Locomotor-Respiratory Coupling Is Maintained In Simulated Moderate Altitude In Trained Distance Runners

By: Timothy J. Fulton, 1 Hunter L. Paris, 1 **Abigail S. L. Stickford**, 2 Allison H. Gruber, 1 Timothy D. Mickleborough, 1 and Robert F. Chapman 1

Abstract

To determine whether acute exposure to simulated moderate altitude alters locomotor-respiratory coupling (LRC) patterns in runners, 13 trained male distance runners performed a running economy and maximal oxygen uptake (Vo2max) test in normoxia (NORM) and hypoxia (HYP) (FIO2= 15.8%; ~2,400 m/8,000 ft) on separate days. Running economy (RE), the degree of LRC, stride frequency-to-breathing frequency quotients (SF/fb), ratings of perceived exertion (RPE), and dyspnea were assessed at three common submaximal speeds and Vo2max. SF/fb were significantly lower at each submaximal speed in HYP (12.9 km/h: 2.91 ± 0.20 vs. 2.45 ± 0.17, 14.3 km/h: 2.53 ± 0.17 vs. 2.21 ± 0.14, 16.1 km/h: 2.22 ± 0.14 vs. 1.95 ± 0.09; $P < 0.05$). The degree of LRC (range: 36–99%) in HYP was not significantly different than NORM at any of the three common submaximal speeds. However, the degree of LRC was significantly higher at Vo2max in HYP than NORM (43.8 ± 3.4% vs. 57.1 ± 3.8%; $P < 0.05$). RE and RPE were similar at all running speeds. Dyspnea was significantly greater in HYP compared with NORM at 16.1 km/h ($P < 0.05$). Trained distance runners are able to maintain LRC in HYP, despite increases in breathing frequency. Within this unique population, years of training may enhance and optimize the ability to maintain LRC to minimize metabolic costs and dyspnea.

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RESEARCH ARTICLE

Locomotor-respiratory coupling is maintained in simulated moderate altitude in trained distance runners

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Fulton TJ, Paris HL, Stickford ASL, Gruber AH, Mickleborough TD, Chapman RF. Locomotor-respiratory coupling is maintained in simulated moderate altitude in trained distance runners. *J Appl Physiol* 125: 1–7, 2018. First published March 8, 2018; doi: 10.1152/japplphysiol.01122.2017.—To determine whether acute exposure to simulated moderate altitude alters locomotor-respiratory coupling (LRC) patterns in runners, 13 trained male distance runners performed a running economy and maximal oxygen uptake ($\dot{V}_{O2max}$) test in normoxia (NORM) and hypoxia (HYP) ($F_{I_{O_2}}$ = 15.8%; ~2,400 m/8,000 ft) on separate days. Running economy (RE), the degree of LRC, stride frequency-to-breathing frequency quotients (SF/f_b), ratings of perceived exertion (RPE), and dyspnea were assessed at three common submaximal speeds and $\dot{V}_{O2max}$. SF/f_b were significantly lower at each submaximal speed in HYP (12.9 km/h: 2.91 ± 0.20 vs. 2.45 ± 0.17, 14.3 km/h: 2.53 ± 0.17 vs. 2.21 ± 0.14, 16.1 km/h: 2.22 ± 0.14 vs. 1.95 ± 0.09; $P < 0.05$). The degree of LRC (range: 36–99%) in HYP was not significantly different than NORM at any of the three common submaximal speeds. However, the degree of LRC was significantly higher at $\dot{V}_{O2max}$ in HYP than NORM (43.8 ± 3.4% vs. 57.1 ± 3.8%; $P < 0.05$). RE and RPE were similar at all running speeds. Dyspnea was significantly greater in HYP compared with NORM at 16.1 km/h ($P < 0.05$). Trained distance runners are able to maintain LRC in HYP, despite increases in breathing frequency. Within this unique population, years of training may enhance and optimize the ability to maintain LRC to minimize metabolic costs and dyspnea.

NEW & NOTEWORTHY Exposure to acute altitude causes increases in ventilation at rest and any submaximal exercising workload, which may alter locomotor-respiratory coupling (LRC). Our data suggest that trained distance runners can maintain LRC during acute exposure to simulated moderate altitude, even when breathing frequency is increased at any submaximal pace.

athletes; entrainment; hypoxia; ventilation

INTRODUCTION

Endurance athletes commonly use altitude training to improve sea level performance. However, even when following best practice guidelines, considerable variation in physiological responses to altitude and subsequent performance exists (9). One of the most immediate and noticeable responses to acute altitude exposure is an increase in ventilation at rest and any submaximal exercising workload. The ventilatory response to exercise is unique in having both physiological outcomes (e.g., defending arterial oxyhemoglobin saturation, but with a metabolic cost of increased work of breathing) and perceptual outcomes (e.g., dyspnea), which can be both positive and negative for exercise performance. As a result, ventilatory control during exercise at altitude can have a strong influence on workload selection, perception of effort, and ultimately the training response at altitude (6, 35, 36).

