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**Original Article**

# Normobaric Intermittent Hypoxia over 8 Months Does Not Reduce Body Weight and Metabolic Risk Factors – a Randomized, Single Blind, Placebo-Controlled Study in Normobaric Hypoxia and Normobaric Sham Hypoxia

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## Key Words

Hypoxia · Weight loss · Physical exercise · Obese · Overweight

## Abstract

**Objective:** Both a 1- to 4-week continuous or intermittent stay and moderate exercise in hypoxia versus normoxia can lead to weight loss. We examined the reproducibility and durability of added hypoxic exposure in a feasible health program of several months. **Methods:** 32 obese persons, randomly assigned to either a hypoxia (age  $50.3 \pm 10.3$  years, BMI  $37.9 \pm 8.1$  kg/m<sup>2</sup>) or a normoxia (age  $52.4 \pm 7.9$  years, BMI  $36.3 \pm 4.0$  kg/m<sup>2</sup>) group, completed 52 exercise sessions within 8 months. Participants exercised for 90 min (65–70% HR<sub>peak</sub>) either at a simulated altitude of 3,500 m or in normoxia, and rested for further 90 min at 4,500 m or normoxia. Before, after 5 weeks, after 3 months, and after the intervention, body composition and exercise capacity were determined. Risk markers (e.g., blood pressure, cholesterol) were measured before, after 3 months, and after the intervention period. **Results:** Body weight, BMI, waist and hip circumference, P<sub>peak</sub> and BP<sub>sys</sub> improved over time ( $p < 0.05$ ) but without group difference. Fat mass reductions correlated with HDL changes ( $r = -0.427$ ;  $p < 0.05$ ) in the entire group. **Conclusion:** Long-term, moderate intensity exercise and rest in hypoxia

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does not lead to higher reductions in body weight than normoxia alone. Therefore, for weight loss and metabolic markers hypoxic exposure does not add effects at least when stimuli (i.e., hypoxia dose, exercise intensity/duration) are unaltered throughout the intervention.

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## Introduction

Overweight and obese individuals have an increased risk of cardiovascular disease, diabetes, and other major diseases [1–5]. Weight management is an important measure in public health because even small reductions in body weight (i.e., 5–7%) have been demonstrated to significantly decrease obesity-related comorbidities [5, 6]. Successful weight and body fat reduction requires sustained lifestyle modifications including restricted caloric intake and physical activity [3, 5, 7]. When considering the latter, the health benefits of increasing physical activity are well established [8–11]. However, in order to promote weight loss large exercise volumes, ranging from 150 to 400 min/week with energy equivalents of 1,200 to >2,000 kcal/week, are necessary [3, 5].

In an attempt to further increase weight loss, some studies [12–15] combined normobaric or hypobaric hypoxia, which appear to increase metabolic rate and leptin levels [15], with a regimen of intermittent exercise for 60–90 min three times a week [12–14] or a continuous stay for 1 week [15]. Results of these studies revealed that after a 3- to 4-week exercise period performed at the same relative intensity [12–14] or one continuous week at rest [15], body fat content decreased more under hypoxia conditions when compared to normoxia conditions [13, 14]. Furthermore, also metabolic risk markers (e.g., triglycerides, HOMA index, and fasting insulin) improved to a greater extent under hypoxia [13]. However, whether or not the durability of these health benefits persist beyond a few weeks is not known. In order to be feasible (feasibility defined as compatible with the work and family life schedule and financing by public health care), a weight and fat loss program with moderate exercise in hypoxia should not only be more effective when compared to exercise in normoxia, but also should persist in the long term [16].

The aim of the present study was i) to investigate if hypoxia exposure combined with moderate intensity exercise over a 8-month period in obese people ( $BMI > 30 \text{ kg/m}^2$ ) is more effective in reducing body weight and body fat when compared to exercising and resting in normoxia and ii) to investigate the long-term effects of such a feasible hypoxia health prevention program on metabolic risk markers.

