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

Running title: Reproducibility of simulated LHTL

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ABSTRACT

Elite athletes often undertake multiple altitude exposures within and between training years in an attempt to improve sea-level performance. **Purpose:** To quantify the reproducibility of responses to live high/train low (LHTL) altitude exposure in the same group of athletes. **Methods:** Sixteen highly trained runners with maximum aerobic power (\(\text{VO}_{2\text{max}}\)) of 73.1 ± 4.6 and 64.4 ± 3.2 ml·kg\(^{-1}\)·min\(^{-1}\) (mean ± SD) for males and females respectively, completed 2 x 3-wk blocks of simulated LHTL (14 h·day\(^{-1}\), 3000 m) or resided near sea-level (600 m) in a controlled study design. Changes in 4.5 km time trial performance and physiological measures including \(\text{VO}_{2\text{max}}\), running economy and hemoglobin mass (Hb\(_{\text{mass}}\)) were assessed. **Results:** Time-trial performance showed small and variable changes after each 3-wk altitude block in both the LHTL (-1.4%; ±1.1% and 0.7%; ±1.3%, mean; ±90% CL) and the Control (0.5%; ±1.5% and -0.7%; ±0.8%) group. The LHTL group demonstrated reproducible improvements in \(\text{VO}_{2\text{max}}\) (2.1%; ±2.1% and 2.1%; ±3.9%) and Hb\(_{\text{mass}}\) (2.8%; ±2.1% and 2.7%; ±1.8%) after each 3-wk block. Compared with the Control group, the LHTL group were substantially faster after the first 3-wk block (LHTL-Control: -1.9%; ±1.8%) and had substantially higher Hb\(_{\text{mass}}\) after the second 3-wk block (4.2%; ±2.1%). There was no substantial difference in the change in mean \(\text{VO}_{2\text{max}}\) between the groups after the first (1.2%; ±3.3%) or second 3-wk block (1.4%; ±4.6%). **Conclusion:** 3-wk LHTL altitude exposure can induce reproducible mean improvements in \(\text{VO}_{2\text{max}}\) and Hb\(_{\text{mass}}\) in highly trained runners, but changes in time trial performance appear to be more variable. Competitive performance is dependent not only on improvements in physiological capacities that underpin performance, but a complex interaction of many factors including fitness, fatigue and motivation. **Keywords:** hemoglobin mass, normobaric hypoxia, maximum aerobic power, repeated exposure, runners
INTRODUCTION

Paragraph 1 Many athletes use altitude training to induce physiological adaptations associated with improved performance (22). Despite more than 40 years of research and widespread support among athletes and coaches, there is little consensus on whether altitude training can enhance sea-level performance in highly-trained athletes. Research findings are confounded by differing methodologies including varying duration, length, and type of altitude training, and training level and status of the athletes. Nonetheless, there is evidence that natural or simulated live high/train low (LHTL) altitude may offer small performance benefits for some athletes (14, 24, 34); although the underlying physiological mechanism(s) remain unclear (22).

Paragraph 2 In our experience, elite endurance athletes often undertake multiple altitude exposures within and between training years to gain a competitive edge (28). However, it has not been established if an individual athlete responds in the same way to repeated bouts of altitude exposure. Small gains in performance following both natural (21, 34, 36) and simulated (4) LHTL have been attributed to hypoxia-induced increases in hemoglobin mass ($H_{\text{mass}}$) and improved maximal aerobic power ($VO_{\text{max}}$). However, a number of studies have observed small ~1% improvements in performance after simulated LHTL, with no substantial change in hematological parameters (14, 24, 31). With shorter daily exposures (8-12 h·day$^{-1}$), other peripherally-mediated mechanisms including improved running economy (31) and enhanced muscle buffering capacity (13) have been observed in the absence of hematological changes. These parameters warrant further investigation to clarify whether small changes in performance following altitude training can be explained independently of increased number of red blood cells (22).
Replication is a fundamental tenet of science and yet no previous study has addressed the reproducibility of physiological adaptations and performance gains to repeated altitude exposure, in the same athletes. Therefore, the aim of this study was to quantify the test-retest reproducibility of both physiological and performance changes in highly trained athletes after two matched 3-wk blocks of simulated LHTL.

