PHYSIOLOGICAL AND PERFORMANCE EFFECTS OF ALTITUDE TRAINING AND EXPOSURE IN ELITE ATHLETES

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ABSTRACT

Despite widespread popularity of altitude training with athletes and coaches, and extensive research over the last 50 years, the transfer of improvements in physiological capacities to competitive performance remains uncertain. This thesis quantified the magnitude of performance gains required to improve placing in international competition, and the performance enhancements and physiological adaptations that can be obtained from altitude training and exposure in elite swimmers and runners.

Performance gains of ~1% will substantially increase the chance of a medal in elite swimmers. This was quantified by a novel analysis of the relationships between lap time and performance, which combined between-athlete correlations and within-athlete effects. Overall, the final lap for 100-m events and the middle two laps for 200-m and 400-m events had the strongest relationship (r~0.7-0.9) with final time. A change in these laps was associated with ~0.4-0.8% improvement in final time for finalists, and ~0.5-1.1% for semi-finalists, depending on sex, stroke and event. However, a similar pattern of lap times was adopted in each event regardless of the sex, finish position, or the best and worst swims for an individual. To gain a competitive advantage, many athletes employ some form of altitude training in an attempt to elicit small enhancements in performance.

Three to four repeated 2-wk blocks of living and training at natural altitude (1350 m) and/or simulated live high/train low exposure (LHTL, 2600 m, 9-10 $h \cdot d^{-1}$) were undertaken by elite swimmers (n=9). Each 2-wk block produced the following mean improvements: haemoglobin mass (Hb_{mass}), 0.9% (±0.8%, 90% confidence limits); 4-mM lactate threshold velocity, 0.9% (±0.8%); 2-km time-trial performance, 1.2% (±1.6%). There was no substantial improvement in competition performance compared with swimmers (n=9) who received no altitude exposure (altitude-control: 0.5%; ±1.0%). To gain substantial enhancements in physiological and performance capacities, a more effective model of altitude training is required.

The final two studies employed 3-wk bouts of simulated LHTL (3000 m, 14 $h \cdot d^{-1}$) in well-trained runners. The test-retest reliability of responses to 2 x 3-wk LHTL were quantified, with reproducible increases in Block 1 and 2 for $\dot{V}O_{2max}$ (2.1%; ±2.1% and 2.1%; ±3.9%) and Hb_{mass} (2.8%; ±2.1% and 2.7%; ±1.8%), but 4.5-km time-trial performance was more variable (-1.4%; ±1.1%, faster and 0.7%; ±1.3%, slower) in the LHTL group (n=8). Compared with

the control group (n=8) who had only trivial changes, the LHTL group were substantially faster after Block 1 (LHTL-control: -1.9%; ±1.8%), had higher Hb_{mass} after Block 2 (4.2%; ±2.1%), but a trivial difference in change in $\dot{V}O_{2max}$ after each 3-wk block. It appears that physiological responses to altitude are reproducible, but transfer to improved time-trial performance is more variable.

Finally, the effect of 3 weeks of intermittent hypoxic training (TH, 2200 m, $4 \cdot wk^{-1}$) or combined LHTL plus TH (LH/TL+TH) were examined. The LH/TL+TH group (n=8) substantially improved $\dot{V}O_{2max}$ (4.8%; ±2.8%), Hb_{mass} (3.6%; ±2.4%) and 3-km time-trial performance (-1.1%; ±1.0%); while the TH group (n=9) improved $\dot{V}O_{2max}$ (2.2%; ±1.8%), but had only trivial changes in Hb_{mass} and time trial. The LH/TL+TH group had substantially higher Hb_{mass} (4.3%; ±3.2%), however, the small increase in $\dot{V}O_{2max}$ (2.6%; ±3.2%) and trivial improvement in time trial performance (-0.9%; ±1.4%) became unclear when adjusted for differences in training ($\dot{V}O_{2max}$: 0.8%; ±3.5% and time trial: -0.3%; ±1.5%). LH/TL+TH was a potent stimulator for improvements in physiological measures, but transfer of these improvements to time-trial performance was limited.

A structured program of 3-wk simulated LHTL, with or without additional hypoxic training, can elicit substantial improvements in $\dot{V}O_{2max}$ and Hb_{mass} and enhance time trial performance by ~1% in well-trained athletes. Evidence of individual responses indicates some athletes respond more favourably than others, and the degree of within-athlete variation to repeated bouts indicates altitude training should be managed carefully in the context of other training and competition. Altitude training and exposure can enhance physiological capacities, but further research is required to improve the direct transfer of these benefits to competitive performance.

CERTIFICATE OF AUTHORSHIP OF THESIS

Except where clearly acknowledged in footnotes, quotations and the bibliography, I certify that I am the sole author of the thesis submitted today entitled:

Physiological and performance effects of altitude training and exposure in elite athletes

I further certify that to the best of my knowledge the thesis contains no material previously published or written by another person except where due reference is made in the text of the thesis.

The material in the thesis has not been the basis of an award of any other degree or diploma except where due reference is made in the text of the thesis.

The thesis complies with University requirements for a thesis as set out in

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Signature of Candidate: .....

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Date: .....

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DECLARATION

This dissertation summarises original work conducted in the Department of Physiology, Australian Institute of Sport, Canberra. This thesis includes research papers for which I am the senior but not the sole author. I took the lead in this research in terms of experimental design, data collection and analysis, and wrote the manuscripts. I was, however, assisted by my co-authors. The research papers which appear as Chapters Three, Four, Five and Six were prepared through substantial, independent contribution by the senior author. Co-authors are listed at the start of each Chapter. Collaborators on the study which appears as Chapter Five, are currently undertaking analysis of additional blood samples collected during the main study and taking the lead on manuscript preparation. Preliminary findings are presented, with details of the working title and list of co-authors for the manuscript, in Appendix 2.

Eileen Y. Robertson

DEDICATION

To my parents Evelyn and Sandy Robertson

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CHAPTER ONE

INTRODUCTION

1.1. Background

For elite athletes, continually improving fitness and performance capabilities within and between national and international competitions is a major challenge. To reach the upper limits of athletic ability, long hours of training are required to maximise aerobic and anaerobic fitness capacities and improve specific strength and power attributes. In endurance-based sports where performance is largely determined by the rate of oxygen transport and oxygen utilisation, training-induced increases in maximal aerobic power ($\dot{V}O_{2max}$) and endurance performance often plateau in elite athletes (Snell & Mitchell, 1984). With only small margins separating competitors in many individual sports, athletes and coaches are continually searching for new and innovative ways of improving performance to gain a competitive edge.

1.2. Competition performance

Evaluation of athletic performance in individual sports is primarily based on analysis of race times. The smallest enhancement in performance that makes a difference to medal winning prospects is determined by variation in an athlete's performance between events (within-athlete variation) and variation in performance between athletes in the same event (between-athlete variation). A key question is the magnitude of the smallest worthwhile enhancement within and between competitions – estimation of this reference value is a growing area of interest for sport scientists. For closely matched opponents, the smallest worthwhile change in performance that will affect the athlete's chance of a medal is approximately half the within-athlete coefficient of variation (Hopkins *et al.*, 1999). Estimates of the variability in competive performance has been derived from overall race times in national level swimmers (Pyne *et al.*, 2004; Stewart & Hopkins, 2000; Trewin *et al.*, 2004), track and field athletes (Hopkins *et al.*, 1999; Hopkins & Hewson, 2001) and elite cyclists (Paton & Hopkins, 2006). In these events, within-athlete variability is ~1-3% depending on race duration and modality. To substantially increase the likelihood of a medal in these events, the smallest worthwhile enhancement in overall performance is ~0.5-1.5%.

In addition to race-to-race variation, pacing strategies are considered an important element for success in many sports (Foster *et al.*, 1994). The appropriate pacing strategy is largely determined by the duration and the physiological requirements of the event (Foster *et al.*, 2004). Short duration (~60 s) events are typically characterised by a fast start (van Ingen Schenau *et al.*, 1994), middle-distance events (2-4 min) are generally more evenly paced (Foster *et al.*, 1993), and longer duration events are typified by a slower start with an increase in pace towards the finish (Tucker *et al.*, 2006). Although the pacing strategy will vary depending on the duration of the event, differences in pacing strategy in competition between top-ranked and lower-ranked competitors are not well characterised. Few studies have addressed differences in pacing strategy between competitors in international competition. Velocity profiles were similar for finalists in international track cycling and speed skating competition (Foster *et al.*, 1994), and pacing profile (pattern of 500-m split times) did not differ between winners and losers in international rowing competition (Garland, 2005). However, variability in lap times and the relationship between change in lap time and overall performance in competition has not been quantified. Modelling of lap times in competition is needed to determine the magnitude of change in lap time that will substantially improve competition performance. These estimates will provide valuable information to the coach and athlete on how to pace a competitive event. Furthermore, establishing the magnitude of change needed in lap times to improve training and competition performance is important to evaluate the effectiveness of various training interventions undertaken by elite athletes.

Athletes and coaches seek advice on the most effective means of gaining small but necessary improvements in performance, through advances in training methodologies and sport science. A popular training methodology for many athletes is altitude training. Altitude training or exposure is used to enhance improvements in fitness (physiological adaptations) that underpin enhanced athletic performance (Wilber, 2007). To substantially increase the likelihood of success for elite athletes, altitude training needs to elicit improvements in overall race time of ~0.5-1.5% in swimming and running events (Hopkins & Hewson, 2001; Trewin *et al.*, 2004). This is equivalent to 0.6 to 1.8 s for a 200-m swimming race lasting ~2 min and 9 to 27 s for 10-km running race lasting ~30 min.

1.3. Altitude training for performance enhancement

There has been considerable interest in the physiological responses and performance benefits of altitude training over the last five decades. Traditional altitude training, where an athlete

lives and trains at moderate altitude for several weeks (live high/train high, LHTH), can elicit beneficial physiological adaptations during acclimatisation that underpin enhanced athletic performance (Rusko *et al.*, 2004). These physiological adaptations will improve competitive performance at altitude (Pugh, 1967) and LHTH has been reported to result in world-class performances in elite endurance athletes on return to sea-level (Daniels & Oldridge, 1970). Athletes choosing to undertake traditional LHTH should live and train at altitudes ≥ 2,000 m for 3 to 4 weeks (Friedmann-Bette, 2008). However, a lack of transfer to improved performance upon return to sea level in the majority of controlled studies has led to several novel approaches to avoid the potentially detrimental effects of chronic hypoxia (Bailey & Davies, 1997). Many athletes undertake several weeks of altitude or hypoxic exposure via either live high/train low (LHTL) for some or most of the day (Levine & Stray-Gundersen, 1997) or live low/train high (LLTH) for a few hours during the day (Hoppeler *et al.*, 2008).

The LHTL model, which facilitates acclimatisation to moderate hypoxia but allows training velocities to be maintained near sea-level values (Levine & Stray-Gundersen, 1997), has been extensively evaluated in both research settings and contemporary practice. It appears that maintenance of high training velocities is a key factor in facilitating the transfer of enhanced physiological capacities to improved performance at sea level in endurance athletes (Stray-Gundersen *et al.*, 2001). In countries where the geography does not readily permit natural LHTL, facilities to simulate altitude have been developed to allow athletes access to this training methodology (Rusko, 1996). The use of nitrogen houses, and other methods of providing normobaric hypoxia such as altitude tents and hypoxic breathing devices, has become increasingly popular. These new methods for simulating altitude have generated interest in the alternate strategy of LLTH, as a potentially time efficient means of stimulating physiological adaptations that underpin enhanced performance (Hoppeler *et al.*, 2008). In LLTH, moderate to severe hypoxia is provided for short durations (~1-3 $h \cdot d^{-1}$) at rest or during exercise. The rationale for training in hypoxia is to increase the metabolic stress on skeletal muscle beyond that achieved in normoxia (Hoppeler & Vogt, 2001). Both LHTL and LLTH are popular training approaches for many athletes, however, the optimal protocols to enhance athletic performance are unclear.

1.3.1. Live high/train low

Overall, natural or simulated LHTL may offer small performance benefits (~1%) at sea-level, in events lasting between 45 s to 14 min (Levine *et al.*, 2005). With sufficient hypoxic

exposure, LHTL stimulates erythropoietin (EPO) production leading to an increase in haemoglobin concentration, red cell mass (or haemoglobin mass, Hb_{mass}) and aerobic power (Levine, 2002). The increase in $\dot{V}O_{2max}$, combined with high rates of oxidative flux, is reported to underpin the effectiveness of this altitude training approach to enhance performance at sea level (Chapman *et al.*, 1998; Levine & Stray-Gundersen, 1997; Stray-Gundersen *et al.*, 2001; Wehrlin *et al.*, 2006). In contrast, a number of studies using simulated LHTL with elite athletes have found no substantial change in Hb_{mass} or erythropoietic markers (Ashenden *et al.*, 2000; Ashenden *et al.*, 1999a; Ashenden *et al.*, 1999b), despite small enhancements in performance (Hahn *et al.*, 2001). The uncoupling of physiological adaptations and performance enhancement at sea-level casts some doubt on the popular paradigm of using altitude training primarily to augment red cell mass and oxygen carrying capacity (Berglund, 1992).

Whether enhanced athletic performance following LHTL is mediated primarily by erythropoietic or non-erythropoietic mechanisms is an ongoing debate (Levine *et al.*, 2005). Some researchers argue that performance enhancement is wholly attributable to increased red cell volume (Levine & Stray-Gundersen, 1997) provided adequate altitude or hypoxic exposure (Rusko *et al.*, 2004). This increase in red cell volume elicits an increase in $\dot{V}O_{2max}$ via increases in cardiac output (from increased total blood volume) or greater oxygen-carrying capacity (from increased haemoglobin concentration). On the other hand, there is growing evidence from other studies that enhanced performance following shorter daily hypoxic exposure ($<12\ h \cdot d^{-1}$) can be obtained via non-haematological mechanisms (Gore *et al.*, 2007). Enhancements in performance following hypoxia have been associated with improved economy (Gore *et al.*, 2001; Neya *et al.*, 2007; Saunders *et al.*, 2004b), enhanced muscle buffer capacity (Gore *et al.*, 2001), reduced lactate production (Clark *et al.*, 2004), increased anaerobic capacity (Roberts *et al.*, 2003), and increased hypoxic ventilatory response (HVR) (Townsend *et al.*, 2002). While not all these findings have been confirmed by other researchers, it is likely that there are a number of factors that contribute to enhanced performance following altitude training which may be dependent on the dose of hypoxic exposure. Current recommendations for using LHTL to enhance sea-level performance are 3 to 4 weeks of natural LHTL at ~2,100-2,800 m (Stray-Gundersen & Levine, 2008) or simulated LHTL at ~3,000 m (Richalet & Gore, 2008). In a meta-analysis incorporating 51 studies of various altitude training interventions (Bonetti & Hopkins, 2009), estimates of the enhancement in performance were largest following natural LHTL in elite and sub-elite

athletes (~4%), while simulated LHTL resulted in a small improvement in performance in sub-elite athletes (~1%), but only a trivial change in elite athletes.

1.3.2. Live low/train high

Brief periods of hypoxic exposure during the day are appealing for athletes who cannot undertake several weeks of LHTL. Following training in hypoxia, there is evidence of reduced lactate accumulation at submaximal intensities (Terrados *et al.*, 1988), improved aerobic capacity (Meeuwsen *et al.*, 2001) and greater anaerobic power (Hendriksen & Meeuwsen, 2003). Short duration severe hypoxia may also stimulate erythropoiesis and increase red blood cell production to enhance aerobic capacity (Rodriguez *et al.*, 1999), although other researchers have failed to confirm this assertion (Gore *et al.*, 2006). Given the wide range of training intensities and frequencies that have been completed under different levels of hypoxia (altitude and duration of exposure), interpretation of the findings from LLTH experimental work is problematic. Nevertheless, there is some support for hypoxic training for ~1-3 weeks at moderate altitude to improve performance (Hendriksen & Meeuwsen, 2003; Meeuwsen *et al.*, 2001; Terrados *et al.*, 1988). While high intensity training in hypoxia for 6 weeks improved performance in well-trained runners (Dufour *et al.*, 2006), the majority of studies have not reported performance benefits with extended periods of hypoxic training (Roels *et al.*, 2005; Roels *et al.*, 2007b; Truijens *et al.*, 2003; Ventura *et al.*, 2003). While there is limited support for intermittent training in hypoxia for elite athletes (Hoppeler *et al.*, 2008), this methodology may be promising for sub-elite athletes who can gain substantial enhancements in performance according to the meta-analysis of altitude interventions (Bonetti & Hopkins, 2009). An unclear improvement in performance following LLTH (~1%) can be enhanced by low to moderate training intensity at a lower training altitude (~2,400 m), for more days (18 days), with a later post-altitude test-day (Bonetti & Hopkins, 2009). The physiological and performance responses to intermittent training in hypoxia require further investigation.

1.3.3. Individual variation

One factor which contributes to the equivocal findings in the literature is the between-athlete variability in physiological and performance responses to hypoxia. A retrospective study attributed individual performance enhancements following LHTL to an EPO-mediated increase in red cell mass (Chapman *et al.*, 1998). However, the relationship between

individual change in EPO and change in Hb_{mass} has not been supported in controlled studies at natural (Friedmann *et al.*, 2005) or simulated altitude (Rusko *et al.*, 1999). It is unlikely that individual variability in response to hypoxia can be explained by up-regulation of EPO alone (Jedlickova *et al.*, 2003). Given both haematological and non-haematological parameters play a role in performance enhancements following altitude training (Levine *et al.*, 2005), an alternative mechanism acting at the molecular level is likely. One such candidate is hypoxia inducible factor-1 (HIF-1), a global regulator of oxygen homeostasis that plays a critical role in cardiovascular and respiratory responses to hypoxia (Semenza, 2000). As such, improvements in performance which have previously been associated with an elevated EPO response may have been mediated by a combination of erythropoietic and non-erythropoietic responses to hypoxia. The underlying mechanism of individual variation has not been elucidated and it is unclear if an individual athlete will respond in the same way to repeated bouts of altitude training. Similarly, it has not been established if there is a dose-response relationship to hypoxia that elicits greater enhancements with longer exposures in the same athlete. Establishing the dose-response and reproducibility of responses to hypoxic exposure are important for many athletes that undertake multiple altitude exposures within and between training years, to evaluate the efficacy of this approach.

1.3.4. Measuring small changes of practical importance

Despite extensive research, the magnitude and time-course of physiological responses to hypoxia and the degree of transfer to athletic performance gains remains unclear. A number of methodological differences such as altitude level, daily duration and length of intervention, training stimulus, and timing of sea-level performance test make direct comparisons difficult. In addition, differences in training status and initial fitness level of athletes may also confound some of the performance outcomes. The optimal time to maximise performance gains at sea-level following altitude training is a key feature of the success of any altitude training intervention. The general consensus among coaches is ~14 days after living and training at altitude (Dick, 1992), however, whether this is the same for other methods of altitude training is unclear. In any altitude training intervention, the critical issue for athletes and coaches is whether enhancements in physiological capacities transfer to improved athletic performance. Subject numbers are often low in studies of elite athletes, so conventional statistical approaches (involving hypothesis testing and statistical significance) may not be able to detect small changes in performance that are important for athletes.