One factor involved in ventilatory control is locomotor-respiratory coupling (LRC). LRC is a stable frequency and phase locking between ventilation and locomotion that can be expressed as the degree (or percentage) of breaths that begin within a specific time point of each stride (2). A lower degree of LRC (i.e., a lower percentage of breaths occurring at the same time point of the stride) may increase the energetic cost of locomotion by increasing the oxygen cost of breathing (2, 18, 21, 34). Increases in the oxygen cost of breathing due to alterations in LRC have also been linked to increases in the perception of breathlessness (i.e., dyspnea) (33). Therefore, any perturbation to the components of LRC could have negative energetic consequences and cause perception-linked decrements in exercise tolerance if the degree of LRC is reduced. A possible perturbation that endurance athletes encounter while utilizing altitude training is hypoxia-induced increases in breathing frequency. However, the impact of hypoxia on LRC has not been fully elucidated.

Paterson et al. (28) found decreases in the degree of LRC during running exercise in hypoxia when compared with normoxia; however, many of the subjects were mountaineers, not trained runners. Moreover, the energetic and perceptual consequences of altering LRC in hypoxia were not examined. Reductions in the degree of LRC may disrupt the coordination of step-driven flows and the duty cycle (15), antagonistically loading the respiratory muscles and causing oxygen uptake to increase. Because oxygen uptake and running economy (RE) are especially important to endurance exercise performance (11, 13, 14), changes to RE could be unfavorable to athletes with acute exposure to altitude.

Therefore, the purpose of this study was to determine whether acute exposure to hypoxia alters LRC patterns typically observed in trained runners and to investigate the effects of potential LRC changes on RE and dyspnea. We hypothesized that when compared with normoxia, hypoxic exercise at

common submaximal speeds would reduce the degree of LRC; furthermore, this reduction would be associated with worsened RE (i.e., increase oxygen uptake) and increased dyspnea.

METHODS

Subjects. Sixteen men volunteered to participate in the study; however, three were unable to meet the maximal oxygen uptake ($\dot{V}O_{2max}$) criteria (>60 ml·kg^{-1}·min^{-1} in normoxia) or voluntarily withdrew from the study. Therefore, 13 trained male distance runners successfully completed the entire study. Women were not included in order to isolate the effects of hypoxia on LRC and to limit any possible cofounding hormonal factors (e.g., progesterone) that could influence our primary variables of interest (e.g., ventilation, oxygen uptake, dyspnea). Subjects were tested at the same time of day for each of the visits. They were instructed to arrive at the laboratory fasted (>5 h) and having abstained from caffeine (>8 h), alcohol (>24 h), and strenuous exercise (>24 h). All subjects provided written informed consent to protocols that were approved by the Institutional Review Board of Indiana University.

Study design. Subjects completed two visits to the laboratory, with visits separated by at least 48 h. Resting pulmonary function was assessed on *visit 1*. *Visits 1* and *2* consisted of a submaximal treadmill test to determine RE and LRC. The treadmill test occurred in normoxia (NORM) or hypoxia (HYP; F_{I_O} = 15.8%; equivalent to ~2,400 m/8,000 ft) and was followed immediately by a ramp to volitional exhaustion to obtain $\dot{V}O_{2max}$. The order of the inspired gas conditions was randomized and counterbalanced, and subjects were blinded to the inspirate.

Protocol. Upon arrival subjects completed physical activity readiness and running history questionnaires followed by anthropometric measurements. Subjects were then instrumented with event switches that were taped to each foot and connected to flexible, lightweight extension cables adhered to the lateral side of each leg and hip. Subjects were subsequently shown and explained the Borg rating of perceived exertion (RPE; original 6–20 scale) and dyspnea (modified 0–10 scale) (3) and performed pulmonary function tests (*visit 1* only). The RE/LRC treadmill test began with three to five minutes of quiet standing to collect resting ventilatory and metabolic data. Following rest, subjects ran for five minutes at each of three constant submaximal speeds of 12.9, 14.3, and 16.1 km/h (7:30, 6:45, and 6:00 min/min) at 0% grade on a motorized treadmill (Model 18-72, Quinton, Bothell, WA). Subjects were given four minutes of rest between each five-minute bout. Treadmill speed was verified using a laser tachometer (Model DT-2234C, Mastech, San Jose, CA). After the fifth minute of running at the 16.1 km/h speed, the incline of the treadmill was raised to 2% for the next two minutes and continued to increase 2% every two minutes thereafter until volitional fatigue (i.e., subjects voluntarily ceased the test by stepping off the treadmill). Measurements of RE and LRC were taken during the fourth minute of each speed (3:00–4:00), while RPE and dyspnea measures were taken during the first 30 s of the final minute at each speed (4:00–4:30) such that any disruption in stride or breathing patterns due to the rating task were not included in the LRC analysis. Dyspnea and RPE were assessed again at the conclusion of the test, followed by completion of an attentional focus questionnaire (5). This questionnaire was utilized to determine association and dissociation scores (0–105 scale) to assess subjects' cognitive strategies and if they tended to focus more on internal cues (e.g., breathing frequency) or external cues (e.g., the surrounding environment) (25).

