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RESEARCH ARTICLE

Individual hemoglobin mass response to normobaric and hypobaric "live high–train low": A one-year crossover study

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Hauser A, Troesch S, Saugy JJ, Schmitt L, Cejuela-Anta R, Faiss R, Steiner T, Robinson N, Millet GP, Wehrlin JP. Individual hemoglobin mass response to normobaric and hypobaric "live high–train low": A one-year crossover study. *J Appl Physiol* 123: 387–393, 2017. First published May 18, 2017; doi:10.1152/japplphysiol.00932.2016.—The purpose of this research was to compare individual hemoglobin mass (Hb_{mass}) changes following a live high-train low (LHTL) altitude training camp under either normobaric hypoxia (NH) or hypobaric hypoxia (HH) conditions in endurance athletes. In a crossover design with a one-year washout, 15 male triathletes randomly performed two 18-day LHTL training camps in either HH or NH. All athletes slept at 2,250 meters and trained at altitudes <1,200 meters. Hb_{mass} was measured in duplicate with the optimized carbon monoxide rebreathing method before (pre) and immediately after (post) each 18-day training camp. Hb_{mass} increased similarly in HH (916–957 g, 4.5 ± 2.2%, $P < 0.001$) and in NH (918–953 g, 3.8 ± 2.6%, $P < 0.001$). Hb_{mass} changes did not differ between HH and NH ($P = 0.42$). There was substantial interindividual variability among subjects to both interventions (i.e., individual responsiveness or the individual variation in the response to an intervention free of technical noise): 0.9% in HH and 1.7% in NH. However, a correlation between intraindividual ΔHb_{mass} changes (%) in HH and in NH ($r = 0.52$, $P = 0.048$) was observed. HH and NH evoked similar mean Hb_{mass} increases following LHTL. Among the mean Hb_{mass} changes, there was a notable variation in individual Hb_{mass} response that tended to be reproducible.

NEW & NOTEWORTHY This is the first study to compare individual hemoglobin mass (Hb_{mass}) response to normobaric and hypobaric live high-train low using a same-subject crossover design. The main findings indicate that hypobaric and normobaric hypoxia evoked a similar mean increase in Hb_{mass} following 18 days of live high-train low. Notable variability and reproducibility in individual Hb_{mass} responses between athletes was observed, indicating the importance of evaluating individual Hb_{mass} response to altitude training.

altitude; training; hypoxia; live high-train low; athletes; hemoglobin mass

SIMULATED AND NATURAL ALTITUDE training methods are commonly used by elite endurance athletes to enhance sea level performance (25, 45). The question as to whether simulated (normobaric hypoxia) altitude and natural (hypobaric hypoxia) altitude differ considerably regarding physiological and performance responses is still debated (5, 26, 32). A frequently used altitude training method that can be performed under either hypobaric or normobaric conditions is the "live high-train low" (LHTL) model (22, 41), where athletes live and sleep at a certain altitude but train at a lower altitude or near sea level (1, 45). However, researchers have rarely directly compared the possible differences between the effects of hypobaric and normobaric LHTL on relevant physiological responses, such as hemoglobin mass (Hb_{mass}) (16) and performance responses (32). Thus far, only one study (16) has compared individual Hb_{mass} responses between normobaric and hypobaric LHTL training camps after the same duration (18 days) and the same hypoxic hours (~230 h) in endurance athletes. Interestingly, these results showed that hypobaric and normobaric LHTL evoked similar group mean increases in Hb_{mass} (4.1 vs. 4.5%) and that there was no difference between the two hypoxic conditions. In line with previous studies (6, 8, 24, 30, 38, 43), individual Hb_{mass} responses demonstrated a wide variability (–1.4 to 10.6%) in hypobaric and normobaric LHTL. Because the number of athletes was small within the hypobaric hypoxia (HH) and normobaric hypoxia (NH) groups ($n = 10, 11$), an uneven distribution of athletes who responded positively or less positive to altitude in Hb_{mass} may have affected the outcome. Thus, the question whether normobaric and hypobaric LHTL results in similar Hb_{mass} responses has not been conclusively answered. The straightforward option to diminish the observed effect is to conduct a same-subject crossover design.

The primary aim of the present study was to investigate whether Hb_{mass} responses differ between 18 days of hypobaric and normobaric LHTL with a same-subject crossover design. The secondary aim was to quantify individual Hb_{mass} responsiveness in HH and NH.

