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Review

Simulated Altitude Training and Sport Performance: Protocols and Physiological Effects

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Featured Application: This article explores diverse hypoxia training protocols to improve sports performance, including hypoxia high-intensity interval training (HHIIT) and incremental hypoxia training.

Abstract: This article explores the physiological mechanisms and effects of simulated hypoxia environment training on sports performance. Different training protocols, including hypoxia high-intensity interval training (HHIIT), incremental hypoxia training, hypoxia submaximal exercise training and combined training, and hypoxia training in the recovery and sleep states, are discussed. HHIIT combines intermittent hypoxia exposure with high-intensity interval training, and has been shown to increase the maximum oxygen intake compare to the state of normoxia, improving cardiorespiratory fitness, skeletal muscle oxygen utilization, power performance, hematological adaptations, and sports performance. Incremental hypoxia training involves the gradual decrease in oxygen concentration while maintaining exercise intensity. It has been found to improve aerobic capacity; however, fewer effects were observed in hematological variables. Hypoxia submaximal exercise training and combined training in a hypoxia environment has shown to increase VO_2 and VE, and only improve hemodynamic function in combined training with hypoxia. Hypoxia during the recovery state has been associated with improvements in maximum oxygen uptake, also providing benefits to sports performance. Overall, exposure to a hypoxia environment has been demonstrated to improve cardiorespiratory endurance, power performance, and specific physiological adaptations in training and resting states. However, the optimal training protocols and their effects on different sports and athlete proficiency require further research to optimize training and enhance athletic performance in hypoxia environments.

Keywords: hypoxia; sports training; cardiorespiratory

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1. Introduction

The physiological effects of the hypoxia environment training protocol have not yet been fully elucidated or examined comprehensively from a holistic perspective. To further understand the sports performance benefits of different hypoxia environment training protocols, the height of the simulated environment, hypoxia concentration, training protocol, duration, and exercise ability level are all still under investigation. Therefore, this study explores the physiological mechanisms and effects of hypoxia environment training and further provides training protocols that match the characteristics of sports to enhance training and athletic performance.

The concept of high-altitude or hypoxia training to improve sea level sports performance has existed for more than decade. Researchers and trainers have proposed different training protocols and strategies, such as live high-training high, live high-training low, and another highland training protocol that has received attention in sports science and training protocols because of the continuous development of equipment to simulate hypoxia environments, which is the live low-training high (LL-TH) protocol [1]. LL-TH is a common training protocol used to improve athletes' performance in sports [2]; in this type of training, athletes or individuals who want to improve their performance in sports, or exercise, choose to live at lower altitudes, while exposing themselves to a lower oxygen environment during training.

Hypoxia is a state in which oxygen intake is reduced, resulting in oxygen levels in the body's tissues falling below the normal range [3,4]. Hypoxic training, also known as altitude training, is a common way to enhance sports and exercise performance [2,5]. If tissue oxygen demand exceeds supply, a cascade of intracellular events is activated increasing the expression of hypoxia-inducible factors (HIFs). Hypoxia-inducible factors (HIFs) are transcriptional factors and key regulators of the cellular response to hypoxia [6,7], and increase hemodynamic function by oxygen transport and utilization ability [5]. Also, hemoglobin levels have a linear relationship with intermittent hypoxia [8]. An increase in hemoglobin mass leads to easier transport of oxygen [9–11], and an adaptive response to high-altitude hypoxia [12].

Recent studies have shown that a simulated hypoxia environment can help improve the cardiorespiratory endurance of endurance-running athletes. It has been shown that the systematic reduction in arterial oxygen saturation (SpO_2) during hypoxia training can trigger various biochemical and structural changes in skeletal muscle, which are beneficial to cellular and muscular oxidation processes [13,14]. It has also been found to increase power performance [15–21], hematological adaptations, anaerobic threshold [22], and muscle conditioning for the transcription of selected genes [14,20]. Durand and Raberin [23] point out that when training in a hypoxia environment, one should monitor SpO_2, to evaluate whether it impairs or facilitates adaption to various training methods. Our study explored the mechanisms and effects of various training protocols in simulated hypoxia environments on athletic performance.

