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Qualitative Study of Altitude Training on Cardio-Metabolic Responses to Endurance Performance: A Systematic Review

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Abstract

Altitude training has been recognized as an effective training strategy for performance optimization based off the various physiological adaptations which the human body gets acquainted to. Exposure to environment with reduced partial pressure of oxygen is believed to trigger various cardio-metabolic responses ranging from the stimulation of erythropoiesis, increased red blood cell mass to improved oxygen carrying capacity, all of which contributes significantly to optimum performance in endurance events. Factors that could serve as barriers towards stimulating responses alongside various forms of training conditions in hypoxic state have been explored by researchers in a bid to aid the attainment of peak performance by athletes. This paper highlights the various acute responses and chronic adaptations of altitude training on the cardio-metabolic indices necessary for optimum endurance-related performance while also pointing out factors, training methodologies and limitations, as well as dispositions of individual variability, when exposed to hypoxic environments

Keywords: Altitude training, training strategy, adaptations, cardio-metabolic, erythropoiesis, hypoxic state, endurance performance, athletes

Introduction

The pursuit of performance optimization in endurance sports has led athletes and coaches to explore a diverse range of training strategies, with altitude training emerging as a prominent and widely adopted technique. The fundamental premise of altitude training rests on the understanding that exposure to hypobaric hypoxia, the reduced partial pressure of oxygen at higher altitudes, triggers a cascade of physiological adaptations designed to enhance oxygen delivery and utilization, ultimately improving endurance capacity. Endurance performance, characterized by sustained submaximal exercise, is primarily limited by the athlete's ability to deliver oxygen to the working muscles and utilize it efficiently for ATP production. Altitude training, characterized by exposure to environments with reduced partial pressure of oxygen, has been widely employed to induce physiological adaptations believed to enhance these critical aspects. The initial rationale centered around stimulating erythropoiesis, leading to increased red blood cell mass and improved oxygen carrying capacity. However, the physiological responses to altitude are far more complex, encompassing adaptations in skeletal muscle, ventilation, and substrate metabolism (Kautz, Jung, Valore, Rivella, Nemeth & Ganz, 2021).

Physiological Responses to Hypoxia

Exposure to altitude initiates a complex series of physiological responses designed to compensate for the reduced oxygen availability (West, 2017). These responses can be broadly categorized as:

A. Acute Responses:

i. Increased Ventilation: Immediate hyperventilation to increase alveolar oxygen tension, leading to a decrease in arterial PCO_2 and respiratory alkalosis.
ii. Increased Heart Rate and Cardiac Output: Compensatory increases in heart rate and cardiac output to maintain oxygen delivery to tissues.

iii. Pulmonary Vasoconstriction: Hypoxic pulmonary vasoconstriction (HPV) redirects blood flow away from poorly ventilated areas of the lung, optimizing gas exchange. Hypoxia induces pulmonary vasoconstriction, leading to an increase in pulmonary arterial pressure. In some individuals, this can lead to the development of high-altitude pulmonary edema (HAPE), a life-threatening condition.
iv. Increased Sympathetic Nervous System Activity: Elevation in sympathetic tone contributes to increased heart rate, ventilation, and vasoconstriction.

Chronic Adaptations

Increased Erythropoiesis:

Hypoxia stimulates the release of erythropoietin (EPO) from the kidneys, leading to increased red blood cell production and elevated hemoglobin concentration, enhancing oxygen carrying capacity (Wang, Jiang, Rue & Semenza, 2019)). The reduced partial pressure of oxygen (PO_2) at altitude triggers a cascade of cellular responses mediated by the Hypoxia-Inducible Factor (HIF). HIF is a transcription factor that regulates the expression of numerous genes involved in oxygen homeostasis, including erythropoietin (EPO). EPO, produced primarily by the kidneys, stimulates erythropoiesis in the bone marrow, leading to an increase in red blood cell production and ultimately, an increase in hemoglobin mass (Hbmass). An increased Hbmass enhances the blood's oxygen carrying capacity, potentially improving VO_2max and endurance performance.

