THE INFLUENCE OF UREA ON NERVOUS STIMULATION OF CARDIAC MUSCLE

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Ya. P. Sklyarov and his co-workers have shown that metabolic products may affect the recovery processes in glandular tissue and in the heart [5-11].

We here report a study of the effect of the products of nitrogen metabolism (urea) on recovery in cardiac muscle. We chose urea, because according to Kh. S. Koshtoyants and his co-workers [4], this substance brings about the splitting off of free sulfhydryl groups from the protein molecule, and these groups play a part in the oxidation-reduction processes in tissues, and are also concerned in neurohumoral regulation.

METHOD

Two kinds of experiments were made: 1) 58 in which frog hearts were prepared by Saima's method, and the sympathetic and vagal supply retained for stimulation, and 2) 13 acute experiments on dogs in which records were made of the blood pressure and pulse pressure. We first found the effect of a 0.5-1% urea solution on the isolated frog heart, and of a 20-40% urea solution on the blood pressure of the dog. Then, in all experiments, a control stimulation was made of the vago-sympathetic or sympathetic nerves, by means of an induction coil. A study was then made of the effect of nervous stimulation of the dog heart; this was done during perfusion of the isolated heart with urea, or after injecting urea intravenously.

RESULTS

Perfusion of the isolated frog heart with 1-2 ml of 0.5 and 1% urea solutions led to an increase in the amplitude of the contractions, and in some experiments also increased the rate. The effect did not last for more than 1-2 minutes. Intravenous injection of 0.5-1 ml per kg of 20-40% urea solution caused a transient reduction in blood pressure and some increase in the pulse pressure.

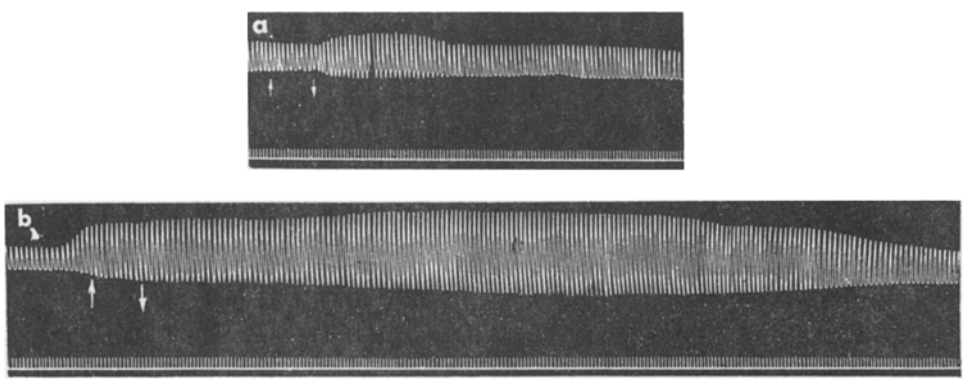

Fig. 1. Stimulation of the sympathetic nerve supply to the frog heart. Experiment made on 23/12/1956. (Distance between the coils of the induction coil - 12 cm; voltage applied to primary winding- 6v.) a) Control; b) after perfusion with 2 ml of 1% urea. Curves, from above downwards: cardiac contractions; time marker (1 second); arrows - time at which nerve was stimulated.

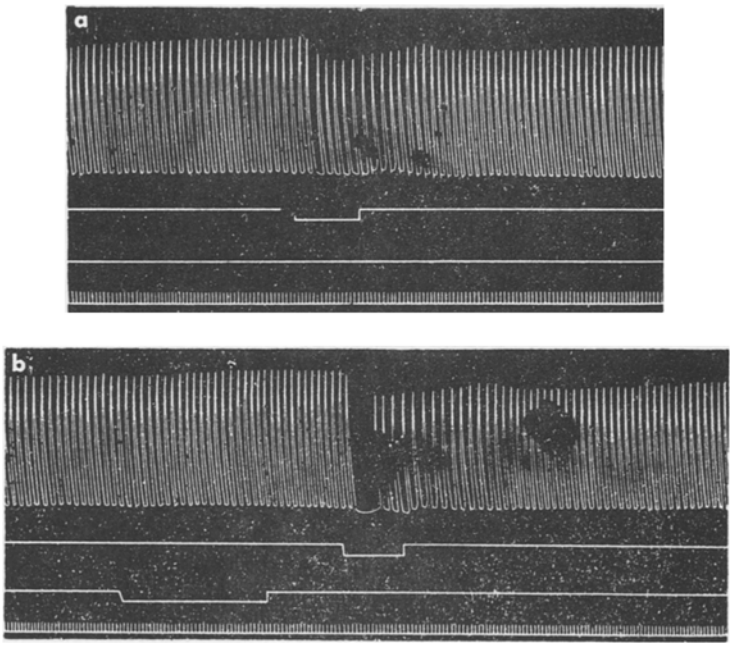

Fig. 2. Stimulation of the vagosympathetic nerve in the frog. Experiment made on 20/1/1956 (distance between coils 8 cm, voltage applied to the primary 6 v). a) Control; b) after perfusing the heart with 2 ml of 1% urea solution. Curves, from above downwards: cardiac contractions; stimulation of the nerve; perfusion with the solution; time marker (1 second).

