A POSSIBLE SPECIFIC STIMULUS OF THE "AUTOMATIC" CENTER OF LYMPHATIC HEARTS

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The lymphatic hearts of amphibians are pulsating structures in the lymphatic system responsible for the transport of tissue fluid in the organism. The rhythmic activity of these hearts is controlled by an "automatic" center, lying in the spinal cord, from which flow rhythmic volleys of impulses leading to contraction of the lymphatic hearts. The automatic activity of this center is under the influence of various reflex agencies [1, 3]. Lymph formation, from the functional point of view, is closely related to the circulatory and respiratory systems; all these systems strive to maintain the constancy of the internal milieu of the organism and, in particular, its pH. One of the characteristics of these systems is their ability to submit to the regulatory influence of the factors whose constancy they maintain.

The object of the present investigation was to study the regulatory action of a change in the hydrogen ion concentration on the rhythmic activity of the center for the lymphatic hearts.

EXPERIMENTAL METHOD

To bring influences to bear on the center for the lymphatic hearts a slight modification of the method of perfusion of the frog's spinal cord developed in the laboratory directed by A. V. Kibyakov was used. The indicator of the state of the centers was the rhythmic contractions of the lymphatic heart, which were recorded on a kymograph. Test solutions were prepared by the addition of a few drops of a 0.001N solution of hydrochloric acid or of a 0.001N solution of sodium hydroxide (or bicarbonate) to Ringer's solution. The hydrogen ion concentration of the solutions was determined by the drop method, using a universal indicator, or by an electrometric method.

EXPERIMENTAL RESULTS

The investigation of the effect of solutions with different pH values on the center for the lymphatic hearts showed that the action of hydrogen ions depends on their concentration. Perfusion with Ringer's solution with a pH of 7.4, as a rule, caused no changes in the rhythmic activity of the center; during perfusion with a solution of pH 7.0 a marked increase in the frequency of contraction was observed in 65% of the experiments; a particularly great increase in the frequency of contraction was recorded during the action of a solution with a pH of 6.6. Perfusion with more acid solutions likewise caused a considerable increase in the frequency of contraction, but it was sometimes accompanied by a considerable period of arrest of rhythmic activity, becoming longer as the hydrogen ion concentration rose.

The results of this series of experiments given in Fig. 1 demonstrate the sensitivity of the spinal centers of the lymphatic hearts to an increase in the hydrogen ion concentration: a fall in the pH to 7.0 is a powerful stimulus for the centers for the lymphatic hearts.

Investigations also were made of the effect of alkaline solutions, or an increase in pH, on the rhythmic activity of these centers. The experiments showed that a change in pH towards the alkaline side also affected the automatic activity of the center for the lymphatic hearts. It is clear from Fig. 2 that a change in pH from its initial value of 7.6 to 8.0 caused a slight slowing of rhythmic activity (by approximately 15%). More strongly alkaline solutions (pH 9.0 and 10.0) had the same action, and not until a solution with a pH of 11.0 was tested was a gradually increasing stimulation of the rhythm observed (by approximately 40%).

