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Skeletal Muscle Mitochondrial Adaptations to Varying Exercise Intensities

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Abstract:
Introduction: Mitochondria play a vital role in skeletal muscle function, and their adaptations to exercise are regulated by key proteins like PGC-1α (mitochondrial biogenesis) and mTOR (muscle hypertrophy). Varying training modalities, including endurance, HIIT, resistance, and concurrent training, induce distinct mitochondrial changes.
Methods: A literature review was conducted using PubMed to identify human studies published after 2014 on exercise-induced mitochondrial adaptations. The accepted articles focussed on different training intensities and their effects on the skeletal muscle mitochondria.
Results: Endurance and HIIT training enhance mitochondrial biogenesis and efficiency, increasing oxidative capacity and mitochondrial density. Resistance training improves mitochondrial function to support muscle growth, though its effects on mitochondrial biogenesis are less pronounced. Concurrent training, combining endurance and resistance training, optimizes both mitochondrial adaptations and muscle hypertrophy by activating both PGC-1α and mTOR pathways.
Discussion: Exercise intensity and modality-specific adaptations are regulated by the interaction of PGC-1α and mTOR pathways, with mitochondrial fusion and fission enzymes playing a crucial role in maintaining mitochondrial function. Endurance and HIIT training focus on mitochondrial function, while resistance training primarily addresses muscle hypertrophy. Concurrent training optimally stimulates both PGC-1α and mTOR pathways, offering synergistic benefits for mitochondrial and muscle adaptations. Due to individual variability in response to exercise stimuli, personalized training approaches are crucial for maximal athletic performance.
Conclusion: Mitochondrial adaptations depend on exercise type and intensity. Concurrent training provides a promising strategy to maximize both mitochondrial function and muscle growth. Future research should explore optimal training sequencing and molecular mechanisms to refine personalized exercise programs.

Keywords: mitochondria; PGC-1α; mTOR; mitochondrial biogenesis; mitochondrial dynamics; oxidative phosphorylation; endurance training; high-intensity interval training; resistance training; concurrent training

Introduction

Mitochondria are essential for skeletal muscle function, serving as the primary sites of energy production and playing a central role in the muscle's adaptation to exercise [1]. These adaptations are tightly regulated by key proteins, particularly the peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) and the mammalian target of rapamycin (mTOR) [2, 3]. PGC-1α in normal cells plays a crucial role in maintaining metabolic balance and protecting from chronic disease [2, 3]. In skeletal muscle, PGC-1α is a critical regulator of mitochondrial biogenesis, driving increases in mitochondrial content and enhancing oxidative capacity [3, 4]. The mTOR protein is responsible for cell growth and survival, immunity, and metabolism in normal cells [4]. In skeletal muscle, mTOR is primarily responsible for regulating muscle growth and strength in response to resistance training by stimulating protein synthesis and cellular growth [4]. In addition to these proteins, the activity of key enzymes such as Opa1, Mfn2, and Drp1 govern mitochondrial fission and fusion dynamics, which help maintain mitochondrial integrity, efficiency, and function [5, 6].

Various exercise modalities such as endurance training, high-intensity interval training (HIIT), resistance training, and concurrent training induce distinct mitochondrial adaptations. Endurance training and HIIT primarily enhance mitochondrial function, promoting greater oxidative phosphorylation efficiency and endurance capacity [7]. Resistance training, while focused on muscle hypertrophy, also improves mitochondrial efficiency during high-intensity activities [8, 9]. Concurrent training, which combines endurance and resistance exercises, offers a synergistic effect by enhancing both mitochondrial biogenesis and muscle growth through the interaction of

PGC-1α and mTOR [2, 3]. An integrated approach maximizes mitochondrial content, oxidative capacity, and muscle performance. This literature review aims to demonstrate the intricate relationship between exercise intensity, duration, and mitochondrial adaptation in skeletal muscle as a determinant in developing effective training regimens for both athletic performance enhancement and disease prevention.

Methods

To conduct this study, a search was conducted through the PubMed database using the key terms "mitochondria", "exercise", "skeletal muscle", "athletic performance", and "intensity". A further exclusion of "diet" was added to the PubMed search to differentiate between nutritional and exercise-induced mitochondrial adaptations. The search was restricted to human studies published after January 2014 (see Figure 1).

