PHYSIOLOGY

Contribution of the Ventral Structures of the Medulla Oblongata to the Hemodynamics and Transcapillary Fluid Exchange in the Lungs

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Neurophysiological and histochemical studies have testified to the involvement of the neuronal populations located in the ventral medulla (VM) in the regulation of the cardiovascular and respiratory systems [1, 3, 4, 9, 14]. There are published data [1-3] which attest to the effect of the above-mentioned brain structures on the circulation in different organs. However, studies of the pulmonary hemodynamics during stimulation of the structures of the VM have not been reported in the literature.

Since a study of the transvascular fluid transfer is important for understanding the exchange processes, changes of the intercellular space, and other processes associated with the homeostasis of the pulmonary circulation during central neuroergic influences, the aim of this study was to investigate the pulmonary macro- and microhemodynamics, as well as the blood indexes of the acid-base equilibrium for electrical activation of VM structures.

MATERIALS AND METHODS

The experiments were carried out on 17 open-chest cats weighing 1.8-3.2 kg under urethane anesthesia (1 g/kg) and artificial lung ventilation (VITA-1 apparatus). The ventilation frequency and volume were chosen individually by monitoring the indexes of the acid-base equilibrium and the partial pressure of gases in the arterial and venous blood (pO_2 and pCO_2), which were measured with the aid of a BMS3 MK2 Radiometer blood microanalyzer (Denmark).

The right posterior pulmonary lobe was perfused with the aid of a constant volume flow rate pump. The pulmonary indexes of the macro- (the perfusion pressure and the venous efflux) and microhemodynamics (the pre- and postcapillary resistance, the mean hydrostatic pressure, and the coefficient of capillary filtration) were assessed as described previously [1].

Nichrome bipolar electrodes were inserted with the aid of a stereotaxic device at a depth of 1500 μ from the ventral surface of the medulla oblongata, 2 mm rostral to and 2 mm caudal to the midpoint of the origin of the roots of the twelfth (XII) cranial nerves (points +2 and -2, respectively). The medulla oblongata structures were electrically stimulated with an EST-14 stimulator at a frequency of 50 Hz (pulse duration 1 msec). The threshold electrical current was determined as the minimal current which caused a shift of perfusion pressure in the zone studied; it varied from 5 to

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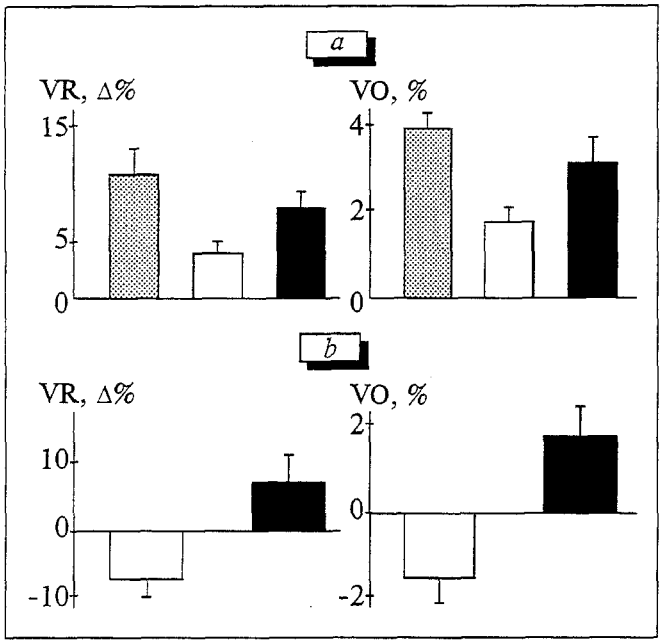

Fig. 1. Changes in vascular resistance (VR) and venous outflow (VO) from the lungs for electrical stimulation of VM and stellate ganglion structures, % of the initial level. Bars: changes of hemodynamic parameters in response to electrical stimulation with a threshold (white bars) or double–threshold (dark bars) current, respectively of rostral (*a*) and caudal (*b*) structures of VM. Grey bars: shifts of hemodynamic indexes for electrical stimulation of stellate ganglion.

120 μA in different animals. The duration of electrical stimulation of the VM structures was 7-8 min, since this amount of time was required to measure the macro- and microhemodynamic indexes. After the completion of the experiments, the VM structures were electrolytically destroyed (with a current of 1500 μA). The location of the electrodes was histologically verified in Nissl-sections, and compared with the atlas [13].

The neuroergic effects of the VM structures on the pulmonary vessels were assessed by comparing the maximal attainable responses to supramaximal electrical stimulation of the regional sympathetic nerves with the responses of the same vessels to electrical stimulation of the brainstem structures. The constrictive responses of the pulmonary vessels to supramaximal electrical stimulation of the stellate ganglion (frequency 10 Hz, pulse duration 1 msec) were taken as 100%.

Since there is evidence [7] that electrical stimulation of the VM structures at the point -2 alters the bronchial resistance, in our experiments atropine was used (0.3 ml of a 0.1% solution) in order to rule out this extravascular factor.

