EFFECT OF STIMULATION OF THE VENTRAL SURFACE OF THE MEDULLA ON ASSOCIATED FUNCTIONS OF SMALL INTESTINAL VESSELS

V. A. Kul'chitskii and B. I. Tkachenko*

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The ventral structures of the medulla play a leading role in regulation of the cardiovascular system and extent on tonic excitatory or inhibitory action on sympathetic preganglionic neurons [6, 7]. The mechanism of this action on associated vascular functions [4] has not been investigated.

The aim of this investigation was to study changes in the resistive, capacitive, and exchange functions of the small intestinal vessels in response to electrical stimulation of varied intensity of structures on the ventral surface of the medulla.

EXPERIMENTAL METHOD

Experiments were carried out on 11 cats of both sexes weighing 2.5-3.8 kg, anesthetized with urethane (1.1 g/kg, intravenously), with an open chest and under artificial respiration.

The vascular bed of the small intestine, hemodynamically isolated, was perfused with the animal's own blood (37.5°C) by means of a constant-delivery pump. To exclude any influence of the extravascular factor (changes in peristalsis) atropine (0.3 ml) was injected intravenously. The capillary hydrostatic pressure and the coefficient of capillary filtration were measured by the method described previously [1], based on the principle of Papperheimer and Soto-Rivera [8]. The pre- and postcapillary resistance and the total regional vascular resistance were calculated by the formulas in [4]. The perfusion and venous pressure in the region of investigation was measured by means of the mechanotron transducers of an electromanometer; the venous outlow was estimated from the change in the blood level in the extracorporeal reservoir. The hemodynamic parameters were recorded on the N-327/5 instrument.

Electrodes were inserted into the ventral part of the medulla 2 mm rostrally to the middle of the point of emergence of roots of the hypoglossal nerves (the point +2 mm) and 2 mm caudally to this level (the point −2 mm) at a distance of 4 mm laterally to the midline at a depth of 2000 μ. Bipolar electrodes were made from nichrome wire 100 μ in diameter, covered with fluorine plastic. The distance between the active regions of the electrodes was 100 μ. Electrical stimulation of the brain was applied with currents of threshold strength and of 2 and 4 times its level with constant frequency and duration of stimulation (50 Hz, 0.5 msec). The threshold strength of the current was defined as the minimal strength causing a change of perfusion pressure in the vascular region studied. It varied in different animals from 5 to 50 μA, in agreement with data in the literature [9]. The duration of electrical stimulation was 240 sec. The numerical results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Stimulation of the brain at point +2 mm by a current of threshold strength lowered the postcapillary resistance by 20% and the capillary hydrostatic pressure (initial level 11.0 ± 0.8 mm Hg) by 10% (Fig. 1a). Activation of the brain at this point by a current of threshold strength thus reduced the hydrostatic pressure in the microvessels of the small intestine and, consequently, shifted filtration-absorption equilibrium predominance of absorption of fluid from the interstitial space into the microcirculation. Raising the threshold of

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

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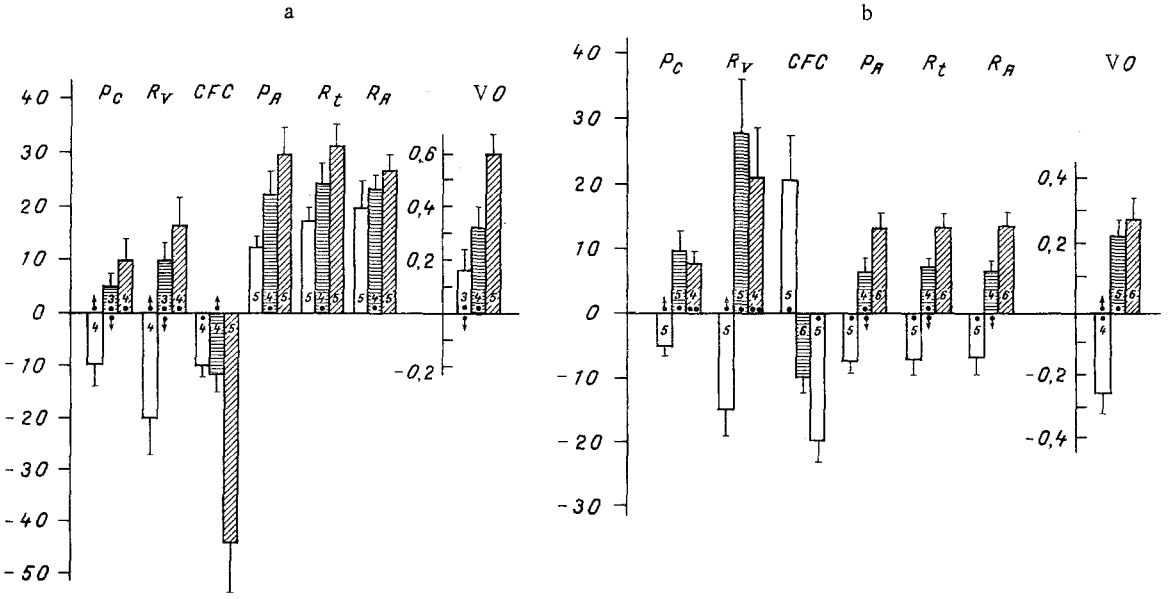

