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CARDIOVASCULAR, METABOLIC AND PLASMA CATECHOLAMINE RESPONSES TO PASSIVE AND ACTIVE EXERCISES

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Eight healthy male volunteers (aged 19.6±3.0 years) were submitted to the unloaded active (AE) and passive (PE) cycling exercise-tests performed on an adapted cycle ergometer at a pedalling rate of 50 rpm. Intensity of active exercise was about 10% of VO_2 max. In the PE exercise test the ergometer was moved electrically. During both tests the systolic time intervals (STI), stroke volume (SV), heart rate (HR), blood pressure (BP), oxygen uptake (VO_2), rating of perceived exertion (RPE), electrical muscle activity (EMG), plasma adrenaline (A), noradrenaline (NE) and blood lactate (LA) concentrations were measured. Exercise induced changes in VO_2, RPE and EMG were significantly higher during AE than PE. Shortening of the pre-ejection period (PEP) and diminishing of the PEP to ejection time (ET) ratio were similar in both types of exercise, whereas HR increased only during AE. A significant increase in cardiac output ($p<0.01$) resulted from increased SV ($p<0.01$) during PE and from increased HR ($p<0.01$) during AE. MAP increased only during PE and it was higher than at rest and during AE ($p<0.01$). Absence of changes in SV and MAP during AE may be considered as a secondary effect of the decrease in TPR. Plasma catecholamines did not increase above resting values in either type of exercise. Blood LA concentration increased during both PE and AE but it reached higher values ($p<0.01$) after the latter test. The present data suggest that the inotropic state depends on the mechanoreflexes originated in skeletal muscles. However, contribution of changes in preload to shortening of PEP can not be excluded.

Key words: *Central command, mechanoreflexes, passive exercise, systolic time intervals, heart rate, blood pressure, stroke volume*

INTRODUCTION

It is commonly accepted that there are two separate mechanisms of neural control of circulation during exercise: the central command and the reflex mechanisms (1, 2). Central command is a feed-forward neural system

functioning in parallel with the system controlling locomotor activity. The command signals from the locomotor brain areas are capable to establish the hemodynamic response to exercise by causing changes in the level of efferent activity of the parasympathetic and sympathetic nervous system to the heart and blood vessels. The reflex mechanisms include afferents from arterial and cardiopulmonary receptors, baroreceptors as well as afferents from contracting skeletal muscles activated by chemical (metaboreceptors) and mechanical stimuli (3—5). *Nucleus tractus solitarius* and the ventrolateral medulla may serve as an integrating sites as they receive neural information from the working muscles as well as from higher brain centers.

In human subjects, the evidence that muscle mechanoreceptors are involved in the control of cardiovascular adjustment to exercise is less plentiful than is the evidence that the central command and metabolic receptors stimulated by the products of muscle metabolism are responsible for circulatory response. Williamson *et al.* (6), Strange *et al.* (7) and Fernandes *et al.* (8) reported that activation of the muscle mechanoreceptors can induce a reflex increase in blood pressure during dynamic exercise. Hollander and Bouman (9) as well as Nobrega and Araujo (10) and Williamson *et al.* (11) concluded that independent activation of mechanoreceptors can promote acceleration of heart rate (HR) at the onset of dynamic exercise. They suggested that the redundant interaction exists between the central command and peripheral mechanisms for the fast HR response at the onset of dynamic exercise. Nobrega *et al.* (12) used passive cycling movement to separate the effect of the reflex mechanism from the central command. The same authors found that the passive cycling movement elicits an increase in stroke volume (SV) and mean arterial pressure (MAP) not occurring during the active unloaded cycling. It was concluded that an elevation of SV may be induced by an increase in venous return from the passively moved lower limbs or by a reflex from muscle mechanoreceptors evoking an increase in myocardial contractility. However, the results obtained by Nurhayati and Boutcher (13) differ from the findings of Nobrega *et al.* (12). These authors found a significant increase in HR with minor changes in SV during passive cycling and suggested that muscle mechanoreceptors largely participate in chronotropic response of heart to dynamic exercise.

The present study was designed to obtain more information on the changes in human left ventricular function and myocardial inotropic state during passive and active exercise. Myocardial effects were assessed by measuring the systolic time intervals (STI) that respond sensitively to exercise and reflect the left ventricular function. In addition, changes in SV, arterial blood pressure (BP), oxygen uptake, and active

muscle electrical activity as well blood lactate concentration (LA) and plasma catecholamine levels were compared during passive and active leg cycling.