Traditional statistical significance testing uses the probability (P value) of obtaining a value larger than the observed effect (regardless of sign) if the null hypothesis were true. An arbitrary value of $P<0.05$ is commonly used to reject the null hypothesis (no relationship or no difference) and report the outcome as statistically significant. However, the P value alone does not account for the direction or size of the effect, or the range of likely values. A non-significant result ($P>0.05$) may mask important effects if there is a combination of small sample size and large measurement variability. New approaches to the analysis of experimental data are emerging in the biomedical, clinical and sports sciences based on interpretation of practical, clinical and sporting significance of effects (changes and differences) rather than traditional statistical significance (Hopkins *et al.*, 2009). This type of analytical approach is particularly useful in an elite athletic population where very small changes or differences can make a substantial difference to performance outcomes (Hopkins *et al.*, 1999).

One such approach is magnitude-based inferences (Batterham & Hopkins, 2006) that centres on the interpretation of small changes of practical or clinical significance, rather than traditional null-hypothesis testing. Magnitude-based inferences quantify the size of the effect as small, moderate, or large (Cohen, 1988) and combined with precision of estimation (confidence limits) permits practical interpretation of effects for coaches and sport-scientists. A three level scale of magnitudes describes the outcome statistic as substantially positive, trivial or substantially negative (Batterham & Hopkins, 2006), which is a more useful approach for interpreting effects than traditional significant/non-significant criteria (Sterne & Davey Smith, 2001). The magnitude of the effect is defined by the smallest worthwhile change (or difference), which is a reference value for the smallest important outcome in a given event or test. The smallest worthwhile change is derived from modelling of competition performance or tests of reliability. To make inferences about population effects, 90% confidence limits will show an outcome is clear if the true value is very unlikely (>5%) to be substantial in a positive and/or negative sense (Batterham & Hopkins, 2006). Use of this analytical approach permits rigorous but practical interpretation of the effects of altitude training on athletic performance. When small differences in competition performance can be the difference between winning and losing, this information should assist coaches and sport scientists in evaluating the practical impact (and cost-benefit analysis) of altitude training interventions on athletic performance.

1.4. Statement of the Problem

Despite many years of research on the performance benefits from either natural or simulated altitude training (Wilber, 2001), there is still no consensus on the optimal duration and length of exposure. Current recommendations suggest a minimum of 3 weeks of altitude exposure for 12 $h \cdot d^{-1}$ to elicit substantial physiological adaptations and performance gains (Rusko *et al.*, 2004). A shortcoming in the existing literature is that previous investigations have focussed on single altitude exposures, yet many athletes typically undertake multiple short duration (<2 weeks) exposures within and between training years. Further research is required to verify the effectiveness, or otherwise, of repeated bouts of simulated and real altitude exposure commonly undertaken by elite athletes to prepare for competition. Contemporary altitude training programs need to be evaluated in combination with controlled studies, in order that improvements or modifications can be identified and implemented in a timely and efficient manner. An observational study of contemporary models of altitude training by elite athletes is required to complement research studies with fully controlled experimental designs.

With so many variables that can be manipulated in LHTL or LLTH methodologies (such as altitude level, daily duration and length of intervention, training stimulus, timing of sea-level performance test) it is difficult to develop definitive guidelines for coaches. The majority of previous research has evaluated 2-4 week LHTL exposures. It is unclear if a dose-response relationship exists and if longer LHTL exposure can elicit greater enhancements in physiology and performance in the same athlete. Moreover, there is an apparent lack of reproducibility in the literature, with many investigators unable to repeat the results using the same experimental protocol. Evidence of individual variation and anecdotal reports following multiple bouts of altitude training indicate that reproducibility of responses is a key consideration for athletes. No previous study has addressed the issue of test-retest reliability of responses to simulated LHTL, or the dose-response relationship of length of hypoxic exposure on physiological and performance effects in the same athletes. Given the equivocal findings of many of the studies of either LLTH or LHTL alone, it is possible that a combined approach may be more effective for enhanced performance. Finally, to address the ongoing debate in the literature, haematological and non-haematological parameters need to be measured in parallel to clarify whether changes in performance following altitude training can be explained independently of increased red blood cells. A greater understanding of the physiological mechanisms and the time-course of their response to hypoxia is fundamental to

establishing the most effective model of altitude training to gain small improvements in performance.

1.5. Research Questions

For elite athletes close to their performance limits, small enhancements in performance are of critical importance. There is little quantitative data on how variations in lap times affect overall performance in international competition. Swimming competition is a useful model to quantify the relationship between lap times and final times, as performance is not affected by environmental conditions and events are essentially against the clock. Estimates of the magnitude of change in lap or training times that will improve competition performance are necessary to evaluate the effectiveness of altitude training (or other) interventions used by athletes. The magnitudes of these enhancements are often too small to be detected using conventional statistical significance approaches, so the use of magnitude-based inferences is more appropriate to interpret practically important effects for athletes. The dose-response of improvements in physiological capacities and the transfer to enhanced athletic performance will be quantified following multiple 2-wk altitude exposures and 3-wk to 6-wk simulated LHTL exposures, and the reproducibility of individual and mean responses examined.

The specific aims of the four investigations in this thesis are outlined below.

Analysis of lap times in international swimming competitions.

- To quantify the magnitude of change needed in lap time and performance for a swimmer to be in medal contention in international competition.
- A secondary aim was to quantify how variations in lap times affect performance by characterising differences in the relationship of specific laps to final time, between finalists and non-finalist in events differing in stroke and distance.

Effect of simulated and real altitude exposure in elite swimmers

- To quantify the physiological adaptations and performance gains in elite swimmers, following three to four 2-wk blocks of combined moderate live high/train high and simulated live high/train low exposure, over a typical preparation for competition.

Reproducibility of performance changes to simulated live high/train low altitude

- To quantify the test-retest reproducibility of physiological responses and performance changes to two matched 3-wk simulated LHTL exposures, with a five week washout, in well-trained runners.

- A secondary aim was to quantify the dose-response relationship of physiological responses and performance changes to altitude exposure following 3-wk (~300 h) and 6-wk (~600 h) LHTL.

Effectiveness of intermittent training in hypoxia combined with live high/train low

- To quantify the physiological adaptations and performance gains following 3-wk intermittent training in hypoxia 4 $d \cdot wk^{-1}$, either while residing near sea-level or combined with 3-wk LHTL exposure.

CHAPTER TWO

REVIEW OF LITERATURE

2.1. Introduction

For elite athletes in individual sports, there are often only small margins between closely matched competitors. A major challenge for highly trained athletes is to continually improve fitness and performance capabilities within and between national and international competitions. As the magnitude of the physiological response to training depends predominantly on the duration, intensity, and frequency of the exercise bouts, athletes spend many hours training to maximise fitness capacities and technique. However, when the limits of training-induced improvements are approached, elite athletes and coaches must seek new and innovative means of enhancing competition performance. One popular approach for many athletes is to live and/or train at altitude in the belief it provides an additional metabolic stimulus to enhance athletic performance.

Despite over 50 years of research into the effects of altitude training, the underlying physiological mechanisms and their subsequent transfer to performance gains on return to sea-level remain uncertain. There is a lack of consistency in the dose of hypoxia (i.e. level of altitude, duration of daily exposure, and number of days or weeks) in the literature which limits our understanding of the physiological mechanisms underpinning enhanced performance upon return to sea-level. Both haematological and non-haematological adaptations are likely contributors to enhanced performance. However, the dose-response relationship of these physiological adaptations and subsequent performance responses to altitude training are unclear. Moreover, it appears that some individuals gain a greater benefit from altitude training than others, and there is evidence of substantial within-athlete variation in response. Given these uncertainties, it is unclear whether short (2-3 week) or longer (6 week) altitude training camps can elicit enhancements in sea-level performance of a sufficient magnitude to substantially improve competition performance, and at what time-point these performance gains are optimised upon return to sea-level. These issues are of particular interest to those athletes and coaches who typically undertake multiple altitude training camps within and between training years in preparation for competition.

For the purpose of this review 'altitude training' refers to the use of any form of natural or simulated altitude by athletes, 'traditional altitude training' refers to living and training at natural altitude, 'altitude exposure' refers to <24 $h \cdot d^{-1}$ at natural altitude and 'hypoxic exposure' refers to <24 $h \cdot d^{-1}$ at simulated altitude (hypobaric chamber or normobaric hypoxia in altitude houses, tent or via breathing apparatus). Given the large volume of scientific literature that pertains to the physiological responses to altitude, where possible this review will be limited to studies at moderate natural altitude or hypoxic exposure (<3,000m). This corresponds to the practices of athletes undertaking traditional altitude training (live and train high, LHTH) or live high/train low (live high/train low, LHTL) exposure. Higher altitudes (>3,000 m) will only be considered in relation to controlled studies examining performance measures and key physiological parameters of short duration intermittent hypoxic exposure (live low/train high, LLTH).

2.2. Performance

At the elite level, athletes are often very close to their performance limits. For these athletes, success in competition relies on a complex interaction of many factors, with small differences often determining a competition outcome (Hopkins & Hewson, 2001).

2.2.1. Evaluation of performance

Traditionally, maximal aerobic power ($\dot{V}O_{2max}$) was considered the most important physiological measure in the assessment of potential for endurance performance (Saltin & Astrand, 1967). More recently, other factors such as lactate threshold (Billat, 1996) and energy cost of submaximal work (Conley & Krahenbuhl, 1980) have been acknowledged to contribute to endurance performance. These parameters can be routinely measured in the laboratory to evaluate the efficacy of various training interventions on physiological determinants of performance. However, enhancing competition performance is the ultimate goal and therefore time trials or performance tests are arguably the most appropriate measures of progress during a season. In many individual sports, competition performance is typically assessed by considering the final time, technical components and pacing strategy. In the lead up to competition, or as an alternative in the absence of scheduled competition, time trial events or criterion efforts may be used and have a similarly high level of reliability as competition (Hopkins *et al.*, 1999).

2.2.2. Competition performance

In the simplest sense, successful performance is determined by an athlete's final time and which competitor is first across the finish line. Small variations in competition performance from race to race can determine an athlete's chance of winning. A key question is the magnitude of the smallest worthwhile enhancement in performance within and between competitions. Estimation of this reference value is a growing area of interest for sport scientists. In international competition, the smallest worthwhile enhancement in performance that will affect the athlete's chance of a medal is approximately half the typical race to race variation (expressed as a standard deviation) of the group (Hopkins *et al.*, 1999). The variability in competition performance has been derived using overall race times in national level swimmers (Pyne *et al.*, 2004; Stewart & Hopkins, 2000; Trewin *et al.*, 2004), elite cyclists (Paton & Hopkins, 2006) and track and field athletes (Hopkins *et al.*, 1999; Hopkins & Hewson, 2001). In these analyses, researchers reported a within-athlete coefficient of variation (CV) of 1.4% for junior level swimmers (Stewart & Hopkins, 2000) and 0.8% for Olympic level swimmers (Trewin *et al.*, 2004). For elite cyclists, CV was 1.0% in the kilo, 1.2% in road time trials and 2.4% in mountain-bike races (Paton & Hopkins, 2006). Similarly, in athletic events, CV was 0.9% for international 100-m sprinters (Hopkins *et al.*, 1999), 1.2 to 1.9% for national cross-country runners, 2.7 to 4.2% in half marathon and 2.6% in marathon runners (Hopkins & Hewson, 2001). Together, these findings equate to a smallest worthwhile enhancement of ~0.4-2.1% depending on event duration and sport, to substantially increase the likelihood of a medal in competition.

The age and experience of athletes appears to influence the reliability of competitive performance. In swimming competition, events differ not only in distance but technique. Junior swimmers were most consistent in performance in the same event between two competitions, less consistent between distances of a given stroke within each competition, and least consistent between strokes for a given distance (Stewart & Hopkins, 2000). In running events, younger runners had greater variability than older runners and males were generally more variable compared with female runners (Hopkins & Hewson, 2001). In contrast, females showed greater variability than males in swimming (Stewart & Hopkins, 2000) and cycling (Paton & Hopkins, 2006) events. Overall, in swimming, cycling and running events the fastest competitors demonstrated less variability than slower athletes (Hopkins & Hewson, 2001; Paton & Hopkins, 2006; Stewart & Hopkins, 2000). In Olympic level swimmers, most

medallists (87%) at the Olympic Games had a top-10 world ranking going into competition, although overall performance times were slower (~0.3%) than world-ranking time. A top-10 ranked swimmer who improved performance by ~0.6% (equivalent to 0.13 s in the 50 m freestyle for men at that time) substantially increased their chance of an Olympic medal (Trewin *et al.*, 2004).

In addition to variability of performance within competition, progression within and between competitions is a key consideration for coaches, athletes and sport scientists interested in the factors that affect performance. Since other athletes also improve their performance between competitions, a given athlete will need to improve by an additional amount equal to the mean progression of all the competitors to be in medal contention. Estimates of progression within and between competition have been quantified in elite swimmers in the year leading up to the Olympic Games (Pyne *et al.*, 2004). In the 12 months prior to the Olympics, competition performance improved ~1% in American and Australian swimmers. An individual swimmer needed an improvement of ~1% between heats and finals within a competition and an additional enhancement of ~0.4% (half the between competition variability) to be in contention for a medal (Pyne *et al.*, 2004).

With small differences in performance determining a competition outcome, information on the best way to expend energetic resources during a race is of considerable value to athletes and coaches. Pacing strategies will vary depending on the length of the event and the physiological requirements of the event. Determining the relationship between individual lap times and overall race performance may assist athletes and coaches on the best way to pace a competitive event. Estimates of the magnitude of change needed in lap time to substantially improve overall race time and competition performance are needed. These estimates can be used to evaluate the effectiveness of various training interventions undertaken by elite athletes to improve training and competition performance.

2.2.3. Effect of pacing on performance

In many individual sports, particularly in middle-distance and distance events, pacing strategies are considered an important element of performance (Foster *et al.*, 1993; Tucker *et al.*, 2006). Appropriate pacing in an event can be the difference between winning or losing for closely matched athletes (Foster *et al.*, 1994; Fukuba & Whipp, 1999). Observations during Olympic competition indicate sprint cycling and speed skating events had a marked reduction

in pace in the latter stages, while longer duration 4000-m cycling and 3000-m speed skating events demonstrated a comparatively even pace (Foster *et al.*, 1993). These findings have been confirmed experimentally. In shorter duration events (<2 min), a fast start to generate high velocities with a progressive slowing has been identified as the most successful strategy (Bishop *et al.*, 2002; Foster *et al.*, 2003; Foster *et al.*, 1994; Foster *et al.*, 1993). The fastest finish times in middle-distance events (2-4 min), are characterised by a fast start followed by a transition to relatively even pacing for the rest of the race (Ansley *et al.*, 2004; de Koning *et al.*, 1999; van Ingen Schenau *et al.*, 1994). Longer duration events such as distance running (Foster *et al.*, 1994; Tucker *et al.*, 2006) and 20km cycle time trial (Mattern *et al.*, 2001) typically have a slower start with an increase in pace towards the finish.

Recent competition analysis has confirmed that world records in 800-m running events (<110 s) are typified by a fast first lap and a notably slower second lap (Tucker *et al.*, 2006). In 2000-m rowing events (6-8 min), the strategy employed by most athletes in international competition is a fast start in the first 500 m, a progressive slowing through the second and third 500 m, and a comparatively faster final 500 m (Garland, 2005). It is clear that pacing strategy is a critical element of many sports and is largely determined by the duration of the event. However, only one study has evaluated lap times in actual competition and found no difference in the pattern of pacing between top-ranked and lower-ranked competitors in 2000-m rowing events (Garland, 2005).

Although reference values for the smallest worthwhile change in overall performance time have been quantified in swimming and running, the relationship between change in lap times, final time and final placing in competition is not well characterised. Estimates of the magnitude of change in lap time modelled in competition are necessary to evaluate the efficacy of various training interventions currently undertaken by elite athletes in preparation for competition. One such training intervention is altitude training, which is popular with athletes and coaches due to their belief that it induces favourable physiological adaptations that enhance performance on return to sea-level.

2.3. Physiological adaptations to altitude

The 1968 Olympic Games in Mexico City (~2,300 m) provoked a great deal of interest in the use of altitude training in preparation for competition. Decreased oxygen availability at altitude, results in a reduction of maximal oxygen uptake ($\dot{V}O_{2max}$) by approximately 1% for every 100 m above 1,500 m (Buskirk *et al.*, 1967). At altitude, performance in events with a

large aerobic component are impaired due to reduced oxygen availability, while shorter duration and wind-resisted events benefit from lower air density (Fulco *et al.*, 1998). The physiological adaptations that occur during acclimatisation to enhance oxygen uptake and transport are very similar to those resulting from exercise training (Wolski *et al.*, 1996). In fact, these enhancements in aerobic performance and oxygen-carrying capacity have been reported to be greater than aerobic training alone (Rusko *et al.*, 2004; Sawka *et al.*, 2000). Therefore, residing and/or training at altitude is believed to provide a potential means of inducing an additive effect over and above regular training for improving performance.

Acclimatisation to hypoxia of altitude is a complex process involving cardiopulmonary, haematological, and skeletal muscle adaptations. Scientists have long been interested in the mechanisms that may explain improvements in athletic performance following altitude training and/or exposure. The current debate on the mechanisms of enhanced sea-level performance is whether haematological and/or non-haematological adaptations primarily account for performance gains at sea level (Levine *et al.*, 2005). This section will examine the physiological adaptations to altitude or hypoxic exposure that underpin performance enhancement on return to sea-level.

2.3.1. Increased oxygen-carrying capacity

The popularity of altitude training with many coaches and athletes is based on the higher haemoglobin concentration ([Hb]) in high-altitude residents relative to sea-level residents (Reynafarje *et al.*, 1959) and evidence of accelerated erythropoiesis and increased number of red blood cells following acclimatisation to altitude (Ekblom & Berglund, 1991). These haematological adaptations and enhancements in oxygen-carrying capacity are believed to improve endurance performance on return to sea-level. However, increased [Hb] in high-altitude residents is not a universal adaptation. Himalayan natives exhibit lower [Hb] compared with Andean natives residing at similar altitudes (Beall *et al.*, 1998), and high-altitude residents of Ethiopia have similar [Hb] compared with fully acclimatised lowlanders (Beall *et al.*, 2002). Moreover, whether intermittent altitude or hypoxic exposure is sufficient to stimulate elevated serum erythropoietin (EPO) concentration, increase the number of young blood cells (reticulocytes) and increase red blood cell volume (RCV) or haemoglobin mass (Hb_{mass}) in already highly trained athletes is a matter of debate (Ashenden *et al.*, 2000).