Fig. 1. Changes in parameters (in % of initial level) of macro- and microhemodynamics in small intestinal vessels in response to electrical stimulation of rostral (+2 mm; a) and caudal (—2 mm; b) regions of ventral surface of medulla. P_C) Capillary hydrostatic pressures; R_V) postcapillary resistance; CFC) capillary filtration coefficient; P_A) perfusion pressure; R_t) total regional resistance; R_A) precapillary resistance; VO) venous outflow (in ml/min/100 g). Unshaded columns — changes in parameters of macro- and microhemodynamics in response to a current of threshold strength; horizontal shading — current of twice threshold strength; oblique shading — current of 4 times threshold strength. Vertical lines indicate mean error of means $\pm m_x$. Numbers in side columns show number of observations. Dots at foot of columns indicate observations during which no hemodynamic shifts were found. Dots with arrows indicate observations during which direction of hemodynamic shifts differed from the dominant direction.

stimulation of the brain at this point two- and fourfold increased the capillary hydrostatic pressure by 5 and 10%, respectively (Fig. 1a) and, consequently, shifted filtration-absorption equilibrium in the vessels of the small intestine toward predominance of filtration of fluid from the microcirculatory bed into the interstitial space.

The increase in venous outflow in the vessels of the small intestine was found to be directly proportional to the strength of electrical stimulation of the brain at point +2 mm (Fig. 1a). The greatest increase in the venous outflow was found in response to a current four times the threshold strength, when it averaged 8% of the total volume (7.5 ml/100 g [8]) of blood contained in the vascular bed of the small intestine.

The initial value of the capillary filtration coefficient in the small intestinal vessels was 0.07 ± 0.007 ml/min/mm Hg/100 g. Electrical stimulation of the brain at point +2 mm by a current of threshold strength and twice its value lowered the capillary filtration coefficient on average by 10%. A current of 4 times the threshold strength had a more marked effect on the capillary filtration coefficient: it reduced it by 45% (Fig. 1a).

Electrical stimulation of the brain at point +2 mm by a current of threshold strength, followed by currents of twice and 4 times threshold strength, raised the systemic arterial pressure by 18, 28, and 34%, respectively. In this case the perfusion pressure in the small intestinal vessels was increased by 12, 22, and 30%, respectively (Fig. 1a). The increase in precapillary resistance and total regional vascular resistance was found to be directly proportional to the strength of electrical stimulation of the brain at point +2 mm (Fig. 1a).

During stimulation of the brain at point —2 mm by a current of threshold strength the postcapillary resistance of the vascular region tested fell by 15% and the capillary hydrostatic pressure by 5%. Thus during stimulation of the caudal zone of the ventral surface of the medulla (—2 mm), just as during stimulation of the rostral zone (+2 mm) by a current of

threshold strength, the hydrostatic pressure in the small intestinal microvessels fell (Fig. 1b) and, consequently, filtration-absorption equilibrium was shifted toward predominance of absorption of fluid from the interstitial space into the microcirculation. This shift was more marked when the brain was stimulated by a current of threshold strength at point +2 mm. When the brain was stimulated at point −2 mm by a current of twice the threshold strength the postcapillary resistance of the small intestinal vessels was increased on average by 28% (about 2.8 times more than when the brain was stimulated at point +2 mm), and the capillary hydrostatic pressure was increased on average by 10% (Fig. 1). During stimulation of the brain at point −2 mm by a current of twice the threshold strength, an increase in hydrostatic pressure was observed in the small intestinal microvessels, leading to a shift of filtration-absorption equilibrium toward predominance of filtration of fluid from the microcirculation into the interstitial space. This shift of filtration-absorption equilibrium in the vascular region studied was more marked in response to stimulation at this strength of the caudal zone of the brain (−2 mm) than of the rostral (+2 mm). About the same increase in capillary hydrostatic pressure and postcapillary resistance was observed in the vessels of the small intestine in response to stimulation of the caudal (−2 mm) and rostral (+2 mm) zones of the ventral surafce of the medulla by a current of 4 times the threshold strength (Fig. 1).

During stimulation of the brain at point −2 mm by a current of threshold strength the venous outflow of blood from the small intestinal vessels was reduced on average by 3.5% of the total blood volume in the vascular bed of the small intestine (Fig. 1b). Increasing the strength of stimulation of this part of the brain to twice and 4 times the threshold strength increased the venous outflow from the vessels of the region studied by approximately the same amount (Fig. 1b). Stimulation of the brain at point −2 mm by a current of threshold strength increased the coefficient of capillary filtration by 20%, whereas stimulation by a current of twice or 4 times the threshold level reduced it by 10 and 20%, respectively (Fig. 1b).

