The Effects of Physical Inactivity on Neuromuscular Electrical Stimulation–Induced mTOR and MAPK Signaling Activation in Rat Skeletal Muscle

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Purpose: We recently confirmed that physical inactivity prior to hind limb unloading accelerated disuse-induced skeletal muscle atrophy through proteolytic signaling transducers up regulation. However, it is unknown that physical inactivity affects the protein synthesis–related signaling such as mTOR and MAPK pathways in response to muscle contraction. Therefore, the aim of this study was to investigate whether physical inactivity blunts muscle contraction–induced mTOR and MAPK signaling activation in rat skeletal muscle.

Methods: Twelve 4-week-old male Wistar rats were assigned randomly into control (CT, n = 6) or physical inactivity (IN, n = 6) groups. Rats in the IN group were housed in narrow cages with half of the usual floor space for 10 weeks to limit their range of movement. After 10 weeks, the lateral gastrocnemius muscles of both groups were electrically stimulated at 100 Hz frequency (pulse duration, 1 ms; duty cycle, 3 s on/6 s off) under anesthesia with isoflurane. The individual stimulation intensity was determined by progressively increasing the stimulus intensity (mA) until there was no further peak twitch force increase. After the stimulation, gastrocnemius muscles were removed and the phosphorylation levels of the mTOR and MAPK signaling pathways were determined by using western blotting.

Results: The phosphorylation levels of Akt at Thr473 and its downstream target S6K1 at Thr389 have significantly increased in the CT and IN groups after NMES in comparison with each control leg. In addition, the phosphorylation of ERK1/2 at Thr202/Tyr204 and its downstream target S6K1 at Thr421/Ser424 have significantly increased in the CT and IN groups after NMES. However, there was no significant difference in these phosphorylation levels between the CT and IN groups.

Conclusion: Physical inactivity has not blunted muscle contraction–induced mTOR and MAPK signaling activation in rat skeletal muscle.

Key words: muscle hypertrophy, electromyostimulation