GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

A Preliminary Course of Transauricular Electrostimulation Mitigates Impairment of Cardiac Contractile Function in Rats with Myocardial Infarction

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A course of transauricular electrostimulation (TES) consisting of 10 sessions was administered to rats before the induction of myocardial infarction by Selye's method and to rats that were left intact. In the latter animals, the electrostimulation did not influence cardiac contractile function at rest (as judged by heart rate, developed pressure, and Katz's index), but exerted beneficial chronotropic and inotropic effects during the maximum isometric tension produced by compression of the ascending aorta. In the TES-pretreated rats with a 2-day-old myocardial infarct, cardiac contractile function was depressed significantly less, both at rest and during isometric tension, than in infarcted rats not exposed to TES.

Key Words: *transauricular electroacupuncture; myocardial infarction; cardiac contractile function; cardiac rhythm*

It has been demonstrated in animal experiments that transauricular electrostimulation (TES), which is widely used in physiotherapy, renders the heart more resistant to various injurious factors. For example, TES has been reported to prevent disturbances of cardiac electrical stability under stress [4] and during ischemia and reperfusion [8], to diminish the size of necrotic areas resulting from ischemia [5], and to increase the body's tolerance for hypoxia [6]. However, the question of whether preliminary TES can be useful as a method of preventing cardiac disorders in animals with experimentally induced myocardial infarction has not been addressed. The present study was undertaken to evaluate how preliminary TES would influence the disturbances of cardiac contractile function caused by myocardial infarction.

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MATERIALS AND METHODS

The study was conducted on four groups of male Wistar rats (body weight around 250 g). Group 1 comprised control rats which had undergone all steps of the operation producing myocardial infarction by Selye's method with the exception of coronary artery ligation (n=9). Group 2 consisted of nonoperated rats subjected to TES (n=11), group 3 of rats with a 2-day-old myocardial infarct (n=11), and group 4 of rats that had undergone a course of TES before myocardial infarction was produced (n=10). TES was carried out with solitary sharp pulses (amplitude 1.5-2 mA, duration 1.5 msec, frequency 200 pulses per minute) delivered by a Lasper CS-504 electrostimulator (Japan) designed for electroacupuncture in hu-

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mans. Needle electrodes were inserted into both auricular conchae near the external acoustic meatus. During such TES, current densities in the skin and subcutaneous layer had a mean value of 1 mA/cm^2 near the electrodes and dropped sharply with increasing distance from these to reach 0.143 mA/cm^2 on the midline. The highest and lower current densities recorded for the cortex and subcortex were 0.386 and 0.057 mA/cm^2, respectively. The electrostimulation was therefore both transauricular and transcranial, and its effects were determined, apart from a reflex action, by the weak electric currents passing through the brain. The TES course consisted of 10 sessions, the first of which lasted 10 min and the other nine 20 min each.

Acute tests were performed in rats with open chest under urethane anesthesia (160 mg/kg) and artificial ventilation. Cardiac contractile function was assessed by the pressure curve obtained for the left ventricle. Ventricular pressure was recorded with a Mingograph-34 apparatus (Siemens-Elema) under conditions of relative physiological rest and during the maximum isometric tension produced by compressing the ascending aorta for 2 min. The following parameters were measured: heart rate; systolic, diastolic, and developed pressure; rates of pressure rise and fall (which reflect the rates of myocardial contraction and relaxation, respectively); and Katz's index, which is the product of the heart rate times the pressure developed. The tests were carried out 2 days after the onset of myocardial infarction on animals with transmural infarcts identified visually and by observing the Q wave on the ECG in lead I (this wave was at least 0.15 mV).

The results were subjected to statistical analysis using the Student and nonparametric Wilcoxon-Mann-Whitney tests.

RESULTS

Data on cardiac contractile function before and during the maximum isometric tension are summarized in Table 1. We see that TES did not have a significant impact on cardiac function in the nonoperated rats (group 2) under conditions of physiological rest, but did render the heart more resistant to the additional load imposed by aortic compression. After 30 sec of compression, the heart rate in this group significantly exceeded the control level by 38 beats/min and the developed pressure was somewhat higher so that Katz's index, which is an integral indicator of cardiac contractile function, was 26.6% higher. The course of TES also led to increased myocardial contraction and relaxation rates in group 2, which were significantly higher than in the control group (by