METHODS

Subjects

Sixteen highly trained male and female middle distance and distance runners (age: 30.6 ± 4.6 y, mean ± SD) undertook 2 x 3-wk blocks of simulated live high/train low altitude (LHTL, n=8) or resided near sea-level (Control, n=8). Athletes were pair matched for time trial performance and randomly assigned to either the LHTL or Control group. Both groups trained together near sea-level (Canberra, ~600 m ambient altitude) and were tested under normoxic conditions at the Australian Institute of Sport (AIS). All participants had been training and running competitively for a minimum of 5 years (LHTL: 11 ± 4y, Control: 14 ± 3 y). Baseline characteristics are presented in Table 1. Written consent was obtained from subjects after they were informed of the experimental procedures and possible risks involved with participation. The study was approved by both the Ethics Committee of the Australian Institute of Sport, and Committee for Ethics in Human Research at the University of Canberra.

Experimental Design

The LHTL group spent 2 x 3 weeks (14 h·day\(^{-1}\), ~300 h) in a normobaric hypoxic five bedroom facility (3000 m), separated by a 5 week wash-out period between Block 1 and 2 (Figure 1).
Time Trial

Paragraph 6  One day prior to and after each 3-wk block a 4.5 km time trial on a road course (6 laps) was completed in the shortest possible time, with split times and final time recorded manually on a stopwatch (Seiko, S120-4020, Japan). This atypical distance was selected to prevent athletes following a pre-determined pacing strategy over familiar race distances such as 3-km or 5-km. Consistent with the approach of others (21, 29) athletes were instructed to follow an experienced pacer for laps 1 and 2 (first 1.5 km). A paced start reduces the chance of individuals going out too fast or too slow, but nevertheless allows ample opportunity for the athlete to change their pacing during the final 4 laps. Individualized starting pace was based on predicted finish time from recent 3-km or 5-km race times. Runners were given feedback on distance completed, but no temporal information on split times during the time trial. The typical error of measurement (TE) established from the Control group pre- to post-test was 1.3 % (1.0 to 2.1%, 90% confidence interval).

Treadmill Test

Paragraph 7  A treadmill test was used to determine $\dot{V}O_{2\text{max}}$, running economy, lactate threshold, and velocity at $\dot{V}O_{2\text{max}}$ ($v\dot{V}O_{2\text{max}}$), on a custom-built motorized treadmill. The test comprised continuous incremental running for 4-5 x 4-min periods, at 0% gradient, with speeds ranging from 14-20 km·hr$^{-1}$, with a 1 min rest between each stage. Five min after the final submaximal stage, a maximal 60 s run (18.5-22 km·hr$^{-1}$) at 4% gradient was completed. After a further 5 min break, subjects recommenced running at 14-16 km·hr$^{-1}$, with speed increasing by 0.5 km·hr$^{-1}$ every 30 s for 5 min. Beyond this point, speed was maintained and gradient increased by 0.5% every 30 s until volitional exhaustion. Heart rate was recorded continuously (Polar Heart Rate Monitor, Kempele, Finland) and capillary blood (5 µL) sampled from the finger tip after each stage and 1 min after completion of the test for
measurement of blood lactate concentration (Lactate Pro, Akray, Japan). Expired ventilation samples were collected by a custom built open-circuit indirect calorimetry system for determination of oxygen consumption (31). The TE established from duplicate trials on a separate group of endurance-trained athletes was 2.1% (1.4 to 4.1%) for \( \dot{V}O_{2\text{max}} \) and 2.4% (1.7 to 4.6%) for submaximal \( \dot{V}O_2 \).

**Paragraph 8** Running economy was derived from steady-state oxygen uptake during the last 60 s of each sub-maximal stage of the treadmill test, to determine \( \dot{V}O_2 \) for a given velocity. Comparisons were made for economy from pooled individual data from four submaximal running speeds. Capillary blood (95 µL) was sampled from the finger tip before and 3 min after the 60 s maximal run, and analyzed on the ABL-700 series analyzer (Radiometer Medical, Copenhagen). Blood pH, bicarbonate (HCO\(_3^\)⁻) and lactate concentration were measured as an indirect means of assessing changes in buffering capacity, with less reduction in HCO\(_3^\)⁻ indicative of augmented buffering capacity.