Increased Capillarization:

Angiogenesis, the formation of new capillaries, increases the capillary density in skeletal muscle, facilitating oxygen diffusion. Angiogenesis, the formation of new blood vessels, is stimulated by hypoxia, leading to increased capillarization around muscle fibers. This increases the surface area for oxygen delivery and waste removal, enhancing oxygen extraction by the muscle (West, 2017). The expression of vascular endothelial growth factor (VEGF), a key regulator of angiogenesis, is upregulated in response to hypoxia.

Mitochondrial Adaptations:

Hypoxia can influence mitochondrial biogenesis and function, potentially increasing oxidative capacity and improving metabolic efficiency, although the specific adaptations are complex and depend on the training protocol and individual response (Murray, 2016). Hypoxia stimulates mitochondrial biogenesis, increasing the number of mitochondria within muscle cells. This enhanced mitochondrial capacity improves oxidative phosphorylation and ATP production, potentially delaying the onset of fatigue during endurance exercise.

Buffering Capacity:

Increased buffering capacity in muscle tissue helps to mitigate the effects of acidosis during high-intensity exercise. Altitude training may improve intracellular buffering capacity, allowing muscles to tolerate higher levels of metabolic byproducts, such as lactate and hydrogen ions (West, 2017).

Ventilatory Acclimatization:

Gradual restoration of arterial pH towards normal levels despite continued hyperventilation. Acclimatization to altitude involves significant adjustments in the ventilatory system. The initial hyperventilation response to hypoxia is driven by stimulation of peripheral chemoreceptors. Over time, this response attenuates, which can impair oxygen unloading in the tissues, and the kidneys excrete bicarbonate to partially compensate for the respiratory alkalosis. This result in an increase in ventilation at any given workload, improving alveolar oxygen tension and facilitating oxygen uptake. However, excessive hyperventilation can lead to respiratory muscle fatigue, which can negatively impact exercise performance (Illi, Held, Frank, Spengler & Göhlert, 2018).

Substrate Metabolism:

Hypoxia can influence substrate metabolism during exercise. Studies suggest that altitude training may increase reliance on carbohydrate oxidation at a given workload, particularly during acute exposure to altitude. This shift in substrate metabolism may be related to increased activity of glycolytic enzymes and a decreased reliance on fat oxidation due to the limited availability of oxygen (Murray, 2016).

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Muscle Fiber Type Transition:

While the evidence is not entirely conclusive, some studies suggest a potential shift towards a higher proportion of type I (slow-twitch, oxidative) muscle fibers in response to chronic hypoxia. This adaptation would favor endurance performance by enhancing oxidative capacity and fatigue resistance. However, other studies have reported no significant changes in muscle fiber type composition following altitude training.

Reactive Oxygen Species (ROS) and Muscle Adaptation:

Hypoxia can increase the production of reactive oxygen species (ROS) within skeletal muscle. While excessive ROS production can be detrimental, moderate increases in ROS may act as signaling molecules, stimulating adaptive responses such as mitochondrial biogenesis and antioxidant defense (Powers, Jackson & Vasilaki, 2019).

The Erythropoietic Response: HIFs, EPO, and Beyond:

The cornerstone of altitude acclimatization is the body's erythropoietic response, primarily mediated by the Hypoxia-Inducible Factor (HIF) pathway. HIFs are transcription factors that regulate the expression of genes involved in oxygen homeostasis, including erythropoietin (EPO), the primary stimulus for red blood cell production. Increases in tHb improve the blood's oxygen-carrying capacity, directly impacting oxygen delivery to the muscles. However, other factors also contribute to improved oxygen transport, including:

i. Pulmonary Diffusion: Increased alveolar-capillary surface area can enhance oxygen diffusion in the lungs.
ii. Cardiac Output: While acute exposure to altitude can increase cardiac output, chronic exposure may lead to adaptations that optimize cardiac function and efficiency.
iii. Peripheral Circulation: Enhanced capillarization and vasodilation in the skeletal muscles improve oxygen delivery to the working tissues.