In order to further investigate the training protocols required for athletes with different sport-specific characteristics in different hypoxia environment settings and training protocols, this study reviewed various studies on the hypoxia training protocols of (1) Hypoxia high-intensity interval training, (2) Incremental hypoxia training, (3) Hypoxia submaximal exercise training and combined training, and (4) Exposure to a hypoxia environment in the recovery and sleep states. This study aimed to identify the potential training effects to consider in the development of training protocols within the context of hypoxia environment training to enhance athletic performance. Furthermore, we prepared a table of simulated altitude protocols and physiological effects in the Supplementary Table S1.

2. Hypoxia Environment Training Protocols

2.1. Hypoxia High Intensity Interval Training (HHIIT)

High intensity interval training is used to increase cardiopulmonary endurance and enhance sports performance, involving short- to moderate-duration exercises (10 s to 5 min) at high intensity, surpassing the anaerobic threshold [24]. Considering that the type of sports training, intensity, and level of exercise of the training target may affect physiological adaptations and hematological changes to improve sports performance, exposure to a hypoxia environment is a more common and widely used training and testing protocol. Intermittent hypoxia interval training (IHIT), or periodic exposure to hypoxia, is also known as LL-TH, and is defined as a protocol in which hypoxia and normoxia alternate during a periodic training session, which may last from a few minutes to several hours of hypoxia exposure, and which is repeated over a period of days to weeks. Hypoxia high-intensity interval training (HHIT) is a combination of an intermittent hypoxia environment and HIIT, and is commonly used in research and interval training. Sprint interval training, a form of HIIT training, involves brief exercise periods lasting approximately 10–15 s at near maximum intensity, followed by recovery intervals of less than 30 s, requiring maximum effort within a short period of time, through the use of repetitive anaerobic testing on a bicycle ergometer. This interval sprint training protocol can improve VO_2max, skeletal muscle oxidative capacity, and endurance performance in two weeks with a total of six "all-out" training sessions [25]. In HIIT, 95% of the lactate threshold load was considered. In this training protocol, athletes perform high-intensity short-duration exercises in a simulated or actual hypoxia environment, alternating between high-intensity (80–90% HR) and low-intensity (60–70% HRR) exercise and recovery exercise [26–28]. This hypoxia exposure is an effective protocol to improve skeletal muscle oxygen utilization capacity and exercise performance, characterized by repetitive sprints of high-intensity exercise at maximum workload, with consideration of short recovery times. Several studies related to hypoxia high-intensity interval training (HHIIT) have shown that participants, whether they were trained athletes [1,19,21,29–31], high-physical-activity performers [22,32], or untrained individuals [13], were able to increase their maximum oxygen intake after more than two weeks of intermittent hypoxia interval training. The studies with relevant post hoc analyses have shown that HHIIT interventions are more effective than normal oxygen interventions in interval training [7].

2.2. Incremental Hypoxia Training

In addition to the more common high-intensity hypoxia interval training, another protocol of hypoxia training is to gradually decrease oxygen concentration and increase exercise intensity. In a study related to oxygen concentration tapering training, Czuba et al. [1] investigated the effect of incremental hypoxia interval training on the aerobic capacity and endurance performance of cycling athletes. This training consisted of 3 weeks of intermittent hypoxia training, three times per week. Each session consisting of four sets of all-out 30 s sprint intervals, accompanied by a 90 s low-intensity recovery state, simulating an altitude of 2500–3000 m. Additionally, the FIO_2 was adjusted as the number of training days decreased, from 17% on day 1 to 14% on day 10; the SpO_2 value was controlled at 88% on days 1–2, 84% on days 3–4, and 82% on days 5–10. The VO_2max increased by 3.98% in the incremental hypoxia interval training group, and so did the lactate threshold, power output, and average speed, while no differences in hematological variables were found in the trained cyclists during the 3 weeks of incremental hypoxia training.

In Bonetti et al. [16]'s study of 10 sub-elite male short-distance sprint light-boat athletes who underwent 3 weeks of incremental hypoxia treatment, while being connected to the system via a face mask, the incremental hypoxia treatment used Wood et al. [33]'s protocol. The incremental hypoxia concentration experiment followed a specific design, starting at 12% in the first week, reducing to 11% in the second week for 6–10 days, and reaching 10.9% in the third week. Pre- and post-tests were conducted, including an incremental step test to assess peak power, VO_2max, exercise economy, lactate threshold, average burst force over 500 m, and short-distance sprints of 5×100 m. Throughout the experiment, intravenous blood samples were collected for analysis of hemoglobin concentration, hematocrit, ferritin, erythrocyte sedimentation rate, and white cell count. The findings demonstrated a 6.8% improvement in peak power, an 8.3% enhancement in mean repeat sprint power, and a 3.6% rise in hemoglobin concentration. However, no notable benefits were observed in lactate threshold, mean 500 m power, VO_2max, or exercise economy.