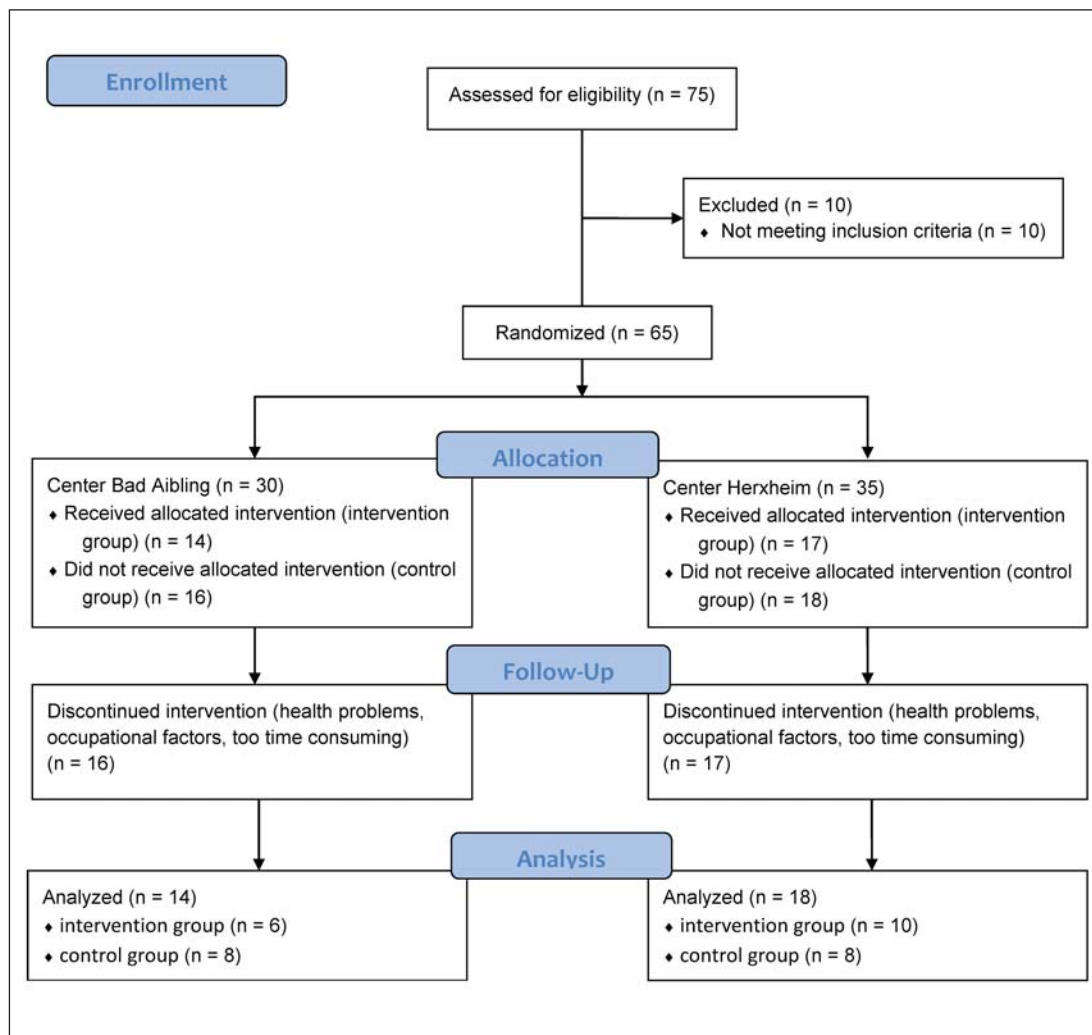
We hypothesized that in the long term, hypoxia exposure combined with moderate intensity exercise is more effective in reducing body weight and body fat mass as well as metabolic risk than resting and exercising in normoxia.

