The Effect of Intermittent Hypoxic Training on Performance

Report to SPARC & Triathlon New Zealand

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ABSTRACT

This study aimed to verify whether the “live low, train high” approach is beneficial for endurance and/or anaerobic cycling performance. Sixteen well-trained athletes completed 90 min of endurance training (60-70% of heart rate reserve) followed by two 30-s all-out sprints (Wingate test), daily for 10 consecutive days. Nine subjects (IHT group) trained with an F_IO_2 set to produce arterial oxygen saturations of ~88% to ~82%, while 7 subjects (placebo group) trained while breathing a normal gas mixture (F_IO_2 = 0.21). Four performance tests were conducted at sea-level including a familiarisation and baseline trial, followed by repeat trials at 2 and 9 days post-intervention. Relative to the placebo group mean power during the 30-s Wingate test increased by 3.0% (95% Confidence Limits, CL ± 3.5%) 2 days, and 1.7% (± 3.8%) 9 days post-IHT. Changes in other performance variables (30-s peak power, 20-km mean power, 20-km oxygen cost) were unclear. During the time trial the IHT participants’ blood lactate concentration, RER and SpO_2 relative to the placebo group, was substantially increased at 2 days post-intervention. The addition of IHT into the normal training programme of well-trained athletes produced worthwhile gains in 30-s sprint performance possibly through enhanced glycolysis.

INTRODUCTION

An increasingly popular method of altitude training is intermittent hypoxic training (IHT); a “live low-train high (LLTH)” approach, where athletes live at or near sea level but train in hypoxic conditions similar to higher altitudes (~2,500 to 3850m) (Geiser et al. 2001). IHT is commonly incorporated into an athlete’s training schedule in preference to living at natural altitude and training at or near sea-level (live high-train low; LHTL) due to the minimal travel, low expense and negligible disruption to training and daily life.

It has been demonstrated that the LHTL method improves sea-level endurance performance in both sub-elite (Levine & Stray-Gundersen 1997) and elite athletes (Brugniaux et al. 2006). The exact mechanisms responsible for enhanced endurance performance following LHTL are controversial (see point-to-point discussion: Journal of Applied Physiology 2005 99:2053-2058). (Levine & Stray-Gundersen 2005) argue that the primary mechanism responsible for improved sea-level endurance performance following repeated, prolonged exposure to hypoxia is an enhanced erythropoietic response, which results in an elevated red blood cell volume and resultant enhanced rate of oxygen transport. In contrast, (Gore & Hopkins 2005) emphasised that an improvement in exercise economy is more likely to be responsible for enhanced performance following LHTL, although this notion is not supported in a recent report (Truijens et al. 2008). Although the exact mechanisms remain debateable, it appears that living at natural altitude and training closer to sea-level improves sea-level endurance performance in most cases (Brugniaux, Schmitt 2006; Chapman et al. 1998; Levine & Stray-

Gundersen 1997; Schmitt et al. 2006; Stray-Gundersen et al. 2001; Wehrlin et al. 2006).

The efficacy of IHT for the enhancement of sea-level performance, however, is more controversial. Several studies have reported an enhanced athletic performance following IHT (Dufour et al. 2006; Ponsot et al. 2006) although a number have failed to demonstrate any significant alteration in post-IHT performance measures (Morton & Cable 2005; Roels et al. 2007).

These conflicting results may be due to methodological differences including the duration and intensity of the hypoxic stimulus, type and intensity of exercise, subject training status, and the time-point following the IHT procedure at which performance was determined. The current IHT research has focused on simulating a specific altitude (2500m – 6000m) despite the knowledge that athletes have a highly variable response to hypoxia (Ainslie et al. 2007). In addition to IHT, much of the research into the effects of hypoxia has involved exposing individuals intermittently to hypoxia while seated at rest (intermittent hypoxic exposure, IHE). Recent IHE studies have individualised the hypoxic stimulus by reducing the arterial oxygen saturation (SpO_2) to a set level (Marshall et al. 2008; Wood et al. 2006). The effectiveness of this methodology, however, remains unclear as IHE has been found to enhance (Wood, Dowson 2006) or have no effect (Marshall, Hamlin 2008) on aerobic performance, and is yet to be utilised during exercise training in hypoxia (IHT).

In addition to potentially improving endurance performance, IHE and IHT may also benefit anaerobic exercise performance (Bonnetti et al. 2006; Hendriksen & Meeuwsen 2003), possibly via increases in muscle buffering capacity (Gore et al. 2001) and glycolytic enzyme activity (Katayama et al. 2004). IHE has been found to increase repeated kayak sprint power by 8.3 ± 6.7% and 6.8 ± 5.2% (mean ± 90% confidence limits) for mean and peak power respectively (Bonnetti, Hopkins 2006) and repeated sprint run times by ~1 – 7 % (Wood, Dowson 2006) 3 days following hypoxia exposures. Similarly, 10 days of IHT at a simulated altitude of 2500m improved anaerobic mean (4.1 %) and peak (3.8 %) cycling power at 9 days post-intervention compared to the placebo sea-level training group (Hendriksen & Meeuwsen 2003). Other studies, however, have reported no beneficial effect of IHT (Morton & Cable 2005) or IHE (Tadibi et al. 2007) on anaerobic performance over and above that of training closer to sea-level.

OBJECTIVES

The majority of studies to date identifying the effects of IHT on anaerobic performance have involved endurance training at altitude with no inclusion of anaerobic training. The aim of the present single-blinded, randomised placebo-controlled study therefore was to determine the effect of 10 consecutive days of combined aerobic and anaerobic cycle training at a set SpO_2 on both aerobic and anaerobic performance.

