EFFECT OF SIMULATED ALTITUDE EXPOSURE ON SEA LEVEL PERFORMANCE

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ATTESTATION OF AUTHORSHIP

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to a substantial extent has been accepted for the award of any other degree or diploma of a university or other institution of higher learning, except where due acknowledgement is made.

Erica Hinckson ----------

Date ----------

CO-AUTHORED WORK

Chapters 4-6 of this thesis represent three separate papers that have been submitted to peer-reviewed journals for consideration for publication. All co-authors have approved the inclusion of the joint work in this doctoral thesis.

Paper 1
Title: Sea level performance in runners using altitude tents: A field study
Chapter in thesis: 4

Percentage contribution: 80% of work is my own, 15% is that of Professor Will Hopkins, 2% of Dr. Jean Fleming, 1% of Pete Pfitzinger, 1% of Dr. Tony Edwards and 1% Dr. John Hellemans.

Paper 2
Title: Reliability of time to exhaustion analyzed with critical-power and log-log modelling
Chapter in thesis: 5
Percentage contribution: 60% of work is my own, 40% is that of Professor Will Hopkins.

Paper 3
Title: Changes in running performance following intermittent altitude exposure simulated with tents
Chapter in thesis: 6

Percentage contribution: 95% of work is my own, and 5% is that of Professor Will Hopkins.

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Peer-reviewed Journal Publications

Chapters 4-6 of this thesis represent individual papers that have been submitted to peer-reviewed journals for consideration for publication. These papers are listed below.

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Technical Reports

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Ingham, E. A., Pfitzinger, P. D., Hellemans, J., Bailey, C., Fleming, J. S, Edwards, T., & Hopkins, W., G. (2001). *Enhancing performance of NZ athletes with intermittent simulated altitude exposure. Final report on the Sport Science New Zealand Research Grant.* Auckland, New Zealand.

Ingham, E. A., Pfitzinger, P. D., Hellemans, J., Bailey, C., Fleming, J. S, Edwards, T., & Hopkins, W., G. (2001). *Enhancing performance of NZ athletes with intermittent simulated altitude exposure. Interim report on the Sport Science New Zealand Research Grant.* Auckland, New Zealand.

ABSTRACT

Exposure to natural altitude using the "live high-train low" method improves athletic endurance performance at sea level by 1-2%. This method can also be employed with hypoxic devices that simulate altitude, but there is limited and conflicting research on their efficacy. Consequently, three studies were undertaken to investigate changes in sea level performance of endurance runners following exposure to altitude simulated with hypoxic tents. The device was chosen because of its potential for incorporation into the athlete's routine. In Study 1, 10 runners received altitude simulated with hypoxic tents (~9 h overnight at 2500-3500 m) and trained at sea level, while 10 runners in the control group performed usual training. Athletes in both groups performed a lactate-threshold test, but only the altitude group performed a run to exhaustion. The effect on 4-mM lactate speed was unclear, owing to poor reliability of this measure. There was a 16% increase in time to exhaustion in the hypoxic conditioning group, equivalent to a 1.9% (90% likely limits, ±1.4%) increase in speed in a time trial. Effects on performance were not apparent four and eight weeks after use of the tents. To improve precision of the effect of the tents and to determine the effects on performance of different durations, a further controlled trial was performed. A reliability study (Study 2) was first conducted to investigate the potential for runs to exhaustion to provide reliable measures of performance. Eight runners performed a test consisting of three runs to exhaustion lasting ~2, ~4 and ~8 min on six occasions over 14 wk. The critical power and log-log models were used to provide factors for converting variability in time to exhaustion into variability in equivalent time-trial time. Variabilities in time to exhaustion expressed as coefficients of variation for predicted 800-3000 m time-trial times were ~1-3%. A crossover study (Study 3) was then conducted in which 11 athletes performed usual (control) training and usual training with altitude exposure by using tents for 25 ± 3 days (mean ± SD) for 8.1 ± 0.6 $h.d^{-1}$, progressing from a simulated altitude of 2500 m to 3500 m above sea level. Washout period between control and altitude treatments was four weeks. Performance was assessed with treadmill runs to exhaustion as in Study 2. Improvements in mean predicted times (altitude-control) for standard competition distances of 800, 1500 and 3000 m derived from the runs to exhaustion were 1.0% (±1.3%), 1.4% (±1.2%) and 1.9% (±1.5%) respectively. There was some evidence that hypoxic exposure favoured

those athletes carrying the I allele for angiotensin converting enzyme. In summary, the main finding from the series of studies is that hypoxic tents are likely to enhance sea level endurance running performance by ~1-2%.

CHAPTER 1: INTRODUCTION

BACKGROUND

Altitude training has gained popularity among athletes, coaches and scientists, because of the belief that adaptations to the oxygen transport system induced by the hypoxia at altitude will enhance endurance performance. Over the last three decades, endurance athletes have lived and trained at altitude to improve performance at sea level, yet results from scientific studies of altitude training provide confusing information. This confusion originates from variation between studies in research design, altitude-exposure duration and frequency, sample size, and athlete calibre. Altitude level ranged from 1600 to 3090 m, the duration of exposure varied from 14 to 28 days, sample size ranged from 6 to 24 subjects, 30% of the studies incorporated no control group, athlete calibre extended from non-athlete to elite, and protocol used at altitude differed (Burtscher, Nachbauer, Baumgartl, & Philadelphy, 1996; Dill & Adams, 1971; Faulkner, Daniels, & Balke, 1967; Levine & Stray-Gundersen, 1992a; H. K. Rusko, Kirvesniemi, Paavolainen, Vahasoyrinki, & Kyro, 1996; Telford et al., 1996). The inconsistency and variation made comparisons difficult, which prevented researchers from making conclusions and practical recommendations.

Although the effects of living and training at altitude are unclear, there is an emerging consensus from scientific literature that altitude exposure using the “live high-train low” method improves athletic endurance performance at sea level by 1-2% (Levine, Stray-Gundersen, Duhaime, Snell, & Friedman, 1991). With this method, athletes reside at high altitude to harness the benefits and commute to train at sea level to avoid compromising training intensity (Levine et al., 1991). However, appropriate altitude facilities that accommodate such an arrangement are not available in most countries. An alternative to natural altitude exposure is simulated altitude using hypoxic devices, including hypoxic apartments, houses, tents or inhalers and hypobaric chambers.

Although hypoxic devices seem to be popular amongst athletes, there is limited and conflicting research on their efficacy on sea level performance (Frey, Zenhausern, Colombani, & Fehr, 2000; Hellemans, 1999; A. D. Roberts et al., 2000; F. A. Rodriguez et al., 1999; H. K. Rusko et al., 1999; Terrados, Melichna, Sylven, Jansson, & Kaijser, 1988). Questions remain concerning the appropriate altitude level and duration, time

course of the effect, appropriate time to compete post exposure, and mechanisms responsible for any changes in performance. For example, in studies where normobaric hypoxic apartments or houses were utilised, researchers have seen improvements (Mattila & Rusko, 1996; H. K. Rusko et al., 1999), little or no change (Piehl Aulin, Svedenhag, Wide, Berglund, & Saltin, 1998; A D Roberts et al., 2003) and impairments (C. J. Gore et al., 1999) in aerobic performance, and some have attributed improvements to anaerobic power (A D Roberts et al., 2003). Similarly, in studies where hypobaric hypoxia was investigated, some researchers have observed increases in aerobic or anaerobic performance (Casas et al., 2000; Hendriksen & Meeuwsen, 2003; Meeuwsen, Hendriksen, & Holewijn, 2001; F. A. Rodriguez et al., 1999). Studies in which hypoxic inhalers were used are limited. Researchers have seen improvements (Hellemans, 1999; Wood, Dowson, & Hopkins, 2004) in endurance performance. Published scientific studies on the efficacy of hypoxic tents on sea level performance are also limited (Hahn et al., 2001). On the basis of limited previous research the purpose of the studies in this PhD thesis was to investigate the effect of intermittent (discontinuous) altitude exposure simulated with hypoxic tents on sea level athletic performance in competitive runners using the "live high-train low" method.

THESIS RATIONALE

Improving athletic performance in an ethical manner is essential to athletes and coaches in preparation for specific competitions. Simulated altitude exposure may provide an avenue for improvement in sea level performance, but more research is needed to determine the effectiveness of devices that provide the altitude stimulus. There is limited published research on the efficacy of hypoxic tents, hence this PhD thesis aimed to contribute to the current knowledge via a series of studies of their efficacy.

Choice of subjects

Athletes of the highest level are often recruited in performance studies, because the variability in their performance is less in comparison to athletes of low calibre. In addition, it is already reasonably clear that altitude or hypoxia exposure produces an enhancement of performance of 1-2% with sub-elite athletes, which is of little use to such athletes. The aim was therefore to recruit athletes at the highest level possible, so that the results from this thesis would apply to athletes at this level.

Runners

Runners were chosen to participate, because the author was familiar with the sport through her involvement as an athlete and coach. For that reason, access to runners from a variety of running clubs was potentially a straightforward process, and coaches' support was gained by including them in the initial discussions in regards to the study design, study requirements, and potential benefit of the experiment.

Rowers

In a pilot study, rowers were also investigated, due to an interest from the New Zealand rowing squad to participate. The similarity of rowing to running events in regards to metabolic requirements, and the high calibre of the rowers secured their inclusion. In this study, the effects of a prototype hypoxic inhaler were investigated on rowing performance. Unfortunately, the results were equivocal, therefore further research investigating the effects of hypoxic inhalers on sea level performance was not pursued. The results of that study are available in Appendix T. The decision was then made to continue studying the effectiveness of the hypoxic tents on sea level performance since there was some evidence of performance improvements that return to baseline four weeks later.

Choice of measures

Performance

Endurance performance is defined as any performance with a large contribution from the aerobic system or any performance that requires pacing, usually activities lasting approximately one minute or longer. Hence, the words "endurance" and "aerobic" are used interchangeably within the thesis.

The primary focus was performance changes following exposure to simulated altitude. Because time trials on the track as a means to monitor performance changes were not possible due to local weather conditions in Study 1, a run time to exhaustion on the treadmill (~5 min) was conducted in the laboratory instead. This test was chosen because, according to the literature (Hopkins, Schabort, & Hawley, 2001), constant

power/speed tests are amongst the most reliable tests available. However, the large variability of time to exhaustion between repeated tests gives an impression that these tests are unsuitable for monitoring athletic performance. This issue was addressed by conducting Study 2 in which the reliability of three runs to exhaustion of different durations (~2, ~4, and ~8 min) was determined. Proper interpretation of run times to exhaustion requires converting them into time trial times using an appropriate model. Critical-power and log-log models were used to convert run times to exhaustion into predicted times on the track for standard competition distances. The models were compared and the log-log modelling was chosen for Study 3.

In addition to run times to exhaustion, the lactate threshold test was utilised to monitor changes in performance. This test was chosen because it has been suggested as a valid predictor of endurance performance, most athletes were familiar with the test, and it was apparently highly reliable. The protocol used was the same as that used in a study by Pfitzinger and Freedson (1998). Their study showed the highest reliability compared to other reliability studies of lactate threshold. The first author of that study was available to assist with the test, so it was expected that his involvement would ensure that the measures obtained would be highly reliable.

Subject characteristics

The secondary focus was the identification of predictors for individual responses to altitude exposure. The variables chosen were the genotype for angiotensin converting enzyme (ACE), percent arterial oxygen saturation immediately following a run to exhaustion, athlete ability, and age.

The ACE gene was chosen because it appears to have a role in adaptation to altitude and training. Of the three forms of the genotype (I-I, I-D, D-D), successful mountaineers were more likely than non-mountaineers to have the I-I form (Montgomery et al., 1998); furthermore, carriers of the I-I genotype showed better physiological adaptation to altitude (Woods, Pollard et al., 2002). A brief review on this topic is found in Chapter 2.

At termination of each time-to-exhaustion test percent arterial oxygen saturation was measured, because desaturation in exercise is linked to hypoventilation, and differences in ventilatory control could account for individual responses. It was speculated that

because hypoventilation induces greater hypoxemia, athletes with reduced ventilatory response would benefit more from hypoxic exposure (Dempsey et al., 1971). On the other hand, it is also possible that athletes exhibiting hyperventilation may respond better to altitude exposure due to their increased sensitivity to hypoxia. While the use of a pulse oximeter was convenient following exercise testing, it only provided a conservative estimation of oxygen saturation. Movement, the time it took for a signal to register and poor perfusion could have potentially interfered with the acquisition of accurate data (Yamaya, Bogaard, Wagner, Niizeki, & Hopkins, 2002).

Differences in ability could also account for individual responses to altitude exposure. Athletes of higher ability may respond less to the altitude treatment if they have a reduced reserve for further improvements.

Mechanisms

The tertiary focus was the investigation of a mechanism by which the observed effects could be explained. For measurement of possible enhancements in buffering capacity (for hydrogen ions), muscle biopsy was considered. The invasive nature of the muscle biopsy technique in conjunction with the uncertainty in the potential changes, made it unrealistic to proceed. The non-invasive technology of Nuclear Magnetic Resonance (NMR) spectroscopy could in principle be used to monitor changes in muscle buffering capacity, but the cost associated with the technique was beyond the allocated budget.

A mechanism that may explain changes in performance is the increase in the oxygen carrying capacity of blood, thus incorporation of measures of red cell volume (via the Evans blue dye technique) or haemoglobin mass (via the carbon monoxide rebreathing technique) were considered. Determination of red cell volume with the Evans blue technique was impractical to perform at the institution's laboratory, and the only hospital capable of conducting this procedure was not set up to accommodate the requirements of the study. Even if the Evans blue technique was incorporated, the errors of measurement associated with this method is apparently too large (5-10%) to track the small changes in blood parameters that would account for the small changes in endurance performance induced by hypoxic exposure (CJ Gore and WG Hopkins, unpublished observations). The carbon monoxide rebreathing device that was constructed at another New Zealand university for measurement of haemoglobin mass

was unreliable and therefore was not utilised in the two studies investigating the tents. Blood analysis was hence performed with standard hospital instrumentation in case substantial changes in haemoglobin concentration and haematocrit occurred that could be measured by this technique. Even so, large shifts in plasma volume could have interfered with accurate interpretation of haemoglobin concentration and haematocrit changes.

Choice of design

The best design for investigating factors that affect performance is a randomised controlled trial (Hopkins, 2000b). Because athletes received exposure at their own homes and had to monitor their own arterial blood oxygen saturation, blinding was not an option. Also randomisation was not possible, as some athletes of higher calibre consented to participate provided that they were included in the experimental group. To reduce problems associated with blinding, eliminate problems with randomisation, and improve the precision of estimation, a cross over design was employed in Study 3 in which all athletes received the hypoxic treatment.

Following consultation with athletes and their coaches it was decided that a field study would be more appropriate to determine whether the chosen device provided a realistic and practical means for improving performance. Controlling daily training regimes, diet, altitude exposures and competition schedules would have made the study unrealistic. Most of the athletes would not have consented to have their training regime and competition schedule altered. It should be noted however, that training and physical responses to the altitude stimulus were monitored with specific detailed training diaries. Perhaps a laboratory study in a controlled environment with non-athletes would have been equally possible to conduct but it would fail to provide results appropriate for a competitive athlete.

Choice of device

The choice of investigating hypoxic tents (Figure 1.1), instead of apartments or houses, was based on the claim that they provided individualised exposure with minimal disruption to family life. At the time when Study 1 was underway another

individualised device (hypoxic inhaler) became available, so the opportunity was taken to investigate its efficacy on sea level performance in rowers (see Appendix T).

Figure 1.1. The hypoxic tent.

Choice of analysis

The statistical approach deviated from the traditional approach of statistical significance. It is the belief of the author and supervisors that it is inappropriate to report performance changes in terms of statistical significance. Instead, changes should be reported in terms of probability of practical benefit or harm. It is possible to have changes in performance of a few percent that are not statistically significant but still provide a clinically realistic chance of a benefit. Conversely, a change in performance can be statistically significant but have a clinically unrealistic chance of benefit (Hopkins, 2002).

To determine whether a change in performance is beneficial or harmful, a threshold value needs to be set. In top runners, the smallest enhancement in performance that has a substantial effect on their chance of a medal is about one third of the typical variation of performance in competition. Top distance runners need to be concerned with changes in performance of ~0.5% (Hopkins & Hewson, 2001). In the two experimental studies the threshold value for determining practical benefit or harm was set at 0.5%.

ORIGINALITY OF THE THESIS

- Since there is limited research available on the effects of hypoxic tents on sea level endurance, the outcomes of this thesis will contribute substantially to the body of knowledge.

- No other study investigating the effects of simulated altitude exposure on sea level performance has monitored changes in performance eight weeks post exposure.

- A more systematic attempt was made, than Rodriguez (2004), to compare performance effects of hypoxic exposure on endurance running performance of several durations.

- The angiotensin converting enzyme genotype has never been included in the analysis of "live high-train low" performance studies as a predictor of individual responses to altitude exposure.

- Conversion of run times to exhaustion to predicted times for standard competition distances using log-log modelling has not been performed previously.

THESIS ORGANISATION

This thesis consists of seven chapters. Chapter 2 is the main review of the literature for the thesis, on the effect of natural and simulated altitude exposure on sea level performance. Chapter 3 is an additional review of the literature of the possible mechanisms contributing to changes on sea level performance with altitude exposure. Chapters 4 to 6 are the experimental studies, and have been submitted to peer-reviewed journals as separate papers.

Study 1, "Sea level Performance in Runners Using Altitude Tents: a Field Study", in which the magnitude and time course of the effect of altitude tent use on endurance performance were determined, is reported in Chapter 4. Study 2, "Reliability of Time to Exhaustion Analyzed With Critical-Power and Log-Log Modelling", in which within-subject variability expected from test to test during normal training was determined, is reported in Chapter 5. Study 3 "Changes in Running Endurance Performance Following

Intermittent Altitude Exposure Simulated With Tents", in which the effectiveness of hypoxic tents on sea level performance over short and long distances using a cross-over design to improve precision of the estimate, is reported in Chapter 6. The sequence of the studies is depicted in Figure 1.2. Finally, Chapter 7 consists of a general discussion of the implications of the results of this thesis for athletes, coaches and sport scientists.

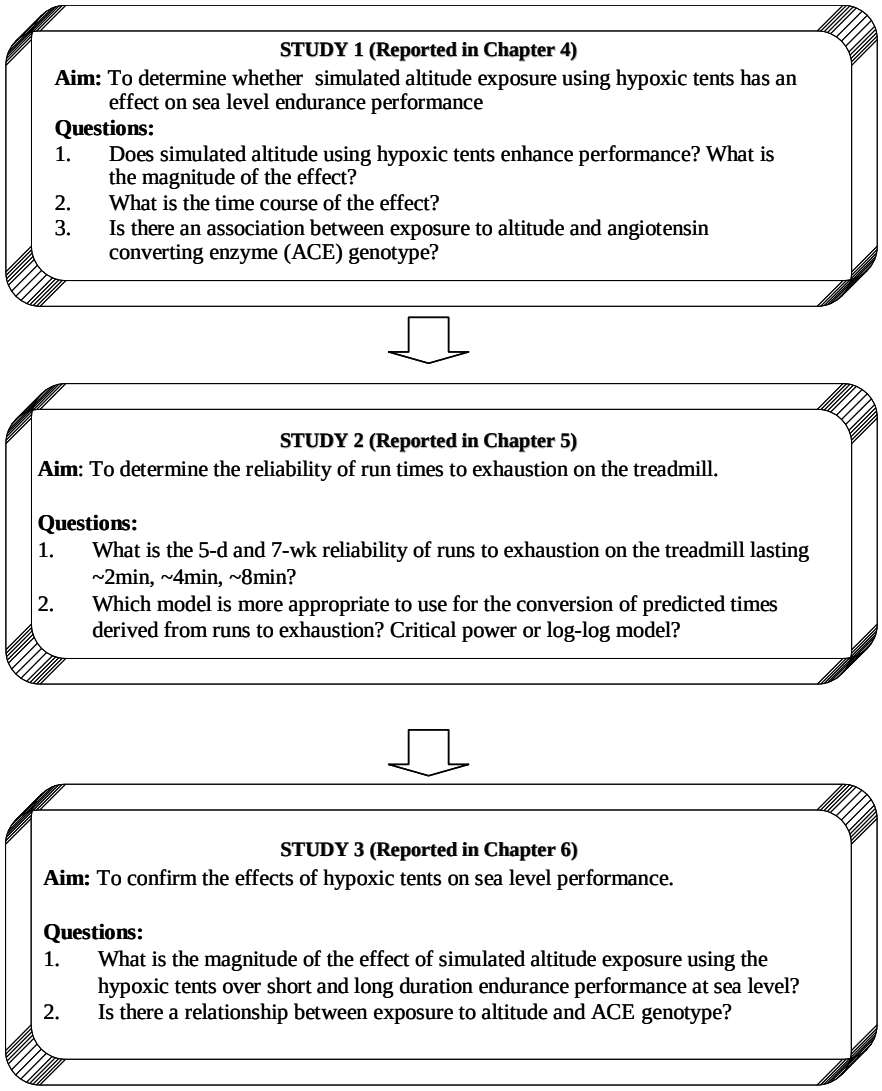

Figure 1.2. The sequence of the studies, aims and questions.

CHAPTER 2: LITERATURE REVIEW-THE EFFECTS OF NATURAL AND SIMULATED ALTITUDE EXPOSURE ON SEA LEVEL PERFORMANCE

INTRODUCTION

There is reasonable evidence to suggest that natural altitude exposure using the "live high-train low" method improves sea level endurance performance (Levine & Stray-Gundersen, 1997). With this approach athletes harness the benefits of altitude exposure during residence at altitude, and continue with regular training at sea level, without compromising training intensity. Currently, athletes who dominate middle and long distance events reside or train at altitude (Entine, 2000). Hence, altitude training or exposure to altitude may improve aerobic performance for sea level events.

The effectiveness of the "live high-train low" approach (in comparison to the live high-train high approach) emerged following decades of equivocal research. In several experimental studies (see Table 1) and reviews (Böning, 1997; Hahn, 1991; Levine & Stray-Gundersen, 1992b; H. R. Rusko, 1996; Wolski, McKenzie, & Wenger, 1996) authors investigated the effects of ***natural*** altitude training or exposure on sea level performance by determining changes primarily in maximal oxygen uptake (VO_2max) and time trial time in athletes involved with distance running, skiing, and rowing. Some authors showed an improvement in VO_2max and/or time trial time (Balke, Nagle, & Daniel, 1965; Burtscher et al., 1996; Daniels & Oldridge, 1970; Dill & Adams, 1971; Faulkner et al., 1967; Klausen, Robinson, Micahel, & Myhre, 1966; Levine & Stray-Gundersen, 1997; J. Stray-Gundersen & Levine, 1994; Terrados, Jansson, Sylven, & Kaijser, 1990), others showed no improvement (Hansen, Vogel, Stelter, & Consolazio, 1967; Ingjer & Myhre, 1990) and some showed a decrease (W. C. Adams, Dernauer, Dill, & Bomar, 1975; Bailey et al., 1998; Levine & Stray-Gundersen, 1992a; Levine et al., 1991; H. K. Rusko et al., 1996; Saltin, 1967).

Similarly, in studies investigating the effects of ***simulated*** altitude exposure authors reported improvements in sea level endurance performance (Hellemans, 1999; F. A. Rodriguez et al., 1999; H. K. Rusko et al., 1999), or no changes (Frey et al., 2000; Levine et al., 1990; Meeuwsen et al., 2001).

In this review a summary of studies examining the effects of natural and simulated altitude training or exposure on sea level performance is presented. Studies were located by using primarily two major databases, Medline and Sport Discus, and cross referencing. The searches were limited to peer review articles, abstracts, and articles published in English. By these means, 169 studies and reviews were selected on the topics of natural and simulated altitude exposure, erythropoiesis and physiological mechanisms. Mechanisms that may explain the physiological changes responsible for changes in performance will be discussed in Chapter 3.

THE EFFECT OF NATURAL ALTITUDE EXPOSURE ON ENDURANCE PERFORMANCE

It is generally accepted that training at altitude improves aerobic performance at altitude (Maher, Jones, & Hartley, 1974). However, it remains unclear whether living and training at altitude provides a greater advantage to sea level performance. Various authors have investigated the effect of natural altitude exposure on sea level performance with conflicting results. In this section, an overview of these studies will be presented and issues relating to altitude exposure methods, altitude level (low altitude <2000 m, moderate altitude ~2000-4000 m, high altitude >4000 m), altitude duration, time course of the altitude effect and subject characteristics will be addressed.

Altitude exposure methods

It was evident from the 1968 Mexico City Olympics that endurance athletes exposed to some form of altitude training prior to competing at altitude performed better than those who were not previously exposed to altitude. Scientists have since sought to determine whether these altitude effects benefit performance at sea level (Dill & Adams, 1971; Faulkner et al., 1967; Levine et al., 1990).

Living and training at altitude

In early studies (Dill & Adams, 1971; Faulkner et al., 1967) authors observed substantial increases in sea level VO_2max in well-trained athletes, but no such changes in elite athletes following training at moderate altitude (2000-3090 m) for 14-17 days. One reason for the lack of change in performance between the two groups was the

difference in conditioning levels. It is possible well-conditioned athletes may not have reached a plateau in their training prior to altitude (See Table 2.1).

Table 2.1. Live high-train high effects on sea level performance. Studies are sorted by the magnitude of the effect in descending order.

Participants	Gender	Altitude Level (m)	Altitude duration (days)	Time of post-altitude test (days)	VO_2 max (%)	Time-trial (%)	Reference
Uncontrolled Studies							
5 men (former runner, runner, student and non-athletes)	M	3800	35	14	+14	- -	(Klausen et al., 1966)
2 athletes (pentathlete, runner) + 3 non-athletes	M	2300	10	2-4	+7	+4% (400m run) 3% (mile run)	(Balke et al., 1965)
6 elite runners	M	2300	14, 14 & 7 over 45	4-5	+5	? (mile run)	(Daniels & Oldridge, 1970)
6 elite runners	M	3100	17	1	+4	- -	(Dill & Adams, 1971)
5 well trained runners + 16 highly trained swimmers	M/?	2300	21	3/21	+1	NS (100, 200, 500 m swim)	(Faulkner et al., 1967)
7 elite skiers	M	1900	21	1/14	un	- -	(Ingjer & Myhre, 1990)
9 elite athletes	M & F	2250	19	?	-	- -	(Saltin, 1967)
Controlled Studies							
10[a] + 12 amateur runners	M	2315	12	3/16	+8 & +10	- -	(Burtscher et al., 1996)
13 [a] + 13 [a] + 13 competitive runners	M & F	2500	28	3/7 14/21	+5	NS (5km run)	(Levine & Stray-Gundersen, 1997)
9 + 9 elite runners	M	1760	28	7	+3	+? (3.2 km run)	(Telford et al., 1996)
16 [a] + 8 soldiers	M	4300	21	1-4, 15-18	un	- -	(Hansen et al., 1967)
14 [a] + 9, 10 [a] + 19 elite runners	M & F	1500-2000	28	10/20	-0.1	+0.4% (4x1km run)	(Bailey et al., 1998)
9 [a] + 10 competitive runners	M & F	2500-3500	28	?	-0.7	-1.7 (2 mile run)	(Levine & Stray-Gundersen, 1992a)
9 + 9 elite rowers	?	1800	21	1	-1	- -	(Jensen et al., 1993)
6 + 6 highly trained runners (crossover)	M	2300	20	1	-2.8	- -	(W. C. Adams et al., 1975)
14 [a] + 7 elite skiers	M	1600-1800	18-28	7	-3.1	- -	(H. K. Rusko et al., 1996)

Uncontrolled , no control group; controlled, with control group; [a] subjects in the experimental group M, male; F, female; VO_2max, maximal oxygen uptake; +, better; -, worse; - -, not measured; ?, data not provided; NS, non significant; un, unclear.

While in the previous two studies the authors observed some evidence of an improvement in performance, it was still unclear whether the improvement was solely due to altitude training or training per se, because of the absence of a control group. In a later study in which they investigated the responses of competitive distance runners, Levine and Stray-Gundersen (1992a) included a control group in their sample. Nine runners resided and trained at moderate altitude, and 10 resided and trained near sea level at an altitude of 1300 m for four weeks. The training intensity was monitored to ensure equivalent training stimulus in both groups. The runners completed a maximal VO_2 treadmill run, and a 5-km time trial, with measurement of sub-maximal heart rate, lactate concentration and plasma volumes. There was a small impairment in VO_2max and 5-km time trial in the altitude group, but the authors reported no significant differences between the two groups in performance and the other physiological measurements. It was concluded that training and residing at high altitude offered no advantage to sea level performance above that obtained through sea level training.

Similarly, Rusko, Kirvesniemi, Paavolainen, Vahasoyrinki, and Kyro (1996) compared the responses in 18 skiers who trained and raced at an altitude of 1600-1800 m with a group of seven skiers who trained and raced at sea level. Performance was monitored through VO_2max testing and maximal and sub-maximal anaerobic power tests at sea level. There were no significant changes in VO_2max values between the two groups. There was, however, a decrease in anaerobic power in the altitude group. The decreased performance was attributed to the enhanced stress and decreased training pace at altitude. Likewise Telford et al. (1996) investigated the responses of nine elite distance runners who trained and resided at an altitude of 1760-2000 m in comparison with a group of nine runners who lived and trained at sea level. There was a 3% improvement in VO_2max in the altitude group and an improvement in the 3.2 km run in both groups but the results were reported as non-significant. It was concluded that living and training at high altitude offered no advantage over sea level training.

In contrast, Burtscher, Nachbauer, Baumgartl, and Philadelphy (1996) showed significant improvements in VO_2max in runners who resided and trained at altitude of 2315 m compared with the group who lived and trained at sea level. The participants in this study were sub-elite athletes, while in the previous studies outlined above the athletes in the experimental groups were elite. The athlete's conditioning level is a contributor to changes in performance along with altitude exposure. The importance of

the athlete's conditioning level and genetic make-up with reference to altitude exposure will be discussed in a later section.

It is not surprising that performances were not improved with the live high-train high approach, as problems exist with residence and training at high altitude. Athletes probably were unable to train at the same intensity as at sea level due to the inadequate oxygen supply in the air, which caused them to detrain, and tended to offset any beneficial effects of altitude on performance (Balke et al., 1965; Buskirk, Kollias, Akers, Prokop, & Reategui, 1967; Faulkner et al., 1967). It is also possible that some athletes did not respond favourably to training at altitude (Roach, Koskolou, Calbet, & Saltin, 1999), due to acute mountain sickness (AMS). The effects of AMS are nausea, loss of appetite, insomnia, fatigue and shortness of breath with exertion (Bovard, Schoene, & Wappes, 1995). These problems hinder the athlete's ability to train at the desired level, hence fitness is lost while training at altitude. Table 2.2 summarises the scientific literature relevant to the live high-train high method and effects on sea level performance.

Living at altitude (2500 m) and training at lower (~1300 m) altitude

In response to the problems experienced at altitude (inability to train at the desired level due to inadequate oxygen supply and AMS) Levine, Stray-Gundersen, Duhaime, Snell, and Friedman (Levine, Friedmann, & Stray-Gundersen, 1996) developed the "live high-train low" method. They hypothesised that athletes who live at altitude but train near sea level will acclimatise to altitude without compromising their training intensity. The authors compared nine athletes living at an altitude of 2500 m and training near sea level (1300 m) with three athletes living and training at sea level. They reported a 4.3% increase in VO_2max and a 25- second improvement in the 5-km time trial in the altitude group. The control group showed no changes in either of the above measurements. Although the authors observed improvements in VO_2max and 5-km time trial the data to support the "live high-train low" method were only preliminary due to the small scale of the study and the conditioning of the athletes involved.

Following the study by Levine and colleagues (1991) authors in similar studies (Dehnert et al., 1997; Levine & Stray-Gundersen, 1997; J. Stray-Gundersen & Levine, 1997) showed improved aerobic power using the "live high-train low" method. In

response to the positive outcomes produced by earlier pilot studies, Levine and Stray-Gundersen (1997) conducted a major study using 39 runners to confirm the results. Thirteen runners lived at “high” altitude (2500 m) and trained at low altitude (1250 m), 13 lived and trained at “high” altitude and 13 lived and trained at sea level. The “live high-train low” and the “live high-train high groups showed an increase in VO_2max but only the “live high-train low” group improved their 5-km time trial time as compared to the low-low group. The authors concluded that the “live high-train low” method offers an advantage to sea level performances over sea level training and that the study provided confirmation of earlier results on the effectiveness of the method. Table 2.2 summarises the studies relevant to the “live high-train low” method.

