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Hypoxic repeated sprint interval training improves cardiorespiratory fitness in sedentary young women

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ABSTRACT

Objective: The purpose of this study was to investigate the effects of repeated sprint interval training (RSIT) under different hypoxic conditions in comparison with normoxic RSIT on cardiorespiratory fitness (CRF) and metabolic health in sedentary young women.

Methods: Sixty-two sedentary young women (age: 21.9 ± 2.8 years, peak oxygen uptake [VO_{2peak}] 25.9 ± 4.5 ml $kg^{-1} \cdot min^{-1}$) were randomized into one of the four groups, including a normoxic RSIT group (N), RSIT simulating an altitude of 2500 m (H_{2500}), RSIT simulating an incremental altitude of 2500 −3400 m ($H_{2500-3400}$) and a non-exercise control group (C). The training intervention (80 × 6 s all-out cycling sprints with 9 s recovery) was performed three times/week for 4 weeks. Anthropometric measures, VO_{2peak}, fasting blood glucose and lipids were assessed during the follicular phase of the menstrual cycle before and after the intervention.

Results: Compared with the control group, significant increases in VO_{2peak} were found in both hypoxic groups (H_{2500}: +8.2%, $p < 0.001$, $d = 0.52$; $H_{2500\text{-}3400}$: +10.9%, $p < 0.05$, $d = 0.99$) but not in the N group (+3.6%, $p > 0.05$, $d = 0.21$) after the intervention, whereas the two hypoxic groups had no difference in VO_{2peak}. Blood glucose and lipids, and body composition remained unchanged in all groups.

Conclusion: The present study indicates that combining hypoxia with RSIT can enhance the improvement of CRF compared with normoxic RSIT alone in the sedentary young population. Yet, compared with RSIT under stable hypoxia, incremental hypoxia stress in the short-term does not additionally ameliorate CRF.

1. Introduction

Low levels of physical activity are associated with a wide range of health consequences, such as all-cause mortality and cardiometabolic diseases.[1] Regular exercise is commonly recommended as an effective mean to improve health outcomes in the physically inactive population.[2] However, this recommendation is difficult to implement, as one of the frequently cited barriers is a lack of time.[3] High-intensity interval training (HIIT) protocols, therefore, are becoming increasingly popular for their advantage of time efficiency over traditional endurance training[4,5] to enhance cardiometabolic health,[6] despite the fact that the feeling of exhaustion during maximal exercise makes the Wingate-based HIIT extremely hard to adhere to.[7] Repeated sprint interval training (RSIT) is a particular form of HIIT characterized by an extremely short exercise duration (≤10 s of work bout) at near to maximal intensity, interspersed with recovery times of less than 30 s.[8] The efficacy of RSIT in improving cardiometabolic health has been well documented.[9] Numerous studies have demonstrated that RSIT effectively improved aerobic fitness in young, healthy adults[4,9] and sedentary individuals,[5] decreased the risk of a complex of metabolic abnormalities such as insulin sensitivity, poor glycaemic control, high blood pressure and body composition in healthy and diseased elderly,[10] overweight/obese,[9,11] and type 2 diabetes

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patients.[12] However, cardiorespiratory fitness (CRF) improvement with a relatively small effect size[4] may weaken the practical implications of RSIT. It would be of great interest to practitioners and researchers for providing more effective solutions to improve cardiometabolic outcomes.

Exercise under hypoxic conditions is becoming a more commonly used strategy for improving cardiometabolic outcomes. It seems that the addition of hypoxia plays an important role in the process of physiological adaptation to insufficient oxygen availability in further ameliorating the effect of physical exercise in improving physical fitness, body composition and lipid profiles.[13–15] Similarly, our previous study demonstrated that training in a moderately hypoxic environment caused greater weight loss and improved blood pressure compared with normoxic training after 4 weeks of residential training.[16] More recently, we found that the addition of hypoxia combined with HIIT conferred greater improvement in CRF than the normoxic protocol in sedentary overweight women.[17] The key mechanisms for this improvement are associated with compensatory vasodilation,[18] elevated vascular oxygen delivery,[19] and increased glycolytic energetic metabolism and mitochondrial function.[20] However, other research has yielded inconsistent results regarding the additive benefits of hypoxia on CRF and metabolic alterations. An optimal combination of time-efficient RSIT and effective dose of hypoxia is incompletely understood. For example, a similar improvement or no difference between normoxic and hypoxic groups on aerobic capacity[21] and body composition[17] was found following short-term RSIT in untrained population. The apparent discrepancy in the literature might be explained by varying exercise regimens and the levels of hypoxia being used in different studies.[14–17]

