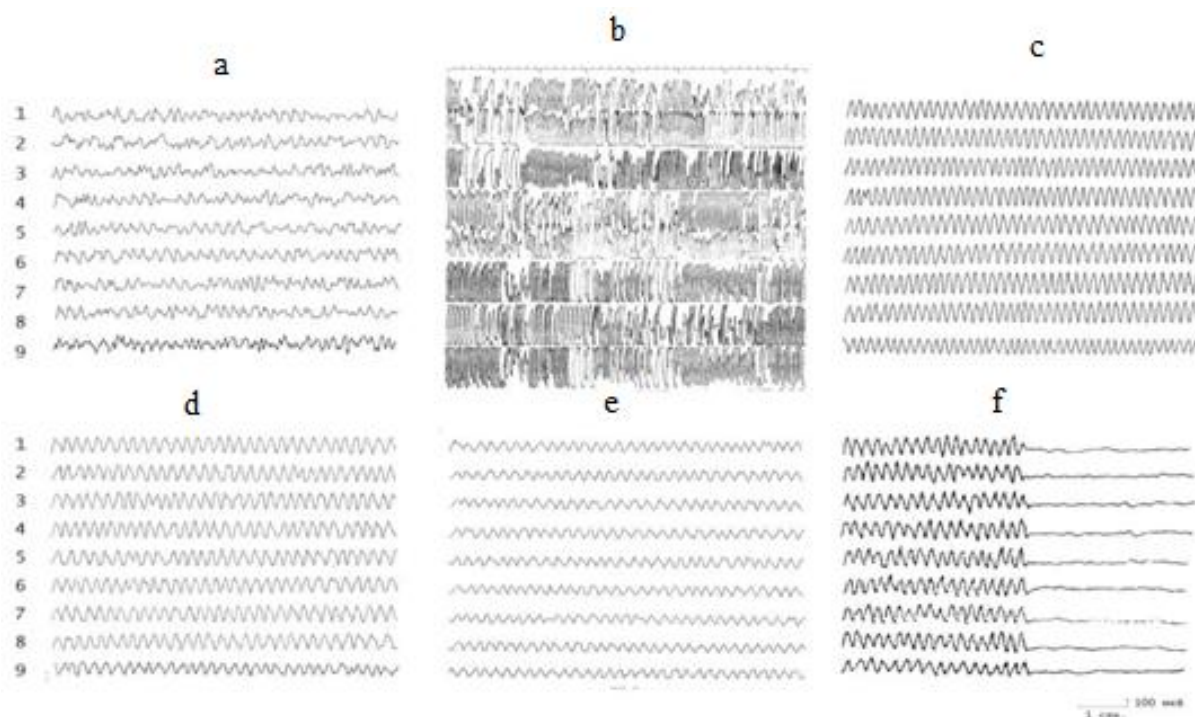


Fig. 1 The influence of electric and chemical stimulation field CA₃ dorsal hippocampus on the electrical activity of the hippocampus.

a—background; b—instant electrical stimulation; c—after application of carbachol; d—after the application of serotonin; e—after application of noradrenaline; f—application of carbachol on the background of the destruction of the dorsal amigdalofugal way. 1, 2) Field CA₁; 3, 4) Field CA₃ of the ipsi- and contralateral hemispheres; 5, 6) Ventral hippocampus of the ipsi- and contralateral hemispheres; 7, 8) Dentate gyrus of the ipsi- and contralateral hemispheres; 9) Medial nucleus of the septum.

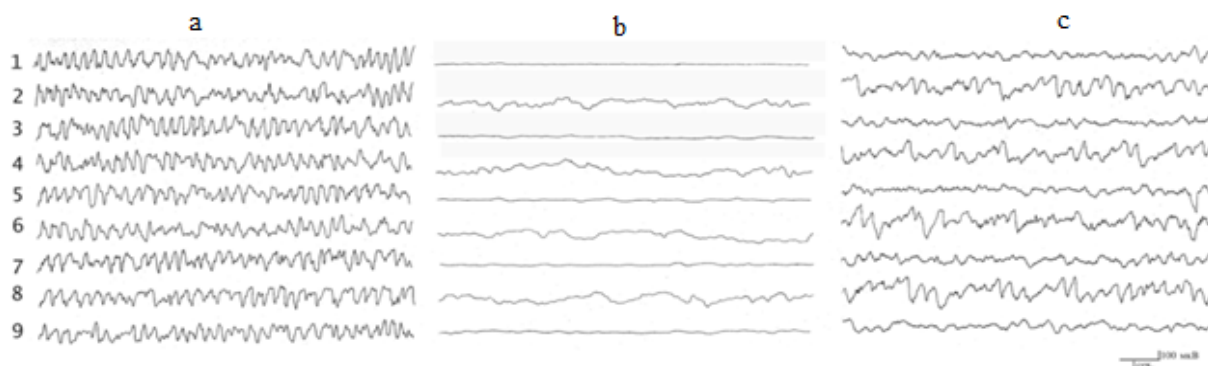


Fig. 2 Changes in hippocampal electrical activity in rabbits under conditions of destruction of the dorsal and ventral amigdalofugal ways.

a—background; b—after destruction of the dorsal amigdalofugal way; c—after destruction of the ventral amigdalofugal way. The rest of the notation is the same as in Fig. 1.

fact that, on the one hand, recovery of electrical activity in the hippocampus and septum occurred spontaneously in all leads, while on the other, there was marked synchronicity in the generation of electrical activity. The effects of carbachol and strychnine were largely similar and were long-lasting.