In non-athletes, incremental hypoxia training was performed in the non-athletic progressive intensity study by Nishiwaki et al. [34]. The first phase consisted of 30 min low-intensity continuous exercise (e.g., walking) at 60–70% of maximum HR; the second phase consisted of eight sets of 2 min high-intensity exercise with 1 min rest between sets at 85–95% of maximum HR. It was observed that in the hypoxia group of women with menopause, the endothelium-dependent vasodilation (FMD) increased from $4.4 \pm 1.8\%$ to $6.4 \pm 2.0\%$ after 10 days of hypoxia training, and the vasodilatory reactivity improved. The physiological benefits of hypobaric hypoxia training in postmenopausal women mainly involve improving the physiological parameters of FMD.

Compared to high-intensity intermittent exercise in a hypoxia environment, progressive hypoxia exposure training can bring about changes and improvements in exercise performance, cardiorespiratory fitness, and anaerobic fitness; however, there are only few studies related to high-intensity intermittent and sub-intensity training. Therefore, if we consider the physiological adaptations associated with exercise, progressive intensity and hypoxia training protocols may provide the time needed to adapt to training, allowing the individual to adapt to physiological changes and bring about better athletic performance; however, more research is needed to further investigate the relevant training protocols.

2.3. Hypoxia Submaximal Exercise Training and Combined Training

As mentioned previously, HIIT and progressive exercise intensity/incremental hypoxia training can provide physiological and performance benefits. Submaximal exercise is a state after completing aerobic exercise training. The blood lactate concentration is lower when exercising at the same absolute intensity [35]. This type of training is another form of hypoxia training. The study conducted by Park et al. [36] investigated the effects of simulated 3000 m hypoxia combined with exercise at 70% of maximal heart rate (HRmax). This condition led to increased anaerobic metabolism and oxygen supply to muscles due to limited oxygen delivery capacity. Moreover, the study found evidence of greater metabolic stress in healthy men, characterized by decreased SpO_2, VO_2, and oxygen pulse, as well as an increased respiratory exchange ratio. Additionally, notable changes were observed in skeletal muscle oxygenation responses.

In another study examining submaximal exercise training in hypoxia, conducted by Jung et al. [37], it was found that endurance submaximal ergometer exercise load at 80%, performed under hypoxia (simulated 3000 m), results in increased metabolic and cardiac responses compared to exercise under normoxia. The hemodynamic function, including parameters such as oxygen uptake, oxygen pulse, and cardiac output, increases. Hemodynamic and autonomic nervous system (ANS) functions also improve, and these improvements do not have adverse effects on immune function.

Overall, submaximal exercise training in hypoxia has shown several effects. It has led to increased anaerobic metabolism in skeletal muscle tissue due to limited oxygen delivery capacity, enhanced oxygen supply to the muscles, and greater metabolic stress. The latter is characterized by decreased SpO_2, VO_2, and oxygen pulse, along with an increased respiratory exchange ratio [15]. Additionally, observable changes have been noted in skeletal muscle oxygenation responses [37]. However, it appears that submaximal exercise training in hypoxia does not have a significant impact on hemorheological properties.

