Sleep Breath (2014) 18:591–597
DOI 10.1007/s11325-013-0922-4

ORIGINAL ARTICLE

Normobaric hypoxia training causes more weight loss than normoxia training after a 4-week residential camp for obese young adults

Zhaowei Kong · Yanpeng Zang · Yang Hu

Received: 10 September 2013 / Revised: 19 November 2013 / Accepted: 27 November 2013 / Published online: 8 December 2013

Abstract
Background Intermittent normobaric hypoxia training, an alternative to altitude training for athletes, may be beneficial to treat overweight and obesity. The purpose of this study is to investigate whether normobaric hypoxia training combined with low-caloric diet has the additive effect on weight loss compared with normoxia training in obese young adults.
Methods Twenty-two subjects (age 17–25 years, body mass index >27.5 kg/m^2) were recruited for a 4-week residential camp of weight loss with low caloric intake, and trained at 60–70 % maximal heart rate of aerobics and 40–50 % of maximal strength of training. They were randomly assigned to either a normobaric hypoxia (HT, FiO_2=16.4–14.5 %) or normoxia training group (NT, FiO_2=21 %), and subjects in HT and NT groups experienced weekly 16-h normoxia and 6-h hypoxia or 22-h normoxia training, respectively. Body composition, resting blood pressure (BP) and brachial-ankle pulse wave velocity (*ba*PWV) were determined before and after the intervention.
Results Weight loss was found in HT (−6.9 kg or −7.0 %, $p<0.01$) and NT groups (−4.3 kg or −4.2 %, $p<0.01$) significantly, and the former lost more weight than the latter ($p<0.01$). Hypoxia training improved systolic BP (−7.6 %) and mean BP (−7.1 %) significantly ($p<0.05$) despite having no effect on *ba*PWV.
Conclusion Four weeks of normobaric hypoxia residential training with low caloric diet has an additive improvement on weight loss. It seems that normobaric hypoxia training might be a promising method to treat obesity.

Keywords Residential camp · Hypoxia training · Normoxia training · Obesity · Weight loss

This article was presented at the 6th Asia-Pacific Conference on Exercise and Sports Science (APCESS 2013), Taipei, Taiwan, November 1–5, 2013.

Z. Kong (✉) · Y. Zang
Faculty of Education, University of Macau, Avenida Padre Tomas Pereira, Taipa, Macao, China
e-mail: zwkong@umac.mo

Y. Hu
Sports Science Research Center, Beijing Sport University, Beijing, China

Introduction

Obesity, one of the most significant public health problems today, is associated with alterations in arterial function including high blood pressure (BP) and arterial stiffness [1, 2]. Weight reduction improves hemodynamic function [3] and vascular stiffness for obese subjects [1]. Young adulthood (18–25 years old), which is characterised by life course changes associated with decreases in physical activity and increases in sedentary behaviours [4], is a risky stage of overweight and obesity.

Losing weight during or after acute high altitude has been reported [2, 5]. However, in the real world, a sojourn at high altitude to lose weight is not only a difficult task but also risks predisposition to acute mountain sickness for obese individuals [2]. With the recent discovery of the potential benefits of intermittent hypoxia exposure on weight loss in obese persons [6, 7], hypoxia training, equivalent to mild altitude, is likely to be an effective means to treat obesity.

It is well known that regular moderate exercise in conjunction with dietary restriction is the most recommended way to reduce weight [8]. However, the common flaw of studies involving normal weight [9, 10] or obese subjects [5–7] undergoing weight loss induced by hypoxia exposure, is that they lack a diet control or only give advice to maintain the current dietary behaviours. The novel method regarding hypoxia exposure or hypoxia training for treating obese needs more supporting evidence.

Interestingly, a residential camp consisting of diet, exercise and lectures is an alternative weight loss pattern for obese children and adolescents [11]. It is worth mentioning that this more controlled intervention ranging from 2 to 8 weeks could reduce body weight by 4.6–13.5 kg, which seems more effective than less controlled programmes [12]. More importantly, as regards adults, one study shows that weight reduction and significant improvements in BP resulting from a 4-week residential programme have been successfully maintained for a fairly long time [13].

