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Aerobic exercise training without weight loss reduces dyspnea on exertion in obese women

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Abstract

Dyspnea on exertion (DOE) is a common symptom in obesity. We investigated whether aerobic exercise training without weight loss could reduce DOE. Twenty-two otherwise healthy obese women participated in a 12-week supervised aerobic exercise training program, exercising 30 min/day at 70–80% heart rate reserve, 4 days/week. Subjects were grouped based on their Ratings of Perceived Breathlessness (RPB) during constant load 60W cycling: +DOE ($n = 12$, RPB 4 , 37 ± 7 years, $34 \pm 4 \text{ kg/m}^2$) and –DOE ($n = 10$, RPB 2 , 32 ± 6 years, $33 \pm 3 \text{ kg/m}^2$). No significant differences between the groups in body composition, pulmonary function, or cardiorespiratory fitness were observed pre-training. Post-training, peak was improved significantly in both groups (+DOE: 12 ± 7 , –DOE: $14 \pm 8\%$). RPB was significantly decreased in the +DOE (4.7 ± 1.0 – 2.5 ± 1.0) and remained low in the –DOE group (1.2 ± 0.6 – 1.3 ± 1.0) (interaction $p < 0.001$). The reduction in RPB was not significantly correlated with the improvement in cardiorespiratory fitness. Aerobic exercise training improved cardiorespiratory fitness and DOE and thus appears to be an effective treatment for DOE in obese women.

Keywords

Shortness of breath; Breathlessness; Obesity; Cardiorespiratory fitness; Exercise

1. Introduction

Obesity rates have been rising to epidemic levels worldwide. In the United States alone, two third of adults are currently classified as overweight or obese (Yang and Colditz, 2015). Obesity is associated with numerous health problems, including type 2 diabetes, hypertension, stroke and heart attacks, sleep disordered breathing, and respiratory disorders (Azagury and Lautz, 2011; Kenchaiah et al., 2002; Van Gaal et al., 2006). Health care providers must decide whether obesity is a contributor or confounder of patient symptoms.

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A common symptom of obesity is dyspnea on exertion (DOE), or the feeling of shortness of breath associated with even low intensity exercise (Gibson, 2000; O'Donnell et al., 2010; Sin et al., 2002; Wasserman, 1982). Approximately one-third of otherwise healthy women and men experience a heightened intensity of DOE during submaximal constant load cycling exercise of ~4 METs (Babb et al., 2008; Bernhardt and Babb, 2014a; Bernhardt et al., 2013). DOE and breathing discomfort in the obese individual are major barriers to physical activity and thus in the management of obesity.

Recommendations for obesity interventions typically include weight loss combined with aerobic exercise training (Anon., 1998; Donnelly et al., 2009). We recently demonstrated that moderate weight loss without aerobic exercise training was effective in reducing DOE in otherwise healthy obese women (Bernhardt and Babb, 2014b). It was still unknown if, conversely, aerobic exercise training without concomitant weight loss could produce similar effects. Aerobic exercise training improves cardiorespiratory fitness and exercise capacity, which in turn could reduce DOE. Exercise is Medicine® is a global health initiative that was put into place by the American College of Sports Medicine (ACSM) to encourage physical activity as an integral part in the prevention and treatments of diseases (ACSM, 2015). Thus, understanding if and how exercise could alleviate DOE in obese individuals is of critical clinical importance.

The main objective of this study was to investigate whether aerobic exercise training via a 12-week exercise program could reduce DOE in otherwise healthy, obese women who experienced DOE at baseline. A secondary objective was to investigate whether changes in cardiorespiratory fitness were associated with the potential reduction in DOE. We hypothesized that aerobic exercise training without weight loss would not significantly reduce DOE in the obese women as we expected no significant changes in body composition, fat distribution, and/or pulmonary function, and we have not found obese subjects to be deconditioned (Lorenzo and Babb, 2011).

2. Methods

2.1. Subjects

Twenty-two obese women participated in the pre-post intervention study. Subjects were initially identified based on BMI ($30-50 \text{ kg/m}^2$), and level of obesity was confirmed by hydrostatic weighing ($30 \text{ total body fat } 55\%$). Exclusion criteria included history of smoking, asthma, cardiovascular disease, sleep disorders, or musculoskeletal abnormalities that would preclude maximal exercise. Subjects participating in regular exercise (i.e., exercise more than $2 \times / \text{week}$) during the last 6 months were also excluded. Written informed consent was obtained before participation in accordance with the UT Southwestern IRB (STU122010-108). Some data have been previously published in abstract form (Bernhardt et al., 2015).

