ЖУРНАЛ ЭВОЛЮЦИОННОЙ БИОХИМИИ И ФИЗИОЛОГИИ, 2020, том 56, № 7, с. 743

## МАТЕРИАЛЫ КОНФЕРЕНЦИИ И ШКОЛЫ

# METABOLISM AND EFFECTS OF SKELETAL MUSCLE SPHINGOLIPIDS IN FUNCTIONAL UNLOADING

**© 2020 г. I. G. Bryndina[1,*], M. N. Shalagina[1], V. A. Protopopov[1], A. V. Sekunov[1], and A. A. Yakovlev[1]**

*[1] FSBEI HE "Izhevsk State Medical Academy", Izhevsk, Russia*

**e-mail: i_bryndina@mail.ru*

**DOI:** 10.31857/S0044452920071572

It is known that sphingolipids (including ceramide – Cer) can act intracellularly as secondary messengers that regulate a number of intracellular processes, such as cell death due to apoptosis, necrosis and necroptosis, autophagy and mitophagy, prooxidant activity, insulin resistance, cytoskeleton rearrangement, and others (Hannun, Obeid, 2017). The role of bioactive sphingolipids in the development of skeletal muscle atrophy and dysfunction during functional unloading is not fully understood, so the study in this area has become the aim of our work. The experiments were performed in male Wistar rats and C57Bl/6 mice. The unloading of the hind limb muscles lasting from 6–12 hours to 30 days was simulated by hindlimb suspension (HS) according to Ilyin-Novikov method. Some groups of the suspended animals were treated with the inhibitors of acid or neutral sphingomyelinases. We have found that HS of different durations is accompanied by an increase in Cer production in m. soleus, and this is characteristic for both the earliest stages (6–12 hours), and more long periods of HS (14, 30 days). The leading mechanism of Cer accumulation is not the de novo synthesis (an increase in SPT expression was not found), but sphingomyelinase hydrolysis. In muscles of animals subjected to HS, clomipramine (aSMase inhibitor) reduces the expression of the components of prooxidant complex (NOX2) and the activity of apoptosis-inducing signaling, attenuates the changes in membrane glucose and amino acids transporters (GLUT4, SNAT2), and also affects the regulator of protein synthesis (mTORC1 system). Special changes have been found in the membranes of muscle fibers. HS is accompanied by the formation of Cer-enriched membrane microdomains; the effect is partially prevented by clomipramine (Bryndina et al., 2018). We have established that the previously described phenomenon of lipid raft destabilization due to short-term muscle unloading (Petrov et al., 2017) may be associated with the effects of activated sphingomyelinase and subsequent accumulation of Cer in sarcolemma (Bryndina et al., 2018, Petrov et al., 2019). In experiments with HS, clomipramine influenced both planar and caveolar rafts, and also affected the submembrane cytoskeleton of muscle fibers. It is important to note that this inhibitor reduced the degree of HS-induced muscle atrophy.

Supported by RSF 16-15-10220.