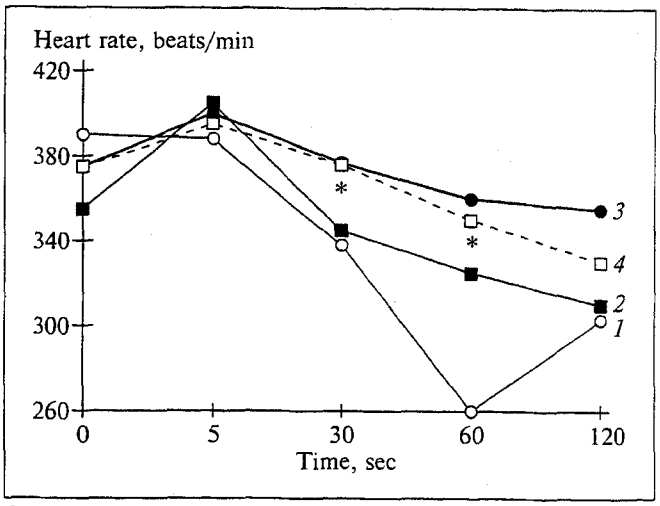

Fig. 1. Effect of preliminary exposure to TES (10 sessions) on the heart rate during the maximum isometric tension caused by compression of the ascending aorta in intact rats and rats with myocardial infarction. Curves *1*, *2*, *3*, and *4* correspond to the four study groups. The asterisk denotes a significant difference between groups 1 and 2 at $p<0.05$ by the Wilcoxon–Mann–Whitney test.

25.8% and 46.8%, respectively). TES thus exerted beneficial inotropic and chronotropic effects on the heart during the period of maximum isometric tension.

In the rats with myocardial infarction pre-exposed to TES (group 4), the depression of cardiac contractile function in the state of relative physiological rest was significantly less than in the unexposed animals with infarction (group 3). Indeed, as shown in the table, group 4 had significantly higher values of developed pressure and heart rate (by 25.6% and 7.9%, respectively), with a resultant 36.1% increase in Katz's index over its value in group 3. TES also considerably increased the infarcted heart's ability to withstand isometric tension, as is evidenced by the significantly higher values of Katz's index at 30 and 120 sec of aortic compression in group 4 (by 24.4% and 36.5%, respectively). This greatly enhanced cardiac resistance to a severe additional load in TES-exposed rats resulted from their tendency to maintain increased heart rates and left ventricular pressures. These rats also exhibited significantly higher myocardial relaxation rates at 30 and 120 sec of aortic compression as compared to their unexposed counterparts, the difference between these groups being 27.2% at 30 sec and 61.2% at 120 sec. On the other hand, the diastolic pressure rose to similar extents by 30 sec of aortic compression in the two groups - from 1.7±1.6 to 35±3.4 mm Hg in group 3 and from 1.6±0.8 to 32±5.5 mm Hg in group 4.

The data presented in Table 1 illustrate two important features of TES action on both intact and infarcted hearts. First, this stimulation produces a beneficial chronotropic effect by maintaining the heart rate at an elevated level during isometric tension. Thus, as shown in Fig. 1, exposure to TES led

TABLE 1. Impact of Preliminary Exposure to TES (10 Sessions) on Left Ventricular Contractility in Rats with Myocardial Infarction

Parameter	Group	Before aortic compression	During aortic compression	
			for 30 sec	for 120 sec
Heart rate, beats/min	1	390±12	337±14	304±24
	2	376±14	375±13*	331±11
	3	354±8	345±15	308±16
	4	382±7**	377±12	354±20
Developed pressure, mm Hg	1	106±6.6	156±7.6	151±8.0
	2	105±6.7	171±6.2	147±13.1
	3	78±1.6	152±7.6	123±14.5
	4	98±6.2**	174±8.8	130±4.6
Katz's index, mm Hg×beats/min	1	48 018±3 275	50 115±4 017	47 872±1 008
	2	44 698±7 093	63 311±3 160*	48 468±4 800
	3	28 289±1 425	51 600±3 300	36 466±3 840
	4	37 106±2 304**	64 217±4 767**	49 794±4 457**
Highest contraction rate, mm Hg/sec	1	8 200±1 300	6 731±489	5 560±520
	2	7 463±768	8 467±644*	7 560±1 600
	3	6 418±455	5 964±364	4 840±660
	4	6 150±950	6 400±760	5 533±733
Highest relaxation rate, mm Hg/sec	1	3 433±375	2 188±250	2 460±280
	2	3 745±335	3 164±400*	3 014±471
	3	2 718±364	1 840±100	1 911±177
	4	3 367±267	2 340±220	3 080±320**