All participants underwent the same testing procedures before and after a 12-week aerobic exercise training program. Testing was performed on four separate visits each before and after the intervention as previously described (Bernhardt and Babb, 2014b). Additional detail on the methods is provided in an online data supplement.

2.2. Visit 1—body composition and pulmonary function

Visit 1 included body composition measurements via hydrostatic weighing as well as spirometry, lung volume, and diffusing capacity determinations via whole body plethysmography (model V62W, SensorMedics) according to ATS/ERS guidelines (Anon, 1995).

2.3. Visit 2—exercise testing

On visit 2, subjects completed a submaximal constant load cycling exercise at 60 W and a graded maximal cycling test.

2.3.1. Submaximal constant load exercise at 60 W—After 3 min of resting baseline measurements, subjects pedaled at 60 W for 6 min (Lode Corival). During minute 6, Ratings of Breathlessness (RPB, Borg scale 0–10) and Ratings of Perceived Exertion (RPE, 6–20) were collected (Borg, 1982). Cardiorespiratory responses, including heart rate (HR), respiratory exchange rate (RER), ventilation ($\dot{V}_E$), and gas exchange ($\dot{V} \text{O}_2$ and $\dot{V} \text{CO}_2$) were measured at rest and throughout exercise.

2.3.2. Peak cardiovascular exercise capacity—Graded maximal cycling test was used to determine peak cardiovascular exercise capacity, $\dot{V} \text{O}_2$ peak. Briefly, the test started with a work rate of 20 W. Subsequently, work rate was increased by 20 W each minute until voluntary termination and/or inability of the subject to maintain pedal cadence above 50rpm. Maximal effort was evidence by achieving predicted peak HR > 90%, [lactate] > 7 mmol/L, and RER > 1.1.

2.4. Visit 3—Oxygen cost of breathing and submaximal constant load exercise at ~50% of $\dot{V} \text{O}_2$ peak

2.4.1. Oxygen cost of breathing—The O_2 cost of breathing was determined from measurements of $\dot{V} \text{O}_2$ and $\dot{V}_E$ at rest and during eucapnic voluntary hyperpnea at 40 L/min and 60 L/min as previously described. O_2 cost of breathing was calculated as the slope of the linear regression between whole body $\dot{V} \text{O}_2$ (mL/min) vs. $\dot{V}_E$ (L/min) at rest and during the two levels of hyperpnea.

2.4.2. Ratings of Perceived Breathlessness during submaximal constant work rate exercise at ~50% $\dot{V} \text{O}_2$ peak—Due to the potential variability in peak aerobic capacity between participants, submaximal constant load cycling at 60 W may represent different relative work rates (i.e., exercise $\dot{V} \text{O}_2$ as a percentage of $\dot{V} \text{O}_2$ peak). Therefore, all subjects completed an identical exercise protocol to the submaximal constant load exercise at 60 W. However the work rate was individually tailored to elicit approximately 50% of their $\dot{V} \text{O}_2$ peak. In order to maintain the relative exercise intensity, work rate at post-testing was set to ~50% of post- $\dot{V} \text{O}_2$ peak, due to the altered $\dot{V} \text{O}_2$ peak post-intervention.

2.5. Visit 4—Body fat distribution

Multiple T2-weighted, water-suppressed, magnetic resonance images were taken to estimate fat distribution in the chest, abdominal, subcutaneous, visceral, and peripheral regions as previously described (Babb et al., 2008; Lorenzo and Babb, 2011). Images were analyzed using custom interactive software (Wafter 1.3)

2.6. Aerobic exercise training program

Each participant completed a 12-week supervised aerobic exercise training program, consisting of 30-min sessions on 4 days/week at 70–80% heart rate reserve. Participants met with a personal trainer 3 days/week and exercised on their own on the fourth day. Each participant received a heart rate monitor (Polar, Lake Success, NY, USA), was instructed on how to use it during the exercise sessions and was provided with their target heart rate range. Heart rate data were downloaded frequently to assess compliance. In the hopes of increasing adherence to the exercise training program, participants were given the choice of equipment to use (e.g. cycle, elliptical, treadmill, rower, etc.). However, they had to exercise at least 10 min per session on the cycle ergometer, as exercise testing in the lab was performed on the cycle.

