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ORIGINAL ARTICLE

Vascular adaptation to aerobic exercise: A new experimental approach

Adaptation vasculaire à l'exercice de type aérobie : une nouvelle approche expérimentale

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Isolated endothelial cells;
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Summary
Purpose. — The purpose of this preliminary study is to assess whether moderate-intensity exercise training is associated with a chronic modification of the cellular response to a mechanical stress-induced with hypo-osmotic shock (regulatory volume decrease process) of 80 mosmoles·kg^{-1}.
Material and methods. — Wistar Kyoto male rats were subjected to a treadmill training protocol (Tr) (60 min per day, 5 days per week, 8 weeks, 15° incline, 20 m·min^{-1}) or not (Sed). The rats were then sacrificed and endothelial cells isolated from the thoracic and abdominal aortas.
Results. — No significant group effect of hypo-osmotic shock was found. A RVD process was observed in cells from the Sed group, cell volume being significantly decreased 20 minutes after the shock (75% of initial volume). However, no RVD was found in cells from the Tr group. These preliminary results suggest that the increase in endothelial cell volume induced by hypo-osmotic shock is modified by chronic exercise as is the subsequent physiological response (RVD

Abbreviations: Ach, ACETYLCHOLINE; BH4, TETRAHYDROBIOPTERIN; ED, ENDOTHELIAL DYSFUNCTION; EDHF, ENDOTHELIUM-DERIVED HYPERPOLARIZING FACTOR; eNOS, NO SYNTHASE ENDOTHELIAL; HTS, HYPO-OSMOTIC SHOCK; NO, NITRIC OXIDE; PGI_2, PROSTACYCLIN; RVD, REGULATORY VOLUME DECREASE; Sed, SEDENTARY; Tr, TRAINED; VRAC, VOLUME-REGULATED ANION CHANNELS; WKY, WISTAR KYOTO.

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process). Therefore, we conclude that isolated endothelial cells from trained rat arteries would provide a good model to assess the effects of chronic exercise on cellular signaling.

MOTS CLÉS
Cellules endothéliales isolées ;
Exercice chronique ;
Rat

Résumé
Objectifs. — Cette étude préliminaire a pour objectif de montrer qu'un entraînement physique d'intensité modérée est associé à des modifications chroniques des réponses cellulaires induites par un choc hypo-osmotique de 80 mosmoles·kg^{-1}.
Matériels et méthodes. — Des rats males de souche Wistar Kyoto sont soumis à un protocole d'entraînement chronique sur tapis roulant (60 min par jour, 5 jours par semaine, pendant 8 semaines, pente de 15°, à 20 m·min^{-1}) ou sont sédentaires. Les rats sont ensuite sacrifiés et les cellules endothéliales isolées à partir des aortes thoracique et abdominale.
Résultats. — Le choc hypo-osmotique induit une augmentation du volume cellulaire dont l'amplitude n'est pas modifiée par l'entraînement. Pour les animaux sédentaires, cette augmentation est immédiatement suivie d'un retour aux valeurs normales (*regulatory volume decrease*, RVD) qui devient statistiquement significative 20 minutes après l'initiation du choc (75 % du volume initial). Le RVD n'est pas observé pour les animaux entraînés. Ces résultats préliminaires suggèrent que l'augmentation de volume, ainsi que la réponse physiologique subséquente (processus de RVD), induites par un choc hypo-osmotique, sont modifiées par l'entraînement. En conséquence, les cellules endothéliales fraîchement isolées d'aortes de rats entraînés à l'exercice constitueraient un bon modèle d'étude des effets de l'exercice sur la signalisation intracellulaire.

1. Introduction

Impaired endothelial function is associated with a number of pathological conditions, including cigarette smoking, dyslipidemia, obesity, diabetes mellitus, hypertension [1]. It is considered as the first step towards atherosclerosis and an independent cardiovascular risk factor. Numerous interventions that improve cardiovascular risk factors and reduce cardiovascular morbidity and mortality also enhance endothelial function. Regular physical activity is one of the most promising factors that are well-known to reduce cardiovascular morbidity and mortality, mainly at primary and tertiary preventive levels.

Regular physical activity improves endothelium-dependent vasodilation in healthy human [2] and animal models [3] as well as individuals with endothelial dysfunction (ED) [4]. Exercise training improves mainly the NO-related vasorelaxation, with a less marked effect on prostacyclin (PGI_2) and endothelium-derived hyperpolarizing factor (EDHF) pathways [3]. Indeed, chronic exercise has been reported to increase both the ACh-induced elevation of intracellular Ca^{2+} in endothelial cells [5] and Akt-dependent phosphorylation of eNOS on Ser1177, and to decrease eNOS interaction with its negative regulator caveolin-1 [6]. Moreover, exercise training prevents eNOS uncoupling by maintaining tetrahydrobiopterin (BH4) stores [7] and activity [4] and eNOS dimer: monomer ratio [6]. Physical exercise also reduces the production of endothelin-1 [8] and the action of angiotensin II [9]. It also lowers oxidative stress and inflammation [9]. However, the precise mechanisms underlying these beneficial effects remain unclear.

Training-induced improvement of endothelial function have often been attributed in the literature to exercise-induced increases in shear stress resulting from a rise in blood-flow to the heart and active skeletal muscle during exercising bouts [10,11]. The limited data obtained from in vivo models also support the notion that increases in mean shear stress provides a stimulus that is anti-atherogenic (for review see Newcomer et al. [12]). However, it is important to acknowledge that the beneficial effects of exercise on vascular health also occur in arteries that are not subjected to robust increases in mean shear stress during exercise. This suggests that the beneficial effects of exercise training on endothelial cells do not result from increased shear stress only and that other stimuli may also play a significant role.

Thus, there is a requirement for new experimental approaches which allow measurements of the training-induced modifications at the intracellular level. In this regard, measurement on isolated endothelial cells previously submitted to whole exercise training may represent a useful tool for investigating intracellular signalization.

Several authors have used hypo-osmotic shock (HTS) to explore the intracellular signaling pathways [13,14] and nitric oxide (NO) synthesis in endothelium. A decrease in external osmolarity results in cell swelling and the immediate activation of a mechanism to restore cell volume, known as regulatory volume decrease (RVD). RVD is a homeostatic mechanism which involves a wide variety of cellular sensors and signalling pathways [15], all of them being also potentially modified by exercise training. Moreover, this process can be easily and reliably quantified by video-imaging technique associated with morphometric analysis [16].

The present study was designed to assess whether exercise training modifies the response of endothelial cells to HTS. Our experiments were conducted in cells freshly isolated from the aorta of either trained or sedentary rats. To