EFFECT OF A RAISED SYSTEMIC BLOOD PRESSURE ON NEUROGENIC VASOCONSTRICTION IN THE RAT SKELETAL MUSCLE MICROCIRCULATION

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Most data on the effectiveness of vasoconstrictor factors depending on intravascular pressure have been obtained either on perfused organs and tissues or on isolated preparations of blood vessels. The conditions of perfusion of isolated organs or vascular regions permit vessels to be perfused under constant pressure or constant flow, and it is considered that this enables a distinction to be drawn between the conditions of operation of vascular smooth muscles in response to vasoconstrictor stimuli [8]. Experiments on the perfused vascular region of the anterior mesenteric artery of the cat have shown that an optimum (between 60 and 80 mm Hg) exists for both perfusion schedules above which an increase in perfusion pressure causes a decrease in the degree of the contractile response of the vessels to noradrenalin [8]. Increasing the perfusion pressure from 80 to 120 mm Hg in experiments on an isolated segment of an artery of the rabbit ear delayed by half the time of development of vasoconstriction in response to noradrenalin [11]. Similar data on the effect of a raised perfusion pressure on the effectiveness of vasoconstrictor neurogenic influences were obtained on preparations of isolated frog and rat limbs [10]. A fall of perfusion pressure also reduces the effectiveness of vasoconstrictor stimuli [2, 10], and in this case the decrease in effectiveness is considered to be due to the effect of the lowered perfusion pressure on basal vascular tone.

Data obtained by a study of this problem at the microcirculatory level are very scanty. A little information can be extracted from the report of an investigation [5] on vessels of the rat small intestine: in response to stimulation of sympathetic nerves, constriction of first-order arterioles, the pressure in which was twice that in the second-order arterioles, was much smaller, although the difference in intravascular pressure cannot evidently be the only factor determining the response of the microvessels in this case. Meanwhile the question of effectiveness of vasoconstrictor stimuli assumes special significance in relation to problems affecting the microcirculation and, in particular, the study of the pathogenesis of hypo- and hypertensive states, for perfusion of the microvascular system is determined by the size of the lumen of the arterioles, which are under considerable nervous control.

The aim of this investigation was to study the effectiveness of the neurogenic vasoconstrictor response in the microcirculation of a rat skeletal muscle (m. extensor hallucis proprius — EHP), judged by the change in diameter of the microvessels at normal and elevated levels of the systematic arterial pressure (BP).

EXPERIMENTAL METHOD

Experiments were carried out on 14 male Wistar rats weighing 190-250 g, anesthetized with pentobarbital (5 mg/100 g intraperitoneally, followed by additional doses during the experiment). The course of the operation involved: tracheotomy, catheterization of the right carotid artery to record the systemic BP, by means of a PE50 catheter (a polyethylene catheter with a diameter of 0.5 mm), catheterization (PE10) of the peripheral end of the caudal artery for injection of substances, implantation of a bipolar nichrome electrode into the sympathetic chain at level L_5-L_6, where it was fixed by means of Tsiakrin MK-7 surgical glue, and dissection of the muscles with a thermocautery by the method in [9]. Biomicroscopy of EHP was undertaken with the MBI-6 microscope, equipped with special constant-temperature stage, so that the

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temperature of the test object could be maintained and the object itself irrigated with Ringer's solution. The muscle was studied in transmitted light under a total magnification of 164 (objective OSF 26×, ocular 6.3×). Because of the great working distance between objective and object, the former did not heat, but for better conditions of microscopy, the muscle was covered with a coverslip. For dynamic recording of changes in diameter of the microvessels, the method of image splitting [1, 3] was used. The sympathetic chain was stimulated by a series of square pulses, generated by a Disa-Multistim stimulator (Denmark). Parameters of stimulation were: 2-10 V, 20 Hz. The pulse duration was 0.5 msec and the period of stimulation 6-10 sec. Felypressin (FP), a vasopressin derivative (from Sandoz, Switzerland) with a marked vasoconstrictor action, was injected into the peripheral end of the caudal artery in 0.1 ml of Ringer's solution in a dose of 6-8 IU/100 g body weight. The experimental data were analyzed by the T and paired T tests.