All participants were instructed to maintain their initial weight. They weighed in before every exercise session to ensure compliance and were advised on slight diet changes if weight increased or decreased by more than 1 kg. Therefore, any changes observed after completing the aerobic exercise program could be attributed to improvements in cardiorespiratory fitness only, and not to changes in weight.

2.7. Data analysis

The subjects were assigned to one of two groups according to their RPB (0–10 Borg scale) during minute 6 of the constant load exercise at 60 W test as previously described (Bernhardt and Babb, 2014b). Women who rated an RPB ≤ 2 were designated as having no or mild DOE (–DOE, $n = 10$) and those who rated an RPB ≥ 4 were designated as having strong dyspnea on exertion (+DOE, $n = 12$). Women who rated an RPB = 3 were excluded from the study in order to better delineate differences between the +DOE and –DOE groups. This grouping has been used in previous studies (Babb et al., 2008; Bernhardt and Babb, 2014a,b; Bernhardt et al., 2013).

Differences between +DOE and –DOE groups before and after the aerobic exercise training program were analyzed using a two-way ANOVA (i.e., group and exercise training) with a repeated measure on one factor (i.e., exercise training). The correlation between changes in RPB and changes in $\dot{V}O_2$ from pre- to post-intervention were analyzed on an individual basis. Data was analyzed using SAS 9.3. Values are presented as mean $\pm$ SD.

3. Results

Our main findings are: $\dot{V}O_2$ peak improved in all obese women, regardless of DOE (Fig. 1). RPB during 60 W cycling was significantly reduced in the +DOE group only, and expectedly remained low in the –DOE group (group * exercise training, $p < 0.001$) (Fig. 2).

However, there was no correlation between the increased cardiorespiratory fitness and the decreased RPB (Fig. 3).

3.1. Comparisons between groups at baseline

Twelve women were categorized as +DOE (37 ± 7 years, 160 ± 7 cm) and ten women as -DOE (32 ± 6 years, 164 ± 6 cm). There were no significant differences between the +DOE and -DOE groups, except for RPB and RPE during submaximal constant load exercise at 60 W and at ~50% $\dot{V}O_2$ peak ($p < 0.05$). Participants were not deconditioned ($\dot{V}O_2$ peak was $92 \pm 13\%$ of predicted $\dot{V}O_2$ peak for all subjects).

3.2. Changes with aerobic exercise training

Adherence to the aerobic exercise training program was $87 \pm 15\%$ in the +DOE group and $90 \pm 11\%$ in the -DOE group.

Table 1 shows the changes in body composition, fat distribution, pulmonary function, oxygen cost of breathing, and cardiorespiratory measures during constant load and peak exercise. There were no significant changes in body composition and fat distribution in most measured variables. Notable exceptions include a small increase in lean body mass and a slight decrease in total torso fat content (i.e., chest and abdomen) following aerobic exercise training ($p < 0.05$). Pulmonary function did not change significantly, except for peak expiratory flow which improved following aerobic exercise training ($p < 0.05$).

Cardiorespiratory measures during submaximal constant load cycling at 60 W were significantly improved following aerobic exercise training. Absolute $\dot{V}O_2$ (i.e., in L/min) during submaximal cycling was unaltered, but relative $\dot{V}O_2$ as a percent of $\dot{V}O_2$ peak was significantly reduced. Similarly, all other cardiorespiratory fitness variables improved following training, including HR, $\dot{V}_{E'}$, RER, and blood lactate concentrations. Along with the significant reduction in RPB, RPE also decreased in the +DOE. However, there were no significant correlations between the improved cardiorespiratory measures during submaximal exercise and the reduction in RPB ($p > 0.05$) (Fig. 3), except for a negative correlation between RPB and $\dot{V}_{E'}$ (%MVV) ($\rho = -0.69$, $p < 0.05$).