Pulmonary function. Resting pulmonary function was assessed using inspired and expired pneumotachographs (Series 3813/4813; Hans Rudolph, Shawnee, KS) and done in accordance with standard ATS procedures (1). Following familiarization, forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and total lung capacity (TLC) were measured. The largest FVC and forced expiratory volume in 1 s (FEV_1) chosen as a representation of the subject's pulmonary function.

Metabolic parameters. Metabolic and ventilatory variables were continuously measured during rest and exercise using open circuit indirect calorimetry with a customized metabolic cart. Subjects wore a facemask (Model 7450, Hans Rudolph) and breathed through a low-resistance, two-way nonbreathing valve (Model 2700, Hans Rudolph) from which expired gases were collected in a 5-liter mixing chamber. Dried samples from this mixing chamber, sampled at 300 ml/min, were used to determine fractional concentrations of O_2 and CO_2 by separate O_2 and CO_2 gas analyzers (S-3A/CD-3A, Ametek Thermox Instruments, Pittsburgh, PA). Analyzers were calibrated pre-test with known gas concentrations within the physiological range and were checked both midway and post-test to correct for any drift. The previously mentioned inspired pneumotachograph was used to measure minute ventilation, and was calibrated pre-test using a 3-liter syringe. Heart rate was measured using a telemetry transmitter (Model FT7, Polar Electro Inc., Lake Success, NY) placed across the subject's chest. Oxyhemoglobin saturation was measured via pulse oximetry (OxiMax N-600x, Nellcor, Minneapolis, MN). All dependent variables were sampled at 50 Hz using a data acquisition system (DASYLab, National Instruments, Norton, MA), with values being averaged over each minute of exercise. RE was calculated as the steady-state $\dot{V}O_2$ (ml·kg^{-1}·min^{-1}) during the fourth minute of each submaximal stage and the slope of the regression line relating steady-state $\dot{V}O_2$ (ml·kg^{-1}·min^{-1}) to running speed (km/h). Steady state was defined as a plateau (<150 ml increase) in $\dot{V}O_2$ from the previous minute. $\dot{V}O_{2max}$ was determined as the

highest recorded $\dot{V}O_2$ over 60 s when the subject met two of the three following criteria: *1*) a heart rate >90% of age predicted maximum (220-age), *2*) a respiratory exchange ratio (RER) of >1.10, and *3*) a plateau (<150 ml increase) in $\dot{V}O_2$ with an increase in workload.

Locomotor-respiratory coupling. Locomotor-respiratory coupling was determined as described previously in our laboratory (32). Briefl to determine the timing of foot strikes during the treadmill tests, fl and lightweight plastic event switches (MA-153, Motion Laboratory Systems, Inc., Baton Rouge, LA) were taped inside the shoe to either the heel or fi metatarsal of each foot depending on the subject's habitual foot strike pattern (heel: ~4 cm distally from the proximal end of the calcaneus; forefoot: approx- imately at the distal end of the fi metatarsal). The switch was positioned so that it was located at the point of initial ground contact and was connected to the data acquisition system by a cable. The timing of inspirations and expirations was determined via pneumotachographs that continuously measured fl rates. The data acquisition system was triggered to start kinematic and ven- tilatory data collection simultaneously to allow post hoc analysis, using only the fourth minute of each stage (the same minute as RE), and the minute during which $\dot{V}O_{2max}$ was achieved for LRC analysis.

An in-house software program allowed for calculation of the stride (i.e., left-to-left and right-to-right foot strike), step (i.e., left-to-right and right-to-left foot strike), and breathing frequencies, as well as time points of foot strike, inspiration, and expiration. Following an origi- nally described protocol (2) that has previously been utilized in our laboratory (32), each stride and step cycle was divided into 10 equal parts (i.e., decile), and the decile in which each inspiration or expi- ration occurred was determined. Subsequently, the highest number of inspirations or expirations beginning in the same decile of the step (or stride) cycle was divided by the total number of breaths to allow for expression of the degree of LRC as a percentage. The highest percentage out of inspirations, expirations, strides, and steps was used as the degree of LRC for that time period. Percentages were summed when coupling appeared to switch between two distinct deciles (determined as two, and only two, deciles encompassing more breaths than expected to occur by chance; binomial probability < 0.05).