METHODOLOGY

Subjects

Sixteen athletes from a variety of cycling backgrounds (8 road cyclists, 3 mountain bikers, 1 triathlete and 4 multisport athletes [athletes that mainly compete in run, cycle and kayak events]) volunteered to participate in the present study, all of whom were well trained and competed at regional or national level in their specific discipline. The research was conducted over the winter period when the cyclists were in the base phase of their training (pre-season). The study was approved by the Lincoln University Human Ethics Committee and conformed to the standards set by the Declaration of Helsinki. Informed voluntary written consent was obtained from each subject prior to the start of the study. Subject characteristics are presented in Table 1.

Table 1. Characteristics and baseline measures of performance of athletes in the two training groups.

	Placebo (n = 7)	IHT (n = 9)
Age (y)	38.7 ± 8.6	29.6 ± 12.3
Body mass (kg)	76.7 ± 12.3	76.6 ± 11.1
Height (m)	1.78 ± 0.1	1.72 ± 0.1
Sex	6 male 1 female	8 male 1 female
Training ($Trimp \cdot d^{-1}$)	224 ± 177	176 ± 82
Wingate 30-s mean power ($W \cdot kg^{-1}$)	8.5 ± 0.8	8.8 ± 0.9
Wingate 30-s peak power ($W \cdot kg^{-1}$)	14.0 ± 2.0	13.6 ± 2.9
20-km mean speed ($km \cdot h^{-1}$)	35.7 ± 3.4	37.2 ± 3.3
20-km mean power ($W \cdot kg^{-1}$)	3.2 ± 0.7	3.5 ± 0.6
Oxygen cost ($ml \cdot W^{-1}$)	12.6 ± 3.1	13.7 ± 1.0

Values are mean ± between subject standard deviation. Trimp; Training Impulse.

All subjects were healthy, free from injury, lived at sea level and had not been resident at altitude within the past 6 months. As some authors suggest maximal exercise performance is unaffected by changes in the menstrual cycle (Beidleman et al. 1999) there was no attempt to test the female athletes in this study in the same phase of their menstrual cycle.

Subjects were matched for initial 20-km cycle time trial performance (i.e. time to complete the 20-km), then randomly divided into two groups: an intermittent hypoxic training group (IHT, n=9) and a control group (placebo, n=8). Due to illness, one placebo group subject had to withdraw from the study.

Study design

The study, based on a training protocol used previously (Hendriksen & Meeuwsen 2003), was a single-blind placebo-controlled trial. Subjects performed four main trials including a familiarisation, baseline, and two post-training trials. The baseline trial was performed 1 week after the familiarisation trial and two days prior to beginning IHT or placebo training. The IHT group trained at simulated altitude (normobaric hypoxia) whereas the placebo group underwent the same training protocol at sea level (normobaric normoxia) on 10 consecutive days. The post-training trials were completed 2 and 9 days

after the training period. The main trials involved a 30-s Wingate anaerobic test followed 1 h later by a 20-km cycle time trial.

Subject preparation

The subjects were asked to refrain from intense exercise for 24 h prior to each main trial. Subjects also recorded their dietary intake prior to the first trial to allow replication of diet prior to subsequent trials. Subjects were provided with a pre-test meal (2 g carbohydrate/kg body mass of Sustagen® Sport, Nestlé, Victoria, Australia) which was consumed, along with 500 mL water, 2 h before arriving at the laboratory. Iron tablets (170 mg ferrous glucomate and 40 mg ascorbic acid; Healtheries Iron & Vitamin C, Auckland) were provided to subjects from one week prior to the familiarisation trial, as altitude-induced erythropoiesis is unlikely to occur in an iron-deficient state (Stray-Gundersen et al. 1992). Subjects consumed one tablet, twice a day with food throughout the study. The subjects were asked to avoid additional training for 2 h before and after each training session.

Resting venous blood samples were drawn from an antecubital vein of seated subjects in a fasted state prior to training (baseline) and ~2 (post-2) and ~9 (post-9) days post training. Blood samples were drawn at the same time for each subject, in the morning prior to breakfast, when subjects were in a fasted state. Samples were assayed by an independent professional testing laboratory (Southern Community Laboratories, Christchurch, New Zealand) for haemoglobin, haematocrit, reticulocytes (XE-2100, Sysmex, Japan), serum iron, serum ferritin and % ferritin saturation (917, Hitachi, Japan).

Training

Subjects trained on their personal road bikes on 10 consecutive days, either at simulated altitude (IHT) or sea level (placebo). The bikes were mounted on a stationary trainer (CycleOps Fluid 2, Madison, WI, USA) and tyre pressure standardised to 120 Psi; bike positioning and tyre pressure were replicated at each training session. The aerobic component of the training lasted 90 min and was performed at 60% -70% of the heart rate reserve. In order to have subjects work at the same relative intensity the IHT group's target heart rate was adjusted to take account of the natural fall in maximal heart rate with decreasing F_IO_2 (Richalet 1992). A regression equation which describes the decrease in chronotropic drive during hypoxia, y (% of sea-level HR_{max}) = 116 – 0.0057x (x = altitude in meters, or SpO_2), was used to predict maximal heart rate for the heart rate reserve calculation (Richalet 1992). Following the continuous cycling, subjects completed two 30-s Wingate tests, separated by 5 min, on an electromagnetically-braked cycle ergometer (Velotron, RacerMate Inc, Seattle, USA).

