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Research Paper

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Do male athletes with already high initial haemoglobin mass benefit from 'live high–train low' altitude training?

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New Findings

- **What is the central question of this study?**
  It has been assumed that athletes embarking on an 'live high–train low' (LHTL) camp with already high initial haemoglobin mass (Hb_{mass}) have a limited ability to increase their Hb_{mass} further post-intervention. Therefore, the relationship between initial Hb_{mass} and post-intervention increase was tested with duplicate Hb_{mass} measures and comparable hypoxic doses in male athletes.
- **What is the main finding and its importance?**
  There were trivial to moderate inverse relationships between initial Hb_{mass} and percentage Hb_{mass} increase in endurance and team-sport athletes after the LHTL camp, indicating that even athletes with higher initial Hb_{mass} can reasonably expect Hb_{mass} gains post-LHTL.

It has been proposed that athletes with high initial values of haemoglobin mass (Hb_{mass}) will have a smaller Hb_{mass} increase in response to 'live high–train low' (LHTL) altitude training. To verify this assumption, the relationship between initial absolute and relative Hb_{mass} values and their respective Hb_{mass} increase following LHTL in male endurance and team-sport athletes was investigated. Overall, 58 male athletes (35 well-trained endurance athletes and 23 elite male field hockey players) undertook an LHTL training camp with similar hypoxic doses (200–230 h). The Hb_{mass} was measured in duplicate pre- and post-LHTL by the carbon monoxide rebreathing method. Although there was no relationship ($r = 0.02$, $P = 0.91$) between initial absolute Hb_{mass} (in grams) and the percentage increase in absolute Hb_{mass}, a moderate relationship ($r = -0.31$, $P = 0.02$) between initial relative Hb_{mass} (in grams per kilogram) and the percentage increase in relative Hb_{mass} was detected. Mean absolute and relative Hb_{mass} increased to a similar extent ($P \geq 0.81$) in endurance (from 916 ± 88 to 951 ± 96 g, +3.8%, $P < 0.001$ and from 13.1 ± 1.2 to 13.6 ± 1.1 g kg^{-1}, +4.1%, $P < 0.001$, respectively) and team-sport athletes (from 920 ± 120 to 957 ± 127 g, +4.0%, $P < 0.001$ and from 11.9 ± 0.9 to 12.3 ± 0.9 g kg^{-1}, +4.0%, $P < 0.001$, respectively) after LHTL. The direct comparison study using individual data of male endurance

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and team-sport athletes and strict methodological control (duplicate Hb_{mass} measures and matched hypoxic dose) indicated that even athletes with higher initial Hb_{mass} can reasonably expect Hb_{mass} gain post-LHTL.

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Introduction

Many elite endurance athletes perform altitude training with the aim of enhancing their oxygen-carrying capacity and eventually their sea-level performance (Wilber, 2007; Bonetti & Hopkins, 2009; Millet *et al.* 2010). During the last decade, hypoxic/altitude training interventions have become increasingly popular in team sports, and innovative methods fitting their physical requirements (combination of aerobic and anaerobic adaptations) have been introduced (McLean *et al.* 2014; Brocherie *et al.* 2017). Compared with endurance athletes, team-sport athletes are generally characterized by a lower maximal aerobic capacity (Girard *et al.* 2013) and possess lower relative haemoglobin mass (Hb_{mass}; Heinicke *et al.* 2001; Wachsmuth *et al.* 2013*a*). The potential main benefit derived from the popular 'live high–train low' (LHTL) altitude training intervention seems to rely on an increase in Hb_{mass} (Levine & Stray-Gundersen, 2005; Gore *et al.* 2013; Wehrlin *et al.* 2016). In a particular sport (e.g. endurance or team sports), considerable individual variation in the Hb_{mass} response to altitude training has been reported (Friedmann *et al.* 2005; Garvican *et al.* 2012; Siebenmann *et al.* 2012; Garvican-Lewis *et al.* 2013; Wachsmuth *et al.* 2013*b*) and quantified as a standard deviation (SD) from the mean change of ±1.7 to ±2.2% (McLean *et al.* 2013; Hauser *et al.* 2017). Although sources of this variability still remain unclear, aspects such as the erythropoietic response to hypoxia (Chapman *et al.* 1998; Friedmann *et al.* 2005), genetic predisposition (Wilber *et al.* 2007), residual fatigue and training history (Garvican *et al.* 2007) and/or intra-individual conditions (Wachsmuth *et al.* 2013*b*) are likely to play a role.