EXPERIMENTAL RESULTS

In the course of the experiment the test objects were arterioles of the muscle with an initial diameter of 28.6 ± 1.4 μ (diameter of lumen 21 ± 1.4 μ, n = 14, M ± m), which occupy an intermediate position betwen second- and third-order arterioles, according to the classification in [6]. The initial values of BP were: systolic 128.3 ± 5 mm Hg and diastolic 96.7 ± 5.3 mm Hg. Measurement of the diameter of the microvessel began 30 sec before stimulation of the sympathetic chain; the external and internal (lumen) diameters could be recorded consecutively. The measurements continued during and after stimulation until the microvessel had regained its original size (Fig. 1b). The degree of vasoconstriction was found to be directly dependent on the intensity of stimulation and its duration. In this experimental situation, the strength of stimulation was thus chosen to be that at which the diameter of the lumen diminished by 20-30%. By itself stimulation of the sympathetic chain of this strength did not lead to any significant fluctuations in the systemic BP (Fig. 1c), but distinct vasoconstriction was observed (Fig. 1a; Table 1). The blood flow in the subjacent microvascular bed and in the capillaries gradually slowed down during stimulation; the process was found to be unequal in different capillaries of the muscle. Sometimes vasoconstriction in the muscle was fragmentary in character: areas whose diameter remained unchanged could be seen along the course of the vessel.

The response to stimulation was reproduced quite well when intervals between stimuli exceeded 3 min.

Injection of FP caused a rapid rise of systemic BP, and stimulation of the sympathetic chain in this case began before vasoconstriction had begun to appear under the influence of FP itself. By the time of stimulation the diameter of the vessels undergoing microscopy did not differ from its initial value: changes (Δ) for the external diameter were 0.9 ± 0.6 μ and for the lumen 1.5 ± 0.7 μ (n = 14, P > 0.05). Meanwhile the rise of pressure, both systolic and diastolic, exceeded 25% (Table 1). Against the background of the raised systemic BP, vasoconstriction to stimulation of the sympathetic chain was considerably less, only 11.5% for the external diameter and 20.4% for the diameter of the lumen (Table 1). The rapid rise of pressure was replaced after injection of FP by a plateau, which corresponded to vasoconstriction induced by FP directly. After a single injection of FP in the above doses the pressor response lasted 20 min or more, after which the pressure and diameter of the vessels returned to their initial values. The next stimulation of the sympathetic chain was applied 15-20 min after injection of FP. By that time the rise of pressure was about half of the value at which stimulation was applied the first time (Table 1), but the diameter of the vessels undergoing microscopy was the same as initially: for the external diameter Δ = 1.1 ± 1.3 μ, for the lumen Δ = 1.2 ± 1.3 μ (n = 13, P > 0.05). In this case, stimulation of the sympathetic chain with the same strength and duration also caused marked vasoconstriction, but to only about half the degree compared with the initial phase of the pressor response to FP. The degree of vasoconstriction which developed in this case did not differ significantly either from the response at the ascending phase of the pressor response or from vasoconstriction under normal conditions before injection of FP (Table 1).

Thus against the background of injection of FP vasoconstriction to stimulation of the sympathetic chain was reduced almost by half. It is unlikely that FP has an inhibitory action on the neuroeffector mechanisms of the vessel wall, for FP itself has a vasoconstrictor action, and it evidently potentiates the action of catecholamines, like vasopressin and its other derivatives [4, 7]. The pressor response to FP, at least in the initial phase, may perhaps be due to an increase in cardiac output, and vasoconstriction and increased peripheral resistance be-

TABLE 1. Changes (Δ) in BP, External Diameter, and Diameter of Lumen of Arterioles of EHP Muscle during Stimulation of Sympathetic Chain (M ± m)

Experimental conditions	Number of measurements	BP, mm Hg		External diameter of arteriole, μ	Diameter of lumen of arteriole, μ
		Systolic	Diastolic		
Stimulation	14	−2,3±2,6	+0,3±2,4	−6,0±0,7 (21)***	−8,2±0,8 (38,9)***
FP	13	+33,6±5,2 (26,2)***	+27,4±3,8 (28,3)***	+0,9±0,6 $P<0,01$	+1,5±0,7 $P<0,001$
FP + stimulation	14	+35,2±5 (27,4)***	+27,5±3,3 (28,6)***	−3,3±0,5 (11,5)***	−4,3±0,9 (20,4)***
20 min after: injection of FP	13	+22,5±3,7 (17,5)***	+20,9±3,1 (21,6)***	+1,1±1,3	+1,2±1,3
FP + stimulation	13	+20,9±8,5 (16)*	+14,0±4,5 (14)**	−5,0±1,3 (17,5)**	−6,5±1,2 (31)***

Legend. Numbers in parentheses are percentages of initial value. *P < 0.05, **P < 0.01, ***P < 0.001 compared with initial value.