## Participants and Methods

### Participants

Participants were recruited through a call in different local media and by means of notices at the two rehabilitation centers where the study was performed (Bad Aibling and Herxheim, Germany). Inclusion criteria for the study were  $BMI > 30 \text{ kg/m}^2$  and the capability to complete moderate intensity exercise (e.g., adequate exercise capacity, absence of orthopedic problems). Exclusion criteria were: New York Heart Association (NYHA) class  $> 3$ , myocardial infarction or stroke within 6 months before the start of the study, instable angina pectoris, malignant hypertension, chronic kidney disease, pregnancy, and an oxygen saturation  $< 70\%$  during 90 min at an simulated altitude of 4,500 m (pre-tested in a normobaric hypoxic chamber).

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**Fig. 1.** Flow chart of the participants throughout the study.

30 persons (21 females and 9 males) in Bad Aibling and 35 persons (19 females and 16 males) in Herxheim followed the call and were eligible for participation according to the inclusion and exclusion criteria. All participants were informed about the study goals and procedures and provided written informed consent for participation before any measurement was performed. Participants then were randomly assigned to a control (CG, n = 34) or an intervention group (IG, n = 31). Due to health problems (not related to the study protocol), occupational factors, or the individual perception that the intervention program is getting too time-consuming, 33 participants (18 females and 15 males) dropped out during the intervention period (fig. 1). Baseline characteristics of the participants finishing the study (22 females and 10 males) are shown in table 1 divided by group allocation (IG: 12 females and 4 males; CG: 10 females and 6 males). Despite the dropouts, group differences at the beginning of the study were not present, except for peak heart rate ( $HR_{peak}$ :  $154 \pm 16$  and  $141 \pm 20$  beats/min for IG and KG, respectively;  $p < 0.05$ ). The study was carried out in conformity with the ethical standards laid down in the declaration of Helsinki, and the study protocol was approved by the ethical committees of the province of Salzburg or University of Salzburg. The study is registered as clinical trial at the WHO and the German Clinical Trial Register under the number DRKS00005479.

*Procedures*

The study was designed as a randomized, placebo-controlled single blinded intervention study and was performed simultaneously in two different centers. One center was located in Bad Aibling, Germany, (at

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**Table 1.** Changes of the physical fitness and body composition parameters over the 8-month intervention period<sup>a</sup>