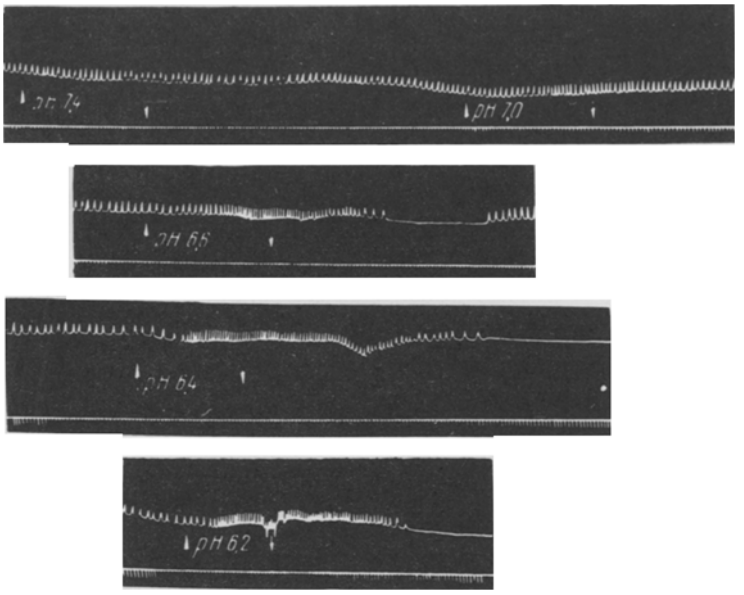

Fig. 1. Rhythmic contractions of the lymphatic heart under the influence of a decrease in the pH of the solution used for perfusion of the spinal cord. Bottom tracing—time marker (60/min). The arrow indicates injection of the solution.

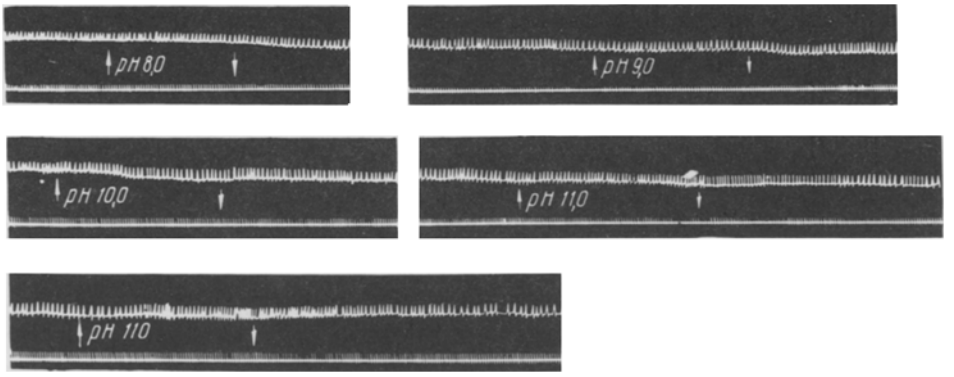

Fig. 2. Change in the rhythmic activity of the center for the lymphatic heart in response to an increase in the pH of the solution used for perfusion of the spinal cord.

Hence, a change in the pH towards the alkaline side had a biphasic action: a slowing of the rhythm in response to a slight increase in pH (probably within the limits of physiological variations), and an increase in its frequency in response to more strongly alkaline conditions (in all probability associated with the marked disturbance of the normal course of the metabolic processes).

Consequently, the spinal center of the lymphatic hearts reacts to changes in pH to both acid and alkaline sides, and the sensitivity of this center to high pH values is much less than to low values. The center of the lymphatic hearts changes its activity very slightly when the pH rises to 8.0, or even to 9.0 (the frequency of the contractions fell by only 15%), and at the same time it reacts by a sharp rise in frequency when the pH falls to 7.0. These facts show that the change in the hydrogen ion concentration may act as a regulator of the automatic rhythmic activity of the center for the lymphatic hearts.

These results agree with those obtained in respect to the respiratory and vasomotor centers. Hydrogen ions thus constitute common stimuli for these three systems. They must evidently be regarded as adequate stimuli, playing an important role in the mechanism of the rhythmic activity of the spinal center of the lymphatic heart.