Very few studies have examined the optimal combination of RSIT and hypoxia. An animal study revealed that a higher level of hypoxia resulted in greater positive adaptation on respiratory system by enhancing carotid body function to increase the ventilatory response.[22] Consistently, our previous study demonstrated that, during a 5-week intervention of HIIT under a stable hypoxia (FiO_2: 0.15), the peripheral oxygen saturation (SpO_2) increased gradually, suggesting a progressive attenuation of hypoxic stress.[17] However, to date there is no clear consensus on the ideal dose of hypoxic training. Physical inactivity is more prevalent among women than among men, and sedentary women are at an increased risk for noncommunicable diseases and are susceptible to mental health problems.[24] The complexities of the menstrual cycle are considered major barriers to the inclusion of women into clinical trials; consequently, the research in sport and exercise medicine was conducted mainly in men.[25] Additionally, sex-specific differences in blood oxygen saturation[26] are an important parameter for determining the differential effects of hypoxia in males and females. Thus, the purpose of the present study was to investigate the effect of short-term RSIT under different levels of moderate hypoxia (i.e. a stable protocol at FiO_2 0.155, and an incremental protocol at FiO_2 0.155–0.135) on CRF and metabolic health in young sedentary women. We hypothesized that the additional stress of hypoxia during RSIT would improve cardiometabolic outcomes, and a higher hypoxic level (i.e. FiO_2: 0.155–0.135), used to maintain the hypoxic stress, would result in more health benefits in comparison with exercise in lower hypoxic levels (i.e. FiO_2: 0.155) throughout the intervention.

2. Methods

2.1. Participants

Participants were publicly recruited through advertising in local media. The inclusion criteria were (1) neither residence at nor travel to altitudes above 1500 m during the past 6 months; (2) no hypoxic training experience and no participation in any regular exercise (less than 90 min of moderate-intensity exercise or 45 min of strenuous exercise per week); (3) general good health and absence of habitual smoking; (4) presence of regular and normal menstrual cycles between 28 and 34 days in length without severe premenstrual syndrome; and (5) absence of known cardiovascular and other associated diseases.

In total, 72 female volunteers (age: 21.9 ± 2.8 years; BMI: 23.0 ± 3.7 kg m^{-2}; $\dot{V}O_{2peak}$: 25.9 ± 4.5 mL $kg^{-1}\cdot min^{-1}$) were recruited. Ten participants were excluded due to consumption of medication for the common cold, irregular menstrual periods, history of exposure to altitude and excess physical activity. After the screening process, all participants provided the written informed consent and were randomized into one of the following: a normoxic RSIT group (N; n = 16), a RSIT group under stable hypoxia simulated at 2500 m (H_{2500}, FiO_2: 0.155; n = 15), a RSIT group under incremental hypoxia simulated at 2500–3400 m ($H_{2500\text{-}3400}$, FiO_2: 0.155–0.135; n = 15) and a non-exercising control group (C; n = 16). To reduce the influence of hormonal fluctuation on physical performance and blood markers, the pre- and post-tests were completed during each participant's individual follicular phase of the menstrual cycle. Participants who reported having a regular menstrual cycle were asked to recall their last two periods to calculate the length of their menstrual period and cycle. If the calculated menses date matched the actual menses onset, it was identified as a regular menstrual cycle. Pre- and post-test measurements were performed in the early follicular stage (3 days after the last day of menses).[27]

The study was approved by the Ethical Committee of the University of Macau for the Use of Human and Animal Subjects in Research and performed according to the Declaration of Helsinki. Before recruitment, a prior power analysis was performed by G*Power Version 3.1 for a repeated-measures ANOVA with four groups and two measures to determine the sample size. When the effect size was set at medium (partial $\eta^2 = 0.05$ or $f = 0.23$), and the correlation among the repeated measures and non-sphericity correction were kept at 0.5 and 1, respectively, a sample size of 14 participants in each group was needed to detect a significant difference in $\dot{V}O_{2peak}$ with a statistical power of 80% at an alpha level of 0.5. Similarly, a total sample size of 36 would be adequate to distinguish differences in training parameters in the three exercise intervention groups with four repeated measures a two-way repeated-measures ANOVA when $\alpha = 0.05$ and $1-\beta = 0.80$.

2.2. Experimental procedure

This was a randomized controlled trial with pre-test and post-test design, which included pre-intervention measurements, a 4-week training intervention and post-intervention measurements. The pre- and post-intervention measurements consisted of blood sampling, anthropometric assessments and a maximal incremental exercise test. All pre- and post-intervention measurements were taken within 3–5 days before and after the intervention, respectively.

2.3. Training protocol

Participants in the N, $H_{2500–3400}$ and H_{2500} groups were subjected to a supervised training intervention at the laboratory with controlled room temperature (22 °C) and humidity (50%–60%). Given that altering hypoxia and normoxia on alternate days may reduce the short-term adaptation to hypoxia and thus cause additional benefits in terms of body composition,[20] the training groups were planned 3 days per week (24 h apart) for 4 weeks within one