METHODS

Subjects. Fifteen well-trained male triathletes, living at or near sea level (age: 23.9 ± 4.0 yr, height: 178.5 ± 4.9 cm, and weight: 64.9 ± 7.6 kg), completed both altitude training camps and fulfilled the following inclusion criteria for participation and data analysis: *1*) a minimum of five years of endurance training and frequent partici-

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pation in endurance competitions, *2*) initial ferritin levels >30 μg/l, and *3*) no doping abuse (OFF score within reference range; see Ref. 11). All athletes provided written informed consent to participate in the study. The study was approved by the local ethical committees (Commission Cantonale Valaisanne d'Ethique Médicale, Agreement 051/09 and French National Conference of Research Ethics Committees, no. CPP EST I: 2014/33; Dijon, France), corresponding to the two training locations. All procedures were conducted in accordance with the Declaration of Helsinki.

Study design. Originally, it was planned to perform a single parallel group study design (*camp 1*). To get a crossover study design, we decided after the first training camp to extend the study with another training camp (*camp 2*), but not all athletes from the first training camp were able to participate a second time. Thus, the present study was based on two training camp phases performed over one year. In the first year (*camp 1*), a total of 24 athletes were randomly assigned to either a hypobaric or a normobaric hypoxic 18-day LHTL training camp. In the second year (*camp 2*), at the same time point during the year and during the competitive season, 15 of the 24 athletes performed a second 18-day LHTL training camp with the opposite hypoxic condition (HH or NH). Individual Hb_{mass} responses of one single training camp have been published; for details, see Hauser et al. (16). To have a same-subject crossover design (Fig. 1), only the results of these 15 athletes were used in this study. The athletes' data were pooled for each hypoxic condition from both camps of the study as follows: HH condition included the pooled values from the HH athletes in *camp 1* ($n = 5$) and the HH athletes in *camp 2* ($n = 10$); the same athletes were considered for the NH condition but reversed ($n = 10$ in *camp 1* and $n = 5$ in *camp 2*). During the one-year washout period, the athletes did not perform any additional altitude training. Under both hypoxic conditions (NH and HH), athletes slept at an altitude of 2,250 meters and trained at altitudes <1,200 meters. Immediately before (pre) and after (post) each training camp, Hb_{mass} was measured in duplicate, and venous blood samples were collected. At *day 13* of the second training camp in HH (*camp 2*), in 10 of 15 subjects, an additional duplicate Hb_{mass} measurement was performed, since it corresponded to the expected hypoxic hours in NH after 18 days (matched hypoxic hours in HH and NH). All measurements were performed at 1,150 meters. During the training camp, training load and hypoxic hours were continuously recorded (Fig. 1).

Hypoxic exposure. For the LHTL training camps under HH, the athletes lived in Fiescheralp, Switzerland [2,250 meters, inspired oxygen pressure ($P_{I_{O_2}}$) 111.6 ± 0.6 mmHg, inspired oxygen fraction ($F_{I_{O_2}}$) 20.9 ± 0.0%, barometric pressure (P_B) 580.2 ± 2.9 mmHg] and traveled by cable car two times daily to the valley (altitude <1,200 m) for training. Daily hypoxic exposures in HH totaled 17.3 ± 2.3 h. The total hypoxic hours after 18 days were 311.6 ± 7.8 h and after 13 days (only measured in the second camp, $n = 10$) 229.5 ± 1.2 h. For the LHTL training camps under NH, the athletes lived in Prémanon, France (1,150 m), and were exposed to normobaric hypoxia equivalent to 2,250 meters in hypoxic rooms (medium size: 15 m^2). Normobaric hypoxia was obtained by extracting oxygen from ambient air in hypoxic rooms ($P_{I_{O_2}}$ 111.9 ± 0.6 mmHg, $F_{I_{O_2}}$ 18.05 ± 0.1%, P_B 666.6 ± 3.6 mmHg). In each hypoxic room, the gas composition was continuously monitored with oxygen and carbon dioxide analyzers (FIELDBROOK, London, UK) that were connected to a central monitoring station under the control of an experienced physiologist. In Prémanon, the athletes left the hypoxic rooms on average 5–6 times/day to eat and train. Daily hypoxic exposures in NH totaled 12.5 ± 0.4 h, and the total hypoxic hours after 18 days were 225.3 ± 9.0 h. During all training camps, the time spent in hypoxia was monitored daily and recorded manually.