In addition, analysis of behavioral reactions provided evidence that conditioned reflex responses persisted in conditions of lesioning of the stria terminalis, with only an element of increase in the latent transfer of the response to the conditioned signal (2.0-2.5 sec as compared with 1.0-1.5 sec before lesioning).

Thus, the analysis of our data allows us to conclude that the actions of various neurochemicals on the EEG activity of the hippocampus possess a number common and differing properties. Among the first include: 1) The occurrence of synchronized theta wave activity; 2) The absence in different areas of the hippocampus differentiation of bioelectric reactions; 3) Violation of the regularity of the theta-wave activity and the emergence of epidischarges by increasing the dose injected into the investigated structure of the brain monoamines. For properties that distinguish the action applied neurochemical agents include: 1) The emergence of dominant frequency 6-7.5 number/s under conditions of cholinergic 5-6 count/s—with serotonergic and 4-5count/s noradrenergic stimulation of the nucleus the amygdale, hypothalamus, midbrain reticular formation, the medial nucleus of the septum and hippocampus; 2) Change in the amplitude of oscillations synchronized potential compared to background EEG activity, which reached its peak on the background of when administered of carbachol, average—with the introduction of serotonin and was below the background level after administration of noradrenaline.

Considering existing data in the literature about the importance of studying brain structures in the regulation of the pituitary-adrenal cortex, it can be assumed that changes in the excitability of hippocampal neurons caused by different electrical and neurochemical impacts on investigated structures of the limbic system, the content are due, apparently to the different concentrations of endogenous corticosteroids in the blood, and seek to compensate for changes caused by in the organism.

In the regulation of the pituitary-adrenocortical system may take part most various transmitters of nerve impulses (acetylcholine, noradrenalin, serotonin, dopamine, gamma-aminobutyric acid, prostanglandiny, etc.) [10]. According to existing literature data, under the influence of large amounts of corticosteroids in the blood occurs in the hippocampus rhythmic activity

with a frequency count of 4-6 Hz, and for topical application of cortisone or hydrocortisone considerably increases the level of the hippocampus pyramidal cells of the hippocampal excitability and formed there in seizure activity [11, 12], which, according to the authors, is proof of direct action of corticosteroids on the dendrites of hippocampal pyramids. In our experiments in hippocampal EEG also synchronized activity is registered frequency 4-6 Hz. However, under the influence of various neurochemicals in the hippocampus are recorded respective frequencies: wave number in the range of 4-5 Hz occurs when activating noradrenergic systems; 5-6 Hz—the serotonergic system; 6-7.5 Hz—the cholinergic system of the brain. Considering existing literature data about the nature and mechanism of action of central neurotropic drugs on adrenocorticotrophic function of the pituitary gland, juxtaposition with the results of our research allows you to conclude the possible involvement of one or another mediator of biochemical systems in the regulation of different frequencies hippocampal theta rhythm, which reflects a different level of activation hypothalamic-pituitary neurosecretory system. The results suggest that the regulation of hippocampal theta rhythm, as well as the functional activity of the hypothalamic-pituitary neurosecretory system, wears polimediation character and is not determined strictly by any single brain monoaminergic mechanism, ensuring the reliability of the pituitary-adrenal response to various influences, because this response is very important to maintain homeostasis. It is in this obviously, are the great compensatory possibilities of the central nervous system.

Complete and irreversible blockade hippocampal EEG caused by destruction of the dorsal amygdalofugal pathway obviously testifies about that in the given conditions the hypothalamic-pituitary-adrenal system works at a lower level—with violation of education of adrenocorticotrophic hormone and the rate of secretion

of corticosteroids. Thus, the results of the research testify to the modulating effect of the limbic brain structures on the hippocampal theta rhythm and apparently on the hypothalamic-pituitary neurosecretory system, as well as the activating the role of the amygdala on the activity of hypothalamic neurons.

All of the above stated testifies that a necessary condition of regulation the excitability of hippocampal neurons is integrity of amygdala-hypothalamic connections means of which the regulatory influence of the amygdala on the activity hypothalamic neurosecretory cells.

4. Conclusions

One of the factors which modulates the excitability of neurons in the septo-hippocampal system might be the disturbance of hypothalamo-hypophysial neurosecretory system under the influence of destruction of amygdala-hypothalamic relations.

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