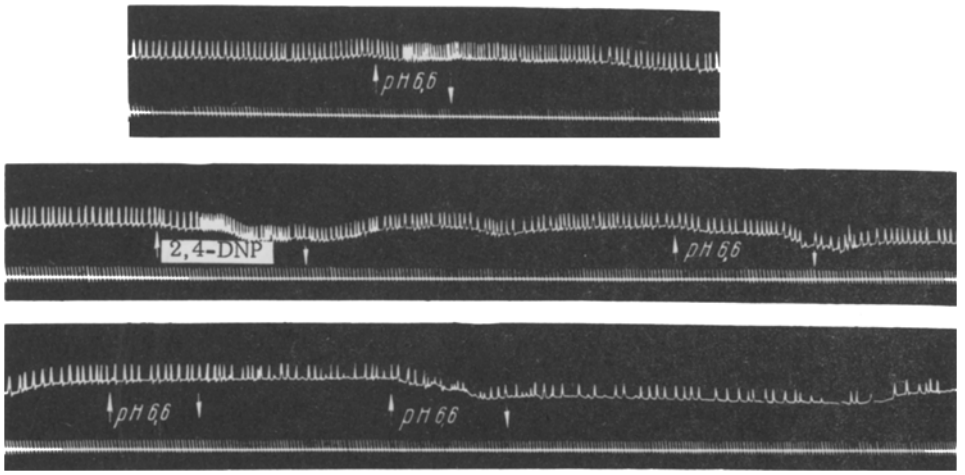

Fig. 3. Blocking of the stimulating action of an acid solution of the rhythmic activity of the center for the lymphatic heart by means of dinitrophenol. Concentration of dinitrophenol (2, 4-DNP) 5 x 10^{-4} M.

In face of these results, indicating the regulatory action of changes in the hydrogen ion concentration of the perfusion fluid on the activity of the center for the lymphatic hearts, experiments were conducted for the object of elucidating the mechanism of action of these ions. The initial theoretical basis for the investigation was the idea put forward by Kh. S. Koshtoyants that the physiological action of various neuro-humoral agents on the activity of various structures is determined by the processes of metabolism taking place in these structures.

In our experiments the hydrogen ions had a marked stimulatory action on the rhythmic activity of the spinal center of the lymphatic heart. It may be suggested that the increase in functional activity must be based on a higher level of metabolism and, in particular, a higher level of metabolism of high-energy compounds. If this suggestion is correct, factors altering the dynamics of metabolism of high-energy phosphorus compounds must also modify the action of hydrogen ions. As an agent modifying the metabolism of high-energy compounds 2, 4-dinitrophenol was used—a substance dissociating the process of respiration from its attendant processes of phosphorylation [5].

It is clear from Fig. 3 that Ringer's solution with pH 6.6 caused considerable stimulation of the rhythmic activity of the center for the lymphatic heart (the frequency of the contractions was doubled). The same solution, when injected 1.5 min after the action of 2, 4-dinitrophenol (1 x 10^{-4} M), caused no increase in the frequency of the rhythmic activity, or even had a slight inhibitory action. The subsequent injection of an acid solution likewise caused no increase in the rhythmic activity of the center for the lymphatic heart. It must be pointed out that the action of higher concentrations of hydrogen ions (pH 5.6) was also weakened considerably by 2, 4-dinitrophenol. However, the action of strongly acid solutions after administration of 2, 4-dinitrophenol had a depressant effect on the rhythmic activity of the automatic center, demonstrating profound disturbances of the normal course of metabolism.

Hence, the stimulant action of hydrogen ions was completely abolished by an agent blocking the synthesis of high-energy phosphorus compounds. It may be concluded from this fact that stimulation of the automatic rhythmic activity of the center for the lymphatic heart caused by hydrogen ions is probably the result of the influence of these ions on the synthesis of high-energy phosphorus compounds. There is no doubt that hydrogen ions may bring about a whole series of changes in the metabolism of the neurons of the automatic center, leading in particular to profound changes in ion exchange, among which the discharge of potassium ions may be especially important. Without doubt all these changes are reflected in the changes in the functional activity of the nervous centers for the lymphatic hearts.

Hence the stimulating effect of hydrogen ions is evidently the result of a chain of changes in the course of various processes, but the effect as a whole must be associated with the synthesis of high-energy compounds, since this is completely suppressed by 2, 4-dinitrophenol. The hydrogen ion, the specific stimulus for the center for the lymphatic hearts, thus influences the fundamental aspect of the metabolism of this center, namely the dynamics of the metabolism of high-energy compounds.

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