MATERIAL AND METHODS

Eight healthy, male students participated in this study. The subjects gave their informed consent to participate in this study. The research procedure was approved by the Local Ethics Committee. The physical characteristics (mean $\pm$ SD) of the subjects were: age = 19.6 $\pm$ 3.0 years, weight = 72.2 $\pm$ 3.2 kg, and height = 177.6 $\pm$ 6.3 cm.

The subjects visited the laboratory three times with one week intervals between the tests. In the first occasion, they became familiarized with the experimental protocol, which consisted of two 5-min exercise-tests performed on an adapted cycle ergometer at a pedalling rate of 50 rpm^{-1}. In the first exercise test the ergometer was moved electrically (passive exercise, PE), and then after 40 min of a resting period the subjects performed 5-min active exercise (AE) without any load. Identical procedure was repeated after one and two weeks to check repeatibility of results. All the tests were carried out at the same time of a day under similar environmental conditions (25—26°C and 50—60 % humidity).

Indices of cardiac functions were recorded continuously before and during exercise tests by the Impedance Cardiography (ICG) technique using the hemodynamic ambulatory monitoring device designed in this Laboratory (14). The measurement is based on the tetrapolar technique: the sinusoidal alternating current (95 kHz) is applied *via* the pair of electrodes placed on the chest, the voltage signal is collected from other electrodes and demodulated. The ECG and the first derivate of the impedance signal are sampled at the rate of 200Hz. The system allows for the off-line, beat-to-beat automatic evaluation of stroke volume (SV), ejection time (ET), pre-ejection period (PEP) and heart rate (HR). Cardiac output (CO) was calculated as a product of the SV and HR. The detailed description of the program for automatic determination of SV and other hemodynamic parameters was previously described (15) and verified in various physiological tests (16—18). For an analysis of ET and total electromechanical systole (QS_2) values, regression lines of ET and QS_2 vs HR were calculated. A standard HR (90 beats $\cdot$ min^{-1}) was chosen to compare the corresponding ET and QS_2 values between the tests.

Blood pressure (BP) was measured before and at the last minute of each exercise using the auscultation method. The total peripheral resistance (TPR) was calculated from the CO and MAP values.

In all tests the electrical activity (EMG) of the rectus femoris, biceps femoris, tibialis anterior and gastrocnemius muscles was simultaneously recorded using EM-10 RI EMG analyzer (mega Electronics LTD., Kuopio, Finland). For this purpose the monopolar technique was used with surface electrodes attached over the muscle bellies after careful cleaning of the skin. The analyzer fully rectifies and integrates the 20—500 Hz band and gives a root mean square of row EMG signals (rms-EMG). The EMG signals were processed with a time constant of 120 ms (19).

Oxygen uptake (VO_2) was measured continuously and computed every 30 s with a cardiopulmonary exercise system CPX (MedGraphics TM, USA).

Before and at the end of each exercise blood samples were taken from the antecubital vein through the previously inserted catheter for determination of blood lactate (LA) and the plasma adrenaline (A) and noradrenaline (NA) concentrations. Blood lactate concentration was determined using commercial kits (Boehringer, Mannheim, Germany). The plasma

catecholamine concentrations were measured by the radio-enzymatic method of Da Prada & Zurcher (20) with kits purchased from Chemapol Co. Ltd. (Czech Republic). The analytical error of this method is 10.8% for adrenaline and 8.7% for noradrenaline concentrations.

Rating of perceived exertion (RPE) was recorded at the end of each exercise using the Borg Scale (21).

Statistics

The data are presented as means with standard errors (SE). Differences between the means were evaluated with nonparametric Wilcoxon signed range test. In addition, correlation and linear regression coefficients were calculated. $P<0.05$ was accepted as the level of significance.

RESULTS

Heart rate (Fig. 1)

There were no significant differences in HR before PE and AE tests. The passive exercise did not induce any significant changes in HR, while the active exercise caused an increase in HR (from 75 ± 2 to 86 ± 3 beats $\cdot$ min^{-1} ($p<0.01$) during the first test and from 78 ± 3 to 88 ± 5 beats $\cdot$ min^{-1} ($p<0.01$) during the second test.