During training, subjects received either a normobaric hypoxic gas (IHT group) or normobaric normoxic gas (placebo group) via the GO_2Altitude® hypoxicator system (Biomedtech, Victoria, Australia). After calibrating the equipment at the start of each training session, the hypoxic or placebo gas was sent to two 100 L Douglas bags connected in series. Subjects breathed from the bags via a leak-free respiratory mask (Hans-Rudolph 8980, Knasas

City, MO, USA) attached to a one-way non-rebreathing valve (Hans-Rudolph 2700, Kansas City, MO, USA). To allow sufficient time for adaptation the oxygen concentration in the hypoxic gas was progressively reduced over the 10-day training period in the IHT group. The fraction of inspired oxygen (F_IO_2) was manually adjusted by the researcher to allow a similar hypoxic stimulus for each subject. SpO_2 levels were ~88% on days 1-2, ~84% on days 3-4, and ~82% on days 5-10 (the equivalent of 3200m, 4000m and 4400m altitude, respectively). The rationale for this protocol is purported to provide a hypoxic stimulus harsh enough to induce acclimatization (Julian et al. 2004). The progressive decrease in F_IO_2 over the course of the study is to provide maximal tolerable hypoxic stress by the end of the training period, but allow progressive acclimatization to minimize symptoms of hypoxic stress and improve tolerance. Subjects were unable to view their inspired oxygen concentration or blood saturation levels during training and we are confident that the blinding procedure worked, as participants were unable to determine which group they were in when asked at the end of the study. SpO_2, F_IO_2 and heart rate (HR) were recorded every 5 minutes.

Subjects were provided with daily logs in which they recorded their daily training information (frequency, intensity, duration and type) as well as their subjective ratings of stress, fatigue, muscle soreness, quality of sleep and quality of training performance. To compare total training load among groups, training impulse (TRIMP) was calculated which was expressed as a product of stress (duration of activity) and strain (subjective rating of training intensity). Subjects reported their subjective feelings with the use of the following 5-point Likert-type scale; excellent =1, good =2, average =3, poor =4, very poor =5.

Performance tests

Hydration status (urine specific gravity; Bayer Diagnostics Multistix®, Leverkusen, Germany) and nude body mass were determined on arrival at the laboratory. Anaerobic and aerobic performances were then evaluated via a 30-s Wingate Anaerobic Test and a 20-km time trial, respectively. Both of these tests were conducted on the Velotron Pro ergometer (Racermate Inc., Seattle, WA). During the performance tests subjects consumed no food but were able to drink water ad libitum. The Wingate test was selected as it is the most widely used anaerobic performance test and commonly used on well-trained athletes. We followed the standard instructions from the Velotron manufacturers (Racermate Inc., Seattle, WA), which are based on the original recommendations of (Inbar et al. 1996). Before each test factory calibration was verified, using the Accuwatt ‘run down’ verification programme (Racermate Inc., Seattle, WA). The Velotron settings (seat, handle bar height and horizontal position) were adjusted during the familiarisation trial to match the subjects’ personal road bike settings as closely as possible. These settings were then noted and replicated for each main trial. The gear ratios of the subjects’ road bike were entered into the Velotron software resulting in a laboratory cycle ergometer as similar to their personal road bike as possible.

After a 10 min self-selected warm-up, interspersed with 3 maximal sprints lasting ~5 s, subjects performed a 30 s Wingate test (Velotron Wingate software, version 1.0, Racermate Inc., Seattle, WA) in which they pedalled

maximally against a constant load (males, 9.8% body mass; females, 9.5% body mass) while seated. The load was applied after an initial acceleration phase of 3 s. Final HR and SpO_2 were recorded by the researcher and the Velotron software calculated peak and mean power output (W). The Wingate test was followed by light pedalling for 5-10 min followed by 50-55 min passive recovery.

Following recovery, baseline data was collected (ventilation and expired gases, SpO_2, HR and blood lactate concentration) followed by a 10-min self-selected warm up for the time trial. Subjects completed the time trial from a standing start, on a gear ratio previously selected during the familiarisation trial. During the time trial subjects were able to change gear when they wished, as they would on their road bike. Subjects were informed of distance covered at 5, 10, 15-km time points and then every 1-km through to 20-km but received no feedback on power output, heart rate, pedal cadence or performance time. The following measurements were taken at 5 km, 10 km, 15 km and 20 km; ventilation and expired gases, HR, SpO_2, blood lactate concentration and rating of perceived exertion (RPE).

Physiological Measurements

Ventilation and expired gases were measured breath-by-breath, and averaged every 5 s, for a period of ~2 min leading up to each measurement time point (for time trial data), or averaged every 1 s (for Wingate data) using a portable gas exchange system (MetaMax® 3B; Cortex Biophysik, Leipzig, Germany). The reported gas variables are the average of the final minute (time trial) or 30-s (Wingate test) of this gas collection. Oxygen consumption ($\dot{V}O_2$), minute ventilation ($\dot{V}_E$), end-tidal CO_2 ($P_{ET}CO_2$) and respiratory exchange ratio (RER) were calculated. Since the time trial is similar to a steady state test in that the subjects show an initial increase in speed and power over the first minute or so and then tend to maintain a relatively stable power output until the final ‘sprint’ in the last 1-2 minutes of the test we have been able to calculate oxygen cost. For each subject, the oxygen cost of exercise, expressed as mL of oxygen per watt (mL/W), was calculated for the last minute of each of the 4 stages (5, 10, 15 and 20 km), then averaged. Before testing, the gas analyser was calibrated for volume (Hans Rudolph 5530 3 L syringe; Kansas City, MO, USA) and gas composition (15% O_2 and 5% CO_2).

During the performance tests and training sessions HR was recorded continuously by means of a HR monitor (S610; Polar, Kempele, Finland). Arterial oxygen saturation was monitored manually by the researcher (Sport-Stat, Nonin Medical, Minneapolis, MN). Subject’s perceived exertion (RPE) was recorded with the use of a Borg scale (6-20). Blood lactate concentration was determined from a finger-prick sample, analysed using a portable lactate analyser (Lactate Pro, Arkray Inc, Kyoto, Japan).

