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Cardioprotective effects mitochondrial ATP-sensitive potassium channel in exercise conditioning

F.-L. Peng, Y.-J. Guo, W.-B. Mo, S.-M. Xu and H.-P. Liao

Department of Physical Education, Guangxi Normal University, Guilin, Guangxi, China

Corresponding author: F.-L. Peng
E-mail: pengfl_2013@163.com

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ABSTRACT. We investigated the mitochondrial ATP-sensitive potassium channel [mito-K (ATP)] in exercise preconditioning of myocardial ischemia-reperfusion injury in rats. Eighty SD rats were randomly divided into high-, moderate-, low-intensity, and control groups. The exercise groups were divided into control and inhibited groups. The control group was divided into model and sham groups. Eight rats were randomly selected from each group for analysis. At 40 and 50 min after ischemia-reperfusion, respectively, J point and T-wave values and QT intervals were significantly higher in the control model group than in the control sham group; ECG parameters were significantly lower in the exercise group than in the control group; ECG parameters were lower in the 5-HD-inhibited group than in the corresponding exercise model group. The trends of serum enzymes (serum muscle kinase isoenzyme, lactate dehydrogenase, aspartate transaminase) were consistent with ECG parameter changes at 40 and 50 min after ischemia and reperfusion, respectively. Compared with the sham group, the control model group showed significantly decreased left ventricular systolic pressure

(LVSP) and maximum rate of left ventricular pressure development (dP/dtmax) and significantly increased left ventricular end-diastolic pressure (LVEDP). LVSP and dP/dtmax were significantly higher and LVEDP was significantly lower in the control group than in the exercise model group. LVSP and dP/dtmax were significantly lower and LVEDP was significantly higher in the inhibited group than in the corresponding exercise group. Long-term exercise can produce a preconditioning effect that exerts an ischemia-reperfusion cardioprotective effect. Mito-K (ATP) mediates the cardioprotective effects of exercise preconditioning.

Key words: Exercise preconditioning; Ischemia-reperfusion injury; Mitochondrial ATP-sensitive potassium channel; Electrocardiogram; Enzymes; Cardiac function

INTRODUCTION

Animal experiments have suggested that endurance exercise training improves cardiac ischemia-reperfusion (I/R) tolerance (Brown et al., 2005). Endurance training protected the heart from anti-I/R injury caused by oxidative stress, and protected the mitochondria from anti-I/R-induced damage (Ascensao et al., 2007). The protective effects of exercise on the heart can occur at different stages and time of ischemia (Quindry et al., 2005). These studies demonstrate that training has a preconditioning effect, but the molecular mechanisms of exercise preconditioning are not yet fully understood. Studies have found that the mitochondrial ATP-sensitive potassium channel [mito-K (ATP)] is an important factor in myocardial protection of ischemic preconditioning. However, its role in exercise preconditioning has not been elucidated, thus this study began with pre-adapted effector mito-K (ATP) to investigate the role of mito-K (ATP) in movement adaptation. We used the mito-K (ATP) blocker 5-hydroxy acid (5-HD) to block mito-K (ATP) opening to investigate the effects of mito-K (ATP) during exercise preconditioning in anti-I/R injury in rats. By analyzing the electrocardiogram (ECG), serum enzymes, and ventricular systolic and diastolic functions in I/R rats, we confirmed the effects of mito-K (ATP) in exercise preconditioning against myocardial I/R injury and describe the basis for the intracellular mechanisms of the cardioprotective effects of exercise preconditioning.

MATERIAL AND METHODS

Experimental animals and grouping

Healthy SD female rats weighing 112.6 ± 16.5 g (means ± standard deviation) were purchased from the Experimental Animal Center of Guilin Medical College. The rats were randomly divided into high-, moderate-, low-intensity exercise, and control groups: each group contained 20 rats that underwent exercise training for 8 weeks. Room temperature and humidity control were applied; the animals had free access to water and food. I/R injury models were established after the exercise training: each exercise group was randomly

divided into a model group and 5-HD-inhibited group (high-intensity model group = HM, high-intensity inhibited group = HMI, moderate-intensity model group = MM, moderate-intensity inhibited group = MMI, low-intensity model group = LM, low-intensity inhibited group = LMI). The 5-HD-inhibited groups received 5-HD (10 mg/kg) through the jugular vein 15 min before the I/R experiment. The control group was randomly divided into a control model group (CM) and control sham group (Sham).