menstrual cycle. For each training session, two research assistants supervised the training process and recorded the training data. Participants in the training groups were blinded to their allocation, and the normoxic or hypoxic condition they were assigned to. Upon arriving at the laboratory, participants were fitted with a facemask connected to a modified gas mixing system (Everest Summit II Hypoxic Generator, New York, NY, USA). The normoxic or hypoxic gas mixtures were generated by this system and were delivered to participants through tubes and a breathing mask. In the N group, participants exercised under normoxic conditions at sea level (FiO_2: 0.209). In the H_{2500} group, participants exercised under stable hypoxic condition (FiO_2: 0.155, stimulating an altitude of approximately 2500 m). In the $H_{2500-3400}$ group, participants exercised under an incremental hypoxic condition, the FiO_2 was set at 0.155 initially (stimulating an altitude of approximately 2500 m) and was decreased by 0.005 every week until the FiO_2 dropped to 0.135 (corresponding to an altitude of 3400 m). The reasons for this gradually incremental hypoxic stress are that, FiO_2 0.155–0.135 is widely adopted in experimental and clinical applications,[27,28] whereas the more severe hypoxic level above might have a deteriorating effect on vascular[29] and metabolic function.[30] After resting 10 min under the corresponding condition, participants warmed up for 5 min and performed RSIT on a cycle ergometer (Monark 894 E, Sweden), which included 80 repetitions of 6 s maximal cycling exercise interspersed with 9 s recovery, followed by a 5-min cool-down at a free pedalling rate. The initial resistance was 1 kg in all training groups. After successfully completing two consecutive training sessions (i.e. the pedalling cadence of all sprint bouts was maintained above 100 revolutions per minute [rpm]), the resistance was increased by 0.5 kg until it reached a workload equivalent to 5% of each participant's individual body mass. Heart rate (HR) and SpO_2 before and after each sprint bout were measured using a pulse oximeter (Polar F4M BLK, Kemele, Finland). Participants could take off the mask after the completion of the cool-down phase.

2.4. Blood profiles

Blood samples were drawn during the early follicular phase of the menstrual cycle. Participants were instructed to refrain from strenuous exercise and caffeine for 48 h before blood sampling and arrived at the laboratory in the morning (7:30 a.m.) after 8 h of fasting. After the subject rested in a supine position for 30 min, 8-ml blood samples were taken from the antecubital vein. The blood samples were left to clot for 1 h and then centrifuged at 3000 rpm for 15 min. After centrifugation, the serum supernatants were aliquoted into 0.5-mL test tubes and stored at −80 °C for later analysis.

Fasting blood glucose, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein (LDL-C) were determined using human metabolic hormone kit on Luminex equipment (Luminex, HMHEMAG-34, KingMed Center for Clinical Laboratory Co. Ltd, Guangzhou, China).

2.5. Anthropometric assessments

After blood sampling, anthropometric measures including height (cm), body mass (kg) and body mass index (BMI, $kg \cdot m^{-2}$) were accessed. Standing height was measured using a wall-mounted stadiometer (with the participant barefoot) and recorded to the nearest 0.1 cm. Body mass was assessed using a bioelectrical impedance analyser (Tanita MC-180 MA, Tanita Corporation, Tokyo, Japan) in light clothing and recorded to the nearest 0.1 kg. BMI (in $kg \cdot m^{-2}$) was calculated by dividing weight (kg) by height squared (m^2).

2.6. Maximal incremental exercise test

Before and after the intervention, participants performed a maximal incremental exercise test on an electric-controlled cycle ergometer (Monark 839 E, Vansbro, Sweden) with gas analyser (Meta-Max 3B, Cortex Biophysik GmbH, Leipzig, Germany), where oxygen consumption (VO_2), carbon dioxide production (VCO_2), and expired minute volume (VE) were recorded continuously. After a 3-min warmup at 50 W, participants started cycling at an initial power output of 25 W, which increased by 15 W every 3 min; the pedalling rate was maintained at 60 ± 5 rpm. The test would be stopped if the participant reached the stage of exhaustion, assessed as meeting two or more of the following criteria: Borg 6–20 rating of perceived exertion (RPE) reached 18; HR reached an exhaustion on age-predicted maximal HR (220 − age); unable to maintain the pedalling rate of 60 rpm; the respiratory exchange ratio (RER) was larger than 1.0 or reached a plateau where the change in VO_2 was less than 150 mL min^{-1}.[31] $\dot{V}O_{2peak}$ was determined as the average of 15 s of the highest oxygen uptake values over the final stage,[17] and HR_{peak} was defined as the highest value attained during the test. Peak oxygen pulse (O_2P_{peak}, $ml \cdot beat^{-1}$) was calculated as the $\dot{V}O_{2peak}$ divided by the HR_{peak}.

2.7. Physical activity and dietary assessments

Participants were required to maintain their regular physical activity and dietary behaviour strictly throughout the training intervention. Daily physical activity was tracked for 6 weeks (i.e. one week before and after the intervention, and 4 weeks during the intervention) using a previously validated pedometer (Yamax Digi-Walker SW-200, Japan). To record their daily food and beverage intake, 3-day diet logs (two weekdays and one weekend day) were kept by all participants for 6 weeks using the Chinese Nutrition Action Plan (CNAP) surveys.[17,32] The nutrition analysis and management system (version 3.1) of the National Research Institute of Sports Medicine (NRISM) was used to measure macronutrient ratios and total energy intake.

