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# Effect of intermittent hypoxic training on 20 km time trial and 30 s anaerobic performance

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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 [intermittent hypoxic training (IHT) group] trained with an $F_1O_2$ set to produce arterial oxygen saturations of $\sim$ 88–82%, while seven subjects (placebo group) trained while breathing a normal gas mixture ($F_1O_2 = 0.21$). Four performance tests were conducted at sea level including a familiarization and baseline trial, followed by repeat trials at 2 and 9 days post-intervention. Relative to the placebo group, the mean power during the 30-s Wingate test increased by 3.0% (95% confidence limits, CL $\pm 3.5$%) 2 days, and 1.7% ($\pm 3.8$%) 9 days post-IHT. Changes in other performance variables (30 s peak power, 20 km mean power and 20 km oxygen cost) were unclear. During the time trial, the IHT participants' blood lactate concentration, respiratory exchange ratio, and $SpO_2$, relative to the placebo group, was substantially increased at 2 days post-intervention. The addition of IHT to the normal training program of well-trained athletes produced worthwhile gains in 30 s sprint performance possibly through enhanced glycolysis.

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 the sea level but train under hypoxic conditions similar to higher altitudes ($\sim$ 2500–3850 m) (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 the 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: Levine and Stray-Gundersen (2005)]. Levine and 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 a resultant enhanced rate of oxygen transport. In contrast,

Gore and Hopkins (2005) emphasized 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 a natural altitude and training closer to sea level improves sea-level endurance performance in most cases (Levine & Stray-Gundersen, 1997; Chapman et al., 1998; Stray-Gundersen et al., 2001; Brugniaux et al., 2006; Schmitt et al., 2006; 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., 2007a, b).

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 (2500–6000 m) despite the knowledge that athletes have a highly variable response to hypoxia (Ainslie et al., 2007a, b). 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 individualized the hypoxic stimulus by reducing the arterial oxygen saturation ($SpO_2$) to a set level (Wood et al., 2006; Marshall et al., 2008). The effectiveness of this methodology, however, remains unclear as IHE has been found to enhance (Wood et al., 2006) or have no effect (Marshall et al., 2008) on aerobic performance, and is yet to be utilized during exercise training in hypoxia (IHT).

In addition to potentially improving endurance performance, IHE and IHT may also benefit anaerobic exercise performance (Hendriksen & Meeuwsen, 2003; Bonnetti et al., 2006), 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 $8.3 \pm 6.7\%$ and $6.8 \pm 5.2\%$ (mean $\pm 90\%$ confidence limits) for mean and peak power, respectively (Bonnetti et al., 2006), and repeated sprint run times by $\sim 1$–$7\%$ (Wood et al., 2006) 3 days following hypoxia exposures. Similarly, 10 days of IHT at a simulated altitude of 2500 m improved anaerobic mean (4.1%) and peak (3.8%) cycling power at 9 days post-intervention compared with 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.

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, randomized 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.

## Methods
### Subjects

Sixteen athletes from a variety of cycling backgrounds [eight road cyclists, three mountain bikers, one triathlete, and four multisport athletes (athletes who mainly compete in run, cycle, and kayak events)] volunteered to participate in the present study, all of whom were well trained and competed at the regional or the 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 before the start of the study. Subject characteristics are presented in Table 1.

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 the initial 20 km cycle time trial performance (i.e. time to complete the 20 km), and then randomly divided into two groups: an IHT group (IHT, $n = 9$) and a control group (placebo, $n = 8$). Because of 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 familiarization, baseline and two post-training trials. The baseline trial was performed 1 week after the familiarization trial and 2 days before beginning IHT or placebo training. The IHT group trained at a simulated altitude (normobaric hypoxia) whereas the placebo group underwent the same training protocol at sea level (normobaric normoxia) for 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 before each main trial. Subjects also recorded their dietary intake before the first trial to allow replication of the diet before 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, New Zealand) were provided to subjects from 1 week before the familiarization trial, as altitude-induced erythropoiesis is unlikely to occur in an iron-deficient state (Stray-Gundersen et al., 1992). Subjects

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

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

Values are mean $\pm$ between subject standard deviation.
Trimp, training impulse; IHT, intermittent hypoxic training.