Living at altitude (2500 m) and training at higher (~3000 m) and lower (1300 m) altitude

A modification of the “live high-train low” method is the “live high-train high and low” method. Athletes live at high altitude and train there at a low intensity, combined with high intensity training at low altitude. In a pilot study of runners (J. Stray-Gundersen & Levine, 1997), who lived at 2500 m and trained at 2700 m and 1250 m for 28 days, it was demonstrated that there were similar improvements in VO_2max and 5000-m time trial as with the original “live high-train low” study (Levine & Stray-Gundersen, 1997). These results were substantiated in a peer reviewed study by Stray-Gundersen, Chapman, and Levine (2001), who observed a 3% improvement in VO_2max and a 0.7% improvement in 5000-m time trial in elite runners who lived at 2500 m for 27 days and trained at 1250-3000 m above sea level. However, the study suffered from the absence of a control group performing a similar training camp at sea level. The inclusion of such a group would have controlled for improvements in VO_2max and time trial time associated with improvements due to being in a camp environment.

Table 2.2. Summary of studies showing the effects of natural altitude exposure on sea level performance using the "live high-train low" method. Studies are sorted by the magnitude of the effect.

Participants	Gender	Altitude level (m)	Altitude duration (days)	Time of post-altitude test (days)	VO_2max (%)	Time trials (%)	Reference
Uncontrolled Studies							
14 elite Olympic distance triathletes	M & F	2100	30	7?	+7.9	- -	(W. D. B. Hiller et al., 2000)
20 Olympic distance triathletes	M & F	2100	38	?	+4.7 (males) +8.0 (females)	- -	(W. D. B. Hiller et al., 2001)
22 elite runners	M & F	2500/1250	27	3	+3.0	+0.7 (3km run)	(J. Stray-Gundersen, Chapman, R. F. and Levine, B. D., 2001)
6 competitive runners	?	2500/1250	28	0 & 14	-3.6 & -4.0	+0.9 & -1.3 (5km run)	(J. Stray-Gundersen & Levine, 1994)
Controlled Studies							
13+13+13 runners	M & F	2500/1250, 2500/2500, 150/150	28	4 (VO_2max) & 21 (5k run)	+5.4	+4.3	(Levine & Stray-Gundersen, 1997)
6 + 3 runners	?	2500/1300	28	?	+3.1	+2.3 (5km run)	(Levine et al., 1991)
13 runners	M & F	2500/2700/1250	28	3-4?	0.0 relative to high-low	+0.2 relative to high low	(J. Stray-Gundersen & Levine, 1997)
11 + 10 well trained athletes	M & F	1950/800	14	7?	7%	?	(Dehnert et al., 2002)

M, male; F, female; VO_2max, maximal oxygen uptake; +, better; -, worse; - -, not measured; NS, non significant; ?, data not provided.

Altitude level

When investigating the effects of altitude on aerobic performance, altitude level becomes an important variable to consider. Authors have used a wide range of altitude levels in their protocols. In the following section the effects of altitude level on performance at sea level are discussed.

Exposure at low altitude

Studies conducted at low altitude (below 2000 m) have shown no significant improvements on sea level aerobic power (Bailey et al., 1998; Ingjer & Myhre, 1990; Telford et al., 1996). For instance, Ingjer and Myhre (1990) investigated seven elite cross-country skiers who lived and trained for three weeks at an altitude of 1900 m. Training ranged from 2-4 h per day. The authors tracked haematological changes through haemoglobin concentration and haematocrit and performance through changes in VO_2max and graded treadmill running. Performance tests were conducted at sea level one and 14 days post altitude training. They reported no significant changes between pre-altitude and post-altitude VO_2max, yet haemoglobin concentration and haematocrit increased significantly. However, they saw a significant improvement in sub-maximal performance.

In a controlled study, Bailey and Davies (1998) investigated elite distance runners training at different altitude levels. One part of the study involved 14 elite distance runners who trained for four weeks at an altitude of 1500-2000 m and a similar group at sea level. The second part of the study involved a group of 10 runners who trained at an altitude of 1640 m and 19 runners who trained at sea level. The athletes continued with their usual training, and performance changes were monitored through VO_2max and a standardized treadmill test for the determination of lactate threshold. Measurements were taken at 10 and 20 days post-altitude with no significant changes in oxygen uptake and lactate threshold. Training at low altitude had no effect on reticulocyte count, haemoglobin concentration or packed cell volume. The authors concluded that training at low altitude produced insufficient stimulus for changes in performance and haematological parameters.

In a similar controlled study, Telford et al. (1996) investigated performance changes through VO_2max, steady-state heart rate at two distances and short duration treadmill test to exhaustion in 18 elite distance runners. Nine trained at 1700 - 2000 m and the other nine at sea level for four weeks. The changes in maximal oxygen consumption and short-duration treadmill test were not significant and both groups improved in their 3.2-km run. The authors concluded that training at lower altitude offered no advantage to sea level performance.

Exposure at moderate altitude

Most studies conducted at moderate altitudes (2000–4000 m) (Dehnert et al., 1997; Levine et al., 1996; Levine & Stray-Gundersen, 1997; Mattila & Rusko, 1996; J. Stray-Gundersen & Levine, 1997) showed a significant improvement in aerobic performance at sea level (see Table 2.3). In fact Weil, Jamieson, Brown, and Grover (1968) had already demonstrated a relationship between altitude level and haematological changes associated with increased aerobic performance. The authors studied healthy men who resided at sea level, 1600 m and 3100 m and attempted to establish a relationship between arterial oxygen saturation and red cell mass. A rise in red cell mass was evident when PaO_2 (partial pressure for oxygen) reached 67 mmHg. This value approximates an altitude level of 2200–2500 m (J. Stray-Gundersen, Alexander, & Hochstein, 1992). More recently, Witkowski et al. (2001) determined the optimal altitude for living high and training low by exposing 48 competitive runners to 1780 m, 2085 m, 2454 m and 2805 m above sea level. High intensity training was conducted at 1250-1780 m, and base training at 1700-3000 m. They concluded that the optimal level for improved VO_2max (~6%) and performance (~2.7% faster) was 2000-2500 m. They speculated that < 1800 m was too low possibly due to inadequate erythropoiesis and > than 2800 m was too high due to the negative aspects of altitude acclimatisation.

Ge et al (2002) investigated the dose-response relationship between altitude and erythropoietin (EPO) to determine the time course and appropriate altitude exposure. EPO is a hormone released by the kidneys in response to hypoxia. Twenty-four distance runners were exposed to simulated altitudes of 1671 m, 2086 m, 2455 m and 2806 m in a hypobaric chamber on four different occasions. The time between exposures was one week. Erythropoietin was measured before, at 6h, and 24h of exposure. There was an increase of EPO at all altitudes by 6 h and EPO continued to increase 24 h at 2455 m

and 2806 m. EPO did not increase after by 24 h at 1671 m and 2086 m. It was concluded that the increase in EPO is dose dependent with the greatest increases achieved above 2440 m. Altitude levels above the recommended range may continue to provide the appropriate stimulus (Weil et al., 1968).

Exposure at high altitude

A high altitude level (approximately above 4000 m) produces catabolic effects, and is unfavourable to improvements in aerobic performance. Green, Sutton, Cymerman, Young and Houston (2000) and Buskirk, Kollias and Akers (1967) showed that at higher altitudes there is a reduction in weight through loss in muscle mass. At higher altitude, oxygen availability continues to decrease, making it harder to produce physical work. Consequently, maximal aerobic power is decreased and athletes are unable to maintain their fitness (Saltin, 1970). According to the literature the most appropriate level for athlete training is between 2200–2500 m.

Altitude duration

Top international coaches generally consider that three weeks at altitude is sufficient to elicit the physiological responses necessary for improved performance at sea level (Dick, 1992). Several investigations were conducted over three and four weeks at moderate altitude (2000-4000 m) (W. C. Adams et al., 1975; Dill & Adams, 1971; Faulkner et al., 1967; Ingjer & Myhre, 1990) with variable outcomes. In most of the "live high-train low" studies athletes received exposure for four weeks, and in some studies for two weeks or less (Burtscher et al., 1996; A D Roberts et al., 2003). On the basis of the experimental studies reviewed, it is recommended that four weeks of altitude-exposure is sufficient to allow physiological changes to be manifested in terms of altitude acclimatisation.

Time course of the effect

The time lapse for testing following altitude exposure has varied among studies. The shortest duration before post altitude testing was one day and the longest duration was three weeks. Tests performed a day after altitude exposure (W. C. Adams et al., 1975; Dill & Adams, 1971) showed no significant changes in VO_2max. In studies where

testing was conducted two to three weeks post altitude the authors provided conflicting results (Faulkner et al., 1967; Ingjer & Myhre, 1990; Klausen et al., 1966). According to Dick (1992) top coaches have seen significant results 14 days following descent. Stray–Gundersen and Levine (1994) showed that the effects of four weeks of living high and training low are evident immediately on return to sea level and lost within two weeks. In a later peer reviewed study (Dehnert et al., 1997; Levine et al., 1996; Levine & Stray-Gundersen, 1997; Mattila & Rusko, 1996; J. Stray-Gundersen & Levine, 1997), the effects of "live high-train low" compared with live high-train high and control live low-train low were similar immediately and three weeks after altitude exposure.

Subject characteristics

In the literature under review, authors have not considered the effect of age, gender, athletic ability and genotypic make up on altitude training or exposure. Most studies have used male endurance athletes in their early and mid twenties of variable athletic abilities.

Age

According to Dick (1992) only mature and experienced athletes should engage in altitude training. Training at altitude is hard and perhaps at times tedious, as athletes have to travel to remote locations. Although the recommended age for engaging with altitude training is 21 and over for the reasons stated above, no one has addressed this issue with a scientific study.

Gender

It is unclear whether altitude exposure in women has the same effect as in men. The ovarian hormones estrogen and progesterone may cause women to acclimatise differently to altitude than men (Braun et al., 1997). It has been shown that there is stimulation of EPO during pregnancy under normal conditions (McMullin, White, & Lappin, 2003; Milman, Graudal, Nielsen, & Agger, 1997), which signifies that systems are in place that could allow women to respond better to a hypoxic stimulus. Levine and Stray-Gundersen (1997) included men and women in their sample, but the effect of

gender was unclear. They speculated that as long as iron supplementation was adequate then the results should be consistent regardless of gender. However, Hiller et al. (2001) saw differences in the effects of the "live high-train low" method in 14 males and 6 females on VO_2max, blood parameters and body composition. The athletes lived at 2100 m for 38 days and commuted daily to sea level facilities for training. Males increased VO_2max by 4.7% and females by 8.0%. Males lost an average of 1.1 kg of fat and gained on average 0.6 kg. Changes in body fat for females were non-significant. While females showed a significant increase in haemoglobin, haematocrit and volume of red blood cells, this was not so in males. Clearly, further research is warranted.

Athletic ability

Athletic ability among participants contributes to the variety of results seen in altitude studies. Table 2.3 categorises the results into non-athletes, sub-elite, and elite athletes. Performance outcome was restricted to VO_2max to allow comparisons of athletic status among studies. Change in VO_2max was unchanged in non-athletes, ranged from 0.7% impairment to 8.0% improvement in sub-elite athletes, and 0.4% impairment and 3.0% improvement in elite athletes. Uncontrolled studies showed a 6.9% improvement in a mixed group of athletes, a range from an impairment of 4.0% to 14% improvement in sub-elite athletes, and a range from worse to an improvement of 5.0% in elite athletes. It is noticeable from the literature that changes in elite athletes are smaller in comparison to non athletes or sub-elite.

Non-athletes

Uncontrolled studies with non-athletes and mixed groups (Balke et al., 1965; Klausen et al., 1966) are hard to interpret because of the training effect that may occur independent of altitude training. Controlled studies with non-athletes (Hansen et al., 1967) show improvements in performance no greater than those achieved with training at sea level. According to Levine (1992a), untrained individuals and recreational athletes are unlikely to benefit from altitude training any more than from training at sea level. Altitude training for these individuals accelerates physiological adaptations that sea level training would have contributed to over a longer period.

Table 2.3. The effect of athletic ability on sea level VO_2max following exposure to natural altitude. Studies are sorted by the magnitude of the effect.

Participants	VO_2max (%)	Reference
Uncontrolled Studies		
Non-athletes		
5 men	+14	(Klausen et al., 1966)
Sub-elite athletes		
5 + 16 runners and swimmers	+1.4	(Faulkner et al., 1967)
6 runners	-4.0	(J. Stray-Gundersen & Levine, 1994)
Elite athletes		
9 runners	+5.0	(Saltin, 1967)
6 elite runners	+5.0	(Daniels & Oldridge, 1970)
6 elite runners	+4.2	(Dill & Adams, 1971)
22 elite runners	+3.0	(J. Stray-Gundersen, Chapman, R. F. and Levine, B. D., 2001)
22 elite runners	+3.4	(Chapman, Stray-Gundersen, & Levine, 1998)
7 elite skiers	NS	(Ingjer & Myhre, 1990)
Mixed group		
1 Olympic pentathlete, 1 middle-distance runner, 1 medical student, 2 laboratory staff	+6.9	(Balke et al., 1965)
Controlled Studies		
Non-athletes		
runners	NS	(Hansen et al., 1967)
21 untrained into 3 groups	NS	(Levine et al., 1990)
Sub-elite athletes		
10 + 12 amateur runners	+2 & +8	(Burtscher et al., 1996)
13 + 13 + 13 runners	+4.9	(Levine & Stray-Gundersen, 1997)
9 + 10 runners	-0.7	(Levine & Stray-Gundersen, 1992a)
14 + 7 skiers	-3.1	(H. K. Rusko et al., 1996)
Elite athletes		
9 + 9 runners	+3.0	(Telford et al., 1996)
14 + 9 runners	-0.4	(Bailey et al., 1998)
2 X 6 runners (crossover)	-2.8	(W. C. Adams et al., 1975)
9 + 9 rowers	-4.0	(Jensen et al., 1993)

+,better; -, worse; NS, non significant.

Sub-elite athletes

Faulkner, Daniels and Balke (1967) investigated five well-conditioned men and fifteen highly conditioned college swimmers trained at an altitude of 2300 m for three weeks. On return to sea level there was an improvement in VO_2max in the five runners in comparison to pre-altitude, but there were no significant improvements in the highly trained swimmers. Yet, Stray-Gundersen and Levine (1994) showed a decrease in oxygen maximal uptake in competitive runners who spent four weeks living at an altitude of 2500 m and training at an altitude of 1250 m.

Controlled studies with sub-elite athletes also show similar contradictory results. Rusko et al. (1996) observed a reduction in VO_2max in 14 skiers who trained at an altitude of 1600-1800 m for 18-28 days. Similalry, Levine and Stray-Gundersen (1992a) observed a reduction in VO_2max in runners who trained at 2500-3000 m for 28 days. But Burtscher et al. (1996) and Levine and Stray-Gundersen (1997) showed an improvement in sea level VO_2max. Burtscher et al. (1996) saw an increase of 8.7% in VO_2max in runners who were tested 16 days following altitude training at 2300 m for 12 days and Levine and Stray-Gundersen (1997) saw a 4.9% increase in VO_2max in runners who spent 28 days at 2500 m. When study results are pooled from the perspective of athletic ability, it is unclear whether sub-elite athletes would benefit from altitude training.

Elite athletes

The responses of elite athletes to altitude training are of particular interest, because they are the ones who seek small but worthwhile changes in performance. In these studies elite athletes were considered those who competed at international level or have won at national championships. Uncontrolled studies with elite athletes show a variety of results in terms of VO_2max. Saltin (1967) observed a reduction in performance in nine runners with altitude exposure initially, but upon acclimatisation to the hypoxic environment VO_2max increased by 1-2%. Daniels and Oldridge (1970) studied the responses of six champion runners who trained at an altitude of 2300 m over a 10-week period. The athletes used the intermittent altitude training method in which they alternated training at sea level with altitude. VO_2max improved by 5% and the athletes ran 14 personal-best times in sea level competitions. Dill and Adams (1971) observed

similar results in six well-trained middle and long distance champions who spent 17 days at altitude at 3090 m. VO_2max increased in these athletes by 4.2%. However, Ingjer & Myhre (1990), who studied the responses of seven elite cross-country skiers who trained for 3 weeks at an altitude of 1900 m, observed no changes in VO_2max and Hiller et al (2000) observed significant changes in 12 out of the 16 elite triathletes who spent 30 days at 2100 m living high and training low.

The above studies were uncontrolled and made it difficult to determine whether the training effects observed in most cases were solely due to altitude. Elite athletes are highly conditioned and arguably a control group is unnecessary because their performances are highly reliable. However, as Hahn (1991) commented in his review, elite athletes do not train at a constant level year-round therefore it is possible that a training effect could occur. In an effort to avoid the possibility of a training effect, Stray-Gundersen, Chapman and Levine (2001) investigated the responses of 22 elite runners who lived at 2500 m and trained at 1250 m shortly after the US National and Track championships. The authors observed significant increases in all parameters tested; EPO, haemoglobin mass, haematocrit concentration, and VO_2max and 3000 m-time performances.

The results of controlled studies with elite athletes are as varied as in the uncontrolled studies. Adams et al. (1975) investigated the responses of 12 elite cyclists in a crossover study. They divided the cyclists into two groups. One group trained at an altitude of 2300 m for three weeks while the other group trained at sea level. No significant changes were observed in VO_2max or time trial time and it was concluded that altitude training did not enhance performance at sea level. Bailey, Davies, Romer, Castell, Newsholme, and Gandy (1998) studied the responses of elite distance runners who trained for four weeks at 1500-2000 m. Overall there was a decrease in oxygen uptake by approximately 0.4% as compared with pre-altitude. Jensen, Nielsen, Fiskestrand, Lund, Christensen, and Secher (1983) observed a decrease in VO_2max by 0.7% in elite rowers who trained at 1800 m for 21 days. Telford et al. (1996) observed an increase in VO_2max by 3.0% in elite runners who trained at 1800 m for 28 days. There is not enough evidence to show whether elite athletes benefit from altitude training. Even though many authors have recorded VO_2 max and primarily saw a decrease or no change, it would be inappropriate to eliminate an effect on performance.

Despite an effort to determine the effects of altitude exposure on sea level performance in elite athletes, the results remain unclear. Some of the uncontrolled studies showed a significant increase in performance followed by several personal best times, whereas some controlled studies showed a decrease in performance. Clearly, more studies need to focus on the effects of altitude training and sea level performance on the elite athletic population.

THE EFFECTS OF NATURAL ALTITUDE EXPOSURE ON SPRINT PERFOMANCE

Altitude exposure method

Very few studies have investigated the effects of training at altitude and sprint performance at sea level (Martino, Myers, & Bishop, 1995; Mizuno et al., 1990; A. Nummela, Jouste, & Rusko, 1996). In most of the studies the altitude method of choice was living and training at altitude.

Living and training at altitude

Karvonen, Peltola, and Saarela (1986) investigated the anaerobic capacity in sprinters in a controlled study employing 3 sprinters at an altitude of 1850 m for 21 days while 6 sprinters trained at sea level. The authors showed an increase in speed production and explosive strength in performances requiring less than seven seconds but no alterations in anaerobic capacity. Mizuno et al. (1990) showed an improvement in exercise time to exhaustion of 17% after altitude training, accompanied by to a 6% increase in buffering capacity. Martino, Myers, and Bishop (1995) observed significant improvements in 100 m sprint swim and upper body Wingate peak power in swimmers who trained at altitude for 21 days at 2800 m above sea level.

Living at altitude and training at sea level

In a study investigating the effects of sprint performance at sea level using the “live high-train low” method, Nummela and Rusko (2000) have observed 0.8% improvements in 400 m performance compared with sea level training in athletes residing at moderate altitude and training low for 10 days.

THE EFFECT OF SIMULATED ALTITUTE EXPOSURE ON ENDRUANCE PERFORMANCE

Athletes without access to natural-altitude training facilities may choose to use simulated altitude in an attempt to reproduce the benefits of altitude acclimatisation experienced with natural altitude exposure. Modalities utilised to simulate altitude are houses, apartments or tents flushed with nitrogen-enriched air, hypobaric chambers, and hypoxic inhalers. Hypoxia refers to the decrease in oxygen concentration, while hypobaria refers to the decrease in barometric pressure.

In this section, studies conducted with simulated altitude will be outlined in terms of device used, method, level, time course of exposure, duration of the altitude effect and subject characteristics. Studies on effects of altitude on sea level performance simulated by different devices are summarised in Table 2.4.

Table 2.4. "Live high-train low" studies and the effect of simulated altitude exposure on sea level performance. Studies are sorted by the magnitude of the effect.

Design	Gender	Age (M±SD) (y)	Duration (hr,d)	Altitude level (m)	Altitude mode	Time Post-altitude (d)	Performance test	Outcome (%)	Reference
Uncontrolled Studies									
5 cyclists	M	?	18 , 11	3000	NH	5	Cycling test	~+3.5	(Mattila & Rusko, 1996)
10 elite athletes	M	?	1, 20	5800-6400	HI	?	Endurance performance	+3.0	(Hellemans, 1999)
17 high altitude expedit.	M & F	28±5	3-5, 9	4000-5500	HC	?	VO_2max	1.3	(F. A. Rodriguez et al., 1999)
20 athletes	M & F	?	1.25, 21	6400	HI	?	VO_2max	NS	(Frey et al., 2000)
6 endurance athletes	M & F	?	12, 10	2000	NH	?	VO_2max	NS	(Piehl Aulin et al., 1998)
10 volunteers	M	19-25 (range)	1, 24	13.5% O_2	HI	?	VO_2max	-0.15	(Melissa, MacDougall, Tarnopolsky, Cipriano, & Green, 1997)
6 elite skiers	F	23±3	14, 11 and 14, 13	2500, and 2200-2800	NH	2-4 / 8-10	-	-	(H K Rusko, Leppavuori, Makela, & Leppaluoto, 1995)
Controlled studies									
16 elite triathletes + 10 athletes	M	21-39 (range)	2, 10	2500	HC	9	VO_2max	+7.0	(Meeuwsen et al., 2001)
12 triathletes	M	29, 30	1.75, 10	2,500/sea level	HC	2/9	Wingate Wingate VO_2max	mean+4.1 peak+3.8 NS	(Hendriksen & Meeuwsen, 2003)
6 + 7 triathletes	M	25±5	8–10, 23	3000	NH	2	VO_2max	-7%	(C. J. Gore et al., 2001)
7 + 6 runners	?	?	16–18, 20–28	2500	NH	1 / 15	-	NS	(Laitinen et al., 1995)
19 cyclists	M & F	28±6	8-10, 5/10/15	2650	NH	1.5	VO_2max MMPO MAOD	? +3.7 +9.6	(A D Roberts et al., 2003)
12 + 10 cross country skiers	M & F	24±4	12–16, 25	2500	NH	1 / 7	VO_2max	+3.0	(H. K. Rusko et al., 1999)
8 + 8 swimmers	M & F	28.9±? 28.8±?	~0.3, 30,	15.3% O_2	HI	3-4	VO_2max 100m swim 400m swim economy	-0.3 -0.08 +0.4	(M. J. Truijens, Toussaint, Dow, & Levine, 2003)

M, male; F, female; HI, hypoxic inhaler; NH, nitrogen house; HC, hypobaric chamber; VO_2max, maximum oxygen consumption; NM, not measured; NS, not significant; MMPO, mean maximal power output; MAOD, maximal accumulated oxygen deficit; ?, data not provided.

Ways to simulate altitude

Nitrogen houses

A number of Finish sport scientists (H K Rusko et al., 1995) pioneered the concept of using nitrogen to simulate altitude by diluting the oxygen content of normal air. Although their preliminary studies did not include performance testing, they showed haematological changes similar to those with natural altitude exposure. In their preliminary study, six female cross-country skiers lived in a nitrogen house, simulating altitude at 2500 m for 14 hours per day. The athletes lived in the house for 11 days but trained at sea level. There was a significant increase in EPO (31%) and reticulocytes (immature red blood cells) (50%) suggesting that simulated altitude may provide an alternative to natural altitude exposure. The authors did not include a control group or performance tests.

But Laitinen et al. (1995) showed in a controlled study that moderate altitude simulated with a nitrogen house is effective in changing haematological parameters. In their study seven athletes lived in the house for 16-18 hours a day for 20-28 days and trained at sea level. They did not conduct performance tests, but they measured erythropoietin (EPO), diphosphoglycerate (DPG) and red blood cell mass. The authors observed an erythropoietic response during residence in the altitude house, using the “live high-train low” approach, similar to that at natural altitude. They concluded that simulated altitude using the altitude house is a worthy alternative to natural altitude exposure.

Similarly in another controlled study, Rusko, Tikkanen, Hamalainen, Kalliokoski, and Puranen (1999) investigated the performance of 12 cross-country skiers and triathletes who lived in normobaric hypoxia simulating an altitude of 2500 m for 12-16 hours per day for 25 days and trained at sea level. The control group lived and trained at sea level. In this study VO_2max was measured before and after altitude exposure. The post-altitude tests were conducted one day and one week following the exposure. Maximal oxygen did not increase significantly a day following exposure, but a week later it increased significantly by 3%. In addition, Mattila and Rusko (1996) investigated the responses of five competitive cyclists who lived in an altitude house at an altitude of 3000 m for 18 hours daily for 11 days, and trained at sea level twice daily. Cycling time

trials were conducted five days before and five days after exposure. Performance improved by 3.5% post exposure.

Another group in Sweden conducted similar studies. Piehl-Aulin, Svedenhag, Wide Berglund and Saltin (1998) studied the effects of normobaric hypoxia on erythropoiesis and physical performance in six subjects who lived at an altitude of 2000 m for 12 hours daily for 10 days. The subjects completed sea level training. A group of five subjects, who served as a control, lived and trained at sea level. The authors found no significant changes in VO_2max and they concluded that ten days of living high in normobaric hypoxia and training low at sea level does not enhance VO_2max. The same authors conducted a similar study at a higher altitude with nine subjects living in normobaric hypoxia at an altitude of 2700 m and training at sea level while a control group of five subjects lived and trained at sea level. They observed no significant differences in VO_2max compared to pre-altitude values.

A group of researchers from Australia conducted comparable studies. Roberts et al. (2000) studied 24 well-trained endurance athletes who slept 8-10 hours per night for 12 nights in normobaric hypoxia that simulated an altitude of 2650-3000 m. Performance tests indicated no increases in the VO_2max, but they observed increases in anaerobic capacity.

Gore et al. (1999) studied the effects of normobaric hypoxia on sub-VO_2max and power in six male triathletes who lived in normobaric hypoxia of 3000 m for 23 days. The control group of seven male triathletes lived and trained at sea level. They conducted tests two days before exposure, 12 days into exposure and two days after exposure. There were no significant changes in any of the parameters in the control group. Sub-VO_2max in the altitude group was lower during mid and post-tests. The ventilatory equivalent (VE/VO_2) was significantly elevated during sub-maximal exercise workloads. The authors concluded that the male triathletes achieved greater hyperpnoea and improved efficiency during sub-maximal exercise following exposure to normobaric hypoxia.

In summary, the Finnish group demonstrated that simulated altitude exposure using nitrogen houses improved sea level performance. They observed significant changes in haematological parameters and performance tests. Residence in a nitrogen house (2500–

3000 m) for 12-18 hours per day for 11-28 days using the “live high-train low” method improved sea level performance. However, the Swedish group showed that 10 days of residence in normobaric hypoxia had no effect on VO_2max. Similarly, studies conducted in Australia showed no significant changes to VO_2max but there were some changes in sub- VO_2max during steady-state sub-maximal exercise. It is clear that further research is necessary to elucidate the effect of nitrogen houses or apartments on performance at sea level.

Altitude tents

There is limited research on the effects of altitude tents on physiological responses and sea level performance (Hahn et al., 2001). Recently three scientific studies (Degia, Emegbo, Stanley, Pedlar, & Whyte, 2003; Emegbo, Pedlar, Stanley, & Whyte, 2003; Stanley, Emegbo, Pedlar, & Whyte, 2003) reported the effects of altitude tents on sleep quality (Kinsman et al., 2002) and cognitive function. Stanley, Emegbo, Pedlar, and Whyte (2003) evaluated the effect of altitude tents on respiratory parameters during sleep in a double blind randomised design in eight recreational athletes who slept in tents at 2500 m for three consecutive nights. Respiratory changes during sleep in the altitude tents were similar to those in normoxia. The authors concluded that the rise of carbon dioxide (CO_2) levels in the tents promoted arterial CO_2 retention promoting the respiratory changes seen under normoxic conditions. In an identical design Emegbo, Pedlar, Stanley, and Whyte (Emegbo et al., 2003) evaluated sleep quality based on several observations. There was no statistical difference between altitude and normoxic conditions. The authors concluded that sleeping in an altitude tent does not disturb sleep. Despite the fact that Kinsman et al.(2002) investigate the effects of sleep using a hypoxic room, the results were contradictory to that of Emegbo et al. (2003). They concluded that overnight sleep in a hypoxic environment at 2650 m is likely to have acute effects on breathing during sleep and that the magnitude of these effects vary among individuals. In another identical design to the prior two studies, Degia, Emegbo, Stanley, Pedlar and Whyte (2003) evaluated the acute effects of altitude tent use on cognitive and psychomotor performance. The authors found no change in performance between the two conditions. It is evident from the literature that few studies investigated the effects of hypoxic tents on cognitive and psychomotor performance and no studies have investigated their effect on sea level athletic performance.

Hypobaric chambers

Few studies are available on the effectiveness of hypobaric chambers on performance at sea level. Some authors (Eckardt et al., 1989) investigated haematological parameters but not performance using a hypobaric chamber. Other authors who measured performance following altitude exposure via the hypobaric chamber showed equivocal results (Meeuwsen et al., 2001; F. A. Rodriguez et al., 1999; Terrados et al., 1988; Vallier, Chateau, & Guezennec, 1996).

Rodriguez et al. (1999) investigated the effects of short intermittent exposure to moderate altitude on aerobic performance and erythropoietic response using a hypobaric chamber. They studied 17 members of high altitude expeditions exposed to three to five hours a day over nine days at an altitude of 4000-5500 m. The authors separated the participants into two groups. They exposed one group to passive hypoxia while the other group was exposed to passive hypoxia combined with low-intensity exercise on a cycle ergometer. The authors showed increases in exercise time and a reduction in blood lactate concentration at sub-maximal exercise intensities in both groups, indicating a possible improvement in endurance. In addition, haemoglobin concentration and reticulocytes increased. There were no differences between the two groups in any of the parameters studied. They concluded that short-term intermittent exposure to moderate altitude in a hypobaric chamber stimulated erythropoiesis and improved endurance. The study was uncontrolled and a training effect independent of altitude exposure may have occurred.

Even though Terrados, Melichna, Sylven, Jansson, and Kaijser (1988) used a control group in their study, the results were still unclear. They investigated the responses of eight male elite cyclists who trained for two to three hours per day for 21 to 28 days either in a hypobaric chamber at a simulated altitude of 2300 m (four cyclists) or in a normobaric laboratory (four cyclists). The authors observed a 33% improvement in total work capacity, which was expressed as the total amount of work performed during an incremental test to exhaustion, at both sea level and altitude in the altitude group. The sea level group showed a 22% increase at sea level and 14% at altitude.

Meeuwsen, Hendriksen, and Holewij (2001) investigated the responses to hypobaric hypoxia in 16 elite triathletes. One group exercised in a hypobaric chamber at an altitude of 2500 m while the other group trained in normobaric hypoxia over 10 days. The authors observed a significant increase of 7% in mean VO_2max and a 7.4% increase in mean maximal power output per kilogram body weight in the hypobaric group. No significant changes were observed in the sea-level group. Haematocrit and haemoglobin concentration did not change after hypobaric training.