Table 1. *Subject characteristics and pulmonary function*

	Value
Age, yr	23 ± 1
Mass, kg	68.7 ± 1.8
Height, m	1.70 ± 0.01
$\dot{V}O_{2max}$, ml·kg^{-1}·min^{-1}	66.8 ± 1.1
FVC, liters	4.92 ± 0.07 (87%)
FEV_1, liters	4.32 ± 0.07 (93%)
FEV1%, FEV_1/FVC	88 ± 2
PEF, liters/s	8.93 ± 0.1 (105%)

Values are means ± SE. Percent predicted (87%, 93%, and 105%), based on Hankinson et al. (20). $\dot{V}O_{2max}$, maximal oxygen uptake; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; PEF, peak expiratory flow.

Hypoxic delivery. Three 1,000-liter weather balloons were placed in-line on the inspired breathing line, distal to the inspired pneumotachograph. The balloons were filled to capacity before subject arrival with a gas composition of 15.8% O_2 and balance N_2 using a nitrogen generator (Model CAT 12, Colorado Altitude Training, Boulder, CO). The balloons were filled during both test days (NORM and HYP) to blind subjects to the inspirate, with the balloon valves staying closed during NORM tests such that the subjects breathed only room air, albeit through the same length of tubing. A secondary O_2 gas analyzer was used to determine the fractional O_2 concentrations of inspired air in real time, and this value was used continuously for calculation of oxygen uptake.

Statistical analysis. Findings were analyzed using SPSS statistical software (Version 24, IBM, Armonk, NY). Descriptive statistics were used to describe group characteristics, with values presented as means ± SE. The data were assessed for normality using the Shapiro-Wilk test and for sphericity using Mauchly's test. A 2 X 4 condition (inspirate) by speed repeated measures ANOVA with a post hoc Tukey's honest significance difference test for simple main effects was used to test for differences in ventilatory, metabolic, LRC, RPE, and dyspnea measures across speeds and between conditions. Paired *t*-tests were used to evaluate association and dissociation measures. The effect size was assessed using Cohen's d_z. The alpha for statistical significance for all comparisons was set at $P < 0.05$.

RESULTS

Subjects. Subject characteristics are displayed in Table 1. All subjects displayed normal pulmonary function, similar to those predicted by sex, age, race, and height (87% of FVC; 93% of predicted FEV_1) (20). Mean heart rate at $\dot{V}O_{2max}$ was 97% of age predicted maximum and RER at $\dot{V}O_{2max}$ was 1.15 ± 0.01.

Locomotor respiratory coupling. Breathing frequency (breaths/min) was signifi increased at each submaximal speed in HYP compared with NORM (12.9 km/h: 30.3 ± 1.9 vs. 35.9 ± 2.2; 14.3 km/h: 34.8 ± 2.0 vs. 39.8 ± 2.2; 16.1 km/h: 40.4 ± 2.4 vs. 45.2 ± 1.9; all speeds $P < 0.05$; effect size (ES) = 0.94–1.52). At $\dot{V}O_{2max}$ the difference in breathing frequency between NORM and HYP was approaching significance (51.8 ± 1.8 vs. 56.2 ± 1.7; $P = 0.07$; ES = 0.55). As expected, stride frequency (strides/min) did not differ between NORM and HYP at any speed (12.9 km/h: 83.8 ± 1.4 vs. 83.9 ± 1.1; 14.3 km/h: 84.3 ± 1.4 vs. 84.2 ± 1.1; 16.1 km/h: 86.0 ± 1.3 vs. 86.1 ± 1.3; <vo2max>: 87.2 ± 1.5 vs. 86.6 ± 1.4; $P = 0.50 - 0.93$; ES = 0.03 – 0.19). The combination of consistent stride frequency with elevated breathing frequencies resulted in significantly lower SF/f_b at the submaximal speeds during HYP compared with NORM (Table 2). Regardless of the inspired gas condition or the speed (i.e., when ratios from all speeds are pooled together) the 2:1 coupling ratio occurred the most frequently (29% of the time), followed by 5:3 (19%) and 5:2 (19%).

Across speeds and conditions, the average degree of LRC was 56.6 ± 15.5%. All subjects displayed an average degree of LRC greater than that expected by chance (~20%). Compared with NORM, the degree of LRC was not significantly different at any of the three common submaximal speeds with exposure to HYP ($P = 0.18 – 0.61$; ES = 0.15–0.39); however, it was significantly increased at $\dot{V}O_{2max}$ (Table 2) (ES = 1.01). The degree of LRC and breathing frequency were significantly inversely correlated when running at 16.1 km/h in NORM ($r = -0.62$); this association also approached significance at16.1 km/h in HYP ($r = -0.48$, $P = 0.096$).

