

THE REFLEX EFFECT OF CARDIOVASCULAR DRUGS ARISING FROM THE VENOUS RECEPTORS OF THE FROG

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The sensitivity of receptors in the veins to various chemical stimulants has been shown in many investigations [3, 4, 6, 10, 11, 12, 13, 15]. V. A. Fedorova [14] observed a hypertensive effect on injecting camphor into a humorally isolated portion of vein in cats and dogs. F. Ia. Bernshtein and L. A. Edel'shtein [2] observed the same effect on injecting adrenalin into the humorally isolated veins of dogs.

In earlier work [8] we were unable to find a specific cardiovascular action of adrenalin, caffeine, strophanthin and ephedrine in injection of these drugs into humorally isolated veins of cats and rabbits; in most of the experiments they caused reflex slowing of the cardiac rhythm and a slight reduction in the arterial pressure.

In the present work we have attempted to compare the action of cardiovascular drugs on reflexes from tissue, venous and other vascular receptors of the hind limbs of the frog.

EXPERIMENTAL METHOD

The experiments were performed on spring and autumn frogs Rana chensinensis. Reflexes arising from the venous receptors of the frog were studied by means of perfusion of a humorally isolated portion of the femoral vein. With the frog fixed dorsum upwards, the sciatic artery and femoral vein were ligated in the region of the hip joint, after which all the tissues of the thigh were divided below the ligature with the exception of the anterior deep branch of the sciatic nerve, going to the femoral vein. Next the trunk was covered with a cloth in which a cut had been made; through this the nerve was brought out. In the femoral vein of the isolated limb, in the region of the knee joint, was inserted a glass cannula which was connected to a vessel placed 15–20 cm above the vein. Oxygenated physiological or test solutions were introduced into the vein through the cannula, escaping from it at the place where it had been divided.

The effects of solutions of caffeine (1 : 500), strophanthin (1 : 1,000,000), adrenalin (1 : 2,000,000) and nitroglycerin (1 : 2,000,000) were investigated. In each experiment the action of the particular drug was tested several times. Electrocardiographic records were made, and respiration was recorded (by the movement of the oral diaphragm).

In order to study the reflex effect of these cardiovascular drugs in the concentrations given from receptors in the whole limb, we perfused the hind limb through the sciatic artery. Humoral isolation of the limb was effected just as in isolation of the vein. All the nerves entering the limb except the anterior deep branch of the sciatic nerve were preserved. The supplying cannula was introduced into the sciatic artery. The upper level of the solutions was kept 30–40 cm above the perfused limb, roughly corresponding to the arterial pressure in the sciatic artery of the frog, from 18 to 57 mm of mercury [7].

EXPERIMENTAL RESULTS

In performing 30 tests of these drugs on 11 frogs, we did not find any marked reflex changes in the electrocardiogram. Thus in our experiments, just as in those of I. N. Davydov [5] on stimulation of the chemoreceptors

of the hind limbs of the frog, these cardiovascular drugs were not found to have any specific effect on reflexes from the venous receptors which influence the activity of the heart. The only reaction which appeared took the form of changes in respiration and of general movements. The results of the 32 experiments in this series are shown in Table 1. Caffeine and strophanthin as a rule produced depression of breathing in the frog, or a motor reaction. In only 4 out of 36 tests was no effect observed. Adrenalin and nitroglycerin produced reflex reactions from the receptors in the vein in only 50 % of cases. It was thus proved that stimulation of the receptors of the vein by these drugs might have a reflex influence on respiration. Depression of respiration is the typical reaction of the frog to stimulation of the receptors in the veins by drugs having an action on the cardiovascular system (Fig. 1, a). In subsequent experiments we studied the reflex action of the same drugs by perfusion of the intact limb of the frog.