	IG					CG					all		ANOVA, p value		
	n	pre	5 weeks	3 months	post	n	pre	5 weeks	3 months	post	pre	post	main effect: time	main effect: sex	interaction: time x group
Body weight, kg	16	105.5 ± 20.0	103.7 ± 20.3*	101.7 ± 20.6 <sup>t1-5</sup>	102.2 ± 20.8*	16	103.2 ± 15.1	102.4 ± 14.6	100.4 ± 13.8 <sup>t1-5</sup>	100.3 ± 14.2 <sup>t-5</sup>	104.3 ± 17.5	101.1 ± 17.3**	0.005	0.990	0.376
BMI, kg/m <sup>2</sup>	16	37.9 ± 8.1	37.2 ± 8.1*	36.5 ± 8.0*	36.6 ± 7.9*	16	36.3 ± 4.2	36.0 ± 4.4	35.4 ± 4.2	35.4 ± 4.6	37.1 ± 6.4	35.9 ± 6.3**	0.018	0.977	0.438
Fat mass, %	16	44.7 ± 8.9	45.3 ± 9.0	44.5 ± 8.9	44.1 ± 8.5 <sup>#</sup>	16	42.4 ± 7.9	42.0 ± 8.9	41.6 ± 9.3	41.5 ± 8.5	43.6 ± 8.4	43.0 ± 9.1	0.439	0.049	0.626
Muscle mass, %	16	24.4 ± 3.7	24.2 ± 3.9	24.5 ± 4.0	24.8 ± 3.8	16	25.7 ± 3.5	26.0 ± 4.1	26.1 ± 4.3	26.1 ± 3.9	25.1 ± 3.6	25.3 ± 4.2	0.522	0.060	0.582
Waist circumference, cm	16	113.0 ± 12.6	112.3 ± 14.5	109.1 ± 14.5	109.1 ± 14.2*	16	112.7 ± 11.4	108.6 ± 11.2*	108.6 ± 11.2*	108.6 ± 10.4*	112.8 ± 11.8	110.5 ± 12.9*	0.001	0.884	0.230
Hip circumference, cm	16	123.7 ± 14.0	121.5 ± 16.0	121.4 ± 15.8	121.4 ± 15.8	16	120.1 ± 9.5	117.8 ± 10.2*	117.8 ± 10.6*	117.0 ± 10.6*	121.9 ± 11.9	119.6 ± 13.4*	0.016	0.380	0.343
WHR	16	0.92 ± 0.08	0.93 ± 0.07	0.90 ± 0.08	0.90 ± 0.08	16	0.94 ± 0.11	0.94 ± 0.11	0.93 ± 0.11	0.93 ± 0.10	0.93 ± 0.09	0.93 ± 0.09	0.116	0.372	0.167
P <sub>peak</sub> W	16	186.8 ± 52.8	193.3 ± 47.1	200.1 ± 50.0	200.1 ± 50.0	14	168.9 ± 39.3	184.9 ± 41.8	187.6 ± 48.9*	187.6 ± 48.9*	178.5 ± 47.1	189.4 ± 44.2	0.005	0.279	0.542
P <sub>peak</sub> W/kg	16	1.79 ± 0.46	1.96 ± 0.54	2.01 ± 0.54	2.01 ± 0.54	14	1.66 ± 0.43	1.87 ± 0.50	1.91 ± 0.55*	1.91 ± 0.55*	1.73 ± 0.44	1.92 ± 0.51	0.002	0.372	0.833
VO <sub>2peak</sub> , l/min	16	2.0 ± 0.7	2.1 ± 0.7	2.0 ± 0.7	2.0 ± 0.7	14	2.0 ± 0.6	1.8 ± 0.5	1.9 ± 0.6	1.9 ± 0.6	2.0 ± 0.7	2.0 ± 0.6	0.858	0.880	0.050
VO <sub>2peak</sub> , ml/min/kg	16	19.3 ± 6.2	20.9 ± 6.2	19.8 ± 6.8	19.8 ± 6.8	14	19.1 ± 5.8	18.5 ± 5.3	19.7 ± 6.3	19.7 ± 6.3	19.2 ± 5.9	19.8 ± 5.8	0.592	0.785	0.027
HR <sub>peak</sub> , b/min	16	154 ± 16	161 ± 14	161 ± 14	161 ± 16	15	142 ± 19	145 ± 17	145 ± 17	145 ± 21	149 ± 18	153 ± 17	0.163	0.485	0.849

IG = Intervention group; CG = control group; P<sub>peak</sub> = peak power output; VO<sub>2peak</sub> = peak oxygen uptake; HR<sub>peak</sub> = peak heart rate.

<sup>a</sup>Except for HR<sub>peak</sub>, no group differences at the beginning of the study were detected.

\*Indicates differences with respect to pre (post hoc t-test with Bonferroni correction).

<sup>#</sup>Indicates differences with respect to 5 weeks (post hoc t-test with Bonferroni correction).

<sup>t-pre</sup>Different by trend with respect to pre (post hoc t-test with Bonferroni correction).

<sup>t-5</sup>Different by trend with respect to 5 weeks (post hoc t-test with Bonferroni correction).

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approximately 490 m above sea level) and one center in Herxheim, Germany, (at approximately 130 m above sea level). Both centers were equipped with the same devices and had access to accredited testing laboratories.