Stroke volume and cardiac output (Fig. 1)

The resting values of SV and CO before the two types of exercises did not differ significantly. The increase in SV (expressed in percentage of resting values) was significant only during the passive exercise. During the first PE test, SV increased by $9.0\pm2.5\%$ ($p<0.05$) and during the second one by $13.2\pm2.0\%$ ($p<0.01$).

The increase in CO (expressed in percentage of resting values) was significant in both types of exercise. During the first PE trial cardiac output increased by $8.95\pm2.21\%$ ($p<0.02$) and during the second trial by $11.74\pm1.81\%$ ($p<0.01$). The first AE test increased CO by $14.21\pm2.86\%$ ($p<0.01$) and the second one by 13.81 ± 1.56 % ($p<0.01$).

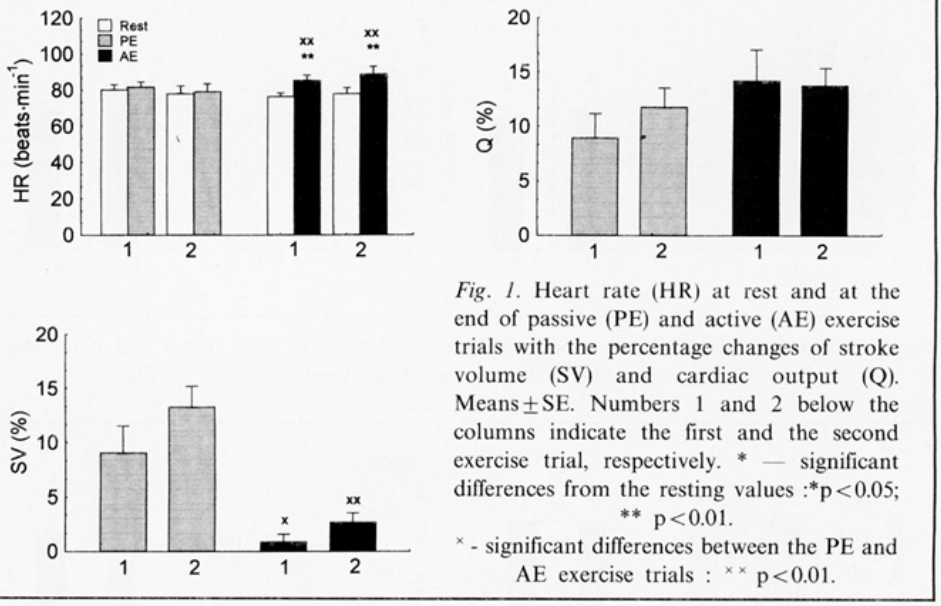

Fig. 1. Heart rate (HR) at rest and at the end of passive (PE) and active (AE) exercise trials with the percentage changes of stroke volume (SV) and cardiac output (Q). Means ± SE. Numbers 1 and 2 below the columns indicate the first and the second exercise trial, respectively. * — significant differences from the resting values :*$p<0.05$; ** $p<0.01$.
$^{\times}$ - significant differences between the PE and AE exercise trials : $^{\times\times}$ $p<0.01$.

Systolic time intervals (Fig. 2)

Resting STI were similar before the two types of exercise. No significant correlation was found between PEP and HR in either exercise type. As shown in *Fig. 2*, PEP was significantly reduced during the both passive exercises ($p<0.03$, and $p<0.01$, respectively) and during the second active exercise ($p<0.01$). Passive exercise decreased PEP to ET ratio in the both PE trials ($p<0.02$ and 0.01, respectively). A significanticant decrease in PEP to ET ratio occurred only during the second AE exercise ($p<0.03$). During the passive exercise PEP and PEP to ET ratio did not differ significantly from those found during the active exercise. The values of QS_2 and ET corresponding to HR equal to 90 beats $\cdot$ min^{-1} (calculated from the regression equations) were not significantly different in the PE and AE tests.

Mean arterial pressure (Fig. 3)

The resting systolic, diastolic and mean arterial pressures were similar before the two types of exercises. A significant increase in MAP above the resting value occurred only during PE test ($p<0.01$).