2.3.1.1. Haemoglobin and haematocrit

Within the first few hours of ascent to altitude, a reduction in plasma volume occurs, resulting in a rise in [Hb] and haematocrit (Hct). This haemoconcentration serves to increase oxygen-carrying capacity for a given cardiac output by increasing the amount of haemoglobin (Hb) per unit of blood, but does not increase the number of red blood cells. While this adaptation is beneficial at rest and during low levels of exercise, a reduction in cardiac output from reduced blood volume reduces the endurance capacity at near-maximal and maximal levels of exercise. While haemoconcentration serves to increase the amount of Hb per unit of blood, a true increase in Hb content of ~1% per week, has been identified from previous altitude studies between ~1,800-3,000 m (Berglund, 1992). Given sea-level residents typically have approximately 11% (Boning *et al.*, 2001b) to 14% (Heinicke *et al.*, 2003) lower Hb content compared to native Andean residents (living at 2,650 m to 3,550 m respectively), it could take up to 3 to 4 months for full adaptation to occur (Berglund, 1992), much longer than the majority of altitude studies which have reported large increases in [Hb] over a few weeks. It is possible in these studies that the large change in [Hb] may be related to reduced plasma volume and haemoconcentration.

2.3.1.2. Accelerated erythropoiesis

There is an increase in serum EPO concentration within a few hours of arrival at altitude, the magnitude of which is directly related to the level of altitude (Eckardt *et al.*, 1989). The threshold altitude for stimulating sustained EPO release is 2,100-2,500 m (Ge *et al.*, 2002). An initial increase in EPO concentration within the first few days of altitude exposure is followed by a gradual decrease towards baseline values despite maintenance of the hypoxic stimulus. The concentration of serum EPO reflects a balance between EPO production and EPO consumption. Therefore the transient increase in EPO concentration on arrival at altitude reflects greater production of EPO, which falls within a few days as EPO consumption by the bone marrow increases (Grover & Bartsch, 2001). The time-course of peak EPO response following living and training at altitude (HiHi), living at altitude and training near sea-level (HiLo) and living and training near sea-level (LoLo) is illustrated in Figure 2.3.1.2. Mean values from different studies suggest that during HiLo, erythropoietin is higher than during HiHi after 2–4 days (Rusko *et al.*, 2004). A peak in EPO has been observed in the first few days at both natural altitude and simulated LHTL in athletes. Interestingly, the same pattern was observed following intermittent simulated LHTL at ~2650 m (3 blocks of 5 nights

separated by 3 nights) with a peak in EPO at the start of the first block but not in subsequent blocks in well-trained runners (Ashenden *et al.*, 2000).

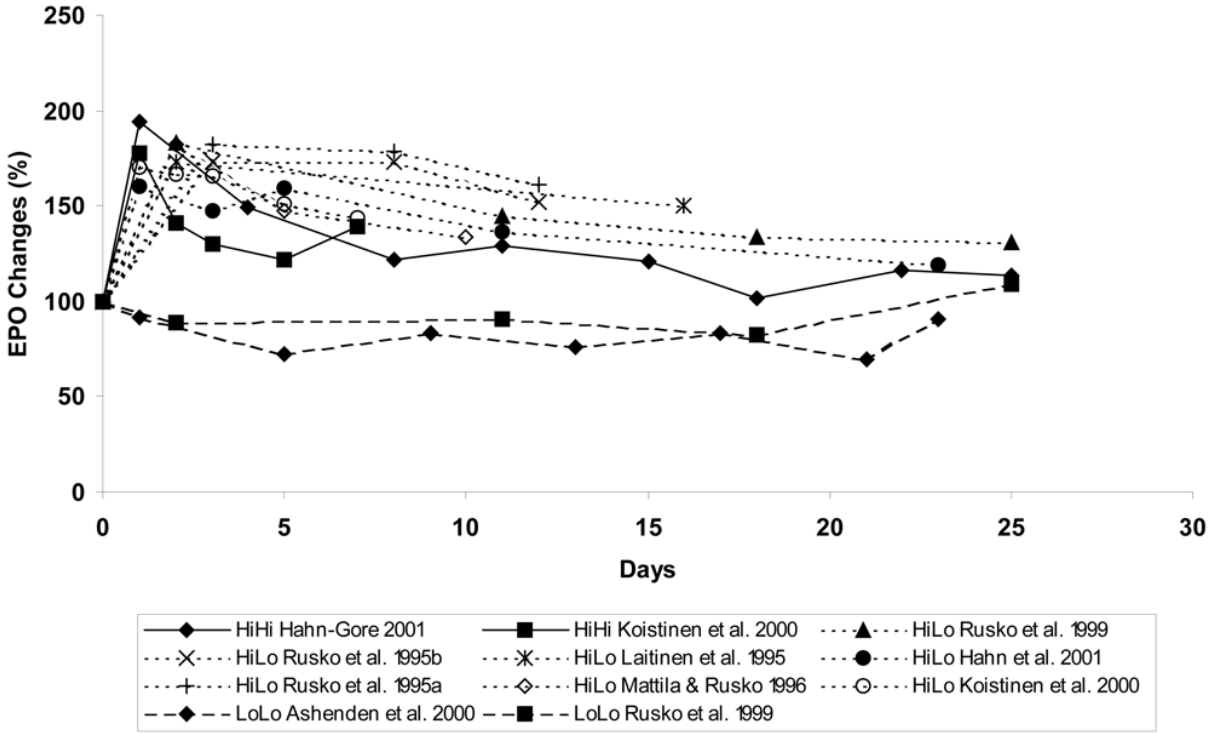

Figure 2.3.1.2. Percentage changes in serum erythropoietin (EPO) concentration during HiHi (live and train at altitude), HiLo (live high/train low) and LoLo (live and train near sea-level). Reproduced from Rusko *et al*. *J. Sports Sci.* 22:928-945, 2004

With sufficient hypoxic exposure, an increase in EPO concentration will stimulate an increase in reticulocytes and increase the number of red blood cells after ~4-7 days (Klausen *et al.*, 1991),. An increase in reticulocyte number has been reported after 1 week living at 1,695 m and training at 2,700 m (Klausen *et al.*, 1991), and 3 weeks living and training at 1,800 m (Friedmann *et al.*, 1999). Although the increase in number of reticulocytes may be related to increased training load in these studies (Friedmann *et al.*, 1999; Klausen *et al.*, 1991) since no control group was used. In other studies, reticulocyte count was increased after 7-10 days (12 $h \cdot d^{-1}$) of simulated LHTL between 2,000-2,700 m in untrained subjects (Koistinen *et al.*, 2000; Piehl Aulin *et al.*, 1998) and after 11 days (12 $h \cdot d^{-1}$) at ~3,000 m in competitive cyclists (Mattila & Rusko, 1996). In contrast, there was no increase in reticulocytes in cyclists or

endurance athletes after 2-3 weeks of simulated LHTL at ~2,650 m (8-11 $h \cdot d^{-1}$), compared with a matched control group, despite initial increases in EPO (Ashenden *et al.*, 2000; Ashenden *et al.*, 1999a; Ashenden *et al.*, 1999b). It is possible that the shorter daily hypoxic exposure in the latter studies failed to provide sufficient stimulus for accelerated erythropoiesis, however, total EPO response to moderate simulated altitude of 2,440 m was not different for 8, 12 or 16 $h \cdot d^{-1}$ of hypoxic exposure (Stray-Gunderson *et al.*, 2000). Therefore it may be the short half-life of EPO (~5.5 h) that explains why LHTL protocols where less than half of the day is spent in hypoxia, may not elevate EPO sufficiently to stimulate accelerated erythrocyte production (Hahn *et al.*, 2001). To obtain a beneficial acclimatisation effect of hypoxia, an increase in EPO concentration and reticulocyte count should increase oxygen transport capacity as measured by RCV or Hb_{mass}. Indeed high-altitude natives resident at 2,600 m to 3,500 m have ~ 10% greater RCV (Weil *et al.*, 1968) and 11 to 14% greater Hb_{mass} compared with sea-level counterparts (Boning *et al.*, 2001b; Heinicke *et al.*, 2003). Long term inhabitants at even higher altitudes above 4,300 m have up to 50% higher RCV (Reynafarje *et al.*, 1959).

2.3.1.3. Expansion of RCV or Hb_{mass}

While athletes and residents of moderate altitude have a higher total Hb_{mass} compared to their sea-level counterparts (Schmidt, 2002), whether a short sojourn to altitude in athletes can augment red cell mass is a matter of debate. The true increase in Hb_{mass} during altitude training has been calculated to be quite small and slow at ~1% per week (Berglund, 1992). No significant change in RCV or Hb_{mass} was observed after living and training for 3-4 weeks at 1,740-1,900 m in endurance athletes (Gore *et al.*, 1997; Svedenhag *et al.*, 1997), 3 weeks at 2,300 m in runners (Dill *et al.*, 1974), or 4 weeks at 2,690 m in elite cyclists (Gore *et al.*, 1998). A comprehensive review has reported that acclimatisation of 3 weeks to altitudes up to 4,000 m failed to demonstrate an increase in RCV (Sawka *et al.*, 2000).

In contrast to these findings, increases in red cell mass of ~9% over 4 weeks were reported in collegiate runners following living and training at 2,500 m (Levine & Stray-Gundersen, 1997). Interestingly, a similar magnitude of increase in Hb_{mass} of 1.9-3.4% per week was reported following administration of moderate doses of recombinant human erythropoietin (r-HuEPO, 50 U/kg, 3 $d \cdot wk^{-1}$, 25 days) (Parisotto *et al.*, 2000). The similarity in the magnitude of increase in red cell mass following 4 weeks of altitude training, despite the peak EPO response only half that of r-HuEPO administration, was speculated to relate to heavy physical

training (Levine & Stray-Gundersen, 1997). Increased red cell turnover following hard training appears to have elicited an erythropoietic response and accelerated the expansion of RCV (Levine & Stray-Gundersen, 1997). A true increase in Hb content of about 1% per week during acclimatisation to moderate natural altitude (Berglund, 1992), has recently been confirmed in highly trained athletes with a ~1% increase in Hb_{mass} (measured using the CO rebreathing technique) for every 100 h of hypoxic exposure (Clark *et al.*, 2009). Although training response may explain some variability in the findings, a genetic predisposition amongst successful endurance athletes (Sawka *et al.*, 2000), or differences in experimental methodology are perhaps more plausible (Gore *et al.*, 2005).

In summary, whether traditional altitude training or LHTL can stimulate accelerated erythropoiesis sufficiently to increase RCV or Hb_{mass} in well-trained athletes is controversial. However, it seems likely that the dose of hypoxic exposure in terms of level of altitude, daily exposure and number of days or weeks is a critical factor. A recent review has confirmed 3-4 weeks of traditional LHTH or LHTL (not less than 14 $h \cdot d^{-1}$) at altitudes above 2,100 m can increase Hb_{mass} by ~6% in highly trained athletes, however, this level of Hb_{mass} remains lower than elite athletes native to altitude (Schmidt & Prommer, 2008).

2.3.2. Skeletal muscle adaptations

A number of adaptations in skeletal muscle have been well-documented at high altitudes (>3,000 m), including increased capillarisation and mitochondrial capacity, decreased lactate production or increased clearance, improved buffer capacity, and alterations in substrate utilisation. These effects may provide an understanding of the mechanisms of acclimatisation, but may have limited application to explain enhanced performance in athletes at sea-level. There is growing evidence of a number of other non-haematological mechanisms that potentially contribute to enhanced athletic performance at sea-level, including improved economy, and enhanced pH regulation and buffer capacity (Gore *et al.*, 2007). This section will examine the physiological adaptations that are likely related to enhanced performance following altitude or hypoxic exposure in athletes.

2.3.2.1. Efficiency and economy

Improved efficiency (reduced oxygen cost for a given task) is an important contributor to performance, especially in highly trained athletes (Snell & Mitchell, 1984). With the association between economy and performance well documented (Saunders *et al.*, 2004a), a

substantial improvement in economy after altitude training should benefit performance. A trivial change in economy was observed in submaximal $\dot{V}O_2$ following altitude or hypoxic exposure (Levine & Stray-Gundersen, 1997; Piehl Aulin *et al.*, 1998), however, well-trained endurance athletes improved net efficiency after 23 nights of LHTL (Gore *et al.*, 2001) and running economy after 20 nights LHTL (Saunders *et al.*, 2004b). Overall, improvements in exercise economy of ~3-8% have been demonstrated following moderate simulated LHTL in athletes from several independent groups (Gore *et al.*, 2001; Neya *et al.*, 2007; Saunders *et al.*, 2004b; Schmitt *et al.*, 2006). Yet a recent review outlined no improvements in economy in athletes following moderate natural LHTL in three studies from one group of researchers (Lundby *et al.*, 2007). Overall, it appears that changes in submaximal $\dot{V}O_2$ from moderate altitude or hypoxic exposure are small and may be confounded by other effects including training (Paavolainen *et al.*, 1999).

The possible mechanisms of improved economy at high altitude include decreased cost of ventilation, preferential utilisation of carbohydrates, or tighter regulation of excitation and contraction processes (Green *et al.*, 2000). An improvement in economy from decreased cost of ventilation is not supported by the ventilatory response to hypoxic exposure which is characterised by a gradual and progressive increase in minute ventilation (V_E) at rest (Townsend *et al.*, 2002), an elevated V_E during submaximal exercise in acute hypoxia (Clark *et al.*, 2007) and higher V_E during maximal exercise following acclimatisation to LHTL (Gore *et al.*, 2001) or traditional LHTH (Faulkner *et al.*, 1967). A greater dependence on glucose metabolism in hypoxia, and decreased reliance on fat metabolism, would be advantageous for athletes in terms of generating more adenosine triphosphate (ATP) per mole of O_2 (Gore *et al.*, 2001; Green *et al.*, 2000). However, in well-trained athletes improved economy following moderate altitude or hypoxic exposure appears to be unrelated to decreased ventilation or a substantial shift in substrate use (Saunders *et al.*, 2004b). Therefore the key mechanisms of improved efficiency are likely to be a change in coupling of adenosine triphosphate (ATP) demand and supply (Hochachka, 1988) and decrease in the ATP cost of muscle contraction (Ponsot *et al.*, 2006).

2.3.2.2. Acid-base balance

On ascent to altitude, hyperventilation is initiated almost immediately to raise the partial pressure of oxygen (PO_2) in the alveoli. The resultant mild respiratory alkalosis decreases the partial pressure of carbon dioxide (PCO_2) and hydrogen ion level [H^+] and elicits a

corresponding increase in pH. The kidneys excrete more bicarbonate to return the plasma bicarbonate to CO_2 ratio to normal. In addition to the compensatory respiratory alkalosis during acclimatisation to altitude, elevated muscle lactate concentration and $[H^+]$ during exercise may explain an increase in buffer capacity (Balsom *et al.*, 1994). An increase in skeletal muscle *in-vitro* buffer capacity (βm) and attenuated acidosis has been reported following altitude training between ~2,000-2,700 m (Mizuno *et al.*, 1990; Svedenhag *et al.*, 1991). Living and training between 2,100-2,700 m for 2 weeks, resulted in a 6% increase in βm in gastrocnemius and triceps brachii in well-trained cross-country skiers (Mizuno *et al.*, 1990). Although a limitation of this study was the lack of control group training at sea-level, the relative increase in βm in gastrocnemius correlated highly (r=0.83) with short term running time (Mizuno *et al.*, 1990).

In two subsequent controlled studies, βm increased ~5-6% in the gastrocnemius in runners after 2 weeks living and training at ~2,000 m (Saltin *et al.*, 1995), and ~18% in endurance trained athletes after 23 nights of simulated LHTL at 3,000 m (Gore *et al.*, 2001). In contrast, βm was unchanged following 20 nights of simulated LHTL at 2,650 m in cyclists (Clark *et al.*, 2004) and decreased in runners living and training at ~2,500 m (Stray-Gunderson *et al.*, 1999), although these latter findings have only been published in abstract form. In line with the enhancements in βm, an increase in maximal accumulated oxygen deficit (MAOD) was observed following 2 weeks living and training at 2,000 m (Svedenhag *et al.*, 1991), and after 15 nights of simulated LHTL at 2,650 m in well-trained cyclists (Roberts *et al.*, 2003). Improvements in blood buffer capacity following acclimatisation may be due to an increased amount of haemoglobin or upregulation of the transport mechanisms that mediate HCO_3^-, lactate or H^+ transport into the red blood cells (Boning *et al.*, 2001a). While enhancements in buffer capacity remain uncertain, collectively there is evidence of an increase in anaerobic capacity which may offer a potential benefit to athletes upon return to sea-level.

2.3.2.3. Lactate metabolism

Acute exposure to altitude elevates blood lactate concentration and lactate release from the muscle at submaximal work rates. In contrast, maximal blood lactate concentration at exhaustion is similar to sea-level values (Brooks *et al.*, 1998). Following 2-3 weeks of acclimatisation, blood lactate at submaximal and maximal levels are reduced and approach values similar to those at sea-level (Brooks *et al.*, 1998). This so-called 'lactate paradox' of unexpectedly low blood lactate levels during exercise despite continuing hypoxia has been

attributed to a number of potential mechanisms (Hochachka, 1988), the most likely of which is improved coupling efficiency of metabolic signals to oxidative phosphorylation (Gladden, 1996). Recent investigations have challenged the classical 'lactate paradox' theory with reports that prolonged acclimatisation (>6 weeks) elicited similar submaximal blood lactate levels compared with sea-level following hypoxic exposure ~5,300 m (van Hall *et al.*, 2001) and altitude exposure of 5,400 m (Lundby *et al.*, 2000). These findings suggest the decrease in lactate may be a transient process, however, there was no control of diet prior to testing in these studies. Although the existence of the lactate paradox is controversial (West & van Hall, 2007) several months of residence at extreme altitudes (>5,500 m) may reduce anaerobic metabolism. However, the use of high and extreme altitudes in the investigation of the lactate response to acute and chronic hypoxia, may limit interpretation of these changes in relation to moderate levels of altitude (<3,000 m) commonly encountered by athletes. Nonetheless, a reduction in blood lactate concentration in elite distance runners training between 1,500-2,000 m is consistent with the experimental findings at higher altitudes (Bailey *et al.*, 1998). Similarly, after 3 weeks of training at 1,900 m in elite cross-country skiers, blood lactate decreased significantly despite no change in $\dot{V}O_{2max}$ (Ingjer & Myhre, 1992). In contrast, sleeping in moderate simulated altitude for 23 nights did not depress lactate accumulation or reduce calculated anaerobic ATP production (Gore *et al.*, 2001). In terms of performance, a rightward shift in the blood lactate curve following natural (Bailey *et al.*, 1998; Ingjer & Myhre, 1992; Pyne, 1998) or simulated (Nummela & Rusko, 2000) altitude, would suggest improved aerobic fitness (Weltman, 1995). However, it is unknown if the mechanisms associated with lower blood lactate after exposure to moderate altitude are the same as after exposure to high altitude (Brooks *et al.*, 1998), and whether this rightward shift after altitude training is caused by the same mechanism as training at sea-level.

In summary, living and training at moderate altitude may offer a potential benefit to sea-level performance, with an increase in red cell mass, buffering capacity, and lower oxygen cost and lactate for a given workload. These adaptations are advantageous for endurance performance; however, transfer of benefits to enhanced performance on return to sea-level is not fully supported by the scientific literature.

