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CHANGES IN THE MICROCIRCULATION IN THE RAT MESENTERY AND SKELETAL MUSCLES CORRELATING WITH THE SYSTEMIC ARTERIAL PRESSURE DURING HYPOTHALAMIC STIMULATION

V. K. Veit and A. M. Chernukh*

UDC 612.135: [612.339+612.741.61]-06: 612.826.4

KEY WORDS: microcirculation of the mesentery and skeletal muscles; pressor response.

No definite experimental data have yet been obtained on the role of the nervous system in the regulation of the microhemodynamics. The difficulty of the problem is that the microcirculatory component of the hemodynamic system is, on the one hand, a sufficiently autonomous system capable of self-regulation, whereas on the other hand, it includes in its structure the nerve fibers which connect the microcirculatory system with the central portions of the sympathetic and parasympathetic systems, and in this connection it can be assumed that the influence of the CNS is not restricted to mechanisms leading to changes in systemic arterial pressure (AP). Influences from the sympathetic nervous system leading to changes in capillary permeability and to local changes in the blood supply to individual regions of the microcirculatory system, and so giving rise to considerable pathological disturbances in those regions, also are interesting.

Since the diencephalon and, in particular, the hypothalamus is considered to be the center for cardiovascular regulation, it must be expected that electrical stimulation of the hypothalamic nuclei would evoke considerable responses of the peripheral blood vessels, not necessarily connected with changes in AP. On the basis of these hypotheses and the results of the first studies of nervous regulation of the microcirculation [4], it was decided to study the dynamics of microcirculatory changes in the mesentery and skeletal muscles of rats in response to stimulation of the hypothalamic nuclei, in correlation with the response of the systemic AP.

EXPERIMENTAL METHOD

Acute experiments were carried out on 20 Wistar rats weighing 250 ± 30 g anesthetized with pentobarbital (50 mg/kg intramuscularly). The hypothalamic nuclei were stimulated through bipolar nichrome electrodes (diameter 200 μ) by a series of square pulses (0.5 msec, 80 Hz, 10-25 V) for 10-45 sec, the electrodes being introduced into the brain structures parallel to one another, taking stereotaxic coordinates from an atlas of the rat's brain [5, 8]. By intravital microscopy in transmitted light, changes in the diameter of the blood vessels and the state of the blood flow were studied in blood vessels from 250 to 5 μ in diameter in the mesentery and the inferior part of the trapezius muscle in rats. The systemic AP was recorded through a catheter in the carotid artery. Synchronization of the stimulation marker and microfilming enabled the microcirculatory changes observed in response to hypothalamic stimulation to be correlated with the dynamics of AP and cardiac activity. The location of the electrodes in the brain was verified histologically after the experiment, using the atlas of the rat's brain as a guide.

EXPERIMENTAL RESULTS

Stimulation of the ventromedial hypothalamic nucleus gave rise, after a short latent period (0-1 sec) to a pressor response with maximal elevation of AP in the course of 3-10 sec; the systolic pressure rose by a greater degree than the diastolic during the first 5-16 sec of stimulation: ΔAP_s was 51 ± 11 mm Hg and ΔAP_d was 34 ± 10 mm Hg (Fig. 1A). The pressor response continued throughout the period of stimulation. Corre-

*Academician of the Academy of Medical Sciences of the USSR.

Laboratory of General Pathology and Experimental Therapy, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 90, No. 8, pp. 139-142, August, 1980. Original article submitted August 6, 1979.