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 before training (baseline) and $\sim 2$ (post-2) and $\sim 9$ (post-9) days post training. Blood samples were drawn at the same time for each subject, in the morning before breakfast, when subjects were in a fasted state. Samples were assayed by an independent professional testing laboratory (Southern Community Laboratories, Christchurch, New Zealand) for hemoglobin, hematocrit, 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 a simulated altitude (IHT) or at sea level (placebo). The bikes were mounted on a stationary trainer (CycleOps Fluid 2, Madison, Wisconsin, USA) and tyre pressure was standardized 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 (HR) reserve. In order to have subjects work at the same relative intensity, the IHT group's target HR was adjusted to take account of the natural decline in the maximal HR with decreasing $F_IO_2$ (Richalet, 1992). A regression equation that describes the decrease in chronotropic drive during hypoxia, $y$ (% of sea-level $HR_{max}$) = 116 − 0.0057$x$ ($x$ = altitude in meters, or $SpO_2$), was used to predict maximal HR for the HR 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, Racer-Mate Inc., Seattle, Washington, USA).

During training, subjects received either a normobaric hypoxic gas (IHT group) or a 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, Kansas City, Missouri, USA) attached to a one-way non-rebreathing valve (Hans-Rudolph 2700). 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. The $SpO_2$ levels were $\sim 88\%$ on days 1–2, $\sim 84\%$ on days 3–4 and $\sim 82\%$ on days 5–10 (the equivalent of 3200, 4000, and 4400 m altitudes, 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 the 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 HR were recorded every 5 min.

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 the 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 five-point Likert-type scale: excellent = 1, good = 2, average = 3, poor = 4 and 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.). 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.), 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 program (Racermate Inc.). The Velotron settings (seat, handle bar height, and horizontal position) were adjusted during the familiarization 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 three maximal sprints lasting $\sim 5$ s, subjects performed a 30-s Wingate test (Velotron Wingate software, version 1.0; Racermate Inc.) 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. The final HR and $SpO_2$ were recorded by the researcher, and the Velotron software calculated the peak and mean power output (W). The Wingate test was followed by light pedalling for 5–10 min, followed by 50–55 min of passive recovery.

Following recovery, baseline data were collected (ventilation and expired gases, $SpO_2$, HR, and blood lactate concentration), followed by a 10 min self-selected warmup for the time trial. Subjects completed the time trial from a standing start, on a gear ratio previously selected during the familiarization 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- and 15 km time points and then every 1 km to the completion of the test, but received no feedback on power output, heart rate, pedal cadence, or performance time. The following measurements were taken at 5, 10, 15, 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 $\sim 2$ 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 min of the test, we have been able to calculate the 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 four stages (5, 10, 15, and 20 km) and then averaged. Before testing, the gas analyser was calibrated for volume (Hans-Rudolph 5530 3 L syringe) and gas composition (15% $O_2$ and 5% $CO_2$).

During the performance tests and training sessions, HR was recorded continuously by means of an HR monitor (S610; Polar, Kempele, Finland). Arterial oxygen saturation was monitored manually by the researcher (Sport-Stat; Nonin Medical, Minneapolis, Minnesota, USA). 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, analyzed 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 modeling procedure (Proc Mixed) in the Statistical Analysis System (Version 8.0, SAS Institute, Cary, North Carolina, USA). We analyzed the natural logarithm of each measure to reduce any effects in non-uniformity of error and to obtain changes in measures and errors as percentages. The fixed effects were trial (pre, post-2 post-9), 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 were 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, uncertainties 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% and 95%, whereas the IHT group's $SpO_2$ decreased during training from $88.8 \pm 1.8\%$ (mean $\pm$ SD), on day 1, to $83.5 \pm 3.1\%$, on day 10. The $F_IO_2$ required to main-

tain the $SpO_2$ at this reduced level for the IHT group declined from $0.17 \pm 0.01$ on day 1 to $0.14 \pm 0.02$ on day 10 (Fig. 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 $224 \pm 177$, $221 \pm 49$, $145 \pm 80$; IHT group $176 \pm 82$, $203 \pm 40$, $165 \pm 55$ Trimps/day 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 $< 0.8\%$. Therefore, it seems unlikely that differences in training load between groups had any influence on the outcomes of this study.

### Performance

Time (min:sec) to complete the 20 km distance decreased in both groups over the study (33:53, 33:38 and 33:27 for placebo, and 32:50, 32:29 and 32:08 for the IHT, for baseline, post-2 and post-9 tests,
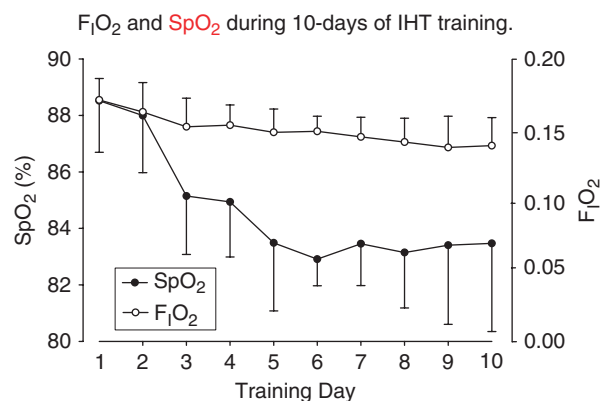


Fig. 1. Oxygen concentration ($F_IO_2$) and arterial oxygen saturation ($SpO_2$) during the 10-day training program for the intermittent hypoxic training (IHT) group. Data are means and SD.

respectively). After adjusting for initial differences in baseline performance between groups (Hopkins et al., 2009) the IHT subjects were $11.8 \pm 40.2$ and $23.7 \pm 46.4$ s (mean $\pm$ 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 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 the 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.

