

Decrements of Muscle Protein Synthesis with Unloading are Not Due to Insufficient Concentrations of Intramuscular Leucine

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Skeletal muscle mass and strength play critical roles in quality of life, and significant muscle atrophy contributes to reduced function and can exacerbate some disease states. It is well-known that persistent reductions of mechanical loading in skeletal muscle result in degeneration. Generally, reductions of muscle protein synthesis are, at least in part, a major culprit with muscle loss under these conditions, and numerous countermeasures such as exercise and nutritional supplements, known to stimulate protein synthesis have been designed to maintain muscle mass under those conditions. Amino acid supplementation, particularly with branched-chain amino acids (BCAAs), has been suggested as a countermeasure to deter muscle loss during spaceflight and bed rest, suggesting that these important protein precursors are not sufficiently available to support muscle protein synthesis during mechanical unloading. The purpose of this study was to examine the effect of muscle loading/unloading on the free amino acid pool of skeletal muscle in order to determine if concomitant alterations of the amino acid availability impact known changes in muscle protein synthesis under these conditions. We hypothesized reduced protein synthesis during periods of chronic unloading would be due to rate-limiting concentrations of one or more amino acids in the cytosolic free pool. Specific amino acid concentrations of 29 amino acids commonly found in the skeletal muscle cytosolic free-pool were assessed with high-performance liquid chromatography (HPLC) in gastrocnemius muscles taken from male Sprague Dawley rats that were assigned to various hindlimb unloading groups or ambulatory controls, with and without exercise countermeasures. Of the 29 amino acids tested, only one amino acid (nonessential aspartic acid) displayed an instance of concentrations significantly below control values ($p \leq 0.05$). Surprisingly, each of the BCAAs, known agonists of muscle protein synthesis, displayed significant elevations in free-pool concentrations in unloaded muscle, even though muscle protein synthesis, and ultimately muscle mass were diminished. Leucine, a potent stimulant of muscle protein synthesis was over two times higher than the leucine concentrations of control muscles, suggesting that leucine was not sufficient to stimulate protein synthesis under conditions of microgravity. It also indicates that amino acid supplementation as a countermeasure may be ineffective, as circulating levels of available BCAAs are already elevated. These results suggest that additional efforts are required to find a suitable defense against muscle atrophy due to mechanical unloading.