Note. *$p<0.05$ in comparison with group 1 by Student's test; **$p<0.001$ in comparison with group 3 by Student's test; +$p<0.05$ in comparison with group 1 by the Wilcoxon–Mann–Whitney test.

to markedly higher heart rates during the entire period of aortic compression in the intact rats (group 2) and starting at 30 sec of compression in rats with myocardial infarction (group 4) as compared to group 1 and group 3 rats, respectively. These data, which indicate that TES is able to inhibit the bradycardia that usually develops during isometric tension, were found to be statistically significant according to the Wilcoxon-Mann-Whitney test. Another important feature of TES is that this experimental physiological procedure largely prevents the fall in myocardial relaxation rate during the period of isometric tension.

In general, the results of the present study indicate that the disturbances of cardiac contractile function occurring in such a grave condition as myocardial infarction can be considerably mitigated by means of repetitive TES. In analyzing the mechanisms of this phenomenon, we should bear in mind that an important component of the overall ischemic damage to the heart is the damage caused by stress, and that a course of TES adapts the heart to stress and activates the stress-limiting systems. Hence, one way by which repetitive TES can protect the heart of animals with myocardial infarction is probably elimination of the stress-related component of the damage. This effect is most likely to be brought about by the following mechanisms: first, through activation of the opioidergic system, as is evidenced by the elevated plasma levels of β-endorphin after a course of TES [7], which limits the myocardial damage due to the excessive adrenergic stimulation accompanying acute myocardial infarction; second, through a reduction of myocardial sensitivity to epinephrine in toxic concentrations [8]; and third, through stabilization of cell membranes, as is indicated by the finding, in a study on isolated hearts, that repeated TES augments myocardial resistance to excess calcium, which is known to play an important part in impairing the functioning of cardiac muscle cells. Finally, the adaptation to TES increases the body's resistance to hypoxia [6] and, consequently, to the myocardial ischemia caused by narrowing of the coronary arteries or compression of the aorta.

The diminished bradycardia observed after TES requires separate consideration. The bradycardia developing while the aorta is compressed is mainly due to activation of the vagus nerve [1]. Adaptation to stress, as shown earlier, makes the heart more resistant to the inhibitory action of this nerve, apparently due to a decreased choline responsiveness [3] of the myocardium and its less severe stress-induced damage. These factors probably contribute to the diminished vagal bradycardia after a course of TES. A role in limiting the bradycardia may also be played by the opioidergic system, which is activated after TES and whose modulating influences have been shown to limit not only adrenergic [2] but also cholinergic [9,10] activation. However, more research is needed to clarify the mechanisms of cardiac protection afforded by TES in myocardial infarction.

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Effects of Adaptation to Intermittent Hypoxia on Oxidative Phosphorylation in Brain Mitochondria of Rats with Different Sensitivities toward Oxygen Deficiency

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After long-term adaptation to intermittent hypoxia, rats with an initially low resistance to acute oxygen deficiency were 2 to 4 times more resistant to it, while highly resistant rats did not show a significant change in resistance. The adaptation was accompanied by weakening of the electron-transporting function of the respiratory chain and increasing efficiency of oxidative phosphorylation in the brain mitochondria oxidizing NAD-dependent substrates, indicating that energy was produced in a more economical way. The succinate oxidase pathway of oxidation was found to be utilized to only a limited extent as a compensatory mechanism in animals exposed to intermittent hypoxia over a prolonged period. The effects of adaptation were more marked in the brain mitochondria of rats initially highly sensitive to oxygen deficiency.

Key Words: *adaptation; intermittent hypoxia; individual resistance; brain mitochondria; oxidative phosphorylation; NADH-oxidase oxidation; succinate-oxidase oxidation*

In an earlier study we demonstrated, for the first time, differences in the work of the brain's mitochondrial respiratory chain between rats differing in susceptibility to acute hypoxia [6]. In the brain of rats with low resistance to hypoxia (LR rats) as compared to the brain of highly resistant (HR) rats, energy production in the mitochondria oxidizing NAD-dependent substrates was found to be less economical and the succinate oxidase pathway to be utilized to a greater extent as a compensatory mechanism during acute hypoxia. The question of how long-term (LT) adaptation to hypoxia influences the energy-synthesizing function of cells remains open. The available information is contradictory. According to Ozawa *et al.* [11], brain mitochondria are more sensitive to hypoxia than liver or heart mitochondria and exhibit reduced respiratory control and lowered efficiency of aerobic energy production as a result of LT adaptation to hypoxia. Other authors, however, failed

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