In a more recent study (Hendriksen & Meeuwsen, 2003) the authors used a train high-live low approach to expose 12 male triathletes to hypobaric hypoxia. The athletes trained at 2500 m on a cycle ergometer over nine days and resided at sea level. The authors observed significant changes in anaerobic power without any significant changes in VO_2max. They concluded that low-intensity training at altitude significantly improves mean anaerobic power.

It is unclear whether exercising or living in a hypobaric chamber would improve endurance performance. Whereas Rodriguez et al. (1999) indicated improvements in endurance performance in conjunction with increases in haemoglobin concentration and reticulocytes, Meeuwsen et al. (2001) and Hendriksen and Meeuwsen (2003) observed improvements in anaerobic parameters without any changes in haemoglobin concentration and haematocrit or VO_2max. On the basis of the recent findings it seems that hypobaric chambers may have an effect on aerobic and anaerobic performance.

Hypoxic inhalers

Another way to simulate altitude is through a technique developed in the former Soviet Union termed intermittent hypoxic training (IHT), a technique by which athletes receive exposure to severe hypoxia (9-12 % oxygen) at rest for 5-7 minutes and alternate with normal air of similar duration. Brief exposure to hypoxia stimulates erythropoietin release (Eckardt et al., 1989) which may increase the oxygen-carrying capacity of blood thus improving endurance performance. Unfortunately results from studies conducted in the former Soviet Union are difficult to access (Serebrovskaya, 2002) and very few studies published in English journals have assessed the effectiveness of this technique on athletic performance.

Hellemans (1999) exposed 10 elite endurance runners to intermittent hypoxic exposure for 20 days breathing a low oxygen concentration air (9-15%) through a mask for five minutes and alternating with normal air for five minutes. The sessions lasted for an hour, twice a day. The athletes trained at sea level as usual. The author saw significant changes in endurance performance, reticulocyte count, haemoglobin concentration and haematocrit. There was no control group in this study.

Contrary to these results, Frey, Zenhausern, Colombani, and Fehr (2000), using moderately trained athletes exposed for 21 days for 75 min daily, saw no changes in haemoglobin concentration, haematocrit and reticulocyte count or exercise performance. There is a great need for more well controlled studies to determine the most appropriate protocol for the use of hypoxic inhalers.

More recently, Hamlin and Hellemans (2004) observed very likely increases in haematocrit and mean cell haemoglobin in a study with 22 multi-sport athletes who completed intermittent hypoxic training for a total of 90 min per day for three weeks, however performance data were not reported. Conversely, Julian et al. (2004), in a balanced, randomised, double blind design reported no effect on VO_2max or 3-km time trial time or any hematological parameters (serum EPO, transferin receptor, reticulocytes) after 28 days of intermittent hypoxic training in national-class distance runners.

Altitude exposure methods

Living at high altitude and training at low altitude

Since “live high-train low” method seems to have a favourable outcome with natural altitude studies, most authors have used this approach in conjunction with simulated altitude exposure to study sea level performance changes (see Table 2.4). Some studies have shown positive effects (see Table 2.4), but there are insufficient confirmatory studies due to inconsistency in protocols and variables measured.

Living at low altitude and training at high altitude

Some authors have investigated and/or compared the effects of moderate exercise in a simulated altitude environment in conjunction with training or residing at sea level. Rodriguez and colleagues (1999) studied the effect of hypobaric hypoxia in subjects either resting or exercising at low intensities for three to five hours per day over nine days. Passive and active exposure showed no significant differences. Similarly, Terrados (1988) found no differences in cyclists either in the altitude or control group who trained for 60-90 min for three to four weeks in a hypobaric chamber or at sea level. Also, Engfred and colleagues (1994) showed that training in a hypobaric chamber does not cause hormonal changes more than those with training at sea level. Casas et al. (2000) showed that exposure to hypobaric hypoxia in combination with low-intensity exercise for three to five hours per day over 17 days at 4000-5000 m was sufficient to improve aerobic capacity and induce altitude acclimatisation. In contrast, Hendriksen and Meeuwsen (2003) showed positive changes in anaerobic, and to a lesser extent aerobic performance, with training two hours per day for 10 days in a hypobaric chamber at 2500 m. Overall there is enough evidence to suggest that benefits of hypoxia can occur in a hypobaric chamber at rest or during exercise. It is unclear however, whether the changes observed benefit aerobic or anaerobic performance.

Altitude level

Altitude exposure at low altitude

According to the literature thus far, no studies investigating simulated altitude exposure have been conducted at low altitude (below 2000 m). Evidence from earlier natural altitude studies (as discussed in previous sections) conducted at low altitudes showed little or no changes in performance.

Altitude exposure at moderate altitude

Most simulated altitude studies have been conducted at moderate altitude (2000-4000 m), but the outcomes of these studies are contradictory. Findings from studies on hypoxic houses or apartments ranged from no effect (Piehl Aulin et al., 1998) to improvement in aerobic (H. K. Rusko et al., 1999) or anaerobic performance (A D

Roberts et al., 2003) to impairment (C. J. Gore et al., 2001) in VO_2max. Studies conducted in a hypobaric chamber showed either an improvement in aerobic (Hendriksen & Meeuwsen, 2003) or anaerobic performance (Meeuwsen et al., 2001) or no change at all (Levine et al., 1990).

Altitude exposure at high altitude

Studies investigating the effect of hypoxic inhalers and hypobaric chambers have generally exposed athletes to high altitudes (above 4000 m). In these studies, the results have also been conflicting (Casas et al., 2000; Frey et al., 2000; Hellemans, 1999; F. A. Rodriguez et al., 1999).

It has been shown recently that a difference exists between normobaric hypoxia and hypobaric hypoxia. Savourey, Launay, Besnard, Guinet, and Travers (2003) showed that when compared to normobaric hypoxia, hypobaric hypoxia leads to greater hypoxemia, hypocapnia, blood alkalosis and lower O_2 arterial saturation. It is therefore possible that the normobaric hypoxia requires a higher simulated altitude than hypobaric hypoxia to elicit the same physiological changes and performance enhancement.

Altitude duration

Only one study by Roberts, Clark, Townsend, Anderson, Gore, and Hahn (2003) investigated the effect of simulated altitude exposure duration in a systematic way. Athletes spent 8-10 hours per night for 5, 10 and 15 days of “live high-train low” in an altitude house. They observed changes in anaerobic rather than aerobic parameters of performance but there were no differences among the three durations of exposure. They concluded that well-trained athletes can use short periods of “live high-train low” to prepare for events lasting ~ four minutes. Their study provided evidence that improvements in performance following “live high-train low” exposure may be due to changes in anaerobic capacity. On the other hand, studies with exposures ranging from one to two weeks (Mattila & Rusko, 1996; Piehl Aulin et al., 1998; F. A. Rodriguez et al., 1999) and studies with expoxurres ranging from three to four weeks (Frey et al., 2000; C. J. Gore et al., 1999; H. K. Rusko et al., 1999) show conflicting results.

Time course of the effect

Generally studies have not tracked the time course of the altitude effect. Post-tests were conducted primarily a few days after altitude exposure (see Table 2.4). No studies have tracked the time course of the effect in terms of performance. Laitinen et al. (1995) conducted post-tests at one and 15 days following exposure but unfortunately none of those measures were related to performance.

Subject characteristics

Age

The age of athletes who participated in simulated altitude studies ranged from 20 to 36 years of age. Authors have not investigated systematically the effect of age on altitude exposure. According to fundamental physiological principles, the body loses the ability to perform at optimal levels with increasing age. It is possible that studies with older participants show a smaller effect than those with younger participants.

Gender

Most studies investigating gender differences in response to altitude exposure have determined the effect of altitude exposure on performance at altitude not sea level (Braun et al., 1997; Harms, Burgett, & Fergusson, 2000; Maes, Riboni, Loeppky, Icenogle, & Roach, 1999; Quintana, Robergs, Parker, & Frankel, 1997; Robergs, Quintana, Parker, & Frankel, 1997; D. A. Sandoval et al., 1997; D. A. Sandoval & Matt, 2000). But in one study, Ashenden, Gore, Martin, Dobson, and Hahn (1999) investigated the effect of “live high-train low” method in female cyclists. The experimental group slept in a simulated altitude of 2650 m for 12 nights in a hypoxic room and trained at sea level, while the control group slept and trained at sea level. The lack of any increases in reticulocyte production and hemoglobin mass led the authors to conclude that 12 nights of simulated altitude was not sufficient to stimulate any haematological changes. In other studies investigating the effect of simulated altitude exposure on sea level performance, men and women were included in the sample, but conclusions on the differences in their responses could not be made with confidence because of the small number of women sampled (Levine & Stray-Gundersen, 1997).

Athletic ability

In studies where the effect of simulated altitude exposure was investigated on sea level performance, researchers have recruited primarily sub-elite athletes (see Table 2.4). Changes in VO_2max for non-athletes were either a 1.3% improvement (F. A. Rodriguez et al., 1999)or a 0.15 impairment (Melissa et al., 1997) and for sub-elite changes were non significant. These studies had no control groups. In controlled studies, authors have seen a 0.3 to 7% impairment in VO_2max, (C. J. Gore et al., 2001; M. J. Truijens et al., 2003), non-significant changes (Hendriksen & Meeuwsen, 2003)or improvements in the order of 3.0% in sub-elite athletes (H. K. Rusko et al., 1999) and 7.0% in elite athletes (Meeuwsen et al., 2001).

Angiotensin Converting Enzyme (ACE) genotype

Genes are responsible for about 50% of the variation observed in physical performance and response to physical training (Wolfarth, 2000). Authors have considered a number of genes as candidates for aerobic performance based on the current knowledge of determinants of VO_2max (Wolfarth, 2000). Some of the candidate genes are: alpha-2-adrenoceptor (ADRA2A), beta-2-adrenoceptor (ADRB2), angiotensin converting enzyme (ACE), angiotensin type 1 receptor (AT1) and angiotensin type 2 receptor (AT2).

Angiotensin converting enzyme (ACE) gene has received considerable attention. The gene is associated with the renin–angiotensin system that controls blood pressure, blood volume and cardiac hypertrophy. Two alleles have been identified: an insertion allele (II) (in the presence of the 287 Alu sequence) and a deletion allele (DD) (in the absence of the 287 Alu sequence) (Fatini et al., 2000). The former is associated with positive responses to the cardiovascular system and improved endurance in climbers (Katsuya et al., 1995) while the latter is associated with cardiac malfunctions such as myocardial infraction, cardiac failure and left ventricular hypertrophy (Cambien et al., 1992; Friedl, 1998; Gharavi, Lipkowitz, Diamond, Jhang, & Phillips, 1996; Hagberg, 1999; Iwai, Ohmichi, Nakamura, & Kinoshita, 1994; Marian, Yu, Workman, Greve, & Roberts, 1993). A likely mechanism for the effects of the ACE gene on performance could be

simply its association with a gene in close proximity that is responsible for changes in the cardiovascular system.

Controversy exists regarding the allele responsible for the improved aerobic performances observed in athletes that have the ACE gene. Gayagay et al. (1998) studied the potential significance of the ACE gene on the development of an elite athlete by investigating the presence of these genes in 64 Australian national rowers and 114 healthy normal volunteers. The results showed a significant association between the excess of the ACE I allele (reduction in D allele) and athletes. The authors suggested that the presence of the ACE I allele may provide an advantage to those athletes that acquire it and are involved in endurance events.

Of the three forms of the genotype (I-I, I-D, D-D), successful mountaineers were more likely than non-mountaineers to have the I-I form (Montgomery et al., 1998). In a recent study, Woods (2002) found an association between the I allele excess among elite mountaineers and arterial oxygen saturation at high altitudes. Hence, carriers of the I-I genotype show better physiological adaptation to altitude. The ACE gene modulates the effects of training on performance in some studies (Wood et al., 2004) but not others (Sonna et al., 2001).

Clearly, athletes who acquire a performance gene will respond more positively to training than those who do not. Hence, variations observed in training responses and performances would influence the results in scientific studies. The athletes' genetic make up is a factor that researchers have to consider when conducting intervention studies.

THE EFFECTS OF SIMULATED ALTITUDE EXPOSURE ON SPRINT PERFORMANCE

Altitude exposure methods

The scientific literature regarding the effects of natural altitude exposure on sprint performance and similarly literature on the effects of simulated altitude exposure on sprint performance are unclear.

Living at high altitude and training at sea level

The effect of normobaric hypoxia on sea level sprint performance of 400-m runners was investigated by Nummela and Rusko (2000). In their study, eight runners lived in an altitude house for 10 days and trained at sea level. It was observed that 400-m running performance improved by 0.8%. The results of this study are encouraging and further investigation is warranted.

Living at low altitude and training at high altitude

Truijens, Toussaint, Dow, and Levine et al. (2003) investigated the effectiveness of hypoxic training without acclimatisation in 16 well-trained swimmers during 100-m freestyle. During training in a swimming flume, swimmers in the experimental group breathed hypoxic air (15.3%), while swimmers in the control group breathed normal air (20.9%). The training sessions lasted ~20 min, and the swimmers trained for six days per week for five weeks. It was observed that both groups improved swim sprint performance, and concluded that hypoxic training did not provide any additional improvements.

CONCLUSION

Following several decades of investigation, the effects of natural altitude exposure on sea level performance have been encouraging. The “live high-train low” method appeared to elicit the haematological changes expected with altitude exposure and those changes were associated with improved performances.

Although studies with natural altitude exposure have been encouraging, little is known about the optimal level, duration, and time course of the effect. In addition the effect of age, gender, athletic ability, ACE genotype and sprint training on sea level performance following hypoxic conditioning has not been systematically evaluated yet.

Results from studies dealing with simulated altitude exposure have been controversial. Studies from the Finnish group using nitrogen houses to simulate altitude observed improvements in endurance performance, yet the Swedish and Australian groups observed unclear effects.

Unlike studies in the natural environment, simulated altitude studies generally show no changes in VO_2max following exposure but substantial changes in anaerobic capacity. One reason might be the difference between the two modes of exposure at least for the studies using nitrogen enriched environments, in which athletes are exposed to normobaric hypoxia instead of hypobaric hypoxia. It is possible that the stimulus provided with normobaric hypoxia is not sufficient to elicit the changes seen with hypobaric hypoxia. It is evident that more research that scrutinizes these issues is necessary to clarify whether simulated altitude exposure benefits sea level performance.

Also, the limited number of studies dealing with other devices of simulated altitude has added little evidence of their efficacy. Few authors have studied the efficacy of barometric chambers and altitude tents, and the use of hypoxic inhalers provided no substantial evidence of a positive effect on performance. The need for more systematic research is apparent.

Nevertheless, several physiological changes occur following exposure to hypoxia that may enhance sea level performance. The particular adaptations include improvement in oxygen carrying capacity of blood, increased buffering capacity or improvements in exercise economy. It is not clear however, which of these adaptations contributes to the enhancement in performance. A favoured mechanism for performance enhancement is expansion of red blood cell mass. However, in some studies there appears to be little change in haemoglobin mass, and the focus has been on buffering capacity and more recently on economy of effort as the mechanisms responsible for the improvements in performance following altitude exposure.

CHAPTER 3: LITERATURE REVIEW-MECHANISMS FOR THE EFFECTS OF ALTITUDE EXPOSURE ON SEA LEVEL PERFORMANCE

Improvements in endurance performance following exposure to natural or simulated altitude can be mediated through increases in power output generated aerobically (oxygen dependent) or anaerobically (oxygen independent) (Figure 3.1). At the next level of explanatory mechanisms, changes in aerobic power can be mediated only by changes in VO_2max, anaerobic threshold expressed as a percent of VO_2max, and exercise economy (power output per unit of VO_2) (Jones & Carter, 2000). There is no similar obvious schema for mechanisms mediating changes in anaerobic power; authors of studies of hypoxic exposure have focused on buffering capacity, because the anaerobic pathway generates hydrogen ions which are thought to contribute to fatigue in brief high intensity exercise. But there could be other mechanisms to explain changes in anaerobic power. Nevertheless it has been shown that at least in the muscle, changes occur at the molecular level after hypoxic exposure and that the hypoxia inducible factor-1 (HIF-1) is specifically involved in the regulation of muscle adaptation (Vogt et al., 2001). In this section, the potential mechanisms responsible for the changes in performance observed with natural or simulated altitude exposure will be discussed.

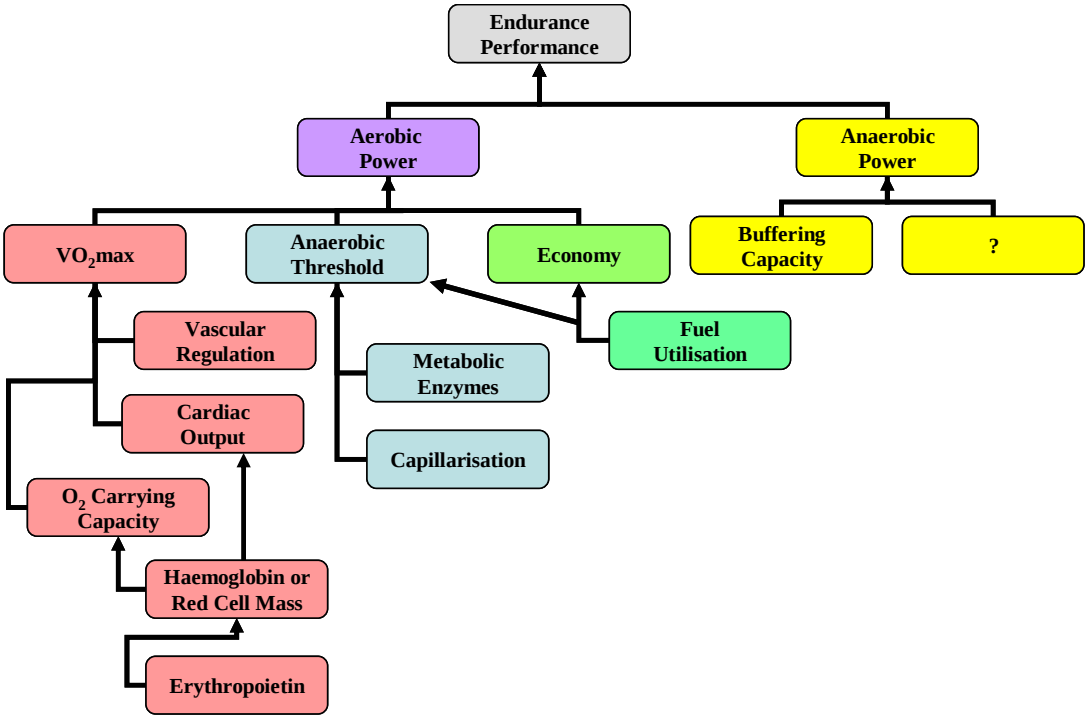

Figure 3.1. Mechanisms that may contribute to improvements in endurance performance following exposure to natural or simulated altitude.

For improvements in VO_2max, authors have identified the oxygen-carrying capacity mechanism. However, other mechanisms may contribute to changes in VO_2max. These potential mechanisms include: improvements in cardiac output and changes in vascular regulation, which would improve VO_2max.

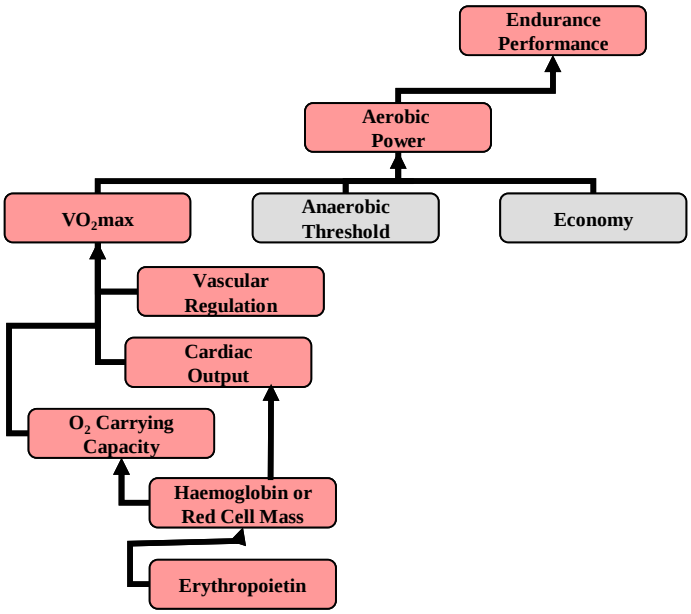

Figure 3.2. Improving VO_2max via changes in oxygen-carrying capacity, cardiac output, and vascular regulation.

Oxygen carrying capacity

Haemoglobin mass increases in response to hypoxia if arterial partial pressure of oxygen is below 65 mmHg, which corresponds to 2200-2500 m (Weil et al., 1968) and there is no iron deficiency in the individuals exposed (J. Stray-Gundersen et al., 1992). This increase is thought to be mediated through erythropoietin (EPO), a hormone secreted by the kidneys, which stimulates red blood cell production.

During hypoxia, chemical agents bind to oxygen sensor cells located by the glomerular capillaries (Bauer & Kurtz, 1989). These cells are responsible for the production of erythropoietin (Berglund, 1992). Erythropoietin release signals the production of red blood cells, and it takes 48-72 hours for reticulocytes (immature red blood cells) to

form in the bone marrow (Berglund, 1992). The reticulocytes are then released to the circulation two days following their production (Berglund, 1992).

Erythropoietin rises significantly after an 114 and 84 min in moderate hypoxia (Eckardt et al., 1989). Mean values increased by 29% at 3000 m and 40% at 4000 m from baseline. Knaupp, Khilnani, Sherwood, Scharf, and Steinberg (1992) showed that continuous exposure to 10.5% oxygenated air for 5 min and 60 min was insufficient to detect a significant rise in EPO secretion. However, after 120 min of continuous exposure and after 240 min of intermittent exposure there was a significant increase in EPO production. They concluded that the duration of O_2 reduction might be more important in stimulating EPO secretion than the magnitude of O_2 reduction.

Maximal levels of EPO during altitude exposure

It takes about 15-72 hours to observe maximal production in erythropoietin release depending upon the level of hypoxic exposure (P. H. Abbrecht & J. K. Littell, 1972; Eckardt et al., 1989; Faura et al., 1969; Hinojosa et al., 2000). Mattila et al. (1996) investigated the EPO responses using the living high and training low method on sea level performance in cyclists. They saw a significant rise in EPO on day five at moderate altitude. Previous studies have shown serum EPO to have remained elevated in the blood for 10 days during high altitude exposure and returning to pre-hypoxic values following that time (P. H. Abbrecht & J. K. Littell, 1972). Studies on cross-country skiers showed elevated serum EPO for two weeks while under a moderate hypoxic stimulus (Laitinen et al., 1995; H K Rusko et al., 1995). Ge et al. (2002) investigated the dose-response relationship between altitude and erythropoietin (EPO) in distance runners exposed to simulated altitudes of 1671 m, 2086 m, 2455 m and 2806 m in a hypobaric chamber. Erythropoietin was measured before, at 6h, and 24h after exposure. The authors observed an increase of EPO at all altitudes after six hours and at 2455 m and 2806 m an increase after 24 hours. There was no further increase by 24h at 1671 m and 2086 m. The level and duration of EPO production seems to be dependent upon the level after the hypoxic stimulus. The more stressful the stimulus the longer EPO takes to reach maximal levels and it seems to remain elevated for a shorter period than at moderate altitude. Milledge and Cotes (1985), however, suggested that the duration for which serum EPO is elevated at high altitude is not dissimilar to that at moderate altitude.

It has been shown that there is greater stimulation of EPO secretion with exercise than with altitude alone (Mairbäurl et al., 1986). Exercise in association with a hypoxic stimulus further accentuates arterial hypoxemia, which may provide a greater stimulus for EPO secretion, and hence increases in haemoglobin mass (Berglund, 1992). Nevertheless, several studies (Laitinen et al., 1995; Mattila & Rusko, 1996; H. K. Rusko et al., 1999) showed an increased EPO secretion with altitude exposure alone rather than in combination with exercise as has been previously indicated. Others (F. A. Rodriguez et al., 1999; Schmidt et al., 1991) showed that exercise in hypoxia has the same effect on erythropoietin production as exposure to hypoxia in the absence of exercise. Both methods of exposure (in the presence or absence of exercise) result in an increase in serum erythropoietin. The only difference is that erythropoietin in the resting group decreases shortly after, while in the exercise group remains elevated over several days (Mairbaurl, 1994).

Time course of EPO

Once erythropoietin production has reached its peak under hypoxic conditions, it decreases back to normal. Little information is known on the fate of EPO (Jelkmann, 2002). The main sites of EPO degradation have not been identified yet but it is frequently suggested that EPO is cleared by the liver and some consider the kidneys to play a role in the removal of circulating EPO (Jelkmann, 2002). Samaja (1997) has suggested that the decrease is probably due to the adequate production of red blood cells to accommodate the decrease in the arterial oxygen tension. Others (Berglund, 1992; Eaton, Brewer, & Grover, 1969; Lenfant, Torrance, & Reynafarje, 1971) suggested that the decrease in erythropoietin secretion after 24 hours was due to the right shift of the oxygen-Hb dissociation curve, which is attributed to the increase of 2,3-biphosphoglycerate. A shift to the right of the oxygen-haemoglobin dissociation curve indicates a low haemoglobin-oxygen affinity, which favours the O_2 release from haemoglobin to the tissues. The substance 2,3-biphosphoglycerate is a metabolite of red blood cell glycolysis, which couples its production to the overall glycolytic activity.

Although EPO levels decrease during hypoxic exposure, red blood cell production continues, evident by elevated reticulocyte presence (Mairbaurl, 1994). The maintenance of red blood cell production at low EPO levels during prolonged hypoxia demonstrates that erythropoiesis is influenced or controlled by other mechanisms to

which EPO has some contribution. It has been suggested that perhaps less EPO is required to maintain erythropoiesis after acclimatisation than during initial hypoxia (P. H. Abbrecht & J. K. Littell, 1972).

Haemoglobin mass and aerobic power

Studies in elite athletes exposed to hypoxia have shown that new red blood cells (reticulocytes) begin to appear after five days (Mattila & Rusko, 1996), and 8 to 10 days of training at a moderate altitude (Berglund, 1992). Reticulocytosis (formation of immature red blood cells) continued throughout the three weeks of altitude training, and a total increase in haemoglobin concentration of 0.5 to 1% was observed (Hartmann, Burrichter, Glaser, Mader, & Oette, 1990). Levine et al (1996) showed that four weeks of training/residing at an altitude of 2500 m elicited a 6.3-11% increase in red blood cell mass, Rusko et al. (1999) observed a 5% increase, Stray-Gundersen, Hochstein, and Levine (1993) a 9% increase and Levine and Stray-Gundersen (1992a) a 10% increase. These increases were retained after a return to sea level. All of the above studies except Rusko et al. (1999) (information not available) have considered changes in plasma volume.

Buick, Gledhill, Froese, Spriet, and Meyers (1980) showed that an increase in haemoglobin mass enhanced aerobic capacity by inducing erythrocythemia in 11 highly trained runners. The runners were tested before and after autologous reinfusion and it was observed that there was a distinct increase in VO_2max following induced erythrocythemia. Ekblom and Berglund (1991) and Berglund and Ekblom (1991) showed a change of 11% in haemoglobin concentration that correlated to a VO_2max of approximately 8%. In mountaineers, after approximately 29 days at an altitude of 4900 - 7600 m, an increase in haemoglobin mass by 14% was observed following the expedition (Böning et al., 1997).

Other studies have shown no significant increase in haemoglobin mass with altitude exposure (W. C. Adams et al., 1975; Bailey et al., 1998; C. Gore et al., 1998; C.J. Gore, Hahn, Burge, & Telford, 1997). Possible reasons for the apparent lack of increase include: insufficient hypoxic stimulus (below 2000 m); insufficient time allowed under the hypoxic stimulus, (less than 14-18 hours at 2500 m, as suggested in Laitinen et al. (1995); short time allowed for acclimatisation effects to be manifested; involvement of

highly trained athletes that have reached their physiological limit and the use of small experimental samples or simply a dilution effect due to an increase in plasma volume.

The increase in haemoglobin mass due to the hypoxia-induced EPO secretion improves VO_2max via increases in the oxygen-carrying capacity of blood and cardiac output. Even though both mechanisms improve VO_2max researchers have focused on the oxygen-carrying capacity mechanism.

In studies of intermittent hypoxia some authors have reported improvements in VO_2max of 1-5% with related increases in blood parameters (W. D. B. Hiller et al., 2000; Levine et al., 1996; Levine & Stray-Gundersen, 1997; Levine et al., 1991; H. K. Rusko et al., 1999; J. Stray-Gundersen, Chapman, R. F. and Levine, B. D., 2001). It is possible however, that hypoxic exposure induces increases in endurance performance mediated not by changes in oxygen-carrying capacity of the blood but by changes in cardiac output or vascular regulation.

Cardiac output

Liu et al (1998) investigated the effects of "live high-train low" on cardiac function in 21 well-trained triathletes. The experimental group lived at 1980 m for 12 hours per day for two weeks and trained at sea level, while the control group trained at sea level. Cardiac function was assessed with Doppler echocardiography. They suggested that "living high-training low" increased cardiac output by improving left ventricular contractility. Svedenhag, Piehl-Aulin, Skog and Saltin (1997) showed increases in left ventricular muscle mass after long-term altitude training. The authors investigated the effect of living and training at altitude (1900 m) for a month in seven elite cross-country skiers on several physiological measures including VO_2 max and cardiac function. Cardiac function was assessed before and after altitude at sea-level. Left ventricular posterior wall thickness increased by 2.7% 35 days post-altitude and VO_2max improved by 2.8% but the results were reported as non-significant. Similarly, Weng, Chen, Wang and Zhuang (1994) observed increased wall thickness with altitude training in swimmers. The reason for the increase in left ventricular muscle mass is unknown but it is conceivable that hypoxia may have a stimulating effect on the myocardium, perhaps via increased cardiac sympathetic activation (E. E. Wolfel, Selland, Mazzeo, & Reeves,

1994), which would facilitate greater cardiac output. Whether the reported changes affect sea level performance remains to be investigated.

Vascular regulation

There have been several studies showing improvements in VO_2max without concomitant changes in blood parameters: Meeuwsen et al. (2001) and Hendriksen and Meeuwsen (2003) reported 7% and 1.9% enhancements in VO_2max respectively, while others saw non-significant increases of 1.3-2.4% (F. A. Rodriguez et al., 2004; Vallier et al., 1996). Some researchers have also reported little to no changes in both VO_2max and blood parameters (Frey et al., 2000; Piehl Aulin et al., 1998; M. J. Truijens et al., 2003). The inconsistencies between these studies could be due to error of measurement in VO_2max (~2-3%) or the method used to measure blood parameters (3-10%), especially when changes are small. A plausible mechanism that would explain the increase in VO_2max independent of an increase in haematological parameters in response to hypoxia could be the activation of the hypoxia-inducible factor (HIF-1) that plays a critical role in the responses of the cardiovascular system (Semenza, 2004). One of these responses could be a change in vascular regulation that would result in greater delivery of blood and therefore oxygen to active muscle.

ANAEROBIC THRESHOLD

The anaerobic threshold represents an intensity of exercise which results in fatigue after 30-60 min (Davis, 1985). It is a threshold for a substantial contribution from anaerobic mechanisms as evidenced by the increase of lactate production by the muscles (Wasserman, 1986). For this reason the term lactate threshold is often used instead of anaerobic threshold. Changes in the enzymes of metabolism (aerobic and anaerobic) could affect the anaerobic threshold. Changes in capillarisation could also change the anaerobic threshold by altering the pattern of uniformity of oxygen distribution to the muscle fibres (Hoppeler & Desplanches, 1992).