To clarify the effectiveness of hypoxia training with exercise and hypocaloric control in obese subjects, we conducted a weight-loss residential training camp for 4 weeks to evaluate the changes of body composition and hemodynamics in a normobaric hypoxia centre, where oxygen levels, food intake and physical activity can be controlled thoroughly. It is hypothesised that both hypoxia and normoxia training can lead to effective weight loss, and hypoxia training has an additive effect on weight loss and hemodynamics when compared with normoxia training in obese young subjects.

Method

Participants

Volunteers were publicly recruited online to participate in the present study, which was approved by the Committee of University Researcher Ethics. Subjects were excluded if they met any one of the following items: older than 30 years, high altitude residents (>1,000 m), previous hypoxia experiences, any barriers to physical activity, smokers, taking medicines to control body weight or to treat metabolic syndromes, involved in sports or structured exercise during the previous 6 months and body mass index (BMI) less than 27.5 kg/m^2 [14].

After a personal interview to ensure adherence to camp requirements and a physical examination to confirm they qualified to do quite heavy exercises, ten males and 12 females of Han ethnicity aged 17 to 25 years were included. The juvenile and her guardian, and 21 adults provided their written informed consent to participate in this study. Subjects were randomly assigned to either hypoxia training (HT) or nomoxia training (NT) group. One female in HT and three females in NT quit midway through the intervention due to personal reasons.

Experimental design

Undertaken in a totally closed residential camp, the accommodation, diet and training were uniformly managed during the 4-week intervention period. Two life assistants accompanied the two groups respectively during the whole course of weight loss, and they all lived in the same building, where the campers could not move in and out freely. Caloric intake was restricted to the energy intake of individual's desirable weight (DW) and a commercial company provided the food supervised by a registered professional dietitian.

Based on the information of hypoxia exposure time in previous studies [6, 7], and the fact that transforming hypoxia and normoxia in alternate days may eliminate the short-term adaptation to hypoxia and thus cause weight loss [15], HT was scheduled on every other day of the week. For pragmatic reasons, 1 week was divided into fourteen 2-h sessions, and two qualified physical fitness instructors jointly supervised the training schemes. With the same training requirements (mode, intensity, time and frequency), both groups had eight sessions of aerobic exercise including running, stepping, cycling and dumbbell exercises, as well as three sessions of strength training. The energy consumption of physical activity was expected to be no less than 4,000 kcal per week. Moreover, three sessions of non-physical activity were scheduled as healthy lifestyle workshop, as well as group visit and shopping led by the assistants every week. All measurements were conducted at the same time of day by the same investigators before and after the intervention. To avoid any unexpected dangers, a doctor was available on-site during the study.

Diet control

Individual target energy intake was calculated as a sedentary adult at 22.5 kcal/kg multiples DW per day [16], whereas DW (kg) was counted as height (cm)−105. In short, the daily caloric intake deficits were 637±333 (270–1,150) kcal in the HT group and 691±330 (270–1,320) kcal in the NT group ($p > 0.05$). The diet consisted of balanced proportions of 60 % carbohydrates, 25 % fat and 15 % protein, and calories were distributed as 30 %, 40 %, and 30 % at breakfast, lunch and dinner, respectively. The dietitian prepared and supervised every individual's meal including fruits. During the study, the menu was changed weekly, and the diet was adjusted each week according to an individual's new weight. All meals were served in the dining hall and supervised by the two life assistants, who would prevent any food from being shared. Opportunities to obtain food outside the training camp were extremely low because of the military-style management.

Training protocol

The aerobic exercise intensity was mostly set at 60–70 % of the subjects' maximum heart rate (HRmax), which was calculated with the formula of 220−age (years). After measuring maximal strength (one repetition maximum [1RM]) in each movement, strength training was implemented at 40–50 % maximal strength for four to six motions, three sets of 15–20 RM with 2–3 min of rest between sets (Table 1). Consistent with 11 sessions of normoxia training (22 h) in NT group per week, subjects in HT group had eight sessions of normoxia

Table 1 Training protocol

Physical activities	Normoxia (h/week)	Hypoxia/normoxia	
		(h/week)	Intensity
Running	4	2	60–70 % HR_{max}; velocity <8 km/h
Cycling	0	1	50–70 % HR_{max}
Stepping	5	1	50–70 % HR_{max}
Dumbbell exercise	3	0	4–6 motions, 3 sets, 10–15 reps with light weight (<5 lb)
Strength training	4	2	40–50 % maximal strength for 4–6 motions, 3sets, 15–20 reps

(16 h) and three times of HT (6 h). With the adaptation to hypoxia, the oxygen concentrations in the HT room (Low Oxygen, Germany) were gradually reduced from 16.4 % (2,000 m) to 14.5 % (3,000 m). In every aerobic training session, a heart rate monitor was used for controlling the exercise intensities, and a pulse oximeter (Nonin Model 9560, USA) measured arterial hemoglobin oxygen saturation (SaO_2). During HT, a real-time monitoring system was used to supervise the oxygen concentration of the hypoxia room and the values of SaO_2 in HT group were kept at 90–92 %.