2.4. Performance following living and training at altitude

The majority of controlled studies examining traditional altitude training have found little advantage over sea-level training for enhancement in performance at sea-level for athletes,

especially in elite athletes (Bailey *et al.*, 1998; Jensen *et al.*, 1993; Svedenhag *et al.*, 1997; Svedenhag *et al.*, 1991). No significant increases in $\dot{V}O_{2max}$ were reported after 2-4 weeks living and training between ~1,750-2,300 m in highly trained runners (Adams *et al.*, 1975; Gore *et al.*, 1997; Svedenhag *et al.*, 1991), rowers (Jensen *et al.*, 1993), or cross-country skiers (Ingjer & Myhre, 1992). However, $\dot{V}O_{2max}$ increased ~5% in athletes who spent 4 weeks between 2,300-3,100 m (Levine & Stray-Gundersen, 1997). The disparity in these findings at different elevations has been attributed to altitudes below ~2200 m being insufficient to increase RCV and therefore $\dot{V}O_{2max}$ (Levine & Stray-Gundersen, 1992). Training at higher altitudes could lead to a relative detraining from reduced workloads (Buskirk *et al.*, 1967). Although most controlled scientific studies do not support endurance training at altitude for improved sea-level performance in athletes (Hahn & Gore, 2001; Rusko *et al.*, 2004; Saltin, 1996), many coaches and athletes still advocate the use of altitude training for optimal endurance performance (Dick, 1992). The favourable disposition to altitude training may relate in part to improvements in performance reported in uncontrolled studies in runners (Daniels & Oldridge, 1970; Dill & Adams, 1971), cyclists (Gore *et al.*, 1998), swimmers (Friedmann *et al.*, 2005; Pyne, 1998) and cross-country skiers (Mizuno *et al.*, 1990; Svedenhag *et al.*, 1997).

The timing of performance after altitude training is an important factor to realise performance gains from physiological adaptations following altitude training. The general consensus among coaches is that performance at sea-level is optimised ~14 days after altitude training (Dick, 1992), although scientific support for this contention is lacking. No significant change in $\dot{V}O_{2max}$ was observed at sea-level between 6 and 12 days (Gore *et al.*, 1998; Svedenhag *et al.*, 1997; Svedenhag *et al.*, 1991), or 21 days (Gore *et al.*, 1998) after descent from altitude. An additional factor contributing to the lack of agreement between studies may be differences in initial fitness levels of the athletes. Altitude training has been associated with regression to the mean, whereby those athletes starting with a relatively low initial value increased $\dot{V}O_{2max}$ and those with a relatively high value decreased $\dot{V}O_{2max}$ (Jensen *et al.*, 1993). It is also possible that highly conditioned athletes have reduced scope to enhance $\dot{V}O_{2max}$ following altitude training (Gore *et al.*, 1998; Ingjer & Myhre, 1992; Jensen *et al.*, 1993; Svedenhag *et al.*, 1991). However, well-conditioned cross-country skiers had a non-significant improvement (2.8%) in $\dot{V}O_{2max}$ after one month at 1900 m (Svedenhag *et al.*, 1997).

Similarly, elite runners who completed 25 days of altitude training at 2,500 m one week after national championships increased $\dot{V}O_{2max}$ by 2.9% (Stray-Gundersen *et al.*, 2001).

The lack of agreement on the effectiveness of living and training at moderate altitude may be in part due to different experimental designs (varying altitude level, duration of exposure, and modality of training), differences in subject characteristics (gender, fitness level and type of sport), or lack of an appropriate performance measure (e.g. unchanged $\dot{V}O_{2max}$ does not account for changes in running economy or anaerobic power). Another limitation of many of the studies is the absence of a control group, to confirm whether any change in performance is a result of altitude *per se* or a training effect. Subject numbers are often low (typically <10), so conventional statistical significance may not be appropriate for detecting small performance changes in this athletic population (Green, 2000). It also appears that some individuals may benefit more than others (Chapman *et al.*, 1998). Given that small mean changes and large variability (biological and test error) may mask individual changes, it is important to quantify individual responses to quantify the typical variability in response to the intervention.

On the whole it appears that traditional altitude training does not substantially enhance subsequent performance at sea-level. This outcome may be due to a number of problems arising from traditional altitude training that potentially negate any positive effect upon return to sea-level.

2.5. Limitations of traditional altitude training

Beneficial training adaptations such as increased oxygen-carrying capacity, enhanced aerobic enzymes and βm which occur at sea-level may be further enhanced by several weeks of training at moderate altitude. However, possible detrimental effects of living and training at moderate to high altitudes include a reduction in total blood volume and $\dot{V}O_{2max}$ and downregulation of key enzymes critical to maintaining membrane excitability, such as Na^+/K^+-ATPase (Aughey *et al.*, 2005) which may counteract the potential for enhanced performance on return to sea-level in some athletes (Wolski *et al.*, 1996). In addition, the combined stress of exercise and hypoxia has been associated with increased incidence of illness in athletes (Bailey *et al.*, 1998; Gore *et al.*, 1998)

At altitude, the reduction in $\dot{V}O_{2max}$ is proportional to that measured in normoxia (Shephard *et al.*, 1988). Accordingly, athletes with a higher sea-level $\dot{V}O_{2max}$ tend to show a greater reduction compared with untrained individuals. In addition, altitudes as low as 580 m have a detrimental effect on $\dot{V}O_{2max}$ in trained cyclists (Gore *et al.*, 1996). Although acclimatisation over 3-5 weeks will improve aerobic capacity at moderate altitude, $\dot{V}O_{2max}$ and endurance performance do not recover fully to sea-level values during that time (Adams *et al.*, 1975; Daniels & Oldridge, 1970; Dill & Adams, 1971; Jensen *et al.*, 1993; Pugh, 1967). Indeed, running performance was greatly reduced after a few days of living and training at 2,270 m (8.5% for 3 miles and 3.6% for 1 mile), and although improved after 4 weeks of acclimatisation (2.8% and 2.1% respectively), remained below sea-level values (Pugh, 1967).

The reduction in $\dot{V}O_{2max}$ at altitude increases the relative exercise intensity for the same power output. An increase in intensity results in higher blood lactate, heart rate, ventilation and perceived effort (Hahn *et al.*, 2001), and therefore may reduce self-selected training power output (Brosnan *et al.*, 2000; Fulco *et al.*, 1998; Levine & Stray-Gundersen, 1992). Runners were only able to maintain 76% and 82% of sea-level 5 km training pace while training at 2,500 m and 1,250 m respectively with interval training pace also reduced (Levine & Stray-Gundersen, 1997). Similarly, in elite cyclists mean power output was impaired across interval training sessions by ~5-6% under hypoxic exposure (Brosnan *et al.*, 2000) and blood lactate accumulation was increased despite a reduction in maximal power during repeated sprints in moderately trained subjects (Balsom *et al.*, 1994). Furthermore a high correlation is evident between maintenance of high training intensity during altitude exposure and improved performance on return to sea-level (Chapman *et al.*, 1998). Together these findings confirm the likelihood of a relative detraining effect at moderate altitude, potentially detrimental to athletes training for extended periods at altitude.

Given the lack of support from the majority of controlled studies, scientists have long been interested in developing new methods of altitude or hypoxic exposure that may be more beneficial for sea-level performance. Alternate periods (7-14 days) of training at altitude and sea-level have been used to minimise losses in speed, power and other neuromuscular capacities from reduced training intensities (Daniels & Oldridge, 1970). In more recent years, discontinuous use of hypoxia each day has been investigated to optimise the stimuli for central and peripheral changes that improve oxygen transport and utilisation, while minimising the detraining effect associated with chronic hypoxia.

2.6. Intermittent altitude or hypoxic exposure

Intermittent altitude or hypoxic exposure is broadly divided into two strategies. Moderate altitude or hypoxic exposure can be provided at rest for some, or most, of the day with the primary goal to facilitate altitude acclimatisation (live high/train low, LHTL). Alternatively, short periods (~1-3 $h \cdot d^{-1}$) of moderate to severe hypoxic exposure (live low/train high, LLTH) can be provided at rest (Intermittent Hypoxic Exposure, IHE), or during part of an athlete's normal daily or weekly training (Intermittent Hypoxic Training, IHT). These popular altitude training methodologies are outlined in Figure 2.6.

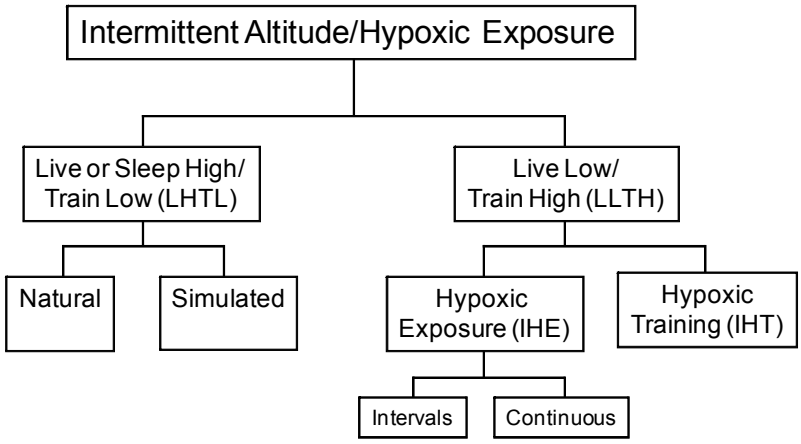

Figure 2.6. Contemporary methods of altitude training. Altitude or hypoxic exposure provided at rest for some or most of the day (LHTL), or for short periods during the day (LLTH). LLTH hypoxic exposure provided at rest (IHE, hypoxic:normoxic intervals or continuous exposure) or hypoxic exposure during training (IHT). Adapted from Wilber. *Med. Sci. Sports Exerc.* 39:1610-1624, 2007.

2.6.1. Live High/Train Low

Natural live high/train low (LHTL), where athletes sleep at altitude to facilitate acclimatisation and train at lower altitudes during the day to maintain training velocities was first described in the early 1990's (Levine & Stray-Gundersen, 1992). A well-designed study in collegiate runners ($\dot{V}O_{2max}$: ~64 $ml \cdot kg^{-1} \cdot min^{-1}$) comprised a 6 week lead-in phase, followed by 4 weeks of living at 2,500 m and training at ~2,500 m (High-High) or ~1,250 m (High-Low) respectively (Levine & Stray-Gundersen, 1997). The control group (Low-Low) lived

and trained at 150 m. Both altitude groups increased RCV (9%) and $\dot{V}O_{2max}$ (5%) to a similar extent, but only the High-Low group improved 5 km run time (1.4%) compared to the pre-test. The change in time trial performance for High-High, High-Low and Low-Low groups are shown in Figure 2.6.1. Enhanced performance following LHTL was attributed to increased RCV and $\dot{V}O_{2max}$, combined with maintenance of training velocities 'near' sea-level (Levine & Stray-Gundersen, 1997). However, it is not clear why the control group were substantially slower (~26 s, 2.5%) following 4 weeks of matched training at sea-level. Interestingly, both altitude groups showed a trend towards performance improvement for three weeks after return to sea-level compared with the immediate post-test.

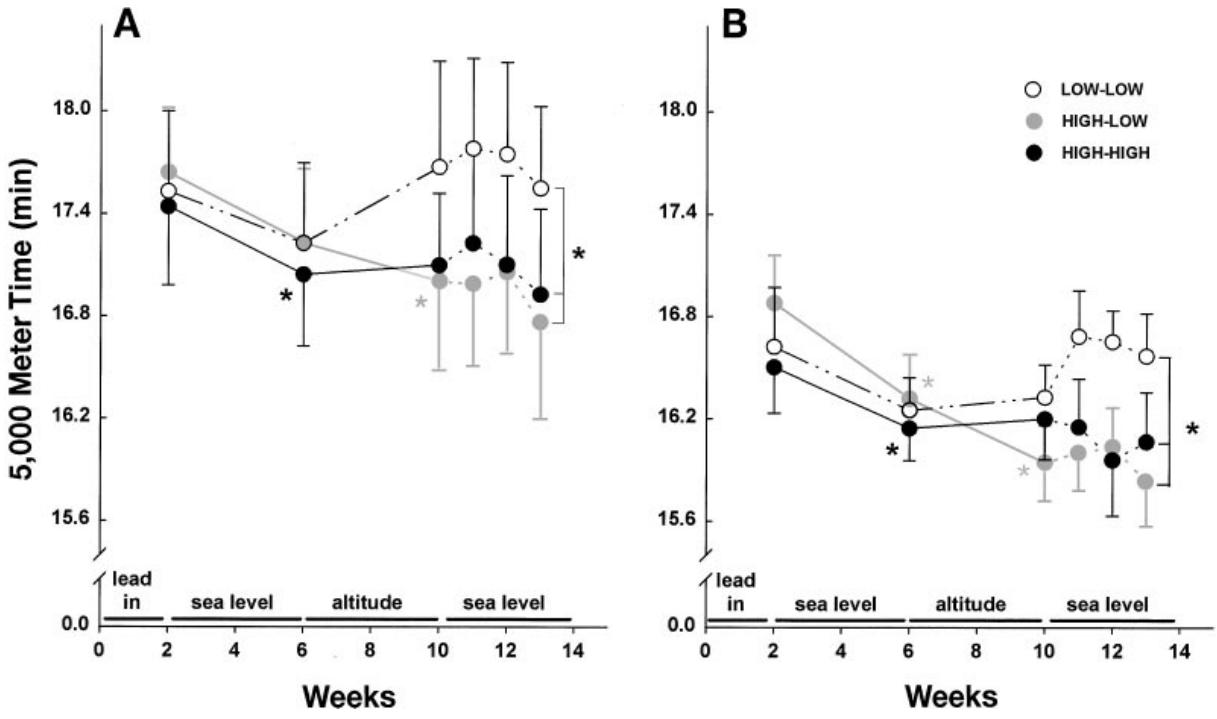

Figure 2.6.1. Time trial (5,000 m) results for all subjects (n=13/group; 9 men, 4 women, A) and also for men only (n=9/group; B) at baseline, after sea-level training in Dallas (sea level), and after altitude training camp or sea-level control (altitude). Time trials (5,000 m) were performed 3, 7, 14, and 21 days after leaving training camp. Three groups: Low-Low = sea-level control group (150 m); High-Low = living at 2,500 m and training at 1,250 1,400 m; and High-High = living at 2,500 m and training at 2,500–2,700 m,*P< 0.05 compared with previous time point. Asterisks next to brackets indicate interaction statistics for analysis of variance, P< 0.05. Reproduced from Levine & Stray-Gundersen. *J. Appl. Physiol.* 83(1):102-112, 1997.

A follow-up study used a modified LHTL approach with national level runners for 27 days (Stray-Gundersen *et al.*, 2001). Athletes lived and performed base training at ~2,500 m and interval training at 1,250 m to minimise travel up and down the mountain (HiHiLo). Although this approach was associated with improvements in $\dot{V}O_{2max}$ (2.9%) and 3 km run time (1.1%), the lack of control group is a limitation of this study. Increases in Hb_{mass} (5%), $\dot{V}O_{2max}$ (4%) and improved 5 km time trial performance (1.6%) were observed in endurance athletes after 24 days of living at 2,500 m and training between 1,000-1,800 m, compared with a control group living between 500-1,600 m (Wehrlin *et al.*, 2006). However, differences in the sporting discipline and initial fitness of the athletes in the altitude (orienteers, ~57 $ml \cdot kg^{-1} \cdot min^{-1}$) and control (cross country skiers, ~70 $ml \cdot kg^{-1} \cdot min^{-1}$) groups make interpretation of these findings more difficult. In addition, training was performed at low to moderate altitudes in both groups, so the possibility of a small hypoxic training stimulus cannot be discounted. In contrast, two weeks of LHTL at lower altitudes (living at 1,956 m and training at 800 m) did not increase Hb_{mass} or $\dot{V}O_{2max}$, although there was a trend towards improved performance in well-trained triathletes (Dehnert *et al.*, 2002). It appears that the level of altitude (>2, 000 m) and the number of weeks of exposure (> 2 weeks) are the critical features of natural LHTL needed to elicit a substantial increase in Hb_{mass} in athletes.

2.6.2. Live or Sleep High/Train Low

Given the performance gains reported in runners following LHTL but not LHTH (Levine & Stray-Gundersen, 1997), normobaric hypoxic chambers were developed to simulate LHTL (Rusko, 1996) in countries where the geography does not readily permit natural LHTL. Further modifications of this protocol have involved the use of hypobaric chambers or normobaric hypoxic tents or breathing apparatus. Using this approach, intermittent exposure to hypoxia at rest is proposed to stimulate acclimatisation to hypoxia while maximal aerobic capacity is maintained through training in normoxia. A summary of the published studies of natural and simulated LHTL with measures of performance and haematological parameters in athletes are reported in Table 2.6.2.

Using simulated LHTL, mean time trial velocity was increased by ~4% in elite cyclists 11 days (18 $h \cdot d^{-1}$) at 3,000 m (Mattila & Rusko, 1996), however there was no control group in this study. At lower simulated altitude, small performance enhancements (~0.8%) were observed in 400m runners after 10 days (16 $h \cdot d^{-1}$) at 2,200 m compared with no change in the control group (Nummela & Rusko, 2000). In a series of studies in elite athletes, there were no

substantial changes in $\dot{V}O_{2max}$ (Gore *et al.*, 2001; Hahn *et al.*, 2001) nor erythropoietic markers/Hb_{mass} (Ashenden *et al.*, 2000; Ashenden *et al.*, 1999a; Ashenden *et al.*, 1999b) following 12-23 days of LHTL (8-11 $h \cdot d^{-1}$) between 2,650-3,000 m. However, performance lasting ~4 min showed a 1% improvement (Hahn *et al.*, 2001). Although it appears that small enhancements in performance can be elicited by simulated LHTL, there is a wide variation in the magnitude of performance gains and uncertainty on the mechanisms underpinning this enhancement.

A multicentre approach was established to examine the effects of 13-18 nights of simulated LHTL (~2,500-3,500 m) in elite athletes. The studies examined physiological and performance responses to LHTL in cross-country skiers (Robach *et al.*, 2006a), swimmers (Robach *et al.*, 2006b) and runners (Brugniaux *et al.*, 2006b). There was no substantial change in $\dot{V}O_{2max}$ of skiers after 18 nights (11 $h \cdot d^{-1}$), and a non-significant increase in swimmers after 13 nights (16 $h \cdot d^{-1}$). Runners improved $\dot{V}O_{2max}$ by 9.6% after 18 nights (14 $h \cdot d^{-1}$) which remained elevated two weeks later (5.2%). Collectively there appears to be a small performance benefit for some elite athletes following LHTL, however the underlying mechanisms of this enhancement is unclear. It seems likely that the dose of altitude exposure (daily exposure and length of exposure) influences the time course and magnitude of adaptations and physiological mechanisms responsible for enhanced performance on return to sea-level (Wilber *et al.*, 2007).