Metabolic variables. All subjects were able to reach a steady state of oxygen uptake (<150 ml increase in $\dot{V}O_2$ from the previous minute) within three minutes at each submaximal speed. Running economy expressed as steady-state $\dot{V}O_2$ (ml·kg^{-1}·min^{-1}) was not statistically different ($P = 0.39 – 0.85$; ES = 0.05–0.25) between NORM and HYP at any submaximal speed (Table 3), nor was running economy expressed as the slope of the regression line relating steady-state $\dot{V}O_2$ to running speed (NORM: 3.10 ± 0.14 vs. HYP: 3.05 ± 0.14; $P = 0.84$). The submaximal running speeds corresponded to $\dot{V}O_2$ values that were 64, 70, and 79% of $\dot{V}O_{2max}$ in NORM, and 72, 79, and 88% of $\dot{V}O_{2max}$ in HYP. The degree of LRC and oxygen uptake were not significantly correlated at any submaximal speed or at $\dot{V}O_{2max}$ in either NORM or HYP, nor were any percent changes in degree of LRC and changes in oxygen consumption from NORM to HYP.

Ventilatory measures are summarized in Table 3. As expected, minute ventilation was significantly higher at each common submaximal speed in HYP compared with NORM but did not differ between inspirates at $\dot{V}O_{2max}$. As tidal volume did not differ between NORM and HYP at any speed, the achievement of increased submaximal exercise ventilation was due to increases in breathing frequency. The ventilatory equivalent for oxygen was significantly greater at each common speed, and at $\dot{V}O_{2max}$, in HYP compared with NORM. Oxyhemoglobin saturation was significantly lower before exercise in HYP

Table 2. *Locomotor-respiratory coupling measures during treadmill running*

	12.9 km/h		14.3 km/h		16.1 km/h		$\dot{V}O_{2max}$	
	NORM	HYP	NORM	HYP	NORM	HYP	NORM	HYP
SF/f_b	2.91 ± 0.20	2.45 ± 0.17*	2.53 ± 0.17	2.21 ± 0.14*	2.22 ± 0.14	1.95 ± 0.09*	1.70 ± 0.06	1.56 ± 0.06
Degree of LRC, %	63.6 ± 4.6	61.4 ± 4.8	60.2 ± 3.7	55.1 ± 5.3	56.8 ± 3.9	53.9 ± 3.0	43.8 ± 3.4	57.1 ± 3.8*

Values are means ± SE. NORM, normoxia; HYP, hypoxia; SF, stride frequency (strides/min); f_b, frequency of breathing (breath/min); SF/f_b, stride frequency-to-breathing frequency quotient, degree of locomotor-respiratory coupling (LRC) percentage of breaths beginning in the same decile of the step or stride cycle. *Significantly different than NORM at the same speed ($P < 0.05$).

Table 3. *Physiological measures during treadmill running*

	12.9 km/h		14.3 km/h		16.1 km/h		$\dot{V}_{O_{2max}}$	
	NORM	HYP	NORM	HYP	NORM	HYP	NORM	HYP
$\dot{V}_{O_2}$, ml·kg^{-1}·min^{-1}	42.9 ± 1.0	43.0 ± 0.8	46.4 ± 1.0	47.0 ± 0.9	52.5 ± 1.0	52.6 ± 0.9	66.8 ± 1.1	59.7 ± 0.8*
$\dot{V}_E$, l/min	71.3 ± 2.3	85.3 ± 3.1*	82.8 ± 2.5	97.3 ± 3.5*	100.6 ± 3.3	119.1 ± 4.4*	157.4 ± 3.7	159.9 ± 4.7
f_b, breath/min	30.3 ± 1.9	35.9 ± 2.2*	34.8 ± 2.0	39.8 ± 2.2*	40.4 ± 2.4	45.2 ± 1.9*	51.8 ± 1.8	56.2 ± 1.7
TV, l/breath	2.44 ± 0.15	2.47 ± 0.16	2.45 ± 0.13	2.52 ± 0.14	2.56 ± 0.13	2.67 ± 0.12	3.06 ± 0.13	2.88 ± 0.12
HR, beats/min	142 ± 4	149 ± 3	155 ± 4	163 ± 3	170 ± 3	176 ± 3	194 ± 2	189 ± 2*
$\dot{V}_E/\dot{V}_{O_2}$	24.2 ± 0.7	29.0 ± 0.8*	26.0 ± 0.7	30.0 ± 0.8*	27.9 ± 0.9	33.0 ± 1.0*	34.3 ± 0.9	39.1 ± 0.9*

Values are means ± SE. $\dot{V}_{O_2}$, volume of oxygen uptake; $\dot{V}_E$, minute ventilation; f_b, frequency of breathing; TV, tidal volume, HR, heart rate, $\dot{V}_E/\dot{V}_{O_2}$, ventilatory equivalent for oxygen. *Significantly different than NORM at the same speed ($P < 0.05$).