**Hemoglobin mass**

**Paragraph 9** Hemoglobin mass (Hb\(_{\text{mass}}\)) was measured twice before, each week during and one week after each 3-wk block using a modified 2-min carbon monoxide (CO) rebreathing test (25). This method accounts for loss of CO due to exhalation and diffusion to the vascular bed. A small bolus (~1 mL·kg\(^{-1}\)) of CO was rebreathed with 3-3.5 L of oxygen for 2 min. Capillary blood (200 µL) was sampled from a pre-warmed finger tip before, and 6 and 8 min post CO inhalation, to measure percent carboxyhaemoglobin (HbCO) in quadruplicate (OSM-3 Hemoximeter, Radiometer Medical, Copenhagen). Change in percent HbCO (baseline to average of 6 and 8 min) was used to calculate Hb\(_{\text{mass}}\) (g). The TE for double baseline Hb\(_{\text{mass}}\) prior to Block 1 was 2.0% (1.6 to 2.6%) in this group.
Hematological parameters

**Paragraph 10** Each subject reported to the laboratory twice prior to Block 1 and 2 in an overnight fasted state and a venous blood sample was collected after 10 min of supine rest. Venous blood was collected into a 2-mL EDTA tube for red blood cell analysis and a 4-mL serum separation tube for biochemical analysis (Vacuette®, Greiner Bio-One) at six time-points (pre-1, pre-2, day 2, day 6, day 20, day 27) in Block 1 and 2 (Figure 1).

**Paragraph 11** Hemoglobin concentration ([Hb]), hematocrit (Hct) and percentage of reticulocytes were determined using the Advia 120 Hematology Analyzer (Bayer Diagnostics, Tarrytown, NY). The analyzer was calibrated against appropriate reference materials and checked daily using 3-in-1 TESTpoint™ quality controls. Whole blood was centrifuged at 4000 rpm for 5 min and the serum aliquoted for storage at -80°C until batch analysis. The concentrations of ferritin and soluble transferrin receptor (sTfR) were determined by immunoturbidimetric assay on a Hitachi 911 Automatic Analyser (Boehringer Mannheim, Germany). Erythropoietin concentration (EPO) was measured on an Immulite (Siemens AG) using an enzyme-amplified chemiluminescence assay with automated bead washing (Immulse® 1000 Test Unit).

**Paragraph 12** All subjects were provided with daily oral iron supplement, Ferrograd C (325 mg dried ferrous sulphate and 562.4 mg sodium ascorbate) to take one week prior, and for the duration of each 3-wk block, to ensure adequate iron stores for accelerated erythropoiesis.

Training quantification

**Paragraph 13** Subjects were instructed to maintain their normal training program throughout the study. Training data was collected from each subject during the study from a
daily training log, global positioning system (GPS) monitoring (Forerunner, Garmin, Kansas) and heart rate monitoring (S-Series, Polar, Kempele, Finland). Data were collated and compared for training distance (km), duration (h) and intensity (%HR_max) within and between groups. Total training distance, duration and intensity did not differ substantially for either group from Block 1 to Block 2 and there was no substantial difference in training duration or training intensity between the groups. However, the LHTL group had a greater mean total training distance compared with the Control group in Block 1 (370 ± 92 km versus 269 ± 62 km) and 2 (379 ± 91 km versus 258 ± 60 km). Given the difference in training distance between the groups, we incorporated individual training distance as a covariate in the analysis of time trial performance (16).

**Statistical Analysis**

*Paragraph 14* We used a contemporary statistical approach (20) because changes in performance of as little as ~0.5% are meaningful for elite athletes (18) and because conventional statistics can be relatively insensitive to such small but important changes. Specifically, we used magnitude-based inferences about effect sizes and precision of estimation expressed as 90% confidence limits (CL), to evaluate differences within and between groups (3). The unequal variances t statistic was used to analyze differences in the mean change for each group during Block 1 and 2, and to compare differences in the change scores between the LHTL and Control groups. All measures were log-transformed for the analyses, to reduce bias arising from any non-uniformity of error, and back-transformed to obtain changes in means and standard deviation (SD) as percents (20). The probability that the true value of the effect was practically positive, trivial or negative accounted for the observed difference, the smallest worthwhile difference, and typical error of measurement (3). A reference value of 1% for the smallest worthwhile change in performance was
calculated from 0.5 x within-athlete coefficient of variation (CV) from competition of similar distance events in elite runners (19). For measures not directly related to performance, the smallest worthwhile change was calculated from Cohen’s smallest standardized effect size of 0.2 multiplied by the pre-test between-athlete SD (8).