Table 2.6.2. Summary of findings following hypoxic (simulated LHTL) or altitude (natural LHTL) exposure in athletes

Type of athletes	n (alt/ con)	Baseline $\dot{V}O_{2max}$	Live High/ Train Low (m)	Live/Train Low (m)	Days; hours per day	Physiological and Performance Outcomes	Haematological parameters	Reference
SIMULATED LHTL								
Cyclists	5	-	3,000/SL	-	11d; 18h·d^{-1}	[1] ↑TT velocity (4%)	↑EPO, ret	(Mattila & Rusko, 1996) [ab]
Endurance	12/10	66/65	2,500/SL	SL	25d; 16h·d^{-1}	[1] ↑ $\dot{V}O_{2max}$ (3%)	↑tHb (4%); ↑EPO	(Rusko *et al.*, 1999) [ab]
Sprinters	8/10	-	2,200/SL	SL	10d; 16h·d^{-1}	[1] ↑400m run (0.8%)	↔[Hb]	(Nummela & Rusko, 2000)
Skiers	6/5	62/59**	<3,500/1,200	1,200	18d; 11h·d^{-1}	[2] ↔ $\dot{V}O_{2max}$ (-2%); ↔T_{exh}	↔RCV; ↑EPO, sTfR;	(Robach *et al.*, 2006a)
Swimmers	9/9	58/58**	<3,000/1,200	1,200	13d; 16h·d^{-1}	[0] ↔ $\dot{V}O_{2max}$ (+5%); ↔TT_{2K} swim (+3%)	↑RCV (8%); ↔EPO, sTfR	(Robach *et al.*, 2006b)
Runners	5/6	63/63**	<3,000/1,200	1,200	18d; 14h·d^{-1}	[2] ↑ $\dot{V}O_{2max}$ (+6%); ↓HR in TT_{10min}	↔RCV, EPO; ↑sTfR	(Brugniaux *et al.*, 2006b)
Endurance	11	-	<3,500/SL	cross-over	25d; 10h·d^{-1}	[1] ↑$TT_{800-3000m}$ (1-1.9%)	↓[Hb], Hct	(Hinckson & Hopkins, 2005)
Runners	10/6	~60	3,000/SL	SL	29d; 11h·d^{-1}	[1] ↓ $\dot{V}O_2$ (3%); ↔VO_{2max} or T_{exh} (+9%)	↔tHb	(Neya *et al.*, 2007)
Runners	9/9	71/71*	2,860/600	600	46±8d; 9h·d^{-1}	[1] ↓ $\dot{V}O_2$ (3%); trivial ↑ $\dot{V}O_{2max}$ (1.5%)	↑tHb (5%)	(Saunders *et al.*, 2009)
Combined	***20/23***	***~4.5****	***2,650-3,000***	***600***	***11-23d***	[0] ↓ ***$\dot{V}O_{2max}$ (2.4%); ↑0.9% TT effort***	↔ ***tHb, ret; ↑EPO***	***(Hahn et al., 2001)***
Cyclists	*5/6*	*3.9/3.7**	*2,650/610*	*600*	*12d; 8-11h·d^{-1}*	[0] ↔ *$\dot{V}O_{2max}$; ↔TT_{4min} (+2%)*	↔ *tHb; ↔ret*	*(Ashenden et al., 1999b)*
Kayakers	*4/5*	*4.1/4.2**	*2,650/610*	*600*	*11d; 8-11h·d^{-1}*	[0] ↔ *$\dot{V}O_{2max}$; ↔TT_{4min} (+2%)*	-	
Runners	*5/5*	*4.7/4.9**	*2,650/610*	*600*	*15d; 8-11h·d^{-1}*	[0] ↔ *$\dot{V}O_{2max}$ (-3%); ↔1500m run*	↑*EPO; ↔ret*	*(Ashenden et al., 2000)*
Endurance	*6/7*	*5.1/5.0**	*3,000/610*	*600*	*23d; 8-11h·d^{-1}*	[0] ↓ *$\dot{V}O_{2max}$ (-4%); ↔TT_{4min}*	↔ *tHb; ↔ret*	*(Ashenden et al., 1999a; Gore et al., 2001)*

NATURAL LHTL

Runners	13/13	64/62	2,500/1,250	150	28d; ~20h·d^{-1}	^{0}↑ $\dot{V}O_{2max}$ (5%); ↑TT_{5K} (1.4%)	↑RCV (9%); ↑EPO	(Levine & Stray-Gundersen, 1997)
Endurance	10/7	57/70	2,500/<1,800	500-1,600	24d; ~18h·d^{-1}	^{1}↑ $\dot{V}O_{2max}$ (4%); ↑TT_{3K} (1.6%)	↑tHb (5%); ↑EPO, ret	(Wehrlin *et al.*, 2006)
Runners	21	72	2,500/1,250	-	27d; ~20h·d^{-1}	^{0}↑ $\dot{V}O_{2max}$ (3%); ↑TT_{3K} (1.1%)	↑EPO, sTfR	(Stray-Gundersen *et al.*, 2001)
Triathletes	11/10	62/60	1,956/800	SL	14d; ~15h·d^{-1}	^{1}↔ $\dot{V}O_{2max}$ (+12%); ↔PPO	↔tHb (con ↓5%); ↑EPO	(Dehnert *et al.*, 2002)

n=number of participants in altitude (**alt**) and control (**con**) groups; **Baseline $\dot{V}O_{2max}$** (maximal aerobic power) in ml·kg^{-1}·min^{-1} or L·min^{-1}; * $\dot{V}O_{2max}$ measured at 600m; ** $\dot{V}O_{2max}$ measured at 1200m; **$\dot{V}O_2$**=submaximal oxygen uptake; **PPO**=peak aerobic power output; **TT**=time trial performance; **T_{exh}**=time to exhaustion; **HR**=heart rate; **EPO**=erythropoietin; **tHb**=haemoglobin mass; **RCV**=red cell volume; **sTfR**=soluble transferrin receptor; **Fer**=ferritin; **ret**=reticulocytes; **[Hb]**=haemoglobin concentration; **Hct**=haematocrit;

Post-test: ^{0} within ~1-3 days; ^{1} within one week; ^{2} after two weeks. ↑ increased/faster; ↓ decreased/slower; ↔ unchanged compared with control group;

All changes marked ↑ or ↓ were statistically significant. Where differences in change scores were non-significant compared with the control condition, percent differences have been calculated from the raw data and differences in performance greater than 1% presented.

2.6.3. Dose-response of LHTL

Those studies which have shown a significant improvement in endurance performance following 3 to 4 weeks of natural LHTL (living at 2,500 m), have also reported a significant correlation between the change in $\dot{V}O_{2max}$ and RCV or Hb_{mass} (Levine & Stray-Gundersen, 1997; Wehrlin & Marti, 2006). On the other hand, there is evidence of improved running economy (Neya *et al.*, 2007; Saunders *et al.*, 2004b) and maximal performance (Gore *et al.*, 2001; Hahn *et al.*, 2001) following 2 to 4 weeks (8-11 $h \cdot d^{-1}$) of simulated LHTL (2,650-3,000 m) in the absence of substantial increases in erythropoietic markers and/or Hb_{mass} (Ashenden *et al.*, 2000; Ashenden *et al.*, 1999a; Ashenden *et al.*, 1999b; Neya *et al.*, 2007; Saunders *et al.*, 2004b). These conflicting findings on whether hypoxia improves Hb_{mass}, $\dot{V}O_{2max}$, running economy and performance indicate a possible threshold for the accumulated altitude dose necessary for effective adaptation.

The optimal altitude level for natural LHTL has been investigated with athletes living at four different altitudes (1,780 m, 2,085 m, 2,454 m, 2,805 m) and training between 1,200-3,000 m for 4 weeks (Levine & Stray-Gundersen, 2006). There was a dose-dependent increase in $\dot{V}O_{2max}$ (8 ml, 206 ml, 308 ml, 301 ml) with increasing altitudes (Witkowski *et al.*, 2001). However, this pattern of increase did not result in a proportionate improvement in 5-km time trial performance outcome. There was ~3% improvement in time trial performance after living at the middle two altitudes (~2,000-2,500 m), and ~1% improvement after living at both the lowest and highest altitudes (Witkowski *et al.*, 2001). The findings of increased $\dot{V}O_{2max}$ and a disproportionate improvement in time trial performance, are consistent with the model that maximal aerobic power is only one of a number of factors that contribute to athletic performance. Although $\dot{V}O_{2max}$ is considered a useful predictor of performance in endurance events (Saltin & Astrand, 1967; Schabort *et al.*, 2000), it is poorly associated with performance in some elite athletes (Snell & Mitchell, 1984). According to the model of di Prampero (di Prampero, 1986), $\dot{V}O_{2max}$, percent of $\dot{V}O_{2max}$ that can be maintained for the duration of the run (fractional utilization), and energy cost of running (economy) account for 70% of between-subject variation in performance. Therefore it is possible that some athletes will gain improvements in performance following altitude training without concomitant increases in Hb_{mass} and $\dot{V}O_{2max}$.

In most natural LHTL studies, athletes 'lived' at altitude for at least 20 $h \cdot d^{-1}$. In contrast, simulated altitude studies have employed daily exposures ranging from 8-18 $h \cdot d^{-1}$. No increase in red cell mass has been reported after simulated LHTL for less than 12 $h \cdot d^{-1}$ (Ashenden *et al.*, 1999a; Ashenden *et al.*, 1999b; Neya *et al.*, 2007; Robach *et al.*, 2006b; Saunders *et al.*, 2004b), whereas increases of ~4-10% have been reported following 14-18 $h \cdot d^{-1}$ (Brugniaux *et al.*, 2006b; Robach *et al.*, 2006a; Rusko *et al.*, 1999). Interestingly, one exception is ~5% increase in Hb_{mass} in well-trained runners after 12 weeks of LHTL (5 $d \cdot wk^{-1}$) for 9 $h \cdot d^{-1}$ (Saunders *et al.*, 2009). These results suggest that the total hours of hypoxia (~400 h) is a key factor for increasing Hb_{mass}, however, this length of intervention may not be practical for most athletes. As Hb_{mass} was only measured before and after the experimental period, it is unknown when Hb_{mass} was first elevated above baseline (i.e. ~250 h is equivalent to 12 $h \cdot d^{-1}$ for 3 weeks). Another finding of note in this study, was that the change in Hb_{mass} was not associated with a corresponding increase in $\dot{V}O_{2max}$ (Saunders *et al.*, 2009). Increases in Hb_{mass} and $\dot{V}O_{2max}$ following moderate hypoxic exposure for >12 $h \cdot d^{-1}$ are consistent with the current recommendations to gain an acclimatisation effect to hypoxia (Rusko *et al.*, 2004). Given the shorter daily exposures of simulated LHTL, higher altitudes up to ~3,000 m can be well-tolerated (Brugniaux *et al.*, 2006a). On the other hand, it appears shorter daily exposures (<12 $h \cdot d^{-1}$) can also improve performance in the absence of increased Hb_{mass} and $\dot{V}O_{2max}$ after 3 weeks, and extended exposure over 3 months (9 $h \cdot d^{-1}$) can substantially increase Hb_{mass} but not $\dot{V}O_{2max}$. The mechanism for the disproportionate mean change in $\dot{V}O_{2max}$ with increased oxygen carrying capacity (Hb_{mass}) remains unclear.

2.6.4. Individual variability

Many altitude studies have shown considerable individual variation in physiological and performance responses to hypoxia. Substantial individual variation, similar to or greater than the mean response, has been observed in performance change following both traditional altitude training and LHTL (Bailey *et al.*, 1998; Jensen *et al.*, 1993; Levine & Stray-Gundersen, 1997; Rusko, 1996; Svedenhag *et al.*, 1991). A number of studies have reported between-athlete variation in the hypoxia-induced increase in EPO and red cell mass (Chapman *et al.*, 1998; Friedmann *et al.*, 2005; Rusko *et al.*, 1999), which has been identified as a potential determinant of change in sea-level performance following altitude training (Chapman *et al.*, 1998). A retrospective analysis of 39 collegiate runners (Chapman *et al.*,

1998) categorised athletes as responders or non-responders based on change in time trial performance (Figure 2.6.4).

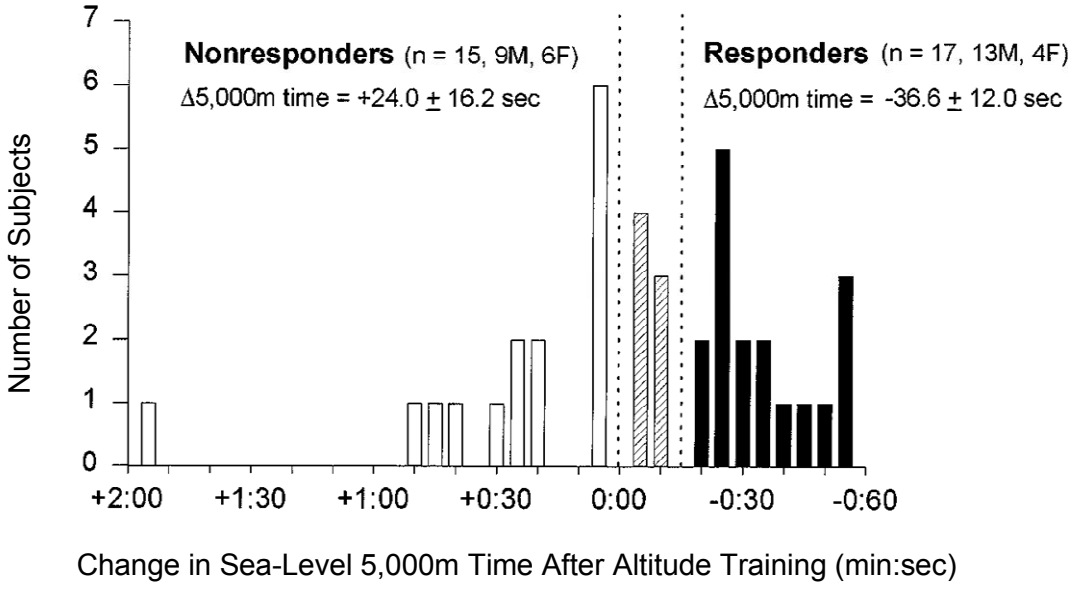

Figure 2.6.4. Histogram displaying variation in change (Δ) in 5,000-m run time after 4 wk of altitude training in 39 athletes. Athletes were retrospectively divided into groups of responders (filled bars), nonresponders (open bars), and indeterminate (hatched bars) on the basis of change in 5,000-m performance. n, No. of subjects; M, men; F, women; +, increase in time; -, decrease in time; dotted lines, cut-off for group definitions. Reproduced from Chapman *et al. J. Appl. Physiol.* 85(4):1448-1456, 1998.

Responders had a larger acute EPO response within 30 h of ascent to altitude, elevated EPO after 14 days at altitude and significant increases in total RCV and $\dot{V}O_{2max}$ compared with non-responders. Although exclusion of individual data (n=7) and overlap in the range of EPO response in responders (57 ± 29%, mean ± SD) and non-responders (37 ± 29%) may limit the strength of their conclusions, improved performance and $\dot{V}O_{2max}$ after a 4 week altitude camp was attributed to an EPO-mediated increase in RCV and maintenance of training intensity near sea-level values (Chapman *et al.*, 1998). The relationship between EPO response and RCV or Hb_{mass} has not been confirmed following living and training at altitude in swimmers (Friedmann *et al.*, 2005) or simulated LHTL in endurance athletes (Rusko *et al.*, 1999) with large between-athlete variability reported in erythropoietic response.

Individuals exposed to varying altitudes (1,780–2,800 m) for 24 hours had a consistent EPO response (individuals with the greatest EPO response at low altitudes had the greatest EPO response at high altitudes) indicating that regulation of the EPO response to hypoxia may be genetically determined (Ge *et al.*, 2002). However, following 24 hours of hypoxic exposure (2,800 m) the differential EPO response to hypoxia (change in serum EPO: -41 to 400 %) was not substantially associated with markers of EPO regulation (Jedlickova *et al.*, 2003). In addition, a recent case-study of a competitive cyclist reported a variable EPO response for an individual athlete (-11 to +38%) to repeated bouts of sleeping at simulated altitude ~2,800 m (Garvican *et al.*, 2007). It appears unlikely that individual variability in the response to hypoxia is related solely to EPO regulation. Another potential candidate at the transcriptional level is the hypoxia inducible factor 1 (HIF-1). HIF-1 acts on almost every tissue in the body in response to hypoxia, and is the global regulator of oxygen homeostasis (Semenza, 2000). HIF-1 is rapidly stabilised under hypoxic conditions and regulates a number of genes involved in erythropoiesis, angiogenesis, glycolysis, pH regulation and ventilation (Lee *et al.*, 2004). The large number of HIF-1 mediated responses to hypoxia implies that an increase in EPO concentration could be concurrent with other physiological changes such as increased carbohydrate metabolism, increased ventilation, enhanced muscle buffer capacity and more efficient use of oxygen in the muscles. All of these other factors could contribute to the improvement in time trial performance which has been (erroneously) attributed to EPO response (Chapman *et al.*, 1998). As yet, attempts to correlate HIF-1α to altitude-induced performance enhancements in athletes have been unsuccessful (Mounier *et al.*, 2006). However, it is conceivable that performance indicators such as $\dot{V}O_{2max}$ or peak power are not sensitive enough to detect more subtle changes that are functionally relevant in elite athletes.

In summary, both natural and simulated LHTL have been evaluated extensively in research settings and contemporary practice. Overall, studies of natural or simulated LHTL have found ~1% enhancement in events lasting between ~45s to 14 min. These improvements in performance have been attributed to haematological (RCV or Hb_{mass}) and/or non-haematological adaptations (such as improved economy and muscle buffer capacity). The magnitude of change in Hb_{mass} following LHTL appears to be dose-dependent, with increases in Hb_{mass} following 3-4 weeks of >12 $h \cdot d^{-1}$ (~250-340 h) or 12 weeks of ~9 $h \cdot d^{-1}$ (~400 h). While a number of studies have reported between-athlete variation in physiological and performance response to hypoxia, it is not clear if the same degree of variation exists for an individual athlete. Identifying the mechanisms underpinning the variability in response and

establishing whether individual athletes respond in the same way to repeated hypoxic exposures requires further investigation.

2.7. Brief intermittent hypoxic exposure

Short duration high to severe hypoxia, is typically provided at rest (IHE) or during exercise or training (IHT) either in a normobaric or hypobaric chamber, or via breathing a gas mixture with reduced oxygen content. IHE typically consists of repeated periods of switching between breathing hypoxic and normoxic air during an indoor session lasting ~1-1.5 hours. The short periods of breathing hypoxic gas (typically 5:5 or 6:4 minutes of breathing hypoxic:normoxic air) allow for application of severe hypoxia (Fraction of inspired oxygen, FiO_2=10-12%, equivalent to 4,500-6,000 m) during these intervals. This method of IHE was primarily proposed as treatment for various illnesses as well as improvement of sea-level performance (Serebrovskaya, 2002). IHE can also be provided at rest in a continuous exposure typically lasting ~1-3 hours at oxygen levels equivalent to ~4,000-5,500 m. Continuous hypoxic exposure at rest was initially introduced for preparation of mountaineers to achieve some level of acclimatisation prior to ascent to high altitudes (Rodriguez *et al.*, 1999). The mechanisms involved with this concept are therefore similar to other forms of altitude training. The practice of training under hypoxic conditions while spending the rest of the day in normoxia (IHT), is based partly on the assumption that muscular responses to training are more pronounced under hypoxia, and partly on the deterioration of skeletal muscle tissue after extended altitude or hypoxic exposure (Hoppeler *et al.*, 1990). The rationale for using hypoxic exposure during exercise (typically ~0.5-2 hours) is to increase the metabolic stress on skeletal muscle to achieve adaptational stimulus beyond that which can be achieved under normoxia (Hoppeler *et al.*, 2008).