Experimental methods

Training methods

Treadmill training lasted 8 weeks: adaptive training was performed in the first week; animals were trained 6 days a week, 60 min a day. The exercise load was developed according to the Bedford findings (Whiteley et al., 2012): high-intensity group, slope 10°, speed 26.8 m/min, which was equivalent to a maximum oxygen consumption (%) of 92.3 ± 2.8; moderate-intensity group, slope 5°, speed 15.2 m/min, which was equivalent to a maximum oxygen consumption (%) of 64.0 ± 4.5; low-intensity group, slope 0°, speed 8.2 m/min, which was equivalent to a maximum oxygen consumption (%) of 52.9 ± 3.1. The control group underwent no training, was fed regularly, and had free activity.

I/R model preparation in vivo

I/R rats were fasted 12 h before surgery; water was provided as required. Urethane (1.2 g/kg) was used for anesthesia, and anesthetized rats were secured to an animal anatomy table. The trachea was isolated, and endotracheal intubation was performed. A ventilator was used to support respiration; the heart rate was 70 beats/min, and tidal volume was 8 mL/beat. A needle electrode was inserted subcutaneously into the limbs and connected with an ECG machine. A biological signal analysis system was connected, and standard lead ECG was recorded.

Thoracotomy was performed along the second to fourth left sternal ribs. The pericardium was dissected open, and the heart and left ventricular surface vessels were exposed. The left main coronary artery was used as the reference point, and a needle was inserted 2 mm beneath the left atrial appendage root. A 5/0 ligature was inserted through the myocardial surface, and the needle emerged beside the pulmonary cone. The thread ring was set at 2 ends of the lines; this line was used as the reperfusion cycle. Tightening the ligature caused myocardial ischemia. Reperfusion would occur when the reperfusion cycle was released. After the ligature was tightened, ECG showed elevation of the ST-segment; after it was released, there was 50% decline of the ST-segment, thus successfully establishing the model, following which the chest was closed. Ischemia and reperfusion lasted 40 and 50 min, respectively. Thoracotomy and lining were performed in the Sham group without the coronary artery ligation; the other operations were the same as with the I/R rat groups. Eight rats with successful modeling were randomly selected from each group and the subsequent experiments and analysis of ECG, serum enzymes, troponin (cTn) T/I, and functional index were performed.

ECG recording

A needle-type electrode was inserted subcutaneously into the limbs; a BL-420S biological experimental system (Chengdu, China) was used for full recording with a 2-lead ECG. ST-segment (J point), Q-wave, and R-wave changes were recorded with the system before ischemia, 40 min after ischemia, and 50 min after reperfusion.

Determination of cardiac function

A carotid artery catheter was inserted into the left ventricle and connected with the external pressure receptors of the BL-420S system. Arterial blood pressure, left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP), heart rate, and maximum rate of left ventricular pressure development (dP/dtmax) were recorded.

Serum myocardial enzymes, cTn-I, and cTn-T measurement

Intraperitoneal blood was collected after I/R following natural coagulation. The blood was centrifuged at 3000 rpm for 15 min and the serum was collected. Serum muscle kinase isoenzyme (CK-MB) was determined by immune suppression method; lactate dehydrogenase (LDH) and AST/aspartate transaminase (GOT) were measured by the colorimetry method. The measurements were carried out according to the kit instructions. cTn-I and cTn-T were measured by ELISA using a microplate reader. The instruments used were a Bio-Rad.550 microplate reader (Bio-Rad company, USA), Eppendorf desktop high-speed refrigerated centrifuge (Eppendorf Company, Germany), F6124 semi-automated biochemical analyzer (Eppendorf Company), and an MDF-382E ultra-low temperature freezer (Sanyo Company, Japan).

Data analysis

SPSS 12.0 (Chicago, IL, USA) was used for single-factor analysis of variance. Data are reported as the means ± standard deviation. $P < 0.05$ and $P < 0.01$ were considered to be statistically significant.