**Paragraph 15** Effects that were simultaneously both >75% likely positive and <5% negative were considered substantial and beneficial. Those effects where the confidence interval overlapped the thresholds for both positive and negative were deemed unclear (17). The true individual response was used to indicate the degree of variability in response to the intervention relative to the magnitude of the mean change. The true individual response expressed as a percent, was calculated as the square root of the difference in the variance in the change scores between the LHTL and Control groups (15). Pearson product-moment correlations were interpreted using a scale of magnitudes (8) comprising of 0.1 (small), 0.3 (moderate), and 0.5 (large). Typical error of measurement (TE) for outcome measures was calculated from the standard deviation of the change scores divided by \(\sqrt{2}\) and presented as a percent.

**RESULTS**

**Reproducibility of Physiological and Performance Changes within Groups**

**Paragraph 16** Following each 3-wk LHTL exposure, there were reproducible mean increases in \(\text{VO}_{2\text{max}}\) (2.1%; ±2.1% and 2.1%; ±3.9%, mean; ±90% CL%) and Hb\text{mass} (2.8%; ±2.1% and 2.7%; ±1.8%). However, changes in 4.5 km time trial performance were less consistent with the LHTL group substantially faster after Block 1 (-1.4%; ±1.1%) but trivially slower after Block 2 (0.7%; ±1.3%). The Control group had only trivial changes after Block 1
and 2 in $\text{VO}_2\text{max}$ (0.9%; ±2.8% and 0.7%; ±3.1%), Hb$_{\text{mass}}$ (1.4%; ±2.7% and -1.5%; ±1.5%) and time trial performance (0.5%; ±1.5% and -0.7%; ±0.8%).

Paragraph 17 Overall, there was a lack of association between percent change in Block 1 versus percent change in Block 2 in physiological and performance measures for the LHTL group. There were moderate but unclear correlations for $\text{VO}_2\text{max}$ and Hb$_{\text{mass}}$, and only a trivial correlation for time trial performance (Figure 2). True individual responses indicating the variability in response to the intervention, were of similar magnitude to the small mean changes in Block 1 and 2 for $\text{VO}_2\text{max}$ (2.6% and 3.7%), Hb$_{\text{mass}}$ (2.4% and 1.4%) and time trial performance (1.5% and 1.6%).

Time Trial Performance

Paragraph 18 Compared with the Control group, the LHTL group was substantially faster (-1.9%; ±1.8%) after Block 1, but possibly slower (1.4%; ±1.5%) after Block 2 (Figure 3). When adjusted for training volume the difference between the groups from pre to post was unclear after Block 1 (-1.1%; ±2.4%) and the LHTL group was substantially slower after Block 2 (2.0%; ±1.9%). In terms of pacing, the LHTL group were faster in the final 4 laps in the post-test after Block 1 (lap 3: -1.5%; ±1.4%, Lap 4: -1.6%; ±1.5%, Lap 5: -2.1%; ±1.7%, Lap 6: -2.9%; ±2.5%), but there were only trivial differences in lap times after Block 2, and after both blocks for the Control group.

Treadmill Test

Paragraph 19 Mean change in $\text{VO}_2\text{max}$ for both groups was reproducible, however, other parameters from the treadmill test were more variable (Table 2). The LHTL group had no substantial improvement in running economy or $v\text{VO}_2\text{max}$ after either block, 4mM lactate running speed was substantially faster only after Block 1, and post-test lactate concentration
was substantially lower after both Block 1 and 2. The Control group demonstrated trivial changes following both 3-wk blocks, with post-test lactate substantially higher only after Block 1. Compared with the Control group, the LHTL group was substantially faster at 4mM lactate running speed after Block 1, had lower lactate post-test after Block 1 and 2, but there were no substantial differences in the change in mean $\text{VO}_{2\text{max}}$, $\nu\text{VO}_{2\text{max}}$ or economy. Following the maximal 60 s test, the difference in blood $\text{HCO}_3^-$ (pre-post) was substantially lower after Block 1 (-3.5%; ±5.0%) in the LHTL group, but there was little difference after Block 2, or when compared with the Control group.

**Hemoglobin mass**

Paragraph 20 The LHTL group exhibited a reproducible pattern of weekly increases in $\text{Hb}_{\text{mass}}$ in both Block 1 and 2; in contrast the Control group showed relatively little change (Figure 4). $\text{Hb}_{\text{mass}}$ measured at week 3 was substantially higher in the LHTL group compared with the Control group after Block 2 (4.2%; ±2.1%), but there was only a trivial difference between the groups after Block 1 (1.3%; ±3.2%).

