REFLEX EFFECTS OF PRESSURE CHANGES IN THE CHAMBERS OF THE FROG'S HEART ON THE PERIPHERAL BLOOD FLOW AND THE HEART RATE

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Hypotension and bradycardia have been observed to develop during mechanical and chemical stimulation of the receptors of the heart [8,9,11,12,14,19-22]. In view of these findings the heart is usually described as the source of exclusively depressor reflexes, and it is so assessed in all the major surveys of the literature on this subject [10,13,16, 18]. As a rule observations suggesting the contrary are of doubtful validity [15,23].

B. S. Kulaev [1,4] has shown that stimulation of the receptors of the epicardium of cats by chemical substances may give rise to both depressor and pressor reflexes. In most experiments conducted with natural respiration, weak stimuli caused an increase of arterial pressure and tachycardia, and strong stimuli a fall of pressure and bradycardia. Admittedly, experimental conditions may be created in which any stimulus applied to the receptors of the epicardium causes depressor reflexes only. This result may most easily be attained if the experiment is conducted with the use of artificial respiration and with the thorax open [3]. It is in these conditions that the receptor functions of the heart have been studied by most investigators who have reported finding enclusively depressor reactions.

It is, therefore, important to ascertain whether mechanical stimulation of the heart, in a near-adequate form, may give rise to constriction of the peripheral blood vessels and to tachycardia in the absence of conditions predetermining a depressor character of the effect. To study this problem in warm-blooded animals it is essential to vary the pressure in the chambers of the heart during natural respiration. Severe operative trauma must be avoided, and the apparatus must not be unwieldy. The present investigation was conducted on winter frogs (Rana temporaria), in which the opening up of the body cavity, isolation of the heart from the vessels, and perfusion of the vascular system by blood substitutes do not have such strong effects on the state of the cardiovascular and nervous systems as in warm-blooded animals.

We know of two researches in which the reflex vasomotor effects of stimulation of the receptors of the amphibian heart were studied. Goto [17], in experiments on toads, always observed dilatation of the vessels. M. I. Lukshina and A. M. Ugolev [5], in experiments on grass frogs, obtained the opposite result—vasoconstriction. In our preliminary experiments [6] we found that if the pressure within the chambers of the frog's heart were changed, both constriction and dilatation of the peripheral vessels can be obtained. In the present study an attempt was made to analyze the conditions determining the pressor or depressor character of the reflexes elicited by stimulation of the mechanoreceptors of the heart.

EXPERIMENTAL METHOD

Experiments were carried out on 90 frogs weighing 20-50 g, lightly anesthetized with ether. An attempt was made to preserve the nervous connections of the heart with the rest of the body but to interrupt all the hemodynamic connections between the heart and the vessels. For this purpose a binocular loupe was used to dissect all the vessels and nerves connected with the heart (the pericardium was incised freely); the vessels were ligated and the nerves remained intact. To stimulate the receptors of the heart its chambers were connected to a vertical graduated glass tube, the level of the fluid in which could be changed rapidly. The connection was made by means of a curved cannula, the end of which was introduced in most experiments through the left aorta into the ventricle, where it was anchored by a ligature passed beneath the conus arteriosus. In the experiments in which only the intra-auricular pressure was varied, the end of the cannula was introduced through the inferior vena cava; after fixation of the cannula a second Stannius