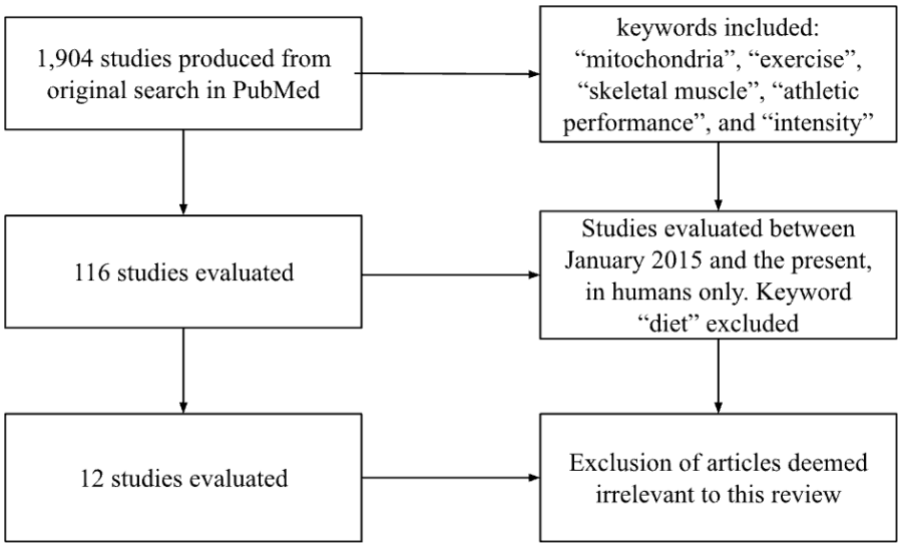

Figure 1. Search Strategy and Article Selection Process. This figure was created using Google Drawings.

Results

Endurance Training

Endurance training, characterized by prolonged submaximal efforts, is performed against a relatively low load over an extended period of time [6]. This training method significantly increases skeletal muscle mitochondrial abundance and capacity [10]. According to Lundby and Jacobs article, this adaptation primarily enhances intermyofibrillar mitochondrial density, where mitochondria reside in close proximity to the myofibrils and make up about 80% of the total mitochondrial content [11]. Increased mitochondrial content is linked to enhanced aerobic metabolism and improved fatty acid oxidation [11]. Additionally, endurance training promotes mitochondrial dynamics by increasing the expression of fusion proteins (Opa1 and Mfn2) and fission proteins (Drp1), essential for maintaining mitochondrial quality control [3, 6]. These processes facilitate the exchange of mitochondrial contents and the segregation of damaged components, promoting a healthy and functional mitochondrial population [6]. Booth et al. demonstrated increased mitochondrial concentration, resulting in increased fatty acid oxidation at a given submaximal workload [6]. The expression of DNM1L, the gene encoding Drp1, is upregulated both following acute exercise and chronic training, correlating with improved mitochondrial metabolism and exercise adaptations [4, 6].

High-Intensity Interval Training

HIIT training is described as reccurring short bursts of near-maximal activity [7]. HIIT enhances mitochondrial oxidative phosphorylation (OXPHOS) efficiency, which is crucial for ATP production during intense, repeated exercise efforts [5]. Fiorenza et al. demonstrated that this improvement was only experienced at high temperatures, such as those experienced during intense exercise [5]. This adaptation is driven by the high metabolic demand of HIIT, which challenges the mitochondria to improve their ability to sustain energy production under high-intensity conditions [5, 7]. Jacques et al. showed that performance markers, including Wpeak, Lactate Threshold, and VO2Peak significantly increased with response to HIIT, though there was significant variability in individual responses to training [7]. Like endurance training, HIIT increases the expression of mitochondrial fission (Drp1) and fusion (Mfn2) proteins, supporting mitochondrial dynamics and functional adaptation [4, 6, 7]. Additionally, HIIT promotes greater ATP transport from the mitochondria to the muscle cell, enhancing performance during brief bursts of intense activity [7].

Resistance Training

Resistance training is primarily associated with muscle hypertrophy, by working to overcome an external force

applied on the body, but it also impacts mitochondrial function in skeletal muscle [2]. Porter et al. showed an increase in coupled mitochondrial respiration in response to resistance training, particularly through the activity of complex I and II, which supports ATP generation during exercise [9]. This suggests an improvement in the muscle's capacity to produce ATP, not just for hypertrophy but also for energy demands associated with resistance training [8, 9]. These adaptations are specifically involved in electron transport and NAD production [9]. However, Zhao et al. demonstrated that resistance training does not consistently lead to significant increases in mitochondrial biogenesis across all studies [8]. While some studies have reported increased mitochondrial protein expression, others show little or no change in the key markers of mitochondrial biogenesis, such as PGC-1α or mitochondrial DNA [8, 12-15]. This suggests that the mitochondrial adaptations to resistance training may be more functional than structural in nature, or that they may be more variable depending on training protocols, muscle fiber type, and other individual factors.