Another suggested reason for this variability relies on the individual's initial Hb_{mass} before embarking upon the altitude training camp. Hence, it has been proposed that athletes with already high initial Hb_{mass} have a limited ability to increase (i.e. ceiling effect) their Hb_{mass} further following altitude training (Gore *et al.* 1998; Robach & Lundby, 2012; McLean *et al.* 2013). A recent analysis of nine LHTL studies (Robach & Lundby, 2012) demonstrated a high correlation ($r = 0.86$, $P < 0.01$) between initial relative Hb_{mass} (expressed in grams per kilogram) and the post-intervention percentage increase in relative Hb_{mass}. However, this analysis had several important limitations, which limit the strength of comparison between the different LHTL training studies. First, different methods (Evans Blue dye *versus* CO-rebreathing methods) for the determination of Hb_{mass}, with different accuracy/reliability levels, have been used (Wehrlin *et al.* 2016). Furthermore, these studies examined different sexes (female athletes demonstrate a 10% lower level of Hb_{mass} compared with male athletes; Schmidt & Prommer, 2008), and 'hypoxic doses' varied greatly, between a total of 200 and 500 h of hypoxic exposure. Lastly, the data analysis was based on averaged values and not on individual values. Nevertheless, one should be cautious when interpreting group mean data because considerable inter-individual variation in the Hb_{mass} response to altitude training exists (Friedmann *et al.* 2005; Garvican *et al.* 2012; McLean *et al.* 2013; Hauser *et al.* 2016).

Given that LHTL is primarily used by elite endurance athletes typically presenting elevated Hb_{mass} values compared with team-sport athletes, the hypothesis that athletes embarking on an LHTL camp with already high initial Hb_{mass} have a limited ability to increase their Hb_{mass} further post-intervention (or at least to a lower extent than their team-sport counterparts) needs to be tested with a more robust study design. Thus, the aim of the present study, which reanalysed already existing data, was to examine the relationship between individual initial Hb_{mass} before LHTL (absolute and relative values) and the percentage Hb_{mass} increase following an LHTL camp with comparable hypoxic doses in male endurance and team-sport athletes.

Methods

Ethical approval

All altitude training studies were approved by the following local ethical committees: Commission Cantonale Valaisanne d'Ethique Médicale, CCVEM (Agreement 051/09), French National Conference of Research Ethics Committees (N°CPP EST I: 2014/33; Dijon, France) and by the Anti-Doping Lab Qatar institutional review board (SCH-ADL-070; Doha, Qatar). All experimental procedures were conducted in accordance with the *Declaration of Helsinki* guidelines, and all athletes provided written informed consent to participate in the respective studies. The study was not registered in a database.

Table 1. Characteristics of the altitude training interventions

Data source	*n*	Sport	Altitude mode	Hypoxic mode	Altitude (m)	Duration (days)	Daily exposure (h)	Hypoxic dose (h)	Hypoxic dose (km.h)
Studies I and II	24	Triathlon	LHTL	NH	2250	18	12.5	225	506
Study II	11	Triathlon	LHTL	HH	2250	13	17.5	230	518
Study III	11	Hockey	LHTL	NH	2500–3000	14	14	200	545
	12	Hockey	LHTL + RSH	NH	2500–3000	14	14	200	545

Abbreviations: HH, hypobaric hypoxia; LHTL, live high–train low; NH, normobaric hypoxia; and RSH, repeated sprints in hypoxia.

Study design

Data from three altitude training interventions (studies I, II and III), with similar hypoxic doses (200–230 h) and identical Hb_{mass} measurement procedures, were re-analysed to determine the nature of the association of individual Hb_{mass} increase with the individual initial absolute and relative Hb_{mass}. The details of the experimental design of the three altitude training interventions have been published elsewhere [see study I (Saugy *et al.* 2014), study II (Hauser *et al.* 2016) and study III (Brocherie *et al.* 2015)].

Participants

For studies I and II, 35 well-trained male endurance athletes (age 24.0 ± 4.5 years, height 177.9 ± 4.8 cm, weight 70.2 ± 6.2 kg, training 10–12 h per week) were recruited. For study III, 23 elite male field hockey players (age 24.4 ± 4.0 years, height 179.7 ± 9.1 cm, weight 77.5 ± 8.7 kg, training 7–9 h per week) were included. A total of 58 athletes were included in the final sample. Inclusion criteria for analysis were as follows: initial ferritin levels >30 $\mu g\ l^{-1}$ (sufficient ferritin stores), male (exclusion confounding factor 'gender'), endurance or team-sport athlete (guarantee high and low initial Hb_{mass} values within the data analysis) and completion of an LHTL altitude training camp with all Hb_{mass} measures done in duplicate by the same investigator before and after the intervention.