Training load. All training sessions during the training camps were advised and supervised by two experienced certified coaches. The intervention groups trained separately (located at two different places: Fiesch, Switzerland, and Prémanon, France) under the supervision of one coach. The training consisted of cycling, running, and swimming. Training load quantification was performed using the Objective Load Scale (ECOs; see Ref. 2), which was specially developed for training load quantification in triathlons. Briefly, the ECOs were calculated by multiplying the total duration of a training session (time in minutes) with a scoring value between 1 and 50, depending on the heart rate-based training zone (1–8) and by a factor of 1.0, 0.75, or 0.5 for running, swimming, or biking, respectively. The daily training loads (ECOs) of each subject were measured based on each subject's physical characteristics and training program intensity.

Hemoglobin mass. Hb_{mass} was measured in duplicate using a slightly modified version of the optimized carbon monoxide (CO)-rebreathing method described by Schmidt and Prommer (36). Briefly, a CO dose of 100 ml (Multigas, Domdidier, Switzerland) was admin-

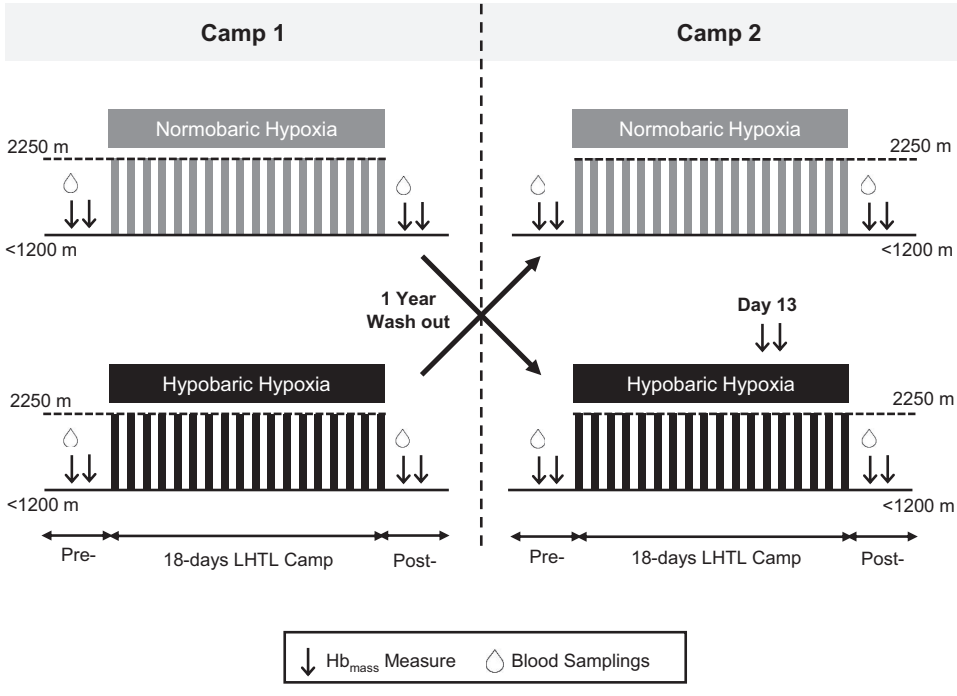

Fig. 1. Illustration of the study design ($n = 15$ subjects). LHTL, live high-train low; Hb_{mass}, hemoglobin mass.

istered and rebreathed with 3.5 liters oxygen for 2 min in a closed circuit system [glass spirometer earlobe blood samples (35 μl) were collected three times before the CO-rebreathing procedure and one time at *minute 6* and *8* after CO rebreathing was started]. Blood samples were analyzed for carboxyhemoglobin (%HbCO) using a CO-oximeter (ABL 800flex; Radiometer, Copenhagen, Denmark). Hb_{mass} was calculated from the mean change in %HbCO before and after CO rebreathing, as described previously by Steiner and Wehrlin (39). Both measurements were performed on two consecutive days (12- to 24-h time lag between the measures), and the results were averaged. The typical error (TE) of Hb_{mass} measurement was calculated from duplicate measurements as the SD of the difference score divided by $\sqrt{2}$ (17). To provide a dimensionless measure of reliability, which is comparable between subjects and studies (17), the TE was translated into a coefficient of variation (CV). The CV is calculated by dividing the TE by the mean value of Hb_{mass} and is expressed in percent. Averaged multiple measurements reduce the TE by a factor of $1/\sqrt{n}$, where n is the number of measurements (17). In this study, the TEs for duplicate measurements of Hb_{mass} at the different time points were as follows: pre-*camp 1*: 1.8% [90% confidence limits (CLs): 1.3–2.5%]; post-*camp 1*: 1.0% (0.7.1–1.3%); pre-*camp 2*: 0.9% (0.7.1–1.3%); *day 13*: 1.9% (1.3–2.6%); and post-*camp 2*: 1.1% (0.8–1.6%). In our mobile laboratory, the overall TE of the CO-rebreathing method was 2.0% (1.5–2.6%), and the TE for the average duplicate measurements was 1.4% (1.1–1.8%).