Statistical analyses

Changes in the mean of the variables and standard deviations representing the between- and within-subject variability were estimated using a mixed modelling procedure (Proc Mixed) in the Statistical Analysis System (Version

8.0, SAS Institute, Cary NC). We analysed the natural logarithm of each measure to reduce any effects in nonuniformity of error and to obtain changes in measures and errors as percentages. The fixed effects were trial (pre, post2 post9), group (IHT, placebo) and their interaction. The random effects were subject variance, residual variance, and additional within-subject variance for the two post-exposure trials combined for the IHT group. Chances that the true effects were substantial was estimated with a spreadsheet (Hopkins 2006), when a value for the smallest worthwhile effect is entered. We used a value of 1% for the performance measures, because this has been shown to represent the smallest worthwhile enhancement for cyclists competing in track or time trial events (Paton & Hopkins 2001) and has been used by previous researchers. For non-performance measures we chose 0.20 standardized units (change in mean divided by the between-subject SD at baseline) as the smallest worthwhile change (Cohen 1988). To make inferences about the true (population) values of the effect of IHT on performance, p values and statistical significance were not used. Instead, uncertainty in the estimate of changes were presented as 95% confidence intervals and as likelihoods that the true value of the effect is a substantial enhancement or impairment. The relationships between parameters were determined by simple linear regression analysis.

RESULTS

Hypoxic exposure

The placebo group's mean SpO_2 during the training sessions remained between 94 – 95 %, whereas the IHT group's SpO_2 decreased during training from 88.8 ± 1.8 % (mean ± SD), on day 1 to 83.5 ± 3.1 %, on day 10. The F_IO_2 required to maintain the SpO_2 at this lowered level for the IHT group dropped from 0.17 ± 0.01 on day 1, to 0.14 ± 0.02, on day 10 (Figure 1, IHT group only).

Training

Both groups decreased their normal road training volume during the 10-day intervention period to accommodate the experimental training loads required for the study. We found no substantial difference in the training volume either between or within the groups before, during or after the study (placebo group 224 ± 177, 221 ± 49, 145 ± 80; IHT group 176 ± 82, 203 ± 40, 165 ± 55 Trimps.d^{-1} for pre, during and post-intervention respectively). However, because of the considerable variation in training we decided to examine whether differences in training load (Trimp) had any influence on performance outcomes. To do this we used the Trimp data as a covariate in the performance analysis as suggested by (Hopkins 2006). To investigate the effects of training load on the performance at 2 days post intervention we averaged the training data completed the week before and the 10 days during the intervention period. Similarly, we used the post-intervention Trimp data to investigate the effects of training on performance 9 days post intervention. Adjusting for training load in this way had little effect on performance outcomes with all measures changing less than 0.8%. Therefore, it seems

unlikely that differences in training load between groups had any influence on the outcomes of this study.

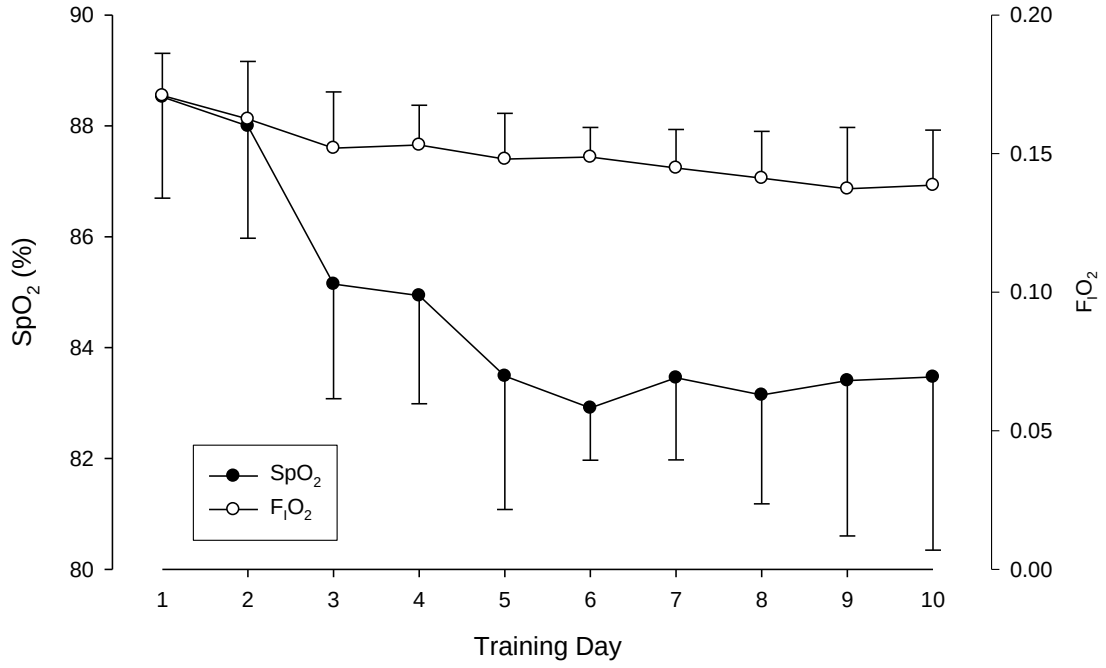

Figure 1. The oxygen concentration (F_IO_2) and arterial oxygen saturation (SpO_2) during the 10-day training programme for the IHT group. Data are means and SD.

Performance

Time (min:sec) to complete the 20-km distance decreased in both groups over the study (33:53, 33:38, 33:27 for placebo, and 32:50, 32:29, 32:08 for the IHT, for baseline, post2 and post9 tests respectively). After adjusting for initial differences in baseline performance between groups (Hopkins et al. 2009) the IHT subjects were 11.8 ± 40.2 and 23.7 ± 46.4 s (mean ± SD) faster than the placebo subjects at 2 and 9 days post-intervention respectively. Table 2 shows the mean changes in performance and economy measures for the placebo and IHT groups and the statistics for the difference in the changes. When differences in athletes initial ability between groups was controlled for by using the baseline performance measures as a covariate, a beneficial effect of IHT on mean 30-s power 2 days post-intervention was likely. This beneficial effect was unclear at 9 days post-intervention. Effects of IHT on 30-s peak power, 20-km mean power and oxygen cost were unclear. Adjusting for subject's body weight had little effect on the performance outcomes.