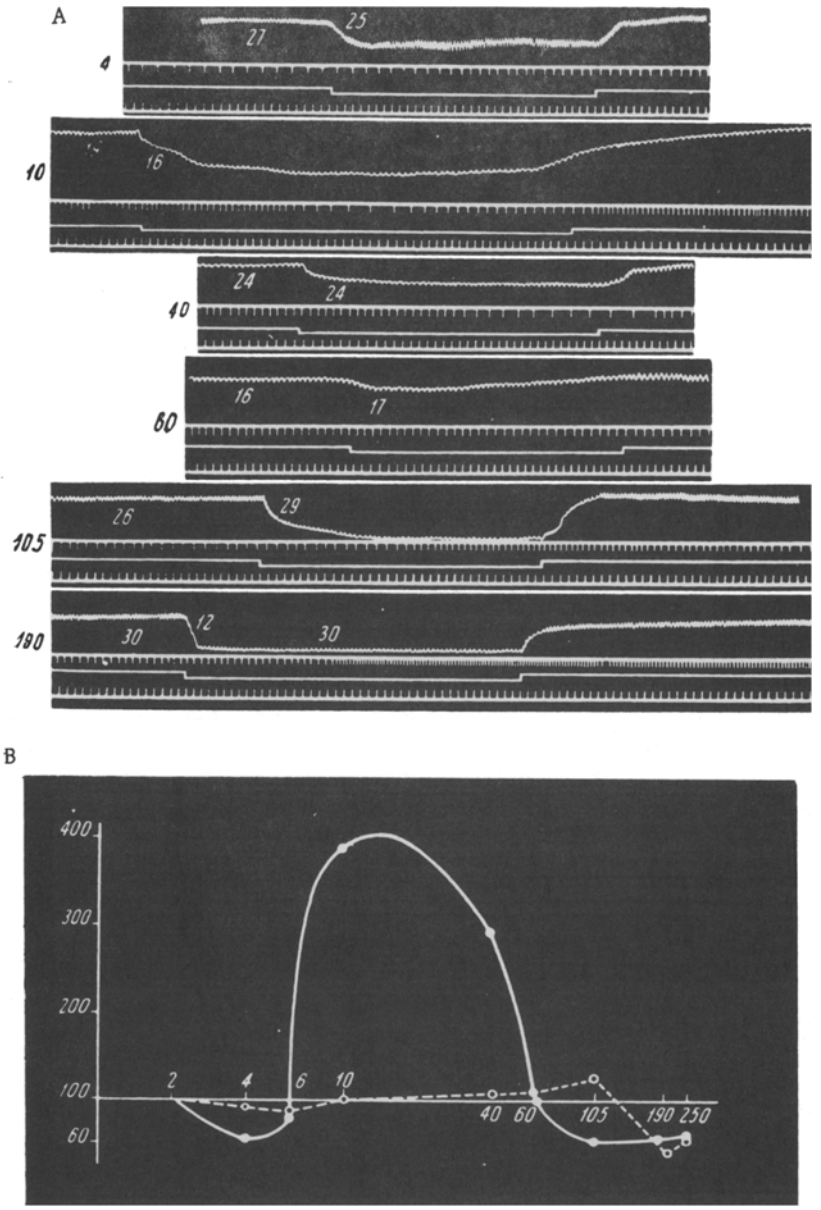

Fig. 1. Relationship between the tone of the peripheral vessels (interval between drops of outflowing perfusion fluid) and the heart rate, and the pressure inside the ventricle. A) 6 kymograms with effects of raising the intraventricular pressure from 0 to the value indicated on the left of each kymogram (in mm water). Significance of the curves on each kymogram (from above down): cardiogram; drop counter; stimulus marker; time marker (2 sec). Numbers below (above) cardiogram: heart rate in beats per minute; B) the same relationship expressed in graphic form. Along the axis of abscissas – pressure inside the heart (in mm water), along the axis of ordinates – value of changes in functions (as percentages of initial value, taken as 100). The solid circles and continuous line joining them denote changes in intervals between drops. The outline circles and broken line joining them denote changes in the rate of the cardiac contractions.

ligature was applied and the ventricle resected. The receptors of the heart were stimulated by introducing 0.1-20 ml of Ringer's solution into the vertical tube, giving rise to a pressure of 2-420 mm water in the chambers of the heart. Minimal stimuli were usually applied initially, gradually changing to stronger stimuli. The intervals between stimuli were 10 min in duration.