The staff in both centers was experienced in exercise training and was retrained together in guiding training in hypoxia and sham hypoxia as well as performing anthropometric measurements (weight, fat mass etc.). Blood samples were taken by one experienced physician and assistant in both centers. The study protocol consisted of a baseline examination, an 8-month intervention, whereby the IG exercised and rested in hypoxia and the CG in normoxia, with an intermediate and a final examination of all subjects. Blinding of the subjects was done by covering any display in the hypoxic rooms and running the ventilation system at the same power with closed windows in both study groups. The success of blinding was assessed by interview of subjects during intervention.

During the study period, participants were advised to use this training regimen and not to change their usual physical activity and nutritional habits. Before the start of the study, after 5 weeks, after 3 months, and at the end of the intervention anthropometry and body composition were assessed. Laboratory assessment and performance testing were performed at the start, after 3 months, and at the end of the intervention. Anthropometric data comprised weight and height measures to the nearest 0.1 kg and 0.5 cm, respectively, and hip and waist circumference measures to the nearest 0.5 cm. Body composition was determined by bioelectrical impedance analysis (OMRON BF511 T Monitor, Healthcare Co., Kyoto, Japan) and included estimation of total body fat and muscle mass. For percent body fat estimation the standard error of the estimate (SEE) of the device is 3.5% (instruction manual, OMRON BF511, technical data). Measurements were completed according to the manufacturer's guidelines.

Laboratory measurements from venous blood samples were performed in accredited laboratories and included the determination of glucose concentration (G), glycated hemoglobin (HbA1c), high-density lipoprotein (HDL), total cholesterol (CHOL) and triglycerides (TG). Resting ECG records and blood pressure measurement were taken before participants did an incremental exercise test to exhaustion on a cycle ergometer (Ergo-Fit Cycle 3000 MED, Ergo Fit, Pirmasens, Germany). The exercise test consisted of cycling for 2 min at 5 W; then work rate was increased by 5 W every 12 s. During the test, heart rate was measured and gas exchange variables, including ventilation (VE), oxygen uptake ( $VO_2$ ) and carbon dioxide production ( $VCO_2$ ) were recorded using an ergospirometric device (MetaVital, Cortex Biophysik GmbH, Leipzig, Germany).

### *Intervention*

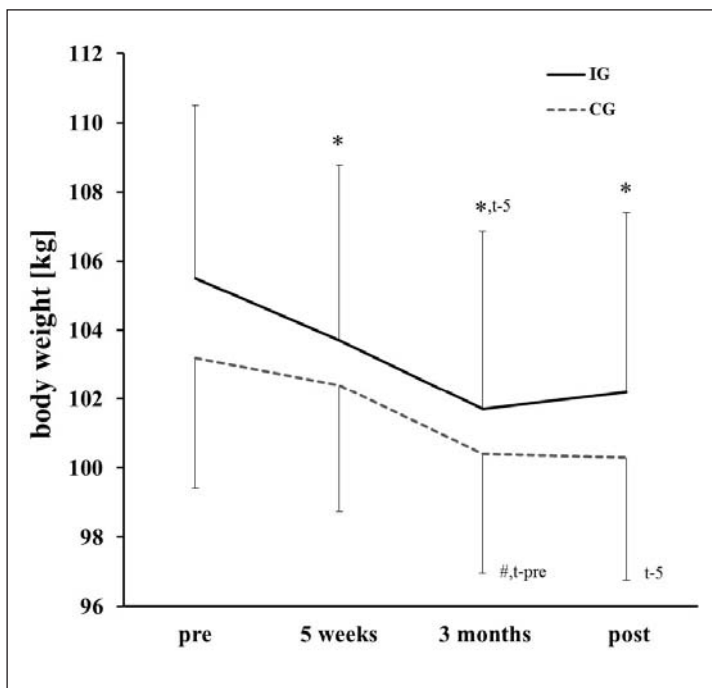
During the 8-month study period, 52 intervention sessions had to be completed. Participants exercised twice a week for 90 min and rested for additional 90 min in normobaric hypoxic chambers. The IG exercised at a  $FiO_2$  of  $14.0 \pm 0.2\%$ , corresponding to approximately 3,500 m and rested at a  $FiO_2$  of  $12.2 \pm 0.3\%$ , equivalent to approximately 4,500 m. The CG followed the same protocol, in the same chambers but under normoxia conditions. Both groups exercised at a moderate intensity of 65–70% of the maximal heart rate, approximately corresponding to the intensity that elicits maximal fat oxidation rates in the untrained (i.e., 47–52% of  $VO_{2max}$ ) [17]. Participants could exercise either on a cycle ergometer, a treadmill, or a cross trainer. When treadmill or cross trainer was used, the target heart rate was increased by 10 beats/min [18]. After 3 months, target heart rate was adapted according to the outcome of an additional incremental exercise test.