2.7.1. Hypoxic exposure at rest (IHE)

2.7.1.1. Hypoxic intervals

Several studies have investigated intermittent hypoxic exposure using repeated cycles of hypoxia:normoxic breathing for 1-1.5 hours in athletes. Following 15 days of IHE (6 x 6:4min, daily; saturation of oxygen, SaO_2 ~90 to 80%) there were improvements in sprint performance and lower blood lactate in hockey and soccer players (Wood *et al.*, 2006). Similarly, 3 weeks of IHE (6x 5:5min, $5 \cdot wk^{-1}$, FiO_2 12 to 10%) improved peak power output by ~7% in subelite kayakers (Bonetti *et al.*, 2006) and ~5% in competitive cyclists (Bonetti *et*

al., 2009). In contrast, endurance trained athletes (mean $\dot{V}O_{2max}$, ~60 ml·kg^{-1}·min^{-1}) failed to substantially improve $\dot{V}O_{2max}$ or anaerobic capacity (Tadibi *et al.*, 2007) after 15 days of IHE (6-7 x 6:4min, daily, FiO_2 ~12 to 10%). Following longer periods of daily exposure, 3 weeks of IHE (9x 5:5min, 5·wk^{-1}, FiO_2 13 to 10%) improved 3 km time trial performance (~2%) in multi-sport athletes of mixed ability (Hamlin & Hellemans, 2007). However, after 4 weeks of IHE (9x 5:5min, 5·wk^{-1}, FiO_2 12 to 10%) there were no substantial improvements in $\dot{V}O_{2max}$ or 3 km time trial performance in well-trained (~72 ml·kg^{-1}·min^{-1}) endurance athletes (Julian *et al.*, 2004). Although reticulocytes were increased after 3 weeks of IHE in multi-sport athletes (Hamlin & Hellemans, 2007) there was no change in erythropoietic parameters after 2 (Tadibi *et al.*, 2007) or 4 weeks (Julian *et al.*, 2004) in endurance trained athletes. Together, these findings do not support the use of hypoxic intervals for accelerated erythropoiesis in highly trained athletes (Julian *et al.*, 2004; Tadibi *et al.*, 2007). Similarly, endurance-trained athletes are unlikely to show improvement in aerobic or anaerobic capacities (Julian *et al.*, 2004; Tadibi *et al.*, 2007), however, less well-trained or team-sport athletes may benefit (Hamlin & Hellemans, 2007; Wood *et al.*, 2006).

2.7.1.2. Continuous hypoxia

Brief periods (~1.5-3 h) of continuous hypoxic exposure have been examined over 2 to 4 weeks in athletes. In well-trained runners (~67 ml·kg^{-1}·min^{-1}), 2 weeks of IHE (3 h·d^{-1}, daily, ~4,300 m) improved running economy and there was a trend towards improvement in 3 km time trial performance (Katayama *et al.*, 2004). After 3 weeks of IHE (1.5 h·d^{-1}, 3 d·wk^{-1}, ~4,500 m) there were no changes in haematological parameters but running economy and 3 km time trial performance were improved (Katayama *et al.*, 2003). In contrast, 4 weeks of IHE (3 h·d^{-1}, 5 d·wk^{-1}, 4,000-5,500 m) in trained runners and swimmers (55-59 ml·kg^{-1}·min^{-1}) did not substantially improve time trial performance, $\dot{V}O_{2max}$, or Hb_{mass} (Rodriguez *et al.*, 2007). Nor were there any changes in economy (Truijens *et al.*, 2008). It remains contentious whether continuous IHE for 2 to 4 weeks (daily or 3-5 d·wk^{-1}) can substantially improve time trial performance or economy in athletes (Katayama *et al.*, 2003; Katayama *et al.*, 2004; Rodriguez *et al.*, 2007; Truijens *et al.*, 2008). The available data are inconclusive on whether hypoxic exposure at rest provides a time-efficient means of inducing adaptations that substantially enhance performance in well-trained athletes. The level of hypoxia, duration and total number of sessions of IHE to improve performance at sea-level or at altitude has not been established (Bartsch *et al.*, 2008).

2.7.2. Hypoxic exposure during training (IHT)

The rationale behind training in hypoxia is to increase the metabolic stress on skeletal muscle, despite lower relative training intensities, while inducing adaptations associated with acclimatisation (Hoppeler & Vogt, 2001). A common finding in the majority of studies is the duration of the hypoxic stimulus is insufficient to induce changes in haematological parameters. Indeed, at least two hours of altitude or hypoxic exposure is required for a measurable increase in serum EPO concentration (Knaupp *et al.*, 1992). Only two studies have reported an increase in Hb and Hct (Hendriksen & Meeuwsen, 2003; Meeuwsen *et al.*, 2001) which may have been related to changes in plasma volume rather than an erythropoietic effect of hypoxia *per se*.

Although brief periods of hypoxia are appealing for athletes who cannot spend more than 12 $h \cdot d^{-1}$ in hypoxia (Rusko *et al.*, 2004), the efficacy of this mode of altitude training remains inconclusive. After 10 days of hypoxic training in well-trained triathletes (2 $h \cdot d^{-1}$, daily, ~2,500 m) improvements in mean and peak power (Hendriksen & Meeuwsen, 2003; Meeuwsen *et al.*, 2001) and $\dot{V}O_{2max}$ (Meeuwsen *et al.*, 2001) have been demonstrated. Similarly, 3-4 weeks of hypoxic training at moderate altitude (~1.5-3 $h \cdot d^{-1}$, 4-5 $d \cdot wk^{-1}$, ~2,300 m) resulted in improved work capacity and reduced submaximal blood lactate concentrations in competitive cyclists (Terrados *et al.*, 1988). The enhancement in work capacity was speculated to be related to improvements in βm (Terrados *et al.*, 1988). In contrast, 4 weeks of hypoxic training (30 min, 3 $d \cdot wk^{-1}$, ~2,750 m) did not improve $\dot{V}O_{2max}$ or anaerobic capacity in team sport players (Morton & Cable, 2005). Similarly there was no improvement in 3 km time trial performance, $\dot{V}O_{2max}$ or Hb_{mass} after 4 weeks (30 min, 3 $d \cdot wk^{-1}$, ~3,000m) in well-trained runners (Neya *et al.*, 2007).

The majority of other studies have employed moderate to high levels of hypoxic exposure for more than 3 weeks. Additional interval training in moderate hypoxia for 5 weeks (total 12.5 $min \cdot d^{-1}$, 3 $d \cdot wk^{-1}$, ~2,500 m) was insufficient to improve $\dot{V}O_{2max}$ and 100-m and 400-m swim times compared with training in normoxia (Truijens *et al.*, 2003). Similarly, 6 weeks of anaerobic threshold training in hypoxia (30 min, 3 $d \cdot wk^{-1}$, ~3,200 m) did not improve $\dot{V}O_{2max}$ or maximal power output in well-trained cyclists (Ventura *et al.*, 2003). One interesting finding was improved $\dot{V}O_{2max}$ in well-trained cyclists who completed their warm-up and recovery in hypoxia (~30 min, 2 $d \cdot wk^{-1}$, ~3,000 m), but the high intensity intervals in

normoxia for 7 weeks (Roels *et al.*, 2005). In contrast, 6 weeks of high-intensity training at the second ventilatory threshold (24-40 min, 2 d·wk^{-1}, ~3,000 m) resulted in improved time to exhaustion at $v\dot{V}O_{2max}$ (velocity at $\dot{V}O_{2max}$) and improved $\dot{V}O_{2max}$ in well-trained runners (Dufour *et al.*, 2006). The mechanisms of this enhanced performance were addressed in two companion papers which reported improved respiratory control and tighter integration between ATP demand and supply (Ponsot *et al.*, 2006) and transcriptional adaptations in skeletal muscle, specifically those involved in redox regulation and glucose uptake (Zoll *et al.*, 2006). Collectively, these findings imply a minimal hypoxic exercise intensity (~80% $\dot{V}O_{2max}$) and duration (>0.5 h) for sufficient stimulus to enhance performance more than equivalent sea-level training.

In summary, there may be some benefit of hypoxic training for enhanced performance in athletes, although given the large number of methodologies and training protocols this area requires further investigation. Under some conditions, some athletes may potentially benefit from hypoxic training as an adjunct to normoxic training, particularly those with a long training history for whom a variety in training stress may be advantageous (Hoppeler *et al.*, 2008). Overall, there is no compelling evidence of an erythropoietic effect and enhanced performance is likely mediated by peripheral adaptations induced by moderate-high intensity training in hypoxia.

2.8 Summary

The findings of this review emphasise that small differences in performance can determine a competition outcome in closely matched competitors. By modelling competition performance, reference values can be established to determine the magnitude of improvements required in lap or split times to substantially increase the likelihood of success. Pacing strategies are an important determinant of performance. Quantifying lap or split times in relation to final time may yield further insight for coaches on where the most improvement to competition performance can be made.

Altitude training is a popular approach for many athletes seeking small enhancements in performance. Both natural and simulated LHTL have been evaluated extensively in both research settings and contemporary practice. Studies of LHTL from four independent laboratories indicate ~1% performance enhancement in events lasting between ~45s to 14 min, which will substantially increase the likelihood of success in competition. However, the

dose-response to hypoxia seems to be a key issue, and differences in the methodologies employed in the literature may be a limiting factor in establishing the most effective protocol. Using the results of the meta-analysis (Bonetti & Hopkins, 2009), it appears traditional LHTH is the most successful strategy to improve performance for elite and subelite athletes. A greater benefit from simulated LHTL may be gained by increasing the altitude level (>3,000 m) and daily hypoxic exposure (14 $h \cdot d^{-1}$), over a shorter duration (~2 weeks instead of ~3 weeks). The LLTH protocols may be enhanced by training at low to moderate intensity at lower altitudes (~2,400 m), for more days of exposure (~18 days) with a later post-altitude test day (Bonetti & Hopkins, 2009)

One major shortcoming of the literature is that the programs of altitude training currently used by elite athletes in preparation for competition often differ from those investigated in research settings. Previous research studies have examined only single altitude exposures, yet athletes typically undertake multiple bouts of altitude training during their preparation for competition. Further research is needed to verify the effectiveness, or otherwise, of repeated bouts of altitude training commonly used by elite athletes. In addition, many athletes undertake a combination of real and simulated altitude in preparation for competition, but the efficacy of this approach has not been established. To complement research studies with fully controlled experimental designs, an observational study of contemporary models of altitude training by elite athletes is required.

Another key issue is that of individual variation in response to altitude, which has previously been considered under the responder or non-responder paradigm based on erythropoietic response. A systematic approach is required to quantify the dose-response relationship of altitude or hypoxic exposure on physiological and performance responses, and ascertain the reproducibility of these responses. Given the equivocal nature of the literature on haematological and non-haematological mechanisms underlying enhanced performance, these parameters should be measured in parallel. Although there is growing interest in brief periods of LLTH (IHE or IHT) as a means of stimulating physiological adaptations to hypoxia, the experimental findings are inconclusive. IHT has emerged as a potentially time-efficient alternative to LHTL for athletes and theoretically could be a useful complement to LHTL. Whether a combined approach is more effective to elicit substantial improvements in performance is unknown.

In any altitude training intervention, the critical outcome for elite athletes is an enhanced performance capability. Unfortunately, despite the abundance of studies, there is a lack of a consistent performance measure (and parallel physiological parameters) which makes the existing experimental results somewhat difficult to interpret. Moreover, there is an apparent lack of reproducibility in the literature, with many investigators unable to repeat the results using the same experimental protocol. With so many variables that can be manipulated in LHTL or LLTH methodologies (such as altitude level, daily duration and length of intervention, training stimulus, timing of sea-level performance measure), combined with substantial individual variability in response, it is difficult to develop definitive guidelines for coaches. Subject numbers are often low in studies of elite athletes, so conventional statistical approaches (involving hypothesis testing and statistical significance) may not be able to detect small changes in performance that are important for athletes. A more appropriate statistical approach to establish the practical significance of altitude training interventions and quantify the variability in response to the intervention is magnitude-based inferences (Batterham & Hopkins, 2006). Use of this analytical approach will permit rigorous but practical interpretation of the effects of altitude training on athletic performance.

Establishing the reproducibility and dose-response of physiological adaptations to short (2-3 week) and longer (6 week) hypoxic exposures in individual athletes is of particular interest to athletes and coaches who undertake multiple altitude training camps within and between training years. Furthermore, quantifying the transfer of physiological adaptations to enhancements in performance at sea-level should assist coaches and sport scientists in evaluating the practical impact (and cost-benefit analysis) of altitude training interventions on performance.

CHAPTER THREE

ANALYSIS OF LAP TIMES IN INTERNATIONAL SWIMMING COMPETITIONS

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E.Y. Robertson, D.B. Pyne, W.G. Hopkins, and J. Anson

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Chapter 3

Robertson, E, Pyne, D, Hopkins, W, & Anson, J 2009, 'Analysis of lap times in international swimming competitions', *Journal Of Sports Sciences*, 27, 4, pp. 387-395.

Abstract

Swimming performances were analysed for the top 16 finishers (semi-finalists, finalists) in nine international competitions over a 7-year period (1530 males, 1527 female). Total race time and intermediate lap times were log-transformed and analysed for effects of sex (male, female), stroke (freestyle, form strokes, individual medley), event (100, 200, and 400 m), and place (1–16). Between-athlete correlations characterized the relationship of each lap to final time, and within-athlete estimates quantified the effect of lap time on improvements in final time. Finalists exhibited very large correlations (r = 0.7–0.9) with final time in the second 50-m lap of 100-m events and the middle two 50-m and 100-m laps of 200-m and 400-m events respectively. For an individual swimmer, an achievable change in lap time was associated with an approximate 0.4–0.8% improvement in final time for finalists and an approximate 0.5–1.1% improvement in final time for semi-finalists, depending on sex, stroke, and event. The pattern of lap times was similar for the top 16 swimmers and between the best and worst swims for finalists. These findings indicate that substantial improvements can be made via the final lap in sprints and the middle two laps of 200- to 400-m events, but the overall pattern of lap times should not be changed.

CHAPTER FOUR

EFFECT OF SIMULATED AND REAL ALTITUDE EXPOSURE IN ELITE SWIMMERS

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Chapter 4

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Online general public	http://journals.lww.com/nsca-jscr/Abstract/2010/02000/Effects_of_Simulated_and_Real_Altitude_Exposure_in.28.aspx
DOI	10.1519/JSC.0b013e3181c06d56

Abstract

The effect of repeated exposures to natural and simulated moderate altitude on physiology and competitive performance of elite athletes warrants further investigation. This study quantified changes in hemoglobin mass, performance tests, and competitive performance of elite swimmers undertaking a coach-prescribed program of natural and simulated altitude training. Nine swimmers (age 21.1 ± 1.4 years, mean ± SD) completed up to four 2-week blocks of combined living and training at moderate natural altitude (1,350 m) and simulated live high-train low (2,600-600 m) altitude exposure between 2 National Championships. Changes in hemoglobin mass (Hb_{mass}), 4-mM lactate threshold velocity, and 2,000 m time trial were measured. Competition performance of these swimmers was compared with that of 9 similarly trained swimmers (21.1 ± 4.1 years) who undertook no altitude training. Each 2-week altitude block on average produced the following improvements: Hb_{mass}, 0.9% (90% confidence limits, ±0.8%); 4-mM lactate threshold velocity, 0.9% (±0.8%); and 2,000 m time trial performance, 1.2% (±1.6%). The increases in Hb_{mass} had a moderate correlation with time trial performance (r = 0.47; ±0.41) but an unclear correlation with lactate threshold velocity (r = -0.23; ±0.48). The altitude group did not swim faster at National Championships compared with swimmers who did not receive any altitude exposure, the difference between the groups was not substantial (-0.5%; ±1.0%). A coach-prescribed program of repeated altitude training and exposure elicited modest changes in physiology but did not substantially improve competition performance of elite swimmers. Sports should investigate the efficacy of their altitude training program to justify the investment.

CHAPTER FIVE

REPRODUCIBILITY OF PERFORMANCE CHANGES TO SIMULATED LIVE HIGH/TRAIN LOW ALTITUDE

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E.Y. Robertson, P.U. Saunders, D.B. Pyne, R.J. Aughey, J. Anson, and C.J. Gore

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Online general public	http://journals.lww.com/acsm-msse/Abstract/2010/02000/Reproducibility_of_Performance_Changes_to.23.aspx
DOI	10.1249/MSS.0b013e3181b34b57

Abstract

Elite athletes often undertake multiple altitude exposures within and between training years in an attempt to improve sea-level performance.

Purpose: To quantify the reproducibility of responses to live high/train low (LHTL) altitude exposure in the same group of athletes.

Methods: Sixteen highly trained runners with maximum aerobic power (V&O2max) of 73.1 ± 4.6 and 64.4 ± 3.2 mL·kg-1·min-1 (mean ± SD) for males and females respectively, completed

2 x 3-wk blocks of simulated LHTL (14 h·day-1, 3000 m) or resided near sea-level (600 m) in a controlled study design. Changes in 4.5 km time trial performance and physiological measures including V&O2max, running economy and hemoglobin mass (Hbmass) were assessed.

Results: Time-trial performance showed small and variable changes after each 3-wk altitude block in both the LHTL (-1.4%; ±1.1% and 0.7%; ±1.3%, mean; ±90% CL) and the Control (0.5%; ±1.5% and -0.7%; ±0.8%) group. The LHTL group demonstrated reproducible improvements in V&O2max (2.1%; ±2.1% and 2.1%; ±3.9%) and Hbmass (2.8%; ±2.1% and 2.7%; ±1.8%) after each 3-wk block. Compared with the Control group, the LHTL group were substantially faster after the first 3-wk block (LHTL-Control: -1.9%; ±1.8%) and had substantially higher Hbmass after the second 3-wk block (4.2%; ±2.1%). There was no substantial difference in the change in mean V&O2max between the groups after the first (1.2%; ±3.3%) or second 3-wk block (1.4%; ±4.6%). Conclusion: 3-wk LHTL altitude exposure can induce reproducible mean improvements in V&O2max and Hbmass in highly trained runners, but changes in time trial performance appear to be more variable. Competitive performance is dependent not only on improvements in physiological capacities that underpin performance, but a complex interaction of many factors including fitness, fatigue and motivation.