Standard deviations representing observed individual responses in performance at 2 and 9 days post-exposure were 30-s mean power, -2.9% (-4.7-2.5%) (mean and 95% confidence interval) and -2.9 (-5.1-3.1%); 30-s peak power, 5.3% (-11.6-15.4%) and 10.1% (-10.1-18.9); 20-km mean power,

-1.0% (-6.2-6.4%) and 10.8% (-5.3-16.8%); oxygen cost, -8.0% (-15.0-11.8%) and 5.4% (-13.2-17.4%) respectively. Variation in response between individuals, represented by a positive standard deviation, in some cases was large relative to the mean effect of IHT shown in Table 2. However, the uncertainty in both the positive and negative standard deviations suggests modest individual responses for all measures, relative to the mean effects, except for 30-s peak power which showed large individual responses.

Observed standard error (typical or within-subject error) of measurement post-intervention for the experimental measures were 30-s mean power, 2.4% and 2.7%; 30-s peak power 7.1% and 6.5%; 20-km mean power, 3.6% and 2.6%; oxygen cost, 8.3% and 6.7% for 2 and 9 days post-intervention respectively. The 95% confidence limits for the true errors were ~ x/÷2.0 for all measures.

Table 2. Mean change in performance and physiological measures post-training, and chances that the true differences in the changes are substantial.

	% Change				Chances that true differences are substantial[a]	
	Days Post-training	IHT	Placebo	Difference; ± 95% CL	%	Qualitative inference
30-s mean power	2	2.8	-0.2	3.0; ± 3.5	91	Likely Positive
	9	2.2	0.5	1.7; ± 3.8	67	Unclear
30-s peak power	2	1.6	-1.1	2.7; ± 11.6	62	Unclear
	9	7.3	-1.3	8.6; ± 12.5	89	Unclear
20-km mean power	2	2.7	0.7	2.0; ± 5.5	65	Unclear
	9	4.7	2.0	2.7; ± 9.2	65	Unclear
20-km Oxygen cost	2	-4.0	5.5	-10.1; ± 15.9	88	Unclear
	9	-3.6	2.6	-6.2; ± 17.3	73	Unclear

[a]Based on a smallest substantial change of 1.0% for all measures. ± 95% CL: add and subtract this number to the mean effect to obtain confidence limits for the true difference.

Physiological variables

Relative to the placebo group the IHT group's post-pre blood lactate concentration was consistently elevated throughout the 20-km time trial 2 and 9 days post-intervention (Table 3). When taking the average change in blood lactate concentration over the entire time trial, the IHT participants blood lactate concentration relative to the placebo group, increased substantially by 1.7 $mmol.L^{-1}$ (-0.6-3.9) (mean and 95% confidence interval)at 2 days and 1.5 $mmol.L^{-1}$ (-0.7-3.7) 9 days post-intervention. Changes in ventilation and $P_{ET}CO_2$ were in most cases unclear. Compared to the placebo group the IHT group's RER during the time trial was elevated 2 days post-intervention. Similarly there were clear and substantial increases in SpO_2 during the time trial in the IHT relative to the placebo group. When taking the average change in RER over the entire time trial, the IHT participants RER relative to the placebo group, increased by 0.08 (-0.01-0.17) at 2 days post-intervention but returned to similar levels by 9 days. Similarly when calculating the average change in SpO_2 over the entire time trail, the IHT participants mean arterial oxygen saturation was elevated by 1.2% (0.01-2.4%) at 2 days and 0.9% (-0.2-2.1%) 9 days post-intervention.

When taking the average change in RER during the 30-s Wingate test, the IHT participants RER relative to the placebo group, showed a clear and

substantial increase of 0.16 (-0.02-0.34) at 2 days post-intervention but returned to similar levels by 9 days post-exposure (0.02, -0.16-0.21). Changes in the other respiratory variables during the 30-s Wingate test were trivial or unclear.

Table 3. Mean post-pre changes between treatments (IHT-placebo) in physiological variables at rest and during the 20-km time trial.

	Days Post-training	Change ± 95% CL				
		Rest	5-km	10-km	15-km	20-km
Blood Lactate ($mmol.L^{-1}$)	2	0.8 ± 1.0*	2.5 ± 3.0*	1.5 ± 2.7	1.2 ± 2.6	1.6 ± 2.9
	9	-0.1 ± 1.2	1.5 ± 2.9	1.0 ± 2.5	1.3 ± 2.6	2.5 ± 2.9*
Heart Rate ($b.min^{-1}$)	2	6.6 ± 13.5	4.7 ± 7.6*	-0.1 ± 9.1	4.8 ± 7.1*	0.7 ± 7.9
	9	4.3 ± 13.1	0.1 ± 7.6	-0.4 ± 9.2	-0.2 ± 7.0	0.2 ± 7.9
$\dot{V}_E$ ($L.min^{-1}$)	2	-1.3 ± 2.9	12.3 ± 18.7	9.2 ± 19.7	4.7 ± 21.9	-6.8 ± 15.1
	9	-1.8 ± 3.2	-4.9 ± 20.3	0.6 ± 21.9	9.8 ± 23.8	14.5 ± 16.6*
$\dot{V}O_2$ ($L.min^{-1}$)	2	-0.00 ± 0.10	0.13 ± 0.45	0.05 ± 0.64	-0.19 ± 0.58	-0.52 ± 0.52*
	9	-0.08 ± 0.12	-0.24 ± 0.48	-0.03 ± 0.69	-0.05 ± 0.64	-0.03 ± 0.59
$P_{ET}CO_2$ (mmHg)	2	2.8 ± 5.1	0.1 ± 3.6	0.1 ± 3.1	0.6 ± 4.9	0.9 ± 3.5
	9	-1.3 ± 5.5	-0.4 ± 3.9	-0.2 ± 3.4	-1.5 ± 5.4	-1.5 ± 4.0
RER	2	-0.07 ± 0.13	0.10 ± 0.11*	0.09 ± 0.09*	0.11 ± 0.11*	0.05 ± 0.10
	9	-0.02 ± 0.14	0.01 ± 0.12	0.01 ± 0.10	-0.01 ± 0.12	0.04 ± 0.11
SpO_2 (%)	2	0.3 ± 1.2	0.2 ± 2.3	1.7 ± 2.4	1.8 ± 1.8*	1.7 ± 2.5
	9	0.6 ± 1.2	2.0 ± 2.3*	1.7 ± 2.4	0.8 ± 1.8	-0.8 ± 2.4

