SWACSM Abstract

Stimulated Muscle Contractions Regulate Membrane-Bound and Soluble TLR4 to Prevent LPS-Induced Signaling and Myotube Atrophy in Skeletal Muscle Cells

JEREMY B. DUCHARME, ZACHARY J. FENNEL, ZACHARY J. MCKENNA, QUINT N. BERKEMEIER, & MICHAEL R. DEYHLE

Exercise Physiology Laboratory; Department of Health, Exercise, and Sports Sciences; University of New Mexico; Albuquerque, NM.

Category: Doctoral

Advisor / Mentor: Deyhle, Michael (mdeyhle@unm.edu)

ABSTRACT

Toll-like receptor 4 (TLR4) activation by lipopolysaccharides (LPS) contributes to chronic inflammation and causes upregulation of muscle atrophy signaling pathways. Exercise can suppress LPS/TLR4 axis activation by reducing the expression of TLR4 on immune cells. It is unknown how this regulation occurs, and it is not clear how exercise affects TLR4 on skeletal muscle. **PURPOSE:** To uncover the nature and mechanisms by which exercise affects TLR4 expression and intracellular signaling using cell culture models and human experiments. **METHODS:** C2C12 myotubes were subjected to electrical pulse stimulation (EPS) with and without subsequent treatment with 500 ng/mL lipopolysaccharide (LPS) along with corresponding control conditions. To investigate the effect of muscle contraction on the regulation of TLR4 *in-vivo*, we analyzed PBMC and serum samples from eight recreationally active men that completed 60-minutes of cycling at a moderate intensity (65% of VO_2max). **RESULTS:** *In-vitro*, LPS decreased membrane-bound TLR4, increased TLR4 signaling (decreased inhibitor of κBα), and induced myotube atrophy. However, stimulated muscle contractions decreased membrane-bound TLR4, increased soluble TLR4 (sTLR4), and prevented LPS-induced signaling and myotube atrophy. In human participants, a single bout of moderate-intensity exercise decreased membrane-bound TLR4 on PBMCs and increased serum-borne sTLR4. **CONCLUSION:** These experiments support exercise may exert a novel anti-catabolic/ anti-inflammatory effect by increasing sTLR4 and decreasing TLR4 expressed on the muscle membrane. These results could help improve interventions for conditions associated with TLR4-mediated inflammation and muscle atrophy, such as diabetes, sarcopenia, and cancer cachexia.