CHAPTER SIX

EFFECTIVENESS OF INTERMITTENT TRAINING IN HYPOXIA COMBINED WITH LIVE HIGH/TRAIN LOW

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E.Y. Robertson, P.U. Saunders, D.B. Pyne, C.J. Gore and J. Anson

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Abstract

Elite athletes often undertake altitude training to improve sea-level athletic performance, yet the optimal methodology has not been established. A combined approach of live high/train low plus train high (LH/TL+TH) may provide an additional training stimulus to enhance performance gains. Seventeen male and female middle-distance runners with maximal aerobic power V O2max of 65.5 ± 7.3 mL kg−1 min−1 (mean ± SD) trained on a treadmill in normobaric hypoxia for 3 weeks (2,200 m, 4 week−1). During this period, the train high (TH) group (n = 9) resided near sea-level (~600 m) while the LH/TL+TH group (n = 8) stayed in normobaric hypoxia (3,000 m) for 14 hours day−1. Changes in 3-km time trial performance and physiological measures including V O2max running economy and haemoglobin mass (Hbmass) were assessed. The LH/TL+TH group substantially improved V O2max (4.8%; ±2.8%, mean; ±90% CL), Hbmass (3.6%; ±2.4%) and 3-km time trial performance (−1.1%; ±1.0%) immediately post-altitude. There was no substantial improvement in time trial performance 2 weeks later. The TH group substantially improved V O2max (2.2%; ±1.8%), but had only trivial changes in Hbmass and 3-km time-trial performance. Compared with TH, combined LH/TL+TH substantially improved V O2max (2.6%; ±3.2%), Hbmass (4.3%; ±3.2%), and time trial performance (−0.9%; ±1.4%) immediately post-altitude. LH/TL+TH elicited greater enhancements in physiological capacities compared with TH, however, the transfer of benefits to time-trial performance was more variable.

CHAPTER SEVEN

SUMMARY OF THESIS

7.1. Summary

Altitude training can elicit substantial improvements in physiological capacities in well-trained athletes, but the transfer to enhanced performance at sea-level is more variable. There is a dose-response relationship of hypoxia-induced changes in physiological parameters, but this does not correspond directly with the magnitude of change (improvements) in performance. A coach-prescribed altitude program of multiple 2-wk natural altitude and simulated LHTL exposures was insufficient to induce substantial physiological adaptations or improve competition performance. Two 3-wk simulated LHTL exposure elicited reproducible small mean increases in Hb_{mass} and $\dot{V}O_{2max}$, however, time trial performance was more variable (~1% faster and ~1% slower after each exposure respectively). Greater enhancements in Hb_{mass} and $\dot{V}O_{2max}$ were elicited following 6-wk LHTL and 3-wk combined LH/TL+TH compared with 3-wk LHTL alone. However, these greater physiological enhancements did not transfer directly to greater improvements in time trial performance. There is an apparent uncoupling between the magnitude of improvements in physiological capacities elicited by hypoxic exposure and changes in performance at sea-level immediately or 2 weeks later. Individual responses, of similar magnitude to the mean, indicate that some athletes may respond more favourably to altitude training than others. However, individual variation in response to repeated 3-wk LHTL exposures, demonstrates that a performance enhancement following one bout of LHTL does not necessarily guarantee the same response in subsequent bouts.

A key issue is the magnitude of improvement required by altitude training (or other training interventions) to substantially enhance performance at the elite level. Prior to conducting the observational study of altitude training in elite swimmers, the magnitude of improvement needed to substantially enhance competition performance had to be established. This became the first step in evaluating the transfer of altitude training-induced physiological adaptations to improved competition performance. The magnitude of change in lap time needed to enhance performance and improve final placing was modelled in international swimming competitions over 7 years. An achievable change in lap time for an individual swimmer was

associated with similar improvements in performance for finalists (~0.4-0.8%) and semi-finalists (~0.5-1.1%) depending on sex, stroke and event. This magnitude of change will substantially increase the likelihood of a medal in top-ranked swimmers (Pyne *et al.*, 2004; Trewin *et al.*, 2004). The novel finding of this study was that the final lap in 100-m events, and the middle two laps of 200-m and 400-m events, had the strongest relationship with final time and needed a smaller change to improve final placing in a race. For example, to move to 1st place from 2nd place in male 200-m freestyle events, an individual swimmer would need ~0.3s improvement in the second 50-m lap or ~0.6s in the final 50-m lap. However, examination of the pattern of lap times revealed a similar pattern for the top 16 swimmers and the best and worst swims for finalists. This finding is in agreement with previous research showing a similar pattern of pacing between winners and losers in 2000-m rowing events (Garland, 2005). The absence of differences in pacing between competitors implies that coaches should first look to address improvements in fitness or technique in the laps which should result in the greatest performance gain. The overall pattern of lap times, however, should not be disrupted. Taken together, these findings confirm that training interventions aimed at enhancing training and competition performance need to elicit improvements greater than ~0.4-1.1%. This magnitude of change in race performance is similar to the smallest important improvement (~0.5-1.5%) in well-trained runners (Hopkins *et al.*, 1999; Hopkins & Hewson, 2001), permitting comparisons of the efficacy of altitude training in swimmers and runners.

The subsequent three studies quantified the physiological and performance responses to different altitude training protocols, to determine the most effective approach to obtain small worthwhile enhancements in competition or time-trial performance in athletes. The main findings for a typical altitude-based preparation (contemporary), two matched 3-wk LHTL exposures (reproducibility), 6-wk LHTL exposure (dose-response), and 3-wk LHTL exposure plus intermittent training in hypoxia (combined) are summarised in Table 7.1. Our analytical approach of magnitude-based inferences permitted rigorous but practical interpretation of the effects of altitude training across each of the studies.

Table 7.1. Summary of the performance changes and physiological responses to multiple 2-wk real and simulated altitude exposure (contemporary), repeated 3-wk LHTL (reproducibility), extended 6-wk LHTL (dose-response) and 3-wk LHTL plus training in hypoxia (combined)

		Contemporary altitude training in swimmers [1]		**Reproducibility** of responses to LHTL [2]		**Dose-response** of LHTL for 3-wk vs 6-wk [2b]		**Combined** LHTL plus TH [3]	
Experimental Group		4 x 2-wk LHTL (10 h·d^{-1}, 2600m) and LMTM (1350m)		2 x 3-wk LHTL (14 h·d^{-1}, 3000m)		6-wk LHTL (14 h·d^{-1}, 3000m)		3-wk LHTL (14 h·d^{-1}, 3000m) + TH (train 4·wk^{-1}, ~2200m)	
Control Group		living/training at ~600m [a]		2 x 3-wk living/training at ~600m		6-wk living/training at ~600m		3-wk TH (train 4·wk^{-1}, ~2200m)	
		Δ combined	**Δ single** [b]	**Δ Block 1**	**Δ Block 2**	**Δ 3-wk**	**Δ 6-wk**	**Δ Post1**	**Δ Post2**
Performance	**Expt**	NC -0.4% (0.9),	CG 0.6% (0.6)	-1.4% (1.1) *	0.7% (2.0)	0.9% (2.5)	-0.3% (1.1)	-1.1% (1.0)	-0.4% (1.1)
	Ctl	NC -0.9% (0.5)*,	CG 1.2% (0.9)*	0.5% (1.5)	-0.7% (1.1)	-0.6% (1.3)	-0.3% (1.1)	-0.1% (1.0)	-0.6% (1.1)
	Diff	NC 0.5% (1.0),	CG 0.6% (0.9)	-1.9% (1.8)	1.4% (1.5)	1.5% (2.5)	0.0% (1.4)	-0.9% (1.4)	0.2% (1.5)
4mM speed	**Expt**	1.7% (1.9) *	0.9% (0.8)	6.5% (2.0) *	1.6% (2.5)	0.4% (2.4)	1.2% (1.4)	2.8% (2.5)	-
	Ctl	-	-	1.1% (1.3)	-0.3% (1.8)	-0.6% (1.6)	-0.9% (3.9)	0.4% (1.5)	-
	Diff	n.a	n.a	5.3% (2.2)	1.9% (2.9)	1.0% (2.5)	2.2% (4.0)	2.4% (2.8)	n.a
VO_{2max} or T_{2K}	**Expt**	2.4% (2.0) *	1.2% (1.6)	2.1% (2.1) *	2.1% (3.9)	3.0% (14.7)	4.3% (6.2) *	4.8% (2.8) *	-
	Ctl	-	-	0.9% (2.8)	0.7% (3.1)	-1.3% (7.1)	-3.1% (5.6)	2.2% (1.8)	-
	Diff	n.a	n.a	1.2% (3.3)	1.4% (4.6)	4.5% (15.4)	7.6% (6.9)	2.6% (3.2)	n.a
Hb_{mass}	**Expt**	-	0.9% (0.8)	2.8% (2.1)	2.7% (1.8)	2.2% (3.6)	4.0% (6.1)	3.6% (2.4) *	-
	Ctl	-	-	1.4% (2.7)	-1.5% (1.5)	-0.7% (3.1)	-1.4% (5.3)	-0.7% (3.8)	-
	Diff	n.a	n.a	1.3% (3.2)	4.2% (2.1)	2.9% (4.0)	5.4% (6.8)	4.3% (3.2)	n.a

Data are percent effects (±90% confidence limits). LHTL, live high/train low; LMTM, live and train at moderate altitude; TH, training in hypoxia; Expt, experimental group; Ctl, control group; **Performance** for each study: [1] competition performance at National Championships (NC) after 3rd block, and Commonwealth Games (CG) after 4th block; [2,2b] 4.5-km time trial performance 1 day after each 3-wk block, [3] 3-km time trial performance 2 days (Post1) and 2 weeks (Post 2) after block (note: negative percent change is faster performance). [a] control group for performance only; [b] average change over each exposure; **4mM speed**, 4mM lactate threshold velocity from 5 x 200m step test (swimmers) and 4 x 4 min submaximal stages (runners); **VO_{2max}**, maximal aerobic power, **T_{2K}**, timed 2000m swim; **Hb_{mass}**, haemoglobin mass; * asterisk identifies substantial difference in post test; ▓ substantial difference between groups (expt-ctl) highlighted in grey shading.

Following contemporary altitude training in elite swimmers, performance at National Championships and Commonwealth Games was not substantially improved compared with a matched group who received no altitude exposure (Table 7.1). There were small enhancements in 4mM speed and 2000m timed swim after two consecutive 2-wk blocks. These changes, however, are of similar magnitude to training-induced enhancements (1.6%) reported in Australian National Team swimmers in preparation for competition (Pyne *et al.*, 2001). It appears this contemporary model of short duration, repeated moderate level altitude exposures is insufficient to elicit substantial mean improvements in physiological or performance measures in elite swimmers. Nevertheless, some individuals will benefit more than others from this type of altitude-based preparation.

The lack of increase in Hb_{mass} following contemporary altitude training confirms short 2-wk exposures are not long enough to elicit substantial increases in oxygen-carrying capacity. These findings are consistent with the current recommendations that a minimum of 12 $h \cdot d^{-1}$ for at least 3 weeks is needed to attain an acclimatisation effect (Rusko *et al.*, 2004). Two matched 3-wk LHTL blocks were sufficient to induce reproducible mean increases in Hb_{mass} (~3%) and $\dot{V}O_{2max}$ (~2%) in well-trained runners (Table 7.1). However, these physiological adaptations did not transfer directly to a consistent improvement in 4.5-km time trial performance, which was only faster (1.4%) after Block 1. This magnitude of improvement in time trial performance is similar to 1.1-1.6% improvements in 3-km (Stray-Gundersen *et al.*, 2001) and 5-km time trial performance (Levine & Stray-Gundersen, 1997; Wehrlin *et al.*, 2006) after 3-4 weeks of natural LHTL. The lack of consistency in the performance response, despite reproducible mean enhancements in physiological capacities, implies an uncoupling in the transfer to performance gains in athletes. The correlations between percent change in Block 1 versus Block 2 for the LHTL group were unclear for time trial performance (r=0.10), $\dot{V}O_{2max}$ (r=0.36) and Hb_{mass} (r=0.46). The lack of association between individual changes in Block 1 and Block 2 indicates enhancements in physiology and performance following one bout of LHTL does not necessarily guarantee the same response in subsequent altitude exposures. Furthermore, individual responses of similar magnitude to the mean indicate that some athletes will respond more favourably than others. Together, these findings demonstrate individual variation and reproducibility of responses are key issues for athletes and coaches incorporating altitude training in preparation for competition.

Protocols to maximise the dose of hypoxia (extended 6-wk LHTL and 3-wk combined LHTL and TH) elicited larger increases in Hb_{mass} (~4-5%) and $\dot{V}O_{2max}$ (~4%) compared with 3-wk LHTL (Table 7.1). However, these greater enhancements in physiological parameters did not transfer directly to the magnitude of performance change. Following 6-wk LHTL (dose-response) there were only trivial changes in 4.5 km time trial performance. It is possible that time trial performance was confounded by a number of factors including individual variation in response to altitude, inadequately managed training with the additional stress of extended hypoxic exposure, and/or timing of the performance test immediately after LHTL. Unfortunately the small sample size in this study limits definitive conclusions. After 3-wk LH/TL+TH (combined), time trial performance was faster immediately after altitude exposure (1.1%), but not two weeks later. The trivially slower time trial performance 2 weeks after LH/TL+TH is consistent with non-statistically significant slower time trial performance 2 weeks after LHTL (Levine & Stray-Gundersen, 1997). These findings are in contrast to the general consensus amongst coaches that optimal performance occurs ~14 days after traditional living and training at altitude (Dick, 1992). Further research is required to elucidate the time course of performance changes following LHTL, LH/TL+TH or TH and the optimal time to maximise performance gains at sea-level.

The results of the 3-wk LHTL (reproducibility) and 3-wk LH/TL+TH (combined) studies allow comparisons to be made between well-trained runners undertaking three types of altitude training (LHTL, LH/TL+TH and TH) and a control group training near sea-level. Combined LH/TL+TH elicited a substantially greater increase in $\dot{V}O_{2max}$ compared with LHTL (LH/TL+TH -LHTL: 2.7%; ±3.3%). However, there was no substantial difference in improvement in trial performance (LH/TL+TH -LHTL: 0.3%; ±1.4%) or change in Hb_{mass} (LH/TL+TH-LHTL: 0.8%; ±3.0%) between the groups. After 3-wk TH alone, there were no substantial differences in $\dot{V}O_{2max}$ (TH-control: 1.3%; ±3.1%) or time trial performance (TH-control: -0.6%; ±1.7%) compared with a control group training near sea-level for 3-wk.

The variable results in time-trial performance, despite small to moderate improvements in $\dot{V}O_{2max}$, are consistent with the model that $\dot{V}O_{2max}$ is only one of a number of factors that contribute to endurance performance in athletes (di Prampero, 1986). Although $\dot{V}O_{2max}$ is considered a useful predictor of performance in endurance events (Saltin & Astrand, 1967), in some top level athletes it is poorly associated with performance (Snell & Mitchell, 1984). For athletes more homogenous in ability, other physiological parameters including the energy cost

(economy) of running (Conley & Krahenbuhl, 1980) and the percent of $\dot{V}O_{2max}$ (fractional utilisation) that can be maintained for the duration of the run (Conley & Krahenbuhl, 1980; Schabort *et al.*, 2000) are important determinants of performance. Our results showed there were no substantial improvements in running economy following LHTL, LH/TL+TH or TH. In fact, there was a trend towards worse economy after the 2nd 3-wk LHTL block in the reproducibility study and after combined LH/TL+TH. This lack of improvement in economy following hypoxic exposure agrees with those studies that have also demonstrated increases in $\dot{V}O_{2max}$ (Lundby *et al.*, 2007). In contrast, other studies with no change or even a reduction in $\dot{V}O_{2max}$ after hypoxic exposure have observed 3-10% improvements in economy (Gore *et al.*, 2007). There were trivial to small improvements in 4mM speed (lactate threshold velocity) across each of the altitude training interventions (Table 7.1). Although 4mM speed improved following contemporary altitude training in swimmers, the lack of a control group limits interpretation of this change. There was an improvement in 4mM speed following Block 1 of the reproducibility study and a trend towards an increase in velocity at 4mM after combined LH/TL+TH. The observed reduction in maximal lactate and increased 4mM running speed may indicate greater reliance on aerobic metabolism (Nummela & Rusko, 2000) or changes in whole body lactate metabolism (Clark *et al.*, 2004) following hypoxic exposure. Together these findings suggest that athletes need to balance their training load during altitude training to maintain or increase $\dot{V}O_{2max}$, while improving other factors that contribute to endurance performance including economy and threshold speed.

A small increase in $\dot{V}O_{2max}$ in the TH group in the absence of any change in Hb_{mass} (Table 7.1) is consistent with no change in Hb_{mass} despite increased $\dot{V}O_{2max}$ (~2%) in well-trained athletes following living and training at 1,740 m (Gore *et al.*, 1997). Similarly, after 3 months of simulated LHTL, there was only a trivial change in $\dot{V}O_{2max}$ despite a ~5% increase in Hb_{mass} (Saunders *et al.*, 2009). In addition to within-athlete variability in change in Hb_{mass} observed in the reproducibility study (r~0.5), there were no substantial correlations between change in Hb_{mass} and change in $\dot{V}O_{2max}$ or time trial performance (r~0.3) following combined LH/TL+TH or TH. This finding is in agreement with the trivial correlation between increased Hb_{mass} (~6%) and change in sea-level performance in junior swimmers after living and training at moderate altitude for 3 weeks (Friedmann *et al.*, 2005). Moreover, the change in Hb_{mass} after 3 weeks was not correlated to acute or sustained EPO response in the swimmers (Friedmann *et al.*, 2005). Similarly, following 3 weeks of simulated LHTL there was only a

trivial correlation between EPO response and increase in red cell volume in endurance athletes (Rusko *et al.*, 1999). No substantial association has been found between individual change in EPO response with markers of EPO regulation (Jedlickova *et al.*, 2003).

An alternative candidate to explain individual variability in response to hypoxia may be found at the molecular level. Hypoxia-inducible factor (HIF-1) is the global regulator of oxygen homeostasis and plays a critical role in cardiovascular and respiratory responses to hypoxia (Semenza, 2004). HIF-1α gene expression was measured in a sub-group of the athletes during the reproducibility study by collaborators. Preliminary data on HIF-1 mRNA response to repeated 3-wk LHTL exposures indicates a peak at day 20 in both Block 1 and 2 for the LHTL group (Appendix 2). There is substantial between-athlete variation and a potential priming effect of the first 3-wk exposure (Block 1) on the response in the second 3-wk exposure (Block 2). Whether the HIF-1 response can account for differential responses to hypoxia and performance enhancement is beyond the scope of this thesis. Nevertheless, these findings confirm the notion that other mechanisms, in addition to accelerated erythropoiesis, may underpin improvements in $\dot{V}O_{2max}$ and performance following altitude training (Levine *et al.*, 2005).