*Clear and substantial changes between groups based on a smallest substantial change of 0.2 of the between-subject standard deviation for all physiological measures. V_E, minute ventilation; $P_{ET}CO_2$, end-tidal CO_2; RER, respiratory exchange ratio; SpO_2, oxygen saturation of arterial blood; ± 95% CL: add and subtract this number to the mean effect to obtain confidence limits for the true difference.

Blood measures

Substantial increases resulting from IHT were likely for haemoglobin and very likely for haematocrit 2 days post-exposure (Table 4). The differences between groups in haemoglobin and haematocrit had decreased by 9 days post-intervention. Relative to the placebo group, reticulocytes in the IHT group were either likely (2 days) or very likely (9 days) to have increased post-intervention. Substantial decreases resulting from IHT were likely or almost certain for serum iron and % Ferritin saturation at both post-intervention days.

Hydration Status

Participants were at similar levels of hydration, as measured by urine specific gravity, prior to all performance exercise trials (IHT group 1.01 ± 0.00, 1.01 ± 0.00, 1.01 ± 0.01; Placebo group 1.01 ± 0.01, 1.01 ± 0.01, 1.01 ± 0.01 for baseline, post2 and post9 tests respectively; mean ± SD).

Table 4. Mean change in haematological measures post-training, and chances that the true differences in the changes are substantial.

	% Change				Chances that true differences are substantial[a]	
	Days Post-training	IHT	Placebo	Difference; ± 95% CL	%	Qualitative
Haemoglobin	2	1.5	-1.5	3.0; ± 4.0	75	Likely
	9	0.3	0.1	0.2; ± 3.6	20	Unclear
Haematocrit	2	2.4	-1.3	3.7; ± 3.5	98	Very likely
	9	0.4	-0.1	0.5; ± 3.6	61	Unclear
Reticulocytes	2	2.1	-7.9	10.0; ± 16.4	85	Likely
	9	-18.0	-2.2	-15.8; ± 16.1	96	Very likely
Serum Iron	2	-17.7	10.1	-27.8; ± 40.4	90	Likely
	9	-21.6	28.5	-50.1; ± 37.1	99	Almost certainly
% Ferritin saturation	2	-17.1	10.0	-27.1; ± 38.6	90	Likely
	9	-18.3	27.3	-45.7; ± 37.9	99	Almost certainly
Serum Ferritin	2	-12.2	-11.9	-0.3; ± 24.4	48	Unclear
	9	-16.3	-6.3	-10.0; ± 21.2	81	Unclear

[a]Based on a smallest substantial change of 0.2 of the between-subject standard deviation for all blood measures.
± 95% CL: add and subtract this number to the mean effect to obtain confidence limits for the true difference.

DISCUSSION

The main novel finding of this study was that 10 consecutive days of IHT substantially enhanced anaerobic power during a 30-s Wingate cycle test. We also found substantial increases in haemoglobin concentration, haematocrit and reticulocyte count 2 days and substantial reductions in serum iron and transferrin 2 and 9 days following IHT. In addition, relative to the placebo group, the IHT group's blood lactate concentration and SpO_2 were substantially higher during the 20-km time trial. Furthermore, the RER was substantially higher during both the 20-km time trial and 30-s Wingate test in the IHT compared to the placebo group. Effects on all other measures were unclear. When considering the smallest worthwhile effects, the performance enhancement found with 30-s mean anaerobic power is likely to be beneficial for well-trained multisport athletes or cyclists.

A larger than expected error of measurement is probably a major reason behind the lack of clarity in many results. The error of measurement for the performance measures in this study ranged from ~ 2% for 30-s mean power to ~ 8% for oxygen cost, compared to much lower errors in similar measures from previous studies ~ 1-2% (Hamlin & Hellemans 2007; Wood, Dowson 2006). The larger error measurement in this study could be due to the cycle erogometry being less reliable than running which was used to assess performance in previous studies (Hamlin & Hellemans 2007; Wood, Dowson 2006). Because of these larger errors of measurement, we would require a larger sample size (>n = 30) to get clear outcomes when the true effect is a change in performance of approximately 2%.

Except for 30-s peak power, individual responses to IHT at 2 days post-intervention were negligible; however at 9 days post-intervention, large individual responses were evident, particularly for 30-s peak and 20-km mean

power. Considering the hypoxic dose was individualised and the training was closely monitored this is an unexpected outcome. At least some of the large individual response may have been due to the larger than expected standard error of measurement of the performance tests at these time periods. It is suggested that such test-retest measurement errors should be no more than 2% (Hopkins et al. 2001), which was obtained for 30-s mean power in this study but was higher for the other performance measures.