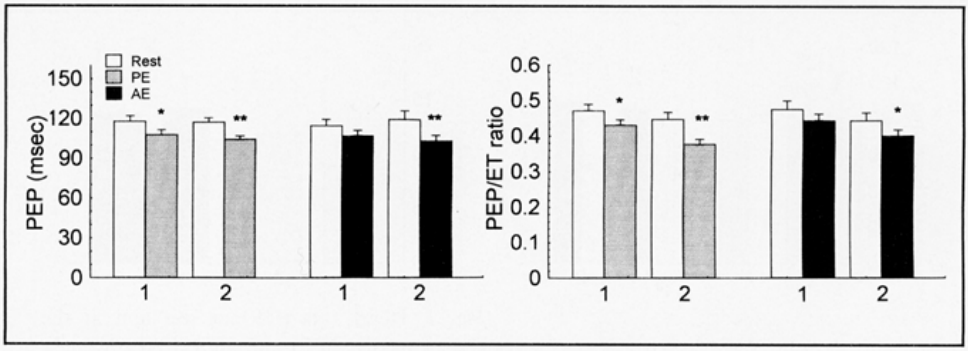

Fig. 2. Pre-ejection period (PEP) and PEP to ejection time (ET) ratio at rest and at the end of passive (PE) and active (AE) exercise trials. Denotations as in *Fig.1.*

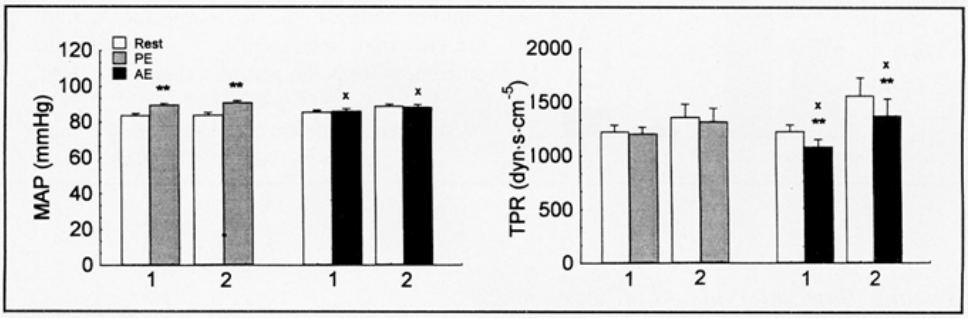

Fig 3. Mean arterial pressure (MAP) and total peripheral resistance (TPR) at rest and at the end of passive (PE) and active (AE) exercise trials (mean $\pm$ SE). Denotations as in *Fig. 1.*

Total peripheral resistance (Fig. 3)

Under resting conditions TPR calculated before all trials was similar and it did not change during the PE test. Active exercise significantly decreased TPR by $11.6 \pm 2.7\%$ ($p < 0.01$) during the first AE trial and by $12.5 \pm 1\%$ ($p < 0.01$) during the second one.

Oxygen uptake

Resting values of VO_2 before both types of exercise were similar. VO_2 increased from 3.64 ± 0.30 to 4.45 ± 0.50 $ml \cdot kg^{-1} \cdot min^{-1}$ ($p < 0.01$), during the first PE trial and from 3.71 ± 0.34 to 4.28 ± 0.40 $ml \cdot kg^{-1} \cdot min^{-1}$ ($p < 0.01$) during the second PE. The increases in VO_2 during AE were more pronounced than those during PE in both repetitions. VO_2 increased from 3.78 ± 0.30 to 5.35 ± 0.41 $ml \cdot min^{-1} \cdot kg^{-1}$ ($p < 0.01$) during the first AE trial and from 4.15 ± 0.30 to 5.74 ± 0.49 $ml \cdot min^{-1} \cdot kg^{-1}$ ($p < 0.01$) during the second one.

Electrical muscle activity (Tab. 1)

Resting muscle activity was similar for all the muscles. It slightly, but insignificantly increased during the first and second PE trial (except the biceps femoris muscle of which electrical activity increased significantly in the second passive exercise). During both AE trials the muscle activity was significantly higher than at rest.