2.8. Statistical analysis

Data analysis was conducted using the PASW software (Release 22.0; IBM, New York, USA). Before the main statistical analyses, Kolmogorov–Smirnov tests were conducted to confirm a normal distribution of all outcome variables. Levene's test was used to assess homogeneity of variance. A two-way ANOVA (time × condition) with repeated measures was used to examine the main effects (time) and interaction effects (time × group) on the outcome variables. Significant interaction effects were further analysed using the Tukey post hoc test. One-way ANOVA test was computed to detect the changes of training workload, duration, mean power output and percentage of maximal HR during the 4 intervention weeks. Regarding effect size (ES) measures of the main and interaction effects, partial η^2 was considered small if $\eta^2 < 0.01$ and large if $\eta^2 > 0.14$. Cohen's d values were also used to access the effect sizes for the difference between variables, which was considered small when d was between 0.20 and 0.49, medium when d was around 0.50–0.79 and large when $d > 0.80$.[33] All data were presented as mean ± standard deviation, and $p < 0.05$ was considered as significant statistical difference.

3. Results

3.1. Training data

During the intervention, the training workload was gradually

increased from week 1 to week 4 in all training groups. Specifically, the workload was increased from 1.1 ± 0.1 kg to 2.3 ± 0.8 kg in the N group ($p < 0.001$), from 1.1 ± 0.1 kg to 2.5 ± 0.8 kg in the H_{2500} group ($p < 0.001$), and from 1.0 ± 0.1 kg to 1.9 ± 0.7 kg in the $H_{2500-3400}$ group ($p < 0.001$, Table 1). Accordingly, mean power output was increased by 0.7 W kg^{-1}, 0.9 W kg^{-1}, and 0.6 W kg^{-1} in the N, H_{2500} and $H_{2500-3400}$ group, respectively ($p < 0.001$, Table 1). Participants were maintained at approximately 90% of the maximal HR (HR_{max} measured as the maximal values from HR_{peak} recorded at the maximal incremental exercise test before intervention or during training sessions) during the intervention without group differences ($p > 0.05$), but the $\%HR_{max}$ was the highest in week 1 compared with the following weeks in all groups. Similarly, training impulse (TRIMP) as the indicator of relative training intensity, was reduced in week 3 and week 4 than that of week 1 or week 2 in all training groups ($p < 0.001$, Table 1). No adverse events were reported during training in either group.

For the SpO_2 of the normoxia and hypoxia groups, the main effects of the time ($p < 0.001$, partial $\eta^2 = 0.402$), group ($p < 0.001$, partial $\eta^2 = 0.402$) and interaction ($p < 0.001$, partial $\eta^2 = 0.344$) effects were significant. During 4 weeks of training, SpO_2 remained constant in the normoxia group, while a significant reduction in SpO_2 occurred in the hypoxic groups ($p < 0.001$, Fig. 1). The reduction of the SpO_2 in the $H_{2500-3400}$ group was highest among all groups (N: −0.4%; H_{2500}: −2.5%; $H_{2500-3400}$: −4.5%), but a trivial effect ($d = 0.046$) was observed when comparing it to the H_{2500} group.

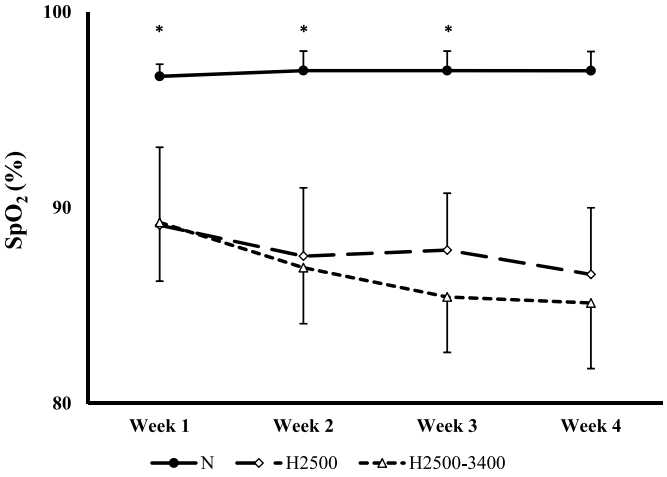

Fig. 1. Blood oxygen saturation (SpO_2) during the intervention Significantly different from N (H_{2500}/$H_{2500-3400}$ vs. N) at *$p < 0.01$.

3.2. Habitual physical activity and dietary profiles

There were no significant differences in daily physical activity among the four weeks (Table 2). The three macronutrient compositions in their diet were similar among the four groups, with 51% carbohydrate, 16% protein and 33% fat. Similarly, no significant differences were found in habitual caloric intake among the four groups or between any time points (Table 2).