Combined training in a hypoxia environment refers to the integration of any two various protocols to optimize performance in sports and exercise. Roels et al. [17] implemented a hypoxia training protocol that involved three weeks of interval training twice a week, along with three sessions of sub-intensity (60% VO_2max) aerobic endurance training; the interval training consisted of three sets of two intervals at a peak power-output (PPO) intensity of 100% for 2 min, with a 2 min rest state between intervals and a 6 min rest state between sets. The results showed that the VO_2max did not improve significantly in either the normoxia training group or the hypoxia training group under normoxia conditions. However, in terms of PPO performance, both the normoxia training group and the hypoxia training group showed a significant improvement of 6.6% and 7.2% under sea level conditions, while only the hypoxia training group showed a significant improvement in power performance under hypoxia conditions (11.3%; $p < 0.05$). In a study by Park and Lim [2], 20 swimmers were exposed to a hypoxia environment for 6 consecutive weeks for 120 min per day, 3 days per week, with a combination of 30 min of sub-intensity running aerobic training (80% HR max), 10 sets of high-intensity stationary bicycle training for 2 min each (90% HR max), and 80–90% maximal resistance training for the remainder of the time. The results showed significant improvements in VO_2max, anaerobic power output, and 50 m and 400 m freestyle performance, as well as significant increases in growth hormone, insulin growth factor (IGF-1), vascular endothelial growth factor (VEGF), and muscle strength and endurance performance.

Based on the aforementioned research, sub-intensity hypoxia exposure and combined hypoxia exposure training can stimulate changes in skeletal muscle oxygenation responses during submaximal exercise training and enhance power performance in combined training. Unlike most hypoxia training in cardiorespiratory demanding sports, such as marathons, triathlons, and endurance sports, sub-intensity hypoxia exposure and combined hypoxia exposure training are also utilized in sports that require cardiorespiratory fitness performance on the field, such as boxing, taekwondo, and badminton, which are open-skill sports that also demand endurance performance. While high-intensity intermittent hypoxia interval training necessitates physical fitness, sub-intensity and integrated hypoxia exposure training protocols can offer sufficient training duration and physical capacity for specialized technical training in the target sports groups.

2.4. Exposure to a Hypoxia Environment in the Recovery and Sleep States

The recovery hypoxia training protocol considers exposure to a hypoxia environment during the recovery state or outside the training time, and further observes physiological and sports performance changes. Exposure to a hypoxia environment during the recovery state was also considered during the training period. In a study conducted by Katayama, Sato, Matsuo, Ishida, Iwasaki, and Miyamura [38], 15 runners in middle- and long-distance training, both in the normoxia group and the hypoxia group, were exposed to submaximal exercise in a normoxia environment with a VO_2max of 75%, while the hypoxia group was exposed to a hypoxia environment only during the recovery state in a tent with a hypoxia environment of 12.3% oxygen concentration. The results of the study showed that the recovery hypoxia exposure group showed a 7.0% improvement in maximum oxygen uptake during the recovery state, with a significant correlation at 3000 m. However, no significant changes were observed in hematological parameters.

Similarly, studies related to hypoxia exposure were conducted outside the training time, e.g., Gore et al. [39] and Saunders et al. [40], where the participants were specially trained long-distance athletes, cyclists, triathletes, and long-distance skiers exposed to 14.3% oxygen in a hypoxia environment for 20–23 days of sleep. Saunders et al. [40] showed that training time with progressive 20-day sleep exposure to a hypoxia environment resulted in a 12.4% improvement in oxygen uptake and improved running benefits in long-distance athletes. In the other study, 23 days of sleep exposure to 14.3% oxygen concentration in a hypoxia environment resulted in a significant increase in peak oxygen uptake (VO_2 peak) and a significant increase in oxygen uptake benefit at submaximal training intensities in trained athletes. In contrast to the recovery state and sleep exposure to hypoxia environments, the oxygen benefits of submaximal training intensity were significantly increased [39]. Truijens et al. [41] set the time of daytime rest and relaxation for trained swimmers and long-distance runners, who were exposed to hypoxia environment for 3 h per day, 5 days per week, for 4 weeks, showed a 0.02% improvement in VO_2max. Hypoxia exposure during the recovery and sleep states reduces the interference of training intensity, which means that the training intensity and technical training can be maintained during the training period.

3. Discussion

3.1. Effects of Hypoxia Exposure Training on Aerobic Fitness Performance in HIIT

After HIIT, physiological adaptations and changes in the relevant hematological variables, including erythropoietin (EPO), hypoxia-inducible factor 1 (HIF-1), levels of nitric oxide, vascular endothelial growth factor (VEGF), and transforming growth factor beta (TGF-β), were observed, and the inflammatory response-related cytokine (TNF-α) levels were significantly increased [7].