The data were statistically processed by the methods of variational statistics using Student's *t* test.

RESULTS

Electrical stimulation of the rostral structures of the VM at the +2 point with a threshold and above-threshold current (twice as high as the threshold current) raised the perfusion pressure in the pulmonary vessels by 5.1±0.9 and 9.6±1.4%, respectively, as against the initial level (Fig. 1). The neuroergic signal delivered from the rostral structures of the VM to the pulmonary vessels was realized by 55.5±4.5 and 80.4±6.7%, respectively. At the same time, the systemic arterial pressure increased by 12.6±2.4 and 21.5±2.8% as compared to the background values (118±5.6 mm Hg).

When the VM structures were stimulated at the +2 point with a threshold and above-threshold current, we observed a 2.2, 5% increase (vs. the total blood volume contained there, which constitutes about 10 ml per 100 g tissue) in the blood efflux from the vessels of the pulmonary lobe (Fig. 1, *a*). The neuroergic signal delivered from the brainstem structures was 38.0±6.5 and 78.2±8.2%, respectively, realized in shifts of the intravascular pulmonary capacity. This drop in the capacity of the pulmonary vascular bed may either be due to the effect of the VM structures on the resistance of this zone to the blood flow, or result from alterations in the organ's filtration-absorption equilibrium.

During stimulation of the neuronal structures of the rostral portions of the VM, the mean hydrostatic pressure in the pulmonary vessels in-

TABLE 1. Changes of the Acid–Base Equilibrium Indexes (pH) and of the Partial Tension of Blood Gases (pO_2 and pCO_2) for Electrical Activation of the VM Structures (*M*±*m*)

Parameters of VM structure	Blood	pH		pO_2, mm Hg		pCO_2, mm Hg	
		baseline	5th min	baseline	5th min	baseline	5th min
+2	A	7.296±0.031	7.278±0.026	102.3±4.7	108.4±5.6	36.4±1.8	33.6±2.2
	V	7.290±0.035	7.275±0.024	75.0±4.5	73.2±3.4	48.0±3.5	49.1±3.6
−2	A	7.280±0.020	7.254±0.025	104.0±4.7	98.6±3.6	40.6±2.4	45.8±2.7*
	V	7.305±0.025	7.310±0.031	76.0±3.8	72.0±2.3	47.2±3.4	49.2±3.8

Note. +2 and −2, respectively, the rostral and caudal structures of the VM; A: arterial blood; V: venous blood. An asterisk indicates $p<0.05$.

creased by 4.5±0.5 and 5.6±1.1%, respectively, vs. the initial level (7.8±0.5 mm Hg). The shifts in the postcapillary resistance constituted 6.5±1.1 and 10.3±1.3% (Fig. 2, *a*). An increase in the capillary hydrostatic pressure shifted the Starling equilibrium toward an increased filtration of the fluid from the pulmonary microcirculatory bed into the interstitial bed.

A rise in the pulmonary precapillary resistance (by 7.8±1.2 and 11.2±1.5%) occurred in response to stimulation of the said neuronal structures (Fig. 2).

A marked drop (to 20% of the initial level - 0.185±0.021 ml/min×mm Hg×100 g) of the coefficient of capillary filtration was noted against the background of slight shifts in the capillary pressure (Fig. 2, *a*). Since the permeability of the microvessels is virtually unchanged for an enhancement or diminution of the sympathetic effects on the pulmonary vessels [7,11,15], it may be assumed that the number of functioning capillaries in the lungs drops when the rostral portion of the VM is stimulated. This conclusion is indirectly corroborated by a 15-20% increase in the oxygen arteriovenous difference (Table 1).

When the caudal structures of the VM were stimulated at the -2 point with a threshold current, this resulted in a drop of the perfusion pressure in the pulmonary vessels (by 7.2±0.9% of the initial level, 21.6±2.3 mm Hg) (Fig. 1, *b*). Under the indicated conditions the systemic arterial pressure dropped 12.6±2.3% (background values were 118.4±5.5 mm Hg). In the majority of observations (11 out of 17) the venous efflux from the vessels of the caudal pulmonary lobe was reduced by 1.5±0.3% of the blood contained there (Fig. 1, *b*) (in the rest of the experiments it was unchanged); the pre- and postcapillary resistance decreased by 4.5±0.6 and 8.2±1.4%, respectively; the capillary hydrostatic pressure fell by 4.6±1.1%. The possible increase in the transcapillary absorption of the fluid in the lungs during activation of the caudal VM structures, which results from a decreased hydrostatic capillary pressure in the pulmonary vessels, may cause an increased venous efflux from this zone. Accumulation of blood in the pulmonary vessels under the above-mentioned conditions could have been due just to an increased intravascular capacity in the organ.