Electrical stimulation of the brain at point −2 mm by a current of threshold strength reduced the arterial pressure a little (by 4-5%). The perfusion pressure in the small intestinal vessels, the total regional vascular resistance, and the precapillary resistance also were reduced (on average by 7-8%; Fig. 1b). Stimulation of the caudal part of the ventral surface of the medulla by a current of twice and 4 times the threshold strength led to an increase in these parameters by 5 and 12%, respectively (Fig. 1b). Thus threshold stimulation of the brain at point −2 mm depressed parameters characterizing the resistive function of the small intestinal vessels, whereas stimulation of this brain zone at above the threshold strength increased them.

The results indicate that changes in the associated vascular functions in the small intestine in response to electrical stimulation of rostral and caudal zones of the ventral medulla differ in character. Stimulation of the brain at point +2 mm by a current of threshold strength leads to an increase in all parameters characterizing the resistive and capacitive functions of the small intestinal vessels and to depression of their exchange function. Electrical stimulation of the brain by a current of threshold strength at point −2 mm leads to reduction of the resistive and capacitive function of the small intestinal vessels, with opposite changes in the parameters of the exchange function of the small intestinal vessels: the capillary hydrostatic pressure falls and the capillary filtration coefficient increases. During activation of the rostral and caudal zones of the ventral medulla (+2 and −2 mm, respectively) by currents of twice and 4 times the threshold strength, an increase in capillary hydrostatic pressure in the small intestinal vessels, a decrease in the capillary filtration coefficient and the pre- and postcapillary vascular resistance, and reduction of the venous outflow from the vessels of the region studied were observed. However, stimulation of the different zones of the ventral medulla by a current of above threshold strength differs in its action on successive segments of the vascular bed of the small intestine: stimulation of the brain at point +2 mm has the strongest action on the precapillary resistance of the vascular bed under investigation, whereas stimulation at point −2 mm led to a more effective change in postcapillary resistance.

The results of these investigations are evidence that arterial and venous vessels in the splanchnic region [2] may respond in different ways, and they support the hypothesis of selective vasomotor control [5], which postulates the central organization of the neuron pool, which projects specifically through the peripheral nervous system to the vascular bed, from both functional and topographic aspects.

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ROLE OF ACETYLCHOLINE RECEPTOR DENSITY IN MECHANISMS PROLONGING POSTSYNAPTIC CURRENT DECAY

R. A. Giniatullin and R. N. Khazipov

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The duration of end-plate currents (EPC) has virtually no effect on transmission of a single signal through the myoneural junction, but plays a decisive role during passage of repetitive series of impulses through a synapse [3]. One approach to the discovery of factors determining the duration of the EPC is to study sensitivity of EPC decay to a change in the density of free acetylcholine receptors (AChR) of the postsynaptic membrane. A decrease in the density of the free AChR due to α-bungarotoxin (α-BT), which binds irreversibly with AChR, quickens EPC decay in tonic muscles [3], and also in phasic muscles, if acetylcholinesterase (AChE) in the latter is inhibited [8]. It has been suggested that α-BT abolishes, and in that way brings to light, the unsynchronized opening of ionic channels present in both cases and associated with repeated activation of AChR by the transmitter during generation of a single signal [8]. However, decay of EPC can be prolonged not only through inhibition of AChE, but also through other influences, such as hyperpolarization of the postsynaptic membrane [6, 11], cooling of the muscle [6], and the action of ethanol [2, 7, 10] and dipyroxime* — a rapid blocker of ionic channels of the postsynaptic membrane [1]. The problem of whether their effect, which conjecturally is realzied through a change in the kinetics of AChR function, may be accompanied by disturbance of synchronization of ionic channel opening, in much the same way as that occurs after inhibition of AChE, has not been investigated systematically.

To solve this problem, it was decided to study the effect of α-BT on the duration of EPC decay under the influence of the various factors mentioned above.

EXPERIMENTAL METHOD

Experiments were carried out on isolated nerve-muscle preparations consisting of the frog sciatic nerve and sartorius muscle. The temperature was measured by a miniature transducer, located next to the muscle. Its mean value was 20.0 ± 0.5°C (except in experiments with cooling). In the course of a single experiment the temperature drift did not exceed 0.1°C. Muscle contractions were abolished by the use of Ringer's solution of the following composition (in mM): NaCl 115.0, KCl 2.5, $CaCl_2$ 0.9, $MgCl_2$ 6.0, $NaHCO_3$ 2.5, pH 7.3. EPC evoked by nerve stimulation were recorded under voltage clamp conditions by the use of two electrodes. Signals were analyzed by a system consisting of digital analyzer and microcomputer, with interrogation frequency of 1 point in 60 μsec, in accordance with special programs (author V. A. Snetkov) for determining the amplitude of the signal, the exponential nature of EPC decay, and the time constant of EPC decay (τ_{epc}). Drugs were used in the follow-

*Trimedoxime bromide.

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