OPEN ACCESS Freely available online

Anatomy & Physiology: Current Research

Short Communication

Cellular Mechanisms of Skeletal Muscle Fatigue and Recovery

Camila Torres*

Department of Functional Anatomy, University of Health Sciences of Bogotá, Bogotá, Capital District, Colombia

DESCRIPTION

Skeletal muscle fatigue represents a reversible reduction in force generating capacity that develops during prolonged or high-intensity muscular activity [1]. It serves as a protective physiological mechanism that limits excessive tissue damage while preserving cellular integrity. Rather than resulting from a single cause, fatigue reflects the interaction of multiple biochemical and physiological processes occurring within skeletal muscle fibers and the nervous system. One of the earliest contributors to muscle fatigue is metabolic disturbance. During repeated muscle contraction, Adenosine Triphosphate (ATP) is rapidly consumed to support cross bridge cycling and ion transport. Although ATP concentrations remain relatively stable under most physiological conditions, the accumulation of inorganic Phosphate (Pi), Hydrogen ions (H), Adenosine Diphosphate (ADP) and other metabolic byproducts impairs contractile protein interactions and calcium sensitivity, reducing force production [2].

These metabolic changes also alter intracellular pH and enzyme activity, contributing to transient declines in muscular performance. Mitochondria play a central role in both fatigue development and recovery. As the primary source of aerobic ATP production, mitochondria sustain prolonged muscular activity through oxidative phosphorylation. However, excessive metabolic demand increases the generation of reactive oxygen species (ROS), which at physiological concentrations function as signaling molecules but, when produced excessively, contribute to oxidative stress and impaired contractile function [3]. Mitochondrial dysfunction has therefore become an important focus of fatigue research, particularly in aging, chronic disease and overtraining syndromes. Calcium regulation is another critical determinant of muscle performance. Efficient excitation contraction coupling depends on the controlled release and reuptake of calcium ions by the sarcoplasmic reticulum.

During sustained exercise, impaired calcium release, altered ryanodine receptor function and reduced calcium sensitivity of contractile proteins contribute to diminished force generation [4]. These changes are generally reversible following adequate recovery but may become prolonged in pathological conditions.

Neuromuscular factors also influence skeletal muscle fatigue. Central fatigue arises when the central nervous system reduces motor neuron activation, limiting recruitment of muscle fibers despite preserved muscular capacity [5].

Neurotransmitter depletion, altered cortical excitability and sensory feedback from fatigued muscles collectively contribute to this protective mechanism. Consequently, skeletal muscle fatigue should be viewed as the result of integrated peripheral and central physiological regulation rather than isolated muscular dysfunction. Recovery begins immediately after exercise through restoration of metabolic homeostasis and activation of cellular repair pathways. Replenishment of ATP and phosphocreatine stores, normalization of intracellular ion concentrations, and removal of accumulated metabolites occur rapidly under appropriate physiological conditions [6]. Simultaneously, blood flow increases to facilitate oxygen delivery and metabolic waste clearance, supporting tissue recovery and reducing residual fatigue.

Inflammation plays a dual role during muscle recovery. Acute inflammatory responses recruit neutrophils and macrophages that remove damaged cellular components while releasing cytokines and growth factors necessary for tissue regeneration [7]. Although excessive inflammation may delay recovery, controlled inflammatory signaling is essential for effective muscle repair.

This evolving understanding has shifted therapeutic strategies toward optimizing rather than completely suppressing post exercise inflammatory responses. Satellite cells are indispensable for skeletal muscle regeneration. These resident muscle stem cells become activated following mechanical stress or injury, proliferate, differentiate into myoblasts and fuse with existing muscle fibers to restore structural integrity [8].

Growth factors such as Insulin like Growth Factor-1 (IGF-1) and Hepatocyte Growth Factor (HGF) regulate satellite cell activity while stimulating protein synthesis and muscle hypertrophy [9]. These regenerative mechanisms contribute to long term improvements in muscle strength and adaptation following repeated exercise [10]. Technological advances have significantly improved the study of muscle physiology.