Although we attempted to individually clamp SpO_2 by manually altering F_IO_2 the IHT subjects showed considerable variation in SpO_2 levels particularly toward the end of the training period (Figure 1.) Under poikilocapnic conditions (i.e. where the $P_{ET}CO_2$ is uncontrolled), hypoxia stimulates hyperventilation via the peripheral chemoreflex (Ainslie et al. 2007). However, the degree of ventilatory-drive to hypoxia is subject to considerable variation (Ainslie & Poulin 2004). This variability may be one reason for the variation witnessed in the IHT subjects SpO_2 levels. Some variation is probably also attributable to the breathing set-up used in this study which included two 100 L Douglas bags connected in series. Such a set-up introduces a large gas reservoir and results in some lag-time in the system between changes in individual SpO_2 levels of the subjects and subsequent adjustment of F_IO_2 levels by the researchers.

Anaerobic Results

Historically, altitude research has investigated changes in aerobic responses to exercise; more recently however, interest has grown into the effects of altitude training on anaerobic ability. The results of the present study demonstrated that IHT overall benefited the anaerobic more than the aerobic performance capacity. Observed changes in mean 30-s power found in this study (~ 3%) were similar to those found by others using similar Wingate protocols but on LODE ergometers (i.e. maximal pedalling against a constant load) (3-4%) (Meeuwsen et al. 2001) (~ 4%) (Hendriksen & Meeuwsen 2003), but lower than mean power in repeated sprint tests (~ 7-8%) (Bonnetti, Hopkins 2006; Wood, Dowson 2006). The difference in the magnitude of the change in mean power between the 30-s Wingate and the repeated sprint tests is probably due to the increased aerobic energy system component used during repetitive sprinting (Bishop & Edge 2006).

As has been shown in sea-level studies, improvement in anaerobic energy supply systems requires high-intensity intermittent training (Lindsay et al. 1996). Therefore, we hypothesized that in addition to the hypoxic aerobic training, the specific anaerobic training during hypoxia would provide a greater stimulus for improvement in anaerobic performance. While the present data indicates that IHT is advantageous for sea-level anaerobic performance it also shows that the specific high-intensity anaerobic training we used added little benefit to anaerobic performance change found with low-intensity hypoxic training alone (Hendriksen & Meeuwsen 2003; Meeuwsen, Hendriksen 2001). With the addition of two maximal 30-s Wingate tests, we based the hypoxic training programme of this study on that of (Hendriksen & Meeuwsen 2003) who used 120 min cycling at 60-70% heart rate reserve. It has been suggested that performance improvements are not likely to occur when

hypoxic training sessions are of insufficient duration or intensity (Ponsot, Dufour 2006). It may well be that the 90 min of aerobic exercise or the very short anaerobic exercise (approximately 1 min at maximum power output) used daily in this study was insufficient in duration or intensity to show clear and substantial increases in the other performance measures. The optimum dose and duration of IHT is still unclear.

Time Trial Results

Controversy exists as to the benefits of intermittent hypoxia on sea-level aerobic performance. The current study found a small (~ 2-3%) but unclear improvement in 20-km time trial average power output in the IHT compared to the placebo group. Ventura and colleagues (2003) also reported a non-significant (unclear) improvement in maximal power output of approximately 4% in the IHT relative to the placebo group (Ventura et al. 2003), while other researchers have found clear improvements in endurance performance of similar magnitude after IHE (~ 2-3 %) (Hamlin & Hellemans 2007; Wood, Dowson 2006) or IHT (~ 1-4 %) (Dufour, Ponsot 2006; Hendriksen & Meeuwsen 2003; Meeuwsen, Hendriksen 2001). A recent study on kayakers found a very large and clearly beneficial increase in peak aerobic power of ~ 7% three days post IHE intervention (Bonnetti, Hopkins 2006), however others have shown aerobic performance decrements ranging from ~ 1-7% after IHE (Julian, Gore 2004), or IHT (Morton & Cable 2005; Roels, Bentley 2007). It is difficult to reconcile these contrasting results, however methodological differences between studies may explain some of this dissimilarity. Most studies that have reported a drop in performance after IHT have used a considerably shorter hypoxic dose. For example, in the present study, and others that have shown performance enhancement after IHT (Hendriksen & Meeuwsen 2003; Meeuwsen, Hendriksen 2001) subjects exercised in a hypoxic state for at least 90 min per day, whereas subjects in studies where performance declined after IHT (Morton & Cable 2005; Roels, Bentley 2007) participants only exercised in hypoxia for up to 30 min per day. It has been suggested that the duration of hypoxic exposure is the most important factor when considering the effects of hypoxia on erythropoietin release (Knaupp et al. 1992). If this is also the case for the mechanisms that are responsible for performance enhancement after hypoxic exposure it may explain the disparity in performance results between studies. However, other factors such as participant's initial athletic ability, variability of the duration and intensity of the hypoxic training employed, and exercise training intensities during hypoxia are all likely to play a role (Levine 2002). For example, Dufour et al. (2006) found an improvement in time to exhaustion of ~ 25% (~ 2% equivalent change in power output) in the IHT compared to placebo group with only moderate duration (48-80 min per week) but high intensity (second ventilatory threshold) hypoxic training (Dufour, Ponsot 2006).

In addition, compared to many of the reports that failed to show any performance enhancement with intermittent hypoxic protocols (Julian, Gore 2004; Morton & Cable 2005; Roels, Bentley 2007), the current study along with others that have found substantial improvements in performance (Bonnetti, Hopkins 2006; Wood, Dowson 2006), used an individualised hypoxic dose, thereby somewhat overcoming the individuals' variability in

response to hypoxia (Ainslie, Barach 2007) which may limit the benefit of the hypoxic exposures to athletic performance. Future research in this area should include investigation into optimal hypoxic dosage (both duration and intensity), effects of individualising the hypoxic dosage, and effects of initial fitness levels and training protocols during the hypoxic period.