Metabolic enzymes

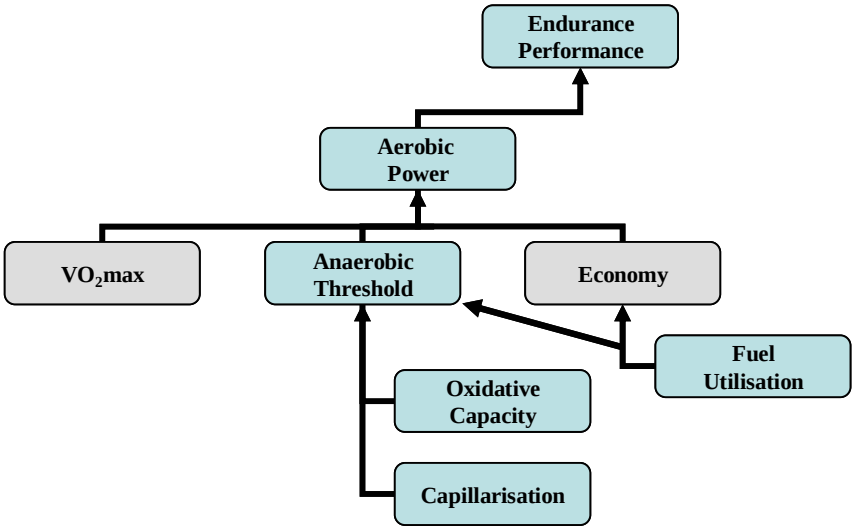

Figure 3.3. Improving anaerobic threshold via changes in oxidative capacity, capillarisation, and fuel utilisation.

Terrados, Jansson, Sylven, and Kaijser (1990) observed an increase in citrate synthase (Krebs cycle enzyme) activity in ten participants who trained one leg under normoxic and the other leg under hypobaric conditions. An increase in the activity of mitochondrial enzymes (along with increased levels of myoglobin) led to faster acceleration of cellular respiration. This acceleration counteracted glycolysis and lactate production. Similarly, Melissa, MacDougall, Tarnopolsky, Cipriano, and Green (1997) saw a greater increase in citrate synthase activity under similar simulated conditions. It was shown that hypoxia stimulated mitochondrial enzyme synthesis.

Jansson, Terrados, Norman, and Kaijser (1992) observed an increase in the oxidative capacity in hypoxic-trained muscles. They attributed this effect to the changes of M and H sub-units of the lactate dehydrogenase enzyme. They suggested that under hypobaric conditions the M sub-unit, favouring the conversion of pyruvate to lactate decreased, therefore allowing the H sub-unit to dominate. The result was less lactate production, which allowed less accumulation of lactate and glycolytic intermediates.

Terrados et al. (1988) noticed a decrease in glycolytic enzymes in eight elite junior cyclists who trained in a hypobaric chamber at 2300 m for 3–4 weeks with no changes in citrate synthase activity. They attributed the unaltered activity of citrate synthase to the already high oxidative capacity of the cyclists. After performance testing the altitude group showed a greater working capacity (expressed as the work performed during an incremental cycle test to exhaustion) following hypobaric exposure compared with the sea level group.

Overall, there is evidence to support that in the presence of hypoxia metabolic enzymes change. Whether there is a decrease in glycolytic enzyme activity with no change in oxidative enzymes, or an increase in oxidative enzyme activity per se, the changes will potentially improve anaerobic threshold and hence aerobic power.

Capillarisation

Most studies that show increases in capillarisation with hypoxic exposure have been conducted on animals (Hudlicka, Brown, Walter, Weiss, & Bate, 1995). Authors who reported changes in capillaries in studies with humans have also observed loss in muscle mass. However, Hoppeler, and Desplanches (1992) found that hypoxia during a limited daily period of an endurance training session enhanced capillarity. Similarly, Terrados et al. (1988) observed an increase in the number of capillaries per unit muscle area following training in hypobaric hypoxia for three to four weeks. Others have reported no changes in fibre capillary ratio (Mizuno et al., 1990) or capillary density (J. Stray-Gundersen, Levine, & Bertocci, 1999). It has been shown, however, that hypoxia stimulates the expression and release of a vascular endothelial growth factor (VEGF) that is involved in vascular development and angiogenesis (Walter, Maggiorini, Scherrer, Contesse, & Reinhart, 2001). If this factor has an effect on capillarisation, then improvements in anaerobic threshold should be expected. For the same amount of oxygen received by the muscle, an increase in capillary number would facilitate a more even distribution of oxygen to muscle fibres, hence delaying fatigue caused by the build up of metabolites associated with the shift to anaerobic energy metabolism.

Fuel utilisation

McClelland, Hochachka, Reidy and Weber (2001) showed that high altitude acclimation greatly stimulated lipolysis in rats. In humans, Young et al. (1982) observed lower glycogen utilisation and respiratory exchange ratio during exercise at altitude in subjects who resided at 4300 m for 18 days. Chronic altitude exposure increased mobilization and use of free fatty acids during exercise resulting in sparing muscle glycogen. Carbohydrate sparing infers delay in accumulation of lactate, and consequently improvements in the anaerobic threshold. However, tracer studies more than ten years later revealed greater use of glucose as a fuel and decrease of free fatty acids (Brooks et al., 1992). The implication of this shift in fuel utilisation is discussed in the following section.

ECONOMY

Exercise economy is the reduction of oxygen consumption at a given sub-maximal workload. Currently there is enough evidence (see discussion below) to suggest that changes in exercise economy improves endurance performance.

Fuel utilisation

Changes in exercise economy are related to changes in oxygen utilisation and subsequently to changes in fuel metabolism. Studies of hypoxic exposure have reported such changes. Saunders et al. (2004) reported a 3.3% reduction in oxygen consumption at sub-maximal workloads, and Gore et al. (2001) observed a 4.4% reduction. Truijens et al. (2004), however, reported no significant effect in sub-maximal economy in runners and swimmers, although their data imply a likely improvement of ~1.6%. Piehl Aulin, et al. (1998) also reported no significant change in economy, but they did not show relevant data.

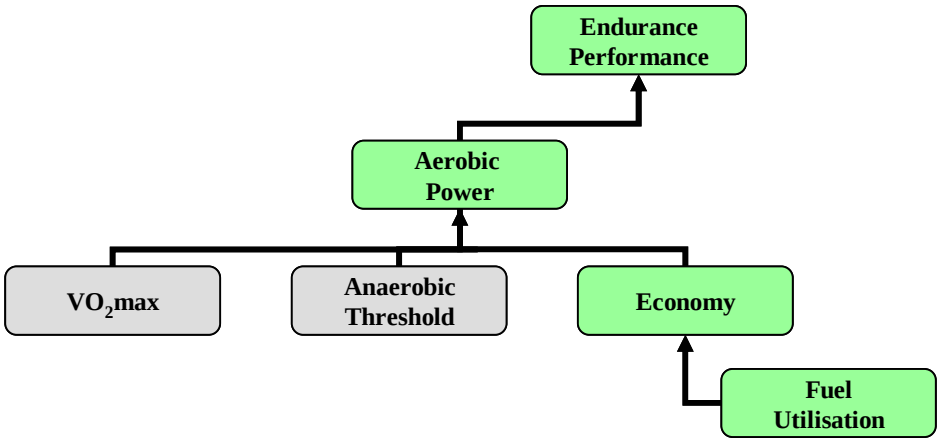

Figure 3.4. Improving economy via changes in fuel utilisation.

In studies where hypoxic exposure occurred at natural altitude, Green et al. (2000) reported a 4.5% reduction in oxygen uptake during sub-maximal exercise and Katayama, Matsuo, Ishida, Mori and Miyamura (2003) observed a significant decrease in oxygen uptake during submaximal exercise while Levine et al. (1991) and Wolfel et al. (1991) reported no significant changes. Overall, it seems likely that there is an enhancement in exercise economy with hypoxic exposure. Suggested mechanisms for improved economy are a shift from fat to carbohydrate oxidation (Brooks et al., 1992; A. C. Roberts, Butterfield et al., 1996; A. C. Roberts, Reeves et al., 1996) or reduced energy requirement during muscle contractions due to metabolic adaptations (C. J. Gore et al., 1999; Saunders et al., 2004).

BUFFERING CAPACITY

Improvements in endurance performance can be attributed to changes in anaerobic power. The obvious mechanism for this change is muscle buffering capacity. An increase in buffering capacity would reduce fatigue associated with decreases in pH. Hydrogen ions interfere with the muscle's contractile mechanisms and disrupt intramuscular homeostasis.

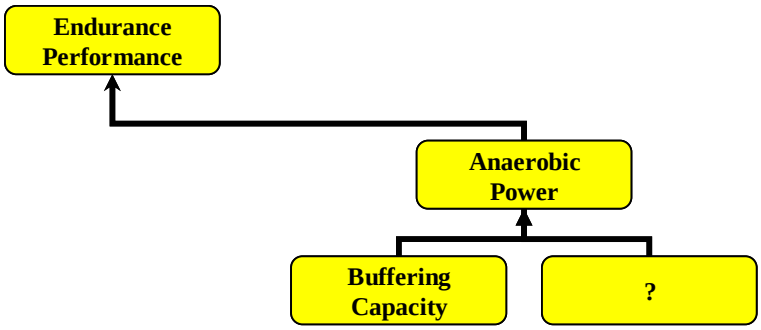

Figure 3.5. Improving anaerobic power via changes in buffering capacity.

Mizuno et al (1990) saw an increase in muscle buffering capacity in elite cross-country skiers who resided at 2100 m and trained at 2700 m for two weeks, even though their training involved long endurance work. On return to sea level they observed no changes to VO_2max, while oxygen deficit and short-term running performance improved. Biopsy obtained from the gastrocnemius and triceps brachii muscles showed increased buffering capacity. The authors concluded that two weeks of training at 2700 m did not improve VO_2max but improved short-term exercise performance due to increased muscle buffering capacity.

Gore et al. (2001) observed an increase in muscle buffering capacity in cyclists who lived high but trained close to sea level. Roberts et al. (2003) provided additional evidence that the “live high-train low” method with simulated exposure provided benefits for anaerobic capacity. They observed substantial changes in maximal mean power output and maximal accumulated oxygen deficit compared with sea level training in 19 well trained cyclists. Clark et al. (2004), however, did not observe a change in buffering capacity following intermittent hypoxia. They also saw a decrease in peak lactate concentration, which was not consistent with an increase in muscle buffering capacity.

Several factors contribute to muscle buffering capacity including phosphocreatine, dipeptide carnosine, and histidine related compounds (Abe, 2000; Parkhouse, McKenzie, Hochachka, & Ovalle, 1985; Sahlin & Henriksson, 1984). Questions remain as to how these factors contribute to changes in buffering capacity.

Buick et al. (1980) suggested that an increase in circulating haemoglobin improves buffering capacity of blood. In fact, Spriet, Gledhill, Froese, and Wilkes (1986) observed a reduction in peak lactate with intense treadmill running following graded

induced erythrocythemia, and Ekblom, Wilson and Astrand (1976) saw a reduction in blood lactate during submaximal exercise following red blood cell reinfusion. Similarly, Russell, Gore, Ashenden, Parisottp and Hahn (2002) observed a reduction in blood lactate with infusion of EPO. However, Goforth, Campbell, Hodgdon, and Sucec (1982) reported no changes in blood lactate values at exhaustion following infusion of red blood cells.

There are possibly other mechanisms that contribute to changes in the anaerobic contribution of endurance performance. Some studies have identified the reduction of the Na^+/K^+ ATPase activity as a likely cause of fatigue unrelated to accumulation of hydrogen ions. Fraser et al. (2002) showed that an acute bout of fatiguing dynamic exercise depressed muscle maximal Na^+/K^+ ATPase activity. Similarly Green et al.(2000) observed down regulation in muscle Na^+/K^+ ATPase activity following a 21-day expedition to 6194 m. It is conceivable that the combination of intense muscular contraction and hypoxia exacerbates disturbances in intracellular ionic concentrations (Fowles, Green, Tupling, O'Brien, & Roy, 2002), which then affect Na^+/K^+ ATPase activity. A possible mechanism could be Ca^{2+} entry via Na^+ channels resulting in accumulation of intracellular Ca^{2+}(Gissel & Clausen, 1999). Increased intracellular Ca^{2+} concentration can decrease Na^+/K^+ ATPase activity (Huang & Askari, 1982) and hence cause fatigue. Other contributing factors to muscle fatigue could be production of reactive oxygen species (Reid, 2001), impaired Ca^{2+} release and uptake (Li et al., 2002), K^+ loss (Sejersted & Sjogaard, 2000), increased intracellular P^+ (Fitts, 1994), or fatigue of the central nervous system (Gandevia, 2001).

The fundamental problem in this field of study, determining the physiological mechanism responsible for the improvement in sea level performance following altitude exposure, remains. Clearly, more research is necessary to identify the mechanism that explains the performance changes observed following exposure to natural or simulated altitude.

CHAPTER 4: SEA LEVEL PERFORMANCE IN RUNNERS USING ALTITUDE TENTS: A FIELD STUDY

This chapter comprises the following paper submitted to Journal of Medicine and Science in Sport: Hinckson, E. A., Hopkins, W. G., Fleming, J. S., Pfitzinger, P., Edwards, T., & Hellemans, J. (2004). Sea level performance in runners using altitude tents: a field study. *Manuscript submitted for publication.*

SUMMARY

In this study of effects of simulated altitude exposure on sea level performance, 10 competitive runners slept in a hypoxic environment achieved with tents for 9.8 ± 1.3 $h.d^{-1}$ (mean ± standard deviation) for 24-30 days at the equivalent of 2500-3500 m above sea level. The hypoxic conditioning group and a control group of 10 runners performed usual training. At ~4-wk intervals before and after exposure both groups performed an incremental test for lactate threshold. The hypoxic conditioning group performed an additional test, a treadmill run to exhaustion lasting ~5 min. One week following exposure lactate threshold speed of the hypoxic conditioning group relative to the control group increased by 1.2% (90% likely limits ± 3.1%), but the effect became slightly negative after controlling for baseline differences in running speed between the groups. A 16% increase in time to exhaustion observed in the hypoxic conditioning group, equivalent to a 1.9% (±1.4%) increase in speed in a time trial, could be a placebo or seasonal training effect. Change in performance had an unclear relationship to total altitude exposure, genotype for angiotensin converting enzyme, and change in haemoglobin concentration.

INTRODUCTION

There is reasonable evidence for an increase in sea level endurance performance after natural altitude exposure using the "live high-train low" method (Levine & Stray-Gundersen, 1997; J. Stray-Gundersen, Chapman, R. F. and Levine, B. D., 2001), but the effects of simulated altitude exposure are unclear. There are several ways to simulate altitude: nitrogen enriched environments (houses, apartments, or tents), barometric chambers, and hypoxic gas inhalers (Wilber, 2001). Inhalers are used to produce a severe intermittent hypoxia, which is quite different from the hypoxia of the other forms

of altitude exposure. Nitrogen enriched environments and hypobaric chambers provide an environment similar to that of natural altitude. Although nitrogen apartments and houses and hypobaric chambers are potentially a cost-effective way to provide altitude exposure to whole teams, the athletes have to live a dormitory lifestyle. Tents provide less disruption to lifestyle and are portable, but there is a potential disadvantage of less daily exposure than with nitrogen apartments.

There has been limited and inconclusive research on the effect of nitrogen apartments or houses and hypoxic inhalers on sea level performance, and no published scientific research on the efficacy of hypoxic tents. Therefore a field study was undertaken to investigate changes in performance of athletes using tents during a competitive season. The extent to which any changes in performance were associated with changes in blood haemoglobin concentration was also investigated, which increases with natural and simulated altitude exposure and could account for changes in endurance performance via changes in the transport of oxygen. Finally, the genotype of our athletes for angiotensin converting enzyme (ACE) gene was determined, which appears to have a role in adaptation to altitude. Of the three forms of the genotype (I-I, I-D, D-D), successful mountaineers were more likely than non-mountaineers to have the I-I form (Montgomery et al., 1998); furthermore, carriers of the I-I genotype showed better physiological adaptation to altitude (Woods, Pollard et al., 2002). The ACE gene also modulates the effects of training on performance in some studies (Montgomery et al., 1998; Woods, World et al., 2002) but not others (Sonna et al., 2001).

METHODS

Subjects

Five altitude tents were available, so three cohorts each of five subjects for the hypoxic conditioning group and three similar cohorts for the control group were recruited. Because recruitment of athletes of the highest competitive level was sought, randomisation to the two groups was not possible due to the lack of such athletes willing to participate. Consequently, recruitment was based on self-selection into either group. Within each cohort, compliance also proved to be difficult: some runners withdrew from the study either because of illness, injury, lack of motivation, or noise of the generator unit of the altitude tents.

The final sample consisted of competitive athletes of national and club level: eight males and two females were in the hypoxic conditioning group (age 25 ± 8 y) and eight males and two females were in the control group (age 37 ± 7 y). The runners' best competitive performance speed at the time of the study as a percent of world record speed in 800-10000 m was 83 ± 6 for the hypoxic conditioning group and 78 ± 5 for the control group (equivalent to 1500 m time of 3:58:08 and 4:18:00 respectively). Maximal oxygen consumption in a standard incremental test with a metabolic cart (Pfitzinger & Freedson, 1998) was 67 ± 6 and 64 ± 7 $ml.min^{-1}.kg^{-1}$ for the altitude and control groups, and 67 ± 6 and 61 ± 7 $ml.min^{-1}.kg^{-1}$ for the male and female runners respectively.

Runners provided informed consent in accord with the institutional ethics committee. Runners were excluded from the study if they were suffering from illness or injury that would interfere with normal training and competition.

Design

In this field study, we investigated the effectiveness of the tents in a setting that was realistic for competitive athletes. Runners in the control group trained and slept in their normal manner throughout the study. Each runner in the hypoxic conditioning group received an altitude tent (Hypoxico, New York), which they set up in their own homes and slept in for a period of approximately four weeks while they continued normal training. Runners in this group monitored their own arterial blood saturation to ensure progressive acclimatisation to altitude exposure. (Self-monitoring was part of the design of this field study and would have prevented blinding of the athletes to the treatment, even if they had complied with randomisation.)

Following familiarisation tests, performance tests were administered at four weeks before altitude exposure, one week before exposure, then at one, five and nine weeks after exposure. Runners in both groups performed the lactate-threshold test and runners in the hypoxic conditioning group performed an additional test, a run to exhaustion, in each testing week. Venous blood was sampled at four weeks before exposure, two days before exposure, then at one to two days, five weeks, and nine weeks after exposure.

Altitude exposure

The tent units simulated an altitude of 2500 m by reducing oxygen concentration in the air flushed through the tent. The model was adapted to allow gradual adjustment of the gas mixture to 3500 m by the end of the fourth week of exposure as the runners became acclimatised to the stimulus, provided that sleep was not unduly disturbed. Runners were encouraged to spend as long as possible in the tents each day (at least 10 hours per day for four weeks) by including extra sessions during the day whenever possible. Runners monitored their blood oxygen saturation via pulse oximeters (Nonin, Plymouth, Minnesota) applied to a finger at the beginning and end of each session in the tent. At the end of each session, athletes recorded in their training diaries the duration of the session (hours and minutes), haemoglobin saturation (%), and perception of nausea, headaches and hard breathing (5-point Likert scales:1=none, 2=low, 3=medium, 4=high and 5=severe). Seven of the 10 runners in the hypoxic conditioning group recorded their exposure data adequately for further analysis.

Training

Runners kept specially prepared daily training diaries in which they recorded session duration (minutes), session intensity (5-point scales: 1=easy, 2=steady, 3=mod-hard, 4=hard and 5=very hard), fatigue and limb pain (5-point scales: 1=none, 2=low, 3=medium, 4=high and 5=severe) and quality of sleep (5-point scale: 1=very good, 2=good, 3=average, 4=bad and 5=very bad).

Performance tests

Laboratory-based tests were chosen, partly because they can be as reliable as field tests, and partly because an indoor track to avoid effects of Auckland weather on field-test performance did not exist. Lack of sufficient control runners willing to visit the laboratory for all performance tests over the course of the study meant that the number of tests had to be minimised for that group. Potential control subjects were prepared to perform a sub-maximal test for lactate threshold, partly because the test provided them with useful information for training. Lactate threshold tests can also be amongst the most reliable of laboratory-based endurance tests (Hopkins et al., 2001). A lactate threshold test was therefore administered to runners in both groups. Runners in the

hypoxic conditioning group were also prepared to perform a maximal effort test. For this test a constant-pace run to exhaustion on the treadmill was chosen, because tests of this type provide probably the most reliable measure of endurance performance (Hopkins et al., 2001). The time course of changes and predictors of individual responses in the run to exhaustion could still be analysed without a control group.

Runners were instructed to perform little or no training one day prior to performance testing. Early in the testing week runners in both groups completed the lactate threshold test on a treadmill (Powerjog M30, Biddeford, Maine). An incremental, discontinuous, 5-min stage protocol (Pfitzinger & Freedson, 1998) was used with one minute between stages to allow sampling of blood from a finger prick. Lactate concentration was measured with a lactate analyser (YSI 1500, Yellow Springs, Ohio) immediately following blood collection. The runners completed the test when lactate concentration neared or exceeded 5 $mmol.L^{-1}$. Concentration was plotted against speed and lactate threshold was determined as the speed at 4 $mmol.L^{-1}$ and at 3 $mmol.L^{-1}$ above exercise baseline. Two measurements of lactate threshold were used to determine whether the two techniques provided similar results.

For the run to exhaustion the slope of the treadmill was fixed at 1.5% and the speed was set initially at the speed corresponding to each runner's current fastest time over 5 km. If the time to exhaustion during a familiarisation session was not between 4.5 and 5.5 min, the speed was adjusted for another familiarisation session a few days later. The speed was held constant for each runner on all subsequent tests, which were performed a few days after the lactate-threshold tests. Changes in time to exhaustion between trials were converted to changes in an equivalent time-trial time on the track via the critical power model (Hopkins et al., 2001). In the model, mean power $P = a/T + b$, where T is time to exhaustion, a is anaerobic capacity, and b is maximum aerobic power. We used values of 15 kJ and 350 W for a and b respectively, on the basis of studies of cyclists (Gaesser & Wilson, 1988; Green, Dawson, Goodman, & Carey, 1994). It was assumed that, for runners, percent changes in power were equal to percent changes in time-trial time (Hopkins et al., 2001). Under these assumptions, a 1% change in time-trial time would result in an 8.1% change in time for a run to exhaustion lasting 5 min. In a more recent study (Study 3) of critical-power modelling in similar competitive runners, it was found a similar relationship between changes in time-trial time and changes in time to exhaustion for tests of this duration (Hinckson & Hopkins, 2003).

Blood tests

Venous blood drawn from the antecubital vein was collected in a 5 ml EDTA tube, 1-7 days following exposure and was analyzed at a haematology laboratory (Middlemore Hospital, Auckland) for the determination of haemoglobin concentration, haematocrit and ferritin concentration. The athletes were seated in a chair, with the arm resting on a table at heart level and blood was drawn. Haemoglobin concentration and haematocrit were determined by automated instrumentation. Athletes in both groups with ferritin concentration <30 $ng.ml^{-1}$ were provided with a daily oral iron supplement under the direction of a physician.

ACE genotyping

Genomic DNA was extracted (Miller, Dykes, & Polesky, 1988) from peripheral venous blood samples. ACE genotype was determined by polymerase chain reaction (PCR) with three primers to distinguish the ACE insertion/deletion polymorphism. As described previously (Evans et al., 1994), PCR was carried out for 30 cycles in a Corbett PC-960 air-cooled thermocycler (Corbett Research, Sydney, Australia) using 50 pmol of primers ACE1 and ACE3 and 15 pmol primer ACE2, with an annealing temperature of 57°C. Amplification products were visualised after electrophoresis in 5% (w/v) Metaphor agarose gels (FMC Bioproducts, Biolab Scientific Limited, Christchurch, New Zealand).

Statistical analysis

Analyses was performed with appropriate repeated-measures modelling using log-transformed times to reduce any non-uniformity of error (Hopkins, 2000a). Performance changes in each post-test relative to the mean of the two pre-tests were expressed as percentages. Uncertainty in the estimates of changes is expressed as 90% confidence limits and as chances that the true value of the effect is a substantial enhancement or impairment (Hopkins, 2002); it was assumed a substantial enhancement on performance for a top competitive runner to be >0.5% and a substantial impairment to be <-0.5% (Hopkins, Hawley, & Burke, 1999). Change scores were analysed using percent of world record and age as covariates to control for any effects in the differences between

altitude and control groups. An attempt was made to quantify individual responses to altitude exposure by analysing within-subject coefficients of variation in performance between consecutive pairs of tests; an increase in the coefficient variation when one of the tests shows a change in the mean due to an experimental treatment is consistent with individual responses to the treatment (Hopkins, 2000a). The possibility that ACE genotype and total exposure to altitude accounted for any individual responses was investigated by plotting individual scores for change in performance between the first post-test and the mean of the two pre-tests against exposure time, with points labelled by genotype. Eight of the subjects volunteered a blood sample for gene analysis. The subject with incomplete exposure data was assigned the group mean in this plot.

Descriptive statistics are shown as means and standard deviations. For repeated measurements within-subject and the usual between-subject standard deviations were derived from the analyses. Data shown in Figure 4.2 are least-squares (adjusted) means to reduce variability arising from missing values. (In the hypoxic conditioning group, two runners missed their tests at Week 5 and three at Week 9; in the control group, four runners missed their test at Week 9.)

For statistics derived from diaries, each runner's data were either averaged or summed over each week; the standard deviations represent the typical variation between subjects in any given week. Six runners in the hypoxic conditioning group and five runners in the control group completed training diaries adequately for analysis.

RESULTS

Figure 4.1 summarises weekly training over the period of the study. Mean weekly training duration over the period of the study determined from the weekly means was 405 min and 385 min for the altitude and control groups respectively (overall standard deviation 165 min). In week 6 the value for the hypoxic group appears to be higher because one of the athletes undertook a day-long hike. Intensity of training, fatigue, and limb pain were slightly higher in the hypoxic conditioning group than the control group, whereas rating of quality of the session was a little higher in the control group (data not shown). In the few weeks before each performance test, these minor differences in volume and intensity did not appear to relate consistently to changes in performance.

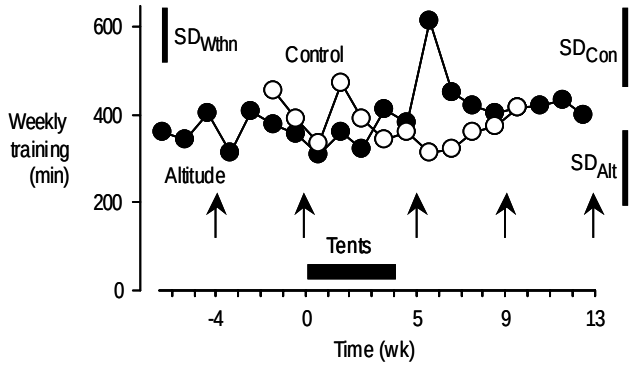

Figure 4.1. Weekly training in the altitude and control groups. Data are least-squares means. Bars indicate between-subject standard deviations in the altitude (SD_{Alt}) and control (SD_{Con}) groups and the overall within-subject standard deviation (SD_{Wthn}). Arrows indicate timing of performance tests.

Mean scores for perception of nausea, headaches, and hard breathing for the hypoxic conditioning group were all between the first two points on the Likert scales (none and low), and there were no obvious changes during the period of altitude exposure. Means in sleep quality for both groups were all between *average* and *good*, with little change throughout the study.

Runners in the hypoxic conditioning group completed 24-34 sessions of altitude exposure over 24-30 days for 9.8 ± 1.3 $h.d^{-1}$. Weekly mean oxygen saturation ranged from 89.6% to 92.5%; there was no clear trend towards decreasing saturation by the end of exposure despite the runners increasing their level of simulated altitude.

Following altitude exposure, mean weight relative to the mean of the two pre-tests in the hypoxic conditioning group decreased by 0.8 kg at the time of the run to exhaustion and by 0.6 kg at the time of the lactate threshold test. In the control group mean weight prior to the lactate threshold test increased by <0.1 kg.

The time course of performance in the run-to-exhaustion and lactate-threshold tests is shown in Figure 4.2. The effects of altitude exposure in the three post-tests relative to the pre-tests are as follows: there was a 1.2% (90% likely limits ±3.1%) and 0.7% (±3.4%) improvement in performance in the hypoxic conditioning group in comparison

to the control group in the 3-mM and 4-mM lactate-threshold tests respectively and a 1.9% (±1.4%) improvement in the run to exhaustion one week following altitude exposure. At Week 5 there was an impairment of 0.9% (±2.7%) and 0.7 (±2.8%) in the 3-mM and 4-mM lactate tests and similar impairment in the run to exhaustion by 0.7% (±1.6%). At Week 9 performance was impaired by 0.4% (±3.2%) in the 3-mM but improved slightly by 0.6% (± 3.7%) in the 4-mM lactate test and was impaired in the run to exhaustion by 0.6% (±1.8%).

When we controlled for the difference in ability in the altitude and control groups, the effect of altitude exposure in the first post-test became a 0.2% (± 3.9%) decline in performance in the 3-mM lactate threshold speed and a 0.7% (± 4.9%) decline in the 4-mM lactate threshold speed. Controlling for age had a trivial effect in the 3-mM and 4-mM lactate threshold speed.

Within-subject coefficients of variation calculated from consecutive pairs of tests showed no consistent pattern indicative of individual responses to altitude exposure. Ranges in the coefficients of variation were: time to exhaustion, 12-22%; equivalent time-trial speed, 1.4-3.0%; lactate threshold speed at 3 $mmol.L^{-1}$ above baseline, 1.6-3.2%; and lactate threshold speed at 4 $mmol.L^{-1}$, 1.5-3.5%. Uncertainty in these estimates (90% confidence limits) were approximately 1.5×/÷ to 1.9×/÷. Calculated from all tests, the overall coefficients of variations were: time to exhaustion, 16%; equivalent time-trial speed, 1.9%; and lactate threshold speeds, 2.8% (for 3 $mmol.L^{-1}$) and 3.4% (for 4 $mmol.L^{-1}$).

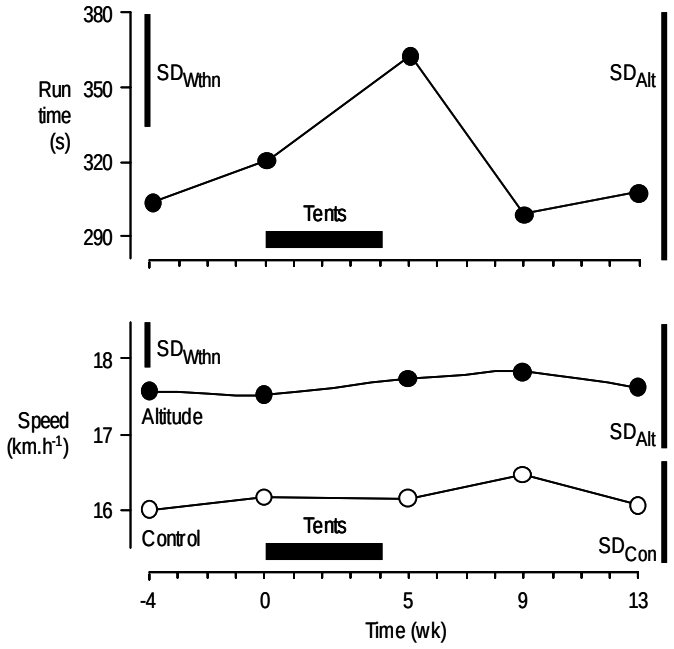

Figure 4.2. Time course of the run time to exhaustion and 4 mmol.L^{-1} lactate-threshold speed. Data are least-squares means; bars are standard deviations, as defined in Figure 4.1.

There was no clear association between the percent change in equivalent time-trial time and either duration of altitude exposure or ACE genotype (Figure 4.3). Effects of duration of exposure and ACE genotype on changes in lactate-threshold speed were similarly inconclusive (data not shown).

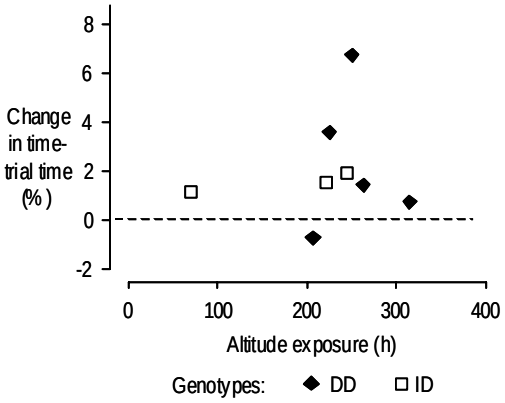

Figure 4.3. Percent change in equivalent time-trial time, duration of altitude exposure, and ACE genotype for each runner in the hypoxic conditioning group.