3.3. Body composition and blood profiles

Participants' demographic characteristics and physiological outcomes before and after the intervention are provided in Table 3. After the 4-week intervention, there were no changes in body mass and BMI in any group. Moreover, all three training modes failed to trigger any changes in fasting glucose and blood lipids (i.e. TG, TC, HDL-C and LDL-C) ($p > 0.05$, Table 3).

Table 1
Training parameters during the intervention.

	N		H_{2500}		$H_{2500-3400}$		Time effect		Group effect		Time × group effect	
							p	partial η^2	p	partial η^2	p	partial η^2
Workload (kg)												
wk1	1.1	±0.1	1.1	±0.1	1.0	±0.1	<0.001	0.707	0.223	0.071	0.097	0.100
wk2	1.6	±0.3[a]	1.5	±0.3[a]	1.5	±0.3[a]						
wk3	2.0	±0.6 [ab]	2.0	±0.6 [ab]	1.8	±0.6 [ab]						
wk4	2.3	±0.8 [abc]	2.5	±0.8 [abc]	1.9	±0.7 [ab]						
Duration (min)												
wk1	16.7	±4.2	16.2	±4.7	14.9	±6.7	0.002	0.133	0.123	0.097	0.479	0.043
wk2	17.3	±3.9	17.7	±2.9	15.1	±4.6						
wk3	14.8	±4.2 [ab]	16.8	±4.3	12.1	±5.0[b]						
wk4	12.9	±5.0 [ab]	14.8	±5.0[b]	12.9	±4.9						
MPO (W•kg^{-1})												
wk1	1.9	±0.2	1.9	±0.2	2.0	±0.4	<0.001	0.367	0.866	0.007	0.760	0.017
wk2	2.3	±0.4 [ab]	2.4	±0.4 [ab]	2.2	±0.6						
wk3	2.5	±0.7 [ab]	2.6	±0.7 [ab]	2.6	±0.9 [ab]						
wk4	2.6	±1.0 [ab]	2.8	±0.8 [ab]	2.6	±1.0 [ab]						
% HR_{max}												
wk1	91.2	±3.6	90.7	±5.6	93.2	±4.1	<0.001	0.202	0.949	0.003	0.142	0.077
wk2	89.0	±3.7[a]	90.4	±3.9	89.4	±4.4[a]						
wk3	89.3	±4.5[a]	88.5	±5.5	89.4	±3.9[a]						
wk4	89.4	±3.9	88.1	±4.9 [ab]	87.7	±7.5[a]						
TRIMP (au)												
wk1	57.3	±16.6	53.6	±16.7	59.5	±18.7	<0.001	0.232	0.876	0.007	0.295	0.062
wk2	54.0	±9.6	56.2	±9.8	50.0	±16.1						
wk3	49.3	±12.1[a]	48.9	±13.5	40.9	±16.5[a]						
wk4	40.8	±12.3 [ab]	43.7	±11.7[b]	44.4	±18.3[a]						

Values are expressed as means ± standard deviation. MPO: mean power output relative to body weight, $\%HR_{max}$: percentage of maximal heart rate, TRIMP (au): training impulse (arbitrary unit), N: repeated sprint interval training in normoxia, H_{2500}: repeated sprint interval training in normobaric hypoxia simulated at 2500 m, $H_{2500-3400}$: repeated sprint interval training in normobaric hypoxia simulated at 2500–3400 m.
Significantly different from the corresponding [a] wk1, [b] wk2 and [c] wk3 values in the same group ($p < 0.05$).

Table 2
Habitual energy intake and physical activity before, during and after intervention.

	C		N		H_{2500}		$H_{2500-3400}$		Time effect		Group effect		Time × group effect	
									p	partial η^2	p	partial η^2	p	partial η^2
Energy intake (kcal•day^{-1})														
Pre	2118	±499	1837	±630	1928	±575	1661	±292	0.439	0.025	0.178	0.120	0.580	0.065
wk1	2164	±423	1497	±404	1719	±599	1764	±460						
wk2	2055	±516	1684	±403	1964	±609	1817	±517						
wk3	1877	±347	1837	±721	1810	±680	1698	±355						
wk4	2029	±771	1687	±209	1918	±750	1776	±490						
Post	2063	±518	1479	±599	1602	±631	1760	±559						
Physical activity (steps•day^{-1})														
Pre	7579	±4451	8770	±2628	8675	±2262	7779	±2750	0.577	0.019	0.845	0.020	0.305	0.082
wk1	9285	±3906	8813	±2663	8842	±2879	8230	±2262						
wk2	7882	±3070	9031	±3744	8011	±3317	7024	±1968						
wk3	8580	±2790	8802	±3753	7697	±1857	8685	±2806						
wk4	7707	±3394	8802	±3753	7764	±2793	8612	±2363						
Post	6168	±3266	8177	±2642	8113	±2344	9530	±3771						

Values are expressed as means ± standard deviation. C: control group, N: normoxic repeated sprint interval training, H_{2500}: hypoxic repeated sprint interval training at 2500 m, $H_{2500-3400}$: hypoxic repeated sprint interval training at 2500–3400 m.

Table 3
Changes in blood outcome measures before and after the intervention.

