Int J Sport Nutr Exerc Metab. 2020 May 25;1-8. doi: 10.1123/ijsnem.2019-0337.
Online ahead of print.

Adaptations in GLUT4 Expression in Response to Exercise Detraining Linked to Downregulation of Insulin-Dependent Pathways in Cardiac but not in Skeletal Muscle Tissue

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PMID: 32454459 DOI: 10.1123/ijsnem.2019-0337

Abstract

Insulin resistance is associated with cardiometabolic risk factors, and exercise training can improve insulin-mediated glucose uptake. However, few studies have demonstrated the reversibility of exercise-induced benefits. Thus, the authors examine the time-response effects of exercise training and detraining on glucose transporter 4 (GLUT4) content, insulin-dependent and insulin-independent pathways in cardiac and gastrocnemius muscle tissues of spontaneously hypertensive rats. Thirty-two male spontaneously hypertensive rats, 4 months old, were assigned to (n = 8/group): T (exercise training: 10-week treadmill exercise, 50-70% maximum effort capacity, 1 hr/day, 5 days/week); D2 (exercise training + 2-day detraining), D4 (exercise training + 4-day detraining); and S (no exercise). The authors evaluated insulin resistance, maximum effort capacity, GLUT4 content, p-IRS-1Tyr1179, p-AS160Ser588, p-AMPKα1Thr172, and p-CaMKIIThr286 in cardiac and gastrocnemius muscle tissues (Western blot). In response to exercise training, there were improvements in insulin resistance (15.4%; p = .010), increased GLUT4 content (microsomal, 29.4%; p = .012; plasma membrane, 27.1%; p < .001), p-IRS-1 (42.2%; p < .001), p-AS160 (60.0%; p < .001) in cardiac tissue, and increased GLUT4 content (microsomal, 29.4%; p = .009; plasma membrane, 55.5%; p < .001), p-IRS-1 (28.1%; p = .018), p-AS160 (76.0%; p < .001), p-AMPK-α1 (37.5%; p = .026), and p-CaMKII (30.0%; p = .040) in the gastrocnemius tissue. In D4 group, the exercise-induced increase in GLUT4 was reversed (plasma membrane, -21.3%; p = .027), p-IRS1 (-37.1%; p = .008), and p-AS160 (-82.6%; p < .001) in the cardiac tissue; p-AS160 expression (-35.7%; p = .034) was reduced in the gastrocnemius. In conclusion, the cardiac tissue is more susceptible to exercise adaptations in the GLUT4 content and signaling pathways than the gastrocnemius muscle. This finding may be explained by particular characteristics of insulin-dependent and insulin-independent pathways in the muscle tissues studied.

Keywords: exercise training; insulin resistance; insulin-dependent signaling; insulin-independent pathways.

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