Exposure to hypoxia elicits an additive erythropoietic response, increasing erythrocyte volume and enhancing oxygen transport efficiency [42]. Studies have shown that hypoxia exposure stimulates the production of erythropoietin (EPO), with longer durations of exposure leading to greater EPO increases [43]. Furthermore, a systematic reduction in hypoxia concentration during training induces physiological and structural alterations in skeletal muscle that promote oxidative processes, ultimately leading to improved athletic performance [13,14].

Hypoxia training in a controlled environment has been found to significantly improve cardiorespiratory fitness indicators, such as ventilation efficiency (VE), heart rate (HR), oxygen consumption (VO), maximal oxygen consumption (VO_2max), blood oxygen saturation (SpO_2), blood lactate levels, HR variability, hemodynamic function, and stroke volume [2,37,38]. Additionally, hemodynamic variables including EPO, HIF1, nitric oxide, transforming growth factor (TGF-β), and the inflammatory response-related cytokine TNF-α have been shown to increase in response to hypoxia training [2,37,38].

The benefits of hypoxia exposure training extend beyond cardiovascular improvements. They also encompass enhanced muscle perfusion, delayed fatigue during intense sprints, improved utilization of fast-twitch muscle fibers, and reduced reliance on anaerobic energy pathways [19]. However, prolonged exposure to a hypoxic environment may lead to a decrease in mitochondrial content in muscle fibers, a shift towards carbohydrate reliance for fuel during oxidative metabolism, and a decrease in intracellular lipid substrate storage [19]. HIF1, a critical regulator of gene expression related to the hypoxic response, has been found to control various genes encoding glucose transporters, glycolytic enzymes, and vascular endothelial growth factor (VEGF) [44].

While hypoxia training has not shown promising effects on performance and physiology, further research is needed to comprehensively explore the specific effects of various hypoxia training protocols. We will address this topic in the section dedicated to training duration and athlete proficiency.

3.2. Effects of Hypoxia Exposure Training on Power Performance

Regarding anaerobic fitness performance, studies have also shown that the power peak in exercise performance [20,31] and the power average increased significantly after hypoxia exposure training [1,19]. The possible reason for this result is a shift in ATP production toward an increased contribution of glycolysis [38]. Additionally, there is a transition towards increased carbohydrate utilization and reduced fat usage in oxidative phosphorylation [17,45]. Furthermore, exercise leads to improved efficiency in excitation–contraction processes [46], or a shift in mitochondrial regulation towards a more oxidative profile [47]. Faiss et al. [19] reported that significant molecular adaptations were observed, demonstrating increased variability in blood perfusion within active muscles. Through interval training during repetitive sprinting, the main action muscle groups may make better use of fast-twitch fibers, potentially delaying fatigue by using less anaerobic energy. Hamlin et al. [21] examined the effects of intermittent hypoxia training on a 20 km time trial and 30 s anaerobic performance, and showed that intermittent hypoxia training improved anaerobic performance but had little effect on 20 km time trial performance. Bonetti et al. [16] collected intravenous blood to determine the hemoglobin concentration, hematocrit, ferritin, erythrocyte sedimentation rate, and white cell count. Their findings indicated a 6.8% enhancement in peak power, an 8.3% improvement in mean repeat sprint power, and a 3.6% increase in hemoglobin concentration.

Hypoxia exposure training and HHIT have shown significant increases in power peak and power average. Intermittent hypoxia intervals lead to improved anaerobic performance and a shift in ATP production. Additionally, adaptations in blood perfusion and muscle fiber utilization contribute to enhanced exercise efficiency. However, the impact on endurance performance appears to be limited. Overall, these findings emphasize the importance of power training and the potential benefits of incorporating specific training protocols to optimize sports performance. Additional research is required to gain a deeper understanding of these mechanisms and to further refine training protocols.

3.3. Training Duration and Athlete Proficiency in HIIT

Studies investigating high-intensity interval training (HIIT) in a hypoxic environment have shown that oxygen concentrations ranging from 14% to 15.3% can lead to improvements in both aerobic and anaerobic performance. Additionally, intermittent high-intensity hypoxia interval training (HHIT) has demonstrated various internal benefits, including enhanced cardiorespiratory endurance, increased maximal oxygen intake, improved power output, and adaptation of hematological variables to hypoxic conditions commonly experienced during plateau competitions and challenging situations faced by athletes dealing with performance stagnation. However, it is important to note that there exists inconsistency between the performance benefits and factors such as athlete proficiency, duration of hypoxia exposure training, and oxygen concentrations.