Ferritin and OFF score. On the first morning in the pre- and posttesting of both training camps, venous blood samples were drawn from an antecubital vein (4.9 ml EDTA tube; Sarstedt, Nümbrecht, Germany) immediately after the athletes woke up (7:00 A.M.). To identify iron-deficient athletes (initial ferritin levels >30 μg/l), serum ferritin concentration analysis was determined with a biochemistry analyzer (Dimension EXL; Siemens Healthcare Diagnostics, Zürich, Switzerland). The CV, which was determined using internal quality controls, was 4.5%. To exclude the potential risk of illegal blood manipulation, athletes were tested for doping by an accredited laboratory (Swiss Laboratory for Doping Analyses, Lausanne, Switzerland). Therefore, the OFF score [OFF score = Hb (g/l) − $60\sqrt{}$(reticulocytes in %)] according to Gore et al. (11) was calculated and compared with cut-off limits for athletes tested at altitude >610 meters with a false positive rate of 1:100.

Statistical analyses. Values are presented as means ± SD. All data were checked for normality (Shapiro-Wilk test) and equality of variance. A two-way repeated-measure analysis of variance was applied to evaluate the differences between the conditions (HH and NH) over time. When a significant global effect was indicated, Tukey's post hoc test was performed to identify significant differences between different levels of time and conditions. For a comparison of the training load between HH and NH, a paired *t*-test was performed. Linear regressions were used to determine the Pearson's correlation coefficient (r) between individual ΔHb_{mass} changes (%) in HH and in NH. The level of significance was set at $P < 0.05$. All analyses were processed using Sigmaplot 11.0 (Systat Software, San Jose, CA).

To assess the likelihood that the differences in percent change in Hb_{mass} between HH and NH were relevant (i.e., more extreme than the smallest worthwhile change in Hb_{mass}, set to ±1%), a contemporary statistical approach according to Hopkins (18) was used. This approach calculates the chances (in %) that the true value of an effect is positive, trivial, or negative. To classify the magnitude of the effects (positive, trivial, or negative), the change in mean and the 90% CL of the individual change scores were used (19). The effect was termed "unclear" if its CL overlapped the positive and negative smallest worthwhile changes. Individual Hb_{mass} responsiveness (i.e., the individual variation in the response to an intervention free of TE; see Ref. 17) for NH and HH is expressed as the SD from the mean Hb_{mass} change and was calculated as the square root of the difference between the variance of the Hb_{mass} change scores in the intervention and the variance in change scores arising from TE only [$(TE \times \sqrt{2})^2$]. To detect significant individual effects, the 95% CL for percent changes of Hb_{mass} was derived from the present overall TE of the Hb_{mass} measurement (95% CL = $\pm 1.96 \times TE \times \sqrt{2} \times 1/\sqrt{2}$; see Ref. 17).

RESULTS

Mean Hb_{mass} responses. After 18 days ($n = 15$), Hb_{mass} increased similarly in HH (916.0 ± 84.6 to 957.1 ± 93.5 g, 4.5 ± 2.2%, $P < 0.001$) and NH (918.0 ± 86.5 to 952.6 ± 92.7 g, 3.8 ± 2.6%, $P < 0.001$; see Fig. 2). For matched hypoxic hours ($n = 10$), Hb_{mass} increased by 4.9 ± 3.7% (891.7 ± 81.7 to 936.2 ± 106.1 g, $P < 0.001$) in HH and by 3.4 ± 2.2% (883.4 ± 72.4 to 914.0 ± 82.5 g, $P = 0.005$) in NH. Hb_{mass} changes did not differ between the conditions after 18 days of LHTL ($P = 0.42$) or for the same hypoxic hours ($P = 0.29$). The chance in percent Hb_{mass} changes being greater in HH compared with NH was 36% following 18 days of LHTL and 61% for matched hypoxic hours (Table 1).

