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Intracellular signaling in human skeletal muscle following different modes of exercise

AKADEMISK AVHANDLING

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ABSTRACT

Resistance and endurance exercise when performed regularly will cause specific adaptations in human skeletal muscle. Resistance exercise is known to increase strength and muscle mass while endurance training increases vascularisation and mitochondrial density which results in enhanced oxidative capacity. To understand how these adaptations occur, it is important to examine the molecular signaling events in muscle. The Akt-mTOR pathway has been shown to have an important function in the stimulation of protein synthesis.

This pathway is stimulated following resistance exercise in human muscle. During the work included in this thesis it has become clear that endurance exercise also stimulates Akt-mTOR signaling in human skeletal muscle. Study (I) revealed an increased phosphorylation of mTOR, Akt and GSK3 and a marked decrease in eEF2 phosphorylation indicating a stimulatory response on elongation and initiation of protein synthesis in the early recovery phase. Furthermore, as shown in study (II), this stimulatory response is followed by an increase in the fractional synthetic rate (FSR), which was progressively increased when measured up to 3 h following endurance exercise.

It is usually recommended that resistance exercise is performed 2-3 times per week. In study (III), markers for anabolic (Akt, mTOR, p70S6k, rpS6, eEF2 and GSK-3 β) as well as catabolic (MAFbx and MuRF-1) processes were investigated following two sessions of resistance exercise separated by 48 hours. From this study it appears that anabolic signaling is slightly enhanced following the second exercise session, and furthermore, the changes in gene expression related to muscle protein degradation (MAFbx and MuRF-1) is attenuated during the second exercise session.

Endurance exercise can compromise the adaptive response of strength training. On the other hand, there is some evidence suggesting that combining endurance training with resistance exercise may have beneficial effects on endurance exercise performance. The final study was designed to evaluate whether resistance exercise can enhance the muscle adaptive response to endurance exercise with respect to molecular signaling related to increased protein synthesis and specific markers for mitochondrial biogenesis. An enhanced signaling response was actually found in the combined exercise protocol. Specifically, expression of genes related to increased mitochondrial biogenesis and oxidative metabolism (PGC-1 α , PRC and PDK-4 mRNA) as well markers for anabolic signaling (mTOR, p70S6k), was enhanced when endurance exercise was followed by a session of heavy resistance exercise. This data support the notion that including resistance exercise in endurance training may be beneficial.

In summary, mixed muscle FSR is gradually increased following endurance exercise when measured during the first 3 h of recovery and this increase is accompanied by stimulation of mTOR signaling. Resistance exercise enhances effects on anabolic signaling and attenuates expression of genes involved in muscle protein breakdown and inhibition of muscle growth during a second exercise session performed two days after the first. Finally, combining endurance and heavy resistance exercise can enhance acute adaptive responses and indicates that combined exercise may be superior to endurance exercise alone.