Body composition and hemodynamics

Body composition and hemodynamic function were measured at a fasting state on two mornings before and 24 h after the last training session of the 4-week of weight loss training camp. Height and weight were determined with light clothing and no footwear in a standardised way and BMI was estimated by weight (kilogram) and square height (metre). Body composition was assessed by a 5-serial of frequent bioimpedance analysis device (Biospace In body 3.0, South Korea). Waist/hip ratio (WHR) was measured using a 3D body scanner (Anthroscan 3D VITUS, Human-solutions, Germany). After at least 10 min of sitting rest, heart rate (HR), BP in the non-dominant arm (BP), brachial-ankle pulse wave velocity (*ba*PWV) and ankle brachial index (ABI) were tested in a supine position by an experienced researcher using a noninvasive automatic waveform measurement system (Colin VP-1000, Komaki, Japan), the same device and method described in previous studies [17, 18]. Mean arterial blood pressure (MBP) was calculated as 1/3 × systolic BP (SBP)+2/3 × diastolic BP (DBP).

Statistics

Data analyses were performed using PASW software (Release 18.0; IBM, New York, USA). All data were firstly analyzed by parametric statistics following confirmation of a normal distribution by the Kolmogorov–Smirnov test. Independent-samples t-test was used to compare the pre-values in these two groups. A two-way repeated measures analysis of variance (group×time) was used to test differences in pre- and post-variables. Following a simple main effect of the within group, paired-samples t-test was applied to compare the pre-and-post difference. One-way ANCOVA (pre-value as covariate) was performed to determine any significance with the factor of group when intervention effect is significant. The Pearson's correlation coefficients were calculated to examine the associations between changes in body composition parameters and changes in BP and arterial stiffness. A p value of <0.05 was accepted as significant. η^2 as an effect size is considered small if $\eta^2<0.06$ and large if $\eta^2>0.14$ [19].

Results

Training data

Total running distance in HT tended to be greater than that in NT ($p=0.064$; Table 2).

Body composition, blood pressure and arterial stiffness

Weight loss decreased in both groups ($p< 0.01$), and the decrement was significantly larger in HT (−6.9 kg or −7.0 %) than that in NT group (−4.3 kg or −4.2 %) ($p< 0.01$, $\eta^2=0.53$). The reduction of fat mass in HT (−6.9 kg or −18.2 %) tended to be significant when compared with NT (−3.9 kg or −10.6 %; $p= 0.08$, $\eta^2=0.18$), and so was

Table 2 Running intensity and amount

	HT	NT
Relative running intensity (% HRmax)	60–70	60–70
Running speed and grade in normoxia	5.5–7.0 km/h, 0–2 % grade	5.5–7.0 km/h, 0–2 % grade
Running speed and grade in hypoxia	6.0–7.5 km/h, 0–4 % grade	
Running distance in hypoxia (km)	33±2	
Running distance in normoxia (km)	88±24	101±17
Total running distance (km)[#]	120±21	101±17

[#] $p=0.064$

Table 3 Changes in body composition at pre and post 4-week weight loss intervention