TABLE 1

Reflex Change in the Respiration of the Frog Due to the Action of Cardiovascular Drugs on the Venous Receptors of the Hind Limb

Drug under test	Total	Findings			
		Motor reaction	Stimulation of respiration	Depression of respiration	No change
		Number of tests			
Caffeine	37	12	—	21	4
Strophanthin	36	15	—	17	4
Adrenalin	23	1	—	11	11
Nitroglycerin	27	3	—	12	12

TABLE 2

The Reflex Effect of Cardiovascular Drugs Arising from the Receptors of the Hind Limb of the Frog on Respiration

Drug under test	Total	Findings			
		Motor reaction	Stimulation of respiration	Depression of respiration	No change
		Number of tests			
Caffeine	18	7	8	—	3
Strophanthin	13	6	7	—	—
Adrenalin	14	3	11	—	—
Nitroglycerin	12	3	6	—	3

A. N. Bakuradze and R. M. Meskhrikadze [1] and V. R. Maisaia [9] found obvious stimulation of respiration on perfusion of the hind limbs of the frog with solutions of adrenalin, caffeine, strophanthin, cytosine and other drugs.

In order to explain the reflex effect of the cardiovascular drugs from the receptors of the intact limb, we carried out 16 experiments, each consisting of 3-5 tests of the drug being investigated (Table 2).

In this series of experiments we did not observe depression of respiration as we did on perfusing the veins. Adrenalin most often (in 11 of 14 tests) produced stimulation of respiration, and a motor reaction only 3 times. The effect of the other drugs was roughly the same.

A typical reaction on perfusion of the intact limb was strengthening of respiration (Fig. 1, b); this most often consisted of increase in the rate of respiratory movements, and less often of increase in their amplitude.

Thus the results of this series of experiments agree with the findings of A. N. Bakuradze and R. M. Meskhrikadze [1] and of V. R. Maisaia [9], although the reactions which we observed differed somewhat in quality.

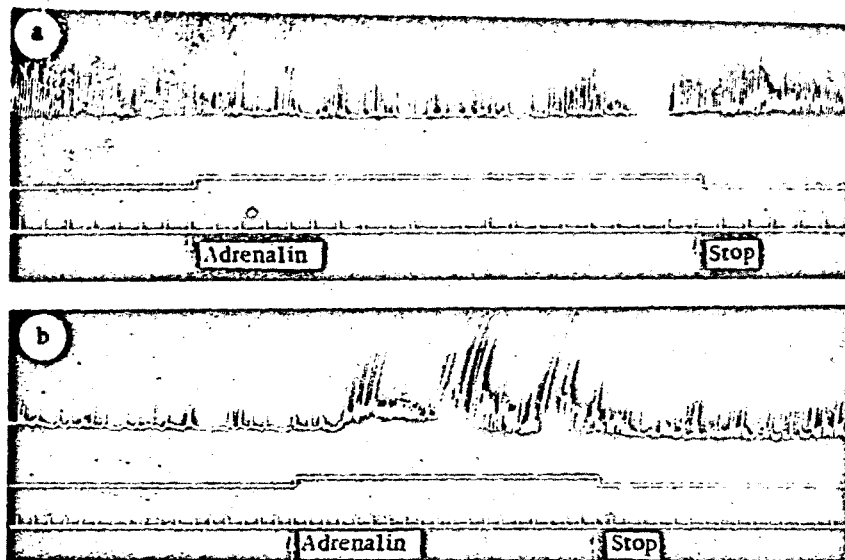


Fig. 1. Reflex changes in the respiration of the frog on perfusion with a 1 : 2,000,000 solution of adrenalin.

a) Of the humorally isolated femoral vein and b) of the humorally isolated limb. Interpretation of the curves (from above downwards): movement of respiration, record of stimulation, time marker.