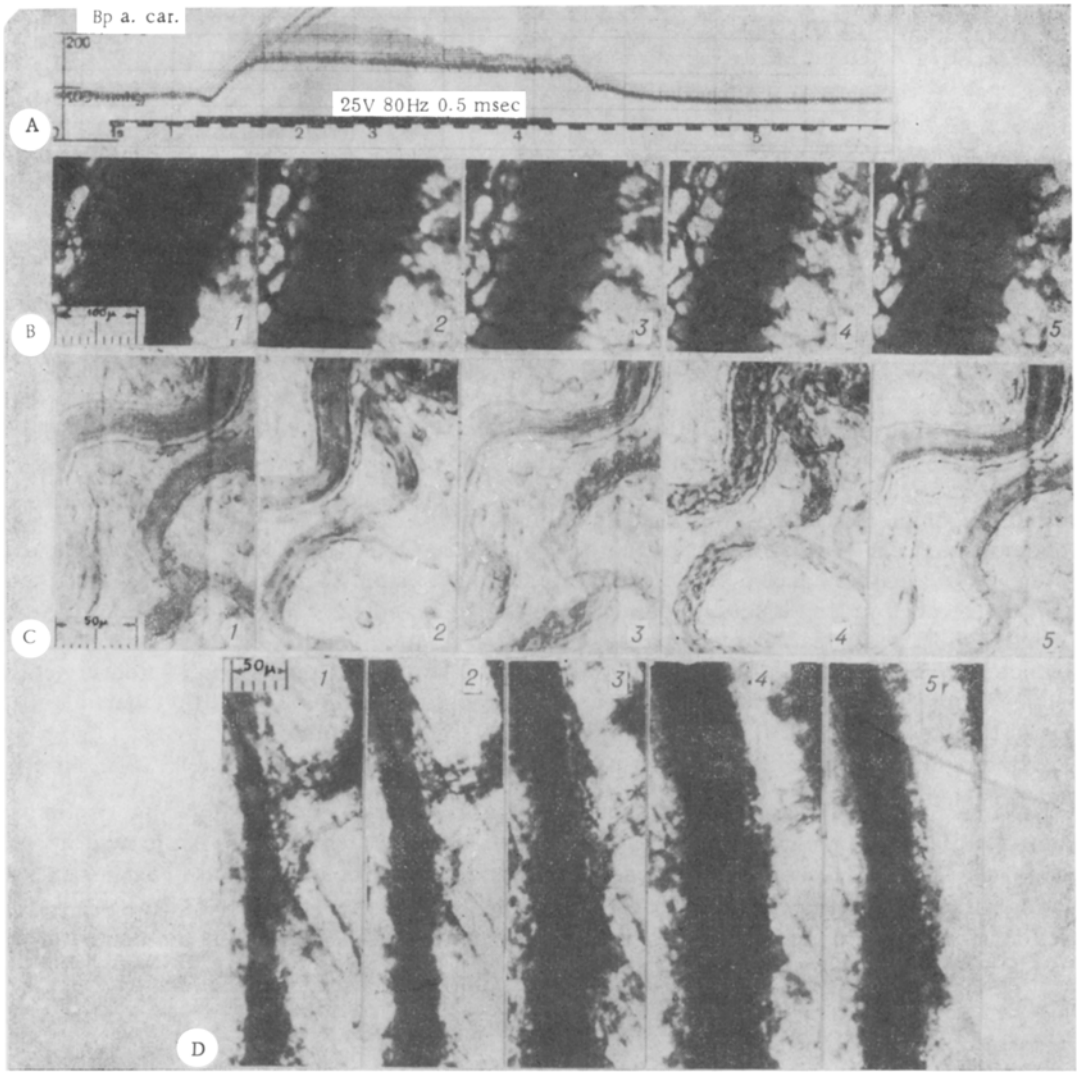

Fig. 1. Dynamics of changes in AP and microcirculatory system in response to stimulation of various hypothalamic nuclei in rats. A) – From top to bottom – arterial pressure; bold line – period of stimulation (25 V; 80 Hz; 0.5 msec); numbers 1-5 correspond to times of microfilming. Time marker (in sec). B, C) Photomicrographs of mesenteric vessels; D) vessels of skeletal muscle: 1) before beginning of stimulation; 2-4) during hypothalamic stimulation; 5) after end of stimulation.