Variable	HT (n=10, 5M5F)			NT (n=8, 5M3F)			Within group			Interaction group		
	Pre	Post	ΔHT	Pre	Post	ΔNT	F	p	Partial η^2	F	p	Partial η^2
Age (y)	19.8 ±2.2[b]*			22.3±1.7								
Weight (kg)	99.0±19.5	92.0±17.9	−6.9±1.9[a]**[b]**	103.4±24.7	99.1±24.2	−4.3±1.5[a]**	186.98	0.00	0.92	9.96	0.01	0.38
FM (kg)	38.0±11.7	31.1±12.0	−6.9±4.3[a]**[b]#	36.7±9.3	32.8±8.0	−3.9±1.8[a]**	44.01	0.00	0.73	3.94	0.08	0.18
MM (kg)	57.1±12.1	57.1±10.9	0.0±4.4	62.6±16.0	62.2±16.4	−0.4±1.3	0.04	0.84	0.00	0.04	0.84	0.00
Water (kg)	44.7±9.4	44.8±8.6	0.1±3.4	49.0±12.6	48.8±13.0	−0.2±1.0	0.00	0.96	0.00	0.51	0.83	0.00
BMC (kg)	3.8±0.7	3.8±0.6	0.0±0.3	4.2 ±0.9	4.1 ±0.9	−0.0±0.1	0.03	0.87	0.00	0.09	0.73	0.00
BMI (kg/m^2)	34.7±5.3	32.1±4.8	−2.5±0.7[a]**[b]#	33.8 ±5.6	33.6 ±4.6	−0.3±3.7	5.63	0.03	0.26	3.79	0.07	0.19
WHR	1.00±0.09	0.94±0.09	−0.06±0.03[a]**[b]#	1.00 ±0.07	0.97 ±0.07	−0.03±0.01[a]**	69.69	0.00	0.81	4.00	0.06	0.20

All values are means±standard deviation

HT normobaric hypoxia training, *NT* normoxia training, *ΔHT* change from pre-intervention in HT, *ΔNT* change from pre-intervention in NT, *FM* fat mass, *MM* muscle mass, *BMC* bone mineral capacity, *BMI* body mass index, *WHR* waist/hip ratio

[a] Comparison with pre-intervention

[b] Comparison with normoxia

*p< 0.05, **p <0.01, [#] p< 0.10

the reduction of BMI (−7.3 % in HT and −0.7 % in NT' p= 0.06, η^2=0.21) and WHR (−6.0 % in HT and −3.1 % in NT; p=0.06, η^2=0.22). No significant changes were found in body water content and muscle mass (Table 3).

There were no significant differences in BP and arterial stiffness between groups; however, resting heart rate significantly decreased in NT (−16.9 %, p< 0.05), and had a trend to decrease in HT (−16.1 %, p=0.054). SBP declined by 7.6 % (p< 0.05) in HT and increased by 0.2 % in NT, while DBP declined by 6.0 % (p=0.10) in HT and 0.7 % in NT. MBP declined by 7.1 % (p< 0.05) in HT and 1.4 % in NT (Table 4). The *ba*PWV values in HT and HT were similar (Fig. 1). ABI tended to be augmented in subjects with normoxia (−6.9 %, p= 0.085) compared with intermittent HT subjects (−4.0 %, p> 0.05) (Fig. 2).

Correlations between changes in body composition and changes in BP and arterial stiffness

The changes in body composition parameters were not significantly related to the changes in BP (p> 0.05). A negative association between the BMI changes and the changes in *ba*PWV was observed (r=−0.64, p< 0.01) and the changes in MM correlated with the ABI changes (r= 0.67, p<0.01) (Table 5).

Table 4 Hemodynamic changes at pre and post 4-week weight loss residential training camp

Variable	HT (n=9, 5M4F)			NT (n=8, 5M3F)			Within group			Intervention group		
	Pre	Post	ΔHT	Pre	Post	ΔNT	F	p	Partial η^2	F	p	Partial η^2
HR (beats/min)	74±10	61±16	−12±16 [a]#	79±19	63±6	−16±18[a]*	11.35	0.00	0.43	0.46	0.51	0.03
SBP (mmHg)	131±12	121±11	−10±12 [a]*	127±29	123±16	−3±21	2.87	0.11	0.16	0.03	0.86	0.00
DBP (mmHg)	70±6	65±8	−4±7	67±12	66±8	−1±9	2.21	0.16	0.13	0.04	0.85	0.00
MBP (mmHg)	90±7	84±9	−6±8 [a]#	87±17	85±10	−2±13	2.66	0.12	0.15	0.04	0.85	0.00

All values are means±standard deviation

HT normobaric hypoxia training, *NT* normoxia training, *ΔHT* change from pre-intervention in HT, *ΔNT* change from pre-intervention in NT, *HR* heat rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MBP* mean blood pressure