compared with NORM (92 ± 0.6% vs. 98 ± 0.3%) and significantly lower at $\dot{V}_{O_{2max}}$ in HYP compared with NORM (80 ± 1.2% vs. 91 ± 0.9%)

Perceptual variables. Dyspnea was significantly higher in HYP than in NORM, but only when running at 16.1 km/h (Fig. 1*A*) (ES = 1.06). No significant differences were found for RPE between conditions (Fig. 1*B*) (P = 0.11–0.50; ES = 0.19–0.48). Dyspnea was significantly correlated to minute ventilation at $\dot{V}_{O_{2max}}$ in NORM (r = 0.82) but not at any other speed or condition. Subjects' association scores (56 ± 2 in NORM and 52 ± 3 in HYP) were significantly higher than their dissociation scores (27 ± 1 in NORM and 26 ± 2 in HYP).

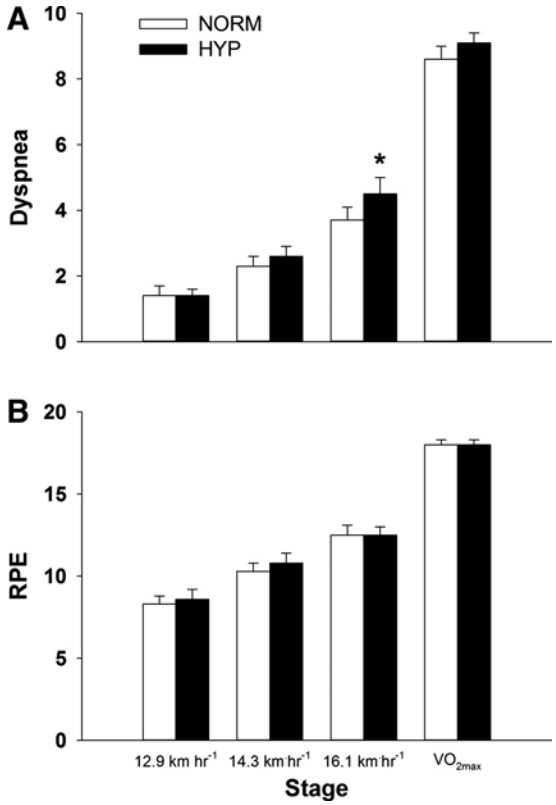

Fig. 1. *A*: ratings of dyspnea (%). *B*: rating of perceived exertion (RPE, %) during normoxia (NORM; open bars) and hypoxia (HYP; 15.8% O_2; filled bars) across all four stages. Values are means ± SE. *Significantly different than NORM at the same speed ($P < 0.05$).

DISCUSSION

The primary finding of this investigation is that in trained distance runners stride-to-breathing frequency ratios during running at constant submaximal speeds in simulated moderate altitude are altered compared with normoxia. However, contrary to our hypothesis, there were no changes to the degree of LRC at submaximal oxygen uptake levels. Additionally, running economy and most measures of perception of effort were not altered during submaximal exercise in HYP compared with NORM. The ability of trained distance runners to maintain LRC in a hypoxic environment may be especially advantageous when training or competing with acute exposure to moderate altitudes. Our data would suggest that declines in exercise tolerance and performance at moderate altitude are not substantially influenced by LRC.

Locomotor respiratory coupling. Due to increased breathing frequencies, the stride-to-breathing frequency ratios were lower during HYP compared with NORM, but in both conditions the most common whole integer ratio was two strides to one breath (2:1). This ratio is consistent with previous work in our laboratory (32), as well as several other investigations on LRC during running (2, 4, 26, 28, 33). An elegant study by Daley et al. (15) suggests that this ratio is used by humans to minimize antagonistic loading of the respiratory muscles by coordinating step-driven flows and breathing such that foot strikes are able to aid in ventilatory transitions.

Although running in hypoxia did increase breathing frequency in the face of a stable stride frequency, it did not reduce the degree of LRC, contrary to our initial hypothesis. Paterson et al. (28) did observe decreases in the degree of LRC during hypoxic running (~65% at 915 m, ~62% at 2,135 m, ~50% at 3,200 m, ~33% at 4,420 m, and ~23% at 5,030 m), suggesting that hypoxia increases breathing frequency to such an extent that it causes uncoupling. Perhaps the reason we did not observe a similar outcome was that our hypoxic stimulus was not strong enough to elicit this response. We chose to utilize a F_{IO_2} of 15.8% (equivalent to ~2,400 m/8,000 ft) as this is most similar to the elevation endurance athletes sojourn to during altitude training camps. Paterson et al. (28) tested subjects across a range of elevations, with the most drastic decreases in the degree of LRC occurring at elevations from 3,000 to >5,000 meters, which are higher than our chosen elevation. The maintenance in the degree of LRC between 915 m and 2,135 m are similar to the maintenance at we observed at 2,400 m.

