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TIME-COURSE CHANGES IN SIGNALING ACTIVITIES ASSOCIATED WITH MUSCLE ATROPHY  
DURING HINDLIMB UNLOADING

**Abstract**

Muscle atrophy is an inevitable incidence caused by weightlessness in space microgravity. Its consequence, however, brings about significant reduction in work capacity which may impair space mission, if extended for weeks. The aim of the current study was to elucidate a precise time-course changes in signaling activities associated with protein synthesis and proteolysis in the Sprague-Dawely rat soleus muscle at 0 d (vivarium control), 1 d, 3 d, 7 d, and 14 d of hindlimb suspension (HS). Relative muscle mass to body mass did not statistically differ between 0 d and 7 d, but decreased (-36%) significantly at 14 d of unloading ( $P < 0.05$ ). Immunoblot analysis on the whole-tissue lysates revealed that the anabolic signaling markers (p-Akt1 and p-mTOR) were only slightly downregulated during the 2-wk unloading while phosphorylation state of FoxO1 decreased 50% at 7 d – 14 d unloading. The levels of ubiquitin E3 ligases (atrogin-1, MuRF1), calpain 1, caspase-3, and autophagy-related LC3-II/LC3-I increased 2.0- to 5.4-fold at 14 d compared to those at 0 d. These data suggest that the significant wasting of the soleus muscle required an HS period at least longer than 7 d, mainly with the upregulated proteolysis rather than the downregulated anabolic activities.