Cardiac Contractility after Acute Cooling of the Organism and Adaptogenic Correction of Its Disorders

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UDC 612.014.43.172.225:615.322

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol.116, № 11, pp.480-482, November, 1993
Original article submitted June, 7, 1993

Key words: *cooling action; natural adaptogens; isolated heart; contractility*

An adaptive defensive stress reaction may turn into an "adaptive disease", as Selye noted, if the response of the organism is excessive or the duration of stress is prohibitively long [7]. The impact of low temperatures on the homoiothermic organism is considered a pathological manifestation of the stress reaction and must be corrected. The different reactions found in cooling are similar to those in other types of stress [2]. However, the mechanism of low-temperature action on the cardiovascular system and, particularly, on the cardiac muscle is far from established. Natural adaptogens, such as *Rhodiola rosea* (RR), have been shown to boost the general resistance of the organism under extreme conditions [6], and may therefore be useful in pathogenic treatment of the cardiovascular disorders induced by low temperatures.

The aim of the present investigation was to study the changes in cardiac contractility at different times after acute cooling of the organism and to assess the efficacy of RR extract for the correction of alterations of inotropic function.

MATERIALS AND METHODS

Isolated hearts of Wistar rats weighing 200-250 g were used in 6 experimental series. The first series was the control, and experiments were carried out on intact animals. The rats of the 2nd and 3rd series were exposed to low temperature (-10°C) during 4 h before the tests. The rats of the 2nd series were examined immediately after cooling, while the animals of the 3rd series were kept at room temperature for 18 h and only then were taken for further experiment (delayed action of cooling stress). RR extract was administered per os in a dose of 1 ml/kg/day to the animals of the 4th-6th series during 8 days prior to the tests. The rats of the 4th series were tested 24 h after the last treatment, while in the 5th and 6th groups they were subjected to cooling and then examined immediately or 18 h later, respectively.

The procedure of isolation and perfusion (60 min) of the spontaneously beating heart was described previously [5]. In the testing the cardiac contractility and coronary flow (CF) were recorded, and the amplitude of contraction was estimated, along with the tension of the cardiac muscle and duration of the cardiac cycle. The results were processed statistically using the Student *t* test.

RESULTS

The impact of cooling markedly altered the contractility of the isolated heart as well as its dynamics during perfusion. The amplitude of contraction immediately after acute cooling (the 2nd series) was initially lower (by 42%) than in the control

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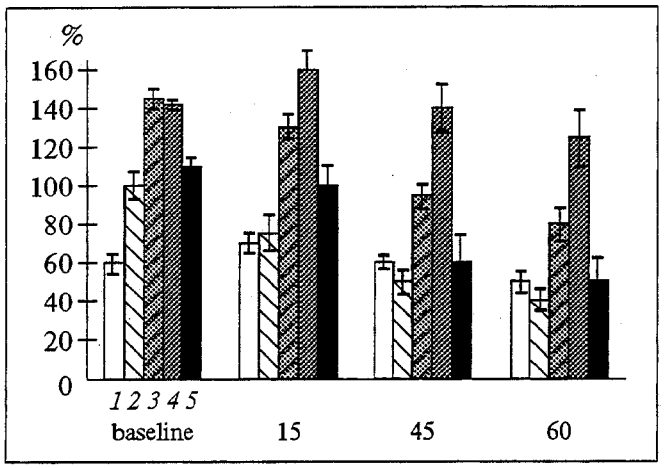

Fig. 1. Amplitude of contraction in isolated hearts of intact and experimental rats. Here and in Figs. 2 and 3: *1*) intact animals in 1st h after cooling; *2*) 18 h after cooling; *3*) adaptogene alone; *4*) adapted animals in 1st h after cooling; *5*) 18 h after cooling. Abscissa: time of perfusion (min); ordinate: amplitude of contraction (in percent of control series; the control value at every time of perfusion is taken as 100%).

($p<0.05$) and remained virtually unchanged to the end of the experiment (Fig. 1). This parameter was in the control range 18 h after cooling at the onset of perfusion, but in the course of perfusion the amplitude of contractions rapidly dropped and by 60 min was significantly lower ($p<0.05$) than the analogous values in the 2nd series.

The stability noted for the parameters of contraction amplitude was a characteristic feature of the CF magnitude immediately after cooling (Fig. 2), a rather high level of CF (up to 80% of the control level) corresponding to an initially low contractility. These findings are consistent with the data reported on the absence of a reliable decrease of the CF in the rat heart under conditions of cooling [8,10].

The initial CF was significantly lower in animals of the 3nd group compared to that in the 1st

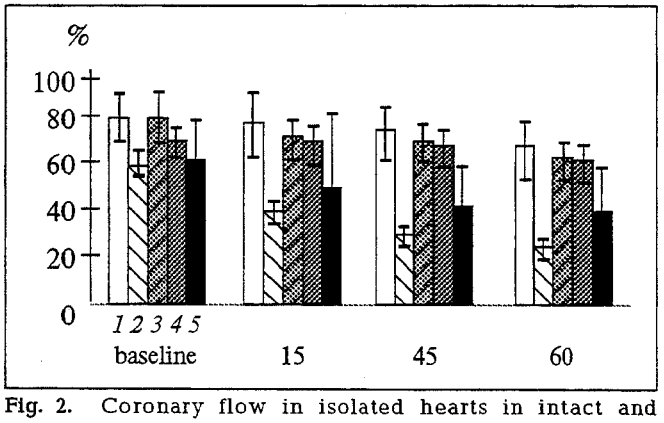

Fig. 2. Coronary flow in isolated hearts in intact and experimental animals. Abscissa: time of perfusion (min); ordinate: CF (in percent of control series; the control value at every time of perfusion is taken as 100%).

and 2nd series. Its decrease during perfusion was also reliably more pronounced in the 3rd series. The fall of the CF in this series might be due to an increase of resistance in the coronary vessels. This conclusion stems from the observation that a low CF in rats 18 h after cooling was found in the very first minutes of perfusion and was not accompanied by inhibition of the inotropic function of the heart. A similar effect has been observed in people exposed to cold [9].