Altitude interventions

For studies I and II (normobaric groups), 24 endurance athletes performed an 18 day LHTL altitude training camp in normobaric hypoxic conditions (∼12.5 h day^{-1} and 225 ± 9 h total hypoxic dose), during which the athletes trained at <1200 m and were exposed to normobaric hypoxia equivalent to 2250 m (Wehrlin *et al.* 2016) in hypoxic rooms [inspired partial pressure of oxygen (P_{I,O_2}) 111.9 ± 0.6 mmHg; fraction of inspired oxygen (F_{I,O_2}) 18.1 ± 0.1%; barometric pressure (P_B) 666.6 ± 3.6 mmHg; 1150 m]. For study II (hypobaric group), as normobaric and hypobaric hypoxia induces similar Hb_{mass} and endurance performance responses after LHTL altitude training (Saugy *et al.* 2014; Hauser *et al.* 2016), an additional 11 endurance athletes were included, who completed a 13 day LHTL camp in hypobaric hypoxic conditions with similar total hypoxic hours (230 ± 1 h, ∼17.5 h day^{-1}). Those athletes lived at 2250 m (P_{I,O_2} 111.7 ± 0.7 mmHg; F_{I,O_2} 20.9%; P_B 580.8 ± 3.3 mmHg) and trained twice daily at <1200 m. For study III, all 23 field hockey players performed a 14 day LHTL training camp in normobaric hypoxic conditions (>14 h day^{-1} and ∼198 h total hypoxic dose); thereby, they trained at sea level and slept in normobaric hypoxic rooms, and simulated altitude was gradually increased from 2500 m (P_{I,O_2} 108.3 mmHg; F_{I,O_2} 15.1%; P_B 768.0 mmHg) up to 3000 m (P_{I,O_2} 101.7 ± 0.8 mmHg; F_{I,O_2} 14.2 ± 0.1%; P_B 765.3 ± 1.5 mmHg) during the 14 days. In addition, they performed six repeated-sprints training sessions during the 14 day training camp in either normoxic (F_{I,O_2} 20.9%; $n = 12$) or normobaric hypoxic conditions (3000 m; F_{I,O_2} ∼14.5%; $n = 11$). In summary, according to the definition of Garvican-Lewis *et al.* (2016), the metrics for hypoxic dose (in kilometre hours) between the LHTL groups were similar and differed within 6%, assuming that the present hypoxic doses were comparable (Table 1).

Haemoglobin mass

In all athletes, Hb_{mass} was measured in duplicate using a slightly modified version (Steiner & Wehrlin, 2011) of the optimized carbon monoxide (CO)-rebreathing method described by Schmidt & Prommer (2005); for details, see Hauser *et al.* (2016) and Brocherie *et al.* (2015). Both measurements were performed on two consecutive days (12–24 h time lag between the measurements), and the results were averaged. The typical error (TE) was calculated from duplicate measurements as the SD of the difference score divided by $\sqrt{2}$ (Hopkins, 2000). In our mobile laboratories, the TEs ranged between 1.6 and 2.0%. As duplicate measurements reduce the TE by a factor of $1/\sqrt{2}$ (Hopkins, 2000), the TEs for averaged duplicate Hb_{mass} measurements ranged between 1.1 and 1.4%. For each athlete, Hb_{mass} measures were performed by the same investigator throughout the studies.

Data analysis

Values are presented as means ± SD. All data were checked for normality (Shapiro–Wilk test). A sample size estimation for a power of 0.8 (80%), a significance level at $P = 0.05$ and a correlation coefficient of $r = 0.4$ was performed and resulted in a minimal number of 46 subjects. Linear regressions were used to determine the Pearson's product–moment correlation coefficients (r) between initial absolute and relative Hb_{mass} and their respective percentage changes in Hb_{mass}, as well as for percentage changes between body weight and Hb_{mass}. The standard error (SE) of the slope of the linear regression was calculated by bootstrapping. Correlation size was interpreted using the correlation classification of Hopkins *et al.* (2009): trivial ($r < 0.1$), small ($0.1 < r < 0.3$), moderate ($0.3 < r < 0.5$), large ($0.5 < r < 0.7$), very large ($0.7 < r < 0.9$), nearly perfect ($r > 0.9$) and perfect ($r = 1.0$). Multiple linear regression analysis was used to determine the effect of body weight changes and initial Hb_{mass} (in grams per kilogram) on percentage changes in relative Hb_{mass}. Student's paired t tests were conducted to compare pre- and post-values in Hb_{mass} and body weight within the athlete group. Student's unpaired t test was performed to compare percentage changes between endurance and team-sport athletes. The level of significance was set at $P < 0.05$. All analyses were processed using Sigmaplot 11.0 (Systat Software, San Jose, CA, USA) and the statistical software package R (Vienna, Austria).

Results

Relationship between initial Hb_{mass} and Hb_{mass} increase

There was no relationship between the absolute initial Hb_{mass} (in grams) and the percentage increase in absolute Hb_{mass} ($r = 0.02$, $P = 0.91$; Fig. 1*A*). The linear regression equation for absolute Hb_{mass} was $y = -0.0004x + 3.5$, and the SE of the slope was ±0.003. A moderate negative correlation between the relative initial Hb_{mass} (in grams per kilogram) and the percentage increase in relative Hb_{mass} ($r = -0.31$, $P = 0.02$) was observed (Fig. 1*B*). The linear regression equation for relative Hb_{mass} was $y = -0.98x + 16.4$, and the SE of the slope was ±0.348. When body weight change (as a percentage) was included in the multiple linear regression model [initial Hb_{mass} (in grams per kilogram) × body weight change (as a percentage)], the initial relative Hb_{mass} (in grams per kilogram) was no longer significantly associated with percentage increase in Hb_{mass} (in grams per kilogram; $P = 0.4$).

Mean Hb_{mass} response

Mean absolute Hb_{mass} increased to the same extent in endurance (from 916 ± 88 to 951 ± 96 g, +3.8 ± 2.9%, $P < 0.001$) and team-sport (from 920 ± 120 to 957 ± 127 g, +4.0 ± 2.9%, $P < 0.001$) athletes ($P = 0.81$). Mean relative Hb_{mass} increased equally in endurance (from 13.1 ± 1.2 to 13.6 ± 1.1 g kg^{-1}, +4.1 ± 4.2%, $P < 0.001$) and team-sport (11.9 ± 0.9 to 12.3 ± 0.9 g kg^{-1}, +4.0 ± 3.2%, $P < 0.001$) athletes ($P = 0.94$).