Table 1. Changes in muscle activities in response to passive and active exercise (rms-EMGμV)

Muscle	Rest	Exercise 1		Exercise 2	
		passive	active	passive	active
rectus femoris	0.8±0.6	1.0±0.5	8.7±5.0*	1.0±0.6	5.4±2.0*
biceps femoris	0.9±0.5	4.0±2.4	0.7±2.6*	3.9±1.6	7.4±2.8*
tibialis anterior	1.6±0.9	4.8±1.0	5.9±1.2*	3.5±2.0	5.4±1.5*
gastrocnemius	1.0±0.2	4.3±1.8	12.3±2.1*	5.5±3.1	11.3±3.2*

Values are means ±SE. * Difference between rest and exercise conditions.

Rating of perceived exertion (RPE)

The RPE during active exercise (10.6±0.5) was significantly higher than during passive (8.1±0.6) exercise ($p<0.01$).

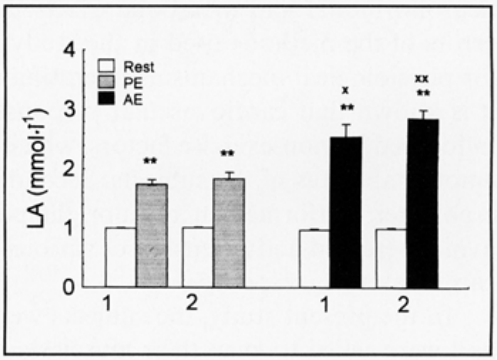

Fig. 4. Blood lactate concentration (LA) at rest and at the end of passive (PE) and active (AE) exercise trials. Means±SE. Denotations as in *Fig. 1.*

Blood lactate (Fig. 4)

The pre-exercise blood LA concentrations were similar in all experiments. During the AE trial blood LA concentration was higher than during PE ($p<0.01$). The first PE trial increased blood LA concentration from 0.99±0.02 to 1.7±0.09 mmol·l^{-1} ($p<0.01$) and during the second one from 1.01±0.01 to 1.83±0.11 mmol·l^{-1}($p<0.01$). Active exercise increased blood LA from 0.99±0.01 to 2.55±0.21 mmol·l^{-1} and from 1.00±0.01 to 2.86±0.14 mmol·l^{-1}in the first and second trial, respectively.

Plasma adrenaline and noradrenaline

There was no significant effects of passive and active exercise on the plasma catecholamine concentrations. Resting values were similar for all tests and there were 0.31 ± 0.02 pmol·l^{-1} and 1.66 ± 0.12 pmol·l^{-1} for A and NA, respectively. The plasma A concentration at the end of passive and active exercise trials was 0.32 ± 0.04 and 0.34 ± 0.04 pmol·l^{-1}, respectively. No significant changes in NA were induced by passive exercise (1.56 ± 0.19 pmol·l^{-1}), but there was a tendency towards higher values of the plasma NA concentration at the end of active exercise (1.88 ± 0.19 pmol·l^{-1}) ($p < 0.06$).

DISCUSSION

It is difficult, if not impossible, to design the experiment in which only one of the neural mechanisms involved in cardiovascular adjustment to exercise is active. The model of passive cycling on the leg cycle ergometer used in the study by Nobrega *et al.* (10), Williamson *et al.* (11) and Nurhayati and Boutcher (13) as well as in the present investigation to evidence the contribution of muscle mechanoreceptors has several limitations. Firstly, the responses to passive exercise can be compared only with volitional exercise of a very low intensity (unloaded cycling) producing rather small circulatory, neurohormonal and metabolic effects. Most of them only slightly exceed the errors of the methods used in the study and the conclusions may be not valid for physiological mechanisms operating at higher exercise loads. Furthermore, it is known that cardiovascular responses to exercise of low intensity may be influenced by non-exercise factors, which are difficult to control, such as e.g. the emotional status of the subjects. Secondly, during passive exercise on a bicycle ergometer, performed in the upright position, it is impossible to completely avoid increased active tension of various muscle groups which may evoke some cardiovascular responses.

In the present study, the subjects were well familiarized with the procedure and were asked to keep their muscles as relaxed as possible during the passive exercise. In spite of it, slight increases in the amplitude of EMG of the leg muscles, enhancement of oxygen uptake, and an elevation of blood lactate concentration were found during passive cycling. Moreover, these effects persisted in the repeated tests. It should be noted, however, that electrical activity of leg muscles, oxygen uptake, blood lactate level and rating of perceived exertion during the active unloaded exercise were all above those noted during the passive cycling. Thus, the involvement of both central command and muscle metaboreceptors during passively induced cycling was much smaller than during active exercise.