	C				N				H_{2500}				$H_{2500-3400}$				Group effect	
	Pre		Post		Pre		Post		Pre		Post		Pre		Post		p	η^2
Age (y)	22.2	±3.8			20.9	±2.6			21.9	±2.0			21.9	±2.2				
Height (cm)	162.6	±5.5			161.7	±4.6			162.4	±5.9			160.9	±4.8				
Weight (kg)	61.0	±7.1	60.8	±6.7	59.1	±8.3	59.4	±8.0	57.3	±7.5	57.2	±7.3	58.8	±11.5	59.0	±11.7	0.602	0.033
BMI (kg•m^{-2})	23.0	±2.3	23.0	±2.1	22.6	±3.1	22.7	±3.0	21.7	±2.4	21.7	±2.4	22.7	±4.2	22.8	±4.3	0.569	0.036
Glucose (mmol•L^{-1})	4.6	±0.4	4.5	±0.4	4.6	±0.2	4.6	±0.3	4.6	±0.3	4.6	±0.3	4.5	±0.3	4.7	±0.3	0.582	0.039
TC (mmol•L^{-1})	4.9	±1.0	5.0	±1.0	4.9	±1.0	4.4	±0.7	4.8	±0.9	4.6	±1.1	4.6	±0.7	4.8	±0.9	0.099	0.119
LDL-C (mmol•L^{-1})	2.9	±0.9	3.0	±0.9	2.9	±0.9	2.6	±0.6	2.9	±0.9	2.7	±0.9	2.9	±0.5	2.8	±0.9	0.486	0.048
HDL-C (mmol•L^{-1})	1.8	±0.3	1.8	±0.3	1.7	±0.4	1.6	±0.5	1.7	±0.6	1.8	±0.9	1.5	±0.3	1.7	±0.4	0.269	0.076
Triglyceride (mmol•L^{-1})	0.9	±0.3	0.8	±0.4	1.0	±0.4	1.0	±0.3	0.9	±0.3	0.9	±0.3	1.0	±0.4	1.2	±0.4	0.071	0.132

Observed values are expressed as means ± standard deviation. C: control group, N: normoxic repeated sprint interval training, H_{2500}: hypoxic repeated sprint interval training at 2500 m, $H_{2500-3400}$: hypoxic repeated sprint interval training at 2500–3400 m, BMI: body mass index, TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol.

3.4. CRF

CRF as reflected by $\dot{V}O_{2peak}$ was significantly increased ($p < 0.01$, Table 4) in the two hypoxic groups following 4 weeks of training. Although not statistically significant, there was a 3.6% increase in $\dot{V}O_{2peak}$ in the N group ($d = 0.21$) compared with the C group. After the intervention, the H_{2500} group showed an 8.2% increase in $\dot{V}O_{2peak}$ (from 1.6 ± 0.2 to 1.7 ± 0.3 L·min^{-1}, $d = 0.52$), while the increment in the $H_{2500-3400}$ group was 10.9% (from 1.5 ± 0.2 to 1.7 ± 0.2 L·min^{-1}, $d = 0.99$). The two hypoxic training groups had higher $\dot{V}O_{2peak}$ than the N group ($p < 0.05$). Group differences were found in $\dot{V}CO_{2peak}$, RER_{peak}, HR_{peak} and O_2P_{peak} were ($p < 0.001$) but not in RPE_{peak}, $\dot{V}E_{peak}$, $\dot{V}E_{peak}/\dot{V}O_{2peak}$ and $\dot{V}E_{peak}/\dot{V}CO_{2peak}$ during the maximal incremental exercise test. Participants in the C group had no change in $\dot{V}O_{2peak}$ and related parameters ($p > 0.05$).

4. Discussion

The main findings of this study were that both of the two hypoxia protocols (H_{2500} and $H_{2500-3400}$ group) were similarly effective at improving CRF compared with the no training controls in sedentary young women, while the normoxia protocol resulted in no significant increase in $\dot{V}O_{2peak}$ after 12 sessions of RSIT in 4 weeks. In terms of metabolic outcomes, no significant alterations were observed in body composition and blood lipids in all groups.

4.1. Effect on CRF

In the present study, $\dot{V}O_{2peak}$ and O_2P_{peak} did not change following 4 weeks of normoxic RSIT when compared with the no training controls. In our previous study, we observed significant CRF improvement using normoxic RSIT with a frequency of four times/week for 5 weeks.[17] With a reduced training frequency and shorter training duration (12 sessions for 4 weeks), the normoxic RSIT failed to show significant improvement in CRF, suggesting that the training dose of normoxic RSIT in the present study is insufficient to induce CRF improvement. In contrast, $\dot{V}O_{2peak}$ was increased by 8.2% in the H_{2500} group (FiO_2: 0.155) and 10.9% in the $H_{2500-3400}$ group (FiO_2: 0.155–0.135), despite having a similar ~13% increase in O_2P_{peak}. These findings provide further evidence for the additional beneficial effects of hypoxia on CRF, which could even compensate for the reduced training dose. The attainment of aerobic capacity under hypoxia is influenced by the mechanism of compensatory vasodilation that occurred during increased pulmonary ventilation.[18] Based on the absence of changes in CRF after normoxic RSIT and a significant improvement in CRF resulting from adding moderately hypoxic stimulus,[34] it is suggested that CRF improvement was initiated earlier under hypoxic conditions than under normoxia. These findings provide further evidence to support the notion that combining hypoxia with short-term RSIT exhibited additional beneficial effects on CRF in the sedentary population.