### *Statistical Analysis*

A power analysis based on the results of our preliminary 3-week investigation [12] revealed that a minimum of 16 persons in each group would have enough statistical power to show significance in differences of body weight and laboratory parameters between hypoxia and sham hypoxia.

Unpaired t-tests were used to investigate baseline differences between groups. To check if the double center approach might have had any influence on the main outcome parameter (body weight), we performed an analysis of variance (ANOVA) with repeated measurement design with center as between-subject and measurement time points as within-subject factor. To investigate the influence of hypoxia and to check for a possible gender effect, ANOVA was also done for repeated measurements with 2 between-subjects factors (hypoxia vs. normoxia, men vs. women) and one within-subject factor (measurement time before, in between, and after the exercise period). When significant time effects were found post hoc t-tests with Bonferroni correction were applied to locate the differences. Pearson's correlation analyses were applied to investigate relationships between physical fitness parameter and body composition changes and changes of the metabolic risk markers. Changes were calculated as post-values minus pre-values. Results are presented as means  $\pm$  SD. Significance was set at  $p \leq 0.05$ .

**Fig. 2.** Weight loss over the course of the intervention for the intervention (IG) and the control group (CG). \*Indicates differences with respect to pre (post hoc t-test with Bonferroni correction). #Indicates differences with respect to 5 weeks (post hoc t-test with Bonferroni correction). <sup>t-pre</sup>Different by trend with respect to pre (post hoc t-test with Bonferroni correction). <sup>t-5</sup>Different by trend with respect to 5 weeks (post hoc t-test with Bonferroni correction).



## Results

No center difference for the main outcome parameter weight was found via ANOVA. Blinding was successful as more than 60% of subjects guessed their group incorrectly. There were no serious adverse health effects recorded in both groups during the study period.

Participants exercised at a mean intensity corresponding to  $68.3 \pm 6.3\%$  of the  $HR_{peak}$ . Changes for parameters of the physical fitness level and body composition over the 8-month intervention period are shown in table 1. Body weight, BMI, waist and hip circumference, and peak power output ( $P_{peak}$ ) improved over time ( $p < 0.05$ ), with no differences between groups and no gender effect.

With respect to the body weight, post hoc tests showed that until month 3 values decreased and then stabilized (fig. 2). Table 2 shows changes for the cardiovascular risk factors. Systolic blood pressure improved over the course of the intervention, with no group difference and no gender effect. No correlation was found for the improvements in  $P_{peak}$  and metabolic risk factors. Reductions in fat mass and increases in muscle mass correlated with changes in HDL ( $r = -0.427$  and  $r = 0.421$ , respectively;  $p < 0.05$ ) Changes in waist circumference and waist-to-hip ratio tended to correlate with changes in TG ( $r = 0.378$  and  $r = 0.346$ , respectively;  $0.05 < p < 0.1$ ).