RESULTS

ECG indicators

Figure 1 depicts the relatively stable status of the ECG parameters 40 min after ischemia and 50 min after reperfusion. Table 1 shows that the J point in the CM rats was significantly higher than that in the Sham rats at 40 min after ischemia and 50 min after reperfusion ($P < 0.01$). The J point in the exercise model rats was significantly lower than that in the CM rats 40 min after ischemia and 50 min after reperfusion ($P < 0.05$). The J point in the 5-HD-inhibited model group was lower than that in the corresponding exercise model group ($P < 0.05$).

Table 2 describes the T-wave area change in each group. The T-wave in CM rats was significantly higher than that in the Sham rats at 40 min after ischemia and 50 min after reper-

fusion ($P < 0.01$). The T-wave in each exercise model group was significantly lower than that in the CM group at 40 min after ischemia and 50 min after reperfusion ($P < 0.05$). The T-wave in the MMI group was lower than that in the MM group ($P < 0.05$).

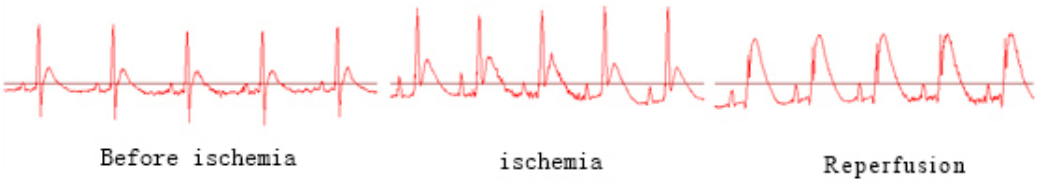

Figure 1. Modeling in rat ECG schematic.

Table 1. Rats of ECG ST (J point) Change (mv).

Category	N	Ischemia 0 min	Ischemia 40 min	Reperfusion 50 min
Sham	8	0.108 ± 0.036	0.110 ± 0.042	0.119 ± 0.045
CM	8	0.107 ± 0.042	0.351 ± 0.056**	0.323 ± 0.047**
LM	8	0.109 ± 0.051	0.242 ± 0.016▲	0.238 ± 0.043▲
LMI	8	0.107 ± 0.036	0.281 ± 0.027#	0.290 ± 0.049#
MM	8	0.109 ± 0.052	0.231 ± 0.041▲	0.227 ± 0.051▲
MMI	8	0.110 ± 0.045	0.274 ± 0.061#	0.271 ± 0.037#
HM	8	0.109 ± 0.043	0.239 ± 0.029▲	0.233 ± 0.045▲
HMI	8	0.110 ± 0.048	0.292 ± 0.034#	0.288 ± 0.029#

Compared with sham group, **$P < 0.01$; compared with the control model group, ▲$P < 0.05$; inhibited group with the corresponding motion model group, #$P < 0.05$.

Table 2. ECG T-wave area change in each group (mV · ms).

Category	N	Before ischemia	Ischemia 40 min	Reperfusion 50 min
Sham	8	27.9 ± 9.4	28.3 ± 9.7	29.4 ± 8.9
CM	8	28.3 ± 8.7	47.1 ± 9.6**	46.6 ± 9.8**
LM	8	28.4 ± 10.1	43.4 ± 9.8▲	38.1 ± 8.7▲
LMI	8	28.1 ± 9.9	44.7 ± 9.4	42.1 ± 9.6
MM	8	27.7 ± 7.6	42.8 ± 8.8▲	39.8 ± 9.1▲
MMI	8	28.5 ± 8.5	46.4 ± 10.2#	44.3 ± 9.9#
HM	8	29.1 ± 9.8	42.3 ± 10.1▲	40.7 ± 11▲
HMI	8	29.1 ± 9.1	44.2 ± 8.4	42.8 ± 8.7

Compared with sham group, **$P < 0.01$; compared with the control model group, ▲$P < 0.05$; inhibited group with the corresponding motion model group, #$P < 0.05$.