We noted that the oxygen content in the arterial blood flowing out of the lungs tended to decrease (from 104±4.7 to 98.6±3.6 mm Hg) in response to activation of the caudal structures of the VM at the -2 point; on the other hand, the carbon dioxide tension increased from 40.6±2.4 to 45.8±2.7 mm Hg (Table 1). Since the ventilation

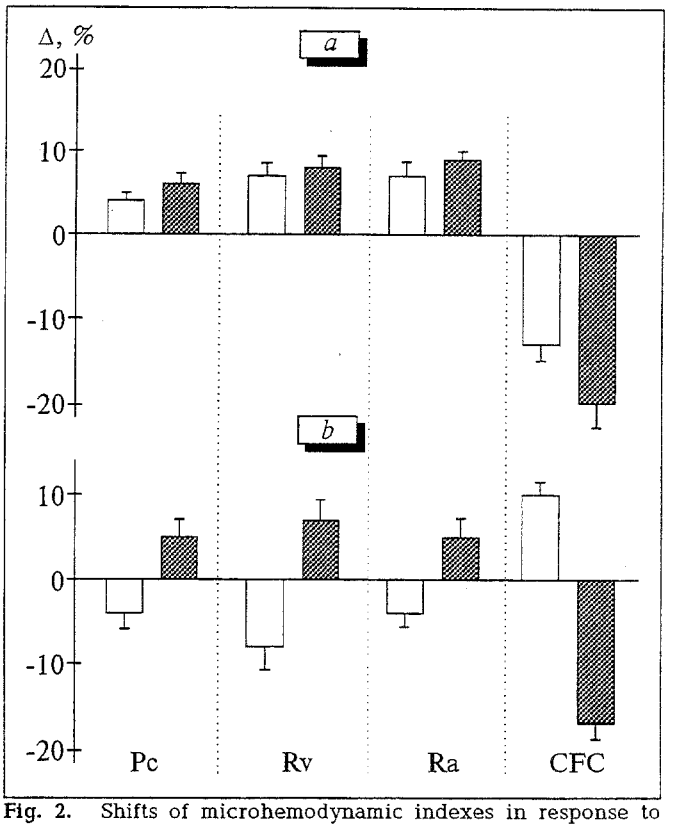

Fig. 2. Shifts of microhemodynamic indexes in response to electrical stimulation of VM structures with a threshold and double-threshold current, % of the initial level. Ra: precapillary resistance; Rv: postcapillary resistance; CFC: capillary filtration coefficient; Pc: mean hydrostatic capillary pressure. Other notation as in Fig. 1.

level in the animal was kept constant owing to the work of an artificial respiration apparatus throughout the experiment, the redistribution in the ventilation-perfusion relationships could have been the cause of the increased carbon dioxide tension in the arterial blood during activation of the caudal VM structures at the -2 point, the increased carbon dioxide content in the final portions of expired air being indirect evidence of this [4]. The increased coefficient of capillary filtration (by 12-16%) may also attest to a possible enlargement of the area of the pulmonary exchange surface (Fig. 2, *b*).

The dilatory response of the pulmonary vessels to stimulation of the caudal structures of the VM may be mediated by the rostral structures of this brain zone, since a mechanism of suppression of the tone of the rostral structures of VM by the caudal neuronal population has been described [6,14]. However, when the intensity of electrical stimulation of the brain structures at the -2 point was raised to a double-threshold value, an inversion of shifts was noted in the indexes of the pulmonary macro- and microhemodynamics (Figs. 1 and 2). Evidently, other central mechanisms, i.e., the structures localized outside the lateral re-

ticular nucleus, altered the trend of hemodynamic shifts for an above-threshold electrical stimulation [1, 2, 6].

Thus, our findings showed the presence of constrictive signals delivered from the rostral structures of the VM (the zone of the paragiant-cell nucleus) to the arterial and venous pulmonary vessels. Conversely, electrical stimulation of the caudal brain structures (lateral reticular nucleus) caused dilatory responses in the vessels involved in the pulmonary circulation. During electrical stimulation of the VM structures, changes of the indexes characterizing the pulmonary hemodynamics (coefficient of capillary filtration and mean hydrostatic capillary pressure) were of opposite phase. This attests to high homeostatic properties of the pulmonary microcirculatory system, which help keep the ventilation-perfusion relationships within physiologically normal limits and maintain the content of blood gases in the organism as a whole. Along with an increase of the capillary filtration coefficient, a decrease of the arteriovenous difference of the blood saturation with oxygen, which was revealed for stimulation of the brain structures by a threshold current at the -2 point, may be explained by the fact that the effect of the reduced oxygen concentration gradient at the blood-tissue boundary prevailed over the effect of the increased area of the exchange vessels in the organ. In addition to the reduced vascular resistance, this was probably due to the preservation of gas diffusion thanks to a reduced volume of the interstitial space resulting from absorption of the tissue fluid.

The marked changes in the pulmonary indexes of the macro- and microhemodynamics, as well as in the transvascular fluid transfer in the lungs during electrical stimulation of the VM attest to an important role of these structures in ensuring the storage or the immediate neuroergic mobilization of blood from the organ.

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