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Training and Cardiovascular Responses from Cigarette Smoke Exposure

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Abstract

The aim of this study was to evaluate the early effect of the endurance training (ET) on systolic blood pressure (SBP), heart rate (HR) and rate pressure-product (RPP) after acute cigarette smoke exposure. Twenty male Wistar rats were randomly allocated into two groups: trained (TEx; n = 10) and control (CEx; n = 10), exposed to smoke. TEx rats undertook ET during 2 weeks (swimming, 5 days/week; 1 h/session) and CEx group was kept in sedentary lifestyle. After ET protocol both groups were exposed to cigarette smoke only once (total 1 h; 2 × 30 min with interval of 10 min between exposures; rate of 10 cigarettes/30 min). SBP, HR and RPP were measured after 2 weeks and just after (5 min) acute cigarette smoke (tail plethysmograph). All parameters did not differ ($P > 0.05$) between TEx (RPP = 45018 ± 1970 mmHg/bpm) and CEx (43695 ± 2579 mmHg/bpm) after ET protocol. However, all cardiovascular parameters increased ($P < 0.05$) only for CEx just after the cigarette smoke exposure. We concluded that ET can attenuate the aggression from acute smoking to cardiovascular system, with a few days of training and even with no chronic effect on these parameters at basal condition.

Key Words: blood pressure, exercise, rate-pressure product, rats, smoke exposure

Introduction

Cigarette smoking is associated with several cardiovascular problems, including atherosclerosis, hypertension and acute myocardial infarction. Tobacco has over 6,700 substances, of which 4,720 were identified as well (15). These constituents and their interactions increase blood pressure and are associated with metabolic, hormonal, vascular and cardiac hypertrophy (3).

The constituents of cigarette smoke are divided into two phases, the vapor phase where the carbon monoxide and particulate phase, as constituent is nicotine (30). Nicotine acts on the autonomic nervous system, central nervous system and cardiovascular system. This interaction is associated with increased cardiac output and heart rate (HR). However, the carbon monoxide has about 250-fold greater affinity for hemoglobin as compared with the oxygen, forming carboxyhemoglobin. Studies have shown that exposure to cigarette smoke increases the concentration of carboxyhemoglobin process leading to hypoxia (5, 9, 14, 30, 31).

It is known that chronic exposure to cigarette smoke results in increased blood pressure. Studies show an increase in blood pressure in rats exposed for three months to cigarette smoke and found a difference of 15 mmHg between the control and exposed to smoke cigarette (9). Others researchers have showed that acute exposure to smoke smoking causes changes in blood pressure, increased peripheral vascular resistance, HR, sympathetic activity and decreased baroreflex activity (4, 6, 16, 24). Thus acutely or chronic tobacco promotes negatives changes in blood pressure

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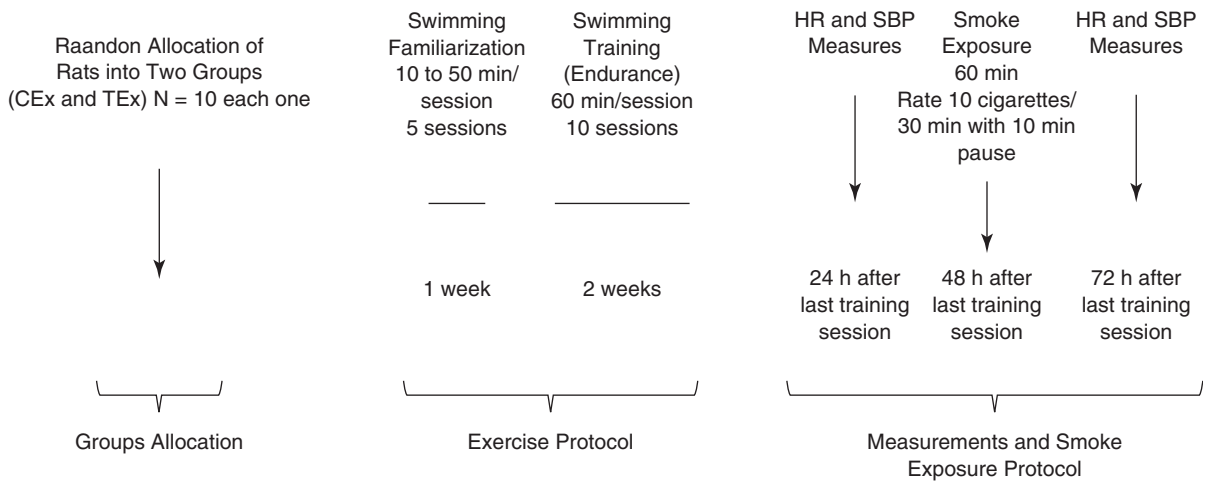