(Tanno, Porayette, Sripichai, Noh, Goodnough, Lozanski & Bunn, 2019)

Factors Limiting Erythropoiesis at Altitude

While hypoxia is a potent stimulus for EPO production, the erythropoietic response at altitude is not unlimited. Several factors can limit EPO production and/or RBCm expansion, including:

Iron Availability:

Iron is a critical component of hemoglobin, and inadequate iron stores can limit erythropoiesis. Hepcidin, a liver-derived hormone that regulates iron absorption and release, plays a central role in iron homeostasis. Hypoxia can induce hepcidin production, potentially limiting iron availability and blunting the erythropoietic response. Effective erythropoiesis requires sufficient iron availability. Hepcidin, the master regulator of iron metabolism, can be elevated by hypoxia and inflammation, potentially limiting iron absorption and hindering erythropoiesis. The interplay between iron homeostasis, inflammation, and erythropoiesis must be considered when designing and implementing altitude training protocols. Strategies to optimize iron status, including iron supplementation and dietary modifications, are crucial for maximizing the benefits of altitude training (Robach, 2021).

Inflammation:

Inflammatory cytokines can suppress EPO production and impair iron utilization, potentially limiting the erythropoietic response to altitude.

EPO Resistance:

In some individuals, the bone marrow may become less responsive to EPO stimulation, resulting in a blunted erythropoietic response.

Hypobaric Hypoxia and Hemodilution:

According to Perini, Milesi, Reggiani, Grassi, Ferretti and Cerretelli (2020), hypobaric hypoxia leads to an increase in RBCm, it is also followed by a plasma volume expansion. This expansion of the blood plasma can cause a hemodilution effect and can limit the concentration of oxygen in the blood.

Other factors involved in the regulation of erythropoietic response to altitude include:

i. Erythroferrone: This hormone, produced by erythroblasts in response to EPO stimulation, suppresses hepcidin production, thereby promoting iron availability for erythropoiesis (Kautz *et al.*, 2021).

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ii. Growth Differentiation Factor 15 (GDF15): GDF15 is another erythroid-derived hormone that can suppress hepcidin expression, potentially contributing to increased iron availability (Tanno *et al.*, 2019).

iii. The Gut Microbiome: Emerging evidence suggests that the gut microbiome can influence erythropoiesis through various mechanisms, including modulating iron absorption and inflammation (Johnson, Vasileiou, & Freyaz, 2020).

Metabolic Adaptations in Skeletal Muscle:

Altitude training induces metabolic adaptations within skeletal muscle, enhancing oxidative capacity and altering substrate utilization.

Mitochondrial Biogenesis and Oxidative Enzyme Activity:

Hypoxia stimulates mitochondrial biogenesis, leading to increased mitochondrial density and oxidative enzyme activity. This enhances the capacity for ATP production via oxidative phosphorylation, improving endurance performance. Alterations in the expression of key metabolic enzymes, such as citrate synthase (CS) and succinate dehydrogenase (SDH), indicate enhanced oxidative capacity within muscle cells (Murray, 2016).

Substrate Utilization and Efficiency:

Altitude training may influence substrate utilization during exercise. While some studies suggest an increased reliance on carbohydrate oxidation at a given workload, others have reported no significant changes in substrate metabolism. The specific adaptations likely depend on the training intensity, duration, and individual metabolic profile. Improvements in metabolic efficiency, potentially due to enhanced mitochondrial function, may contribute to improved endurance performance.

Lactate Metabolism and Buffering Capacity:

Altitude training may enhance lactate clearance and improve muscle buffering capacity, enabling muscles to tolerate higher levels of metabolic byproducts during high-intensity exercise. Improved lactate threshold and reduced lactate accumulation during exercise can enhance endurance performance (Feriche, 2014).

Altitude Training Methodologies

Live High, Train Low (LHTL)

LHTL involves living at a moderate altitude (2000-3000m) to stimulate erythropoiesis and other acclimatization responses, while training at or near sea level to maintain high-intensity training quality. This approach aims to maximize the benefits of altitude exposure while minimizing the negative impact of hypoxia on training intensity and volume. This strategy is predicated on the idea that the hypoxic stimulus of altitude can be exploited to enhance oxygen carrying capacity without compromising the ability to perform demanding training sessions. Numerous studies have demonstrated that LHTL can improve endurance performance in some athletes, primarily through increased Hbmass. However, the success of LHTL depends on sufficient altitude exposure (typically >12 hours per day), proper monitoring of individual responses and adequate iron status to support erythropoiesis. This method is widely considered the gold standard for altitude training, as it theoretically balances the benefits of hypoxic exposure with the need for high-intensity training (Brocherie, Girard, Faissol & Millet, 2017; Schmidt & Prommer, 2018; Bonetti, & Hopkins, 2019).