**Hematological parameters**

Paragraph 21 There was evidence of accelerated erythropoiesis in the LHTL group with substantially higher EPO concentration at day 2 and day 6 of each exposure, increased sTfR concentration at day 6 which remained elevated until day 20, and a corresponding decrease in ferritin concentration over each 3-wk LHTL exposure (Figure 5). The Control group had no substantial differences in sTfR or ferritin concentration in either block, although EPO concentration was substantially lower at day 20 and 27 in Block 1. Percent reticulocytes were substantially increased in both Block 1 and 2 for the LHTL group at day 6 and 20, and the Control group at day 6, 20 and 27.
Paragraph 22 Compared with the Control group, EPO was substantially elevated in Block 1 and 2 at day 2 (70%; ±30% and 90%; ±24%), day 6 (37%; ±29% and 34%; ±28%) and day 20 (16%; ±21% and 32%; ±28%), and sTfR was higher at day 20 (19%; ±13% and 11%; ±11%) in the LHTL group. There were no substantial differences in ferritin between the groups.

DISCUSSION

Paragraph 23 This is the first study to demonstrate that 3 weeks of simulated LHTL exposure elicited reproducible mean increases in $\dot{V}O_{2\text{max}}$ (~2%) and Hb$_{\text{mass}}$ (~3%). However, these physiological enhancements did not transfer to reproducible improvements in 4.5 km time trial running performance. There was an apparent uncoupling in the relationship between underlying improvements in physiological capacities and changes in endurance performance following altitude training in highly trained athletes. The mean changes in performance measures with hypoxic exposure were small and variable. Therefore, our results suggest that the timing of competition following altitude exposure and the management of training may be particularly important factors in realizing performance gains following altitude exposure.

Performance

Paragraph 24 After the first 3-wk block, the ~1% performance improvement in the LHTL group compares favourably with the previously reported 1.1-1.6% improvements in 3-km (34) and 5-km time trial performance (21, 36) after LHTL. These improvements in performance corresponded with ~3-4% increases in $\dot{V}O_{2\text{max}}$ and were attributed to increased hemoglobin mass or red cell volume (21, 34, 36). However, a slower time trial performance after the second 3-wk block in the current study, despite equivalent increases in Hb$_{\text{mass}}$ and
\( \text{VO}_{2\text{max}} \) suggests that non-erythropoietic factors also influence endurance performance (22). The failure to enhance performance after the second 3-wk block is similar to previous studies in well-trained athletes where little or no improvement was reported following simulated LHTL (6, 10, 13, 26, 27).

**Paragraph 25** The lack of association between performance changes in Block 1 versus Block 2, demonstrates that enhancement of performance following one bout of LHTL exposure does not guarantee the same response in subsequent altitude exposures. While a reduction in performance at the end of the second block is a concern for those athletes who regularly engage in repeated altitude exposures in a training year, it may be that the 5-wk recovery period between exposures in the current study was too short and/or athletes were unable to produce best performances possibly due to fatigue. Further investigation of longer wash-out periods of several months or up to a year between repeated altitude exposures is warranted, as well as careful quantification of fatigue. The inconsistent performance outcome in this study is at odds with a previous investigation that categorized athletes as ‘responders’ based on greater performance improvement relative to the mean following a single bout of LHTL (5). In the current study, the true individual responses to the intervention for performance, as well as \( \text{VO}_{2\text{max}} \) and \( \text{Hb}_{\text{mass}} \), were of similar magnitude to the mean response which indicates that performance is relatively labile. It furthermore suggests that, after adequate altitude exposure, attributing performance increases of ~1-2% solely to increased erythropoiesis may be too simplistic (22).

**Paragraph 26** The variable results in time-trial performance, despite similar mean improvements in \( \text{VO}_{2\text{max}} \), are consistent with the model that maximal aerobic power is only one of a number of factors that contribute to athletic performance. Although \( \text{VO}_{2\text{max}} \) is considered a useful predictor of performance in endurance events (30, 32), in some top level
athletes it poorly associated with performance (33). For athletes more homogenous in ability, other physiological parameters including percent of $\dot{V}O_{2\text{max}}$ at a given velocity (9, 32) and energy cost of running (9), account for most of the variation in running performance. According to the model of di Prampero (11), $\dot{V}O_{2\text{max}}$, percent of $\dot{V}O_{2\text{max}}$ that can be maintained for the duration of the run (fractional utilization), and energy cost of running (economy) accounts for 70% of between-subject variation in performance. Consequently, a portion of the variability in performance in this study could be related to other factors such as fatigue, training status and motivation. All of these factors presumably require careful management to realize enhanced performance following altitude training, without or without an increase in hemoglobin mass.