Cardiorespiratory measures at peak exercise were also significantly improved following aerobic exercise training. Both +DOE and -DOE groups increased in relative $\dot{V}O_2$ peak as a percent of predicted (Fig. 1), as well as in absolute $\dot{V}O_2$ peak (Table 1). Mean change in $\dot{V}O_2$ peak was $12 \pm 7\%$ (range = 1–29%) in the +DOE and $14 \pm 8\%$ (range = 2–25%) in the -DOE group. A slight (~4 beats/min), yet significant, decrease in peak HR was observed, while blood lactate concentration remained unchanged.

RPB at constant load exercise at ~50% of $\dot{V}O_2$ peak was higher in the +DOE compared with the -DOE group, as it was at 60 W cycling. After aerobic exercise training, the work rate to elicit ~50% of $\dot{V}O_2$ peak was significantly greater due to the increased $\dot{V}O_2$ peak.

RPE was significantly reduced only in the +DOE group (Group*exercise training interaction $p < 0.05$).

4. Discussion

Twelve weeks of aerobic exercise training significantly reduced dyspnea on exertion in otherwise healthy, obese women, contrary to our hypothesis. However, the physiological mechanism(s) of the reduction in breathlessness remains unclear since there were no remarkable changes in body weight, fat distribution, or pulmonary function; and the increased $\dot{V} \text{O}_2$ peak as well decreased $\dot{V} \text{O}_2$ during submaximal constant load cycling at 60 W was not associated with the decrease in RPB. Nevertheless, the significant decrease in DOE is very encouraging for obese individuals who struggle with breathlessness when exercising and affirms ACSM's "Exercise is Medicine[®]" statement.

At baseline, the subjects in the present study were physically very similar to our previous cohort undergoing a weight loss intervention in terms of age, BMI, fitness level, etc. (Bernhardt and Babb, 2014b). Moderate weight loss in the previous study significantly reduced RPB from 4.7 ± 1.1 to 3.1 ± 1.6 in the +DOE group. Here, we found a similar reduction from 4.7 ± 1.0 to 2.5 ± 1.0 . Thus, weight loss without aerobic exercise training as well as aerobic exercise training without weight loss can independently alleviate DOE. Either method appears to be effective in treating DOE in otherwise healthy obese women. While exercise training has been shown to reduce dyspnea ratings in patients with COPD (Carrieri-Kohlman et al., 1996) and cystic fibrosis (O'Neill et al., 1987), this is the first study to show that exercise training is also effective at reducing DOE in otherwise healthy, obese women.

4.1. Aerobic exercise stimulus

The most recent position stand on physical activity by the American College of Sports Medicine recommends moderate intensity cardiorespiratory exercise training for 30 min/day on 5 days/week for a total of 150 min/week, vigorous intensity cardiorespiratory exercise training for 20 min/day on 3 days/week (75 min/week), or a combination of moderate- and vigorous-intensity exercise to achieve a total energy expenditure of 500–1,000 MET/min/week (Garber et al., 2011). The exercise training program employed in the present study of 120 min/week of moderate to vigorous intensity fulfills those recommendations. This program showed a significant improvement in cardiorespiratory fitness as evidenced by increased $\dot{V} \text{O}_2$ peak in all obese subjects (mean increase of $13 \pm 7\%$). Thus, an exercise load of 120 min/week is a sufficient stimulus in this population.

4.2. Body composition, fat distribution, and pulmonary function

There were no differences in body composition, fat distribution, or pulmonary function between the +DOE and –DOE groups, nor were any major changes observed following the aerobic exercise training, indicating that these factors do not contribute to the perception of DOE in these individuals.

As expected, subjects did not lose weight throughout the exercise training program. In fact, there was a small (~1 kg), yet statistically significant, increase in body weight (Table 1). Subjects were instructed to not alter their daily food intake or make other lifestyle changes, except for attending the four exercise training sessions per week. For the most part, body weights were maintained in a narrow range and no intervention was needed. There was a small, yet significant decrease in total torso fat mass (i.e., in the chest and abdomen); however, this was counterbalanced by a small increase in total lean body mass. The absence of weight loss with increased physical activity is in agreement with other studies showing that physical activity and weight control are not necessarily strongly correlated (Cook and Schoeller, 2011; Wilks et al., 2011). However, even though physical activity by itself may not lead to weight loss, it certainly is important for improving physical fitness and cardiovascular health, as well as reducing dyspnea on exertion, which could play a major factor in exercise program adherence. When regular physical activity is combined with a healthy diet, it could combat and prevent obesity (Donnelly et al, 2009; Lemmens et al., 2008; Wing, 1999).