Live High, Train High (LHTH)

LHTH involves both living and training at altitude. While this approach maximizes exposure to hypoxia, it can also significantly impair training intensity and volume. The reduced oxygen availability can limit the athlete's ability to perform high-intensity workouts, potentially negating the benefits of increased Hbmass. However, some athletes may be able to tolerate LHTH and achieve performance gains, particularly if they are well acclimatized and able to adapt their training accordingly (Brocherie *et al.*, 2017).

Intermittent Hypoxic Training (IHT):

IHT involves repeated short exposures to hypoxia, typically delivered through breathing hypoxic gas mixtures, interspersed with periods of normoxia. IHT can be performed at rest (intermittent hypoxic exposure, IHE) or during exercise (intermittent hypoxic exercise, IHE). Intermittent Hypoxic Exposure (IHE): Involves resting in normobaric or hypobaric hypoxia for short periods of time, and is proposed to stimulate acclimatization mechanisms without the cost of high-intensity training sessions in hypoxia. "Altitude Simulation": Using hypoxic tents or chambers at sea level to mimic the

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physiological effects of altitude exposure. This method offers the advantage of controlling the hypoxic dose and minimizing the logistical challenges associated with traveling to altitude (Feriche, 2014).

The rationale behind IHT is to stimulate HIF activation and induce cellular adaptations without the limitations associated with prolonged exposure to altitude. While IHT can induce some physiological changes, such as improved ventilatory control and muscle buffering capacity, its effectiveness in improving endurance performance remains controversial, with inconsistent findings reported in the literature. The optimal IHT protocols, including the intensity, duration, and frequency of hypoxic exposures, are still under investigation. IHT is often used as a supplement to traditional training and may be beneficial for enhancing peripheral adaptations, such as mitochondrial function and buffering capacity, without the need for prolonged altitude residence.

Repeated Sprint Training in Hypoxia (RSH)

This specific form of hypoxic training is primarily used to enhance the adaptations of anaerobic metabolism. Athletes perform maximal sprints with short recovery periods at altitude or while breathing hypoxic air. RSH represents a specialized implementation of IHT where high-intensity sprint exercise is performed under hypoxic conditions, followed by recovery periods in normoxia. This form of training appears to be successful to increase glycolytic capacity and muscular power. This method focuses on local muscular adaptations rather than the cardiorespiratory adaptations commonly associated with traditional altitude training. The application of RSH is more suited for short burst athletes, rather than endurance athletes (Brocherie *et al*., 2017).

Individual Variability in Response to Altitude:

A significant challenge in altitude training research is the marked individual variability in response to hypoxic exposure (Bonetti & Hopkins, 2019). Some athletes experience significant performance gains, while others show little or no improvement, and a small percentage may even experience performance decrements. Factors that may contribute to this variability include: genetic predisposition, iron status, baseline physiological characteristics, training history, monitoring response, altitude dose, nutrition and hydration, sleep quality and gut microbiome:

Conclusion

Altitude training remains a popular and potentially effective strategy for improving endurance performance. While the underlying mechanisms involving erythropoiesis, skeletal muscle adaptations, and ventilatory changes are well-established, the individual variability in response poses a significant challenge. The "live high, train low" (LHTL) approach appears to be the most effective strategy for many athletes, allowing for sufficient altitude exposure to stimulate physiological adaptations without compromising training intensity. Future research should focus on optimizing altitude training protocols for individual athletes based on their genetic profile, iron status, training history, and physiological responses.

Suggestions for Further Study

i. Future research should look into the optimization of altitude training protocols for athletes based on individual variability.
ii. The need for targeted studies towards optimizing intermittent hypoxic training for endurance gains is encouraged.
iii. Comparison of the efficacy of altitude training protocols across diverse athletic population to establish best practices.

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