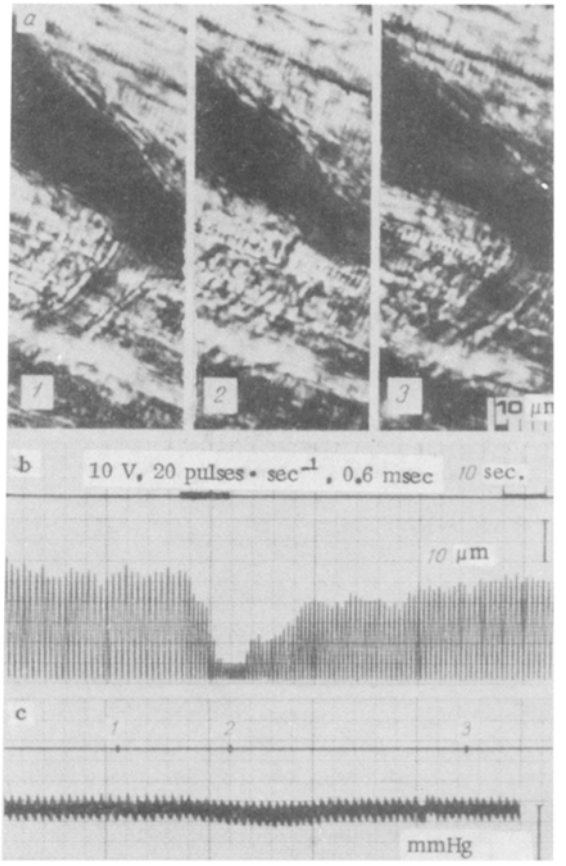

Fig. 1. Vasomotor changes in microcirculatory bed of rat skeletal muscle and dynamics of BP during stimulation of sympathetic chain: a) vessels of EHP muscle; b) recording of diameter of lumen of vessel by image splitting method [1]. Straight line above is marker of stimulation; c) BP in carotid artery. 1) Before stimulation; 2) during stimulation (maximal degree of constriction of small vessel arising from larger vessel); 3) after stimulation.

gin to appear later. The absence of marked vasoconstriction in this phase of the pressor response, at least in arterioles of this particular order in the rat skeletal muscle, suggest that the intravascular pressure in them rises and modifies vasoconstrictor responses in a certain manner.

The results of this investigation confirm those of experiments *in vitro*, which revealed a reduction in the effectiveness of vasoconstrictor stimuli when the intravascular pressure rises, and considering the conditions of intravital microscopy of the muscle, they suggest that in this case limitation of the tissue blood flow, evoked by sympathetic vasoconstriction, also is inhibited under these circumstances. This may indicate that the rise of intravascular pressure in the arteriolar part of the microvascular bed may play a protective role. Elevation of the intravascular pressure in the arterioles modifies the action of vascular smooth muscles, in the same way as is observed in perfusion experiments [8], transforming it to isometric operation, when vasoconstrictor stimuli can only potentiate the tonic contraction of the vascular smooth muscles, without changing the lumen of the microvessel in so doing. It can be tentatively suggested that a fall of microvascular pressure acts in the opposite way, considerably strengthening the likelihood of vascular occlusion during potentiation of vasoconstrictor influences.

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MOTOR RESPONSES IN RATS DURING CRITICAL GROWTH PERIODS IN EARLY POSTNATAL LIFE

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During adaptation to environmental factors and physical exercise in the early periods of postnatal ontogeny (a state of stress) the functions of the body return to those typical of previous stages of ontogeny [8, 9]. The question arises whether this return takes place only during adaptation to new environmental conditions (conditions of development) or whether similar changes also take place at critical periods of growth. Several critical growth periods in rats are distinguished in the literature [3, 4].

To study this problem an attempt was made to evaluate the physiological features and, in particular, the character of motor responses (MR) of jerking type, specific for the early age, in rats during critical growth periods, and also to determine the character of the physiological mechanisms of the return of functions to forms typical of these animals at previous stages of development.

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