Table 3 lists the QT interval change in each group. The QT interval in the CM rats was significantly higher than that in the Sham rats at 40 min after ischemia and 50 min after reperfusion ($P < 0.05$ or $P < 0.01$). The QT interval in each exercise model group was significantly lower than that in the CM group at 40 min after ischemia and 50 min after reperfusion ($P < 0.05$ or $P < 0.01$). The QT intervals in the LMI and MMI groups were higher than that in the corresponding exercise groups ($P < 0.05$).

Serum myocardial enzymes, cTn-I, and cTn-T changes

Table 4 shows that at 40 min after ischemia and 50 min after reperfusion CK-MB,

LDH, and GOT activity in the CM group was significantly higher than that in the Sham group ($P < 0.01$). The CK-MB, LDH, and GOT activity in the exercise groups was significantly lower than that in the CM group ($P < 0.05$ or $P < 0.01$). Serum CK-MB and LDH activity in the LMI and HMI groups was significantly lower than that in the corresponding exercise groups ($P < 0.05$ or $P < 0.01$). Serum CK-MB and LDH activity in the MMI group was significantly lower than that in the corresponding exercise group ($P < 0.05$ or $P < 0.01$). Serum cTn-I and cTn-T levels in the CM group were significantly higher than those in the Sham group ($P < 0.01$). Serum cTn-I and cTn-T levels in the exercise groups were lower than those in the CM group ($P < 0.05$ or $P < 0.01$). Serum cTn-I levels in the 5-HD-inhibited groups were significantly lower than those in the corresponding exercise groups ($P < 0.01$). The same was true of the serum cTn-T levels in the 5-HD-inhibited groups ($P < 0.05$).

Table 3. ECG Q-T interval change in each group (ms).

Category	N	Before ischemia	Ischemia 40 min	Reperfusion 50 min
Sham	8	86 ± 8	88 ±12	89 ± 13
CM	8	88 ± 7	111 ± 14**	102 ± 13*
LM	8	85 ± 7	92 ± 8▲	94 ± 11▲
LMI	8	86 ± 10	97 ± 9#	101 ± 11#
MM	8	86 ± 9	90 ± 7▲▲	92 ± 11▲
MMI	8	86 ± 8	94 ± 9#	95 ± 10#
HM	8	86 ± 7	91 ± 8▲	96 ± 7▲
HMI	8	87 ± 8	93 ± 10	96 ± 11

Compared with sham group, *$P < 0.05$, **$P < 0.01$; compared with the control model group, ▲$P < 0.05$, ▲▲$P < 0.01$; inhibited group with the corresponding motion model group, #$P < 0.05$.

Table 4. Serum enzyme levels.

Category	N	CK-MB (U/L)	LDH (U/L)	GOT (U/mL)	cTn-I	cTn-T
Sham	8	291.34 ± 34.11	6910.78 ± 231.12	7.12 ± 1.89	0.11 ± 0.02	0.02 ± 0.00
CM	8	911.45 ± 45.62**	8768.23 ± 451.54**	13.55 ± 2.31**	2.63 ± 0.73**	1.26 ± 0.33**
LM	8	490.37 ± 37.87▲▲	7543.75 ± 452.95▲	10.22 ± 1.54▲	1.56 ± 0.32▲▲	0.89 ± 0.20▲▲
LMI	8	621.45 ± 54.91#	8429.16 ± 553.13#	11.26 ± 3.05	2.24 ± 0.54##	1.03 ± 0.24#
MM	8	377.59 ± 61.23▲▲	7314.92 ± 389.12▲	9.88 ± 1.99▲▲	1.09 ± 0.28▲▲	0.77 ± 0.26▲▲
MMI	8	611.52 ± 53.89##	8265.56 ± 523.34#	10.36 ± 2.22#	2.07 ± 0.61##	0.94 ± 0.31#
HM	8	389.45 ± 57.23▲▲	7492.25 ± 414.24▲	10.11 ± 1.89▲	1.76 ± 0.38▲	1.05 ± 0.34▲
HMI	8	632.47 ± 45.09##	8475.56 ± 471.63#	11.44 ± 2.25	2.52 ± 0.53##	1.21 ± 0.35#

Compared with sham group, **$P < 0.01$; compared with the control model group, ▲$P < 0.05$, ▲▲$P < 0.01$; inhibited group with the corresponding motion model group, #$P < 0.05$, ##$P < 0.01$.