Table 4
Changes in maximal gas exchange data and related parameters before and after the intervention.

	C				N				H_{2500}				$H_{2500-3400}$				Group effect	
	Pre		Post		Pre		Post		Pre		Post		Pre		Post			
				Δ%	*d*			Δ%	*d*			Δ%	*d*			Δ%	*d*	*p*	η^2
VO_{2peak} (L•min^{-1})	1.6	±0.3	1.6	−1.0	0.06	1.5	±0.3	+3.6	0.21	1.6	±0.2	1.7	+8.3	0.52	1.5	±0.2	1.7	+11.9	0.99	0.027	0.153
VO_{2peak} (ml•min^{-1}•kg^{-1})	25.8	±3.9	25.8	±4.5	−0.1	0.01	25.5	±3.6	26.4	+3.6	0.27	27.8	±3.5	30.0	+8.2	0.68	26.4	±5.0	29.3	+10.9	0.63	0.009	0.189
VCO_{2peak} (L•min^{-1})	1.7	±0.3	1.7	±0.3	−5.3	0.28	1.9	±0.3	2.0	+4.7	0.29	2.1	±0.2	2.3	+6.5	0.53	2.0	±0.2	2.3	+12.4	1.20	<0.001	0.447
RER_{peak}	1.1	±0.2	1.3	±0.1	−6.5	0.42	1.3	±0.2	1.3	+3.8	0.29	1.2	±0.1	1.3	+6.5	0.61	1.2	±0.1	1.3	+11.7	1.06	<0.001	0.280
HR_{peak} (bpm)	176	±11	180	±9	+2.2	0.40	176	±12	170	−3.7	0.50	181	±10	173	−4.4	0.82	173	±12	173	−0.4	0.07	0.020	0.162
RPE_{peak}	18	±2	18	±2	+0.7	0.07	19	±2	19	+1.1	0.12	19	±1	19	−3.1	0.45	19	±1	19	+0.4	0.07	0.572	0.035
VE_{peak} (ml•min^{-1})	71	±14	64	±11	−9.8	0.55	61	±10	64	+3.8	0.20	66	±10	67	+2.7	0.18	62	±11	71	+13.4	0.70	0.101	0.106
VE_{peak}/VO_{2peak}	45	±9	41	±4	−10.7	0.69	39	±5	39	−0.6	0.05	40	±6	38	−4.7	0.34	39	±7	40	+2.9	0.16	0.693	0.026
VE_{peak}/VCO_{2peak}	41	±5	39	±5	−4.1	0.36	32	±3	31	−0.9	0.09	31	±3	30	−3.2	0.30	31	±4	31	+0.8	0.06	0.066	0.122
O_2P_{peak} (ml•beat^{-1})	8.9	±1.5	8.6	±1.2	−3.4	0.22	8.7	±1.3	9.2	+5.6	0.39	8.8	±1.2	9.9	±1.6[b]†	+13.4	0.83	8.8	±1.0	9.9	±1.5[b]†	+12.9	0.89	<0.001	0.257

Observed values are expressed as means ± standard deviation. C: control group, N: normoxic repeated sprint interval training, H_{2500}: hypoxic repeated sprint interval training at 2500 m, $H_{2500-3400}$: hypoxic repeated sprint interval training at 2500–3400 m, Δ%: change rate from pre to post-intervention, VO_{2peak}: peak oxygen uptake, VCO_{2peak}: peak carbon dioxide production, RER_{peak}: peak respiratory exchange ratio, HR_{peak}: peak heart rate, VE_{peak}: peak minute ventilation, RPE_{peak}: peak ratings of perceived exertion, O_2P_{peak}: peak oxygen pulse.Significantly different from pre-training at [a] $p < 0.05$, [b] $p < 0.01$. Significantly different from C at † $p < 0.05$. Significantly different from N at ‡$p < 0.05$.