The vessels of the trunk were perfused at constant pressure with Ringer's solution for frogs containing 6.5% polyglucin. No edema developed in a period of 3-4 h. Perfusion was carried out through the right aortic arch, into the

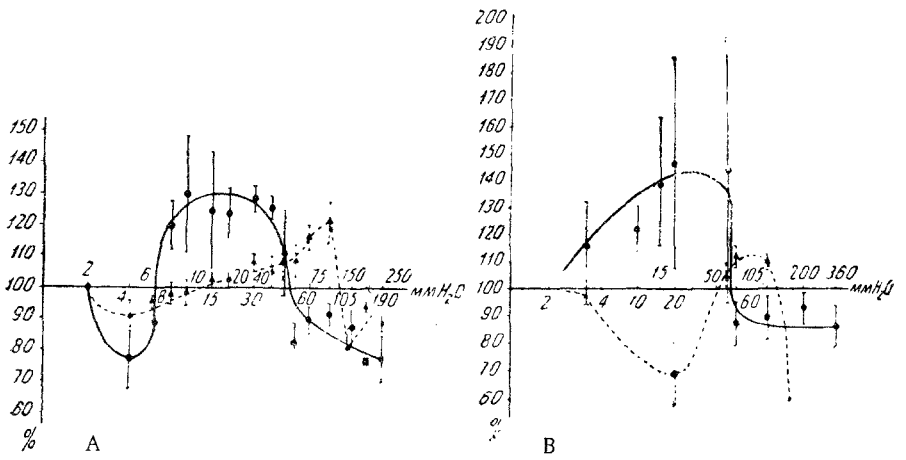

Fig. 2. Relationship between the tone of the peripheral vessels and the heart rate, and the magnitude of the pressure in the ventricle (A) and auricles (B). The points denote the mean values of the changes in the blood flow (circles) and in the heart rate (triangles). The vertical lines intersecting them give the value of the standard error of the mean (m). Remaining legend as in Fig. 1.

distal end of which was inserted a cannula connected to a Marriott's vessel. The outflow of perfusion fluid from the anterior abdominal vein was recorded by means of a drop counter, consisting of contacts closed by the falling drops, a single-stage amplifier, and an electromagnetic marker. The work of the heart was recorded by placing on it a light rod, firmly joined to a light Engelmann's lever by a short arm.

Experiments in which the fluid passed from the perfused vessels into the empty heart, meaning that the hemodynamic connection was maintained between the heart and vessels, were regarded as unsuccessful.

EXPERIMENTAL RESULTS

In 45 experiments the effect of an increase in the intraventricular pressure on the rate of outflow of perfusion fluid from the abdominal vein was studied. In each case the pressure was raised from 0 to a definite value. In two experiments no changes were found even in response to a considerable increase of pressure. In all the remaining cases even a slight increase in pressure led to obvious changes in the outflow of perfusion fluid from the abdominal vein.

Tracings of six such effects are shown in Fig. 1, A. The creation of a pressure of 4 mm water in the ventricle caused an increase in the outflow from the abdominal vein (the interval between the drops was shortened by 40%). An increase in pressure to 10 and 40 mm water had the opposite effect—a decrease in the outflow (the interval between the drops increased by 293 and 200% respectively). A pressure of 60 mm water did not lead to changes in the outflow, whereas the effects caused by an increase of pressure to even higher levels (105 mm water or higher) were shown by a shortening of the interval between the drops flowing from the abdominal vein by more than half. As a rule the heart rate was only slightly changed. However, if the numbers marked above the heart rate curve are examined (the drop in this curve during stimulation is the result of the increased volume of the heart), it is clear that an increase in the pressure inside the heart to 4 mm water caused a slowing of the heart, an increase to 10 mm water caused no change in the heart rate, an increase to 40-105 mm water did not cause an increase in the heart rate, while an increase to 150-250 mm water usually caused a biphasic change in the rhythm: a transient slowing, rapidly followed by the return of the rhythm to normal or to above the normal level. This last effect can be understood in the light of reports in the literature [7] according to which a significant increase in the pressure inside the heart leads to a decrease in its sensitivity to the influence of the vagus nerves, the slowing of the cardiac contractions becomes short in duration, and "escape" easily takes place, sometimes changing to tachycardia in the course of stimulation.