Cardiac function index

As shown in Table 5, at 40 min after ischemia and 50 min after reperfusion, the LVSP and dP/dtmax was significantly decreased and the LVEDP significantly increased in the CM group as compared with the Sham group ($P < 0.01$ or $P < 0.05$). At 40 min after ischemia and 50 min after reperfusion, the LVSP and dP/dtmax were significantly higher and the LVEDP significantly lower in the exercise groups than in the CM group. Compared with each exercise group, at 40 min after ischemia and 50 min after reperfusion, the LVSP and dP/dtmax in the corresponding inhibited groups were significantly lower, and the LVEDP was significantly higher ($P < 0.01$ or $P < 0.05$).

Table 5. Rats in each group changes in blood pressure and heart function.

Category	N	+dp/dtmax (mmHg/ms)		-dp/dtmax (mmHg/ms)		LVSSP (mmHg)		LVEDP (mmHg)	
		Ischemia 40 min	Reperfusion 50 min	Ischemia 40 min	Reperfusion 50 min	Ischemia 40 min	Reperfusion 50 min	Ischemia 40 min	Reperfusion 50 min
Sham	8	4.56 ± 0.94	4.33 ± 0.78	3.48 ± 0.67	3.46 ± 0.70	128.22 ± 8.79	128.98 ± 9.45	5.13 ± 2.91	5.28 ± 5.65
CM	8	2.43 ± 1.12**	2.54 ± 0.87**	2.02 ± 0.56*	2.06 ± 0.47*	103.45 ± 8.89**	95.15 ± 10.21**	11.88 ± 3.22**	13.65 ± 7.28**
LM	8	4.21 ± 1.44▲	4.64 ± 1.66▲	4.10 ± 0.78▲▲	3.81 ± 0.62▲▲	118.66 ± 8.75▲	114.22 ± 9.01▲	6.74 ± 2.33▲▲	6.79 ± 2.83▲▲
LMI	8	3.11 ± 1.65#	2.77 ± 1.03#	3.07 ± 0.69#	2.66 ± 0.69#	111.35 ± 9.64#	109.54 ± 10.13#	9.05 ± 2.64#	11.38 ± 4.18#
MM	8	5.48 ± 1.94▲▲	5.33 ± 1.88▲▲	4.78 ± 1.33▲▲	4.44 ± 1.45▲▲	122.75 ± 10.33▲▲	118.22 ± 9.66▲▲	4.04 ± 2.07▲▲	4.69 ± 2.05▲▲
MMI	8	3.67 ± 1.46#	3.23 ± 1.23##	3.66 ± 1.41#	3.04 ± 1.19##	111.36 ± 10.73##	108.46 ± 9.81##	7.29 ± 2.55##	8.68 ± 3.03##
HM	8	5.23 ± 1.58▲▲	5.02 ± 1.35▲▲	4.64 ± 0.67▲▲	4.23 ± 0.58▲▲	119.29 ± 9.77▲	116.68 ± 10.36▲▲	5.07 ± 2.06▲▲	6.11 ± 2.05▲▲
HMI	8	3.33 ± 1.75#	3.08 ± 1.15#	3.24 ± 0.74#	2.83 ± 0.75##	112.63 ± 9.95#	109.42 ± 9.66##	9.77 ± 2.52##	a10.41 ± 3.03##

Compared with sham group, *P < 0.05, **P < 0.01; compared with the control model group, ▲P < 0.05, ▲▲P < 0.01; boycott group with the corresponding motion model group, #P < 0.05, ##P < 0.01.

DISCUSSION

Myocardial I/R injury

Clinical studies and animal studies have demonstrated that ECG abnormalities occur in myocardial I/R damage: myocardial enzymes and cardiac cTn complex are released into the bloodstream, causing these substances to become concentrated in the blood within a certain time. CK-MB and cTn have high specificity and sensitivity in the myocardium. Changes in serum myocardial enzyme and cTn levels can reflect the extent of myocardial damage more accurately, especially cTn, which has become the gold standard for diagnosis of myocardial injury (Thygesen et al., 2007; Whiteley et al., 2012). At 40 min after ischemia and 50 min after reperfusion, the ST-segment, T-wave value, and QT interval in the CM group were significantly higher than that in the sham group. The levels of cTn-I, cTn-T, and myocardial enzymes (CK-MB, LDH, GOT) in CM rats were significantly higher than those in sham rats, indicating successful creation of the I/R injury model.