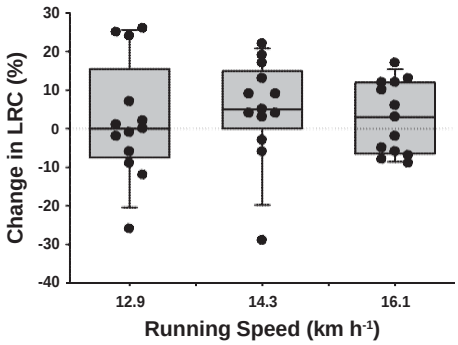

Fig. 2. Box plot of change (%) in locomotor-respiratory coupling (LRC) from normoxia to hypoxia across three submaximal running speeds. A positive change in LRC (%) indicates a greater LRC (%) in normoxia. Shaded box indicates first and third quartiles with median value. Error bars represent 90% confidence interval.

Another difference that merits comment is that Paterson et al. (28) utilized hypobaric hypoxia, whereas we (due to logistical constraints) tested subjects in normobaric hypoxia. Possible differences in breathing frequency between these two stimuli are especially relevant to our study. Although the data are inconclusive, a recent systematic review suggests that breathing frequency may increase more in normobaric hypoxia than in hypobaric hypoxia (12). Therefore, it is unlikely the degree of LRC would be altered to a greater extent in hypobaric hypoxia due to changes in breathing frequency alone. However, air density is less in hypobaric hypoxia than in normobaric hypoxia, which could increase flow rates and alter the duty cycle. Alterations to the duty cycle may affect the timing of inspirations and expirations and therefore when each occur within the stride cycle, ultimately affecting the degree of LRC.

The maintenance of the degree of LRC between normoxia and hypoxia in our study is consistent with the findings of Fabre et al. (17) and Seebauer et al. (31). Fabre et al. (17) did not observe any changes in the degree of LRC in rowers while exercising in hypoxia compared with normoxia. While ventilation and frequency of breathing increased as expected with exposure to hypoxia, the rowers concomitantly increased their stroke rate, which also resulted in a consistent LRC ratio (stroke rate-to-breathing frequency). It was suggested that the neuro-mechanical stimuli linking the specific locomotor aspects of rowing with respiration was stronger than the peripheral chemoreceptor stimuli induced by hypoxia. We believe our results mirror this conclusion, as the rowers completed the hypoxic tests at an elevation of 2,877 meters, only slightly higher than our FI_{O_2} equivalent. Seebauer et al. (31) found comparable effects of hypoxia during cycling exercise, where no decrements in the degree of LRC were observed at any of three separate workloads. In fact, the degree of LRC was increased at a workload of 95% peak oxygen uptake. This fi is parallel to our results, as we observed a signifi higher degree of LRC at $\dot{V}_{O2max}$ in hypoxia compared with normoxia. This increase in the degree of LRC at maximal and near-maximal workloads, as well as maintenance at submaximal workloads in hypoxia, may be an additional illustration of the established ability of trained endurance runners to self-optimize kinematic and physiological variables (7, 22, 32).

Perceptual measures. We hypothesized that dyspnea would increase in hypoxia compared with normoxia at each common submaximal speed if the degree of LRC was reduced. While no reductions in the degree of LRC were observed, dyspnea was increased at the fastest speed (16.1 km/h). In hypoxia, this speed elicited an average oxygen uptake of 88% of $\dot{V}_{O2max}$. These data suggest that the combination of the high relative workload along with an increase in ventilation from normoxia to hypoxia was enough to alter subjects' perceptions of ventilatory effort independent of any significant changes to the degree LRC. Even though subjects were able to maintain the degree of LRC at this speed, a combination of input from other mechanisms (chest wall mechanoreceptors, auditory feedback) may have outweighed the maintenance of the degree of LRC to alter dyspnea.

Subjects in our study exhibited a much higher associative than dissociative focus during exercise in both normoxia and hypoxia. These results are consistent with the hypothesis that