Physiological Responses

Mechanisms underlying the improved sea level performance after altitude training have received much debate recently (Gore & Hopkins 2005; Levine & Stray-Gundersen 2005). Some investigators suggest the enhanced sea-level performance is due to the hypoxic conditions causing an increase in red cell volume along with an associated increase in maximum oxygen uptake thereby allowing a greater oxygen delivery to, and uptake by, the working muscles (Levine & Stray-Gundersen 1997). Alternatively, other researchers have suggested the hypoxic-induced performance enhancement at sea level is caused by changes in the skeletal muscles buffering capacity (Gore, Hahn 2001) or improved exercise efficiency through producing more ATP per molecule of oxygen consumed (Katayama, Sato 2004).

Changes in the blood parameters in this study were similar to previous IHE (Hamlin & Hellemans 2007; Rodriguez et al. 2000) and IHT studies (Hendriksen & Meeuwsen 2003; Meeuwsen, Hendriksen 2001) and would tend to support enhanced erythropoiesis after IHT. When the relationship between changes in haemoglobin and mean power output during the time trial were analysed via linear regression analysis, we found large correlations at day 2 ($r = 0.60$), and 9 ($r = 0.48$) post-intervention, suggesting the small increase in mean power output after IHT may be explained in part by increased haemoglobin concentration.

Previous investigations have shown that intermittent hypoxic exposure results in increased ventilation and consequently elevated SaO_2 during exercise (Ainslie et al. 2008; Katayama et al. 2001). Calculating the overall mean changes in the respiratory variables during the 20-km time trial, the results of this study similarly indicate increased ventilation and SpO_2. It has been suggested that IHT causes increased chemoreflex sensitivity to hypoxia (Ainslie, Hamlin 2008; Katayama, Sato 2001) resulting in increased ventilation and therefore a smaller drop in SpO_2 during exercise.

Intermittent hypoxia may also have an effect at the cellular level, altering mitochondrial energy production. As suggested by Katayama et al. (2004) this change may increase the amount of ATP produced per mole of oxygen consumed, thereby resulting in less oxygen required for the same amount of energy produced. Although not conclusive, but similar to previous studies (Gore, Hahn 2001; Green et al. 2000; Katayama et al. 2003), our results showed a trend downward in oxygen cost (i.e. improved cycling economy) in the IHT compared to the placebo group during the time trial. However, this result was unclear and should be considered preliminary until further research has been completed.

It has been suggested that the improved economy after hypoxic exposure is related to the decreased cost of ventilation (Green, Roy 2000). Indeed, in this study, at the final stage of the time trial 2 days post-intervention, $\dot{V}_E$ and $\dot{V}O_2$ were lower in the IHT compared to the placebo participants, however, this change in $\dot{V}_E$ was too variable to make firm conclusions about whether the decreased $\dot{V}O_2$ was due to reduced $\dot{V}_E$.

A lower $\dot{V}O_2$ may also arise from a shift toward increased glycolytic contribution in ATP production (Katayama, Sato 2004), a move towards greater carbohydrate and less fat utilisation in oxidative phosphorylation (Roels et al. 2007), a more efficient excitation-contraction process during exercise (Green, Roy 2000) or a shift in the mitochondrial regulation to a more oxidative profile (Ponsot, Dufour 2006). While the last two hypotheses were not able to be tested in this study some evidence exists for a hypoxia-induced change in metabolism. At 2 days post-intervention we found a shift in the RER in the IHT compared to the placebo group that would indicate greater carbohydrate utilisation during both 30-s and 20-km exercise. We found a moderate to large negative correlation (r = -0.47) between RER and oxygen cost at day 2, reducing to a small to moderate correlation at 9 days post-intervention (r = -0.16). These data, while not conclusive, suggest that after IHT, the reduced oxygen cost during the time trial may be explained in part, by a shift toward carbohydrate utilization. Further evidence for this shift comes from the substantial increase in blood lactate production in the IHT compared to the placebo group during the time trial. Recently Peronnet et al. (2006) also found substantial increases in blood lactate concentration accompanying a shift in carbohydrate utilization in subjects exercising in hypoxic conditions (Peronnet et al. 2006). These data are consistent with the suggestion that under hypoxic conditions, increased carbohydrate flux reflects a shift towards carbohydrate utilization which is a more efficient fuel in terms of ATP generation per mole of O_2 consumed (Hahn & Gore 2001).

In conclusion, the results of this study demonstrate that training in a hypoxic environment for ~91 min per day for 10 consecutive days resulted in a clear 3.0% improvement in mean 30-s power 2 days post-intervention, and beneficial but unclear changes in 30-s peak power, 20-km mean power and 20-km oxygen cost 2 and 9 days post-intervention. Changes in the physiological and haematological indices indicate IHT may work to increase the blood oxygen carrying capacity but also change the metabolic fuel source towards enhanced breakdown of carbohydrate.

PRACTICAL IMPLICATIONS

Many athletes continue to use live-low, train-high techniques to improve sea-level performance. Such training is controversial with a recent review stating such training cannot be recommended for athletes because of a lack of sufficient evidence (Hoppeler et al. 2008). The results of the current study add little to resolve the debate on whether live-low train-high improves endurance performance. However, our results do indicate that the true effect of such training on anaerobic performance (30-s Wingate test) of well-trained athletes

can be a change in performance anywhere from a small decrease of 0.5% through to a large increase of 6.5% (95% confidence interval). The chances that the true effects are beneficial was 91%, whereas the chances that this effect is detrimental was 1%. Given these odds, most well-trained athletes would be likely to benefit from such training. However, it remains to be seen whether such changes also occur in very elite athletes.

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