**Paragraph 27** There were no substantial improvements in running economy or $\dot{V}O_{2\text{max}}$ in the LHTL group, despite increased $\dot{V}O_{2\text{max}}$. This lack of improvement in economy following hypoxic exposure is in agreement with those studies who have also demonstrated an increase in $\dot{V}O_{2\text{max}}$ (23). In contrast, those studies with no change or even a reduction in $\dot{V}O_{2\text{max}}$ have observed 3-10% improvements in economy (12). Improvements in $\dot{V}O_{2\text{max}}$ were associated with lower post-test blood lactate concentration after each 3-wk block in the LHTL group. The reduction in maximal lactate and increased 4mM running speed after Block 1 in the LHTL group may indicate greater reliance on aerobic metabolism or changes in whole body lactate metabolism following hypoxic exposure (24).

**Paragraph 28** There were no clear differences in change in blood bicarbonate ($\text{HCO}_3^-$) or pH, measured as a surrogate of muscle buffer capacity ($\beta_m$), compared with the Control group. It is possible that our indirect means of assessing buffering capacity may not have been sensitive enough to detect subtle changes following altitude training, as direct measurement has previously demonstrated an enhancement in $\beta_m$ (13).
**Hemoglobin mass**

**Paragraph 29** The reproducible small increases in Hb\textsubscript{mass} indicate that 14h·day\textsuperscript{-1} of hypoxic exposure for two to three weeks was sufficient to induce accelerated erythropoiesis and elicit measureable changes in Hb\textsubscript{mass} in highly trained runners. The ~3\% mean increase we observed after each block (~300 h) is consistent with a 1\% increase in Hb\textsubscript{mass} for every 100 h of hypoxic exposure (7). Although this small mean increase is somewhat lower than ~5-10\% increases in Hb\textsubscript{mass} (4, 36) previously reported, the individual changes in Hb\textsubscript{mass} we measured lends support to the notion that some highly trained athletes can demonstrate moderate to large increases in Hb\textsubscript{mass} (~4-7\%) after LHTL (35). The capacity for repeated Hb\textsubscript{mass} measurement with CO rebreathing (25) allows confidence in identifying small changes in Hb\textsubscript{mass} and elucidating the time-course of Hb\textsubscript{mass} change in relation to hematological responses. Our results following 14 h·d\textsuperscript{-1} of LHTL, confirm that the length of daily hypoxic exposure is critical for stimulating the acute increase in EPO concentration and augmented erythropoiesis. Indeed, other researchers using daily exposures shorter than 12 hours have failed to observe increased red blood cell production in athletes (1, 2, 26, 31).

**Limitations**

**Paragraph 30** It was not possible to have a period of controlled training prior to Block 1, due to the training and competition demands on the athletes. Nevertheless, there was no substantial difference in their training load between Block 1 and 2. A limitation of the 4.5 km time trial performance within one day of altitude exposure is the possibility of residual fatigue. Nonetheless, substantial improvements in time trial performance following the first 3-wk block indicate that the LHTL group did not suffer any ill-effects from time-trialling immediately after simulated altitude exposure. It appears the performance response to altitude training may be mediated by prior training, and individual athletes in this study may not have
adequately managed their training load with the additional stress of a second bout of altitude exposure.

**CONCLUSION**

*Paragraph 31* A 3-wk simulated LHTL block can induce reproducible mean increases in Hb$_{mass}$ and VO$_{2\text{max}}$ in highly trained runners, but these enhanced physiological capacities did not transfer directly to reproducible improvements in 4.5 km time trial performance. There was large individual variation in change in physiological and performance measures after each block, with true individual responses of similar magnitude to the mean response. Competitive performance is dependent not only on physiological adaptations, but a complex interaction of fitness, training status, and fatigue. All these factors require careful, individual management to improve performance following altitude training particularly when multiple exposures are undertaken within a training year.