Changes in the mean values of haemoglobin concentration and haematocrit from test to test in each group were typically ~1-2%, but the percent changes for both variables in both groups tended to track each other. Relative to the control group, there was a small increase in haematocrit for the hypoxic conditioning group of 0.2 percent of blood volume (%BV) (confidence limits of –1.0 to 1.4 %BV) from the average of 44 %BV between the first post-test and mean of the previous two pre-tests. For haemoglobin the corresponding change was 2.7 $g.L^{-1}$ (confidence limits –2.2 to 5.5 $g.L^{-1}$) or an increase of 1.8% from the average of 149 $g.L^{-1}$.

DISCUSSION

In this study, tents were used to provide altitude exposure to distance runners. An improvement in performance of about 1% in the lactate-threshold test and an improvement in the time to exhaustion test that was equivalent to about 2% in a time trial was observed. The error of measurement of the lactate threshold (overall coefficient of variation ~3.0%) was approximately twice that in the reliability study by Pfitzinger and Freedson (1998), even though the same protocol was used. The larger error in our study may be due to the longer duration between tests (four-five weeks) than in the reliability study (≤two days). Other possible causes include greater variability in training and in carbohydrate intake in this study compared with that in the controlled conditions of a reliability study, because variability in training (Hurley et al., 1984) and diet (Yoshida, 1984) might have a substantial effect on lactate threshold via changes in carbohydrate metabolism. Any such changes appeared to have less effect on the error of time to exhaustion, because the within-subject coefficient of variation of the equivalent time trial time (1.9%) was substantially less than that of lactate threshold. Although the improvement in the time to exhaustion test was very likely to be substantial, there was no control group for this test, so at least part of the improvement might not be due to altitude exposure.

However, further analysis indicated that when controlling for differences in ability and age between the two groups, the effect of altitude disappeared. In particular when percent world record was included as a covariate to control for ability, there was a slight decline in performance in both the 3mM and 4mM lactate tests in the hypoxic conditioning group in comparison to the control group. Controlling for age had little or no effect. Gains observed in the run time to exhaustion could be attributed to training as the lactate threshold speed change showed a trend towards improvement in athletes of

better ability regardless of the intervention. On the basis of the extended analysis of the data simulated altitude exposure using the tents may not provide the necessary stimulus for sea level performance improvements. Further research is necessary to clarify whether the changes observed in time to exhaustion were partly due to the hypoxic effect.

The moderate changes in haemoglobin and haematocrit concentration that occurred in both groups probably arose from day-to-day variation in calibration in the haematology laboratory. The net difference in the changes between the groups following altitude exposure was less than that in natural-altitude studies (Levine & Stray-Gundersen, 1997; Sharpe et al., 2002) but similar to changes observed in simulated-altitude studies (Piehl Aulin et al., 1998). In light of the absence of change in blood parameters it is possible that exposure to a nitrogen rich environment does not provide the stimulus necessary for erythropoiesis at altitude equivalent above 2500 m for less than 10 $h.d^{-1}$. Rodriguez et al. (1999) showed that small doses of hypobaric hypoxia elicited the expected blood changes. However, Rusko et al. (1999) showed changes in performance and blood parameters after 16 $h.d^{-1}$ for four weeks of hypoxia in a nitrogen enriched environment. It seems that athletes will need to spend more than 10 $h.d^{-1}$ in the tent to gain the expected benefits.

Previous studies using the “live high-train low” method have not tracked the time course of the effect for as long as nine weeks post altitude. According to the data of this study, it is unlikely that there would be an enhancement in performance five or nine weeks post altitude.

The within-subject variation observed from test to test and the analysis based on the ACE genotype and altitude exposure (Fig. 2) provided no clear evidence of individual responses to altitude exposure. If the dose was sufficient, some sort of a relationship between change in performance and the ACE genotype was expected, given the apparent role of this gene in recent studies of adaptation to altitude (Montgomery et al., 1998; Woods, Pollard et al., 2002). The mechanism responsible for such adaptations seems to be related to aerobic than anaerobic mechanisms. In these studies the I-I genotype was more beneficial than the other two genotypes (I-D and D-D), but in our study no athletes carried the I-I genotype. To resolve the issue of the role of the ACE genotype on the effects of altitude exposure on performance, a larger sample size and a

proportion of athletes carrying the I-I genotype are needed. A range of exposures within such a study would also clarify the minimum threshold required and the effects of exposure duration.

The final issue to address is the practicality of altitude tents. The most recent version of the tents do not present the noise problems of earlier models and the tents are otherwise easy to use and not prohibitively expensive for serious athletes.

CONCLUSION

- Simulated altitude exposure using the tents may not provide the necessary stimulus for sea level performance improvements.

- Effects on performance were not apparent five and nine weeks after use of the tents.

- Further research is necessary to determine the minimal threshold required necessary to improve performance at sea level using perhaps a crossover design to avoid problems with compliance and to investigate performance changes other than endurance.

CHAPTER 5: RELIABILITY OF TIME TO EXHAUSTION ANALYZED WITH CRITICAL-POWER AND LOG-LOG MODELLING

This chapter comprises the following paper submitted to Medicine and Science in Sports and Exercise: Hinckson, E. A., & Hopkins, W. G. (2004). Reliability of time to exhaustion analysed with critical power and log-log modelling. *Manuscript submitted for publication.*

SUMMARY

The large variability of time to exhaustion between repeated tests at constant power output or speed gives an impression that these tests are unsuitable for monitoring athletic performance. This issue was addressed using critical-power and log-log models of the speed-duration relationship to analyse treadmill runs to exhaustion. Application of differential calculus to the models provided factors for converting variability in time to exhaustion into variability in equivalent time-trial time. Values for the factors and variabilities from a reliability study were estimated. Eight male competitive runners performed a test consisting of three constant-speed runs to exhaustion lasting ~2, ~4 and ~8 min, with 30 min rest between runs. A pair of such tests five days apart was repeated seven and 14 weeks later within a summer competitive season. The models were also used to predict times for fixed distances from each set of three runs. Repeated-measures analysis of log-transformed times provided estimates of variability expressed as coefficients of variation. Variabilities of time to exhaustion were 9%, 13% and 16% (shortest to longest runs). Converted to their equivalents in time-trial time, the variabilities were 2.6%, 1.7% and 1.0% via critical-power modelling, and 1.3%, 1.7% and 2.2% via log-log modelling (90% likely limits ×/÷1.2). The conversion factors varied typically by 28% from runner to runner (×/÷1.5). Variabilities in times predicted for fixed distances were similar but more uniform for the log-log model. Runs to exhaustion are inherently reliable, but conversion of changes in time to exhaustion at a single fixed speed into changes in equivalent time-trial time is model- and individual-specific and therefore only approximate. Log-log modelling of runs at several speeds provides accurate conversion.

INTRODUCTION

For many years researchers have used time to exhaustion in tests performed at constant power output or speed to study treatments that affect endurance performance. (See, for example, the publications of R.J. Maughan and coworkers) This measure regularly revealed statistically significant large effects, but the fact that it showed large test-retest variability in reliability studies (coefficients of variation of ~15-25%) led some researchers to conclude that it was unsuitable for investigating the small changes in endurance performance that matter to competitive athletes (Jeukendrup, Saris, Brouns, & Kester, 1996). These researchers suggested that performance tests in which the athlete attempts to maximize power output during performance of a constant amount of work, or over a constant distance, or for a constant duration, were not only more race specific but were apparently more reliable. Indeed, an athlete's performance in such tests varies typically by only a few percent in reliability studies (Hopkins & Hewson, 2001).

Other researchers have argued that the apparently poor reliability of time to exhaustion is an artefact of the hyperbolic relationship between exercise duration and power output (Hopkins et al., 2001). The relationship is such that small random changes in a subject's ability to output power from test to test (~1%, say) result in much larger random changes in time to exhaustion (~10-20%). But a treatment that produces a substantial change in a subject's ability to output power will also result in a large change in time to exhaustion, which will stand out against the large random changes. When these researchers used duration-power relationships to convert changes in time to exhaustion into equivalent changes in power output in a constant-duration time trial, they found that time to exhaustion was amongst the most reliable of measures of endurance performance (Hopkins et al., 2001). They suggested that the measures derived from race-specific constant-work or constant-duration time trials are, if anything, less reliable, because optimal performance in such time trials requires subjects to set a pace appropriate for the distance or duration and appropriate for their current state of fitness. In contrast, tests conducted at constant power, along with incremental tests to maximum effort, require no self-selection of pace and potentially less familiarisation with the test protocol.

Notwithstanding the strength of these arguments, we continue to encounter scepticism about the utility of time to exhaustion as a measure of performance. The scepticism may arise in part from lack of understanding of the calculus used to derive the relationship between changes in power output and changes in time to exhaustion. One aim of the present study was therefore to provide a detailed account of the application of calculus to convert changes in time to exhaustion into changes in a time trial of similar duration. This account should help researchers understand why the high test-retest variability of time to exhaustion does not imply poor reliability. A further aim was to present empirical evidence of high reliability of time to exhaustion. For this aim, a reliability study was performed in which subjects ran to exhaustion at three speeds, then repeated the set of runs at various times over 14 weeks. For each set of three runs, the critical-power modelling and log-log modelling were used in the relationship between run distance and run time to predict time-trial performance over standard competition distances. It was reasoned that high reliability for these predicted times would be indirect but compelling evidence of functionally high reliability in times to exhaustion, from which they were derived.

METHODS

Choice and use of models

The relationship between exercise duration and the maximum work or mean power output that can be achieved during the exercise is the key to understanding test-retest variation in time to exhaustion. In the present study the exercise duration was restricted to 1- to 10-min, a range in which the critical-power model can be used for the relationship (Hill, 1993).

The critical-power model is based on the following assumptions: work is derived from aerobic and anaerobic mechanisms; the aerobic system provides power at maximum (m, the so-called critical power) for the entire duration (T) of the exercise; and the point of exhaustion coincides with the depletion of the anaerobic work capacity (a) needed to sustain the supra-aerobic-maximal exercise. It follows that $W = a + mT$, where W is the total work done (Hill, 1993). For running, the model is $D = a + mT$, where D is the total distance run, a is the distance run purely anaerobically, and m is the maximum aerobic running speed (Hill, 1993). Researchers have used the critical-power model to make

inferences about reliability of the parameters *a* and *m* and about effects of experimental treatments on these parameters. Remarkably, researchers have used the model to predict and analyze performance times for set distances or set work in only one previous study (Hughson, Orok, & Staudt, 1984); the prediction was for a 10-km running time, which is far beyond the theoretical maximum time (~10 min) for the critical-power model. To make predictions in the present study, we expressed T as a function of D: $T = D/m - a/m$.

The fit of the critical-power model to performance times and distances produces extremely high correlations (Vandewalle, Vautier, Kachouri, Lechevalier, & Monod, 1997). Although the data of this study were no exception, analysis of residuals showed systematic and non-uniform deviations from the model (see Results), a phenomenon that appears to have gone unnoticed in previous studies. An additional model was therefore chosen for the relationship between T and D, an empirical log-log model with a long history (Billat, Koralsztein, & Morton, 1999). The model is easiest to understand in the form $\log(S) = k\log(T) + c$, where S is running speed or power, and *k* and *c* are constants. By applying differential calculus, $dS/S = k dT/T$, so the model implies that percent changes in speed ($100dS/S$) are proportional to percent changes in exercise duration ($100dT/T$), and *k* is the constant of proportionality. To make predictions of performance times for set distances, we used $S = D/T$ to express the model as $\log(T) = \log(D)/(1+k) - c/(1+k)$, or $\log(T) = k'\log(D) + c'$.

To derive the relationship between change in time to exhaustion at a constant speed and change in time in a constant-distance time trial of similar duration, it is necessary to express the critical-power model first as a relationship between speed (S) and distance travelled (D). The critical-power model is $D = a + mT$, therefore $T = (D-a)/m$, and so $S = D/T = D/((D-a)/m) = mD/(D-a)$. Figure 5.1 shows this relationship as a curve over the range of distances corresponding to run times of 1-8 min for the mean values of *a* and *m* observed in this study. Figure 5.1 also shows the new curve when *a* and *m* change by small arbitrary amounts, and the inset of Figure 5.1 shows the resulting small change in S for a constant-distance time trial and small change in D for a constant-speed run to exhaustion at a given value of S and D. The ratio $-\delta S/\delta D$ is approximately the slope of either curve. But, using differential calculus, the slope of the curve $= dS/dD = -am/(D-a)^2 \approx -\delta S/\delta D$. Rearranging, $\delta S/S \approx [am/(D-a)^2]\delta D/S = [a/(mT)]\delta D/D$. Therefore $100\delta S/S$ = percent change in speed in a constant-distance time trial $\approx [a/(mT)]100\delta D/D$

= a/(mT) times the percent change in distance in a constant-speed run to exhaustion. But D = ST, so again using differential calculus, δD = SδT, and therefore 100δD/D = 100SδT/D = 100δT/T = a small percent change in time to exhaustion. Therefore the constant to convert small percent changes in time to exhaustion into small percent changes in a constant-distance time trial is a/(mT). By a similar analysis, the constant to convert small percent changes in time to exhaustion into small percent changes in a constant-*time* time trial is a/(a+mT), although this constant is not used in this study. Similarly, the conversion constants derived from the log-log model for constant-distance and constant-duration time trials are k/(1+k) (or 1-k') and k (or (1-k')/k') respectively.

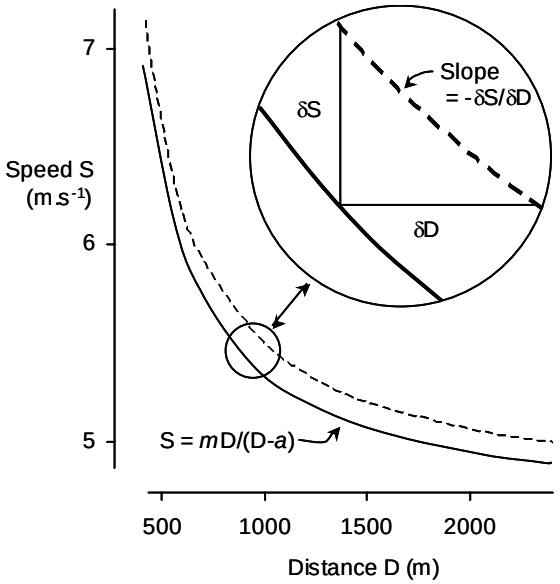

Figure 5.1. Curves showing relationship between running speed and distance travelled under the assumptions of the critical-power model. Solid curve is for mean values of anaerobic capacity (a) and maximum aerobic power (m) observed in this study for treadmill running at an inclination of 1.5%; dashed curve is for arbitrary small increases in a (5%) and m (2%). Inset shows that the resulting small change in S (δS) for a constant-distance test divided by the small change in D (δD) for a constant-speed test is approximately equal to the slope of the curves at the given value of S and D.

Subjects

Eight male distance runners (age 27 ± 9 y, mean ± standard deviation) of regional and national competitive level participated in the study. The runners' current best competitive performance speed as a percent of world record in the 800-10,000 m was 79 ± 11 (mean ± standard deviation). They provided informed consent and the study was conducted in accord with the institutional ethics policy. Runners were excluded from the study if they were suffering from illness or injury that would interfere with normal training and competition.

Design

Variability of a subject's performance can depend on the time between tests. This reliability study was therefore designed to determine variability of performance over a period of a few days (during which changes in performance should be close to minimal) and over a period of several months (which is typical for training or other long-term interventions). To this end, runners were recruited on the understanding that they would maintain their usual training (~7 $h.wk^{-1}$) over a 15-wk period in a summer season, and that during this time they would visit the laboratory on seven separate occasions to perform a set of three runs to exhaustion. The first visit was a familiarisation session, and the remaining six visits, beginning one week later, were testing sessions. Pairs of testing sessions were scheduled five days apart every seven weeks for a total of 14 weeks. One subject failed to report to the lab for his last test.

As models with two parameters, the critical-power and log-log models require at least two runs to exhaustion for derivation of slope and intercept parameters and for subsequent prediction of time-trial times. Three or more runs allow derivation of goodness of fit and more accurate estimation of parameters and predictions. The number of runs were limited to three, because we were concerned that more runs might compromise the performance of the runners in some runs.

The sample size for the reliability study produced 20 degrees of freedom for the estimate of 5-day test-retest error of measurement (within-subject variability). The sample size is the equivalent of 21 subjects tested twice (after familiarisation), which is more than that of most studies of reliability of performance (Hopkins et al., 2001). The

resulting precision of error of measurement (90% confidence limits, 1.2) is adequate although not ideal for comparison of errors (Hopkins, 2000a).

Runs to exhaustion

The runners were instructed to engage in little or no training for at least one day prior to each visit. At each visit, the runners performed three runs to exhaustion on a treadmill (Powerjog M30, Biddeford, Maine) at three speeds. In a pilot study with two runners, and during the familiarization session, the runners indicated (perceived exertion) they had recovered sufficiently to perform the set of three runs with 30 min rest between runs. In the familiarization session the speed of the treadmill was adjusted to elicit exhaustion times of approximately 1-2 min, 3-4 min and 7-10 min, in that order. The first speed was based on the individual's current best 800 or 1500 m time. Each runner's speeds were then held constant for the six testing sessions. The slope was fixed at 1.5% for all runs. The runners received no feedback about elapsed time or distance travelled during the runs.

For two of the runners, speed of the third run was changed after the first testing session to keep time to exhaustion within 10 min. Analysis of variability of time to exhaustion requires the speed of the treadmill to be constant for the given runner, so for these runners we excluded the times for the third run in the first test from the analysis. These times were, however, included in the critical-power modelling and were therefore included in reliability analyses of parameters and estimates derived from the critical-power modelling. The third run of one runner in the fifth test was also excluded, because the standardized residual of this run in the reliability analysis was 6.2. Critical-power modelling was not applied to this runner's other two runs in the fifth test.

Statistical analysis

For the prediction of time-trial times, a least-squares straight line was fitted to the run time and run distance (critical-power predictions) and to the natural logarithms of run time and run distance (log-log predictions) for each runner's set of three runs. The parameter estimates were then used to predict times for the standard competition distances of 800, 1500, and 3000 m, as illustrated in Figure 5.2 for the set of three runs with the worst fit for the critical-power model. Each runner's times were also predicted

for the group-mean distance run in each of the three runs (640, 1200, and 2300 m). Measures of goodness of fit for each set of three runs were the adjusted correlation coefficient (square root of the R^2 adjusted for degrees of freedom) and the standard error of the estimate; the latter were averaged over all six runs of all runners (via averaging of their squares). Residuals and predicteds for each set of three runs were also output for plotting and averaging to assess the uniformity of fit.

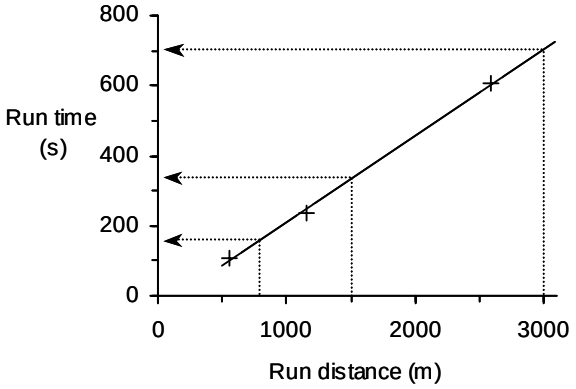

Figure 5.2. Run time and run distance for a runner with the set of three runs showing the worst fit of the critical power model T = (D-a)/m, illustrating prediction of run times for 800, 1500 and 3000 m from the least-squares line. Adjusted correlation = 0.998, standard error of estimate = 13 s.

Mixed-model analyses of log-transformed times (Hopkins, 2000a) provided estimates of test-retest variability of times to exhaustion, predicted times, and model parameters as coefficients of variation (percent of each subject's mean). The mixed model had a single fixed effect for identity of trial (six levels, excluding the familiarisation trial), a residual representing within subject variation (error of measurement) between any pair of trials, a random effect representing additional within-subject variation between trials seven or 14 weeks apart, and a random effect for subject identity.

RESULTS

The adjusted correlation coefficients for the critical-power and log-log modelling of the sets of three runs were all at least 0.998, and mean standard errors of the estimate were 4.8 s and 2.0% for the critical-power and log-log models respectively. A plot of residuals against predicteds from the critical-power modelling of all sets of three runs showed clear evidence of non-uniformity of error (Figure 5.3): the means of residuals for the three runs (shortest to longest) were 1.4, -2.4 and 1.0 s; the standard deviations were 2.0, 2.9 and 1.2 s. (The root-mean square of all the residuals in the figure, appropriately corrected for degrees of freedom, is the mean standard error of the estimate, 4.8 s.). The residuals from the log-log modelling showed a similar pattern of non-uniformity, but with reversed sign for the means for the three runs (shortest to longest): -0.7%, 1.0% and -0.3%; the standard deviations were 0.8%, 1.2% and 0.6%.

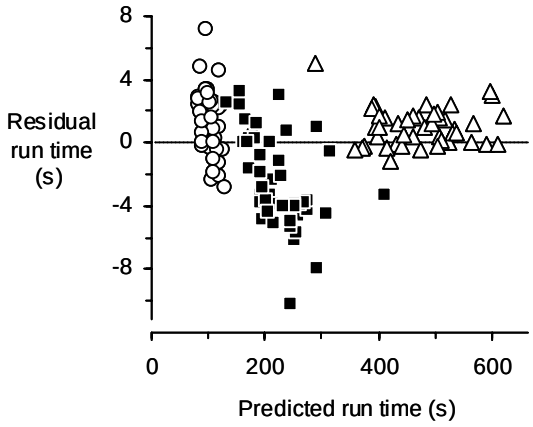

Figure 5.3. Residual and predicted run times derived from fitting the critical power model T = (D-*a*)/*m* to each runner's set of three runs (first, ○; second, ■; third, △).

Table 5.1 shows values of parameters derived from the modelling as means and variabilities.

Table 5.1. Reliability analysis of parameters derived from the critical-power and log-log models for each set of three runs over the six trials: overall mean, between-runner variability in any one trial, and within-runner variability from trial to trial.

		Variability	
Parameter	**Mean**	**Between-runner (%)**	**Within-runner (%)**
a	139 m	24	14
m	4.57 $m.s^{-1}$	11	1.8
a/(*m*T)	0.506/T	28	16
k′ - 1	0.137	27	11

a, anaerobic capacity; *m*, maximum aerobic power; *a*/(*m*T), factor for converting percent changes in time to exhaustion into changes in an equivalent constant-distance time trial, where T is time to exhaustion in minutes; *k*′ - 1, similar factor derived from log(T) vs log(D) model, where *k*′ is the slope of the model.

Variabilities are expressed as coefficients of variation.

Uncertainty in variabilities (90% confidence limits): between-runner, ×/÷1.7; within-runner, ×/÷1.2.

The reliability analyses for time to exhaustion in each of the three runs over the six tests produced negative estimates for additional error variance when tests were seven weeks apart. Since it is unrealistic that there should be better reliability between tests seven weeks apart than between tests five days apart, the additional variance was set to zero, and the resulting estimates of variability (in which the six tests contribute equally) are shown in Table 5.2. Also shown in the table for each of the three runs is the within-runner variability of an equivalent constant-distance time trial estimated from the within-runner variability in time to exhaustion via the critical-power and log-log models.

Table 5.2. Analysis of time to exhaustion for each of the three runs over the six trials: overall mean, between-runner variability in any one trial, within-runner variability from trial to trial, and within-runner variability of an equivalent constant-distance time trial estimated from the critical-power and log-log models.

		Variability of time to exhaustion (%)		Estimated within-runner variability of equivalent time trial (%)	
Run	Mean time to exhaustion (min)	Between-runner	Within-runner	via critical-power model[a]	via log-log model[b]
1	1.8	13	9.2	2.6	1.3
2	3.7	24	13	1.7	1.7
3	7.8	17	16	1.0	2.2

Variabilities are expressed as coefficients of variation.

Uncertainty in variabilities (90% confidence limits): between-runner, ×/÷1.5; within-runner, ×/÷1.2.

[a]Within-runner variability multiplied by 0.506/T, where 0.506 is the mean value of *a/m* and T is the mean time to exhaustion in minutes.

[a]Within-runner variability multiplied 0.137, the mean value of *k′* - 1.

The reliability analysis of time-trial times predicted for the distances of each run and for standard competition distances using the critical-power and log-log models is summarized in Table 5.3. The analysis for the shortest distance produced negative estimates for additional error variance when tests were seven weeks apart. As in the analysis of times to exhaustion, the additional variance was set to zero, and the resulting estimates of 5-d and 7-wk variability in the table are therefore equal. Variabilities of the time-trial times for the other distances were greater for tests seven weeks apart than for tests five days apart, as shown in the table.

Table 5.3. Within-runner variability of constant-distance time-trial times predicted for various distances from each runner's set of three runs using the critical-power and log-log models. The distances are the mean distance in each of the three runs to exhaustion (for comparison with variabilities in Table 5.2) and standard competition distances.

Distance (m)	Predicted time (min)	Within-runner variability (%)			
		via critical-power model		via log-log model	
		5-d	7-wk	5-d	7-wk
Mean distances of the three runs					
640	1.8	2.5	2.5	1.3	1.3
1200	3.9	1.1	1.2	1.1	1.3
2300	7.9	1.0	1.3	1.5	2.3
Standard competition distances					
800	2.4	1.8	1.8	1.1	1.1
1500	5.0	0.9	1.1	1.2	1.6
3000	10.4	1.1	1.4	1.8	2.8

Variabilities are expressed as coefficients of variation.

Uncertainty in variabilities (90% confidence limits): 5-d, ×/÷1.3; 7-wk, ×/÷1.5.

DISCUSSION

In the present study, several approaches were used to derive estimates of test-retest error of measurement from times to exhaustion in tests conducted at constant running speed. All estimates were <3%, and some were ~1%, which represents excellent reliability in comparison with other tests of endurance performance (Hopkins et al., 2001). These findings should lay to rest any concerns that time to exhaustion is inherently an unreliable measure of endurance performance.

Although the errors were small, there were considerable differences in the estimates (up to a factor of 2) between the different approaches. Given the uncertainty in the estimates represented by the confidence limits (×/÷1.2–1.3) these differences are likely to represent substantial real differences rather than simply sampling variation. The most noteworthy differences are for the within-runner equivalent time-trial variabilities estimated from single runs to exhaustion (Table 5.2, last two columns): the variabilities derived from the critical-power model get smaller for longer runs; the trend is in the other direction and less marked for variabilities derived from the log-log model. These differences arise presumably from the systematic lack of fit of the models revealed by the mean values of the residuals for the three runs. Evidently, there is some curvature in the relationship between run time and run distance, and log-log transformation overcompensates by inverting the curvature. The factors for converting variation in time to exhaustion into variation in equivalent time trial time are based on the slope of the appropriate version of each model, so failure to fit curvature in the data will result in systematic errors in the factors. The biological within-subject variability in mean power output for exercise durations over the range of 1 to 10 min is practically constant, when expressed as a coefficient of variation. The trends shown in the last two columns of Table 5.2 are therefore artefacts of the models. A model that fits the curvature would probably produce equivalent time-time trial variability of ~1.7% (the variability for both models for the second of the three runs) for runs of any duration in the 1- to 10-min range.

Although neither model produced an ideal fit for predicting time-trial times from single runs to exhaustion, Table 5.3 provides some evidence for the superiority of the log-log model when combining three runs. The 5-d variability from the log-log model differs little for the shortest and longest of the three runs (640 and 2300 m). The variability for the middle run (1200 m) is a little lower, as one might expect for a prediction for the middle of a set of points in comparison with predictions for the extremes. In contrast, the 5-d variability from the critical-power model appears to have a systematic trend towards less variability for longer runs similar to that in Table 5.2.

The estimates of 7-wk variability for run times predicted from each set of three runs (Table 5.3) were similar to the variability of times derived from single runs (Table 5.2). Variability over five days, where it could be estimated, was a little smaller. Greater variability is expected as time between tests increases, so the failure to find any such

increase for the shortest runs in Table 5.3 could represent simply sampling variation. It is also possible that over the 14 weeks of the study the runners tended to experience more variability in the aerobic (endurance) component of their fitness.

Estimability of 5-d and 7-wk variability for predicted times for 1200- and 2300-m runs (Table 5.3) was not matched by such estimability for corresponding runs to exhaustion (Table 5.2). Thus, single runs to exhaustion appear to have less sensitivity to subtle changes in reliability. There are two likely explanations. First, there is a large increase in variability of the time to exhaustion (9.2% to 16%) as the duration of the run increases from the shortest (1-2 min) to the longest (5-10 min). Within a single run, there is a two-fold range of run time between runners. It follows that variability of time to exhaustion within a single run will be greater for the runners with longer run times. This "variability of variability" presumably tends to mask the random effect representing additional variability for tests seven weeks apart. The other likely explanation is a similar variability of variability arising from individual differences in the constants that convert changes in time to exhaustion into changes in equivalent time-trial time (27-28%, Table 5.1). Both these sources of variation are eliminated when the critical-power or log-log models are used to predict times for specific distances from two or more runs.

An incidental outcome in our study is estimation of the reliability of parameters in the critical-power model. The only comparable studies were performed over a shorter time frame (≤1 wk) on cycle ergometers (reviewed in Hopkins et al., 2001). In these studies, aerobic power was more variable (2.3-7.6%) and anaerobic capacity was less variable (8.4-14%), possibly reflecting the different time frame and mode of exercise.

In conclusion, it is clear that time to exhaustion is a reliable measure, but it is now also clear that converting change in time to exhaustion from trials at one speed or power output into change in time-trial time can only be approximate. During testing, researchers or sport scientists may still wish to use time-to-exhaustion tests, because of their potential to avoid the problems of self-selection and familiarization associated with pacing. It is recommended that they use at least two trials differing widely in speed or power, then combine the trials with an appropriate model to predict time-trial times or mean power over race-specific distances. Choice of the model can make substantial differences to the predictions for the race distances. For time to exhaustion in the 1- to

10-min range, the log-log model appears to be appropriate and superior to the critical-power model. For longer times the critical-power model is theoretically inappropriate, and more research is needed to determine whether the log-log model will be suitable. Further research should investigate the reliability of predicted time trial times to actual measured time trials.

CHAPTER 6: CHANGES IN RUNNING ENDURANCE PERFORMANCE FOLLOWING INTERMITTENT ALTITUDE EXPOSURE SIMULATED WITH TENTS

This chapter comprises the following paper submitted to European Journal of Sport Science: Hinckson, E. A., & Hopkins, W. G. (2004). Changes in running performance following intermittent altitude exposure simulated with tents. Manuscript submitted for publication.

SUMMARY

The effect of intermittent hypoxia on sea level endurance performance was assessed by simulating altitude with hypoxic tents. Eleven male competitive runners and triathletes participated in a crossover study of usual training (control) and usual training with altitude exposure (altitude). Altitude treatment consisted of 25 ± 3 days (mean ± SD) of sleeping in tents for 8.1 ± 0.6 $h.d^{-1}$, progressing from a simulated altitude of 2500 m to 3500 m above sea level. Time allowed for the effect to reverse between control and altitude treatments was 4 wk. Three treadmill runs to exhaustion lasting ~2, ~4 and ~8 min were completed 7 and 12 days after control and altitude treatments. Times for standard competition distances (800, 1500 and 3000 m), predicted using a log-log model, improved by 1.0% (90% confidence limits, ±1.3%), 1.4% (±1.2%) and 1.9% (±1.5%) respectively. Improvements were greater in the six athletes with an I allele for angiotensin converting enzyme (ACE): 2.3% (±1.5%), 2.2% (±1.5%), and 2.1%, (±2.1%) respectively. Effects of altitude on haemoglobin concentration were unclear. Altitude exposure simulated with hypoxic tents is likely to enhance performance substantially in middle-distance endurance running events, especially for athletes with an I allele of the ACE gene.

INTRODUCTION

There is reasonable evidence that exposure to natural altitude using the “live high-train low” method (<16 $h.d^{-1}$ at ~2500 m) enhances endurance performance at sea level (Levine & Stray-Gundersen, 1997; J. Stray-Gundersen, Chapman, R. F. and Levine, B. D., 2001). With this method, athletes reside at moderate altitude to harness its benefits and commute to train near sea level to avoid compromising training intensity. Because

such an arrangement is not available in many countries, athletes have the alternative to live at simulated altitude under normobaric or hypobaric conditions and train at sea level.