The relationships observed in this experiment between the character of the changes in the peripheral blood flow and cardiac rhythm and the magnitude of the pressure increase in the ventricle can be compared from the graphs in Fig. 1, B. The heart and vessels reacted with functionally opposite changes, and the relationship between these reactions and the strength of stimulation was found to consist of three phases. However, the thresholds of the transition from one phase of such a relationship to another do not coincide, so that it is possible to observe an increase in the

outflow and at the same time a slowing or quickening of the heart rate, or no change in the heart rate. In the experiment demonstrated here (see Fig. 1) an increase in the pressure inside the ventricle to 10 mm water caused no changes in the frequency of the cardiac contractions, although the outflow fell by almost 75%; a pressure of 60 mm water did not lead to changes in outflow, although the heart rate increased. These values of the pressure were intermediate between those which caused opposite functional changes, so that a suitable name for them would be the term "zone of silence" suggested by M. G. Udel'nov [7].

The relationships we have examined are typical; they were repeated in all the experiments of this series. The differences lay in the thresholds of appearance of the reflex changes, and in the duration of the latent period, varying from 2 to 40 sec. In some experiments no "zone of silence" was present, differences were observed in the intensity of the reactions, and so on, although the general pattern remained the same. Statistical analysis of the values of the maximal changes during each reaction in all 43 experiments in response to an increase in pressure to a definite level enabled a general graph to be plotted (Fig. 2, A), which confirms the significance of the relationships described.

In 12 experiments we varied the pressure in the auricles only (Fig 2, B). Comparison of the curves showing the relationship between the character and intensity of the reflex responses and the magnitude of the pressure in the ventricle (see Fig. 2, A) and auricles (see Fig. 2, B) reveals, besides features of similarity, definite differences. In the zone of moderately strong and strong stimulation (from 10 to 250 mm water) the curves characterizing the vascular changes practically coincided; the very slight differences in the course of the curves were not statistically significant. In the zone of weak stimulation (4 mm water) the differences between the curves are quite obvious: as the intraventricular pressure rose vasodilatation took place; with the same increase of pressure in the auricles in 10 experiments constriction was observed and dilatation of the vessels in only two. The difference between the reactions of the vessels to weak stimulation of the receptors of the auricles and ventricle may be attributed to the fact that the pressure in the auricles was increased, not from 0 but from 2 mm water. This was due to the fact that the completely emptied auricles do not contract. Because of the high elasticity of the thin-walled auricles in the frog, the first phase of the relationship must become apparent when the pressure was increased within the range from 0 to 2 mm water.

After injection of novocain into the chambers of the heart (5 experiments), as after destruction of the brain (4 experiments), division of the vago-sympathetic trunks (3 experiments) or intracranial division of the roots of the vagus nerve (10 experiments), all the reactions to an increase in the pressure inside the heart disappeared. Conversely, extirpation of the 4 anterior ganglia of the sympathetic chain, including the stellate ganglion (6 experiments), had no effect on the character and intensity of these reactions. From this it can be concluded that all the reactions described are reflex in nature and that the afferent pathways of these various reflexes run in the vagus nerves.

Experiments involving removal of the anterior sympathetic ganglia showed that the efferent pathways of the cardio-cranial reflexes also ran in the vagus nerve trunks. This was also demonstrated by 5 experiments in which the spinal cord was removed, in which these reflexes were preserved, although no changes could be observed in the blood flow with these values of the pressure in the heart. This means that the efferent pathways of the cardio-vascular reflexes pass through the spinal cord.

The conclusion reached from experiments in which the receptors of the heart in cats were stimulated chemically [1-4], namely that both pressor and depressor reflexes may be caused by stimulation of the same receptors of the heart, was confirmed by the results of the present investigation. During the active life of the frog, when the pressure within the heart may reach values exceeding those which we used for stimulation, but when the elasticity of the heart is limited by the intact pericardium, the second and third stages of the relationship we have discovered must play an important part. It seems probable that the mean intracardiac pressure must be maintained at a level corresponding to the "zone of silence" of the vascular reactions. In this way it is easy to imagine the mechanism of the compensatory, buffer functions of the reflexogenic zone of the heart.

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