Partial or Complete Unloading of Skeletal Muscle Leads to Specific Alterations of Anabolic Signal Transduction.

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ABSTRACT

Consequences of disuse atrophy of skeletal muscle observed during spaceflight on astronaut health and performance are a focal point of space research. Decrements of both muscle mass and protein synthesis rates have been observed with exposure to varying muscle loading environments (1G > partial loading > 0G), and most of the reduced muscle mass can be attributed to diminished rates of synthesis. However, specific mechanisms behind unloading-dependent reductions of protein synthesis are not well defined.

PURPOSE: To determine whether or not alterations of anabolic signal transduction was responsible for the changes previously observed in fractional synthesis rates with specific gravitational loading paradigms. METHODS: Female BALB/cByJ were normalized by bodyweight and assigned to normal cage ambulation (1G), partial weight bearing suspension titrated to approximately 33% bodyweight (G/3), partial weight bearing titrated to 16% bodyweight (G/6) and full unloading of hind limbs (0G) in specially designed cages. All mice were subjected to that loading environment for 21d prior to tissue harvest, and monitored daily. Immunoblotting of the gastrocnemius (n=23) was carried out to analyze alterations of anabolic signal transduction. Although numerous signaling intermediates were assessed, the focus of this abstract will be on ribosomal protein S6 kinase (p70-S6K). This important protein has served as a marker of protein synthesis signal transduction as well as the anabolic capacity in skeletal muscle. RESULTS: Regardless of loading paradigm, no differences were detected among groups for the activation of p70-S6K (as indicated by the phospho: total protein content). Total protein content, however, was ~27% lower than control in 0G and G/3 (P=0.008) with G/6 not being different from control (P>0.05). CONCLUSION: In combination with previous data (unpublished observations), Partial gravitational fields at least partially rescues anabolic signaling, suggesting that a threshold level of stimulus is necessary to maintain anabolic capacity in muscle. These results may have important implications towards the development of strategies designed to counter the effects of partial/complete unloading on skeletal muscle based on how the anabolic capacity of muscle is affected.