Redox modulation of contractile function in skeletal muscle

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For the last half century, scientists have studied the biological importance of free radicals in respiratory and limb muscles. We now know that muscle fibers continually produce both reactive oxygen species (ROS) and nitric oxide (NO) and that both cascades play critical roles in contractile regulation. Under basal conditions, muscle-derived ROS and NO exert opposing effects. Low-level ROS activity is an essential part of the homeostatic milieu and is required for normal force production whereas NO derivatives function as a brake on the system, limiting force. The modulatory effects of ROS and NO are disrupted by conditions that exaggerate production including mechanical unloading, inflammatory disease, and strenuous exercise. Marked increases in ROS or NO levels cause contractile dysfunction, resulting in muscle weakness and fatigue. Loss of force may reflect alterations in intracellular calcium regulation or myofilament function, processes controlled by redox-sensitive regulatory proteins. These principles provide a foundation for ongoing research to identify the mechanisms of ROS and NO action and develop interventions that protect muscle function.

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