# ROLE OF THE DORSAL HIPPOCAMPUS AND MESENCEPHALIC RETICULAR FORMATION IN THE MECHANISM OF THE AVOIDANCE REACTION IN RABBITS

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UDC 612.833.81-06:[612.825.263+612.826.4

KEY WORDS: dorsal hippocampus; reticular formation; avoidance.

Analysis of the central mechanisms responsible for the formation of defensive motivation in animals and of the avoidance reaction developing on its basis provides convincing evidence of the decisive role of the limbicomesencephalic formation in the genesis of this reaction. However, the role of individual formations of the limbic system and, in particular, of the dorsal hippocampus (DH), is still unexplained. Besides the results of investigations in which facilitation of onset of the avoidance reaction was observed in hippocampectomized animals [12], there are indications of interference with the formation of this behavioral reaction [9, 11]. There are no convincing data on the character of relations between DH and the mesencephalic reticular formation (MRF), whose role in the development of the avoidance reaction in animals, according to some investigations [6, 8, 13], is extremely complex.

In the investigation described below the effects of stimulation and coagulation of DH and MRF was studied on the avoidance reaction induced in an animal by electrical stimulation of the ventromedial hypothalamus (VMH) (the center for "affective reactions"), and the role of the limbicomesencephalic structures mentioned above in the mechanisms of spread of excitation from VMH to regions of the neocortex also was examined.

## EXPERIMENTAL METHOD

Experiments were carried out on 25 unimmobilized, unanesthetized rabbits weighing 2.5-3 kg. Nichrome electrodes 0.1 mm in diameter were inserted into the region of VMH and the animal's behavior was tested. In accordance with maps in the atlas of the rabbit's brain (Sawyer et al., 1957) electrodes also were inserted into DH and MRF, ipsilaterally or contralaterally relative to the stimulated hypothalamic center of "affective reactions." In the course of the experiment either DH or an area of the MRF was coagulated (3 mA for 10 sec) by means of the implanted electrode. Cortical electrical activity was recorded on a 15-channel Alvar-Electronic electroencephalograph. The EEG was processed (harmonic analysis, estimation of the powers of the rhythms) by means of an Estergom analyzer and integrator. The location of the subcortical electrodes and the dimensions of the foci of coagulation were determined histologically. The results of the observations were subjected to statistical analysis.

## EXPERIMENTAL RESULTS

An avoidance reaction of "escape" type, which is based on motivational excitation arising in the hypothalamic center for "affective reactions," after a short period of orienting behavior, was expressed as the animal's avoiding the place where it received brain stimulation. This behavioral reaction was accompanied by significant changes in the "autonomic components" of behavior; the heart rate and the depth and frequency of respiration. During analysis of the principal rhythms constituting the electrical activity of the subcortical structure and various regions of the cortex studied, an increase in power of the theta-rhythm in DH and MRF and also a tendency for the amplitude of all rhythms to decrease in the neocortex were observed. Analysis of ascending influences of VMH on cortical electrical activity during formation of the avoidance reaction in the animals revealed the important role of DH and MRF. In particular, statistically significant agreement was obtained between the char-

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0007-4888/81/9209-1139$07.50  

TABLE 1. Effect of Electrical Stimulation and Unilateral Coagulation of DH and MRF on Threshold of Stimulation of VMH Evoking an Avoidance Reaction in Rabbits

| Type of action | No. of animals | Effect on threshold of avoidance reaction | | |
|---|---|---|---|---|
| | | increase | decrease | uncertain |
| Stimulation of DH | 19 | 17 (89,47%) | — | 2 (10,53%) |
| Coagulation of DH | 14 | 14 (100%) | — | — |
| Stimulation of MRF | 7 | — | 7 (100%) | — |
| Coagulation of MRF | 10 | 7 (70%) | — | 3 (30%) |

acter of the ascending influences on electrical activity of the frontal cortex from VMH and DH ($P = 0.7$), and between VMH and MRF ($P = 0.4$). Different relationships were found between the effects of ascending hippocampal influences and influences during stimulation of VMH on occipital electrical activity ($P < 0.001$). Meanwhile the character of the changes in electrical activity in the occipital region of the neocortex during stimulation of MRF and VMH largely coincided ($P = 0.035$).

Electrical stimulation of DH hindered the appearance of an avoidance reaction in the animals in response to threshold stimulation of VMH, as expressed in a significant ($P < 0.001$) increase in the latent period of the response (in 89.47% of cases). Conditioning stimulation of MRF, on the other hand, in every case reduced the latent period of the avoidance reaction, evidence of the facilitatory character of reticular influences on the formation of this type of behavior.