## Discussion

To the best of our knowledge, this was the first long-term (several months) and two-center randomized sham controlled study for health improvement as well as weight and fat loss in simulated hypoxia. It was also the first study where a financially responsible and acceptable time-consuming hypoxia training prevention program was performed. The main findings refute the hypothesis in that the present study found that long-term exposure and



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**Table 2.** Changes of the cardiovascular risk factor parameters over the 8-month intervention period<sup>a</sup>

	IG		CG		All		ANOVA, p value							
	n	pre	3 months	post	n	pre	3 months	post	main effect: time	main effect: sex	interaction: time × group			
BP <sub>sys</sub> , mm Hg	13	134.2 ± 9.7	129.6 ± 12.1	129.5 ± 11.5	14	125.8 ± 15.2	123.0 ± 21.4	118.6 ± 14.3	129.8 ± 13.4	126.2 ± 17.5	123.9 ± 14.0 <sup>t-pre</sup>	0.033	0.344	0.577
BP <sub>dia</sub> , mm Hg	13	91.7 ± 11.0	88.7 ± 8.1	89.8 ± 8.2	14	86.8 ± 9.4	84.6 ± 12.2	82.4 ± 7.8	89.1 ± 10.3	86.6 ± 10.5	86.0 ± 8.7	0.061	0.531	0.489
HDL, mg/dl	12	49.4 ± 14.3	50.3 ± 18.0	50.4 ± 13.0	15	53.1 ± 16.0	52.1 ± 13.7	52.7 ± 13.3	51.5 ± 15.1	51.3 ± 15.4	51.7 ± 13.0	0.845	0.411	0.939
Cholesterol, mg/dl	12	206.9 ± 29.7	208.3 ± 34.0	213.8 ± 33.0	15	208.7 ± 37.5	208.1 ± 47.2	197.7 ± 37.7	207.9 ± 33.6	208.1 ± 41.1	204.8 ± 36.9	0.818	0.423	0.123
Triglyceride, mg/dl	12	210.5 ± 100.2	205.4 ± 115.0	224.3 ± 105.0	15	176.1 ± 62.0	176.3 ± 68.0	154.1 ± 51.6	191.4 ± 81.4	189.3 ± 91.1	185.2 ± 85.8	0.862	0.814	0.467
HbA1c, %	16	5.8 ± 0.8	5.5 ± 0.8	6.0 ± 0.6	15	5.9 ± 0.9	5.9 ± 1.2	5.8 ± 0.4	5.9 ± 0.8	5.7 ± 1.0	5.9 ± 0.5	0.053	0.110	0.117
Glucose, mg/dl	12	123.0 ± 41.3	111.1 ± 18.6	120.1 ± 40.4	15	117.3 ± 39.0	116.3 ± 40.1	111.7 ± 16.8	119.8 ± 39.4	114.0 ± 32.0	115.4 ± 29.3	0.853	0.341	0.411

IG = Intervention group; CG = Control group; BP<sub>sys</sub> = systolic blood pressure; BP<sub>dia</sub> = diastolic blood pressure; HDL = high-density lipoprotein; HbA1c = glycated hemoglobin.

<sup>a</sup>No group differences at the beginning of the study were detected.

<sup>t-pre</sup>Different by trend with respect to pre (post hoc t-test with Bonferroni correction).

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moderate intensity exercise in hypoxia does not enhance loss of body weight or improve metabolic markers more than with resting and exercising in normoxia alone. Thus the health prevention strategy against obesity using hypoxia has no advantage over regular obesity prevention and healthy lifestyle programs with moderate exercise. Independent of hypoxia, however, the level of moderate intensity exercise led to beneficial reductions in body weight, BMI, waist and hip circumference as well as improvements in  $P_{\text{peak}}$  and systolic blood pressure. With respect to the body composition, the greatest effects were found within the first 3 months of the intervention, with only slight changes thereafter.