Concurrent Training

Concurrent training, which combines endurance and resistance exercise, promotes skeletal muscle mitochondrial adaptations through the activation of both the PGC-1α and mTOR pathways according to Zhao et al. and Booth et al. [6, 8]. The PGC-1α pathway, a master regulator of mitochondrial biogenesis, is primarily activated by endurance training, while the mTOR pathway is crucial for muscle hypertrophy in response to resistance training [6, 8]. Interestingly, recent research suggests that mTOR may enhance PGC-1α signaling, facilitating mitochondrial biogenesis even in the presence of resistance training [8]. This combined activation of pathways likely contributes to the enhanced mitochondrial content and function observed with concurrent training.

Discussion

The literature review herein collectively highlights the integral role of mitochondria in mediating skeletal muscle adaptations to varying exercise intensities and durations. These adaptations are not a consequence of exercise, but rather an essential component of the muscle's response to the metabolic demands imposed by varying training stimuli.

Exercise Intensity and Mitochondrial Efficiency

There is a crucial link between exercise intensity and mitochondrial adaptations. High-intensity exercise, such as HIIT, specifically enhances OXPHOS efficiency at elevated temperatures, stimulating the conditions within intensely contracting muscles [5]. This suggests that HIIT induces adaptations specifically aimed at maximizing mitochondrial function under challenging metabolic conditions [4, 5]. The temperature-dependent adaptation suggests HIIT primes muscle mitochondria to function optimally in the conditions created by intense activity [5]. Conversely, while resistance training effectively improves mitochondrial respiratory capacity, it may not consistently elicit significant increases in mitochondrial biogenesis [8, 9]. Lundby et al. demonstrates a 2-fold increase in coupled mitochondrial respiration supported by complex I substrates, indicating improved respiratory capacity [11]. However, transcripts involved in mitochondrial biogenesis remained unchanged, suggesting that the improvements were primarily qualitative rather than quantitative [11]. This discrepancy underscores the distinct impact of varying intensities on mitochondrial adaptations, tailoring the muscle's metabolic responses to effectively meet the specific demands of each training modality.

Endurance Training and Mitochondrial Dynamics

The sources offer a nuanced perspective on the dynamic interplay between endurance training and skeletal muscle mitochondrial adaptations. Endurance training stimulates both mitochondrial fusion, the merging of mitochondrial facilitated proteins like Opa1 and Mfn2, and fission, the division of mitochondria regulated by Drp1 [4-6]. This coordinated response ensures a healthy and functional muscle mitochondrial population capable of meeting the energy demands of prolonged physical activity. Enhanced fusion allows for the exchange of mitochondrial components, effectively rejuvenating damaged mitochondria [5, 6, 16]. Concurrently, fission segregates damaged mitochondrial components, enabling their removal through mitophagy [5, 6]. This intricate balance between fission and fusion, finely tuned by endurance training, is crucial for maintaining mitochondrial quality control. Notably, Drp1 is highlighted as a pivotal player in exercise-related adaptations, suggesting that Drp1-mediated fission plays a direct role in optimizing muscle mitochondrial function [4]. It is suggested that this fine-tuning of mitochondrial dynamics contributes to improved ATP production, enhanced muscle endurance, and protection against muscle damage [4]. This interplay between mitochondrial dynamics and endurance training underscores the complexity of skeletal muscle adaptation and highlights the essential role of mitochondria in facilitating sustained physical activity.

Concurrent Training and Synergistic Adaptations

There is a compelling argument for the benefits of concurrent training, the combination of endurance and resistance training, in maximizing skeletal muscle mitochondrial adaptations. This synergistic effect challenges the traditional view that the mTOR pathway, activated by resistance training, and the PGC-1α pathway, stimulated by endurance training, are antagonistic [2, 3]. Rather, these pathways interact cooperatively to enhance mitochondrial biogenesis [2, 3].

