PROTEIN BIOSYNTHESIS IN THE FIBRILLATING PERFUSED HEART WITH NORMAL OXYGENATION AND AFTER ANOXIA

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UDC 616.12-009.3-008.939.6-092.4

Incorporation of methionine-S^{35} into proteins of the fibrillating dog's heart perfused with a donor's circulation, was investigated. During electrically induced fibrillation and with an adequate oxygen supply the incorporation of methionine-S^{35} into contractile proteins of both ventricles of the heart increased by 50-55%. In the case of fibrillation following prolonged anoxia, incorporation of methionine-S^{35} was reduced into atrial proteins (by 40-60%) and also into the sarcoplasmic (by 36-53%) and contractile (by 18-30%) proteins of both ventricles.

KEY WORDS: isolated heart; protein biosynthesis; perfusion; fibrillation.

Ventricular fibrillation frequently arises during cardiac hypoxia, hypothermia, electric shock, and so on. In operations on the open heart with an artificial circulation ventricular fibrillation may be specially induced by weak electric discharges so that manipulations can be carried out on the "quiet" heart [9]. Prolonged fibrillation frequently arises also during keeping of the isolated heart and its transplantation. Investigations of metabolism in the fibrillating heart have dealt mainly with energy metabolism.

In this investigation the biosynthesis of contractile and sarcoplasmic proteins of the isolated dog's heart were studied during artificially induced fibrillation with an adequate oxygen supply and during spontaneous fibrillation arising after prolonged anoxia.

EXPERIMENTAL METHOD

Coronary perfusion of the isolated dog's heart was carried out as described previously [1]. In the experiments of series I protein biosynthesis was investigated in the normally contracting isolated heart perfused from a donor. Throughout the experiment the heart was kept in the chamber of a ultrathermostat at 38°C with adequate oxygenation and it contracted in the sinus rhythm (100-120 beats/min). In the experiments of series II fibrillation of the heart was induced under exactly the same conditions (alternating current, voltage 12 V). In the experiments of series III the heart was removed from the animal and placed for 60 min in the chamber of an ultrathermostat at 38°C without perfusion, after which it was connected to the circulation of a donor dog.

Active fibrillation began 0.5-1.5 min after the beginning of perfusion and it lasted throughout the experiment. In all experiments the duration of perfusion was 1 h.

At the beginning of perfusion a solution of methionine-S^{35} (specific activity 200-300 μCi/mg) was injected into the systematic circulation of the donor dog in a dose of 35,000-40,000 counts/min/g body weight. At the end of perfusion, contractile [3] and sarcoplasmic [2] proteins were isolated from all parts of the

Biochemical Laboratory and Laboratory of Experimental Surgery, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. A. Vishnevskii.*) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 81, No. 2, February, 1976. Original article submitted May 20, 1975.

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TABLE 1. Incorporation of Methionine-S^{35} into Myocardial Proteins of Donor's and Perfused Hearts (in counts/min/mg protein)

Test object	Left atrium	Left ventricle		Right atrium	Right ventricle	
	total protein	sarcoplasmic proteins	contractile proteins	total protein	sarcoplasmic proteins	contractile proteins
Donor's heart	607	554	573	560	560	508
Perfused heart:						
normal contractions	657±36,62	520±117,57	536±46,59	611±66,91	648±47,57	599±41,67
P	>0,2	>0,5	>0,2	>0,2	>0,05	>0,05
artifically induced fibrillation	565±45,55	671±105,72	898±90,37	640±126,99	656±74,09	753±37,55
P	>0,2	>0,2	<0,01	>0,5	>0,2	<0,001
fibrillation after anoxia	376±35,08	260±43,39	402±22,89	227±12,75	359±47,01	418±26,73
P	<0,001	<0,001	<0,001	<0,001	<0,01	<0,01

Note. Here and in Table 2 criteria of significance of differences between donor's and perfused hearts are shown.

TABLE 2. Concentration of Free Methionine-S^{35} in Different Parts of Myocardia of Donor's and Perfused Hearts (in counts/min/2 mg wet weight of tissue)

Test object	Left atrium	Left ventricle	Right atrium	Right ventricle
Donor's heart	518	489	568	504
Perfused heart:				
normal contractions	530±5,88	558±25,59	631±21,25	584±80,82
P	>0,1	>0,05	>0,05	>0,2
artificially induced fibrillation	514±29,52	514±36,21	548±45,42	488±19,62
P	>0,5	>0,5	>0,5	>0,2
fibrillation after anoxia	409±43,09	509±34,46	456±43,65	464±39,29
P	>0,05	>0,5	>0,05	>0,2

isolated heart and the donor's heart and their radioactivity was determined. Nonprotein radioactivity also was determined in all parts of the heart.

EXPERIMENTAL RESULTS AND DISCUSSION

It will be clear from the results in Table 1 that the incorporation of methionine-S^{35} into myocardial proteins during perfusion of the normally contracting isolated heart with adequate oxygenation was virtually the same as into the myocardial proteins of the donor dog. During artificially induced fibrillation of the perfused isolated heart incorporation of methionine-S^{35} was increased into the contractile proteins of the left (by 56.7%) and right (by 48.2%) ventricles. During spontaneous fibrillation of the perfused heart after a period of anoxia, much less methionine-S^{35} was incorporated into proteins of all parts of the myocardium than into the corresponding proteins of the heart of the donor dog. The inhibition of incorporation of methionine-S^{35} into the contractile proteins of the ventricles was less marked in this case than into other myocardial proteins.

It will be clear from Table 2 that, regardless of the state of the perfused heart, the level of free methionine-S^{35} in all its parts was the same as in the heart of the donor dog. Since it is reasonable to consider that in the early stages after administration of the labeled amino acid the level of nonprotein radioactivity in the organ reflected the intensity of entry of the label into it, these results indicate that the changes in methionine-S^{35} incorporation into proteins of the fibrillating heart were due to changes in the ability of the myocardium to synthesize protein rather than to a disturbance of permeability of the cell membranes.

Activation of processes of protein synthesis in the fraction of myocardial contractile proteins during artificial fibrillation of the heart may perhaps be explained to some degree by the higher oxygen demand of the fibrillating heart [4-9]. The sharp inhibition of protein biosynthesis in the fibrillating heart when perfused after a period of anoxia, however, was in all probability due not to the fibrillation itself, but to disturbance of the metabolism of the myocardium during the period of anoxia, which was not fully restored to normal during the subsequent oxygenation.

When oxygenation is adequate, fibrillation of the heart by itself thus does not inhibit the biosynthesis of sarcoplasmic and contractile proteins.

LITERATURE CITED

1. A. A. Vishnevskii, V. F. Portnoi, and G. K. Bandyaev, Éksper. Khir., No. 2, 8 (1969).
2. R. N. Korotkina, V. I. Nikulina, and A. S. Konikova, Vopr. Med. Khimii, No. 5, 527 (1968).
3. V. V. Oppel' and T. P. Serebrenikova, Biokhimiya, No. 4, 648 (1959).
4. S. Goldschmidt and G. Lamprecht, Hoppe-Seyler's Z. Physiol. Chem., 307, 132 (1957).
5. W. Lamprecht, in: Hämodynamik and Stoffwechsel, Stuttgart (1964), p. 241.
6. V. Lorber, Circulat. Res., 1, 298 (1953).
7. V. Lorber, Physiol. Rev., 35, 137 (1955).
8. M. H. Paul, E. O. Theilen, D. E. Gregg, et al., Circulat. Res., 2, 573 (1954).
9. A. Senning, cited in: Zentralorg. Ges. Chir., 126, 157 (1953).