[a] Comparison with pre-intervention

*p< 0.05, [#] p< 0.10

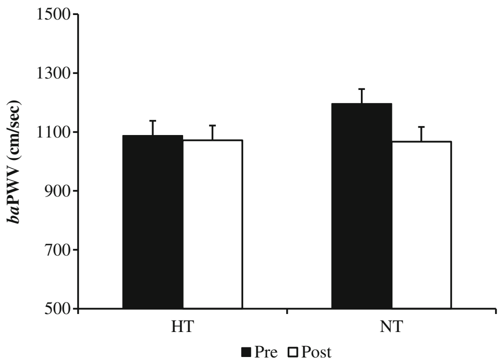

Fig. 1 Changes in brachial-ankle pulse wave velocity (*baPWV*) at pre- and post-training. *HT* normobaric hypoxia training, *NT* normoxia training

Table 5 Correlations between changes in body composition and blood pressure and arterial stiffness

	ΔSBP	ΔDBP	ΔMBP	Δ*ba*PWV	ΔABI
ΔWeight	0.19	0.05	0.13	−0.38	0.03
ΔFM	0.44	0.34	0.40	−0.26	−0.43
ΔMM	− 0.32	− 0.39	− 0.36	−0.23	0.67**
ΔBMI	0.05	−0. 11	− 0.03	−0.64**	− 0.34
ΔWHR	0.41	0.23	0.33	−0.32	−0.35

Δ represents a change between post-intervention and pre-intervention. *FM* fat mass, *MM* muscle mass, *BMI* body mass index, *WHR* waist/hip ratio, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MBP* mean blood pressure, *baPWV* brachial-ankle pulse wave velocity, *ABI* ankle brachial index

**$p<0.01$

Discussion

It is a big challenge to maintain the required caloric intake and expenditure strictly for an intervention programme in free-living subjects, who may exhibit such behaviours as reduction in habitual daily activities and enhancement in food intake to compensate for the extra energy deficits [20]. In order to avoid the subjective assertion to interpret weight change, a 4-week weight loss residential training camp was carefully conducted to observe the difference between normobaric intermittent hypoxic training and normoxic training. To our knowledge, this is the first study to evaluate the effect of weight loss following exercise training in intermittent hypoxia combined with well-controlled calorie intake for every meal in obese subjects.

The present study shows that 4 weeks of intensive exercise under normobaric intermittent hypoxia or normoxia with calorie diet restriction leads to significant improvement in body weight, BMI, WHR and FM as well as a trend to ameliorate SBP and MBP, whereas there is no significant change in vascular stiffness expressed as *ba*PWV and ABI in young obese individuals. Further, HT also improves effect in BW, BMI, WHR, FM and, potentially, in SBP, when compared with normoxia. Despite consistency with the previous findings [6, 7], our study reveals a statistically additive weight loss (2.7 %) rather than a trend to lose more weight (1.3–1.8 %) induced by HT in obese subjects. Nevertheless, the similar rate of weight loss (1.5 % or 1.6 kg) after only a 1-week stay at 2,650 m [5] illustrates that previous studies most likely underestimate the weight-loss influence of HT because of uncontrolled diet and extra physical activity. The mechanisms of hypoxia exposure resulting in an additional improvement in body composition might be more energy expenditure [5], appetite suppression because of continuous adaptation to the environment [21] and responses of neuroendocrine factors relevant to energy balance [2].

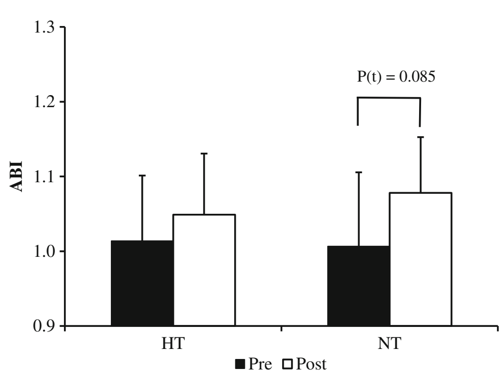

Fig. 2 Changes in ankle brachial index (*ABI*) at pre- and post-training. $p<0.10$ vs. pre-training. *HT* normobaric hypoxia training, *NT* normoxia training

On the other hand, the present study shows that hypoxia and exercise exhibits a trend of synergistic effect in ameliorating BP. Although most studies reveal that short-term weight loss improves BP [3], some studies also report no changes of BP following weight loss [7, 9]. In this study, only significant decreases in SBP and MBP were found in hypoxia after the intervention. The changes in FM could explain 19.4 %, 11.6 % and 16.0 % of the reductions in SDB, DBP and MBP, respectively, although no significant relationship was found. The decreased arterial BP may be attributed to hypoxia inducing the increase of arteriole diameter and then producing peripheral vasodilatation [21] and decreased peripheral resistance in the systemic circulation [22].