Body weight

The mean pretraining body weight for endurance and team-sport athletes was 70.2 ± 6 and 77.5 ± 9 kg, respectively, and the mean post-training body weight was 70.0 ± 6 and 77.4 ± 8 kg, respectively. The changes in body weight pre- to post-training did not differ between the groups ($P \geq 0.53$). There was no relationship ($r = -0.006$, $P = 0.96$) between individual percentage changes in body weight and absolute Hb_{mass} (Fig. 2*A*). A large inverse relationship ($r = -0.64$, $P < 0.001$) occurred between individual percentage changes in body weight and relative Hb_{mass} (Fig. 2*B*). Furthermore, the multiple linear regression model for percentage changes in relative Hb_{mass} [initial Hb_{mass} (in grams per kilogram) × body weight changes (as a percentage)] showed that percentage changes in body weight were significantly associated with percentage changes in Hb_{mass} (in grams per kilogram; $P < 0.001$).

Discussion

To our knowledge, the present study is the first to demonstrate trivial (absolute values) to moderate (relative values) relationships between initial Hb_{mass} and the percentage change in Hb_{mass} following LHTL altitude training in male endurance and team-sport athletes using individual data. Mean absolute and relative Hb_{mass} increased to the same extent in endurance and team-sport athletes following sport-specific LHTL interventions. Furthermore, a large inverse relationship occurred between individual percentage changes in body weight and relative Hb_{mass}.

Effect of absolute initial Hb_{mass} on Hb_{mass} response

The observed trivial relationship ($r = 0.02$) between absolute initial Hb_{mass} and percentage changes in absolute Hb_{mass} might suggest that absolute initial Hb_{mass} in our athlete cohort had no impact with regard to further Hb_{mass} improvements following LHTL. Thus far, no study has focused on this relationship using absolute Hb_{mass} values, with the rationale that absolute Hb_{mass} values are not an indicator for an individual's maximal aerobic