The observed standard errors (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%; and oxygen cost, 8.3% and 6.7% for 2 and 9 days post-intervention, respectively. The 95% confidence limits for the true errors were $\sim x/ \div 2.0$ for all measures.

## 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 $(-0.6-3.9)$ (mean and 95% confidence interval) at 2 days and 1.5 mmol/L $(-0.7-3.7)$ 9 days post-intervention. Changes in ventilation and $P_{ET}CO_2$ were unclear in most cases. Compared with 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 trial, 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 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* | |
|---|---|---|---|---|---|---|
| | Days Post-training | IHT | Placebo | Difference; $\pm$ 95% CL | % | Qualitative inference |
| 30 s mean power | 2 | 2.8 | $-0.2$ | 3.0; $\pm$ 3.5 | 91 | Likely Positive |
| | 9 | 2.2 | 0.5 | 1.7; $\pm$ 3.8 | 67 | Unclear |
| 30 s peak power | 2 | 1.6 | $-1.1$ | 2.7; $\pm$ 11.6 | 62 | Unclear |
| | 9 | 7.3 | $-1.3$ | 8.6; $\pm$ 12.5 | 89 | Unclear |
| 20 km mean power | 2 | 2.7 | 0.7 | 2.0; $\pm$ 5.5 | 65 | Unclear |
| | 9 | 4.7 | 2.0 | 2.7; $\pm$ 9.2 | 65 | Unclear |
| 20 km Oxygen cost | 2 | $-4.0$ | 5.5 | $-10.1$; $\pm$ 15.9 | 88 | Unclear |
| | 9 | $-3.6$ | 2.6 | $-6.2$; $\pm$ 17.3 | 73 | Unclear |

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

IHT, intermittent hypoxic training.

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) | 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) | 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) | 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) | 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. ± 95% CL: add and subtract this number to the mean effect to obtain confidence limits for the true difference.

$\dot{V}_E$, minute ventilation; $P_{ET}CO_2$, end-tidal $CO_2$; RER, respiratory exchange ratio; $SpO_2$, oxygen saturation of arterial blood; IHT, intermittent hypoxic training;

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

| | | % Change | | | Chances that true differences are substantial* | |
| --- | --- | --- | --- | --- | --- | --- |
| | Days Post-training | IHT | Placebo | Difference; ± 95% CL | % | Qualitative |
| Hemoglobin | 2 | 1.5 | − 1.5 | 3.0; ± 4.0 | 75 | Likely |
| | 9 | 0.3 | 0.1 | 0.2; ± 3.6 | 20 | Unclear |
| Hematocrit | 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 |

*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.

IHT, intermittent hypoxic training.

## Blood measures

Substantial increases resulting from IHT were likely for hemoglobin and very likely for hematocrit 2 days post-exposure (Table 4). The differences between groups in hemoglobin and hematocrit 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, before all perfor-

mance 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, post-2 and post-9 tests, respectively; mean ± SD).

## 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 the hemoglobin concentration, hematocrit, 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 the 30-s Wingate test in the IHT compared with the placebo group. The effects on all other measures were unclear. When considering the smallest worthwhile effects, the performance enhancement found with a 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 the major reason behind the lack of clarity in many results. The error of measurement for the performance measures in this study ranged from $\sim 2\%$ for 30 s mean power to $\sim 8\%$ for oxygen cost, compared with much lower errors in similar measures from previous studies of $\sim 1–2\%$ (Wood et al., 2006; Hamlin & Hellemans, 2007). 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 (Wood et al., 2006; Hamlin & Hellemans, 2007). Because of these larger errors of measurement, we would require a larger sample size ($>n = 30$) to obtain 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 that the hypoxic dose was individualized 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 a considerable variation in $SpO_2$ levels particularly toward the end of the training period (Fig. 1.) Under poikilocapnic conditions (i.e., where the $P_{ET}CO_2$ is uncontrolled), hypoxia stimulates hyperventilation via the peripheral chemoreflex (Ainslie et al., 2007a, b). 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 observed 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 in 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. The changes observed in the mean 30 s power found in this study ($\sim 3\%$) 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) ($\sim 4\%$) (Hendriksen & Meeuwsen, 2003), but lower than the mean power in repeated sprint tests ($\sim 7–8\%$) (Hopkins, 2006; Wood et al., 2006). The difference in the magnitude of the change in the 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, an improvement in anaerobic energy supply systems requires a 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 an improvement in anaerobic performance. While the present data indicate that IHT is advantageous for sea-level anaerobic performance, it also shows that the specific high-intensity anaerobic training we used led to little benefit to anaerobic performance change found with low-intensity hypoxic training alone (Meeuwsen et al., 2001; Hendriksen & Meeuwsen, 2003). With the addition of two maximal 30-s Wingate tests, we based the hypoxic training program of this study on that of Hendriksen and Meeuwsen (2003), who used 120 min of cycling at 60–70% HR reserve. It has been suggested that performance improvements are not likely to occur when hypoxic training sessions are of an insufficient duration or intensity (Ponsot et al., 2006). It may well be that the 90 min of aerobic exercise or the very short anaerobic exercise (approximately 1 min at the 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 ($\sim 2–3\%$) but unclear improvement in a 20 km time trial average power output in the IHT compared with the placebo group.