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REFERENCES


Hopkins, WG. Spreadsheets for Analysis of Controlled Trials, with Adjustment for a Subject Characteristic. Sportscience. 2006;10:46-50.


### TABLE 1. Baseline characteristics of the elite runners in the simulated live high/train low (LHTL) and control groups at the start of each block (mean ± SD)

<table>
<thead>
<tr>
<th>Block 1</th>
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<tbody>
<tr>
<td><strong>Body Mass</strong> (kg)</td>
<td><strong>VO(_{2}\text{max})</strong> (mL.kg(^{-1}.\text{min}^{-1}))</td>
<td><strong>Time trial</strong> (mm:ss)</td>
<td><strong>Hb(_{\text{mass}})</strong> (g.kg(^{-1}))</td>
</tr>
<tr>
<td><strong>LHTL</strong> 6 Male, 2 Female</td>
<td>61.8 ± 6.8</td>
<td>72.4 ± 4.5 (^{\wedge})</td>
<td>13:34 ± 0:45</td>
</tr>
<tr>
<td><strong>Control</strong> 5 Male, 3 Female</td>
<td>60.2 ± 8.7</td>
<td>68.4 ± 6.7</td>
<td>14:10 ± 1:09</td>
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<tr>
<td><strong>Block 2</strong></td>
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<tr>
<td><strong>LHTL</strong> 6 Male, 2 Female</td>
<td>62.3 ± 7.2</td>
<td>72.9 ± 6.2</td>
<td>13:31 ± 0:45</td>
</tr>
<tr>
<td><strong>Control</strong> 5 Male, 3 Female</td>
<td>60.1 ± 8.4</td>
<td>69.2 ± 4.0</td>
<td>14:14 ± 1:08</td>
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\(VO_{2}\text{max}\), maximal aerobic power; Time trial, 4.5 km road course; Hb\(_{\text{mass}}\), hemoglobin mass. 
\(^{\wedge}\) substantially different from Control.
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<tr>
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<th>Block 1 Test 1</th>
<th>Block 1 Test 2</th>
<th>Δ Test 1-2</th>
<th>Block 2 Test 3</th>
<th>Block 2 Test 4</th>
<th>Δ Test 3-4</th>
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<tr>
<td>$\dot{V}O_{2\text{max}}$ (mL·kg$^{-1}$·min$^{-1}$)</td>
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<tr>
<td>LHTL</td>
<td>72.4 ± 4.5</td>
<td>73.9 ± 4.3</td>
<td>2.1; ±2.1% *</td>
<td>72.9 ± 6.2</td>
<td>74.3 ± 5.8</td>
<td>2.1; ±3.9%</td>
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<tr>
<td>Control</td>
<td>68.4 ± 6.7</td>
<td>69.1 ± 6.9</td>
<td>0.9; ±2.8%</td>
<td>69.2 ± 4.0</td>
<td>69.2 ± 6.4</td>
<td>0.7; ±3.1%</td>
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<td>Economy (L·min$^{-1}$)</td>
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</tr>
<tr>
<td>LHTL</td>
<td>3.68 ± 0.45</td>
<td>3.67 ± 0.44</td>
<td>-0.3; ±1.7%</td>
<td>3.82 ± 0.58</td>
<td>3.89 ± 0.52</td>
<td>2.2; ±2.7%</td>
</tr>
<tr>
<td>Control</td>
<td>3.48 ± 0.65</td>
<td>3.43 ± 0.65</td>
<td>-1.2; ±1.3%</td>
<td>3.55 ± 0.70</td>
<td>3.46 ± 0.70</td>
<td>-0.1; ±1.8%</td>
</tr>
<tr>
<td>Difference</td>
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<tr>
<td>$v\dot{V}O_{2\text{max}}$ (km·h$^{-1}$)</td>
<td></td>
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<tr>
<td>LHTL</td>
<td>20.0 ± 1.2</td>
<td>20.3 ± 1.2</td>
<td>1.3; ±1.5%</td>
<td>20.1 ± 1.2</td>
<td>19.6 ± 1.4</td>
<td>-1.4; ±2.7%</td>
</tr>
<tr>
<td>Control</td>
<td>19.4 ± 1.6</td>
<td>19.6 ± 1.6</td>
<td>1.2; ±2.4%</td>
<td>19.7 ± 1.5</td>
<td>19.9 ± 1.9</td>
<td>-0.1; ±2.3%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
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<tr>
<td>4mM speed (km·h$^{-1}$)</td>
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<tr>
<td>LHTL</td>
<td>17.8 ± 1.0</td>
<td>19.0 ± 1.1</td>
<td>6.5; ±2.0% *</td>
<td>18.4 ± 1.1</td>
<td>18.7 ± 1.3</td>
<td>1.6; ±2.5%</td>
</tr>
<tr>
<td>Control</td>
<td>17.8 ± 1.3</td>
<td>18.0 ± 1.5</td>
<td>1.1; ±1.3%</td>
<td>18.2 ± 1.4</td>
<td>18.1 ± 1.7</td>
<td>-0.3; ±1.8%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
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<tr>
<td>Post [La$^-$] (mM)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>LHTL</td>
<td>12.3 ± 2.7</td>
<td>11.0 ± 3.4</td>
<td>-12.2; ±8.3% *</td>
<td>12.5 ± 2.2</td>
<td>9.0 ± 2.1</td>
<td>-28.0; ±13.5% *</td>
</tr>
<tr>
<td>Control</td>
<td>10.7 ± 2.7</td>
<td>11.8 ± 2.1</td>
<td>11.5; 10.8% *</td>
<td>10.8 ± 1.9</td>
<td>10.9 ± 1.6</td>
<td>-0.9; ±24.2%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
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</table>