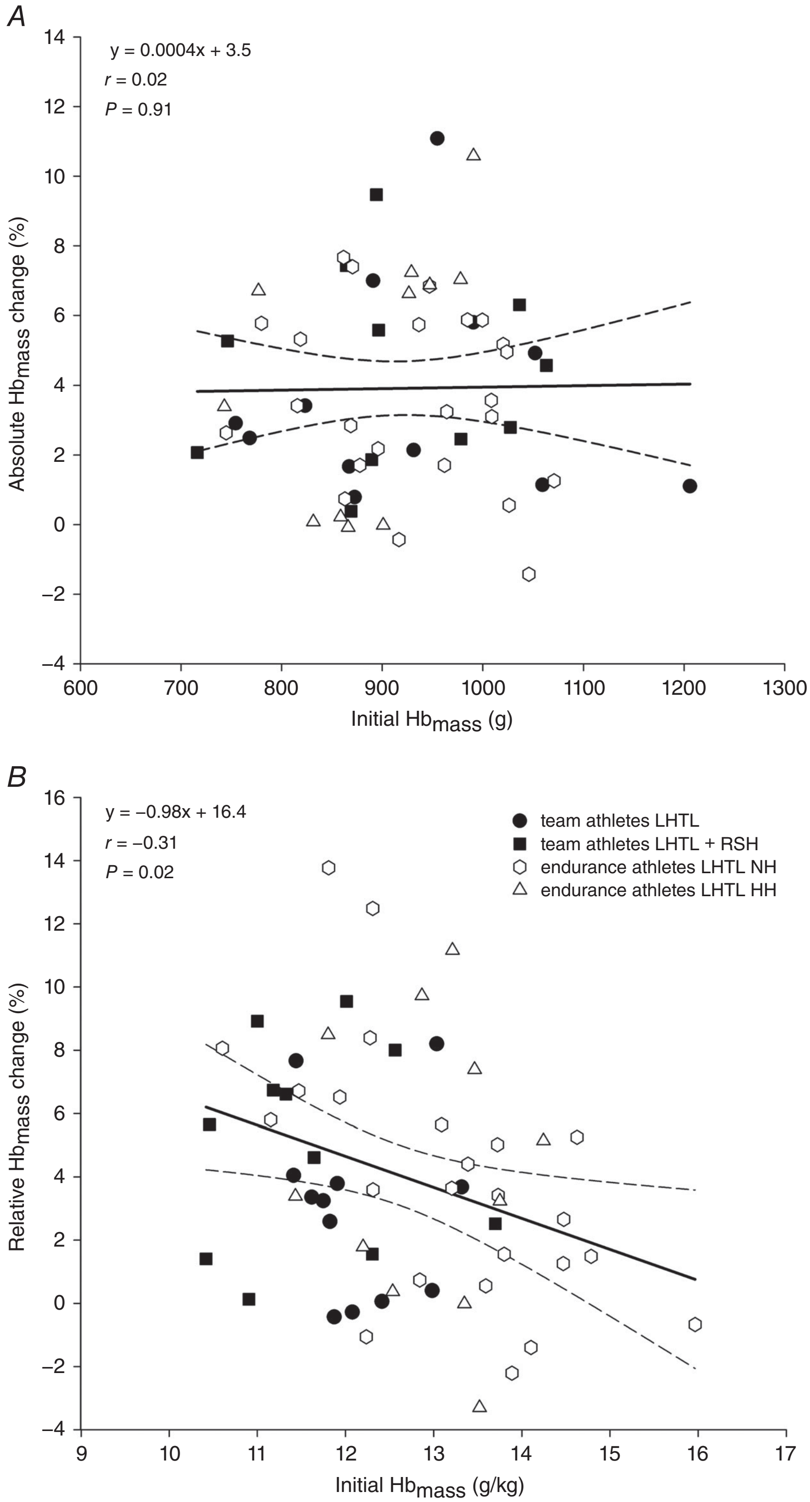

Figure 1. *A*, linear regression between the individual's initial absolute Hbmass (in grams) and the individual's absolute Hbmass change (as a %) following LHTL. *B*, linear regression between the individual's initial relative Hbmass (in g/kg) and the individual's relative Hbmass change (as a %) following LHTL

Regression slope (continuous line) and 95% confidence limits (dashed lines) are shown. $n = 58$. Abbreviations: Hb_{mass}, haemoglobin mass; HH, hypobaric hypoxia; LHTL, live high–train low; NH, normobaric hypoxia; and RSH, repeated sprints in hypoxia.

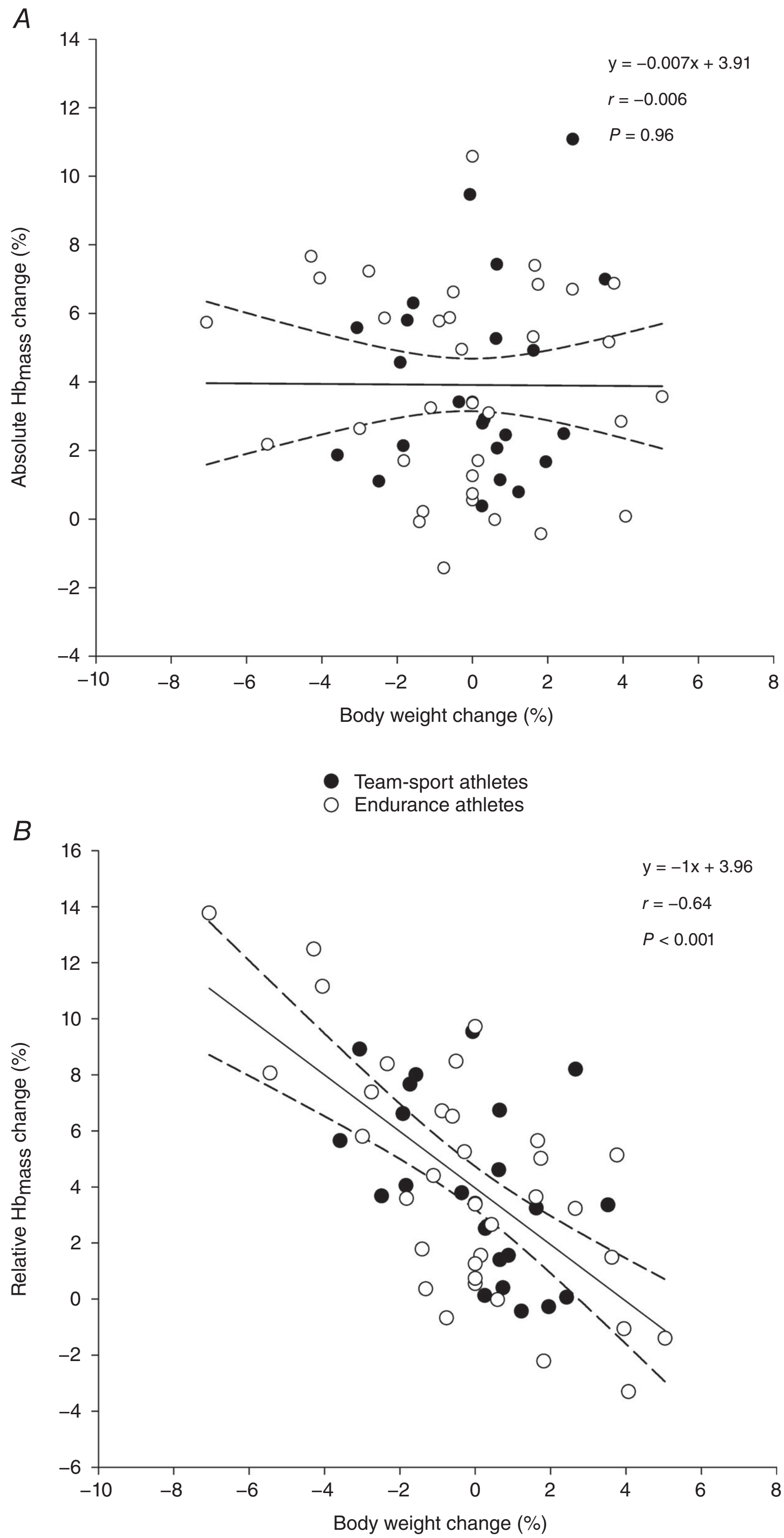

Figure 2. Linear regression between individual body weight change (as a percentage) and individual absolute Hb_{mass} change (as a percentage; *A*) and individual relative Hb_{mass} change (as a percentage; *B*) after live high-train low training
Regression slope (continuous line) and 95% confidence limits (dashed lines) are shown. $n = 58$.