Several devices have been used to examine the effect of simulated altitude on sea level performance. Researchers investigating the use of apartments, houses or tents to provide normobaric hypoxia (C. J. Gore et al., 1999; Ingham et al., 2001; Mattila & Rusko, 1996; A. Nummela & Rusko, 2000; Piehl Aulin et al., 1998; A D Roberts et al., 2003) have observed changes in sea level cycling and running performance ranging from trivial to 3.7% improvement. With hypobaric chambers (Meeuwsen et al., 2001; F. A. Rodriguez et al., 1999; F. A. Rodriguez, Murio, & Ventura, 2003; F. A. Rodriguez et al., 2004) changes in endurance cycling performance were either trivial or small, but sprint cycling performance improved by 5.0%. Outcomes from studies of hypoxic inhalers (Frey et al., 2000; Hellemans, 1999) range from little effect to improvements in performance of ~3%. Many of these findings are still only in abstract form, so the effects of the various methods of hypoxic exposure on performance of different durations are still unclear. Also unclear are the potential mechanisms for any enhancements in performance. Some researchers attribute enhancements following natural altitude exposure to erythropoiesis (Levine & Stray-Gundersen, 1997), which would increase aerobic power. Other researchers have attributed enhancements following simulated altitude exposure to increases in anaerobic power (C. J. Gore et al., 2001; Hendriksen & Meeuwsen, 2003; Mizuno et al., 1990; A D Roberts et al., 2003; Saltin et al., 1995).

The present study was undertaken to investigate the effect of altitude exposure simulated with tents on running performance over middle-distance durations differing substantially in the contribution of aerobic and anaerobic power. Competitive runners participated in the study, and performance was assessed over standard competition distances of 800, 1500, and 3000 m. The relationship between changes in performance and the athletes' genotype for angiotensin converting enzyme (ACE) was also investigated. The ACE gene appears to have a role in adaptation to altitude and training: high altitude mountaineers are more likely to carry the I allele than the general population (Montgomery et al., 1998), and mountain climbers carrying the II genotype showed less arterial oxygen desaturation with ascent to high altitude (Woods, Pollard et

al., 2002). Whether this association is due to some direct effect of the ACE gene or other genes in close proximity to the ACE locus is unclear.

METHODS

Subjects

Five hypoxic tents were available, so 10 athletes were recruited for a crossover study. Three athletes withdrew from the study because of illness, injury, or lack of time. An additional cohort of five athletes was recruited. Data for one athlete were excluded from the analysis because he participated in competition the day before testing. The final sample consisted of 11 male runners and triathletes (age 31 ± 9 y, height 178.2 ± 9.7 cm, body mass 72.9 ± 6.1 kg, mean ± standard deviation) of regional, national and international competitive level. None was suffering from illness or injury that would interfere with normal training and competition. The athletes' current best competitive performance speed as a percent of world record speed in the 800-10,000 m was 81 ± 7 s. Athletes provided written informed consent and participated with the approval of the institutional ethics committee.

Experimental design

For the crossover design athletes either received altitude exposure using hypoxic tents and performed daily training near sea level (the altitude treatment) or continued usual training without exposure to altitude (the control treatment) for four weeks. Time for the reversal of the effect between control and altitude treatments was four weeks based on previous data from a preliminary study.

Familiarisation tests were conducted one to two days prior to the first altitude or control treatment. Performance tests were conducted seven days following either treatment and repeated five days later to improve precision of the estimate. Venous blood was sampled at four weeks before the first treatment, then 1 week before and 1-7 days after altitude and control treatments. The experimental design of the study and timing of performance tests is shown in Figure 6.1.

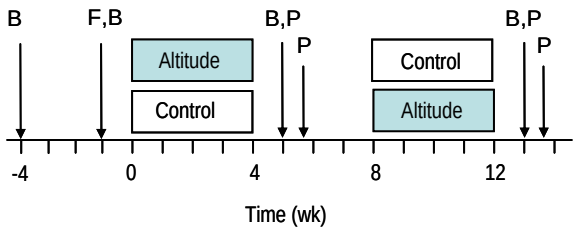

Figure 6.1. Experimental design for the crossover study, indicating duration of the altitude-exposure and control conditions. Labels on the arrows indicate blood tests (B), familiarisation for the performance (F) and performance tests (P).

Performance tests

Changes in performance were monitored with runs to exhaustion on a treadmill (Powerjog M30, Biddeford, Maine). A laboratory-based test was chosen because changeable weather conditions in the region would compromise reliability of outdoor time trials, and there was no indoor track facility available. Runs to exhaustion at constant speed were chosen, because these and other constant-power tests are amongst the most reliable endurance tests (Hopkins et al., 2001). Treadmill calibration (as described in Adams, 2002) was conducted twice, prior to pre and post testing. Each test consisted of three runs to exhaustion at different speeds to permit prediction of performance times for standard competition distances, as suggested by Hopkins et al. (2001). In preparation for this study, the reliability of the predicted times derived from runs to exhaustion was investigated to confirm high reliability (Hinckson & Hopkins, 2004). Athletes completed three runs to exhaustion lasting ~2 min, ~4 min and ~8 min with 30 min rest between runs at a fixed slope of 1.5%. All athletes performed a familiarisation test to determine the appropriate speeds necessary to elicit exhaustion for the required durations. The speeds for the different durations were held constant for each athlete for all subsequent tests. At termination of each run to exhaustion arterial oxygen saturation was measured with a pulse oximeter (see below) as a potential predictor of individual responses, because desaturation in exercise is linked to hypoventilation (Dempsey et al., 1971), and differences in ventilatory control could account for individual responses. The variable examined as a potential predictor was the saturation at the end of the longest control run and the mean saturation at the end of

all three control runs. While the use of a pulse oximeter was convenient following exercise testing, it only provided a conservative estimation of oxygen saturation. Movement, the time it took for a signal to register and poor perfusion could have potentially interfered with the acquisition of accurate data (Yamaya et al., 2002).

Times for standard competition distances (800, 1500 and 3000 m) were predicted from each set of three runs to exhaustion via a log-log model, $\log(T) = k\log(D) + c$, where T is exercise duration, D is the distance run, and k and c are constants. In Study 3 (Hinckson & Hopkins, 2004), 5-d test-retest reliability of the predicted times, expressed as coefficients of variation, were 1.1%, 1.2%, and 1.8% (90% confidence limits; ×/÷1.3) for 800, 1500 and 3000 m respectively.

Training

During the course of the study, athletes maintained their fitness as they transitioned from cross-country to summer events. Each athlete kept specially prepared detailed daily training diaries in which they recorded session duration (minutes), session intensity (5-point scales: 1=easy, 2=steady, 3=mod-hard, 4=hard and 5=very hard), and quality of sleep (5-point scale: 1=very good, 2=good, 3=average, 4=bad and 5=very bad). Means and standard deviations were calculated for the athletes' average weekly training for the altitude and control training periods.

Hypoxic tents

The tent unit consisted of a tent and a generator (HYP 100, Hypoxico, New York). The unit simulated an altitude of 2500 m by reducing oxygen concentration in the air flushed through the tent. The generator allowed gradual adjustment of the gas mixture from 2500 m to 3500 m by the end of the fourth week of exposure as the athletes became acclimatised to the stimulus. Prior to the study, altitude level achieved in all tent units was evaluated following at least an hour of operation at the lowest and highest settings by measurement of percent oxygen content with a portable oxygen analyzer (Metamax 3B, Cortex, Germany).

Each athlete was encouraged to aim for a total of 10 hours in the tents per day for four weeks by including an extra session during the day along with the overnight session

whenever possible. This regime of exposure was the most that the athletes would be expected to adopt, and on the basis of previous studies (Ingham et al., 2001; Laitinen et al., 1995; Mattila & Rusko, 1996; H. K. Rusko et al., 1999) it seemed likely that it would improve performance substantially.

Athletes received altitude exposure at their homes and monitored their own blood oxygen saturation via pulse oximeters (Onyx, Plymouth, MN; accuracy claimed to be a standard deviation of ±2 units of percent saturation for saturations of 70-100%) applied to the index finger at the beginning and end of each session in the tent.

To ensure progressive acclimatisation to the hypoxic stimulus and to account for individual hypoxic ventilatory response (Terblanche, Fahlman, Myburgh, & Jackson, 2004) target saturations for Weeks 1-4 ranged from 88-92%, 84-88%, 80-84% and 76-80% respectively. At the end of each session, athletes recorded in their training diaries the duration of the session (hours and minutes), oxygen saturation (%), and perception of nausea, headaches and hard breathing (5-point scales: 1=none, 2=low, 3=medium, 4=high and 5=severe). Seven of the 11 athletes recorded their exposure data in a training diary, the remaining four provided data through a subsequent interview process due to their non-compliance with the training diary to the required level of detail.

Blood tests

Previously, researchers reported substantial changes in haemoglobin concentration with intermittent exposure to altitude (Levine & Stray-Gundersen, 1997; F. A. Rodriguez et al., 1999), hence these measurements were incorporated in our study. Subjects were seated for five minutes and venous blood drawn from the antecubital vein was collected in a 5 ml EDTA tube, 1-7 days following exposure. Venous stasis (tourniquet application) was kept to a minimum. Blood samples were analyzed at a haematology laboratory (Middlemore Hospital, Auckland) for the determination of haemoglobin concentration, haematocrit and ferritin concentration. Haemoglobin and haematocrit were determined by the coulter method (Beckman Coulter GEN-S analyser, Fullerton, USA) in which number and size of cells are determined by changes in electrical resistance when a red blood cell in a conduitive liquid goes through a small aperture. The packed red cell volume (heamatocrit) was a calculated parameter (PCV= mean cell volume x red blood cell/1000). Ferritin was analysed using microparticle enzyme

immunoassay technology (Abbott Diagnostics Axsym, Illinois, USA). With this method ferritin is bound to microparticles, incubated, washed, hydrolysed and the rate at which the hydrolysed product is generated, which is proportional to the concentration of ferritin, is measured by fluorometry.

Stray-Gundersen et al. (1992) showed the importance of adequate iron stores for the increase in red cell mass with altitude exposure. Therefore, ferritin was assayed four weeks before altitude exposure to ensure each athlete's concentration was above 20 $ng.ml^{-1}$. Athletes below this value were supplemented daily with iron tablets (Ferro-Gradumet, Abbott Laboratories, Lower Hutt, New Zealand). Each tablet contained 325 mg of anhydrous ferrous sulphate. One athlete received iron supplementation.

Genomic DNA was extracted (Miller et al., 1988) from peripheral venous blood samples. ACE genotype was determined by polymerase chain reaction (PCR) with three primers to distinguish the ACE insertion/deletion polymorphism. As described previously (Evans et al., 1994), PCR was carried out for 30 cycles in a Corbett PC-960 air-cooled thermocycler (Corbett Research, Sydney, Australia) using 50 pmol of primers ACE1 and ACE3 and 15 pmol primer ACE2, with an annealing temperature of 57°C. Amplification products were visualised after electrophoresis in 5% (w/v) Metaphor agarose gels (FMC Bioproducts, Biolab Scientific Limited, Christchurch, New Zealand).

Statistical analyses

Most analyses were performed with the Statistical Analysis System (Version 8.2 SAS Institute, Cary, NC). Prediction of times for standard competition distances via the log-log model were performed with a regression procedure (Proc Reg) (Hinckson & Hopkins, 2004). Predicted times were then log transformed for further repeated-measures analyses to reduce non-uniformity of error and to express effects as percent changes (Hopkins et al., 2001). The repeated-measures analyses were performed with a mixed-modelling procedure (Proc Mixed). Fixed effects were treatment (two levels, control and altitude), order (two levels, first treatment and second treatment), and their interaction. The treatment effect provides the estimate of the effect of altitude on performance time while the order effect and the interaction controlled for any overall changes in performance due to seasonal or training effects. Random effects were the

identity of the athletes, the residual (representing error of measurement between the tests separated by five days), and a variable representing additional within-subject variation due to the altitude treatment (athlete*xvaralt where athlete = athlete identity and xvaralt = 1 for altitude and 0 for control). The term athlete*xvaralt includes variance due to within-subject variation attributable to random changes in performance over the seven-week period.

Proc Mixed provided the value for each athlete's individual response, which was plotted against potential predictors (total hours of exposure to altitude and arterial oxygen saturation following the control treatment), with points identified by ACE genotype. Another potential predictor was athlete ability, which was provided by the solution for the random effect for athlete identity in the mixed model for each of the competition distances. Only the ACE genotype showed a substantial relationship with individual responses, so this effect was quantified by including an additional fixed effect, the interaction of treatment with ACE genotype (two levels, II or ID, and DD).

To compare the extent to which predicted times for 800 and 3000 m differed, their difference was analyzed via the paired t statistic using a spreadsheet. (For those athletes who performed two tests post altitude or post control five days apart, the predicted times were averaged.)

To make inferences about true (population) values of the effect of altitude on performance, p values and statistical significance were not used. Instead, uncertainty in the estimate of changes were presented as 90% confidence limits and as likelihoods that the true value of the effect is a substantial enhancement or impairment (Hopkins, 2002). A substantial enhancement was assumed to be a reduction in performance time of more than 0.5% and a substantial impairment to be an increase in performance of more than 0.5% (Hopkins & Hewson, 2001).

RESULTS

The characteristics for the eleven athletes who completed the requirements of the study are shown in Table 6.1.

Table 6.1. Characteristics and baseline data of the 11 athletes who completed the study.

	Mean ± SD
Age (y)	31 ± 9
Body mass (kg)	72.9 ± 6.1
% World Record	
800 m	83.5 ± 4.9
1500 m	84.7 ± 4.1
3000 m	81.8 ± 3.8
Training ($h.wk^{-1}$)	7.1 ± 3.0
Baseline blood parameters	
Haemoglobin ($g.L^{-1}$)	153 ± 11
Haematocrit (%)	45.1 ± 3.4
Reticulocytes ($10^9.L^{-1}$)	43 ± 13
Ferritin ($\mu g.L^{-1}$)	72 ± 62

Mean weekly training duration was 6.8 ± 3.6 $h.d^{-1}$ and 7.1 ± 3.0 $h.d^{-1}$ (mean ± SD) during altitude and control treatments respectively. During altitude treatment, athletes spent 16%, 20%, 32%, 25% and 8% in easy, steady, moderate hard, hard and very hard intensity of training; during control treatment the athletes spent 6%, 23%, 23%, 17% and 8% of their training in these respective intensities. Athletes completed an average of 8.1 ± 0.6 $h.d^{-1}$ in the tents over 25 ± 3 d. On questioning, athletes reported difficulty in reaching the target daily exposure because of work, training and family commitments. Weekly mean percent oxygen saturation was 89 ± 3. Mean hard breathing, nausea and headache during altitude treatment were recorded as “none” or “low”, and sleep quality was “good” in both altitude and control conditions.

The effects of altitude exposure on predicted performance times over standard competition distances (800, 1500 and 3000 m) are shown in Table 6.2. Also shown are the effects of altitude exposure when ACE genotype is taken into account. The mean effect for all athletes showed an overall improvement in the predicted times; however, athletes with either the II or ID allele showed greater improvements than those with the DD allele especially for the shorter distance.

Table 6.2. The effects of altitude exposure on performance over standard competition distances for all athletes and for subgroups with II or ID allele and DD allele of the ACE gene. Percent changes in constant-distance time-trial times, when times are predicted for three standard competition distances from each athlete's set of three runs using the log-log model.

	Observed effect (%) and 90% likely limits	Likelihood (% and qualitative) that the real effect is a substantial[a] improvement or impairment	
		improvement	impairment
All athletes			
800 m	-1.0; ±1.3	76; likely	3; very unlikely
1500 m	-1.4; ±1.2	90; likely	1; very unlikely
3000 m	-1.9; ±1.5	94; likely	1; very unlikely
3000 vs 800 m	-0.8; ±1.2	67; possibly	4; very unlikely
ACE subgroups: 800 m			
II/ID	-2.3; ±1.5	98; very likely	0.3; almost certainly not
DD	0.3; ±1.6	16; unlikely	40; possibly
II/ID vs DD	-2.6; ±2.1	95; very likely	1; very unlikely
ACE subgroups: 1500 m			
II/ID	-2.2; ±1.5	97; very likely	0.5; very unlikely
DD	-0.4; ±1.7	46; possibly	17; unlikely
II/ID vs DD	-1.8; ±2.3	84; likely	5; very unlikely
ACE subgroups: 3000 m			
II/ID	-2.1; ±2.1	90; likely	3; very unlikely
DD	-1.6; ±2.3	80; likely	7; unlikely
II/ID vs DD	-0.5; ±3.2	29; possibly	50; possibly

[a]Assuming the smallest substantial change in performance time is 0.5%

Individual responses of altitude exposure expressed as standard deviation about the mean effect of exposure were 1.0% (90% confidence limits, -2.3, 2.8), 1.6% (-1.3, 2.6) and 1.0% (-2.4, 2.8) for the 800, 1500 and 3000 m respectively. An example of the relationship between each athlete's individual response (derived from the random effect representing individual responses in the mixed model) and potential predictors (ACE genotype and hours of exposure for the 1500 m performance) is shown in Figure 6.2. The effect of ACE genotype on the response to hypoxic exposure is evident in this

figure, but hours of exposure had little apparent relationship with the response. Similar plots showed little effect of athlete ability or arterial saturation at the end of the control runs on the response to hypoxic exposure (data not shown: see Appendix S for plots of athlete ability).

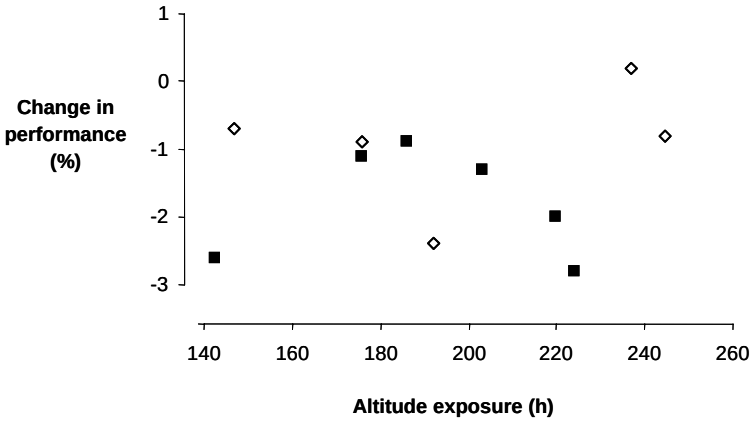

Figure 6.2. Individual responses to altitude for predicted 1500-m time-trial time, hours of altitude exposure, and ACE genotype (◇ DD, ■ II or ID) for each athlete.

The percent seasonal effect on performance (the change in performance between the first and second treatment conditions) was an enhancement of 1.6, 1.7 and 1.8% in the 800, 1500 and 3000 m times, respectively (90% confidence limits, ± 1.3%). These effects were controlled for in the above analysis of the effects of the altitude treatment. Error of measurement for repeated tests five days apart in the three competition distances expressed as coefficients of variation were 1.6, 1.1 and 2.0% for the three distances respectively (×/÷1.7).

There was a decrease in mean values for haemoglobin concentration and haematocrit a week following altitude treatment. Percent mean changes were -3.3 (90% confidence limits, ±3.6) and -3.1 (±3.0) respectively.

DISCUSSION

The principal finding of this study was that in well trained endurance runners, times predicted for 800-3000 m from runs to exhaustion improved by a mean of ~1-2%

following three to four weeks of “live high-train low” exposure in hypoxic tents. The uncertainty in the mean effect was such that substantial improvements in performance were likely and impairments in performance were very unlikely. There appeared to be no technical problems or variability in motivation of the athletes in relation to the performance test, because errors of measurement in the present study were similar to those in a reliability study (Hinckson & Hopkins, 2004), which was performed during a similar phase of training and competition, and with athletes of similar calibre.

These results agree with those of other researchers who found substantial improvements in cycling, running or swimming performance lasting ~1-10 min at sea level following exposure to intermittent hypoxia. Hellemans (1999) observed an ~3% increase in cycling power, Roberts et al. (2003) observed a 3.7% increase in 4-min cycling power while Rodriguez et al. (1999) observed a substantial drop in lactate at a fixed sub-maximal workload on a cycle ergometer that would be consistent with an enhancement of endurance performance. Improvements were also reported for sea level running, cycling or running performance lasting <1 min following exposure to hypoxia. Nummela and Rusko (2000) observed a 0.8% improvement in 400-m running performance while Meeuwsen et al. (2001) reported a 5% increase in power output in a 30-s all-out test on a cycle ergometer. Most recently the data of Rodriguez et al. (2004) showed some substantial improvements in 100- and 400-m swimming performance and a substantial impairment in 3000-m running performance, but the true effects were unclear. This study represents a more systematic attempt to compare the performance effects of hypoxic exposure on endurance running performance of several durations. The effect on 3000-m performance was possibly better than that on 800-m and was very unlikely to be worse. More studies are needed to confirm the effect of simulated altitude exposure on sea level running performance of various durations.

The only potential physiological mechanism investigated in this study was the change in haemoglobin concentration and haematocrit. An increase in these parameters would be consistent with improvements in performance being due to increases in oxygen-carrying capacity of blood. However, decreases were observed in this study. Unfortunately, even automated haematocrit measurements have a source of variability. The electrical impulse produced by the cell is only approximately proportional to the volume of the cell and some of the “noise” impulses do not actually represent cell size (d'Onofrio, 2001). In addition, haematocrit is sensitive to changes in plasma volume, as well as red

cell volume. According to Thirup (2003) normal within subject variation would be as high as 3% but the variation among athletes could be even greater due to training. For these reasons, haematocrit might not the best parameter for red cell quantitative assessment. Haemoglobin on the other hand is a better measurement and represents more directly the oxygen carrying capacity of blood. Nevertheless, the results of this study are consistent with those in a recent study by Hendriksen and Meeuwsen (2003), whose data showed a net 3.6% decline in haemoglobin concentration and a 6.5% decline in haematocrit nine days following exposure to hypobaric hypoxia. Others have observed either an increase (Hamlin & Hellemans, 2004; Hellemans, 1999) or little change (Casas et al., 2000; Frey et al., 2000; Piehl Aulin et al., 1998; F. A. Rodriguez et al., 1999; M. J. Truijens et al., 2003; Vallier et al., 1996) 7-12 days post-exposure.

Several investigators (Ashenden, Gore, Martin et al., 1999; Friedman, Jost, Rating, Mairbaurl, & Bartsch, 1996; C. Gore et al., 1998; Levine & Stray-Gundersen, 1997; Levine et al., 1991; H. K. Rusko et al., 1999; Saunders et al., 2004; J Stray-Gundersen et al., 2004; Svedenhag, Saltin, Johansson, & Kaiijser, 1991) have addressed the issue of the role of oxygen-carrying capacity in adaptation to hypoxic exposure using the more direct measures of red cell volume (via the Evans blue dye technique) or haemoglobin mass (via the carbon monoxide rebreathing technique). In studies conducted at natural altitude researchers have either observed an increase (Levine & Stray-Gundersen, 1997; Levine et al., 1991) or a decrease (Friedman et al., 1996) in red cell volume, or no change in haemoglobin mass (C. Gore et al., 1998; Svedenhag et al., 1991). Equally conflicting are the data from studies at simulated altitude. Ashenden et al. (1999), Saunders et al. (2004) and Stray-Gundersen et al. (2004) reported little change in haemoglobin mass, while Rusko et al. (1999) reported a substantial increase in red cell mass. The errors of measurement with these techniques, especially the Evan's Blue methods, are apparently too large (5-10%) to track the small changes in blood parameters that would account for the small changes in endurance performance induced by hypoxic exposure (CJ Gore and WG Hopkins, unpublished observations). The uncertain outcomes from these assays combined with logistical difficulties in setting them up in our laboratory prevented us from using either method in our study.

Although VO_2max was not quantified, an obvious mechanism linking an increase in oxygen-carrying capacity and enhancement of endurance performance following hypoxic exposure is an increase in maximal oxygen consumption. In studies of

intermittent hypoxia some authors have reported improvements in VO_2max of 1-5% with related increases in blood parameters (W. D. B. Hiller et al., 2000; Levine et al., 1996; Levine & Stray-Gundersen, 1997; Levine et al., 1991; H. K. Rusko et al., 1999; J. Stray-Gundersen, Chapman, R. F. and Levine, B. D., 2001). It is possible however, that hypoxic exposure induces increases in VO_2max mediated not by changes in oxygen carrying capacity of the blood but by some other mechanism. Indeed, there have been several studies showing improvements in VO_2max without concomitant changes in blood parameters: Meeuwsen et al. (2001), and Hendriksen and Meeuwsen (2003) reported 7% and 1.9% enhancements in VO_2max respectively, while others reported non-significant increases of 1.3-2.4% (F. A. Rodriguez et al., 2004; Vallier et al., 1996). Frey et al (2000) reported little to no changes in both VO_2max and blood parameters following 21 d, 75 $min.d^{-1}$ at 6440 m. Similarly Piehl Aulin et al.(1998) reported little change after 10 d, 12 $h.d^{-1}$ at 2000 or 2700 m. Truijens et al (2003) also saw little changes after 22 min three times a week for 5 weeks inspiring 15.3% oxygen fraction. The inconsistencies between these studies could be due to error of measurement in VO_2max (~2-3%) or the method used to measure blood parameters (5-10%), especially when changes are small. If the observed changes in VO_2max from the above studies are real and independent of changes in blood parameters, a possible mechanism that could explain increases in VO_2max is a change in vascular regulation through activation of HIF-1 that plays a critical role in the responses of the cardiovascular system (Semenza, 2004), resulting in greater delivery of blood and therefore oxygen to active muscle.

Regardless of whether there is an increase in VO_2max with hypoxic exposure, enhancement of endurance performance could be mediated in two other ways: enhancement of exercise economy (which represents an increase in power output for the same oxygen consumption) or an enhancement of anaerobic threshold as a percent of VO_2max (which represents greater power output for the same development of fatigue). Increases in exercise economy have been reported in some studies of hypoxic exposure. Saunders et al. (2004) reported a 3.3 % reduction in oxygen consumption at sub-maximal workloads, Gore et al. (2001) observed a 4.4% reduction and Katayama et al. (2003) reported significant reduction in oxygen uptake during submaximal exercise. Truijens et al. (2004), however, reported no significant effect in sub-maximal economy in runners and swimmers, although their data imply a likely improvement of ~1.6%. Piehl Aulin et al. (1998) also reported no significant change in economy, but they did not show relevant data. In studies where hypoxic exposure occurred at natural altitude,

Green et al. (2000) reported a 4.5% reduction in oxygen uptake during sub-maximal exercise, while Levine et al. (1991) and Wolfel et al. (1991) reported no significant changes. Overall, it seems likely that there is an enhancement in exercise economy with hypoxic exposure. Suggested mechanisms for improved economy are a shift from fat to carbohydrate oxidation or reduced energy requirement during muscle contractions due to metabolic adaptations (C. J. Gore et al., 1999; Saunders et al., 2004).

The other potential mechanism for improvement in endurance performance could be changes in the anaerobic threshold. In the only study of hypoxic exposure in which anaerobic threshold was expressed as a percent of VO_2max, Casas et al. (2000) reported a substantial increase in the anaerobic threshold in elite climbers. Others who studied one-legged training in hypoxia have reported changes in enzymes of energy pathways that could result in changes in anaerobic threshold and performance (Melissa et al., 1997; Terrados et al., 1990).

As already noted, our data are consistent with those of authors who observed improvements in short duration exercise. Such improvements could be mediated through increases in power output generated anaerobically. Although there are several possible mechanisms for such an effect, authors have focused on increases in muscle buffering, which would reduce fatigue associated with decreases in pH. Mizuno et al. (1990) saw an increase in muscle buffering capacity in elite cross-country skiers who lived at 2100 m and trained at 2700 m. Gore et al. (2001) observed an increase in muscle buffering capacity in cyclists who lived high but trained close to sea level. Roberts et al. (2003) saw an increase in maximal accumulated oxygen deficit (9.6%), which they suggested could be due to an increase muscle buffering capacity. Clark et al. (2000), however, did not observe a change in buffering capacity following intermittent hypoxia; they also saw a decrease in peak lactate concentration, which is not consistent with an increase in muscle buffering capacity. If the increases in muscle buffering are real, they could be due to increases in muscle phosphocreatine or dipeptide carnosine concentration (Abe, 2000; Parkhouse et al., 1985; Sahlin & Henriksson, 1984), but the precise mechanism has not yet been identified.

It could be argued that the changes in performance observed in this study were due to a placebo effect, because athletes were not blind to the treatments. Performance effects from a crossover design are less likely to be biased by a placebo effect than those of a

controlled trial. Athletes participating in a crossover have the opportunity to test the suitability of the treatment on their performance, hence motivation during performance following treatment and control conditions are expected to be similar. The association of performance with the ACE genotype also represents some evidence that the effect in performance was not simply a placebo effect.

There was some evidence for individual responses in performance, and the ACE genotypes accounted partly for these in the predicted 800 and 1500 m and to a lesser extent in the 3000 m. However, the genotypes were separated in the analysis in a manner that provided the largest difference between groups (II/ID vs DD). Hence, it is possible that the apparent effect was at least partly due to sampling error in our small sample of athletes. Further research is warranted, since no other studies have investigated the effect of ACE gene using the "live high-train low" method on sea level performance. The other three potential predictors of individual responses that we investigated—arterial oxygen saturation in the exercise test, duration of exposure to altitude, and athlete ability (See appendix S)--did not show substantial relationships with performance. Until a larger sample is investigated, the possibility that these variables have some substantial effect cannot be excluded. Duration of exposure could also be deliberately manipulated to determine its effect. In the one study in which this was attempted (A D Roberts et al., 2003), there was apparently little difference between 5, 10 and 15 days of exposure, but the lack of p values or confidence limits in the paper precludes any useful assessment of the uncertainty of the differences. In any case, longer studies of longer duration of exposure are warranted.

CONCLUSIONS

- Hypoxic tents provide a 1-2% improvement in running performance for athletes involved with events lasting ~2 to 10 min.
- ACE genotype may account for individual responses due to altitude in performances of ~2 to 5 min duration.
- Inconvenience and expense of the tents warrant further evidence of benefit before they can be recommended for improvement of endurance performance.

CHAPTER 7: GENERAL DISCUSSION

In this section the results of the three studies will be discussed in terms of their implications for coaches and their athletes. In later sections the implications for sport scientists, (de)limitations, conclusion and recommendations will also be presented.

SIMULATED ALTITUDE EXPOSURE: DOES IT WORK?

Athletes who dominate middle and long distance running events have often been born or raised at altitude. For this reason, runners worldwide believe that some form of altitude training will benefit their sea level performance. The magnitude of the altitude benefit however, and the best way to achieve it are somewhat unclear to athletes and coaches.

In recent years, a new approach termed ""live high-train low"" has been developed, in which athletes can live at moderate altitude for ~16 $h.d^{-1}$ to gain the benefits and train near or at sea level so that training intensity is not compromised. It is generally accepted among scientists that the "live high-train low" method at natural altitude improves endurance running performance by 1-2%. However, facilities to accommodate this arrangement are not available in most countries hence athletes are willing to invest in devices that simulate altitude.

Anecdotal evidence suggests that athletes who have used hypoxic devices improved their competitive performance more than those who engaged only in sea level training. However, researchers who investigated the effect of simulated altitude exposure on endurance performance using the "live high-train low" method via a variety of hypoxic devices have provided little and confusing information. For this reason several studies were undertaken to investigate the effect of hypoxic tents on sea level endurance performance in runners.

IMPLICATIONS FOR COACHES AND ATHLETES

Magnitude of the effect

Athletes ranging from club to national level should expect an improvement in endurance running performance following altitude exposure using the “live high-train low” method with the hypoxic tents in the order of 1-2%. In elite athletes, the smallest enhancement in performance that has a substantial effect on their chance of winning a medal is about one third of the typical variation of performance in competitions (Hopkins et al. 1999). Hence, elite athletes need to be concerned with changes in performance of the magnitude of ~ 0.5% in middle and long distance events. The magnitude of the effect observed following exposure to hypoxic tents is potentially substantial for an elite athlete.