Perfusion of the isolated frog heart with 0.5 and 1% urea solutions markedly increased and prolonged the positive inotropic effect (Fig. 1, a, b).

Similar changes were observed in the experiments on dogs. After intravenous injection of 10 ml of a 40% urea solution, the hypertensive effect of stimulating the sympathetic nerve was more clearly shown. These results agree with those of Kh. S. Koshtoyants [3] on the fatigued striated frog muscle. He found that a given strength and duration of stimulus applied to the sympathetic nerve supplying a fatigued muscle treated with urea caused a far greater increase in the height of the contractions than it did when the muscle was immersed in Ringer solution.

In the presence of urea, the effect of vagosympathetic stimulation is different from that in the control animal (Fig. 2, a, b). When the heart is perfused with urea, the inhibitory effect from the vagus is enhanced.

A similar effect was observed also in acute experiments on dogs. After injecting 20% urea solution intravenously, the depressor vagosympathetic action was enhanced, and it lasted longer than it did in the control experiment. This result agrees with those of Kh. S. Koshtoyants, T. M. Turpaev and K. S. Logunova [1,2], who found that urea restored the inhibitory effect of the vagus, which is destroyed when sulfhydryl groups become bound by thiol poisons; they found that it also eliminated the phenomenon of "escape" of the heart from vagal inhibition.

Urea therefore enhances the effect of sympathetic and vagal stimulation in both the frog and dog. A possible explanation is that the functional change is due to the liberation of active sulfhydryl groups from the protein molecules, and that these groups influence the cardiac response to neurohumoral action.

SUMMARY

A study was made of the effect of urea on regeneration in cardiac muscle. Urea was chosen because according to results obtained by Kh. S. Koshtoyants, this substance promotes the liberation of free sulfhydryl groups from the protein molecule, and so plays an important part in the oxidation-reduction processes in the tissues, and in neurohumoral regulation.

The experiments reported here were carried out on isolated frog hearts, and the sympathetic and vagus nerves were retained for stimulation. Blood pressure and fluctuations in pulse amplitude were recorded in acute experiments on dogs. Usually, the vagosympathetic or sympathetic nerves were first stimulated by current from an induction coil. A study was then made of the specific features of the effect exerted by these nerves on an isolated frog heart perfused by 0.5-1% urea solution, or on the heart of an intact animal which was given an intravenous injection of 20-40% urea solution. In evaluating these results, attention was paid to the frequency and amplitude of the cardiac contractions, and in dogs to the blood pressure and pulse pressure. Perfusion of the isolated frog heart with 1-2 ml of 0.5 or 1% urea solution caused transient changes in both the amplitude and the rate of the heart beat, but intravenous injection of 0.5-1 ml per kg of 20-40% urea solution caused no significant drop in blood pressure but produced a rise in the amplitude of the pulse pressure. Treatment with urea considerably intensified the effect of stimulation of the cardiac sympathetic and vagosympathetic nerves.

LITERATURE CITED

1. Kh. S. Koshtoyants and T. M. Turpaev, Doklady Akad. Nauk SSSR, 54, 2 (1946) p. 181.
2. Kh. S. Koshtoyants and K. S. Logunova, Doklady Akad. Nauk SSSR, 73, 2 (1950) p. 429.
3. Kh. S. Koshtoyants, Doklady Akad. Nauk SSSR, 72, 5 (1950) p. 981.
4. Kh. S. Koshtoyants, Protein Bodies, Metabolism, and Nervous Regulation [in Russian] (Moscow, 1951).
5. A. A. Mazurok, Fiziol. Zhurn., 5, 5 (1959) p. 622.
6. A. A. Mazurok, Abstracts of Reports of the Conference on the Problem of the Mechanism of Action of the Hormones [in Russian] (Kiev, 1957) p. 101.
7. A. A. Mazurok, Fiziol. Zhurn. SSSR, 3 (1960) p. 326.
8. Ya. P. Sklyarov, Reports of the 2nd Ukrainian Conference on Problems of Physiology, Diseases, and Morphology of the Digestive System [in Russian] (Odessa, 1948) p. 53.
9. Ya. P. Sklyarov, Results on the Analysis of Secretory Function of the Gastric Glands during Their Prolonged Stimulation [in Russian] Dissertation for Doctorate (Chernovitsy, 1948).
10. Ya. P. Sklyarov, in book: Problems of Physiology [in Russian] (Kiev, 1951) 1st ed., p. 20.
11. Ya. P. Sklyarov, L. N. Karpenko, and B. S. Savron', Abstracts of Reports of the Scientific Conference on Problems of the Physiology and Pathology of Digestion [in Russian] (Kiev, 1954) p. 156.

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