capacity (Gore *et al.* 1998; Lundby *et al.* 2012; Robach & Lundby, 2012). However, to evaluate precisely the sole effect of the initial Hb_{mass} on the Hb_{mass} response to altitude training, both absolute and relative Hb_{mass} values should be assessed to exclude the confounding factor 'body weight changes' during altitude training. Furthermore, the average percentage increase in absolute Hb_{mass} was of a similar magnitude in endurance and team-sport athletes (+3.8 *versus* +4.0%). This increase is in accordance with LHTL studies of similar total hypoxic hours (230–240 h), showing a measurable mean absolute Hb_{mass} increase in elite triathletes (+3.2%; Humberstone-Gough *et al.* 2013) and semi-professional Australian footballers (+6.7%; Inness *et al.* 2016). Furthermore, to fit the team sport's physical requirements better, some team-sport athletes in the present study performed a combination of LHTL and repeated-sprints training sessions in hypoxia, the so-called 'live high–train low and high' method (Brocherie *et al.* 2015). However, as the mean Hb_{mass} response did not differ between the two hypoxic groups (LHTL *versus* LHTL and high), it seems that the additional hypoxic sprints had no beneficial effect on the mean Hb_{mass} response. Overall, in the present sample absolute initial Hb_{mass} demonstrated no adverse effect for further absolute Hb_{mass} improvement following LHTL.

Effect of relative initial Hb_{mass} on Hb_{mass} response

We found a moderate inverse correlation between initial relative Hb_{mass} and the percentage increase in relative Hb_{mass} ($r = -0.31$) following LHTL. Compared with the analysis of Robach & Lundby (2012) and a classic altitude training study on Australian footballers (McLean *et al.* 2013), the present correlation coefficient was much smaller than in those studies ($r = -0.51$ to -0.86). The above-mentioned studies suggested that athletes starting with high relative Hb_{mass} values have smaller chances to increase their relative Hb_{mass} further after altitude training, with the rationale that those athletes would already have maximized their relative Hb_{mass} by training at sea level (Robach & Lundby, 2012; McLean *et al.* 2013). However, in the present study it seems that the moderate inverse relationship between initial relative Hb_{mass} and the percentage change in relative Hb_{mass} could not be attributed to the physiological limit of an athlete.

Changes in an individual's body weight from pre- to post-intervention could explain the moderate relationship between initial relative Hb_{mass} and its percentage Hb_{mass} increase following LHTL. There was a large inverse relationship ($r = -0.64$) between individual percentage changes in body weight and relative Hb_{mass}, whereas no relationship between individual percentage changes in body weight and absolute Hb_{mass} occurred. Furthermore, percentage changes in body weight were significantly associated with percentage changes in relative Hb_{mass} ($P < 0.001$) in contrast to initial relative Hb_{mass} ($P = 0.4$). This assumes that, primarily, individual changes in body weight from pre- to post-LHTL camp led to the moderate relationship between initial relative Hb_{mass} and the percentage change in Hb_{mass} after the LHTL camp. Whether the body weight changes were attributable to alterations in fat and/or muscle mass or because of the weekly fluctuation in body weight/fluid (Orsama *et al.* 2014) remains unclear. With a lack of significant relationship between individual changes in body weight and absolute Hb_{mass}, it can be assumed that body weight alterations did not negatively influence the absolute Hb_{mass} response in the present study. Thus, we propose that lean body mass-adjusted relative Hb_{mass} values would be a better unit for future comparisons.

A further point that must be considered when assessing the relationship between change and initial values is the statistical phenomon of 'regression to the mean' (Galton, 1886; Bland & Altman, 1994). Although in the present study there was no relationship between initial absolute Hb_{mass} and percentage changes in absolute Hb_{mass}, the 'regression to the mean' effect could still have appeared. Furthermore, given that individual changes in body weight from pre- to post-LHTL camp occurred, it could also be possible that the 'regression to the mean' effect arose within the relationship between initial body weight and body weight changes. This makes the speculation that, in the present study, part of the inverse relationship between initial relative Hb_{mass} and percentage changes in relative Hb_{mass} following LHTL camp could be attributable to the statistical phenomenon 'regression to the mean'. However, this needs to be confirmed with a larger dataset, involving athletes of different performance levels and from various sport disciplines as well as using different altitude training protocols with various characteristics (e.g. duration, altitude severity, hypobaric *versus* normobaric hypoxia). Lastly, one should also keep in mind that the chosen metric for total 'hypoxic dose', i.e. 'kilometre hours' (Garvican-Lewis *et al.* 2016), is still debated in the literature (Millet *et al.* 2016).