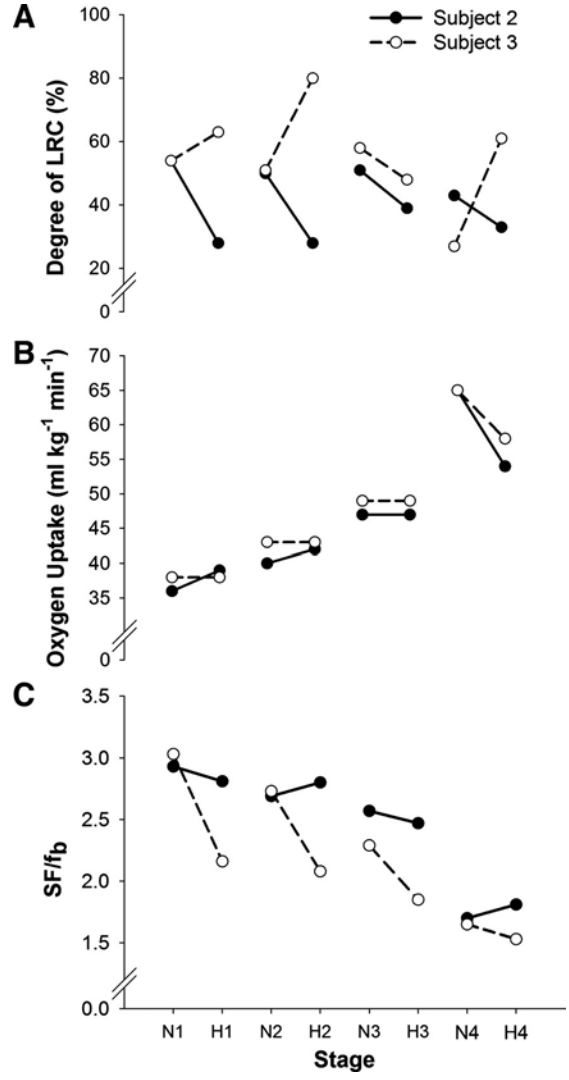

Fig. 3. Degree of locomotor respiratory coupling (LRC) (*A*), oxygen uptake (*B*), and stride frequency to breathing frequency ratio (SF/f_b) (*C*) for *subject 2* (line and filled circle) and *subject 3* (dashed line and open circle) across all four stages (*N*, normoxia; H, hypoxia; at 15.8% O_2, 1 = 12.9 km/h, 2 = 14.3 km/h, 3 = 16.1 km/h, 4 = $\dot{V}_{O2max}$).

trained distance runners tend to use associative attentional strategies during exercise instead of dissociative strategies employed by novice individuals to maximize exercise performance (5, 10, 27). It is plausible that subjects in our study utilized an attentional strategy to monitor changes in physiological variables such as breathing frequency and stride frequency to maintain the degree of LRC in hypoxia, and therefore maintain running economy.

Individual responses to hypoxia. For endurance athletes training or competing acutely at altitude, physiological responses to hypoxia show substantial individual variation (8). Despite the lack of mean differences, the ability to maintain LRC in hypoxia was not universally seen across our cohort of well-trained runners (Fig. 2). Select subjects (e.g., *subject 2* in Fig. 3*A*) displayed large decreases in the degree of LRC from NORM to HYP across stages, while others (e.g., *subject 3* in Fig. 3*A*) had a similar, or even elevated, degree of LRC between conditions. Concurrent with the decreases in the degree of LRC, *subject 2* also had increased oxygen uptake from NORM to HYP at the fi two stages, while *subject 3* was able to maintain oxygen uptake (Fig. 3*B*). While both subjects saw decreases in $\dot{V}O_{2max}$ from NORM to HYP, *subject 3*, who had a substantial increase in the degree of LRC in HYP, had less of a decrement in $\dot{V}O_{2max}$ than *subject 2*. The responses of *subject 2* suggest that if there are substantial reductions in the degree of LRC in hypoxia it may, as others have shown (18, 21, 34), lead to increases in submaximal oxygen uptake, while the responses of *subject 3* may be evidence that the maintenance of the degree of LRC in hypoxia is benefi for maintaining RE and mitigating the decline in $\dot{V}O_{2max}$ at altitude. Due to the established presence of individual variation in the response to acute hypoxic exposure (8), future inquiries into factors limiting exercise performance at altitude should consider including LRC as a variable of interest.

A factor related to the individual ventilatory response to exercise in hypoxia is expiratory flow limitation (8). Although this was not directly measured, we believe its influence on the group results is minimal. The exercise intensities during the running economy tests were, on average, 75% of $\dot{V}O_{2max}$. Additionally, even at the fastest speed of the RE test, subjects' minute ventilation in HYP was only 75% of minute ventilation at $\dot{V}O_{2max}$. Studies quantifying flow limitation in trained runners, both in our laboratory and others, have not observed a large prevalence of flow limitation at similar exercise intensities or ventilations (16, 23). However, this may be especially important in the context of sex-based respiratory differences, as women have a higher prevalence of flow limitation than men due to smaller diameter airways (19). Furthermore, increases in progesterone during the luteal phase have been shown to alter both ventilatory drive during exercise and hypoxic ventilatory responses (30), possibly influencing oxygen uptake (24) and dyspnea (29). Future studies may wish to include flow limitation measurements as well as female subjects to tease out individual variations.

Conclusion. Trained distance runners are able to maintain LRC with acute exposure to simulated moderate altitude, even when breathing frequency is increased at any submaximal pace. It is possible that within this unique population, years of training enhance and optimize the ability to make adjustments to LRC to minimize metabolic costs. However, there may be individual differences to LRC that could affect performance or the response to training at altitude.

DISCLOSURES

No confl of interest, fi or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

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

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