Pulmonary function was not altered after the aerobic exercise training, except for a small increase in peak expiratory flow. This is in agreement with recent findings in highly fit, but obese, athletes (Lorenzo and Babb, 2013), which showed that an increased PEF is one of the reasons for the high cardiorespiratory fitness and exercise capacity in these athletes. Thus, PEF may be an early adaptation that occurs with exercise training. The absence of changes in pulmonary function with exercise training is in agreement with other studies in older obese adults (Womack et al, 2000) and lung disease patients (Casaburi et al., 1991).

4.3. Oxygen cost of breathing

Oxygen cost of breathing reflects the total amount of oxygen required by the respiratory muscles to complete ventilatory work and is used as a noninvasive surrogate for the work of breathing. Due to the additional weight on the chest and abdomen in obese individuals, the O_2 cost is typically greater in obese compared with nonobese people (Kress et al., 1999). Also, weight loss decreases the O_2 cost of breathing (Bernhardt, 2014). We have published conflicting results on the association between the O_2 cost of breathing and RPB (Babb 2008; Bernhardt, 2014). The findings of the present study confirm our latter study in that no differences in O_2 cost of breathing were found between the +DOE and -DOE groups. As expected, aerobic exercise training had no effect on the O_2 cost of breathing as the weight on the chest and abdomen did not change significantly. Thus, O_2 cost of breathing does not seem to contribute to DOE in these individuals.

4.4. Exercise testing

Cardiorespiratory fitness improved in all subjects, as evidenced by the increased $\dot{V} O_2$ peak, peak work rate, and time to exhaustion (Table 1). Accordingly, the metabolic cost of the constant load submaximal cycling at 60 W was reduced, such that $\dot{V}_{E'}$, HR, and lactate, among others, were significantly lower after exercise training. However, neither the increase in $\dot{V} O_2$ peak nor the decrease in $\dot{V} O_2$ at submaximal cycling was associated with the decreased RPB. Interestingly, the greater the reduction in $\dot{V}_{E'}$ at submaximal exercise, the

smaller was the change in RPB, indicating that ventilation was not contributing to the improved breathlessness. Thus, cardiorespiratory fitness, per se, does not seem to play a major role in the perception of DOE.

4.5. Potential mechanism for dyspnea on exertion

It is possible that psychophysiological, rather than pure physiological mechanism(s), might contribute to the perception of DOE, especially the affective dimension of breathlessness. Respiratory sensations are thought to reach consciousness (i.e., the sensory cortex) via a subcortical threshold-gated mechanism (Chan and Davenport, 2008; Davenport and Reep, 1995). Reduced respiratory sensory gating has been found with anxiety (Chan et al, 2012) and smokers after nicotine withdrawal (Chan and Davenport, 2010). Also, negative affect has been shown to modulate neural processing of respiratory perception (von Leupoldt et al, 2011a, 2008, 2010). It is likely that the obese women in the present study who rated high breathlessness during moderate exercise had a negative emotional experience associated with exercise, which would reduce respiratory sensory gating and flood the sensory cortex with respiratory stimuli, leading to increased perception of breathlessness. We excluded subjects who had a diagnosis of anxiety or depression but we cannot be certain that some did not have underlying tendencies or would have been diagnosed if seen by a specialist.

Aerobic exercise training resulted in improvements in exercise tolerance and cardiorespiratory fitness; however, these changes were not associated with the reduction in breathlessness in the women who experienced heightened DOE at the beginning of the study. This could indicate that the respiratory gating mechanism was altered to appropriately filter incoming respiratory stimuli. Experience, emotions, or attention can modulate this process (Chan et al., 2012; Tsai et al., 2013; von Leupoldt et al., 2011a). It seems that experience, or habituation to exercise could play a main role. Habituation is a psychophysiological term to describe a decrease in the response to a repeated stimulus and indicates an adaptive response to frequently recurring exposure (Thompson and Spencer, 1966). In this case, the repeated stimulus is an exercise session and the response is dyspnea. Habituation in the neural processing of repeatedly experienced respiratory sensations during the exercise sessions may elicit the reduced respiratory perception (von Leupoldt et al., 2011b). Emotional changes regarding exercise may also have occurred, where the subjects successfully complete exercise sessions and developed a positive experience with exercise. Establishing the habit of successfully performing regular exercise may have habituated the subjects to the exercise, therefore increasing sensory gating and decreasing the conscious awareness of breathlessness.