Individual Hb_{mass} responses. Percent changes in individual Hb_{mass} ranged from +0.4 to 8.7% in HH and from −1.4 to +7.7% in NH (Fig. 3) after 18 days of LHTL. The 95% CL for individual percent Hb_{mass} changes was ±3.9%, and the upper CL was exceeded by 8 out of 15 athletes in HH and by 7 out of 15 athletes in NH. Individual responsiveness was ±0.9% in HH and ±1.7% in NH. For matched hypoxic hours, individual responsiveness was ±3.4% in HH and ±0.9% in NH. There was a significant correlation between individual ΔHb_{mass} changes (%) in HH and in NH after 18 days of LHTL ($r = 0.52$, $P = 0.048$).

Ferritin and OFF score. Initial ferritin levels were >30 μg/l in all athletes. Preferritin values were 108.1 ± 36.0 and 107.3 ± 36.3 μg/l in HH and NH, respectively. All athletes were within the cut-off limits for the OFF scores (<125.3) for pre (91.7 ± 5.4 vs. 94.6 ± 14.1)- and post (97.2 ± 6.3 vs. 97.9 ± 5.1)-testing in HH and NH, respectively.

Training load and body weight. No differences were found in daily average training loads between the two groups, HH (217.6 ± 87.9 ECOs) and NH (229. ± 80.0 ECOs), during the 18-day LHTL training camps of the crossover study ($P = 0.54$). In *camp 1*, the daily training load was similar to that in *camp 2* in HH (231.7 ± 42.1 vs. 210.6 ± 105.6 ECOs, $P = 0.68$) and NH (229.4 ± 25.2 vs. 228.6 ± 7.9 ECOs, $P = 0.98$). Body weight did not differ over time between HH and NH after 18 days ($P = 0.72$). The average pre body weight was 70.3 ± 6.3 and 71.6 ± 7.6 kg, and the average post body weight was 69.8 ± 5.3 and 70.6 ± 6.4 kg for HH and NH, respectively.

DISCUSSION

This is the first study to compare individual Hb_{mass} responses to normobaric and hypobaric LHTL using a same-subject crossover design. The main findings indicate that HH and NH evoked a similar mean increase in Hb_{mass} following 18 days LHTL. The mean changes in Hb_{mass} did not differ between HH and NH. Notable variability in individual Hb_{mass} responses following 18 days LHTL in HH and NH was observed as well as a significant correlation between individual ΔHb_{mass} changes (%) in HH and NH.

Mean Hb_{mass} responses. Both hypoxic conditions (HH vs. NH) demonstrated a similar mean Hb_{mass} increase (+4.5 vs.