The main causes of myocardial I/R injury include intracellular acidosis, Ca^{2+} overload, and increased oxygen free radicals. The myocardial I/R process causes a decrease in cytosolic pH, which can decrease sarcoplasmic reticulum Ca^{2+}-ATPase activity. Following the decrease in sensitivity toward Ca^{2+} activation, the number of active calcium pumps also decreases. The pH decrease can also decrease the speed of formation and deformation of intermediate high-energy phosphate in the sarcoplasmic reticulum, which will inhibit the calcium uptake rate and lead to Ca^{2+} overload. The excess Ca^{2+} activates the calcium-dependent proteases and phospholipases, and destroys the structural integrity of the biofilm. In the membrane phospholipid decomposition process, lysophospholipids are generated and brought into the mitochondria to inhibit ATP synthesis. A large amount of Ca^{2+} enters the mitochondria in the form of calcium phosphate deposition, thereby damaging the oxidative phosphorylation of the mitochondria. Ca^{2+} overload can aggravate acidosis. H^+ can be released during the binding process of Ca^{2+} and phosphate in the mitochondria. Meanwhile, calcium overload can also activate ATP enzymes to decompose ATP, and H^+ is released during the ATP decomposition process. As the increase in H^+ can promote acidosis, it thereby increases reperfusion injury (Anzawa et al., 2012).

As electron transfer in the mitochondrial respiratory chain is disordered during myocardial ischemia, large amounts of oxygen free radicals are generated. In reperfusion, coen-

zyme IV (NADH), which accumulates during ischemia, is provided sufficient oxygen, thus producing large amounts of oxygen free radicals (Ahmed et al., 2012). These free radicals have high chemical activity that can damage membrane lipid composition. Cell membranes undergo lipid peroxidation, which changes the lipid microenvironment of the membrane receptors, membrane proteases, and membrane ion channels, altering their functions. The mitochondrial membrane undergoes lipid peroxidation, or lipid peroxides that form in the cell affect the mitochondrial membrane. Thus, the liquid and mobility changes to the latter lead to its dysfunction, and ATP production is decreased while that of free radicals is increased (Guo et al., 2012). The lysosomal membrane undergoes lipid peroxidation, following which permeability is increased, plasmin release is induced, and destruction of the cell structure and surrounding tissue follows. Free radicals attack proteins and enzymes. Under the action of free radicals, cytoplasmic and membrane proteins and the molecules of certain enzymes are cross-linked and polymerized, and the peptide bonds are broken, damaging the proteins and enzyme structures and causing loss of activity (Heusch and Schulz, 2011). Changes in the lipid membrane microenvironment also affect the function of membrane proteins and enzymes, such as Na^+-K^+-ATP enzyme inactivation, increasing Na^+ influx. Na^+-Ca^{2+} exchange is enhanced, leading to intracellular Ca^{2+} overload (An et al., 2001). In I/R, microsomal and plasma membrane lipoxygenase and cyclooxygenase are activated. It also catalyzes arachidonic acid metabolism, increasing free radicals and lipid peroxidation while forming highly reactive substances such as prostaglandins, thromboxanes, and leukotrienes (Takahashi et al., 2004). Free radicals can damage DNA and chromosomes and cause nucleic acid base changes, DNA breaks, and chromosome aberrations; 80% of these changes are caused by oxygen free radicals (OH•). OH• can easily react with and alter deoxyribose and bases. Subsequently, it can destroy the intercellular matrix. Oxygen free radicals can degrade hyaluronic acid and cross-link collagen to detach stromal cells, decreasing elasticity (Valko et al., 2004).