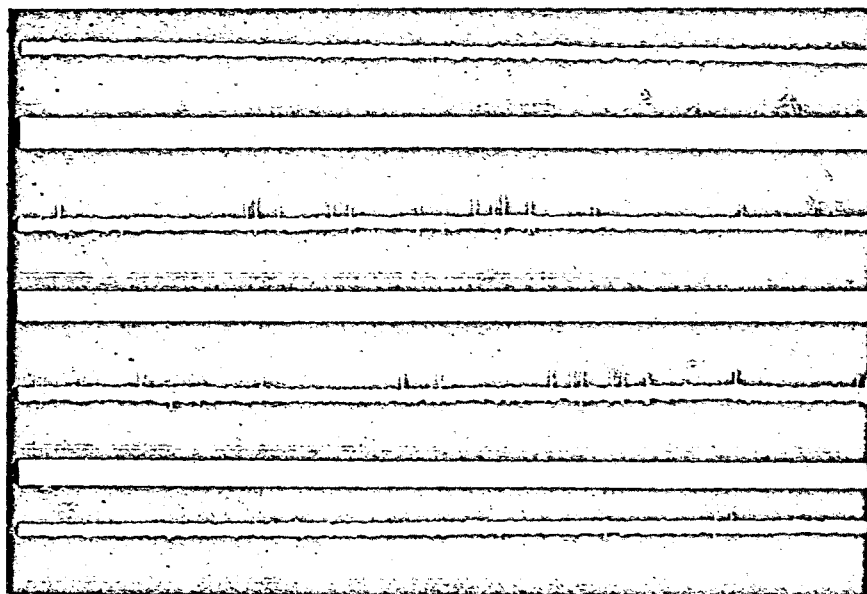


Fig. 2. Changes in the impulse activity of the venous receptors on perfusion of the vein with a 1 : 500 solution of caffeine.

1) Initial activity during passage of Ringer's solution through the vein;
2, 3) activity after 1-2 minutes perfusion with caffeine solution; 4) activity 2 minutes after rinsing out the caffeine with Ringer's solution.

In order to confirm the reflex character of these reactions which we have described, we carried out 6 experiments in which we blocked the receptors with novocain. A preliminary perfusion with a 2 % solution of novocain for 5 minutes brought about a complete blockade of the receptors, which was shown by absence of reflex reactions on perfusion of the vein and the intact limb with the drugs being tested.

By means of a cathode oscillograph, we studied the impulse activity of the venous receptors, recording the biopotentials in the peripheral end of the anterior deep branch of the sciatic nerve. On perfusion of the isolated section of the vein with caffeine solution a considerable increase in the frequency of impulses was observed in 12 out of 14 tests. In some experiments the impulse activity of the venous receptors was increased between 5 and 10 times by the action of caffeine (Fig. 2). By the action of the other drugs no clear changes in the impulse activity of the venous receptors could be found.

The technic which we used for preparing the femoral vein excludes the possibility of leakage of perfusion substances into the general circulation of the frog. Cardiovascular drugs, acting on the receptors in the femoral vein, cause reflex depression of respiration and sometimes a motor reaction but have no effect on the activity of the heart. Stimulation by these drugs of the receptors of the intact limb produced reflex stimulation of respiration or a motor reaction.

Thus reflex changes in respiration, opposed in character, may be produced from the receptors of the femoral vein and of the intact limb. This conclusion is in agreement with the view of A. G. Bukhtiarova [3] on the variation in the reactions arising from receptors in arteries and veins.

SUMMARY

The reflex effect on the heart and respiration of caffeine, strophanthin, adrenalin and nitroglycerin was studied in conditions of perfusion of the humorally isolated femoral vein or of the whole frog's extremity. The impulse activity of the venous receptors was also registered.

These substances act on the receptors of the isolated parts of the vein and depress the respiration and cause motor reaction by reflex effect. However, they do not change the heart activity. Reflexes which come from receptors of the whole extremity stimulate respiration or cause motor reaction. The frequency of the afferent impulses from receptors of the femoral vein is increased by 5 to 10 times by the action of caffeine.

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