The small and variable changes in time-trial performance, and lack of direct association between time trial performance and measures of physiological capacity, make it difficult to identify the underlying mechanisms of performance enhancement following altitude training. Without repeated performance tests over a longer period post-altitude, it is not possible to ascertain if the lack of transfer to performance is related to individual variability in the optimal time for performance post-altitude. Nonetheless, the lack of a corresponding enhancement in time trial performance with greater increases in $\dot{V}O_{2max}$, is consistent with other researchers who have demonstrated 1.1-1.6% improvements in time trial performance which were not directly proportional to ~3-5% increases in $\dot{V}O_{2max}$ (Levine & Stray-Gundersen, 1997; Stray-Gundersen *et al.*, 2001; Wehrlin *et al.*, 2006). Furthermore, despite a reduction in $\dot{V}O_{2max}$ (~2%) there was a trend towards improved performance (~1%) in 4-min maximal efforts, following simulated LHTL (Hahn *et al.*, 2001). It is possible that while altitude training can substantially enhance $\dot{V}O_{2max}$ in well-trained athletes, there is only limited scope to improve time trial performance substantially more than ~1-2% with the current methodologies. Interestingly, a recent meta-analysis has suggested modifications to a variety of altitude training protocols that may further enhance performance outcomes (Bonetti

& Hopkins, 2009). Recommendations for modification to simulated LHTL protocols include more hours of hypoxia (~14 $h \cdot d^{-1}$) with less days of exposure (~11 d). For LLTH protocols, modifications include a reduction in training intensity and altitude (~2,400 m), more days of exposure (~18 d) and a later post-test (~5 d after exposure). Whether these enhanced protocols (Bonetti & Hopkins, 2009) can result in larger and more robust performance changes will require experimental confirmation.

In conclusion, 3 to 6-wk LHTL and 3-wk combined LH/TL+TH can elicit small improvements in physiological capacities that underpin endurance performance in well-trained athletes. Extended 6-wk LHTL and 3-wk combined LH/TL+TH elicit greater enhancements in Hb_{mass} and $\dot{V}O_{2max}$, however, there is a lack of direct transfer to the magnitude of improvement in time trial performance. There is substantial individual variation in physiological and performance response to repeated 3-wk LHTL, of similar magnitude to the mean changes. This level of variation indicates some athletes may respond more favourably than others, however, enhanced performance following one hypoxic exposure does not necessarily guarantee the same response in subsequent bouts. Athletes can expect improvements in performance of ~1% following LHTL or LH/TL+TH which will increase the likelihood of success in competition in top ranked athletes. Lower ranked athletes will also need improvements in other areas such as fitness, technique and motivation. It appears a number of different factors may contribute to performance enhancement following hypoxic exposure. The mechanisms that underpin individual variation in response to hypoxia remain unclear and the optimal time after altitude training for consistent enhancements in performance has not yet been established.

7.2. Practical Applications

The findings of this thesis are directly applicable to athletes and coaches who seek advice on effective altitude training for enhanced performance.

- Multiple 2-wk exposures at moderate altitude are unlikely to induce substantial improvements in physiology or competition performance.

- Repeated 3-wk LHTL exposure elicits small mean increases in Hb_{mass} and $\dot{V}O_{2max}$, but transfer to time trial performance within 1-2 days post-altitude is more variable.

- Extended LHTL (6-wk) or additional training in hypoxia (LH/TL+TH) stimulate greater increases in physiological capacities compared with 3-wk LHTL. However, this level of exposure does not transfer directly to greater enhancements in time trial performance within 1-2 days post-altitude. In addition, these modalities of altitude training may be impractical to implement for many athletes, so other combinations of altitude training and exposure are needed for substantial enhancements in time trial performance.

- Individual variation exists in physiological and performance responses. Some athletes are likely to respond more positively than others, however, enhanced performance following one hypoxic exposure does not guarantee a similar response in repeated bouts of altitude training. Moreover, altitude training should be carefully managed in the context of other training and competition.

- The small and variable changes in competition performance (~1-3 weeks) and time-trial performance (~2 days to 2 weeks) following altitude training preclude the preparation of definitive guidelines for the optimal time for enhanced performance on return to sea-level. Coaches and athletes should work to define the optimal time for an individual athlete based on objective data as well as subjective feelings and performance results.

7.3. Future Directions

Using an analytical approach to detect practically important changes for athletes, we have demonstrated ~1% improvements in performance following altitude training. However, the underlying mechanisms of within-athlete variation to repeated exposures and the optimal time point to maximise performance gains following altitude training have not been established.

Future studies should look to identify the mechanisms underpinning individual variation in response to hypoxic exposure. While athletes who have a positive performance response to LHTL have previously been characterised by an accelerated erythropoietic response, the within-athlete variability in change in Hb_{mass} in this thesis demonstrates other mechanisms may contribute to enhanced time trial performance. The number of HIF-1 mediated responses to hypoxia implies that an increase in EPO concentration could be concurrent with other physiological changes such as increased carbohydrate metabolism, increased ventilation, enhanced muscle buffering and more efficient use of oxygen in the muscles. It seems possible that improvements in performance, which have previously been associated with a sustained elevated EPO response, may have been caused by some or all of these other factors. Further investigation of the regulation of hypoxia-dependent gene expression in relation to various altitude training methodologies may offer some clues about the precise mechanisms underpinning the large degree of variability in response to hypoxia within- and between-athletes. Whether an understanding of the underlying mechanisms can help develop protocols to improve the consistency of performance response to altitude or hypoxic exposure is yet to be established.

In addition, future research is required to elucidate the time-course of physiological and performance response after hypoxic exposure. Although some researchers, including our laboratory, have tried to measure performance immediately and between 1 to 3 weeks after altitude training, the optimal time to realise performance gains has not been substantiated. This time point is important for coaches and athletes not only in terms of when to come 'out' of hypoxic exposure prior to competition, but also in terms of managing training load. The additional stress of repeated hypoxic exposures, typically separated by short 4-5 week wash-out periods, also needs careful management. These studies are needed to clarify the physiological mechanisms and the time-course of their response to various forms of altitude training and exposure. This information will assist coaches and sport scientists to plan and monitor effective altitude training programs for individual athletes and squads.

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APPENDIX 1

DOSE-RESPONSE OF 3 WEEKS AND 6 WEEKS SIMULATED LIVE HIGH/TRAIN LOW ALTITUDE

INTRODUCTION

No previous study has addressed the dose-response relationship of extended LHTL altitude exposure on performance, hemoglobin mass and $\dot{V}O_{2max}$ in highly trained athletes. A secondary aim of Chapter 5 was to quantify the dose-response relationship of 3-wk (~300 h) and 6-wk (~600 h) consecutive LHTL exposure.

METHODS

Subjects

Eight well-trained male and female middle distance and distance runners undertook simulated live high/train low altitude (LHTL, n=4) or resided near sea-level (Control, n=4) in a randomized controlled design. Both groups trained in Canberra (~600 m ambient altitude). All athletes were tested under normoxic conditions at the Australian Institute of Sport (AIS), Canberra. Baseline characteristics are presented in Table 1.

TABLE 1. Baseline characteristics of the runners in the simulated live high/train low altitude (LHTL) and control groups at the start of Block 2 (mean ± SD)

		Mass (kg)	VO_{2max} ($mL.kg^{-1}.min^{-1}$)	Time trial (mm:ss)	Hb_{mass} ($g.kg^{-1}$)
LHTL	3 male, 1 female	66.4 ± 5.9 ^	69.4 ± 8.6	14:16 ± 1:53	13.7 ± 2.2
Control	1 male, 3 female	56.2 ± 9.4	66.8 ± 4.4	14:59 ± 1:05	13.3 ± 1.3

$VO_{2max,}$ maximal aerobic power; Time trial, 4.5 km road course; $Hb_{mass,}$ hemoglobin mass.
^ substantially different from control.

Experimental Design

The LHTL group spent 2 x 3 weeks (14 h·day-1, ~300 h) in a normobaric hypoxic five bedroom facility (3000 m), separated by a 5 week wash-out period between Block 1 and 2 (Figure 1). An additional 3 weeks of LHTL (Block 3) was completed immediately following Block 2, for a total of 6 weeks (~600 h) altitude exposure. A matched sub-group of the control group continued living and training in the same location for Block 3.

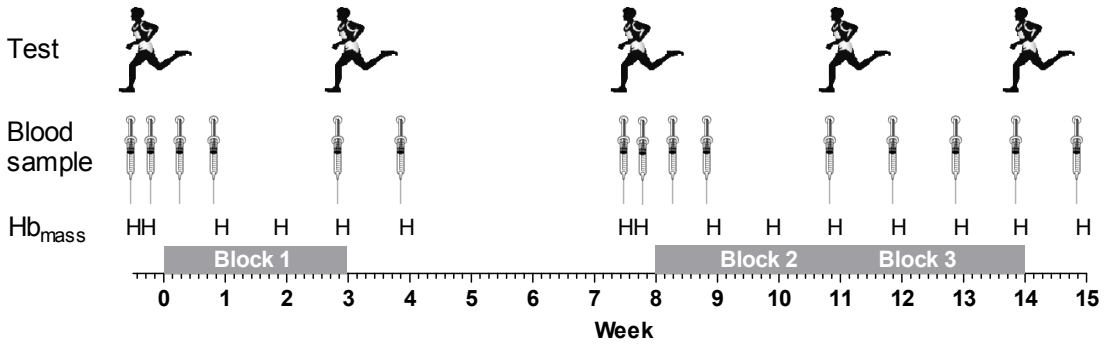

FIGURE 1–Schematic diagram of testing during each 3-wk simulated live high/train low or near sea-level training block (Block 1, 2 and 3). Test=time trial and treadmill test performed on separate days; Blood sample=venous blood collection; Hb_{mass}=hemoglobin mass.

Time Trial

A 4.5 km time trial on a road course (6 laps) was completed in the shortest possible time, before Block 2, within 1 day after Block 2 and within 1 day after Block 3.

Treadmill Test

A treadmill test to determine $\dot{V}O_{2max}$, running economy, lactate threshold, and velocity at $\dot{V}O_{2max}$ ($v\dot{V}O_{2max}$) was completed within 1-2 days after each time trial.

Hemoglobin mass

Hemoglobin mass (Hb_{mass}) was measured using a modified 2-min CO rebreathing test, twice before Block 2, weekly during Block 2 and 3 and one week after Block 3.

Hematological parameters

Venous blood was collected at six time-points (pre-1, pre-2, day 2, day 6, day 20 and day 27) in Block 2 and at three further time-points in Block 3 (day 34, day 41, day 48).

Details of all testing methods and Statistical Analysis are fully described in Chapter 5.

RESULTS

For the eight athletes who completed the additional 3-wk block, change in time trial performance was trivial after both Block 2 (LHTL: 0.9%; ±2.5%, control: -0.6%; ±1.3%) and Block 2+3 (LHTL: -0.3%; ±1.1%, control: -0.3%; ±1.1%). $\dot{V}O_{2max}$ was substantially higher in the LHTL group after Block 2+3 (4.3%; ±6.2%), but was not different after Block 2 or for the control group in either block. There were trivial changes in Hb_{mass} after Block 2 (LHTL: 2.2%; ±3.6%, control: -0.7%; ±3.1%) and Block 2+3 (LHTL: 4.0%; ±6.1%, control: -1.4%; ±5.3%). Compared with the control group, the LHTL group had substantially higher $\dot{V}O_{2max}$ (7.6%; ±6.9%) and Hb_{mass} (5.4%; ±6.8%) after Block 2+3, but there was no substantial difference between the groups in 4.5 km time trial performance (0.0%; ±1.4%).

The LHTL group had substantially higher submaximal $\dot{V}O_2$ and lower post-test lactate after 3 weeks, but substantially improved $\dot{V}O_{2max}$ and velocity at $\dot{V}O_{2max}$ ($v\,\dot{V}O_{2max}$) after 6 weeks (Table 2). The control group had only trivial changes in parameters measured during the treadmill test after 3 weeks, and a substantial reduction in $\dot{V}O_{2max}$ after 6 weeks. Compared with the Control group, the LHTL group had substantially poorer economy and lower post-test lactate after 3 weeks, but were substantially faster at $v\,\dot{V}O_{2max}$ and had a higher $\dot{V}O_{2max}$ after 6 weeks. There were no substantial differences in the change (pre-post) in blood bicarbonate (HCO_3^-) or pH for either group after either 3 weeks or 6 weeks.

DISCUSSION

We are not aware of any studies that have examined the dose-response relationship of hypoxic exposure to performance, Hb_{mass} and $\dot{V}O_{2max}$. Despite greater enhancements in Hb_{mass} and $\dot{V}O_{2max}$ after ~600 h LHTL exposure, time trial performance was not substantially improved compared to ~300 h of LHTL. The small number of athletes completing Block 3 precludes any definitive conclusion on the efficacy of extended LHTL exposure on performance. However, further enhancements in the physiological adaptations and the absence of a substantially harmful effect on performance lends support to the efficacy of even longer periods of LHTL in already well-trained athletes.

TABLE 2. Physiological parameters for treadmill tests 3, 4 and 5 for the simulated altitude and control groups. Percent change (pre- to post-test) after Block 2 (Δ 3 weeks) and Block 2 and 3 (Δ 6 weeks) within each group, and difference between the groups.

	Test 3	Test 4	Test 5	Δ 3 weeks	Δ 6 weeks
VO_{2max} ($ml.kg^{-1}.min^{-1}$)					
LHTL	69.4 ± 8.6	69.9 ± 7.0	72.2 ± 5.8	3.0; ±14.7%	4.3; ±6.2% *
Control	66.8 ± 4.4	64.4 ± 5.5	64.8 ± 6.0	-1.3; ±7.1%	-3.1; ±5.6% *
Diff (LHTL-Control)				4.4; ±15.5%	7.6; ±6.9% ^
Economy ($L.min^{-1}$)					
LHTL	3.90 ± 0.70	4.04 ± 0.61	3.89 ± 0.57	3.8; ±3.5% *	0.0; ±4.2%
Control	3.11 ± 0.70	3.07 ± 0.65	3.05 ± 0.68	-1.1; ±1.6%	-1.7; ±1.7%
Diff (LHTL-Control)				4.9; ±3.4% ^	1.8; ±4.1%
vVO_{2max} ($km.h^{-1}$)					
LHTL	19.2 ± 2.3	18.9 ± 1.7	19.8 ± 2.1	-0.3; ±9.7%	3.2; ±2.3% *
Control	18.7 ± 1.3	18.9 ± 2.2	18.7 ± 1.8	0.9; ±5.4%	-0.2; ±3.7%
Diff (LHTL-Control)				-1.1; ±8.9%	3.5; ±3.7% ^
4mM speed ($km.h^{-1}$)					
LHTL	17.5 ± 1.8	17.6 ± 1.6	17.8 ± 1.9	0.4; ±2.4%	1.2; ±1.4%
Control	17.3 ± 1.3	17.2 ± 1.6	17.1 ± 1.9	-0.6; ±1.6%	-0.9; ±3.9%
Diff (LHTL-Control)				1.0; ±2.5%	2.2; ±4.0%
Post [La^-] (mM)					
LHTL	13.6 ± 1.7	9.7 ± 2.8	12.9 ± 1.5	-32; ±36% *	-5; ±6%
Control	11.2 ± 1.9	10.9 ± 1.4	11.0 ± 2.3	-7; ±30%	-2; ±10%
Diff (LHTL-Control)				-27; ±35% ^	-3; ±10%

Values are mean ± SD, and effects as percent (mean; ±90% CL). LHTL (n=4), Control (n=4). VO_{2max}, maximal aerobic power; Economy, pooled submaximal VO_2 from four running speeds; vVO_{2max}, velocity at VO_{2max}; 4mM speed, lactate threshold speed; [La-] blood lactate concentration. * substantially different within group, ^ substantially different from control.

APPENDIX 2

HIF-1α RESPONSE TO REPEATED BOUTS OF LIVE HIGH: TRAIN LOW ALTITUDE

R.J. Aughey, N.S. Stepto, F. Serpiello, E.Y. Robertson, P.U. Saunders, D.B. Pyne, and C.J. Gore

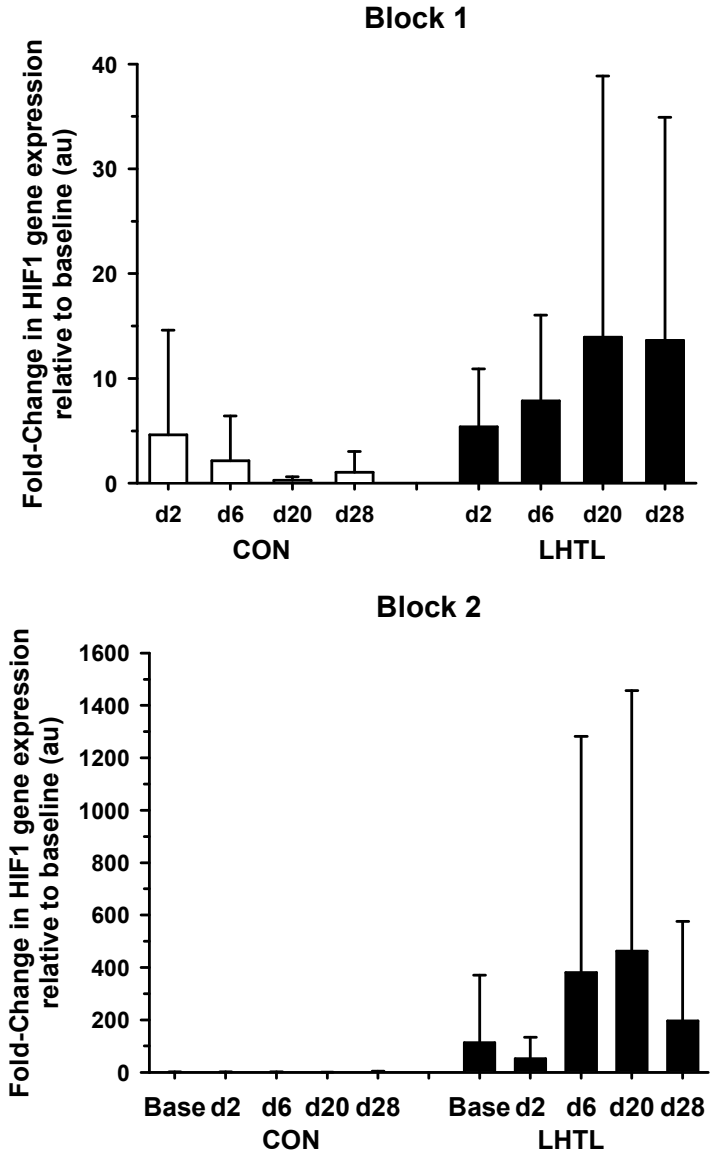

Figure 1. Fold change in HIF-1α. Data are mean and error bars are SD.

Table 1. Differences in HIF-1α gene expression, relative to baseline. Data are difference between LHTL (n=6) and CON (n=6) groups and presented as the difference in fold change between groups, a qualitative descriptor, and effect size (±90% confidence limits).

			BLOCK 1		
	Baseline	day2	day6	day20	day28
Fold Change Δ	n/a	0.78	5.69	13.65	12.58
Qual Descriptor	n/a	Trivial - Large ↑	Mod - V Large ↑	Large- V Large ↑	Mod - V Large ↑
ES (±90% CL)	n/a	0.90 (1.00)	1.62 (0.92)	2.06 (0.72)	1.73 (0.88)
			BLOCK2		
	Base 2	day2	day6	day20	day28
Fold Change Δ	112.70	51.86	379.93	462.41	194.94
Qual Descriptor	Mod - V Large ↑	Large - V Large ↑	Mod - V Large ↑	Large - V Large ↑	Large - V Large ↑
ES (±90% CL)	1.83 (0.72)	2.03 (0.66)	1.75 (0.73)	2.04 (0.55)	1.92 (0.70)