Fig. 1. Experimental design of the study.

and left ventricular function (2, 9, 14).

Differently the harmful effect exerted by cigarettes smoking on cardiovascular parameters, physical training has been used as a non-pharmacological tool in the prevention of cardiovascular disease (33). Chronic exercise performed properly and organized as the duration and intensity have beneficial effects on blood pressure (1, 25). It is believed that the exercise hypotensive effect come from several changes on the body, like decreased cardiac output, increased antioxidants and increased endothelial activity due to increased synthesis of nitric oxide, decreased systolic, diastolic and mean blood pressure, improved baroreflex/ compliance arterial and decreased sympathetic activity (25). The majority of these beneficial from exercises are achieved from at least 10 weeks of physical training, because at this time the body already obtained chronic physiological effects. However, Jen *et al*. showed beneficial effects of short-term exercise training eliminating negative changes caused by high-cholesterol diet intervention from 2 weeks of training (20).

On the other hand it is unknown if a short time of exercise intervention (*i.e.* less than 4 weeks) could protect cardiovascular system from aggression cigarettes. Thus, the aim of this study was to evaluate the early effect of endurance training (ET) on systolic blood pressure (SBP), HR and rate pressure-product (RPP) after acute cigarette smoke exposure in rats.

Considering the short time of physical training (only 2 weeks), we hypothesized that it would not be possible to find chronic effects caused by ET but, nevertheless after acute smoke exposure, rats trained could have lower effects on cardiovascular parameters than control animals.

Materials and Methods

Experimental Animals

Twenty male Wistar rats (200-250 g) were kept at 25 ± 2°C with day/night cycle of 12 h and free access to rat chow and water following the guidelines of the institutional animal care and use committee. Animals were randomly allocated into two experimental groups: control exposed to smoke (CEx, n = 10) and trained exposed to smoke (TEx, n = 10). All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication 85-23, revised 1985). The study was in accordance with the ''Principles of laboratory animal care'' (NIH publication No. 85-23, revised 1985), and was approved by the local Institution's Animal Care (protocol number 032/2010). Fig. 1 illustrates the experimental design of the study.

Exercise Training

There are several studies using animal model with swimming exercise in the literature, including from our laboratory (1, 7, 13, 25). One explanation for that is the greater effectiveness in exercise intensity in rats, once Wistar rats usually presents no satisfactory performance in treadmill protocols (12, 17). Therefore, here we performed swimming exercise protocol. Only the group TEx participated of this swimming protocol. Animals were firstly familiarized to water during five days (10 min 1st day, 20 min 2nd day, 30 min 3rd day, 40 min 4th day and 50 min at 5th day). In the familiarization the animals swimming in a tank with water (28 ± 2°C) level that allowed the rats tail tip hillside in the background.

Table 1. Endurance training prevented the increases in heart rate and systolic blood pressure

	Control Exposed (n = 10)		Trained Exposed (n = 10)	
	HR (bpm)	SBP (mmHg)	HR (bpm)	SBP (mmHg)
Pre-Smoke Exposure	443 ± 23	98 ± 5	411 ± 11	106 ± 4
Post-Smoke Exposure	469 ± 14*, #	121 ± 4*, #	416 ± 11	110 ± 4

Data presented by mean ± SD. HR (heart rate); SBP (systolic blood pressure). *$P < 0.05$ *vs.* pre-smoke exposure. #$P < 0.05$ *vs.* trained exposed.