Conclusion

Our results indicate that trivial (absolute values) to moderate (relative values) relationships occurred between initial Hb_{mass} and Hb_{mass} increase following LHTL altitude training in endurance and team-sport athletes. This indicates that even athletes with higher initial Hb_{mass} can reasonably expect Hb_{mass} gains post-LHTL. Furthermore, it seems that in the present study the moderate relationship between initial relative Hb_{mass} and percentage increase in relative Hb_{mass} following LHTL could be attributed to changes in body weight and possibly to the statistical phenomenon 'regression to the mean', rather than to a pure physiological effect.

References

Bland JM & Altman DG (1994). Regression towards the mean. *BMJ* **308**, 1499.

Bonetti DL & Hopkins WG (2009). Sea-level exercise performance following adaptation to hypoxia: a meta-analysis. *Sports Med* **39**, 107–127.

Brocherie F, Girard O, Faiss R & Millet GP (2017). Effects of repeated-sprint training in hypoxia on sea-level performance: a meta-analysis. *Sports Med* **47**, 1651–1660.

Brocherie F, Millet GP, Hauser A, Steiner T, Rysman J, Wehrlin JP & Girard O (2015). "Live high–train low and high" hypoxic training improves team-sport performance. *Med Sci Sports Exerc* **47**, 2140–2149.

Chapman RF, Stray-Gundersen J & Levine BD (1998). Individual variation in response to altitude training. *J Appl Physiol* **85**, 1448–1456.

Friedmann B, Frese F, Menold E, Kauper F, Jost J & Bartsch P (2005). Individual variation in the erythropoietic response to altitude training in elite junior swimmers. *Br J Sports Med* **39**, 148–153.

Galton F (1886). Regression towards mediocrity in hereditary stature. *The Journal of the Anthropological Institute of Great Britain and Ireland* **15**, 246–263.

Garvican LA, Martin DT, Clark SA, Schmidt WF & Gore CJ (2007). Variability of erythropoietin response to sleeping at simulated altitude: a cycling case study. *Int J Sports Physiol Perform* **2**, 327–331.

Garvican LA, Martin DT, Quod M, Stephens B, Sassi A & Gore CJ (2012). Time course of the hemoglobin mass response to natural altitude training in elite endurance cyclists. *Scand J Med Sci Sports* **22**, 95–103.

Garvican-Lewis LA, Clark SA, Polglaze T, McFadden G & Gore CJ (2013). Ten days of simulated live high:train low altitude training increases Hbmass in elite water polo players. *Br J Sports Med* **47**(Suppl 1), i70–i73.

Garvican-Lewis LA, Sharpe K & Gore CJ (2016). Time for a new metric for hypoxic dose? *J Appl Physiol* **121**, 352–355.

Girard O, Amann M, Aughey R, Billaut F, Bishop DJ, Bourdon P, Buchheit M, Chapman R, D'Hooghe M, Garvican-Lewis LA, Gore CJ, Millet GP, Roach GD, Sargent C, Saunders PU, Schmidt W & Schumacher YO (2013). Position statement—altitude training for improving team-sport players' performance: current knowledge and unresolved issues. *Br J Sports Med* **47**(Suppl 1), i8–i16.

Gore CJ, Hahn A, Rice A, Bourdon P, Lawrence S, Walsh C, Stanef T, Barnes P, Parisotto R, Martin D & Pyne D (1998). Altitude training at 2690m does not increase total haemoglobin mass or sea level VO2max in world champion track cyclists. *J Sci Med Sport* **1**, 156–170.

Gore CJ, Sharpe K, Garvican-Lewis LA, Saunders PU, Humberstone CE, Robertson EY, Wachsmuth NB, Clark SA, McLean BD, Friedmann-Bette B, Neya M, Pottgiesser T, Schumacher YO & Schmidt WF (2013). Altitude training and haemoglobin mass from the optimised carbon monoxide rebreathing method determined by a meta-analysis. *Br J Sports Med* **47**(Suppl 1), i31–i39.

Hauser A, Schmitt L, Troesch S, Saugy JJ, Cejuela-Anta R, Faiss R, Robinson N, Wehrlin JP & Millet GP (2016). Similar hemoglobin mass response in hypobaric and normobaric hypoxia in athletes. *Med Sci Sports Exerc* **48**, 734–741.

Hauser A, Troesch S, Saugy JJ, Schmitt L, Cejuela-Anta R, Faiss R, Steiner T, Robinson N, Millet GP & Wehrlin JP (2017). Individual hemoglobin mass response to normobaric and hypobaric "live high–train low": a one-year crossover study. *J Appl Physiol* **123**, 387–393.

Heinicke K, Wolfarth B, Winchenbach P, Biermann B, Schmid A, Huber G, Friedmann B & Schmidt W (2001). Blood volume and hemoglobin mass in elite athletes of different disciplines. *Int J Sports Med* **22**, 504–512.

Hopkins WG (2000). Measures of reliability in sports medicine and science. *Sports Med* **30**, 1–15.

Hopkins WG, Marshall SW, Batterham AM & Hanin J (2009). Progressive statistics for studies in sports medicine and exercise science. *Med Sci Sports Exerc* **41**, 3–13.