Data are mean ± SD, and effects are percent (mean; ±90% CL). LHTL (n=8), Control (n=8) $\dot{V}O_{2\text{max}}$, maximal aerobic power; Economy, pooled submaximal $\dot{V}O_{2}$ from four running speeds; $v\dot{V}O_{2\text{max}}$, velocity at $\dot{V}O_{2\text{max}}$; 4mM speed, lactate threshold speed; [La$^-$] blood lactate concentration *substantially different within group, ^substantially different from Control.
FIGURES

FIGURE 1—Schematic diagram of testing during each 3-wk simulated live high/train low or near sea-level training block (Block 1, 2 and 3). Test, 4.5 km time trial and treadmill test performed on separate days; Blood sample, venous blood collection; Hb\text{mass}, hemoglobin mass.

FIGURE 2–Percent change (Δ) in Block 1 versus Block 2 for 4.5 km time trial performance, maximum aerobic power (\text{VO}_2\text{max}) and hemoglobin mass (Hb\text{mass}) for the LHTL (n=8; filled circles) and Control (n=8; open circles) groups. The regressions are the line of best fit and 90% confidence interval (dashed line) for each group.

FIGURE 3–Individual percent change in time trial performance. Group mean ± SD are shown in heavy black and offset slightly for clarity, for LHTL (n=8; filled circles) and Control (n=8; open circles) groups. Negative values indicate a decrease in time and improved performance. Grey shaded area indicates the range of trivial changes from baseline.

FIGURE 4–Individual percent change in hemoglobin mass (Hb\text{mass}) measured before, weekly and one week after Block 1 and 2. Pre-test values for each block are the mean of the two pre-tests. Group mean ± SD are shown in heavy black and offset slightly for clarity, for LHTL (n=8; filled circles) and Control (n=8; open circles) groups. Grey shaded area indicates the range of trivial changes from baseline.

FIGURE 5–Mean change in serum erythropoietin (EPO), soluble transferrin receptor (sTfR) and ferritin concentration measured before, on day 2, day 6, day 20 and day 27 in Block 1 and 2 in the LHTL (n=8; filled circles) and Control (n=8; open circles) group. Pre-test values for each block are the mean of the two pre-tests. Data are raw mean ± SD. *substantially different from pre-test.
FIGURE 1

Test
Blood sample
Hb mass

HH  H  H  H  H  H
HH  H  H  H  H  H

Week
0  1  2  3  4  5  6  7  8  9  10  11  12

Block 1
Block 2
FIGURE 2

LHTL: $r = 0.10$
$y = -0.13x + 0.49$

Control: $r = 0.49$
$y = 0.24x + 0.19$

FASTER

SLOWER

Δ Time Trial Block 1 (%)

Δ Time Trial Block 2 (%)
FIGURE 4

![Graph showing Δ Hb mass (%) over weeks for LHTL and Control groups.]
FIGURE 5

- EPO (mU.mL$^{-1}$)
- sTfR (mg.L$^{-1}$)
- Ferritin (ng.mL$^{-1}$)

LHTL vs Control

Week

Block 1
Block 2