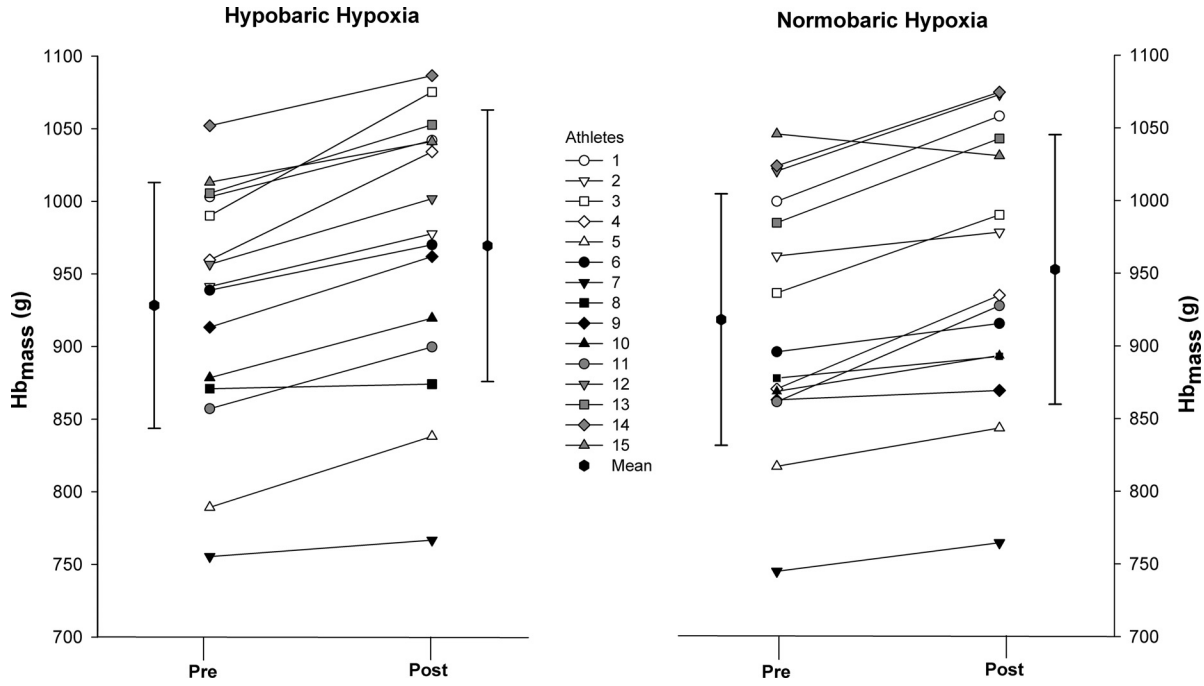

Fig. 2. Individual Hb_{mass} (g) before (Pre) and after (Post) 18 days of LHTL in either hypobaric or normobaric hypoxia, $n = 15$.

3.8%) following 18 days of LHTL. Furthermore, the chance in percent Hb_{mass} changes being greater in HH compared with NH was only 36%. Recently, the part study (16) of the crossover study also reported similar Hb_{mass} responses after an 18-day LHTL training camp in either HH or NH despite larger total hypoxic hours in HH compared with NH. A recent meta-analysis estimated that Hb_{mass} increases at a mean rate of 1.1%/100 h of exposure at simulated or natural altitude (14), which would have expected lower mean Hb_{mass} responses (~1–2%) in the present study. However, in this meta-analysis, the "upper 95% individual response limits" for 225 and 310 h were around 5 and 6%, respectively, indicating that group composition can noticeably influence the mean Hb_{mass} response. The present mean Hb_{mass} increases were of similar magnitude to previous LHTL studies with longer hypoxic exposures (>300 h; see Refs. 15 and 44) and were of greater magnitude than in LHTL studies with similar hypoxic hours (4, 20, 28). The current recommendation suggests an adequate hypoxic exposure of >12 h/day at natural or simulated altitude >2,000 meters for >21 days; that is, ~300 h are required to substantially increase Hb_{mass} (4, 31). However, the data for the NH group after 18 days (225 h) and for the HH group after 13 days (230 h) suggest that a relevant Hb_{mass} increase can be achieved with less hypoxic hours (<300 h) in some subjects. Recently, studies have examined earlier time courses (8, 43) and shorter hypoxic exposure (9, 27) on changes in Hb_{mass} to moderate altitude (2,500–3,000 m). The data from these studies showed measurable Hb_{mass} increases (2.1–3.7%) within a shorter time period (11–13 days) or lower hypoxic exposure (<210 h) than recommended (14, 31). However, the present study and the reported studies (8, 9, 27, 43) used different athlete populations and applied different altitude protocols, which may limit generalization. Therefore, further research is needed to better understand the time course and dose-response relationship of Hb_{mass} to different altitude protocols in different athlete populations.

Table 1. *Likelihood of magnitudes of Hb_{mass} changes between HH and NH after 18 days of LHTL camp and after matched hypoxic hours (230 and 225 h)*

HH vs. NH	ΔMean, %	90% CL	Positive, %	Trivial, %	Negative, %
18 Days LHTL	0.7	±1.4	36	61	3
Same hypoxic hours	1.4	±2.3	61	34	5

Hb_{mass}, hemoglobin mass; ΔMean, differences in mean; CL, confidence limits; HH, hypobaric hypoxia; NH, normobaric hypoxia. With references to a smallest worthwhile change of 1% for Hb_{mass}. Comparison of groups always first group minus second group.

