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L-ARGININE ADMINISTRATION AS A POSSIBLE COUNTERMEASURE PREVENTING FUNCTIONAL AND BIOCHEMICAL CONSEQUENCES OF MUSCLE DETRAINING IN MICROGRAVITY

Abstract

For the last several years data were accumulated about protective, corrective, and stimulating activity of NO in the complex signaling orchestra of a functioning muscle fiber. It is known that NO is involved in calpain inhibition, enhancement of anabolic signaling and AMPK-dependent energy metabolism regulation, control of slow myosin mRNA expression and satellite cells activation. Since most of the mentioned functions are known to be impaired in real or simulated microgravity, the administration of L-arginine, the well-known NO predecessor, could be useful in spaceflight practice. We performed several rat studies in order to reveal the signaling and functional consequences of the L-arginine administration during exposure to simulated microgravity (tail-suspension model). First of all we established that the NO content in m. soleus during 14-Day unloading dramatically decreased (60%). The L-arginine administration brought about to dystrophin, titin and nebulin preserving in m. soleus after unloading. Moreover, administration of NO predecessor prevented growth of expression level of genes of E3-ubiquitine ligases (atrogin-1/MAFbx, MuRF-1) during functional unloading. In our study with NO predecessor L-arginine administration during functional unloading of muscles we did not observe loss of HSP90 content in the group administered with L-arginine in contrast to the pure unloading group. We cannot exclude, that decrease of soleus atrophy level in this group could be the result of HSP90 protection of muscle proteins from proteasome degradation. Functional unloading is known to stimulate expression of the fast isoforms of myosin heavy chains (MHC) leading to changes in soleus contractile properties. Unexpectedly, in our study we found, that L-arginine administration prevented also decrease of type I MHC expression level

in soleus. Thus, nNOS activity can regulate contractile proteins expression as well. We also studied the effect of L-arginine administration in rats subjected to unloading and treadmill running training (20 min/day, 3 bouts with the speed 40 m/min). We found that the hindlimb extensor maximal voluntary strength in L-arginine fed and exercised animals did not differ from the control levels (in contrast to the decreased level in pure unloading group). Thus the L-arginine administration could be considered as the possible countermeasure means against leg muscle detraining in spaceflight. The study was supported by the RAS Presidium Program "Basic studies for the new technologies in medicine"