Correspondence to: Camila Torres, Department of Functional Anatomy, University of Health Sciences of Bogotá, Bogotá, Capital District, Colombia, E-mail: camila.torres@uhsb.edu.co

Received: 02-May-2025, Manuscript No. APCR-25-43595; **Editor assigned:** 05-May-2025, PreQC No. APCR-25-43595 (PQ); **Reviewed:** 19-May-2025, QC No. APCR-25-43595; **Revised:** 26-May-2025, Manuscript No. APCR-25-43595 (R); **Published:** 02-Jun-2025, DOI: 10.35248/2161-0940.25.15.551

Citation: Torres C (2025). Cellular Mechanisms of Skeletal Muscle Fatigue and Recovery. Anat Physiol. 15:551.

Copyright: © 2025 Torres C. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

CONCLUSION

In conclusion, skeletal muscle fatigue and recovery are complex physiological processes involving metabolic changes, mitochondrial function, calcium regulation, neuromuscular activity, inflammation, and cellular regeneration. Understanding these interconnected mechanisms provides valuable insights into how muscles respond to physical stress, restore their functional capacity, and adapt to repeated exercise. Advances in muscle physiology research and emerging technologies are further improving the assessment of fatigue, recovery, and muscle performance. Adequate rest, appropriate nutrition, and individualized exercise programs are essential for supporting effective recovery and reducing the risk of excessive fatigue and injury. Ultimately, continued research into the molecular and physiological mechanisms of skeletal muscle fatigue will contribute to improved athletic performance, rehabilitation strategies, and the management of muscle dysfunction associated with aging and chronic diseases.

REFERENCES

1. Dey S, DeMazumder D, Sidor A, Foster DB, O'Rourke B. Mitochondrial ROS drive sudden cardiac death and chronic proteome remodeling in heart failure. Circ Res.2018;123(3):356-371.
2. J.J. Rayner et al.Myocardial energetics in obesity: enhanced atp delivery through creatine kinase with blunted stress Circulation. 2020.
3. Murashige D, Jang C, Neinast M, Edwards JJ, Cowan A, Hyman MC, et al. Comprehensive quantification of fuel use by the failing and nonfailing human heart. Science. 2020;370:364-368.
4. Dávila-Román VG, Vedala G, Herrero P, De Las Fuentes L, Rogers JG, Kelly DP, et al. Altered myocardial fatty acid and glucose metabolism in idiopathic dilated cardiomyopathy. J Am Coll Cardiol. 2002;40:271-277.
5. Wilkens MR, Nelson CD, Hernandez LL, McArt JAA. Symposium review: Transition cow calcium homeostasis-Health effects of hypocalcemia and strategies for prevention. J Dairy Sci. 2020;103(3): 2909-2927.
6. Manuelian CL, Penasa M, Visentin G, Zidi A, Cassandro M, De Marchi M. Mineral composition of cow milk from multibreed herds. Anim Sci. 2018.
7. Goff JP. The monitoring, prevention, and treatment of milk fever and subclinical hypocalcemia in dairy cows. Vet J. 2008;176(1):50-57.
8. Neves RC, Leno BM, Bach KD, McArt JAA. Epidemiology of subclinical hypocalcemia in early-lactation Holstein dairy cows: The temporal associations of plasma calcium concentration in the first 4 days in milk with disease and milk production. J Dairy Sci. 2018;101(10):9321-9331.
9. Leno BM, Martens EM, Felippe MJB, Zanzalari KP, Lawrence JC, Overton TR. Short communication: Relationship between methods for measurement of serum electrolytes and the relationship between ionized and total calcium and neutrophil oxidative burst activity in early postpartum dairy cows.J Dairy Sci 2017;100(11):9285-9293.
10. Caixeta LS, Ospina PA, Capel MB, Nydam DV. Association between subclinical hypocalcemia in the first 3 days of lactation and reproductive performance of dairy cows. Theriogenology.2017;94:1-7.