Thus, acute cooling resulted in a decrease of cardiac contractility, but the tonus of the coronary vessels was not affected immediately after stress, whereas 18 h later vascular disorders developed (a drop of the CF). The rise in the amplitude of contraction to the control level in the 3rd series is not to be considered the result of the total recovery of contractile activity. The changes noted can be regarded as a negative consequence of the organism's having used up its internal reserves after normalization of the temperature conditions.

The differences in the dynamics of cardiac muscle tension for perfusion that developed during 18 h postcooling attested to the incomplete recovery of the amplitude of contraction. Thus, the animals in the 3rd group exhibited a more rapid rise ($p<0.05$) in tension in comparison with the changes of this parameter in rats of the 2nd series (Fig. 3). Such alterations in the process of diastolic relaxation testified to a decrease of myocardial efficiency [1] and may be related to the development of metabolic disturbances in rat cardiomyocytes after exposure to low temperatures.

The duration of the cardiac cycle was not affected in our experiments, contrary to the findings of other investigators, who noted an increase of the heart rate in cooling [2]. Such a discrepancy may be related to the use of the isolated heart model in the absence of central regulation of hemodynamics, which has an undoubted effect on the experimental results when the whole organism is studied.

The baseline amplitude of contraction was 40% higher (Fig. 1) and the CF was relatively low (Fig. 2) in the isolated hearts of animals treated with RR (the 4th series) in comparison to intact rats. Acute cooling did not affect the initial parameters of heart contraction in these animals immediately after its termination.

Myocardial contractility in perfusion was similar to the intact value 18 h after acute cooling with (6th series) or without (3rd series) RR administered, and was significantly lower than the levels obtained in the 4th and 5th series. A low CF was observed in all tests with adaptogen pretreatment.

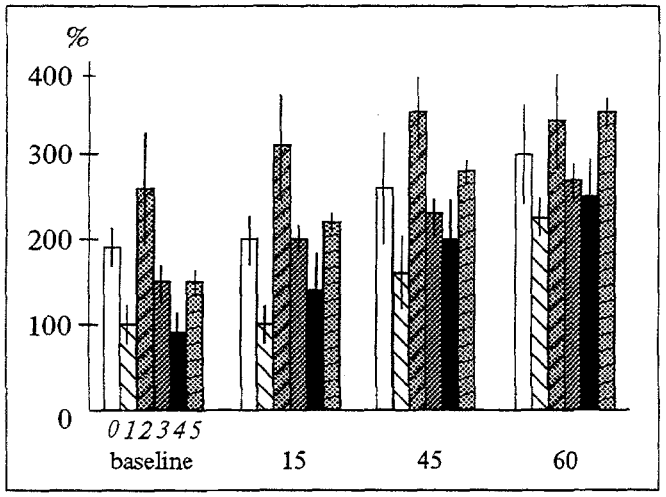

Fig. 3. Dynamics of tension of isolated rat heart during 60 min of perfusion. 0) intact animals; abscissa: time of perfusion (min); ordinate: tension (in percent; baseline value of parameter in every series is taken as 100%).

The stimulating effect of RR [4] may account for the higher baseline amplitude of contraction in the 4th and 5th groups in comparison with nonadapted rats. This is also indicated by the high level and stability in the parameters of contraction during the perfusion of rat hearts pretreated with adaptogen (5th series) and tested immediately after cooling, while measurements 18 h later did not demonstrate a similar stability (Fig. 1).

The perfusion procedure itself resulted in a slow decline of the amplitude of contraction, which dropped to 60% of the baseline level toward the end of the experiment in the 6th series. The dynamics of this parameter behaved in much the same way as it did 18 h after cooling in nonadapted animals, but the level of the amplitude was higher. Changes in the CF in the 4th group also replicated the dynamics noted in the 3rd series, but were less pronounced and the CF itself was higher (Fig. 2).

It may be assumed that the course of administration of RR to intact animals was accompanied by an enhanced cardiac contractility due to the activation of the same natural protective mechanisms which are involved 18 h after cooling in myocardium recovery without RR (3rd group). Our findings suggested that RR is more likely to be a mobilizing agent than a drug expanding the biochemical and functional reserves of an organism, as was believed previously [3].

Thus, the data obtained demonstrate that acute cooling decreases myocardial contractility, which is restored over the subsequent 18 h. However, this recovery is not total, as it does not provide for stable contractility of the isolated heart during perfusion. Preventive adaptation by a course of administration of RR extract prevents the amplitude of contraction in the isolated heart from dropping immediately after acute cooling and provides for stable contraction during 60 min of perfusion. However, RR does not abolish disorders in diastolic function and results in a decrease of the CF under all experimental conditions. It may be assumed that the effect of RR on the myocardium may follow the same path as the restoration process noted in cardiac muscle after cooling.

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