In the next 2 weeks animals were exercised in deep water without touching the tip of the tail at the bottom during 60 min per session, without overload. In the first week the rats trained 5 sessions (Monday to Friday) and rested on Saturday and Sunday. In the second (and the latest) week they trained exactly like on the first week. But, on Saturday we measured HR and SBP (see specific section) from both groups (CEx and TEx). On Sunday all rats performed the smoke exposure (see specific section) and, immediately after (~ 5 min), we measured again HR and SBP.

HR and Arterial Blood Pressure Measures

Arterial blood presure was measured with in a rest conscious state by noninvasive tail cuff method (8) coupled to a photoelectric sensor to detect the arterial pulses (Model 29-SSP, IITC, Life Science Instruments, Woodland Hillsm, CA, USA). A three-channel recorder (Model RG300, Funbec) thermo-sensitive was attached to the system.

Prior to arterial blood pressure recordings, animals were conditioned for 7 consecutive days, 20 min each day, inside a plexiglass restrainer. All posterior recordings were conducted on a constant environment, during the morning (0700-0900h). To measure the systolic pressure rats were placed in plexiglass restrainer with appropriate dimensions to the animal size. The container was connected to photoelectric sensor and the wrist cuff around the animal's tail. The compartment temperature was maintained at 28 ± 2°C. The cuffs were preheated to temperature stabilization. Animals were acclimatized for 3 days prior to fitting 10 min, and the fourth day collecting itself lasting 40 min. The procedure performed was inflating the cuff with two min between the next blow. The procedure was performed by the same staff, so there would be minimal stress on the animal.

Smoke Exposure

Rats were placed in the exposure apparatus with dimensions (89 × 86 × 55 cm). The cigarette smoke was taken during 60 min by motor/fan and vented through pipe camera divided into two phases (29). The smoke was released at a rate of 10 min cigarettes/30 min during 30 min and after 10 min intervals this protocol was repeated. Both groups (CEx and TEx) was exposure to only one session of smoke cigarette.

Statistical Analysis

Data was expressed as mean ± standard deviation of the mean (SD). Two way ANOVA and *post hoc* Tukey test was used for comparisons between groups. Statistical procedures were made in SigmaStat for Windows (SPSS v.3.5, San Raphel, CA, USA). Statistical significance was established at the $P < 0.05$ level.

Results

Before the smoke exposure there were no differences ($P > 0.05$) between TEx and CEx groups in relation their SBP and HR. However, after the acute smoke exposure the CEx group presented higher values ($P < 0.05$) for SBP and HR (Table 1).

On the same line, RPP increased ($P < 0.05$) only for the CEx group after smoking stress (Fig. 2).

Discussion

Our main finding is that ET could protect the trained animals from acute aggression cigarettes even without chronic effect of training on the cardiovascular parameters, due the short-time of intervention (2 weeks), corroborating our initial hypothesis. Thus, it is possible to get beneficial from exercise early against smoke cigarettes exposure. To our knowledge, this is the first study that tested the acute effect of smoke exposure on the cardiovascular responses after a short time intervention with physical training.

Our results are similar to other studies acutely exposed to cigarette smoke, which was found increased HR and SBP, probably due decreases in baroreflex activity and increases in peripheral vascular resistance and sympathetic activity (4, 6, 16, 24). The use of rate

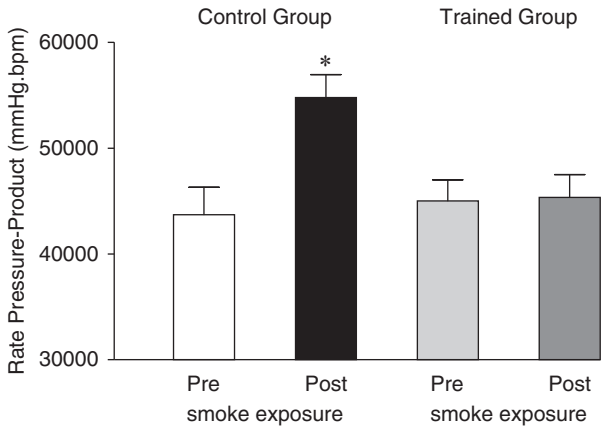

Fig. 2. – Rate-Pressure Product pre- and post-smoke exposure protocol. CEx pre Exp: control group before smoke exposure; CEx post Exp: control group after smoke exposure; TEx pre Exp: trained group before smoke exposure; TEx post Exp: trained group after smoke exposure. *$P < 0.05$ *vs.* CEx pre Exp and TEx pre and post.

pressure-product used in the current study aimed to evaluate if the exercise may affect the changes in these parameters. As an easy and powerful parameters to determine the cardiovascular overload (27). In addition, other studies have been demonstrated alterations on HR blood pressure after nicotine exposure (19).