In a 4-week IHIT program with a reduced oxygen concentration of 14.6% (FiO_2 = 14.6%), trained cyclist athletes showed significant changes in hematological variables. These changes included increased VO_2max, higher frequency of interval training, molecular adaptations, improved blood perfusion in crucial muscle groups, and notable enhancements in blood perfusion within major muscle groups [19]. Similar findings were observed in a study by Buchheit et al. [48], which involved long-distance athletes but at lower oxygen concentrations. Their research demonstrated that up to 4 weeks of training led to increased VO_2max and alterations in hematological variables. However, studies have shown that physiological adaptations and performance changes resulting from intermittent hypoxia training beyond four weeks can vary.

Another study conducted by Roels et al. [30] involved a 7-week simulated hypoxia training at an altitude of 3000 m with an oxygen concentration of 14.6% in the HIIT group. Surprisingly, no clear trend of improvement in VO_2max was observed for triathletes and cyclists. However, significant enhancements in VO_2max were evident only during intermittent training periods when the recovery intervals were exposed to hypoxic conditions. Moreover, there were no significant differences in VO_2max between the intermittent training group in the hypoxia chamber and the control group. Therefore, further research is necessary to clarify and establish appropriate hypoxia interval training protocols tailored to dedicated athletes, considering the specific characteristics of the training subjects and the duration of training [29].

In terms of athlete proficiency, several studies have examined the effects of hypoxia high-intensity interval training (HHIT) on different groups of participants. In one study, basketball players training at a 15% hypoxia concentration and a simulated altitude of 2500 m experienced a significant 7.8% increase in VO_2max and a notable decrease in Delta-lactic acid after 3 weeks of HHIT. However, no significant changes in relevant hematological variables were observed during the intermittent hypoxia intervals [29].

Another study focused on repeated sprint training as part of hypoxia HHIT, involving 50 professionally trained cyclists randomly assigned to different groups. The groups included a normoxia group at sea level (485 m altitude), a hypoxia group at 3000 m altitude, and a control group without interval training but exposed to hypoxia. The results revealed that the hypoxia group showed greater improvements in sports-specific performance, significant molecular adaptations, and increased blood perfusion within the active muscles when compared to the sea level group [19].

In a study involving long-distance athletes with a mean age of 18.9 years, aerobic and anaerobic exercise performance and physiological parameters during HHIT were investigated. Participants were randomly assigned to a normoxia group (FiO_2 = 20%) and a hypoxia group (FiO_2 = 15.4%) to perform three sets of HIIT sessions over a 2-week period. The physiological changes in ventilation (VE), heart rate (HR), and oxygen saturation (SpO2) showed lower values in the hypoxia group, although statistical significance was not reached [48]. Additional research is needed to fully understand the optimal protocols and parameters for different levels of athlete proficiency.

4. Conclusions and Future Directions

The relevant oxygen concentrations, exposure protocols, and training periods should be considered to determine training prescriptions for different sports. In the hypoxia high-intensity interval training protocol, there is an increase in physiological changes to cardiorespiratory function, power output, hemodynamic function, and performance efficacy. However, improvements in these parameters do not always produce effective results, as they depend on the training duration and the athlete's proficiency. By implementing HHIIT protocols in high-altitude areas, competitors could potentially reap significant benefits. Not only can hypoxia high-intensity interval training protocols enhance aerobic and anaerobic performance, but incremental protocols, submaximal exercises, intergraded training, and recovery states can also contribute to physiological adaptation and improved performance for athletes across different sports.

Further research is needed to establish tailored hypoxia interval training protocols considering specific characteristics and physiological demands of athletes and individuals who need to improve their sports or exercise performance. Progressive hypoxia exposure training enhances exercise performance, cardiorespiratory fitness, and anaerobic performance; however, studies on high-intensity intermittent and sub-intensity training are limited. Sub-intensity and integrated hypoxia exposure training protocols may be utilized in sports like boxing, taekwondo, and badminton, providing sufficient duration and physical capacity for specialized technical training. Hypoxia exposure during the recovery and sleep states minimizes interference with training intensity, enabling its maintenance.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app132011381/s1, Table S1: Simulated Altitude Protocols and Physiological Effects.

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