sponding to the pressor response, 5-10 sec after the beginning of stimulation, clear constriction (by 32 ± 10%) of the small arteries of the mesentery 250-90 μ in diameter (Fig. 1B), and gradual slowing and stoppage of the blood flow in the microvessels of the mesentery 70-10 μ in diameter, with no change in their diameter (Fig. 1C), were observed. In response to stimulation of the central hypothalamus, changes in the blood volume in the microvessels were observed in the trapezius muscle of the same animal, with dilatation or constriction of their lumen respectively and opening of capillaries. Meanwhile, during stimulation of the posterior hypothalamic nucleus a marked rise in AP, with a more evident systolic component (ΔAP_s + 68 ± 18 mm Hg, ΔAP_d + 44 ± 15 mm Hg), coincided in time with dilatation by 39 ± 10% of the microvessels 5-40 μ in diameter in the skeletal muscle, and with an increase in the volume of blood in them (Fig. 1D).

The most characteristic response to stimulation of the lateral hypothalamus was a depressor response with a more marked diastolic component (ΔAP_s – 18 ± 3 mm Hg, ΔAP_d – 33 ± 8 mm Hg), and stimulation of the dorsal part of the lateral hypothalamus evoked a purely depressor response. If the stimulating electrode was located in the ventral part of the lateral hypothalamus, however, a biphasic response of AP was obtained: a rapid rise followed by a fall. During stimulation of the lateral hypothalamus constriction of the small arteries and gradual slowing and stoppage of the blood flow in the microvessels were observed in the mesenteric micro-

circulatory network, but these responses were observed comparatively less frequently than during stimulation of the central part of the hypothalamus. In the rat trapezius muscle no significant changes could be found in response to stimulation of the lateral hypothalamus.

The initial phase of the microcirculatory response to stimulation of different zones of the hypothalamus, corresponding in time to the beginning of the rise in AP, was manifested as a transient acceleration of the blood flow in the vessels under the microscope.

The results of this investigation thus demonstrate that electrical stimulation of hypothalamic structures evokes different types of changes in AP, largely depending on the nucleus in which the stimulating electrodes were situated. In experiments of a similar type on rats under pentobarbital anesthesia, the same three different types of change in systemic AP was found during differential stimulation of the diencephalic structures, with no change in the pulse pressure or cardiac rhythm [6, 7]. In the present experiments at the beginning of the pressor response we observed transient acceleration of the blood flow in the microvessels of the mesentery and skeletal muscles. It can be tentatively suggested that this acceleration was due to an increase in cardiac output as the result of the positive inotropic effect on the heart. The cardiac frequency of the rat was unchanged in our experiments also, but the pulse pressure difference was increased. Changes in the microcirculatory system in response to stimulation of the hypothalamic nuclei were more uniform in type. Irrespective of the response of the AP in the microcirculatory network to stimulation, a brief acceleration of the blood flow, followed by its slowing or even complete arrest, were recorded, with no change in the diameter of the mesenteric microvessels, but with marked constriction of the small arteries. Contraction of these vessels is evidently an important component in the pressor response of AP.

When the experimental data are analyzed and compared with those of previous investigations in which peripheral parts of the sympathetic system were stimulated [1, 3], it must be emphasized that it is at the level of the deep brain structures that, because of the richness of the interneuronal connections, excitatory processes may be formed that are realized at the level of the microcirculation in the form of disturbance of the tone of individual regions of the microcirculatory system, more or less local disturbances of permeability, and so on. Recently published data are evidence of the unique specificity of the response of the microcirculatory network to stimulation of parts of the CNS and of the possibility of separate activation of metarterioles and precapillary sphincters during stimulation of the reticular formation and ventromedial thalamic nucleus in rats [2]. Nevertheless, in our own experiments we did not detect any specific responses in the dynamic course of the microcirculatory changes in the rat mesentery which differed from responses to stimulation of the peripheral portion of the sympathetic system.

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