There is a limited number of studies investigating the influence of 4 weeks of hypoxia exercise on body composition and metabolic risk markers in the obese. The authors showed that fat mass and body weight was reduced to a greater extent and diastolic blood pressure reduction tended to be higher after 4 weeks of hypoxia exercise ( $\text{FiO}_2$  approximately 15%) performed at the same relative intensity when compared to normoxia conditions [12, 14, 19]. Furthermore, in a non-obese population Haufe et al. [13] showed better improvements in body fat content, triglycerides, HOMA index, and fasting insulin when exercising for 4 weeks under hypoxia conditions compared to normoxia. The authors of these studies speculated that altered catecholamine, thyroid hormone, and/or leptin levels might be involved in changing substrate metabolism and food intake patterns and thus could have affected body composition [12, 14]. In contrast, the present investigation found no added effects of hypoxia on body composition after 5 weeks.

With respect to the long-term effects (i.e., 8 months), hypoxia exercise had no additional effect on body composition and metabolic risk factors when compared to normoxic exercise. This results are in accordance with those of Engfred et al. [20], who suggested that there could be an upper limit for the degree of endocrine adaptation to exercise and that hypoxia and normoxia training elicit comparable adaptations of the glucoregulatory hormones and of metabolites reflecting fat and carbohydrate metabolism. Interestingly after 3 months of exercise no further weight loss was found (fig. 2). It could be suggested that after 3 months the adaptations to the same stimulus might be abolished and leads to a stabilization of the effects.

Beside the unaltered exercise stimulus, the rather moderate exercise intensity applied in the present investigation might also have influenced outcomes. As mentioned, the intervention improved body composition,  $P_{\text{peak}}$  and systolic blood pressure, independently of the hypoxia stimulus, but did not enhance  $\text{VO}_{2\text{peak}}$ . This could indicate that exercise intensity was too low to improve maximal aerobic capacity. Accordingly Powell et al. [9] stated that vigorous activity seems to induce larger improvements in physical performance and to be more cardioprotective than moderate intensity exercise. In the present study the exercise program was not designed to improve performance but to enhance fat and body weight loss [17], and as such improvements in body composition, though not to a dramatic extent, were achieved. Nonetheless, higher exercise intensity might have been necessary to achieve enhancements of maximal aerobic capacity and to reveal a cardioprotective effect. It has to be mentioned that when exercising at the same relative intensity the cardiovascular strain is the same in hypoxia or normoxia even though the mechanical strain is reduced under hypoxia [14]. Therefore, the finding of a comparable body weight loss under both conditions could be of particular importance for the obese patient who cannot attain a given work load because of orthopedic or spinal comorbidities.

Some points of the study protocol have to be critically discussed as limitations. During the 8-month intervention period, no information on food intake and physical activity patterns were collected. Even though participants were instructed not to change their usual physical activity and nutritional habits, some favorable behavioral alterations might have occurred outside the study protocol. However, as such alterations would be desirable in real life



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settings, their influence, which should be low, should not constrain present conclusions. The dropout rate of our study population (51.7%) is comparable to earlier long-term clinical trials of exercise [21] and behavioral life changing studies dealing mainly with nutritional intervention [22–24], but is somewhat lower than current studies reporting adherence rates of approximately 75% [25]. Importantly, according to the pre-study power analysis the number of finishing participants suggested statistical power was achieved. Nevertheless, the loss of participants might have led to a selection bias with those already more motivated and fit continued and those, who could have even more gained from the program because of a less physical fitness and higher body weight, dropped out. However, we do not think that this changed the outcome of the study to a critical extent. The assessment of percent body fat with a relatively large SEE of approximately 3.5% represents a further limitation of the study and could explain why percent body fat did not significantly decrease.

## Conclusions

In conclusion, short- and/or long-term exercise at a moderate intensity led to reductions in body weight, BMI, and waist and hip circumferences as well as to improvements in  $P_{\text{peak}}$  and systolic blood pressure. Furthermore, data from the present study indicate no added effect by hypoxia in the long term, at least when stimuli (i.e., hypoxia dose, exercise intensity, and duration) are unaltered. Nonetheless, overweight persons with orthopedic problems might profit from such training as comparable adaptations, despite lower absolute workloads and thus lower mechanic strain, can be obtained.

## Disclosure Statement

The authors declared that have no conflict of interest.

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