Competing post altitude

Athletes should compete within a week following exposure to hypoxic tents. Improvements in performance are unlikely four and eight weeks following exposure. Therefore, more than one exposure per year will be necessary depending on the athlete’s competitive schedule. Athletes and their coaches must plan the exposures ahead of time to ensure maximum benefit.

Protocol

Altitude in the tents is achieved by diluting the concentration of oxygen in the air with more nitrogen. The recommended time to spend in the tent is at least 8-10 hours overnight combined with supplementary daytime sessions for a total exposure period of approximately four weeks. The initial altitude level is 2500 m and which is progressively increased to approximately 3500 m during the last week of exposure.

While in the tent, athletes need to monitor their percent oxygen blood saturation via a pulse oximeter to ensure progressive acclimatisation to altitude. The oximeter is a small device that can be purchased commercially and it is applied to the index finger. The pulse oximeter shines infrared and red light through the tissue to determine oxygen saturation. At sea level arterial oxygen saturation at rest ranges from 98-100%. As altitude increases arterial oxygen saturation decreases. The athlete is advised to begin at 88-91% and progressively increase altitude level as acclimatisation occurs. During the last week of exposure athletes should focus on bringing their saturation close to 80% but not below 76%. However, differences in individual hypoxic ventilatory response to

the hypoxic stimulus may influence blood oxygen saturation levels and may differ from the recommended ranges.

Symptoms during exposure

During exposure sleep quality is good and the incidences of hard breathing, nausea and headaches are low to none. Overall fatigue during exposure may increase slightly.

Individual responses

Any coaches considering hypoxic exposure as part of their annual training plan, should realise that some athletes may not benefit from the experience due to individual responses to altitude. A potential predictor of individual responses is the angiotensin converting enzyme (ACE) genotype. The ACE gene comes in two forms—I (for insertion) and D (for deletion)—and individuals carry one of the three copies of the genotype (II, ID or DD). It has been previously shown that the II genotype is more prevalent among competitive athletes of endurance sports than in the general population. The I form of the genotype has also been associated with altitude exposure. On the basis of the results from this study athletes having the II or ID genotype may respond better to altitude exposure than those with the DD genotype. The answer is not definitive and more studies are necessary to substantiate these results.

Haematological changes

Values for haemoglobin concentration and haematocrit (% red blood cells) decrease following hypoxic exposure at least in our study. An increase in these parameters would be consistent with improvements in performance due to increases in oxygen-carrying capacity of blood. This decrease in both blood parameters signifies that the mechanism responsible for the improvements in performance observed could be other than blood based. Among others, potential mechanisms include changes in vascular regulation, economy of effort, changes in muscle enzymes or buffering capacity.

Practicality

In general hypoxic tents are easy to assemble and reasonably practical. The accompanying generator is relatively portable, and the tent can be erected over a queen size bed or on the floor. The tents have the potential to become part of the athlete's daily routine, but may disrupt family lifestyle to a degree. The most recent model is less noisy but equally expensive.

IMPLICATIONS FOR SPORT SCIENTISTS

Performance tests

The performance tests chosen to monitor changes in performance were the lactate threshold and time to exhaustion. Surprisingly, the error of measurement of the lactate threshold in the incremental treadmill test was ~3.0% (overall coefficient of variation). With appropriate choice of athletes or modes of exercise, it should be possible to achieve error of measurement in performance closer to 1% (Hopkins et al., 2001), with concomitant reduction in uncertainty in the change in performance. The larger error observed may have been due to a longer duration between tests (four to five weeks), variability in carbohydrate intake, or training employed as compared to that of a reliability study. Even though most of the athletes performed the test on a regular basis the athletes were unreliable in this test. The low reliability is probably an inescapable feature of the lactate test in a practical setting. Hence caution is recommended when using the lactate threshold test to monitor performance changes. The error of measurement of the equivalent time-trial time derived from runs to exhaustion was substantially less (1.9%) than that of lactate threshold. Hence, run times to exhaustion provide a good measure of performance.

Time to exhaustion is a reliable measure of performance, but converting change in time to exhaustion from a single run at one speed into change in time-trial time can only be approximate due to the associated variation observed with the factor used for the conversion. Sport scientists may still wish to use time to exhaustion tests, because of their potential to avoid the problems of self-selection and familiarisation associated with pacing.

For time to exhaustion in the 1- to 10-min range, the log-log model appears to be appropriate and superior to the critical-power model. For longer times the critical-power model is theoretically inappropriate, and more research is needed to determine whether the log-log model will be suitable.

The appropriate speed of a time to exhaustion is determined for the required duration during a familiarisation session. When more than one run to exhaustion is performed it is recommended that athletes rest for at least 30 min between runs. The slope (1.5%) of the treadmill must remain constant during subsequent testing.

Individual responses

There was some evidence for individual responses in performance, and the ACE genotypes accounted partly for these. However, genotypes were separated in a manner that provided the largest difference between groups (II/ID vs DD). It is possible that the apparent effect was at least partly due to sampling error in the small sample of athletes. ACE genotype was chosen as a potential predictor of individual responses because other researchers have observed an association between ACE II genotype and maintenance of arterial oxygen saturation at high altitude (Woods, Pollard et al., 2002). Whether this association is due to some direct effect of the ACE gene or other genes in close proximity to the ACE locus is unclear. Further research is warranted, since no other studies have investigated the effect of the ACE gene using the “live high-train low” method on sea level performance. If indeed ACE is a predictor of individual responses then sport scientists should consider performing DNA testing on their subjects prior to intervention to minimise individual differences to the treatment.

Mechanisms

There was an expectation that improvements in performance would be mediated through improvements in the oxygen carrying capacity of blood due to increases in red blood cell production. Changes in haemoglobin concentration and haematocrit were either small increases or moderate decreases. Others have observed either an increase (Hamlin & Hellemans, 2004; Hellemans, 1999), little change (Casas et al., 2000; Frey et al., 2000; Piehl Aulin et al., 1998; F. A. Rodriguez et al., 1999; M. J. Truijens et al.,

2003; Vallier et al., 1996) or a decrease (Hendriksen & Meeuwsen, 2003) 7-12 days following hypoxic exposure.

If there are no real changes in blood parameters consistent with increases in oxygen carrying capacity, it is possible that the exposure duration or level utilised might not have been appropriate to induce the necessary haematological changes. Rodriguez et al. (1999) showed that small doses of hypobaric hypoxia at 5000 m elicited the expected blood changes, and Rusko et al. (1999) found changes in blood parameters following exposure to hypoxia in a nitrogen house when exposure lasted 16 h per day for four weeks at 2500 m. It could be suggested that athletes would need to spend more than 8-9 per day in the hypoxic tent than experienced in this study to see the expected blood changes.

Measurement of red cell volume (via Evans blue technique) or haemoglobin mass (via carbon monoxide rebreathing technique) would have been more appropriate, however the large error of measurement of the Evan's blue (5-10%) made it unreasonable to proceed with this technique, so as the low reliability of the carbon monoxide breathing devise in our laboratory . When the expected change is in the order of 1-4%, it would be unrealistic to track changes in blood parameters. Until a more reliable method is found, the large errors in these procedures will only provide scientists with unclear results.

Researchers have suggested that other mechanisms unrelated to changes in blood could account for changes in endurance performance with intermittent hypoxia. These potential mechanisms include: (a) change in vascular regulation; (b) enhancement in exercise economy via a shift from fat to carbohydrate oxidation (C. J. Gore et al., 2001) or reduced energy requirement during muscle contractions (S. A. Clark et al., 2004); (c) changes in muscle enzymes; (d) changes in muscle buffering capacity, (e) muscle ion pumps (Fowles et al., 2002; Fraser et al., 2002; H. Green et al., 2000; Huang & Askari, 1982)and (f) hypoxia inducible factor (HF-1). More studies are necessary to determine the mechanism responsible for the observed changes in performance.

(DE)LIMITATIONS

There were some potential weaknesses with the three studies reported in this thesis. Attempts have been made, however to account for these.

- In Study 1, randomisation into control and experimental groups was difficult, because the top athletes had agreed to participate in the study provided that they participated in the experimental group. As a consequence the experimental group consisted of younger and faster athletes than the control group. For that reason, differences in ability and age among athletes were accounted for by including them in the analysis as covariates. To avoid the issue of randomisation in Study 3, a crossover design was employed.

- There was no control for the run time to exhaustion as athletes in the control group were not interested in performing this test. Since the run time to exhaustion test is motivation dependent, it seemed unreasonable to subject the athletes to it. To avoid the issue of motivation in Study 3, a crossover design was employed.

- Blinding was difficult because athletes monitored their own saturation at home. It could be argued that the changes in performance observed were due to a placebo effect. This issue was addressed by employing a crossover design in Study 3. Performance effects from a crossover design are less likely to be biased by a placebo effect than those of a controlled trial. Athletes participating in a crossover have the opportunity to test the suitability of the treatment on their performance, hence motivation during performance following treatment and control conditions are expected to be similar.

- The error of measurement in the lactate test was very high and did not provide a good measure of performance. To avoid the use of an unreliable measure of performance in Study 3, the lactate threshold test was not included in the design.

- A mechanism to explain performance changes was not determined. The methods available for measuring red cell volume and haemoglobin mass were impractical, and beyond the allocated budget. The large error of measurements of the Evan's blue technique (5-10%) made it unreasonable to proceed with this technique. When the expected change is in the order of 1-4%, it would be unrealistic to track changes in blood parameters. A more reliable method is needed.

- Even though a mechanism was not determined, at least individual responses to simulated altitude exposure were investigated. ACE genotype was included in the analysis and accounted partly for individual responses.

- Several devices are capable of simulating altitude. In this PhD thesis the main focus was on the effect of hypoxic tents on sea level performance. The effect of hypoxic inhalers on sea level performance investigated in a pilot study was unclear.

CONCLUSIONS

The overall effects and conclusions from this thesis are outlined below and illustrated in Figure 7.1.

- Exposure to intermittent hypoxia via hypoxic tents using the “live high-train low” method provides a 1-2% improvement in running performance in athletes involved with events lasting approximately 1 to 10 min.

- Performance effects were apparent approximately one week following exposure. Effects on performance were not apparent four and eight weeks later.

- Time to exhaustion is a reliable measure for monitoring performance. When converting time to exhaustion to predicted time-trial time in the 1- to 10-min range, the log-log model appears to be more appropriate than the critical-power model.

- Improvements in running performance following the use of hypoxic tents could not be explained via changes in haemoglobin concentration and haematocrit.

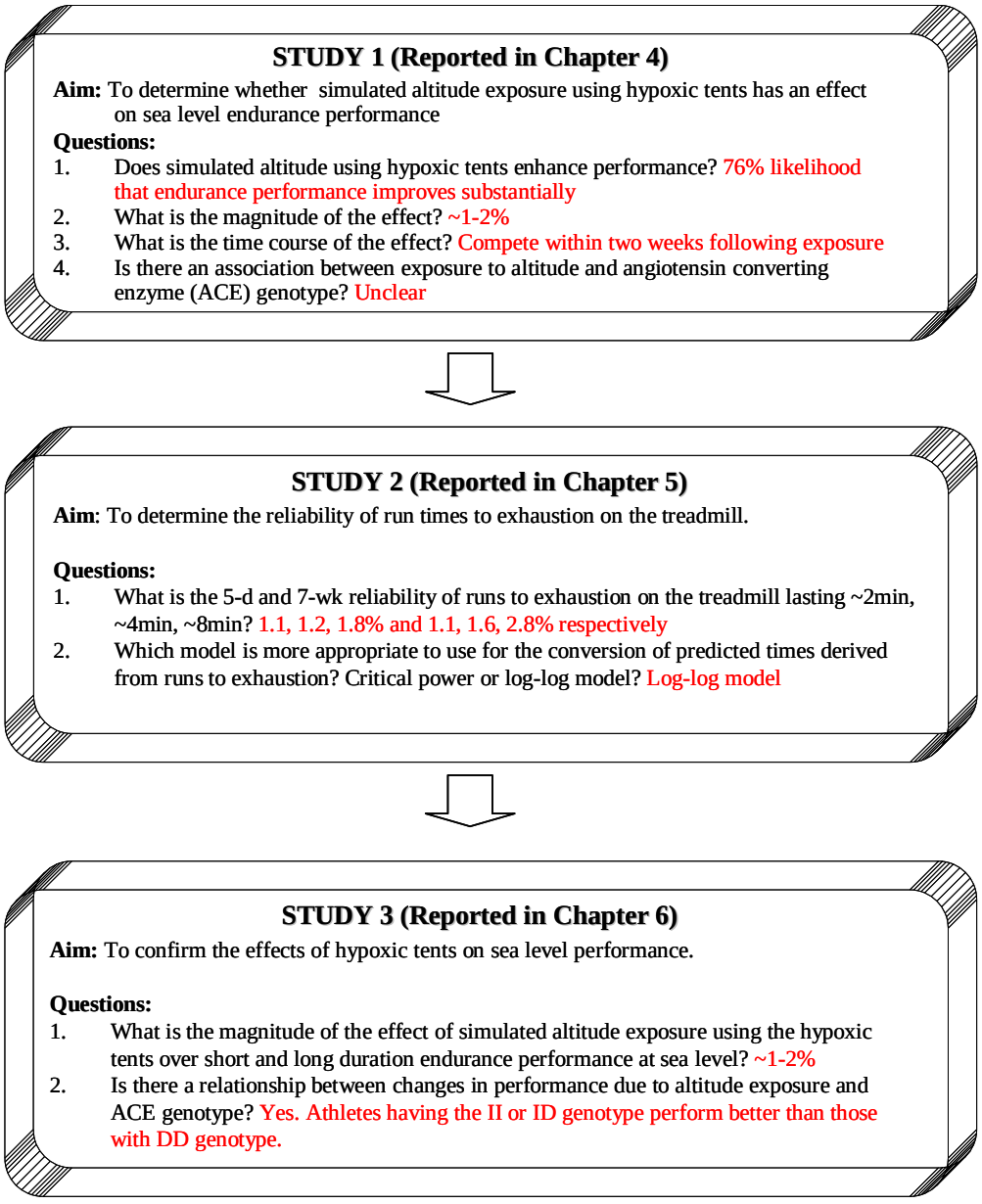

Figure 7.1. The results and conclusions of the three studies.

FUTURE RESEARCH

This thesis reported the effects of simulated altitude exposure via hypoxic tents on sea level performance in competitive and elite athletes. Sea level performance following the use of the hypoxic tents for ~8 $h.d^{-1}$ over ~25 days at 2500 to 3500 m above sea level, improved by 1-2%, however, there was some uncertainty in the estimate. Further studies

investigating the effect of “live high-train low” with the hypoxic tents are recommended as follows:

- The effect of various exposure durations on sea level performance.
- The effect of different exposure levels on sea level performance.
- The effect of hypoxia on blood parameters using CO rebreathing or Evans blue methods. This study may provide a more valid measurement of changes in the blood provided that the methods are made more reliable.
- Effect of the changes in muscle enzymes, vascular regulation or economy of effort with hypoxic exposure on sea level performance. This study would identify a likely mechanism attributable to changes in performance that is unrelated to blood changes.
- The effect of hypoxic exposure on sea level performance of males and females.
- The effect of repeated exposures to maintain improved sea level performance.
- Effect of hypoxic exposure on sea level sprint performance.

This thesis also reported results of runs to exhaustion on a treadmill. It was shown that time to exhaustion is a reliable measure of performance. Predicted times for standard competition distances were determined via log-log and critical power modelling. For time to exhaustion in the 1- to 10-min range, the log-log model was more appropriate to the critical-power model. Further studies investigating runs to exhaustion are recommended as follows:

- Suitability of log-log modelling to predict time trial times from runs to exhaustion lasting more than 10 min.
- The use of at least two runs differing widely in speed analysed with log-log modelling.

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APPENDICES

APPENDIX A: PARTICIPANT INFORMATION SHEET FOR THE ALTITUDE GROUP (STUDY 1)

THE EFFECT OF INTERMITTENT SIMULATED ALTITUDE EXPOSURE ON ENDURANCE PERFORMANCE

INFORMATION SHEET FOR PARTICIPANTS AND COACHES IN THE GROUP RECEIVING ALTITUDE EXPOSURE

Thank you for showing an interest in this project. Please read this information sheet carefully before deciding whether or not to participate. If you decide to participate we thank you. If you decide not to take part there will be no disadvantage to you of any kind, and we thank you for considering our request.

The Aim of the Project

This project is being undertaken as part of the requirement for a Doctorate in Philosophy (Erica Ingham) and a Masters of Science (Chris Bailey).

The major aims of this project are as follows:

a) to enhance performance using simulated altitude exposure (nitrogen tents or masks)

b) to measure the effect of intermittent altitude exposure via performance testing and blood samples

c) to determine effective methods of utilising the tents or masks before a major competition

d) to track the effects or repeated altitude exposure

e) to compare the effectiveness between the tents and the masks

f) to determine whether simulated altitude exposure raises your haematocrit (percent of red cells in your blood) to a limit that would bar you from competing.

Participant Criteria

The participants recruited for this project should fulfil the following criteria:

a) male or female

b) competitive athlete

c) runner participating in 400m, 800m, 1500m, 3000m, or 5,000m events or a cyclist participating in kilo, pursuit, road events, or triathlons.

Exclusion Criteria

The following people will not be allowed to participate

a) anyone suffering from illness or injury that would interfere with normal training and competition

b) anyone who has a haematocrit of 54% or more (males) or 47% or more (females) in the first blood test.

What will Participants be Asked to Do?

As a participant you will be involved with this study for about 36 weeks. During this time you will acclimatise to simulated high altitude and train at sea level for two 12-week cycles. The first cycle will consist of 4 weeks of pre-testing, 4 weeks of altitude exposure and 8 weeks of follow-up. The second cycle will consist of a further 4 weeks of altitude exposure. The benefit gained would be performance enhancement in competitive events.

If you agree to take part in this project, you will be asked to do the following:

Runners: You will receive one of five Hypoxico tents for each period of altitude exposure. These tents are connected to a unit that produces air containing less oxygen than at sea level to simulate an altitude of up to 4200 m. The tents are portable and can be erected on a normal bed, but the unit that removes oxygen from the air may seem noisy and will to be located in another room. You will have an opportunity to try the tent for a day or two several weeks before the study begins, to see if you are likely to be happy using it for periods of 4 weeks. A few people do not get used to the noise.

You will sleep and rest in the tents for a minimum of 10 continuous hours per day. As you become acclimatised in the first two weeks, the simulated altitude will be raised from 2500 m to 3500 m, then to 4200 m, provided that you are not unduly disturbed by symptoms of altitude sickness (see below). The overnight continuous

exposure will be supplemented with at least one daily rest of at least 1.5 hours at 4200 m, the highest altitude the tents can produce.

You will be provided with a portable hemoximeter and you will be required to measure your percent arterial oxygen saturation after you have been in the tent for a few minutes (or after half an hour if the nitrogen-enriching pump is switched on or if the altitude setting is changed when you enter the tent).

No serious discomforts have been reported previously from use of the tents, but **if at any time you feel uncomfortable with any symptoms of altitude sickness (headaches, poor sleep, or feeling sick, dizzy or drowsy), you must exit the tent and contact either Dr Hellemans in Christchurch at (03) 383 6290 or Dr Edwards in Auckland at (09) 528 0561. You must also exit the tent and contact Dr Hellemans if your arterial saturation drops below 77%.** He will discuss any symptoms you might have and make a decision about reducing your altitude or stopping your exposure to altitude. He is happy to be contacted any time at work as above or after hours at (03) 351 6684.

Cyclists: You will visit a clinic for daily or twice-daily 1- to 2-hour sessions breathing air containing less oxygen than normal (down to 9% oxygen, equivalent to an altitude of 6000 m) generated by an *Hypoxicator*. This is a commercially available device.

You breathe through a mask, then breathe normal air alternately for repeated, short periods. The time you have the mask on and the period it will be taken off will be determined by your body's response to the low oxygenated air. This response is monitored by a pulse oximeter, which is comfortably attached to one of your fingers and measures the percent saturation of oxygen in your blood. The oxygen percentage delivered from the mask will be reduced until the percent saturation of the blood is in the range 65-85%. The percent of oxygen in the air will be lowered during the course of the four weeks as you get used to the "simulated altitude".

No serious discomforts have been reported previously from use of the masks, but **if you are unduly disturbed by a headache or by feeling sick, dizzy or drowsy, you must ask to see Dr Hellemans (or if he is not there, the doctor on duty at the clinic).** The staff at the clinic are specialists in this field of study, they are familiar with the Hypoxicator, and Dr Hellemans has used the device himself.

All participants will also do the following:

a) You will give a blood sample every four weeks before and after altitude exposure: three samples before, and three samples after, for two cycles (a total of 9 samples). During each visit to the lab your skinfold thickness will be measured, to track any changes in body fat throughout the study.

b) You will take iron supplements if your initial blood test shows iron deficiency, and you will take iron supplements during the periods of altitude exposure, as prescribed by a sports nutritionist and sports doctor.

c) You will perform a standard incremental test to maximum effort in the laboratory, for measurement of maximum oxygen consumption. (This test will not be necessary, if you have already performed it in the last six months.)

d) You will participate in simulated laboratory time trials appropriate for your specialty event. There will be three trials before and three trials after the first cycle of altitude exposure.

e) You will participate in laboratory tests to determine anaerobic threshold. The test consists of a series of 5-min sub-maximal stages of exercise at increasing intensity. At the end of each stage a few droplets of blood are taken from a finger or earlobe for measurement of blood lactate (lactic acid). There will be five tests altogether, at four-weekly intervals.

f) You will complete a questionnaire to provide basic information about your age, weight, height, and competitive status.

g) You will complete a daily diary of your training, response to training, and response to the altitude exposure each day throughout the whole study.

Can Participants Change their Minds and Withdraw from the Project?
Your participation throughout the study will allow us to make the best assessment of the effects of altitude exposure on you personally and on the group as a whole. But, as for any research project of this nature, you are free to withdraw from the study at any time without having to give a reason.

What Data or Information will be Collected? What Use will be Made of it?
The data collected are as follows:

a) Blood samples to measure haematocrit and haemoglobin. These two parameters will demonstrate whether there is an increase in red blood cell mass with altitude exposure. Also to measure ferritin in your blood, to determine your iron status for prescription of iron supplements. This is to ensure your health status is not compromised.
b) A saliva sample to determine your genotype for angiotensin converting enzyme. We think that people who have the one or two copies of the "I form" of this gene will have a better response to altitude exposure than those who have one or two copies of the "D form".
c) Maximum oxygen consumption. This is a standard measure to describe the calibre of endurance athletes in a research study.
d) Anaerobic threshold. This measure of performance is not affected by motivation. It is one of the best objective measures of endurance performance currently available.
e) Time trials to monitor changes performance over distances similar to your specialty event. These data will help us determine when performance peaks after each period of altitude exposure (immediately, 4 weeks, or 8 weeks later). Runners will run on a treadmill for 4-8 min at a constant speed to exhaustion. Cyclists will ride as fast as possible for a simulated distance of 16 km on a cycle ergometer.
f) Training and altitude data in the daily diary.

Results of this project may be published but any data included will in no way be linked to any specific participant. The data collected will be securely stored in such a way that only those mentioned above will be able to gain access to it. At the end of the project any personal information will be destroyed immediately except that, as required by the University's research policy, any raw data on which the results of the project depend will be retained in secure storage for at least five years.

You will be given a copy of the results of the project, along with an assessment of your individual response to altitude exposure.

What if Participants have any Questions?

If you have any questions about our project, either now or in the future, please feel free to contact either:

Erica Ingham
Department of Health Science
UNITEC
Work Number: (09) 8154321 ext.8043

Chris Bailey
Department of Physical Education, Canterbury University
Work Number (03) 3642987 ext. 8416

Will Hopkins
Department of Physiology
University of Otago
Work Number: (03) 4797330

Dr Tony Edwards
Unisports Medicine
University of Auckland
Work Number: (09) 528 0561

Dr John Hellemans
Sports Med QEII
Work Number: (03) 383 6290
Home Number: (03) 351 6684

This project has been reviewed and approved on 4th March 1999 by the Ethics Committee of the University of Otago, reference number 99/018.

APPENDIX B: PARTICIPANT INFORMATION SHEET FOR THE CONTROL GROUP (STUDY 1)

THE EFFECT OF INTERMITTENT SIMULATED ALTITUDE EXPOSURE ON ENDURANCE PERFORMANCE

INFORMATION SHEET FOR PARTICIPANTS AND COACHES IN THE CONTROL GROUP

Thank you for showing an interest in this project. Please read this information sheet carefully before deciding whether or not to participate. If you decide to participate we thank you. If you decide not to take part there will be no disadvantage to you of any kind, and we thank you for considering our request.

The Aim of the Project

This project is being undertaken as part of the requirement for a Doctorate in Philosophy (Erica Ingham) and a Masters of Science (Chris Bailey).

The major aims of this project are as follows:

a) to enhance performance using simulated altitude exposure (hypoxic tents or masks)

b) to measure the effect of intermittent altitude exposure via performance testing and blood samples

c) to determine effective methods of utilising the tents or masks before a major competition

d) to track the effects or repeated altitude exposure

e) to compare the effectiveness between the tents and the masks

f) to determine whether simulated altitude exposure raises haematocrit (percent of red cells in your blood) to a limit that would bar athletes from competing (cyclists).

Participant Criteria

The participants recruited for this project should fulfil the following criteria:

a) male or female

b) competitive athlete

c) runner participating in 800m, 1500m, 3000m, or 5,000m events or a cyclist participating in kilo, pursuit, road events, or triathlons.

Exclusion Criteria

The following people will not be allowed to participate

a) anyone suffering from illness or injury that would interfere with normal training and competition

b) anyone who has a haematocrit of 54% or more (males) or 47% or more (females) in the first blood test.

What will Participants in the Control Group be Asked to Do?

As a participant you will be involved with this study for about 36 weeks. Most of the action occurs in the first 20 weeks, when the experimental group is being exposed to simulated altitude. Your role as a member of the control group is to train and be tested in the same manner as the experimental group.

If you agree to take part in this project, you will be asked to do the following:

a) You will give a blood sample every four weeks (a total of 6 samples). During each visit to the lab your skinfold thickness will be measured, to track any changes in body fat throughout the study.

b) You will take iron supplements if your initial blood test shows iron deficiency, as prescribed by a sports nutritionist and sports doctor.

c) You will perform a standard incremental test to maximum effort in the laboratory, for measurement of maximum oxygen consumption. (This test will not be necessary, if you have already performed it in the last six months.)

d) You will participate in laboratory tests to determine anaerobic threshold. The test consists of a series of 5-min sub-maximal stages of exercise at increasing intensity. At the end of each stage a few droplets of blood are taken from a finger or earlobe for measurement of blood lactate (lactic acid). There will be five tests altogether, at four-weekly intervals.

e) You will complete a questionnaire to provide basic information about your age, weight, height, and competitive status.

f) You will complete a daily diary of your training, response to training, and response to the altitude exposure each day throughout the whole study.

Can Participants Change their Minds and Withdraw from the Project?

Your participation throughout the study will allow us to make the best assessment of the effects of altitude exposure. But, as for any research project of this nature, you are free to withdraw from the study at any time without having to give a reason.

What Data or Information will be Collected? What Use will be Made of it?

The data collected are as follows:

a) Blood samples to measure haematocrit and haemoglobin. These two parameters will demonstrate whether there is an increase in red blood cell mass with altitude exposure. Also to measure ferritin in your blood, to determine your iron status for prescription of iron supplements. This is to ensure your health status is not compromised.

b) Maximum oxygen consumption. This is a standard measure to describe the calibre of endurance athletes in a research study.

c) Anaerobic threshold. This measure of performance is not affected by motivation. It is one of the best objective measures of endurance performance currently available.

d) Training data in the daily diary.

Results of this project may be published but any data included will in no way be linked to any specific participant. The data collected will be securely stored in such a way that only those mentioned above will be able to gain access to it. At the end of the project any personal information will be destroyed immediately except that, as required by the University's research policy, any raw data on which the results of the project depend will be retained in secure storage for at least five years.

You will be given a copy of the results of the project.

What if Participants have any Questions?

If you have any questions about our project, either now or in the future, please feel free to contact either:

Erica Ingham
Department of Health Science
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Work Number: (09) 8154321 ext.8043

Chris Bailey
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Work Number: (03) 383 6290
Home Number: (03) 351 6684

This project has been reviewed and approved on 4th March 1999 by the Ethics Committee of the University of Otago, reference number 99/018.

APPENDIX C: CONSENT TO PARTICIPATION IN RESEARCH (STUDY 1)

THE EFFECT OF INTERMITTENT SIMULATED ALTITUDE EXPOSURE ON ENDURANCE PERFORMANCE

CONSENT SHEET FOR PARTICIPANTS AND COACHES

I have read the Information Sheet concerning this project and understand what is about. All my questions have been answered to my satisfaction. I understand that I am free to request further information at any stage.

I know that:-

1. my participation in the project is entirely voluntary;
2. I am free to withdraw from the project at any time if absolutely necessary without any disadvantage;
3. the data will be destroyed at the conclusion of the project, but any raw data on which the results of the project depend will be retained in secure storage for five years, after which they will be destroyed;
4. the only discomfort involved in this project is the prickling of the needle or small lancet during blood sampling, and the maximum effort in time trials;
5. I will be compensated with petrol vouchers for travel to the testing facility;
6. the results of the project may be published but my anonymity will be preserved.

I agree to take part in this project.

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(Signature of participant) (Date)

This project has been reviewed and approved on the 4th of March 1999 by the Ethics Committee of the University of Otago, reference number 99/018.

APPENDIX D: APPROVAL LETTER FROM THE UNIVERSITY OF OTAGO ETHICS COMMITTEE (STUDY 1)

APPENDIX E: TRAINING AND ALTITUDE DIARY FOR RUNNERS (STUDY 1)

TRAINING and ALTITUDE DIARY: Runners

athlete

1 2 3

- Use one box per digit. Please CHECK you have used the correct number from the correct scale.
- Record training and daytime altitude data soon after the sessions. Measure saturation at end of session.
- In the evening record alcohol and extent of feeling stressed out or anxious during the day.
- Next morning record overnight altitude data. Measure saturation at end of session. CHECK your time in the tent.
- Record weight after voiding before breakfast, and record quality of sleep.

show details in comments box

1 = weights
2 = run continuous
3 = run intervals
4 = cycle continuous
5 = cycle intervals
6 = swim continuous
7 = swim intervals
8 = other

TRAINING SESSIONS

symptoms during the session

1 = easy
2 = steady
3 = mod-hard
4 = hard
5 = very hard

1 = none
2 = low
3 = medium
4 = high
5 = severe

1 = very good
2 = good
3 = average
4 = bad
5 = very bad

ALTITUDE EXPOSURE

symptoms in the tent

1 = none
2 = low
3 = medium
4 = high
5 = severe

Comments:

session no. today

day month

1 2 3 4

type of session | duration of session (min) | Intensity | fatigue | limb pain | session rating

#1 5 | 6 7 8 | 9 | 10 | 11 | 12

#2 13 | 14 15 16 | 17 | 18 | 19 | 20

#3 21 | 22 23 24 | 25 | 26 | 27 | 28

Daytime

saturation (%) | time in tent today hours mins | altitude setting | breathing hard | nausea | head-ache

29 30 | 31 32 33 34 | 35 36 | 37 | 38 | 39

alcohol today cans glasses | overall stress

40 41 | 42

1 = none
2 = low
3 = medium
4 = high
5 = severe

Overnight

saturation (%) | time in tent last night hours mins | altitude setting | breathing hard | nausea | head-ache

43 44 | 45 46 47 48 | 49 50 | 51 | 52 | 53

weight (kg) | sleep

54 55 56 | 57

1 = very good
2 = good
3 = average
4 = bad
5 = very bad

show details in comments box

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Overnight

saturation (%) | time in tent last night hours mins | altitude setting | breathing hard | nausea | head-ache

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TRAINING SESSIONS

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ALTITUDE EXPOSURE

symptoms in the tent

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Comments:

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day month

1 2 3 4

type of session | duration of session (min) | Intensity | fatigue | limb pain | session rating

#1 5 | 6 7 8 | 9 | 10 | 11 | 12

#2 13 | 14 15 16 | 17 | 18 | 19 | 20

#3 21 | 22 23 24 | 25 | 26 | 27 | 28

Daytime

saturation (%) | time in tent today hours mins | altitude setting | breathing hard | nausea | head-ache

29 30 | 31 32 33 34 | 35 36 | 37 | 38 | 39

alcohol today cans glasses | overall stress

40 41 | 42

1 = none
2 = low
3 = medium
4 = high
5 = severe

Overnight

saturation (%) | time in tent last night hours mins | altitude setting | breathing hard | nausea | head-ache

43 44 | 45 46 47 48 | 49 50 | 51 | 52 | 53

weight (kg) | sleep

54 55 56 | 57

1 = very good
2 = good
3 = average
4 = bad
5 = very bad

APPENDIX F: PROTOCOL FOR GENERATOR OPERATION (STUDY 1)

WEEK	Flow-meter	Hoses
1	**75%**	**Install only the two hoses as described in the assembly instruction sheet**
2	**50%**	**Install all 3 hoses**
3-4	**80%**	**Install all 3 hoses**

Notes:

- Please remain in contact with Erica Ingham (473-0090) as you raise the altitude level from week to week.
- If your sleep is NOT disturbed during the 3rd week of exposure at the highest setting (80%) then remain at that level for the remainder of the exposure. If it is disturbed then lower the level to 60-70% for the duration of the 3rd week and then increase it to the highest level on the 4th week.
- Remember to check your saturation 5 min after you have entered the tent but make sure you have run the generator for at least an hour and a half (1.5h) before checking.