It is suggested that the integration of resistance and endurance training can amplify mitochondrial biogenesis compared to single-mode exercise programs [9]. This is a potential mechanism by which mTOR signalling, typically associated with muscle hypertrophy, may promote PGC-1α activity, a key regulator of mitochondrial biogenesis [6, 9]. This proposed interaction offers a novel perspective on the interplay between these critical pathways.

The traditional view in exercise physiology has often stated that resistance training and endurance training induce opposing effects on muscle adaptations [8]. Resistance training activating mTOR, and endurance training stimulating PGC-1α [6-9]. This has led to the common practice of separating resistance and endurance training sessions to maximize the specific adaptations of each modality. Currently, research suggests concurrent training exploits the interplay between mTOR and PGC-1α to enhance mitochondrial adaptations [6, 9]. This effect could offer a superior approach to maximizing both muscle growth and oxidative capacity, leading to improved overall fitness and athletic performance. While further studies are needed to fully support this, the evidence presented strongly challenges the traditional view of these pathways as strictly antagonistic.

Inter-Individual Variability and Personalized Training

It is important to emphasize recognizing the significant variability in individual responses to exercise training. While studies often report average improvements in performance markers, the actual range of responses among participants can be substantial [7]. This inherent variability emphasizes the intricate nature of exercise adaptations and highlights the need for personalized training programs that cater to individual needs and responses.

Jacques et al. demonstrated that while all participants in their study regarding HIIT training experienced improvements in peak power output, lactate threshold, and peak oxygen uptake, the magnitude of these improvements varied considerably between participants [7]. The study also highlighted the challenges in assessing training-induced changes in muscle mitochondrial enzyme levels due to the inherent variability within individuals [7].

Research suggests that genetic factors can contribute significantly to individual variability in training responses. A review by Platen on exercise training adaptations notes that approximately 50% of the adaptations associated with endurance training can be attributed to genetic factors [2]. While genetic testing for exercise-related genes is not yet widespread, it may become a valuable tool in the future for personalizing training programs.

Future Research Directions

The sources illustrate the crucial role of mitochondria in skeletal muscle adaptation to exercise but also point to several areas requiring further research [8, 11]. Concurrent training requires more research to precisely clarify the molecular mechanisms underlying the interaction between the mTOR and PGC-1α pathways [8]. This could involve investigating specific signalling molecules and downstream targets involved in the crosstalk between these pathways [8]. Understanding this interaction is crucial for developing optimized concurrent training programs that maximize mitochondrial adaptations [8, 9]. Further, the sequencing of exercise modalities within a concurrent training program could significantly influence mitochondrial adaptations. Performing resistance training before endurance training might pre-activate the mTOR pathway, potentially priming the muscle for enhanced PGC-1α activation during the subsequent endurance session. Conversely, endurance training prior to resistance training could enhance mitochondrial function and substrate availability, possibly affecting the hypertrophic response to the subsequent resistance training. Determining the optimal sequencing strategy could lead to more effective concurrent training programs for enhancing mitochondrial function and overall athletic performance.

Conclusions

Mitochondria play a central role in skeletal muscle adaptation to exercise, with different training modalities driving distinct mitochondrial responses. Endurance training and HIIT primarily improve mitochondrial efficiency and oxidative capacity, while resistance training focuses more on enhancing mitochondrial function to support muscle hypertrophy. Concurrent training, which combines endurance and resistance training, offers a unique advantage by activating both the PGC-1α and mTOR pathways, promoting mitochondrial biogenesis and muscle hypertrophy. However, inter-individual variability in response to exercise underscores the importance of personalized training approaches to optimize both mitochondrial function and muscle performance. Future research should continue to explore the molecular mechanisms behind these adaptations, particularly in concurrent training, and investigate the most effective sequencing of exercise modalities to maximize benefits for athletic performance and overall health.

List of Abbreviations

DNM1L: dynamin 1 like
Drp1: dynamin-related protein 1
HIIT: high intensity interval training
Mfn2: mitofusion 2
mTOR: mammalian target of rapamycin
Opa1: optic atrophy 1
OXPHOS: oxidative phosphorylation
PGC-1α: peroxisome proliferator-activated receptor γ coactivator 1α

Conflicts of Interest

The author declares that they have no conflicts of interest.

Ethics Approval and/or Participant Consent
No ethics/participant consent was required to conduct this study.

Authors' Contributions
AMV: made contributions to the design of the study, collected and analysed data, drafted the manuscript, and gave final approval of the version to be published.

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