



The Effects of Sphingosine-1-Phosphate on Physical Performance and on AMPK and Akt phosphorylation in the Skeletal Muscle of Mice

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Abstract

Here we sought to determine the effect of S1P administration on physical performance and on AMPK and Akt phosphorylation in the muscle of mice. Methods: Mice were divided in four groups: Wild-Type, Placebo, Exercise and Exercise plus intramuscular S1P during 3 consecutive days. Thereafter, the animals performed an incremental exercise test. Results: We demonstrate a relation between S1P and physical exercise in response to markers of mitochondrial biogenesis. Immunoblotting analysis showed an increase in phosphorylation of AMPK and AKT in response to S1P administration. The placebo group ran significantly less in comparison to S1P and Exercised groups. Conclusions: These preliminary findings suggest that physical exercise and S1P may enhance oxidative metabolism in the skeletal muscle and performance in mice.

Key words: Sphingosine-1-Phosphate, Physical Exercise, Mitochondrial Biogenesis.

Introduction

Background: Sphingosine-1-phosphate (S1P) is a potent bioactive lipid, and has recently emerged as a key player in skeletal muscle metabolism, through actions to specific kinases (SKs) and receptors (S1PRs). Although the literature demonstrated beneficial effects of S1P metabolism in skeletal muscle regeneration, cellular growth, resistance to fatigue and directly responses in physical exercise, the effects of S1P administration in comparison to physical exercise into metabolic pathways, including AMPK and Akt, remain to be elucidated.

Therefore, since exercise promotes several benefits in mitochondrial function and S1P promotes benefits in Ca²⁺ release and resistance to fatigue, we aimed to investigate the effects of short-term of S1P intramuscular (i.m) administration, in physical performance and AMPK and Akt phosphorylation.

Methods: 40 male mice were divided into groups: Wild-Type, Placebo, Stimulated and Exercise. After, they received for 3 days i.m. S1P-injections, vehicle or none. Then, animals performed an incremental exercise until exhaustion and after 18h they were euthanized (**figure 1**). We analyzed physiological and performance parameters of animals. Furthermore, we use immunoblotting to analyze protein content of mitochondrial biomarkers in skeletal muscles of animals.

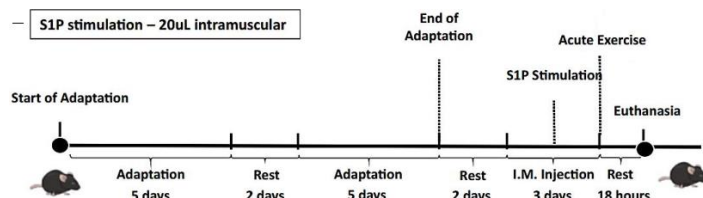


Figure 1. Experimental design. Rats were adapted to exercise for 2 weeks. After 3 days of intervention, they a Maximal Power Test (MPT) was performed until exhaustion. Animals were euthanized 18 h after acute exercise.

Results and Discussion

Figure 2 presents body weight in animals were not different after 3 days of S1P intervention, although a tendency in GS1P to lose weight. Regardless, basal lactate was measured between intervention groups and

demonstrated an increase tendency in lactate for GS1P related to other groups.

Placebo group ran less than other groups, which suggests that the injection of S1P or vehicle during 3 days may have damage skeletal muscle of animals. Also, although the damage caused by the intervention, GS1P shows to ran similar to GEX, suggesting a protective effect of S1P in skeletal muscle, or enhancements in resistance to fatigue, although damage caused.

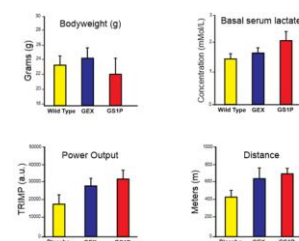


Figure 2. Physiological analysis of body weight (2A) and basal lactate concentrations (2B). In addition, performance results related to internal load (TRIMP; 2C) and external load (Distance, 2D). GEX – Group Exercised and GS1P Group Stimulated + Exercise. Statistical evaluated using one-way Anova and Turkey t-test.

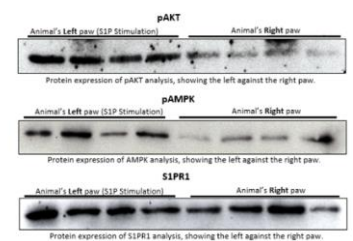


Figure 3. Western Blotting analysis of S1P receptor 1 (S1PR1), pAKT and pAMPK. Samples were for left (stimulated) vs right (control) paw for animals. (n = 4).

In these preliminary analysis, we observed that S1P administration induced pAKT and pAMPK in the skeletal muscle of mice (**figure 3**). However, S1P administration did not change the S1PR1 expression (**figure 3**).

Conclusions

These preliminary findings suggest that physical exercise and S1P may enhance oxidative metabolism in the skeletal muscle and performance in mice.

Acknowledgement

We would like to thank FAPESP and CNPq for the financial support and grants for this project