J. Health Biol Sci. 2025;13(1):1-3 doi: 10.12662/2317-3076jhbs.v13i1.5510.p1-3.2025

SHORT COMMUNICATION

Physical exercise and anti-inflammatory agents in an animal model of seizures: insights into lipid peroxidation and antioxidant activity

Exercício físico e agentes antiinflamatórios em modelo animal de crises epilépticas: ideias sobre peroxidação lipídica e atividade antioxidante

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Abstract

A previous study revealed the protective effect of an aerobic exercise protocol on behavioral and inflammatory aspects in an animal model of epileptic seizures. The previously collected samples in that investigation were now analyzed from the perspective of oxidative stress. Five experimental groups of Wistar rats were used (sedentary, diazepam, two physical exercise groups, and naive). Analyzes of lipid peroxidation, sulfhydryl content levels, and quantification of reduced glutathione were performed in the cortical and hippocampal tissues of the animals. There was no change in any parameter in any of the analyzed tissues.

Keywords: seizure; physical exercise; oxidative stress.

Resumo

Um estudo anterior revelou o efeito protetor de um protocolo de exercícios aeróbicos sobre aspectos comportamentais e inflamatórios em modelo animal de crise epiléptica. As amostras anteriormente recolhidas naquela investigação foram agora analisadas na perspectiva do estresse oxidativo. Foram utilizados cinco grupos experimentais de ratos Wistar (sedentários, diazepam, dois grupos de exercício físico e naive). Análises de peroxidação lipídica, teor de sulfidrilas e quantificação de glutationa reduzida foram realizadas nos tecidos corticais e hipocampais dos animais. Não houve alteração em qualquer parâmetro em ambos os tecidos analisados.

Palavras-chave: crises epilépticas; exercício físico; estresse oxidativo.

INTRODUCTION

A recent study by our research group linked an amelioration of oxidative markers with an improvement in epileptic seizures, suggesting that oxidative modulation may be useful in the treatment of epilepsy[1].

This short communication presents new results from a previously original article that performed a kindling protocol of epileptic seizures with physical exercise as a treatment[2]. The objective of this new approach is to investigate changes in oxidative markers in cerebral samples of animals subjected to the aerobic exercise protocol with or without concomitant treatment with anti-inflammatory drugs.

MATERIALS AND METHODS

Experimental Groups

A total of 52 male Wistar rats (2-month-old) were separated into five experimental groups, each with n = 8-12 (exercise + saline; exercise + prednisolone; sedentary; diazepam 2 mg/kg; naive (baseline control)). The animals were obtained and kept at the Federal University of Rio Grande do Sul Central Vivarium (CREAL) under conventional conditions. All animals received daily doses of intraperitoneal diazepam, saline, or prednisolone. The experiments followed the "Guide for the Care and Use of Laboratory Animals, DHEW, publication n° (NIH) 80-23, 1985" and were authorized by the local ethical committee.

Epileptic Seizures Model

A model of induced seizures[3,4] was employed. The protocol consisted of intraperitoneal injections every 2 days for 14 days of subconvulsant doses of PTZ (25 mg/kg body weight).

Aerobic protocol

The exercised animals performed aerobic exercise on a rodent treadmill during these 14 days. The maximum indirect oxygen

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Conflict of interesse: There is no conflict of interest on the part of any of the authors.
Received: 2024 Oct 4; Revised 2025 Feb 25; Accepted 2025 Feb 27

uptake (VO2 max) was measured, and the animals ran daily for 30 minutes at a speed corresponding to 60% of the VO2 max, with resting on days 5 and 10 of the protocol.

Tissue preparation and assays

On the 15th day, the animals were sacrificed by decapitation. Cortical and hippocampal areas were dissected and homogenized with 1:10 PBS buffer. The homogenate was centrifuged at 800g for 10 minutes, and the supernatant was collected.

Thiobarbituric acid reactive species (TBA-RS) were measured according to the methods of Ohkawa[5]. Sulfhydryl determination was performed according to a previously described methodology[6]. GSH levels were measured with a few modifications from the original protocol[7]. All quantifications were normalized by protein.

Statistical Analyzes

One-way ANOVA was performed for parametric data, and the Kruskal–Wallis test was performed for nonparametric data. A p-value < 0.05 was considered to indicate statistical significance. The results for each group are expressed relatively to the sedentary group (saline group).