Other studies have identified dysfunction in left ventricular diastole in response to exposure to cigarette smoke (2, 14). It could have increased endothelium peripheral vasoconstriction in response to substances in tobacco (*e.g.* carbon monoxide or nicotine), which pass through the vascular endothelium and releases endogenous vasoconstrictors such as endothelin-1 and angiotensin II (21). It results in a smaller flow of venous return to the heart, reducing the amount of blood pumped by the ventricle and with the possible consequence of elevated blood pressure.

Additional vasoconstrictor substances are also released in response to the process of hypoxia caused by carbon monoxide. It was showed that carboxiemoglobin is increased suddenly in non-smokers exposed to cigarette smoke during 30 min, corroborating the effect to chronic exposure (9, 14).

In this hand, physiological variables as HR and blood pressure should be monitored. The association between them may provide information that correlates with myocardial oxygen consumption, which is denominated RPP and is calculated by multiplying SBP by HR. Thus, RPP is an indirect indication of heart energy demand. Due its practice measures RPP if has been investigated by studies with exercise, which aims to investigate stress caused by different exercise protocols on cardiovascular system (18, 22) . In this way, our study showed that exercise avoided an increase in RPP by maintenance of both HR and SBP. Therefore exercise seems to protect cardiovascular system from cigarette smoke acute damage.

It is known that epinephrine increase with stress and it can collaborate to elevation in blood pressure. It is also demonstrated that few weeks' physical training reduces epinephrine concentration to the same load of exercise (submaximal) (10, 11). So we may explain, at least in part, that due lower epinephrine release TEx group did not increase the RPP like as CEx after smoke exposure.

Considering that the passive smoke exposure is common in several countries where there is no law against smoking (28) and it is associated to hypertension, atherosclerosis, acute myocardial infarct, we suggest that even a short ET (*i.e.* 2 weeks) may protect the cardiovascular system. Once hypertension is the major risk factor to the cardiovascular diseases, it seems that regular physical activity is an interesting non pharmacological tool for public health policies.

Additionally, there is a clear association between acute exposure to cigarette smoke and genesis of inflammatory and reactive oxygen species (32) and both of them can induce a negative scenario cardiorespiratory (23). In this sense, van der Vaart *et al*. (32) found 37 studies examining the acute effects of cigarette smoke in animal models. Interestingly their data showed that in animals most markers of oxidative stress change in the first 6 h after acute cigarette smoking and return to normal within ~ 24 h. In our study we measured the SBP and HR exactly 24 h after exposure and, therefore, we did it within the "window" of time quoted by them (32). Therefore, it is possible that our results still had influence from oxidative stress induced by cigarette exposure.

Oppositely, regular exercise confers protection against inflammatory diseases by reducing inflammatory response in human or experimental animals (26).

Although our aim here was not exactly explain the mechanisms, but only verify the effect of short training on cardiac demand (RPP) of animals after acute cigarette exposure, we agree would be interesting to have an evidence about the mechanism. In this sense, blood epinephrine concentration, for instance, would be proper. However, once is already clearly stated in the literature that endurance training (even in a few days) decreases the blood epinephrine concentration (10, 11), we consider that this mechanism may explain the effects reported here. However, this issue should be explored in future research with more analysis (*e.g.* blood samples) including also inflammatory, stress and oxidative stress markers.

Thus, we conclude that early endurance training can attenuate the aggression from acute smoking to the cardiovascular system (SBP, HR and RPP) in rats,

with two weeks of training and even with no significant effect on these parameters at rest conditions.

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