



Original article

## Effects of aerobic and resistance training of long duration on pro- and anti-inflammatory cytokines in rats

C.M.S. Silva<sup>a</sup>, R.C. Vieira-Junior<sup>b</sup>, J.C.R. Trombeta<sup>c</sup>, T.R. Lima<sup>a</sup>, G.A. Fraga<sup>a</sup>, M.S. Sena<sup>a</sup>, E.T.P. Ávila<sup>a</sup>, R.A. Tibana<sup>d</sup>, J. Prestes<sup>d</sup>, J.W. Navalta<sup>e</sup>, F.A. Voltarelli<sup>a,\*</sup>

<sup>a</sup> Federal University of Mato Grosso (UFMT), Cuiabá, Brazil

<sup>b</sup> State University of Mato Grosso (UNEMAT), Cáceres, Brazil

<sup>c</sup> University of Campinas (UNICAMP), Campinas, Brazil

<sup>d</sup> Post-Graduate Program on Physical Education, Catholic University of Brasília (UCB), Brasília, Brazil

<sup>e</sup> University of Nevada Las Vegas, NV, United States

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### ABSTRACT

**Objective:** To determine possible changes in serum concentrations of pro- and anti-inflammatory cytokines of eutrophic rats subjected to aerobic or resistance physical training.

**Methods:** This study examined serum concentrations of TNF- $\alpha$ , IFN- $\gamma$ , IL-6, IL-10 and IL-1- $\beta$  in rats that performed aerobic or resistance training for 16 weeks. Thirty-five Wistar rats (male adult) were divided into three groups: Control Group (CG), Aerobic Group (AG) and Resistance Group (RG). Rats were sacrificed 48 h after the final training session. Serum concentrations of cytokines were analysed by ELISA.

**Results:** TNF- $\alpha$  levels were higher in the RG, followed by the AG and CG groups ( $p < 0.001$ ). IFN- $\gamma$  and IL-10 levels were not significantly different between groups ( $p = 0.097$  and  $p = 0.17$ , respectively). The levels of IL6 and IL1- $\beta$  were higher in AG compared to RG and CG ( $p = 0.0004$  and  $p = 0.003$ , respectively). In general, our results indicate a higher pro-inflammatory profile in AG and probably RG animals.

**Conclusion:** Further studies are required in order to better clarify the effects of aerobic and resistance exercise training on pro- and anti-inflammatory cytokines. Additionally, future studies should address the metabolic and molecular pathways involved in these responses.

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## Efectos de entrenamientos aeróbico y de resistencia de larga duración acerca de citocinas pro y antiinflamatorias en ratas

### RESUMEN

**Objetivo:** Determinar posibles cambios en las concentraciones séricas de citoquinas pro y antiinflamatorias de ratas eutróficas sometidas a entrenamiento físico aeróbico y de resistencia.

**Método:** Se examinaron las concentraciones séricas de TNF- $\alpha$ , IFN- $\gamma$ , IL-6, IL-10 e IL-1- $\beta$  en ratas sometidas a entrenamiento aeróbico o de resistencia de 16 semanas de duración. Treinta y cinco ratas Wistar (macho adulto) fueron divididas en 3 grupos: Grupo Control (GC), Grupo Aeróbico (GA) y Grupo Resistencia (GR). Las ratas se sacrificaron 48 horas después de la sesión de entrenamiento final. Las concentraciones séricas de las citoquinas se analizaron por ELISA.

**Palabras clave:**

Entrenamiento aeróbico

Entrenamiento de resistencia

Citoquinas

Inflamación

\* Corresponding author at: Faculty of Physical Education – Federal University of Mato Grosso, Fernando Corrêa da Costa Avenue, n.º. 2367, Boa Esperança, Cuiabá, MT 78060-900, Brazil.

E-mail address: [favoltarelli@ufmt.br](mailto:favoltarelli@ufmt.br) (F.A. Voltarelli).

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**Resultados:** Los niveles de TNF- $\alpha$  fueron mayores en el GR, seguido por los grupos de GA y GC ( $p < 0.001$ ). Los niveles de IFN- $\gamma$  e IL-10 no fueron significativamente diferentes entre los grupos ( $p = 0.097$  y  $p = 0.17$ , respectivamente). Los niveles de IL-6 y IL-1- $\beta$  fueron mayores en GA comparado con GR y GC ( $p = 0.0004$  y  $p = 0.003$ , respectivamente). En general, nuestros resultados indican mayor perfil antiinflamatorio en GA y probablemente en GR.

**Conclusión:** Se necesitan estudios adicionales para aclarar mejor los efectos de un entrenamiento aeróbico o de resistencia en las citoquinas pro y antiinflamatorias. Además, los estudios futuros deben abordar las vías metabólicas y moleculares involucradas en estas respuestas.

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## Efeitos do treinamento aeróbico e de resistência na longa duração sobre as citocinas pró e anti-inflamatórias de ratos

### R E S U M O

**Objetivo:** Determinar as possíveis alterações nas concentrações séricas de citocinas pró e anti-inflamatórias de ratos eutróficos submetidos a treinamento físico aeróbico ou resistência.