Humberstone-Gough CE, Saunders PU, Bonetti DL, Stephens S, Bullock N, Anson JM & Gore CJ (2013). Comparison of live high: train low altitude and intermittent hypoxic exposure. *J Sports Sci Med* **12**, 394–401.

Inness MWH, Billaut F & Aughey RJ (2016). Live-high train-low improves repeated time-trial and Yo-Yo IR2 performance in sub-elite team-sport athletes. *J Sci Med Sport* **20**, 190–195.

Levine BD & Stray-Gundersen J (2005). Point: positive effects of intermittent hypoxia (live high:train low) on exercise performance are mediated primarily by augmented red cell volume. *J Appl Physiol* **99**, 2053–2055.

Lundby C, Millet GP, Calbet JA, Bartsch P & Subudhi AW (2012). Does 'altitude training' increase exercise performance in elite athletes? *Br J Sports Med* **46**, 792–795.

McLean BD, Buttifant D, Gore CJ, White K & Kemp J (2013). Year-to-year variability in haemoglobin mass response to two altitude training camps. *Br J Sports Med* **47**(Suppl 1), i51–i58.

McLean BD, Gore CJ & Kemp J (2014). Application of 'live low-train high' for enhancing normoxic exercise performance in team sport athletes. *Sports Med* **44**, 1275–1287.

Millet GP, Brocherie F, Girard O, Wehrlin JP, Troesch S, Hauser A, Steiner T, Peltonen JE, Rusko HK, Constantini K, Fulton TJ, Hursh DG, Noble TJ, Paris HL, Wiggins CC, Chapman RF, Levine BD, Kumar VH & Schmidt WF (2016). Commentaries on viewpoint: time for a new metric for hypoxic dose? *J Appl Physiol* **121**, 356–358.

Millet GP, Roels B, Schmitt L, Woorons X & Richalet JP (2010). Combining hypoxic methods for peak performance. *Sports Med* **40**, 1–25.

Orsama AL, Mattila E, Ermes M, van Gils M, Wansink B & Korhonen I (2014). Weight rhythms: weight increases during weekends and decreases during weekdays. *Obes Facts* **7**, 36–47.

Robach P & Lundby C (2012). Is live high–train low altitude training relevant for elite athletes with already high total hemoglobin mass? *Scand J Med Sci Sports* **22**, 303–305.

Saugy JJ, Schmitt L, Cejuela R, Faiss R, Hauser A, Wehrlin JP, Rudaz B, Delessert A, Robinson N & Millet GP (2014). Comparison of "live high-train low" in normobaric versus hypobaric hypoxia. *PLoS One* **9**, e114418.

Schmidt W & Prommer N (2005). The optimised CO-rebreathing method: a new tool to determine total haemoglobin mass routinely. *Eur J Appl Physiol* **95**, 486–495.

Schmidt W & Prommer N (2008). Effects of various training modalities on blood volume. *Scand J Med Sci Sports* **18**(Suppl 1), 57–69.

Siebenmann C, Robach P, Jacobs RA, Rasmussen P, Nordsborg N, Diaz V, Christ A, Olsen NV, Maggiorini M & Lundby C (2012). "Live high–train low" using normobaric hypoxia: a double-blinded, placebo-controlled study. *J Appl Physiol* **112**, 106–117.

Steiner T & Wehrlin JP (2011). Does hemoglobin mass increase from age 16 to 21 and 28 in elite endurance athletes? *Med Sci Sports Exerc* **43**, 1735–1743.

Wachsmuth NB, Kley M, Spielvogel H, Aughey RJ, Gore CJ, Bourdon PC, Hammond K, Sargent C, Roach GD, Sanchez RS, Claros JC, Schmidt WF & Garvican-Lewis LA (2013*a*). Changes in blood gas transport of altitude native soccer players near sea-level and sea-level native soccer players at altitude (ISA3600). *Br J Sports Med* **47**(Suppl 1), i93–i99.

Wachsmuth NB, Volzke C, Prommer N, Schmidt-Trucksass A, Frese F, Spahl O, Eastwood A, Stray-Gundersen J & Schmidt W (2013*b*). The effects of classic altitude training on hemoglobin mass in swimmers. *Eur J Appl Physiol* **113**, 1199–1211.

Wehrlin JP, Marti B & Hallen J (2016). Hemoglobin mass and aerobic performance at moderate altitude in elite athletes. *Adv Exp Med Biol* **903**, 357–374.

Wilber RL (2007). Application of altitude/hypoxic training by elite athletes. *Med Sci Sports Exerc* **39**, 1610–1624.

Wilber RL, Stray-Gundersen J & Levine BD (2007). Effect of hypoxic "dose" on physiological responses and sea-level performance. *Med Sci Sports Exerc* **39**, 1590–1599.

Additional information

Competing interests

None declared.

Author contributions

J.P.W., G.P.M., O.G., L.S. and A.H. conceived and designed the research. All authors performed the research and analysed or interpreted the data for the work. A.H., S.T., J.P.W. and G.P.M. drafted the manuscript. All authors edited and revised the manuscript critically and approved the final version of the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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