PWV is a non-invasive indicator of arterial stiffness and is also an independent marker for cardiovascular disease [23], and a low ABI indicates high risks of cardiovascular and cerebrovascular accidents [17]. The observations with respect to different oxygen levels having no effect on *ba*PWV and normoxia tending to increase ABI, imply that arterial stiffness is mostly independent of the improvements in weight loss and BP. This issue differs from some published studies in which weight loss improves vascular stiffness by diet control [24] or aerobic exercises [25]; however, it is partially in agreement with some recent studies: strength training increases arterial stiffness without the changes of adipose tissue in young adults due to increased sympathetic activities [18]. It suggests that aerobic combined with strength exercise and aerobic exercises alone have different influences on vascular stiffness [18].

Given the strict diet control, the same requirements of training conditions, exercise encouragements and daily life routines in the present study, it is reasonable to conclude that the group differences in body composition and hemodynamics are most likely the effects of hypoxia or hypoxia-induced changes. Surprisingly, according to our observation, the hypoxia subjects completed better training quality than the subjects in normoxia. The former tended to accomplish a longer distance than the latter. Similar to the results obtained in athletes [26] and even in healthy subjects [10], we speculate that intermittent HT could improve exercise performance and then make for an additively physiological effect. Nevertheless, because of the un-blinded design, we could not exclude whether between-group differences in weight loss may result from a placebo effect of hypoxia. It is evident that HT paradigms involved in different types (sustained or intermittent), severity (mild or severe) and duration (exposure time per day and number of exposure days) are critical in determining whether intermittent hypoxia is beneficial or harmful to the subjects [22]. Our findings along with 90–92 % of arterial oxygen saturation are, at least partially, supported by the study of Bailey et al. [9], which shows no adverse effect of power output during HT even if the arterial hypoxemia decreases to 88 % SaO_2.

Additionally, chronic intermittent hypoxia may lead to persistent sympathetic activation and to hypertension [27], and hence the use of hypoxia exposure in obese individuals should be undertaken with caution. However, the lack of significant elevations in resting HR and BP after 4 weeks of hypoxia exposure in HT group shows that the present intermittent hypoxia paradigm, three times of a 2-h mild hypoxia simulated at 2,000–3,000 m, does not lead to remarkably deleterious effect in systemic hemodynamics and even arterials stiffness, despite possibly sympathetic nerve activity being activated by intermittent hypoxia [28].

There are several limitations in this study. Firstly, the sample size was small. Given the strength in experimental design, the military-style camp and strict management for 4 weeks of obese adults, we recruited limited qualified volunteers. Nevertheless, the partial statistical power for weight, fat mass, BMI and WHR is 0.533, 0.211, 0.216, and 0.390, respectively, which represent large effect sizes [19]. Therefore, the weight-loss difference between hypoxia and normoxia is true but not a type II error. Secondly, gender difference in weight loss was not compared. The aim of this study was not mainly gender difference of weight loss, especially regarding the small sample size. Thirdly, the psychological effect of hypoxia on weight loss should be considered in future studies. Finally, this study does not fully quantify all the components in the multi-component model involving nutrition status, hypoxia exposure, physical activities and daily activities, though we tried to manage as much as we can. It is very difficult for the subjects to accept only running and/or cycling as the exercise intervention, in order to estimate the amounts of exercise in a residential camp for several weeks. Further investigations, if possible, could strictly control all model components and it would be helpful to identify the contribution rate of each factor of weight loss in a relatively longer intervention period.

In conclusion, the present study shows that intermittent HT causes significant weight loss and possibly improves BP when compared with normoxia training in obese young individuals. Hypoxia could have a considerable role in multiple-component interventions including diet and physical activity of weight management in treating overweight and obesity and their related disorders. Further, the conclusion is strengthened by the fact that we used residential camp for caloric intake restriction and physical activity control to assess the effect of hypoxia.

Acknowledgements The study was supported by a research grant from the University of Macau (MYRG027(Y1-L1)-FED11-KZW).

Conflict of interest The authors declare that they have no conflict of interest.

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