The pattern of duration of exposure and levels of hypoxia differentiate mechanisms of respiratory and metabolic response.[35] Moderate hypoxia (>10% inspired O_2) with or without exercise appears to present a safe method to elicit beneficial effects with minimal detrimental effect.[36,37] However, mechanisms that maintain balance between efficacy and side effects are still unclear. To our surprise, we did not observe a significant difference between the two hypoxic groups. Both hypoxic groups had similar SpO_2, demonstrating that the hypoxic stress was comparable. Nevertheless, during the last training week, the mechanical workload during $H_{2500-3400}$ stimulus was lower compared with that during H_{2500} stimulus. This was possibly because of the reduced PO_2 in the hypoxic condition that made it more difficult for the $H_{2500-3400}$ group to complete the whole training session with the same intensity compared with the H_{2500} group; thus, they failed to progressively increase the workload. Although there was no significant difference, the large effect size (ES = 0.99) suggested that the cardiorespiratory strain in the $H_{2500-3400}$ group was greater so that the mechanical workload was compromised. It is possible that the mediation between the mechanical workload and cardiorespiratory strain affected the final outcomes. The insignificant cardiorespiratory outcome might be accounted for in part by difference between distinct levels of triggering stimulus in the two hypoxic groups. Therefore, it is emphasised that the hypoxic level plays a crucial role in physiological processes. Perhaps the slight difference indicates that a higher dose (i.e. either a longer duration or more stimulation from hypoxia) is necessary to impose a higher cardiorespiratory load, which could be responsible for the greater beneficial effects of a higher vs. a lower level of hypoxia.[1–3]

4.2. Effect on cardiometabolic risk factors (body mass and blood lipids)

In the current study, we found that hypoxic RSIT did not change BMI, body weight, triglycerides, TC, LDL-C, HDL-C and glucose levels in all groups. The potential reason for this observation regarding metabolic-related factors may be related to the characteristics of the study subjects. In view of short-term RSIT, body weight, BMI, body fat percentage and waist circumference was less pronounced in normal weight, non-obese and healthy individuals than in overweight individuals.[9,15] A population-based study reported that sedentary, normal weight subjects may have a lower metabolic impact on lipid profiles compared with overweight people.[15] Some evidence revealed that fat mass was decreased after 4 weeks RSIT under hypoxia compared with normoxic RSIT in obese women,[39] although others reported no difference.[17,40]

Training stimulus is another potent inducer of metabolic change.[41] It seemed that the hypoxic dose of the present training protocol was insufficient to evoke metabolic alterations such as body composition and blood lipid changes in the short term. More experimental hypoxic exercise protocols are required to provide additional evidence about the effectiveness of hypoxic variation as an extra stimulus. To illuminate the potential strategy for improving body composition, blood glucose and lipid profiles, it is worthy of future research at a range of FiO_2 0.12–0.15, which has been commonly used without negative physiological[13,27,28] and psychological effects.

Intermittent hypoxia alone or combined with exercise has been proposed as a valuable and viable strategy to improve health outcomes in different populations.[23] The present study demonstrated that RSIT, regardless of whether the training was performed in normoxia or hypoxia, had an exceptional completion rate with no adverse events, suggesting that this protocol is a well-tolerated exercise option for sedentary young women. Our results were further supported by the previous findings that exercise

incorporating short-term intermittent hypoxia ameliorated exercise tolerance by improving stress resistance and oxygen delivery in obese individuals,[11] and elderly men with and without coronary artery disease.[10] Nevertheless, hypoxic RSIT are warranted to further confirm the application in clinical cohorts.

4.3. Strengths and limitations

There are several strengths of our study. First and foremost, the experiment was performed at the same point in the menstrual cycle in all participants to exclude the potential impact of the menstrual cycle on physical performance and blood markers. Moreover, hormonal differences are potentially involved in physiological responses to hypoxic exercise; therefore the menstrual cycle and gender difference should be taken into consideration in future studies. Another strength was that habitual physical activity and diet were controlled throughout the study period. Moreover, our study was strengthened by the randomized control trial design, which was commonly neglected in previous research.[17,19,42–44] There are a few limitations that should be considered. The 20 min, relatively high-volume RSIT regimen used in this study might be too long and intense to sustain, resulting in diminished working outputs for the subjects.[45] Future studies could adopt modified low-volume RSIT protocols covered in several minutes (e.g. $\leq$ 10 s all out exercise) to achieve more favourable health outcomes.[34] In addition, the hypoxic response varied from person to person, related to the hypoxic ventilatory response.[46] To offer less SpO_2 variation among individuals, future research may consider using fixed SpO_2 instead of fixed FiO_2.[47,48] For instance, FiO_2 can be individually titrated based on the oxygenation response to maintain a target SpO_2. We did not measure haematological parameters (i.e. haemoglobin and haematocrit) in the present study. These biochemical biomarkers need to be examined to facilitate understanding of cardiorespiratory adaptation following different exercise modalities. Finally, considering that studies of hypoxic RSIT longer than 12 weeks significantly improved body composition and metabolic risk factors.[9,49,50] further studies could extend the intervention duration, and involve varied hypoxic stimulus to avoid weakening hypoxic effects.[38]

5. Conclusion

The present study indicates that combining hypoxia with RSIT can enhance the improvement of CRF compared with normoxic RSIT alone in a sedentary population. Nevertheless, compared with RSIT under stable hypoxia (FiO_2 0.155), gradually incremental hypoxia stress (FiO_2 0.155–0.135) in the short term does not have an additive effect on facilitating CRF.

Authors statement

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All authors read and approved the final version of the manuscript.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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