A hypoxia-induced increase in Hb_{mass} seems to be one of the main physiological mechanisms leading to improved sea level endurance performance after altitude training (14, 22, 23, 42). Hb_{mass} is closely related to maximal oxygen uptake ($\dot{V}O_{2max}$), that is, a gain of 1 g in Hb_{mass} results in a 4 ml/min increase in $\dot{V}O_{2max}$ under normoxic conditions (37). Furthermore, Hb_{mass} correlates with time trial performance and maximal incremental power output in highly trained endurance athletes (21). In both 18-day LHTL camps, the athletes performed a 3-km running time trial near sea level before and after each camp. The mean performance data of both LHTL camps have been already published (34). If we correlate the percent changes in individual Hb_{mass} data (in g/kg) of the present article with the individual performance data from the already published article (34), we obtain a correlation of $r = -0.47$ ($P = 0.07$) in HH and a correlation of $r = -0.57$ ($P = 0.03$) in NH. This is comparable to our previously published paper (16) where we reported also a correlation ($r = -0.64$, $P = 0.002$) between running performance improvements and increase in Hb_{mass} (g/kg) after 18 days of LHTL ($n = 21$), suggesting that the enhancement in endurance performance was directly linked to

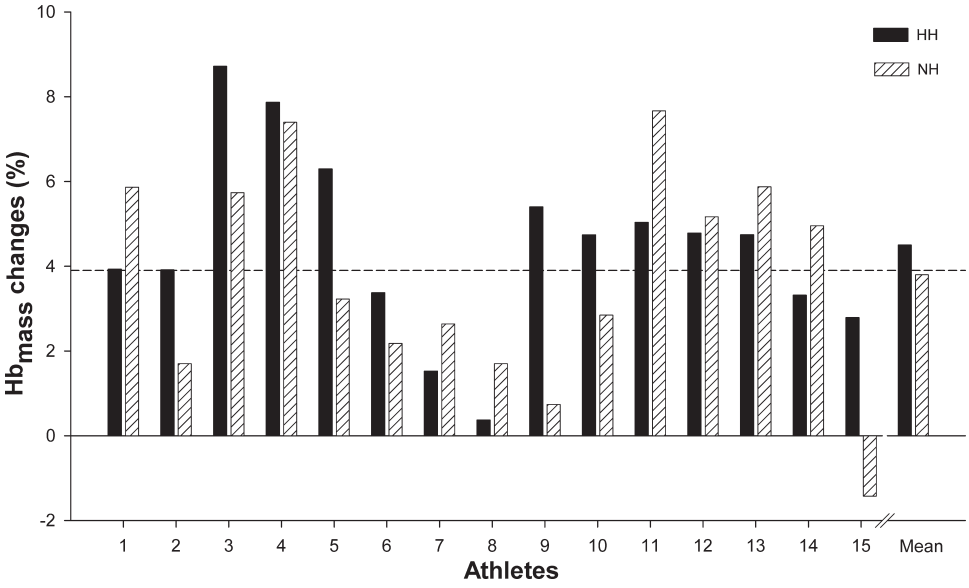

Fig. 3. Individual Hb_{mass} changes (%) after 18 days of LHTL in hypobaric hypoxia (HH, 312 h) or in normobaric hypoxia (NH, 225 h). The 95% confidence limits are indicated by broken lines.

changes in Hb_{mass} after LHTL, whereas there was no significant correlation between percent changes in individual performance and Hb_{mass} (in g) in HH ($r = -0.14$, $P = 0.61$) or NH ($r = -0.35$, $P = 0.20$). This in turn supports the literature showing an increase in Hb_{mass} following altitude training with different performance outcomes (7, 12, 30). Furthermore, it seems that also nonhematological mechanisms such as improved mitochondrial efficiency and/or muscle pH regulation (13) can contribute to enhanced sea level performance following altitude training. Thus, the impact of Hb_{mass} increase on performance benefits following altitude training remains unclear.

To date, whether the type of hypoxia (e.g., NH or HH) differs considerably regarding physiological and performance responses is still debated (5). Short-term exposure (<26 h) to HH seems to evoke greater hypoxemia, lower oxygen arterial saturation (35), and more altered cycling time trial performance (33) compared with NH, whereas long-term exposure of the same duration (e.g., following LHTL) to HH and NH induced similar Hb_{mass} (16) and performance improvements (32, 34). The present crossover study confirmed that 18 days of LHTL training at 2,250 meters either in HH or in NH induced similar mean Hb_{mass} responses despite a larger number of hypoxic hours in HH compared with NH. Thus, from a practical point of view, it seems that both hypoxic conditions (HH or NH) can be used equally for LHTL camps to enhance Hb_{mass}. However, it must be considered that HH conditions can accumulate hypoxic hours much faster than NH, while NH conditions are logistically easier and more customizable than HH.