Ventura et al. (2003) also reported a non-significant (unclear) improvement in the 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 a similar magnitude after IHE ($\sim$ 2–3%) (Wood et al., 2006; Hamlin & Hellemans, 2007) or IHT ($\sim$ 1–4%) (Meeuwsen et al., 2001; Hendriksen & Meeuwsen, 2003; Dufour et al., 2006). A recent study on kayakers found a very large and clearly beneficial increase in peak aerobic power of $\sim$ 7% 3 days post-IHE intervention (Bonnetti et al., 2006); however, others have shown aerobic performance decrements ranging from $\sim$ 1% to 7% after IHE (Julian et al., 2004) or IHT (Morton & Cable, 2005; Roels et al., 2007a). 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 decline 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 (Meeuwsen et al., 2001; Hendriksen & Meeuwsen, 2003), 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 et al., 2007a), participants only exercised in hypoxia for up to 30 min/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 used 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 $\sim$ 25% ($\sim$ 2% equivalent change in power output) in the IHT compared with the placebo group with only a moderate duration (48–80 min/week) but a high-intensity (second ventilatory threshold) hypoxic training (Dufour et al., 2006).

In addition, compared with many of the reports that failed to show any performance enhancement with intermittent hypoxic protocols (Julian et al., 2004; Morton & Cable, 2005; Roels et al., 2007a), the current study, along with others that have found substantial improvements in performance (Hopkins, 2006; Wood et al., 2006), used an individualized hypoxic dose, thereby somewhat overcoming the individuals' variability in response to hypoxia (Ainslie et al., 2007a, b) that may limit the benefit of the hypoxic exposures to athletic performance. Future research in this area should include an investigation into the optimal hypoxic dosage (both duration and intensity), effects of individualizing 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 been debated considerably (Gore & Hopkins, 2005; Levine & Stray-Gundersen, 2005). Some investigators suggest that 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 that the hypoxic-induced performance enhancement at sea level is caused by changes in the skeletal muscles' buffering capacity (Gore et al., 2001) or improved exercise efficiency through producing more ATP per molecule of oxygen consumed (Katayama et al., 2004).

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

Previous investigations have shown that IHE results in increased ventilation and consequently elevated $SaO_2$ during exercise (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 (Katayama et al., 2001), resulting in increased ventilation and therefore a smaller decline 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 (Green et al., 2000; Gore et al., 2001;

Katayama et al., 2003), our results showed a downward trend in the oxygen cost (i.e., improved cycling economy) in the IHT compared with 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 et al., 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 with 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 et al., 2004), a move toward greater carbohydrate and less fat utilization in oxidative phosphorylation (Roels et al., 2007a, b), a more efficient excitation–contraction process during exercise (Green et al., 2000) or a shift in the mitochondrial regulation to a more oxidative profile (Ponsot et al., 2006). While the last two hypotheses could not 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 with the placebo group that would indicate greater carbohydrate utilization 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 with 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 under hypoxic conditions (Peronnet et al., 2006). These data are consistent with the suggestion that under hypoxic conditions, increased carbohydrate flux reflects a shift toward 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 $\sim 91$ min/day for 10 consecutive days resulted in a clear 3.0% improvement in the 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 hematological indices indicate that IHT may work to increase the blood oxygen-carrying capacity but may also change the metabolic fuel source toward enhanced breakdown of carbohydrate.

## Perspectives

Many athletes continue to use live-low, train-high techniques to improve sea-level performance. Such a training technique 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 this effect is 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.

**Key words:** altitude, intermittent hypoxic exposure, cycling performance, Wingate test, efficiency.

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