The results of the present study showed several differences in circulatory responses to the passive cycling and volitional unloaded cycling. An increase in HR and a decrease in TPR were found only during the active exercise while the significant increases in SV and MAP occurred only during the passive cycling. The increases of CO tended to be greater during active than passive cycling. These data confirmed the results previously obtained by Nobrega *et al.* (12) who applied similar experimental protocol but differ from those of Nurhayati and Boutcher (13). The new finding is that the passive and active cycling evoked similar shortening of PEP and a decrease in PEP to ET ratio.

The lack of significant increases in HR during the passive exercise suggests that muscle mechanoreceptors are not involved in the chronotropic response to dynamic exercise. It cannot be, however, excluded that they contribute to the initial HR response as it was postulated by Nobrega *et al.* (10) on the basis of data obtained during passive cycling lasting only 4s. This possibility was further supported by Willamson *et al.* (11) who reported that the first R-R interval in electrocardiogram recorded during passive cycling is shortened but only when the cycling is combined with electrical stimulation of muscles to increase mechanoreceptor activation.

The present data on HR changes recorded during volitional and passive exercise are in agreement with the concept of the role of both central command and metaboreflex in the HR control during dynamic exercise. It is believed that metabolic receptors are not activated during a light dynamic exercise, however, in spite of the low exercise intensity during the active unloaded cycling the contribution of afferents stimulated by chemical changes in muscles to the cardiovascular response might be noticeable since the subjects showed an increase in blood lactate concentration.

An increase in SV during the passive cycling may result from increased venous return to the heart, increased ventricle contractility or both. The recent experiments by O'Leary and Augustyniak (22) performed on dogs demonstrated that cardiac contractility may be increased due to the activation of muscle metabolic receptors by ischemia without changes in the central venous pressure. The shortening of PEP and decreasing of the PEP to ET ratio without concomitant changes in HR during the passive exercise suggest that muscle mechanoreceptors may participate in the enhancement of the heart contractility during exercise although increased venous return by itself may also result in reduction of PEP (23).

According to the current view an increase in blood pressure during exercise is due to the rapid resetting of the arterial baroreflex which is mediated by the central (central command) or peripheral (exercise pressor reflex) mechanisms. The latter involve both metaboreceptors and mechanoreceptors (24). A significant increase in MAP during the passive cycling found in the present study confirm contribution of mechanically sensitive afferents to the blood

pressure regulation during exercise. The lack of the increase in MAP during low intensity active exercise can be explained by a decrease in peripheral resistance which depends mostly on local metabolic and endothelial vasodilatory factors released in working muscles (see Laughlin *et al.* (25).

During the passive exercise there was no changes in plasma catecholamines while during the active exercise a tendency towards an elevation of plasma noradrenaline occurred. The study employing the sympathetic microneurography showed that the plasma noradrenaline concentration during exercise is highly correlated with the muscle sympathetic nervous activity (MSNA) (26). Exercise-induced elevation in the plasma noradrenaline level depends largely on the enhanced sympathetic impulse traffic to muscles which, according to the commonly accepted opinion, is attributed to both the central command and reflexes initiated by stimulation of muscle metabolic receptors (27). However, the recent study of Herr *et al.* (28) suggested that mechanically sensitive afferents contribute importantly to the MSNA response, and these afferents may be sensitized by the chemical products of muscle contraction. The present data indicate that during passive cycling the rhythmic stimulation of muscle mechanoreceptors with minimal activation of the central command or metabolic receptors is not sufficient to induce an elevation of the plasma noradrenaline concentration. The exercise intensity during the active cycling was also below the level which is associated with marked elevation of plasma noradrenaline (29). It should be noted, however, that the plasma noradrenaline concentration provides only an indirect information about the activity of the sympathetic nervous system and is much less sensitive than microneurography in assessment of the sympathetic input to various organs or tissues.

In summarizing, comparison of the cardiovascular responses to passively induced cycling and active unloading leg exercise indicates that muscle mechanoreceptors are not involved in heart rate acceleration during dynamic exercise but they may contribute to the enhancement of cardiac contractility. The latter effect may be partly responsible for an increase in stroke volume and cardiac output during the passive exercise. The study confirmed also the muscle mechanoreceptor involvement in so called "exercise pressor reflex".

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