Individual Hb_{mass} responses and reproducibility. Individual variability in Hb_{mass} response to altitude training camps in either HH or NH has previously been shown and discussed (6, 8, 16, 38, 43); however, not many altitude training studies quantified individual responsiveness (24, 27, 29, 30). In the present study, individual Hb_{mass} responsiveness (measure of individual responses that is free from the TE) was ±0.9% in HH and ±1.7% in NH, which was slightly lower compared with other studies demonstrating individual Hb_{mass} responsiveness of ±1.3 to ±2.6% in HH (24, 29) and of ±1.4 to ±2.9% in NH (27, 30). Interestingly, after the same hypoxic hours in HH, the magnitude of individual Hb_{mass} responsiveness was ±3.4%. This result was much greater than expected, suggesting that it was the result of measurement imprecision and that, even with duplicate Hb_{mass} measurements, there is still a chance of random noise (14). The reason for individual variability in Hb_{mass} response to altitude training remains to be clarified and can be attributed to many factors, such as individual variation in erythropoietic response to hypoxia (3, 6), genetic predisposition (46), occurrence of a mild neocytolysis after descending after return to sea level (6), or different baseline conditions such as low prealtitude ferritin levels (40). Regarding the latter, in the present study, all individual ferritin levels were above >30 μg/l, and an inverse correlation between the prealtitude ferritin level and Hb_{mass} (in g) changes ($r = -0.30$, $P = 0.10$) was shown, suggesting that, in the present study, initial ferritin levels did not influence individual variability in Hb_{mass} response. However, there is also evidence that low iron stores (<30 μg/l) may impair Hb_{mass} production, and thus an individualized iron supplementation strategy during altitude training is recommended (10).

To detect significant individual Hb_{mass} responses, the 95% CLs for the percent changes of Hb_{mass} were derived from the present overall TE, which was ±3.9%. The upper CL was exceeded by one-half of the athletes in both hypoxic conditions (HH: 8 of 15 and NH: 7 of 15; Fig. 3). Because Hb_{mass} was measured in duplicate, which reduces the TE by a factor of $1/\sqrt{2}$ (17) and thus enhances the measurement precision, the athletes who exceeded the 95% CL were likely responders in Hb_{mass} to the altitude training in the current study. Furthermore, most of the athletes who increased their Hb_{mass} during the first LHTL altitude camp demonstrated a reproducible Hb_{mass} response after the second LHTL altitude camp, suggesting that those athletes who responded one time to altitude training will very likely respond another time regardless of the type of hypoxia. Previous studies focusing on reproducibility of Hb_{mass} responses in athletes to altitude training camps (24, 43) have demonstrated reproducible mean percent Hb_{mass}

changes but only a small trend toward reproducible individual Hb_{mass} changes, which is not in line with the present results. Thus, whether reproducibility in individual Hb_{mass} responses to altitude training camps and/or to different hypoxic conditions (HH vs. NH) exists remains unclear. Overall, the variability in individual Hb_{mass} response to hypoxia detected in the present study emphasizes the importance of evaluating the individual Hb_{mass} response of an athlete to altitude training camps. Therefore, we recommend measuring Hb_{mass} in duplicate directly before and after an altitude training camp within a time lag of $<$24 h between the two measurements.

Conclusion. The findings of the present crossover study indicate that hypobaric and normobaric LHTL evoked a similar mean increase in Hb_{mass} following 18 days of LHTL. There was no difference in Hb_{mass} changes between HH and NH. Notable variability in individual Hb_{mass} responses between athletes was observed, indicating the importance of individual evaluation of Hb_{mass} responses to altitude training.

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GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

A.H., L.S., G.P.M., and J.P.W. conceived and designed research; A.H., S.T., J.J.S., L.S., R.C.-A., R.F., T.S., N.R., G.P.M., and J.P.W. performed experiments; A.H., S.T., J.J.S., L.S., R.C.-A., R.F., T.S., N.R., G.P.M., and J.P.W. analyzed data; A.H., S.T., J.J.S., L.S., R.C.-A., R.F., T.S., N.R., G.P.M., and J.P.W. interpreted results of experiments; A.H., S.T., T.S., G.P.M., and J.P.W. prepared figures; A.H. and J.P.W. drafted manuscript; A.H., S.T., J.J.S., L.S., R.C.-A., R.F., T.S., N.R., G.P.M., and J.P.W. edited and revised manuscript; A.H., S.T., J.J.S., L.S., R.C.-A., R.F., T.S., N.R., G.P.M., and J.P.W. approved final version of manuscript.

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