APPENDIX G: PRE TEST QUESTIONNAIRE (STUDY 1)

NAME_____

ALTITUDE SIMULATION STUDY: PRETEST QUESTIONNAIRE

Before each lactate threshold test you are advised to do the following:

a) consume a normal carbohydrate diet three days before testing
b) report for testing 4hrs after a meal
c) perform workouts of similar intensity and duration before each test
d) do not perform exercise before the test
e) drink 500 ml of water during the 3hrs prior to testing
f) do not ingest caffeine at least 8h before testing

Questions:

1. Have you had a normal CHO diet 72 hours before the test? YES / NO
2. Have you had any caffeine today? YES / NO. If yes list the caffeine-containing item and when it was consumed.
3. Have you exercised today? YES / NO. If yes what was the intensity and duration of the exercise?
4. How many hours since you ate your last meal?
5. Have you consumed alcohol during the last 24 hrs? YES / NO. If yes list the type and quantity.

APPENDIX H: DATA COLLECTION SHEETS (STUDY 1)

ALTITUDE SIMULATION STUDY: VO_2MAX DATA SHEET

Name: _____

Date: _____

Cycle: _____

Weight: _____

Temp: _____

Stages	Km/h	Slope	Time / stage
1		1.5	3 min
2		1.5	3 min
3		1.5	3 min
4		1.5	3 min
5		3.5	1 min
6		5.5	1 min
7		7.5	1 min

Finish time	HRmax	%SpO2	VO_2max

ALTITUDE SIMULATION STUDY: LACTATE TEST DATA SHEET

Name: _____

Date: _____

Cycle: _____

Weight: _____

Temp: _____

Resting Lactate: _____

Time: _____

Warm up details:

Time	Speed	Grade %	HR4	HR5	[La]
0-5		1.5			
6-11		1.5			
12-17		1.5			
18-23		1.5			
24-29		1.5			
30-35		1.5			
36-41		1.5			
42-47		1.5			

ALTITUDE SIMULATION STUDY: TIME TO EXHAUSTION TEST DATA SHEET

Name: _____

Date: _____

Time: _____

Cycle: _____

Weight: _____

Temp: _____

Speed of TM: _____

HRmax: _____

%SpO2: _____

Metres run: _____

Actual Speed: _____

TTE: _____

Warm up :

APPENDIX I: SAS PROGRAMME AND LISTINGS (STUDY 1)

The information is available on a CD at the back of the document.

APPENDIX J: PARTICIPANT INFORMATION SHEET (STUDY 2)

Participant Information Sheet

For Athletes and Coaches

ENHANCING PERFORMANCE OF NZ ATHLETES WITH INTERMITTENT SIMULATED ALTITUDE EXPOSURE:-*RELIABILITY STUDY*

You are invited to take part in this study for five weeks. Please read this information sheet carefully before deciding whether to participate. If you decide to participate, we thank you. If you decide not to take part, there will be no disadvantage to you of any kind and we thank you for considering our request.

What is the purpose of the study?

Erica Hinckson is undertaking this project as part of her studies for a Ph.D. (Doctor of Philosophy).

The major aim of this project is as follows:

a) To determine the reliability of the tests used in the study to evoke maximal efforts lasting approximately 1, 4 and 8 min.

How is a person chosen to be asked to be part of the study?

The participants recruited for this project should fulfil the following criteria:

d) male

e) competitive middle or long distance runner

Can I join the study?

You can join the study unless you are suffering from illness or injury that would interfere with normal training and competition.

What happens in the study?

In this part of the study, you will be asked to come to the lab once a day for five weeks. The first visit will be a familiarisation visit to determine the appropriate treadmill speed. On the second and third visits you will perform the 3 tests. Then you will have 7 weeks off. At the end of the 7th week you will be asked to visit the lab for the next two weeks. In other words:

Test 0
One Week off
Test 1
Test 2
Seven weeks off
Test 3
Test 4

What is a Reliability Study?

Reliability is the consistency of the measurement, or the degree to which an instrument measures the same way each time. Therefore, in this study we want to determine the repeatability of our measurement which in this case is the maximal time to exhaustion that would be elicited in approximately 1, 4 and 8 min. A measure is considered reliable when the person's score on the same test given is similar. Then the results will be compared with actual track times during your competitive season.

What are the discomforts and risks?

No major discomforts or risks. The athletes will be required to reach maximal levels.

What compensation is available for injury or negligence?

In the unlikely event of a physical injury as a result of your participation in this study, you will be covered by the accident compensation legislation with its limitations. If you have any questions about ACC please feel free to ask the researcher for more information before you agree to take part in this trial. You may withdraw from the study

and medical care will be available to you. The Doctor monitoring this project is **Dr Edwards from the Adidas Sport Medicine Centre in Auckland at (09) 521 9811**

How is my privacy protected?

Results of this project may be published but any data included will in no way be linked to any specific participant. The data collected will be securely stored in such a way that only those mentioned above will be able to gain access to it. At the end of the project any personal information will be destroyed immediately except that, as required by the University's research policy, any raw data on which the results of the project depend will be retained in secure storage for at least ten years.

Costs of Participating

There will be no cost to you and travel will be compensated.

Invitation

If you have any questions about our project, and would like to be part of this study please feel free to contact either:

Erica Hinckson
School of Community Health and Sports Studies
Auckland University of Technology
Contact Number: 021-476-200
Work Number: (09) 815-4321 ext 8012

Associate Professor Will Hopkins
Department of Physiology
University of Otago
Work Number: (03) 479-7330

Associate Professor Patria Hume
School of Community Health and Sports Studies
Auckland University of Technology
Work Number: (09) 917-9999 ext 7306

Dr Tony Edwards
Adidas Sports Medicine
University of Auckland
Work Number: (09) 521-9811

Participant Concerns:

Any concerns regarding the nature of this project should be notified in the first instance to the Project Supervisor. Concerns regarding the conduct of the research should be notified to the Executive Secretary, AUTEC, Madeline Banda, madeline.banda@aut.ac.nz ,917 9999 ext 8044.

Approved by the Auckland University of Technology Ethics Committee on 27th August 2001 **AUTEC Reference number** 01/87.

APPENDIX K: PARTICIPANT CONSENT FORM (STUDY 2)

Consent to Participation in Research

Title of Project: **Enhancing Performance of NZ Athletes with Intermittent Simulated Altitude Exposure- Reliability Study**

Project Supervisor: **Dr Patria Hume and Dr Will Hopkins**

Researcher: **Erica Hinckson**

- I have read and understood the information provided about this research project.
- I have had an opportunity to ask questions and to have them answered.
- I understand that I may withdraw myself or any information that I have provided for this project at any time before completion of data collection, without being disadvantaged in any way. If I withdraw, I understand that all relevant information and transcripts, or parts thereof, will be destroyed.
- I agree to take part in this research.

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
	Other languages to be added following		

	consultation with relevant communities.		

Participant signature: .....

Guardian signature: ……..

Participant name:

Date:

Contact Details:

Erica Hinckson
School of Community Health and Sports Studies
Auckland University of Technology
Contact Number: 021-476-200
Work Number: (09) 815-4321 ext 8012

Associate Professor Will Hopkins
Department of Physiology
University of Otago
Work Number: (03) 479-7330

Associate Professor Patria Hume
School of Community Health and Sports Studies
Auckland University of Technology
Work Number: (09) 917-9999 ext 7306

Approved by the Auckland University of Technology Ethics Committee on 27th August 2001 **AUTEC Reference number** 01/87.

APPENDIX L: APPROVAL LETTER FROM THE AUCKLAND UNIVERSITY OF TECHNOLOGY ETHICS COMMITTEE (STUDY 2)

MEMORANDUM

Academic Registry - Academic Services

To: Patria Hume

From: **Madeline Banda**

Date: 17 July 2001

Subject: 01/87 Enhancing performance of NZ athletes with intermittent simulated altitude exposure - pilot treadmill reliability study

Dear Patria

Your application for ethics approval was considered by AUTEC at their meeting on 27 August.

Your application has been approved subject to amendment and/or clarification of the following :

- Clarification of risks – they appear to be understated. Give risks adequate weighting, for example, 'exhaustion' – how close to being serious might it come? A doctor should be on hand if this is possible.

Please provide evidence of the above to me as soon as possible.

Please quote the application number and title in all correspondence.

Yours sincerely

Madeline Banda

Executive Secretary

AUTEC

APPENDIX M: SAS PROGRAMME AND LISTINGS (STUDY 2)

The information is available on a CD at the back of the document.

APPENDIX N: PARTICIPANT INFORMATION SHEET (STUDY 3)

Participant Information Sheet

For Athletes and Coaches

ENHANCING PERFORMANCE OF NZ ATHLETES
WITH INTERMITTENT SIMULATED ALTITUDE EXPOSURE

You are invited to take part in this study for 14 weeks. Please read this information sheet carefully before deciding whether to participate. If you decide to participate, we thank you. If you decide not to take part, there will be no disadvantage to you of any kind and we thank you for considering our request.

What is the purpose of the study?

Erica Hinckson is undertaking this project as part of her studies for a PhD (Doctor of Philosophy).

The major aims of this project are as follows:

a) To determine the effect of simulated altitude exposure (hypoxic tents) on short duration endurance events.

b) Determine the association between the ACE genotype and performance with altitude exposure. In particular to see how a certain genetic characteristic affects the response to altitude exposure and determine which athletes are likely to benefit from altitude exposure.

How was a person chosen to be asked to be part of the study?

The participants recruited for this project should fulfil the following criteria:

a) male

b) competitive runner participating in 800 m, - 5,000 m events

Can I join the study?

You can join the study unless you are suffering from illness or injury that would interfere with normal training and competition.

What happens in the study?

As a participant, you will be involved with this study for about 14 weeks. The first week you will be tested for familiarisation purposes. The next four weeks you will be given a tent and asked to sleep in the tent overnight every night. During this time you will acclimatise to simulated moderate-high altitude and train at sea level. A week after the exposure you will be tested. Then you will continue training as normal for four weeks for the washout effect to occur. Following the washout effect the second group of five athletes receives exposure for four weeks while you continue training as normal. Following that period you will be tested again. If you agree to take part in this project, you will be asked to do the following:

1. You will receive one of five Hypoxico tents for one of the two altitude exposure periods. These tents are connected to a unit that produces air containing less oxygen than at sea level to simulate an altitude of up to 4200 m. The tents are portable and can be erected on a normal bed, but the unit that removes oxygen from the air may seem noisy and will need to be located in another room.

2. You will sleep and rest in the tents for a minimum of 10 continuous hours per day. As you become acclimatised in the first two weeks, the simulated altitude will be raised from 2500 m to 3500 m, then to 4200 m, provided that you are not unduly disturbed by symptoms of altitude sickness (see below). The overnight continuous exposure will be supplemented with at least one daily rest of at a higher altitude.

3. You will be provided with a portable hemoximeter and you will be required to measure your percent arterial oxygen saturation after you have been in the tent for a few minutes (or after half an hour if the nitrogen-enriching pump is switched on or if the altitude setting is changed when you enter the tent).

All participants will also do the following:

a) You will give a blood sample before and after the study for determination of your haematocrit levels, iron deficiency and testing for the ACE gene.

b) You will take iron supplements if your initial blood test shows iron deficiency, and you will take iron supplements during the periods of altitude exposure, as prescribed by a sports nutritionist and sports doctor.

c) You will participate in simulated laboratory time trials in 800 m and 3000 m on a running treadmill. There will be 15 trials at three different distances (including familiarisation).

d) You will complete a questionnaire to provide basic information about your age, weight, height, and competitive status.

e) You will complete a daily diary of your training, response to training, and response to the altitude exposure each day throughout the whole study.

What are the discomforts and risks?

No serious discomforts have been reported previously from use of the tents, but **if at any time you feel uncomfortable with any symptoms of altitude sickness (headaches, poor sleep, or feeling sick, dizzy or drowsy), you must exit the tent and contact Dr Edwards in Auckland at (09) 521 9811. You must also exit the tent and contact Dr Edwards if your arterial saturation drops below 77%.** He will discuss any symptoms you might have and make a decision about reducing your altitude or stopping your exposure to altitude. However, the majority of people also adapt and experience little or no further discomfort after a few days. We do not know the exact proportion of people who continue to experience symptoms, but it is probably very small. The moment the discomfort is too unpleasant at any time, leaving the tent or switching off the unit will stop the symptoms. And, of course, you can also stop taking part in the study at any time. Also some tiredness will be felt towards the end of the maximal treadmill tests. The majority of people experience some discomfort during acclimatisation to the moderate altitudes that the tents simulate.

What are the benefits?

You will be given a copy of the results of the project, along with an assessment of your individual response to altitude exposure.

What compensation is available for injury or negligence?

In the unlikely event of a physical injury because of your participation in this study, you will be covered by the accident compensation legislation with its limitations. If you have any questions about ACC please feel free to ask the researcher for more information before you agree to take part in this trial. You may withdraw from the study and medical care will be available to you. The Doctor monitoring this project is **Dr Edwards from the Adidas Sport Medicine Centre in Auckland at (09) 521 9811**

How is my privacy protected?

Results of this project may be published but any data included will in no way be linked to any specific participant. The data collected will be securely stored in such a way that only those mentioned above will be able to gain access to it. At the end of the project any personal information will be destroyed immediately except that, as required by the University's research policy, any raw data on which the results of the project depend will be retained in secure storage for at least ten years.

Costs of Participating

There will be no cost to you. In fact travelling time will be compensated with petrol vouchers.

Invitation

If you have any questions about our project, and would like to be part of this study please feel free to contact either:

Erica Hinckson
School of Community Health and Sports Studies
Auckland University of Technology
Contact Number: 021-476-200
Work Number: (09) 815-4321 ext 8012

Associate Professor Will Hopkins
Department of Physiology
University of Otago
Work Number: (03) 479-7330

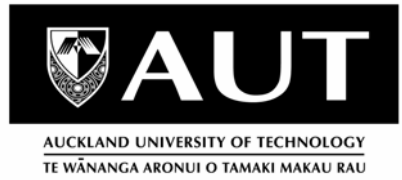
Associate Professor Patria Hume
School of Community Health and Sports Studies
Auckland University of Technology
Work Number: (09) 917-9999 ext 7306

Dr Tony Edwards
Adidas Sports Medicine
University of Auckland
Work Number: (**09) 521 9811**

Participant Concerns:
Any concerns regarding the nature of this project should be notified in the first instance to the Project Supervisor. Concerns regarding the conduct of the research should be notified to the Executive Secretary, AUTEC, Madeline Banda, madeline.banda@aut.ac.nz, 917 9999 ext 8044.

Approved by the Auckland University of Technology Ethics Committee on 28th August 2001 **AUTEC Reference number** 01/45

APPENDIX O: PARTICIPANT CONSENT FORM (STUDY 3)



Consent to Participation in Research

Title of Project: **Enhancing Performance of NZ Athletes with Intermittent Simulated Altitude Exposure – Altitude Study**

Project Supervisors: **Dr Patria Hume and Dr Will Hopkins**

Researcher: **Erica Hinckson**

- I have read and understood the information provided about this research project.
- I have had an opportunity to ask questions and to have them answered.
- I understand that I may withdraw myself or any information that I have provided for this project at any time prior to completion of data collection, without being disadvantaged in any way. If I withdraw, I understand that all relevant information and transcripts, or parts thereof, will be destroyed.
- I agree to take part in this research.

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

Participant signature: .....

Guardian's signature…….

Participant name:

Date:

Contact Details:

Erica Hinckson
School of Community Health and Sports Studies
Auckland University of Technology
Contact Number: 021-476-200
Work Number: (09) 815-4321 ext 8012

Associate Professor Will Hopkins
Department of Physiology
University of Otago
Work Number: (03) 479-7330

Associate Professor Patria Hume
School of Community Health and Sports Studies
Auckland University of Technology
Work Number: (09) 917-9999 ext 7306

Approved by the Auckland University of Technology Ethics Committee on 28th August 2001 **AUTEC Reference number** 01/45

APPENDIX P: APPROVAL LETTER FROM THE AUCKLAND UNIVERSITY OF TECHNOLOGY ETHICS COMMITTEE (STUDY 3)

MEMORANDUM

Academic Registry - Academic Services

To: Patria Hume

From: **Madeline Banda**

Date: 17 July 2001

Subject: 01/45 Enhancing performance of NZ athletes with intermittent simulated altitude exposure - ACE study

Dear Patria

Your application for ethics approval was considered by AUTEC at their meeting on 28 August.

Your application has been approved subject to the following:

- Receipt of letter of approval from Auckland Ethics Committee

Please provide evidence of the above to me as soon as possible.

Please quote the application number and title in all correspondence.

Yours sincerely

Madeline Banda

Executive Secretary

AUTEC

APPENDIX Q: APPROVAL LETTER FROM THE AUCKLAND ETHICS COMMITTEE (STUDY 3)

APPENDIX R: SAS PROGRAMME AND LISTINGS (STUDY 3)

The information is available on a CD at the back of the document.

APPENDIX S: ACCOUNTING FOR ABILITY LISTING (STUDY 3)

```
Pred800m indiv responses vs athlete ability                  105
                                          13:49 Thursday, June 10, 2004

      Plot of IndivResp*AthleteTime.  Symbol is value of ACEgene.

IndivResp |
          |
      0.5 +
          |
          |                D
          |         i
          |
      0.0 +
          |
          |
          |
          |
     -0.5 +         i
          |                     D  I
          |
          |
          |
     -1.0 +
          |                   i
          |        D
          |                                                    I
          |
     -1.5 +
          |
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          |                                                  D
     -2.0 +           i
          |
          Š-+------------+------------+------------+------------+------------+--
         130.00       140.00       150.00       160.00       170.00       180.00

                                AthleteTime

NOTE: 1 obs hidden.


Pred1500m indiv responses vs athlete ability                 113
                                          13:49 Thursday, June 10, 2004

      Plot of IndivResp*AthleteTime.  Symbol is value of ACEgene.

IndivResp |
          |
      0.0 +
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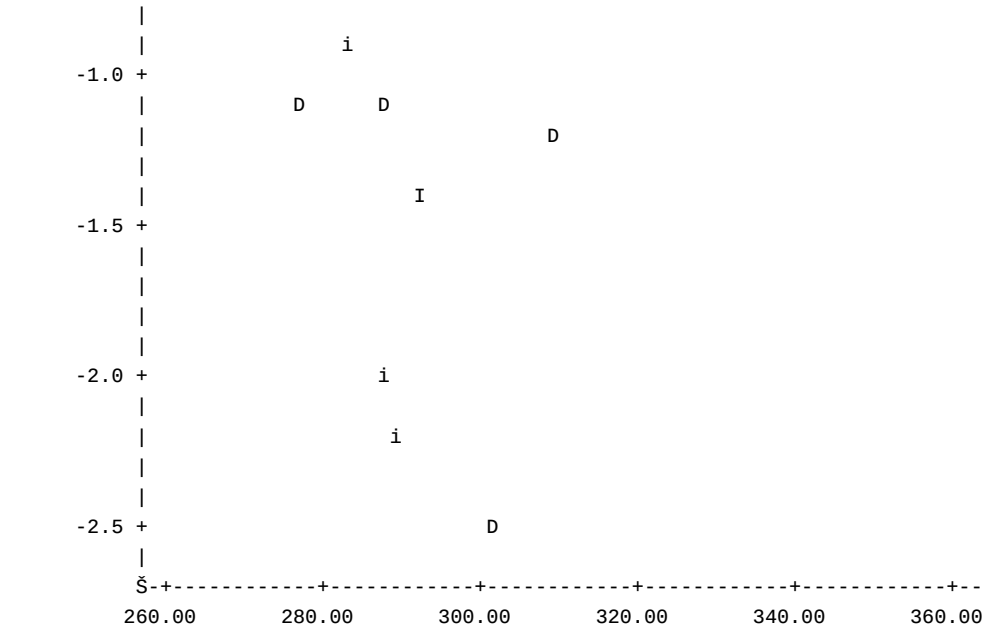
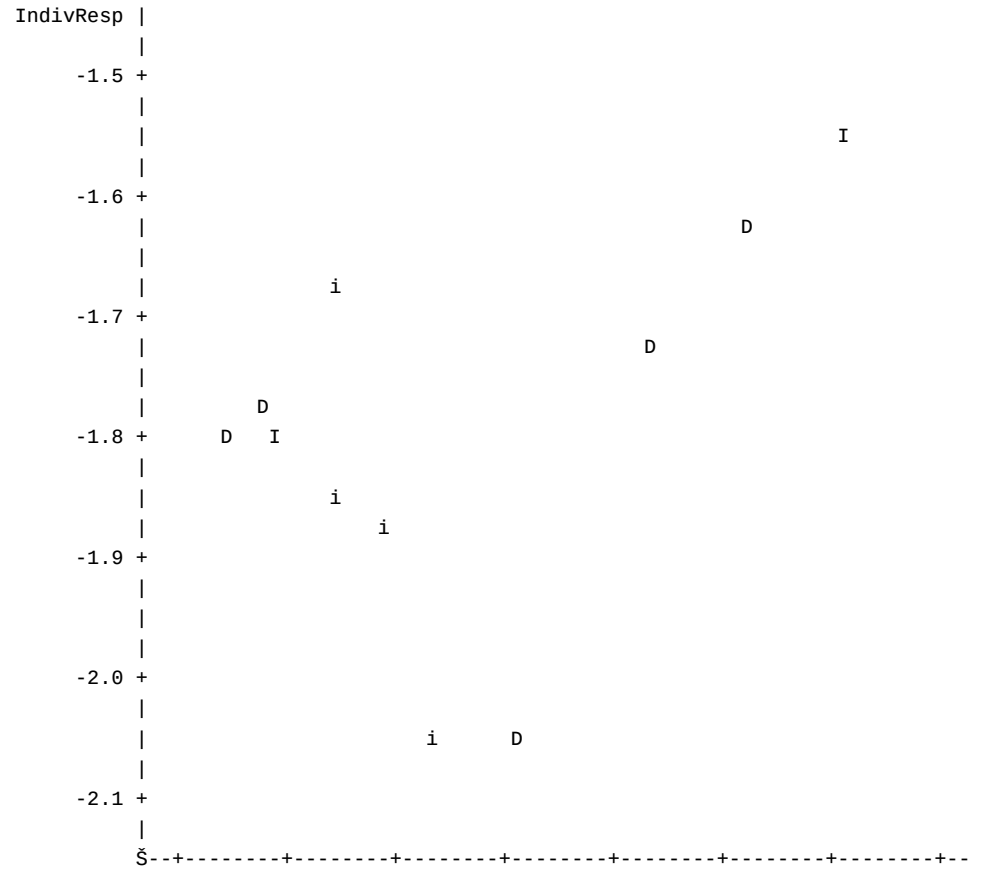
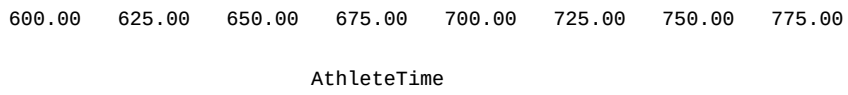


Pred3000m indiv responses vs athlete ability 121
13:49 Thursday, June 10, 2004

Plot of IndivResp*AthleteTime. Symbol is value of ACEgene.




600.00
625.00
650.00
675.00
700.00
725.00
750.00
775.00
AthleteTime

APPENDIX T: PILOT STUDY

The Effect of Hypoxic Inhalers on Sea level Performance in Rowers

This paper was submitted to Journal of Medicine and Science in Sport: Hinckson, E. A., Hopkins, W. G., Downey, B., & Smith, B. (2004). The effect of hypoxic inhalers on sea level performance in rowers. *Manuscript submitted for publication.*

Introduction

The effects of natural altitude exposure on sea level endurance performance using the "live high-train low" method have been favourable (Wilber, 2001). In New Zealand there are no appropriate altitude training facilities, therefore athletes have to resort to other resources to experience altitude exposure. Currently there are a variety of means available to athletes, including hypoxic apartments, tents or inhalers, and hypobaric chambers (Wilber, 2001). In these devices reduced partial pressure of oxygen is achieved by either dilution of air with nitrogen or by reducing the barometric pressure.

In this pilot study we investigated the effect of a new inhaler on a small sample of elite rowers, who were exposed to reduced partial pressure of oxygen through rebreathing a portion of their expired gas. A carbon dioxide (CO_2) absorbent in the device reduces the build-up of CO_2 in the inspired gas that would otherwise stimulate hyperventilation and thereby limit the fall in arterial oxygen saturation.

Methods

Subjects and design

We randomised nine female and three male members of the elite national team to an hypoxic conditioning group (five females, two males) or placebo group (four females, one male). The male in the placebo group withdrew, owing to injury. The rowers' age was 25 ± 4 y (mean ± standard deviation). The rowers provided informed consent, and the study was conducted within the institution's guidelines for experimental research with human subjects.

Each rower completed performance tests within one week before exposure and seven to ten days after exposure. The exposure sessions were performed daily for three weeks. Venous blood was sampled a day before and three to nine days after altitude exposure.

Altitude Exposure

Each rower received either an inhaler or a placebo device. The CO_2 absorbent (soda lime) in the inhaler used by the hypoxic conditioning group allowed the athletes to experience simulated altitude by re-breathing expired air. The placebo device contained an inert substance (pebbles) in place of CO_2 absorbent. During the session the athletes breathed through their devices for 6-min periods, alternating with 4-min periods of normal air, for a total of 90 min. Blood oxygen saturation was monitored with oximeters (Nonin, Plymouth, Minnesota) applied to a finger. The addition of compartments increased desaturation through an increase in dead space. Each athlete's inhaler in the hypoxic conditioning group was adjusted to produce a saturation of 88-92% in the first week of the study, decreasing to 80-84% (equivalent to an altitude of 6000 m) in the final week. In an attempt to maintain blinding, compartments were added to the inhalers in the placebo group without substantial reduction in arterial saturation. However, the active devices produced heating in the inspired air, so that by the end of the study the athletes all guessed correctly which group they were in.

Training

The rowers were followed a periodised plan consisting of four phases: general, specific pre-competition and competition. At the time of the study the rowers were in the specific phase. They trained as a squad twice daily throughout the study.

Performance Tests

Performance was monitored with a lactate-threshold test and time trials over 500 m and 5000 m on a rowing ergometer (Concept II, Morrisville, Vermont). Rowers were performing the 5000-m time trial routinely every two months, but the last 500-m time trial had been performed one year previously. Rowers did little or no training the day prior to testing.

For the lactate threshold test, we utilised a discontinuous incremental protocol of 6-min stages with 1-min rest periods to collect blood samples. Lactate concentration was measured with a lactate analyser (YSI 1500, Yellow Springs, Ohio). The performance measure was power at 4 $mmol.L^{-1}$.

Blood test

Venous blood samples were analysed by a local haematology laboratory for the determination of haematocrit and ferritin. Under the direction of the team's physician daily iron supplementation was given to those athletes with ferritin concentration <30 $ng.ml^{-1}$.

Statistical analysis

Analyses were performed with appropriate repeated-measures modelling after log-transformation (Hopkins, 2000a). In the analyses of the time trials we multiplied the log-transformed times by three to convert changes and errors for time into their equivalent for mean power (Hopkins et al., 2001). Uncertainty in the estimates of changes in mean power is expressed as 90% confidence limits and as chances that the true value of the change is substantial (Hopkins, 2002). We chose 0.5% as the threshold for a substantial change in performance (Hopkins et al., 1999).

Results

All rowers completed pre and post lactate threshold tests, but only nine completed the 5000-m time trials, and 10 completed the 500-m time trials. The effects of altitude exposure on performance are shown in Table 1. The difference in the changes was small compared with the uncertainty, and it is possible that the true effect of altitude exposure on 5000-m time trial and lactate threshold performance could be a substantial improvement or impairment. The effect on 500-m time trial was more likely to be an impairment. Further analyses of the chances of improvement or impairment showed that the natural effect of altitude exposure in the 5000-m time trial and lactate threshold test is unlikely to exceed ±3%, while the effect on 500-m time trial is unlikely to exceed ±4%.

Table 1. Changes in performance (post-pre) of the altitude and control groups, difference in the changes (altitude-control), and chances that the true difference represents a substantial improvement or impairment in performance.

	Change in mean power (%)		**Difference (%) and confidence limits**	**Chances (% and qualitative) of a substantial[a] improvement or impairment**	
	Altitude	Control		improvement	impairment
500-m time trial	1.9	4.2	-2.2; ± 4.1	13; unlikely	77; likely
5000-m time trial	0.3	-0.3	0.6; ± 3.7	53; possibly	29; possibly
Lactate threshold	-1.1	-1.5	0.4; ±3.5	48; possibly	33; possibly

[a]Change in performance of >0.5% for improvement or <-0.5% for impairment.

The within-subject coefficients of variation in the three tests were not consistently higher in the hypoxic conditioning group compared with those in the control group, and the uncertainty in the estimates of these coefficients was large (data not shown). There was therefore no clear evidence of individual responses to altitude exposure. For the two groups combined, the coefficients of variation were 1.7% for 5000-m time trial, 2.5% for the 500-m time trial, and 2.5% for the lactate threshold.

The lowest saturations achieved each week of exposure expressed as the mean of the individual's lowest saturation attained at each session for the hypoxic conditioning group were 89±3%, 84±3% and 84±5% respectively. Seven rowers completed 19-20 sessions of exposure from the total of 20 sessions, while the rest completed 15-18 sessions.

There was a small decrease in the haematocrit for the control group and a small increase for the hypoxic conditioning group after the period of altitude exposure. The difference in the change in haematocrit was 2.0% of blood volume (-0.6 to 4.6%).

Discussion

The devices for achieving simulated altitude exposure were practical and fitted in well with the athlete's daily routine. Athletes could use these devices without supervision, provided they monitored arterial saturation with a pulse oximeter.

We could not expect to determine precisely the effect of the device on performance in this pilot study, but we have at least limited its effectiveness with the current exposure protocol to a likely range of ±3-4%. A larger sample and/or more reliable tests will allow more precise characterization of the effect on mean performance, the extent of any individual differences in the effect, and the role of haematocrit or other physiological parameter in the response. The effects of different exposure protocols also need investigating.

With appropriate choice of athletes or modes of exercise, it should be possible to achieve error of measurement in performance closer to 1% (Hopkins et al., 2001), with concomitant reduction in uncertainty in the change in performance. In the present study, the athletes were relatively unreliable in the 500-m test, presumably because they had not performed this test for a year. However, the athletes performed the lactate threshold test on a regular basis, so the poor reliability of this test is probably an inescapable feature of the lactate threshold in a practical setting.

The fact that the subjects knew before the post-test whether they had been using a placebo or active device would have presented us with a problem of interpretation if the hypoxic conditioning group had shown an enhancement of performance similar to that seen in studies of the placebo effect (V. R. Clark et al., 2000). In any future study, it would be desirable to design a placebo device that ensures successful blinding of the athletes to the treatment.