Exercise preconditioning and myocardial protection

During the I/R process, myocardial cells are damaged, cell membrane integrity and permeability changed, and intracellular substances leak into the peripheral blood circulation. These substances, which can be detected in the circulation, are known as markers of myocardial injury. Serum cTn, CK-MB, LDH, and AST are commonly used laboratory enzymatic indicators to detect myocardial injury (O'Brien, 2008). cTn and CK-MB have the highest degree of cardiac specificity, making their detection the gold standard in clinical diagnosis of myocardial injury (Thygesen et al., 2007; Jamshidi et al., 2012; Whiteley et al., 2012). Therefore, we examined serum enzymes, cTn-I, and cTn-T changes in myocardial I/R to verify the extent of myocardial injury. ECG monitoring was carried out simultaneously to collect evidence from the electrophysiological aspect. To investigate mito-K (ATP) following exercise preconditioning of myocardial I/R injury in rats, exercise groups were further divided into control model and 5-HT-inhibited model groups. Following I/R, serum myocardial enzymes and cTn were detected. Serum CK-MB, LDH, and GOT activity, cTn-I, and cTn-T in the exercise model groups were significantly lower than that in the CM group. At 40 min after ischemia and 50 min after reperfusion, the J point, T-wave, and QT interval values in the exercise groups were significantly lower than that of the CM group, indicating that high- and low-intensity training can produce myocardial protection. Serum CK-MB, LDH, and GOT

activity, cTn-I, and cTn-T concentration in the 5-HD-inhibited groups were significantly lower than that in the corresponding exercise model groups. At 40 min after ischemia and 50 min after reperfusion, the J point, T-wave, and QT interval values in the 5-HD-inhibited groups were significantly lower than that in the corresponding exercise model groups. It indicated that the mito-K (ATP) inhibitor 5-HD could effectively cancel exercise-induced myocardial protection, albeit partially, suggesting that the mito-K (ATP) may mediate the cardioprotective effects of exercise. The mechanism of exercise preconditioning-induced cardioprotective effects was not clear; exercise may induce a series of endogenous protective mechanisms. It is also possible that myocardial morphology adaptive changes caused by exercise increased the myocardial ischemic tolerance. Our results showed that mito-K (ATP) was an effector of preconditioning functions, playing a role in the myocardial protective effects of exercise preconditioning.

Exercise preconditioning and left ventricular function

Cardiac function depends on the ventricular systolic and diastolic functions. Various hemodynamic indicators can reflect cardiac function. LVSP and dP/dtmax reflect the chamber systolic function and LVEDP and -dP/dtmax reflect left ventricular diastolic function. LVSP primarily reflects myocardial contractility, and LVEDP reflects left ventricular preload and indirectly reflects ventricular diastolic compliance. The dP/dtmax reflects the pace changes in wall tension to some extent; it is greatly affected by cardiac preload and afterload reflecting the systolic and diastolic myocardial contractile functions, respectively (Jamshidi et al., 2012). Changes to cardiac functional status are the main manifestations in myocardial I/R injury, the specific manifestations being cardiac function recovery that is inconsistent with or worse than the restoration of blood flow after reperfusion (Qi et al., 2011). The LVSP and dP/dtmax were significantly decreased and the LVEDP significantly increased after myocardial I/R in rats, indicating that I/R caused the decline in cardiac function. The LVSP and dP/dtmax were significantly higher in the high- and low-intensity training groups as compared with that in the I/R model group. The LVEDP in the exercise groups was significantly lower than that in the I/R model group, suggesting that exercise can protect I/R cardiac function. Comparing the myocardial systolic and diastolic functions in the 5-HD-inhibited group and the exercise model groups, we found that the LVSP and dP/dtmax in the 5-HD-inhibited group was significantly lower than that in the exercise model group. The LVEDP was significantly higher than that in the exercise model group, suggesting that 5-HD partially cancelled the I/R cardiac function protection conferred by exercise. The mito-K (ATP) may be an important target of exercise preconditioning for cardioprotective effects. Further research of the specific mechanisms of mito-K (ATP) in exercise preconditioning is required.

CONCLUSION

Endurance exercise of different intensities can produce preconditioning cardioprotective effects. Whether different exercise training intensities confer myocardial protection through the same mechanisms has not been determined. The mito-K (ATP) played a mediating role in the cardioprotective effects of exercise training of different intensities. The specific mechanisms involved require further experimental study.

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