SHORT-TERM STRENGTH TRAINING INCREASES CLUSTERIN RECEPTOR LEVELS AND IMPROVES INSULIN SIGNALING IN SKELETAL MUSCLE OF OBESE MICE

Chadi Pellegrini Anaruma [1]
Rodrigo Pereira Martins [2]
Kellen Cristina da Cruz Rodrigues [3]
Diego Gomes de Melo [4]
Thaís Dantis Pereira de Campos [5]
Leandro Pereira de Moura [6]

Introduction: Recently related to insulin signaling, clusterin (CLU) protein, a hepatokine, can be found in several tissues as well in serum. In skeletal muscle, CLU acts via its receptor LRP2, participating in ~50% of insulin signaling cascade. It is known that physical exercise plays a positive role in insulin pathway. However, the effect of exercise on CLU levels remains unknown. **Objective:** We investigated the effect of short-term strength training (STT) in glucose homeostasis and muscular CLU and LRP2 in obese mice. **Methods:** Study protocol was approved by ethics committee nº 4773-1/2018. Swiss mice were divided into 3 groups: CTS (n=12): fed with chow diet and; OBS (n=12) and OBF (n=12): fed with high fat diet (60% Kcal fat), for 14 weeks. The OBF group underwent a STT, which consisted of 20 climbing on stairs at 75% of their maximum voluntary carrying capacity for seven consecutive days. Mice were euthanized and skeletal muscle (gastrocnemius) was excised for protein content and mRNA analysis. Data are presented as mean±S.E.M., ANOVA one-way followed by Tukey post hoc test were used for comparisons between groups. Correlation coefficients were calculated using Pearson or Spearman's test and $p<0.05$ was considered statistically significant. **Results:** Obese mice presented worsened glucose homeostasis and insulin signaling compared with CTS, which was improved by the STT. Fasting blood glucose levels were increased in OBS compared with CTS as well as serum insulin and the STT was efficient in improving both parameters, but no changes were found in HOMA-IR. During the ipITT, OBF group presented reduction in AUC and blood glucose decay was improved by 62%, when insulin-stimulated. No differences were found in muscle CLU protein content and gene expression between groups, however, the STT was able to increase LRP2 protein levels in skeletal muscle as well as AKT phosphorylation. CLU protein levels

[1]Ph.D. in Movement Sciences at Sao Paulo State University (UNESP) – SP, chadi.anaruma@hotmail.com;
[2]Ph.D. student in Science of Nutrition, Sports and Metabolism at School at Applied Sciences, University of Campinas - SP, rodrigo_mpereira@hotmail.com;
[3]Ph.D. student in Science of Nutrition, Sports and Metabolism at School at Applied Sciences, University of Campinas - SP, kellen.rodrigues.nut@gmail.com;
[4]Ph.D. student in Science of Nutrition, Sports and Metabolism at School at Applied Sciences, University of Campinas - SP, diego.fca.unicamp@gmail.com;
[5]Ph.D. student in Science of Nutrition, Sports and Metabolism at School at Applied Sciences, University of Campinas - SP, thais.dantis@outlook.com;
[6]Advisor professor: Ph.D. Professor at Applied Sciences, University of Campinas – SP, mouralp@unicamp.br

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positively correlated with physiological parameters, among them, serum insulin (r=0.60; p=0.02) and HOMA-IR (r=0.67; p=0.008). **Conclusion:** According to presented data, we concluded that the STT was able to improve insulin signaling in obese mice skeletal muscle regardless of body weight changes, also, CLU plays an important role on glucose homeostasis due to its positive correlation with several physiological parameters and can be modulated by insulin stimulus. Additionally, we are the first study to show the effect of the short-term strength training in skeletal muscle in CLU levels, unveiling new mechanisms by which the exercise can improve insulin signaling, working as an important non-pharmacological tool in the management of diabetes.