RESULTS AND DISCUSSION

The aerobic exercise protocol, either with prednisolone administration or performed alone, did not alter any oxidative stress parameters in the tissues analyzed ($p > 0.05$, Kruskal-Wallis test or One-Way ANOVA test) (Figures 1-2).

Figure 1. Effect of aerobic exercise alone or combined with prednisolone on the levels of sulfhydryl groups, TBARS, and GSH in cortical tissue. One-way ANOVA test for the sulfhydryl groups. Kruskal–Walli's test for the TBARS and GSH analyses. N: 8-10. Data expressed as relative to the sedentary group. Pred: Prednisolone.

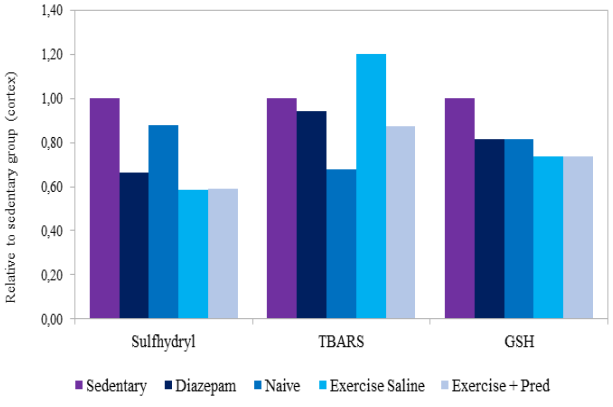
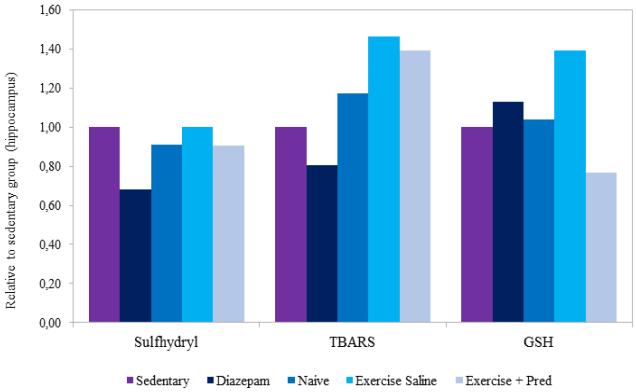


Figure 2. Effect of aerobic exercise alone or combined with prednisolone on the levels of sulfhydryl groups, TBARS, and GSH in hippocampus. One-way ANOVA test for the sulfhydryl groups. Kruskal–Walli's test for the TBARS and GSH analyses. N: 8-10. Data expressed as relative to the sedentary group. Pred: Prednisolone.



According to the evidence obtained in recent years, the importance of the participation of oxidative stress processes in epilepsy is remarkable. It can act both on the etiological basis of epileptic seizures and due to this condition[8,9].

Although the behavioral and inflammatory aspects of the rats in the exercise groups improved in the previous study, there were no changes in the parameters of oxidative stress, indicating that the exercise was not intense or long enough to exert any effect on this signaling pathway. No differences were found in the sulfhydryl groups in the cortex or the hippocampal tissue, which is different from what was observed in other studies by our research group, in which the improvement in behavioral parameters was associated with an increase in sulfhydryl groups in the hippocampus[1]. The level of lipid peroxidation was not altered in any of the analyzed tissues, corroborating the previously mentioned study, which also revealed no difference. Unaltered GSH levels were an unexpected result since it has already been established that physical exercise leads to modifications in the enzymatic antioxidant system, although often with conflicting results. We believe that longer protocols, both for seizures and for the aerobic approach, may result in different outcomes.

CONCLUSION

The protocols of aerobic exercise alone and aerobic exercise combined with an anti-inflammatory drug did not change any marker of oxidative stress, indicating that this protective effect on seizures did not involve oxidative signaling.

FUNDING AND ACKNOWLEDGMENTS

This study was made possible by grants from the National Council of Scientific and Technological Development (CNPq) and the Coordination for the Improvement of Higher Education Personnel (CAPES).

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How to cite this article/Como citar este artigo:
Rosa GL, Guzzo EM, Nunes SE, Faverzani JL, Padilha RB, Lima AM, et al. Physical exercise and anti-inflammatory agents in an animal model of seizures: insights into lipid peroxidation and antioxidant activity . J Health Biol Sci. 2025; 13(1):1-3.