**Método:** Este estudo examinou a concentração sérica de TNF- $\alpha$ , IFN- $\gamma$ , IL-6, IL-10 e IL-1- $\beta$  em ratos que realizaram treinamento aeróbico e de resistência durante 16 semanas. Trinta e cinco ratos Wistar (macho adulto) foram divididos em 3 grupos: grupo controle (GC), grupo aeróbico (GA) e grupo de resistência (GR). Os ratos foram sacrificados 48 horas após a sessão de treino final. As concentrações séricas de citocinas foram analisadas por ELISA.

**Resultados:** Os níveis de TNF- $\alpha$  foram maiores no GR, seguindo-se os grupos GA e GC ( $p < 0.001$ ). IFN- $\gamma$  e os níveis de IL-10 não foram significativamente diferentes entre os grupos ( $p = 0.097$  e  $p = 0.17$ , respectivamente). Os níveis de IL-6 e IL-1- $\beta$  foram maiores em GA, quando comparados com GC e GR ( $p = 0.0004$  e  $p = 0.003$ , respectivamente). Em geral, os nossos resultados indicam um perfil pró-inflamatório maior nos animais do GA e, provavelmente, no GR.

**Conclusão:** Mais estudos são necessários para melhor esclarecer os efeitos do treinamento físico aeróbico e resistência sobre as citocinas pró e anti-inflamatórias. Além disso, estudos futuros devem abordar as vias metabólicas e moleculares envolvidas nestas respostas.

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### Palavras-chave:

Treinamento aeróbico  
Treinamento de resistência  
Citocinas  
Inflamação

## Introduction

Noncommunicable chronic diseases (NCCDs) are currently responsible for the majority of deaths in many countries. The main NCCDs related to these deaths are cardiovascular disease, cancer, chronic respiratory diseases, diabetes *mellitus* and mental illness. It is known that the emergence of NCCDs is related to exposure to risk factors such as hypertension, smoking, hypercholesterolemia, low consumption of fruits and vegetables, overweight and obesity, alcohol abuse and physical inactivity<sup>1</sup>.

In relation to a sedentary lifestyle, physical activity levels have declined worldwide, with sedentary behaviour at work and during leisure time, as well as the use of "passive" means of transport partly explaining this phenomenon. Physical inactivity is responsible for causing 6% of all deaths and is the fourth major global mortality risk factor. Several authors have demonstrated an association between physical inactivity and NCCDs.<sup>1</sup> Moreover, the association between NCCDs and its risk factors (metabolic syndrome, type 2 diabetes *mellitus*, obesity and atherosclerosis, for example) and systemic low-grade inflammation in different populations has been investigated and established.<sup>2,3</sup>

Obesity is a clear example of this association since the increase in visceral fat induces increased secretion of pro-inflammatory cytokines, and results in the initiation of low-grade chronic inflammation.<sup>4</sup> Cytokines can be classified according to their function, namely pro-inflammatory (interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), interleukin-8 (IL-8), tumour necrosis factor alpha (TNF- $\alpha$ ), interferon (IFN), among others) or anti-inflammatory (interleukin-4 (IL-4), interleukin-10 (IL-10), interleukin-13 (IL-13), and receptor antagonist IL-1 (IL-1ra)),

characterized by inducing the increase in the inflammatory process or its decrease, respectively. Thus, chronic low-grade inflammation is due, among other factors, to the increased production of pro-inflammatory cytokines.<sup>5,6</sup>

Studies have shown the protective effect of regular exercise against inflammation. This may be attributed, at least in part, to the anti-inflammatory response generated by exercise, which is partly mediated by IL-6 derived from skeletal muscle. Physiological concentrations of IL-6 stimulate the appearance of anti-inflammatory cytokines in the circulation and inhibit the production of pro-inflammatory cytokines.<sup>7</sup>

In addition, IL-6 appears to stimulate lipolysis and fat oxidation. The anti-inflammatory effects of regular exercise may protect against insulin resistance induced by TNF- $\alpha$ . It has also been proposed that IL-6 and other cytokines, which are produced and released by skeletal muscles (i.e., IL-15), exert their effects on other organs. Thus, they may be termed myokines,<sup>8</sup> which may mediate the beneficial effects of physical exercise as they play an important role in protecting the body against diseases associated with systemic low-grade inflammation. On the other hand, when the IL-6 is not produced by the skeletal muscle, but by the adipose tissue (in this case, IL-6 it would become an adipokine), it exerts pro-inflammatory effects.<sup>4,9</sup>

However, important issues regarding the performance of physical exercise still need to be elucidated, that is: what is the best exercise (aerobic or resistance) for the production of anti-inflammatory cytokines at the expense of pro-inflammatory that, in turn, will act positively on healthy bodies, via the blood stream, on other tissues? Another area that needs further investigation is the ability of exercise-induced skeletal muscle contraction to

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