Unilateral coagulation in the region of MRF ipsilateral and contralateral to VMH, stimulation of which evoked an avoidance reaction, mainly hindered the formation of this behavioral reaction in the animals (Table 1). Animals with unilateral coagulation of MRF were characterized by a lower level of motor activity and by less marked "autonomic" manifestations of respiration. The experiments showed that coagulation of MRF did not prevent DH from exerting inhibitory influences on the formation of the avoidance reaction.

Coagulation of DH hindered the appearance of an avoidance reaction in all experimental animals upon electrical stimulation of VMH. By contrast with animals with destructive lesions in the region of MRF, rabbits with a coagulated DH were characterized by motor disinhibition, by more frequent and at times violent orienting-investigative reactions. However, an avoidance reaction proper appeared in response to stronger stimulation of the hypothalamic center for "affective reactions."

These investigations demonstrated the different roles of DH and MRF in the mechanisms of spread of motivational excitation from VMH to the frontal and occipital regions of the cortex. Experiments with coagulation and with stimulation of the subcortical structures indicated the predominantly inhibitory influences of DH and facilitatory influences of MRF on excitability of the hypothalamic center for "affective reactions." The inhibitory character of the influences of DH has been established by many workers [1, 2, 3, 4, 5, 11] when studying the formation of different motivational reactions in animals. Meanwhile, during assessment of the role of DH in the formation of the avoidance reaction the polyfunctional nature of that structure and its role in different physiological processes constituting the initial stage of the behavioral act must be borne in mind [3]. Very probably the depression of the fear reaction in hippocampectomized animals described by some workers [7, 10] could be the reason why in animals with destructive lesions in DH, against the background of intensified orienting-investigative activity, an avoidance reaction proper arose in response to stronger stimulation of VMH.

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# EFFECT OF ATP AND ADENOSINE ON SPONTANEOUS ELECTRICAL AND CONTRACTILE ACTIVITY OF PORTAL VEIN SMOOTH MUSCLE CELLS

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UDC 612.18:612.816]:612.733.014.46:547.963.32

KEY WORDS: ATP; adenosine; portal vein.

Blood vessels are highly sensitive to adenine nucleotides, although their mechanism of action has not yet been explained. Interest in the vasomotor effects of adenine-containing substances has increased in the last decade, in particular, following the discovery of purinergic neuromuscular transmission in smooth muscles. According to recent investigations, the mediator for this transmission is evidently ATP [2], the inhibitory effect of which on smooth muscle cells of the gastrointestinal tract is effectively blocked by apamin [1]. The existence of purinergic neuromuscular transmission has also been postulated in smooth muscles of blood vessels [3].

The object of this investigation was to study the action of ATP and adenosine (AD) on spontaneous contractile and electrical activity of the smooth-muscle cells of the portal vein and also the action of apamin on the vascular effects of ATP and AD.

## EXPERIMENTAL METHOD

Experiments were carried out on smooth-muscle cells of the portal vein of guinea pigs, rats, and rabbits. Longitudinal strips not more than 1.5 mm wide and 7 mm long were cut from the blood vessel. The muscle strip was kept under isometric conditions of contraction. To record electrical potentials the single sucrose gap method was used. Contractile activity was recorded by the 6-MKhlS mechanotron. Electrical potentials and contractile activity were recorded on a type KSP-4 automatic potentiometer.

Continuously flowing Krebs' solution (36°C, pH 7.4) used in the experiments had the following composition: NaCl 120.4 mM, KCl 5.9 mM, $NaHCO_3$ 5.5 mM, $NaH_2PO_4$ 1.2 mM, $MgCl_2$ 1.2 mM, $CaCl_2$ 2.5 mM, glucose 11.5 mM (made up in bidistilled water). The action of AD and ATP in concentrations of $10^{-6}$-$10^{-3}$ M was studied on spontaneously active muscle strips from the portal vein. Apamin, a polypeptide from bee venom, was used in a concentration of $10^{-7}$-$10^{-6}$ M. Because of the development of desensitization of the portal vein muscle cells to AD and ATP, an interval of 15-20 min was provided between the repeated action of these substances.

## EXPERIMENTAL RESULTS

Under the influence of AD ($10^{-6}$-$10^{-5}$ M) a small increase in the frequency of a spontaneous action potentials (AP) and of phasic contractions of the muscle strip of the guinea

Department of Neuromuscular Physiology, A. A. Bogomolets Institute of Physiology, Academy of Sciences of the Ukrainian SSR, Kiev. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 92, No. 9, pp. 261-264, September, 1981. Original article submitted March 27, 1980.

  