4.6. Limitations

Subject recruitment and retention for this study was challenging due to various factors, such as intensive time commitment for the multiple testing sessions and the supervised aerobic exercise training program for 12 weeks. The relatively small number of subjects, the small, yet remarkable, reduction in RPB, and the small, yet significant, increase in exercise capacity, may have contributed to the inability to detect a stronger correlation between changes in exercise capacity and dyspnea. The limited number of subjects may reduce the

generalization of the results, especially to higher obesity levels, older individuals, or patient populations.

5. Conclusions

In conclusion, we found that aerobic exercise training of 120min/week was effective in reducing breathlessness on exertion in obese women who experienced DOE at baseline. Thus, health care providers may recommend aerobic exercise training without weight loss to those otherwise healthy obese patients with strong exertional dyspnea. Exercise training may be easier to implement considering the difficulties in achieving weight loss for the majority of obese individuals. The physiological mechanism(s) of the reduction in DOE remains unclear since the decrease in RPB was not significantly associated with the improvements in cardiorespiratory fitness and exercise tolerance.

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Fig. 1.

$\dot{V}O_2$ peak (as% of predicted weight) increased significantly in all subjects following aerobic exercise training. Values are mean $\pm$ SD. * $p < 0.0001$.

Fig. 2. RPB decreased significantly following aerobic exercise training in the +DOE group, but remained low in the -DOE group. Values are mean $\pm$ SD. * $p < 0.001$ group* exercise training interaction.

Fig. 3.

The change in breathlessness ratings (Δ RPB) was not significantly correlated with the change in oxygen uptake. Δ VO₂ is the change in oxygen uptake at 60W following aerobic exercise training.

Table 1

Pre- and post-intervention values of body composition, fat distribution, pulmonary function, oxygen cost of breathing, and cardiorespiratory exercise variables with aerobic exercise training (mean $\pm$ SD). p -value of interaction only shown when significant. NS, non-significant.

	+DOE		-DOE		p -value Exercise Training	p -value Group Differences	p -value interaction
	PRE	POST	PRE	POST			
Body composition							
Weight (kg)	87.5 $\pm$ 12.1	88.6 $\pm$ 12.4	89.3 $\pm$ 13.1	89.9 $\pm$ 13.4	0.0463	NS	
Body mass index (kg/m ²)	34.0 $\pm$ 3.6	34.4 $\pm$ 3.8	33.0 $\pm$ 3.0	33.0 $\pm$ 3.1	NS	NS	
Body fat (%)	46 $\pm$ 4	46 $\pm$ 4	45 $\pm$ 4	44 $\pm$ 4	NS	NS	
Lean body mass (kg)	46.9 $\pm$ 6.8	47.8 $\pm$ 7.2	48.9 $\pm$ 6.9	49.8 $\pm$ 6.8	0.0038	NS	
Waist-hip ratio	0.91 $\pm$ 0.06	0.90 $\pm$ 0.07	0.87 $\pm$ 0.08	0.88 $\pm$ 0.09	NS	NS	
Fat distribution ^a							
Total torso fat (kg)	25.8 $\pm$ 5.2	24.5 $\pm$ 4.9	22.7 $\pm$ 6.2	22.3 $\pm$ 6.8	0.0326	NS	
Chest fat (kg)	5.4 $\pm$ 1.5	6.9 $\pm$ 3.8	4.8 $\pm$ 1.02	4.7 $\pm$ 1.1	NS	NS	
Abdominal fat (kg)	12.0 $\pm$ 2.7	10.2 $\pm$ 3.9	10.0 $\pm$ 3.6	10.0 $\pm$ 4.0	NS	NS	
Visceral fat (kg)	5.0 $\pm$ 2.0	4.1 $\pm$ 2.0	4.1 $\pm$ 2.1	4.1 $\pm$ 2.1	NS	NS	
Subcutaneous fat (kg)	15.4 $\pm$ 2.6	13.4 $\pm$ 5.0	13.8 $\pm$ 4.3	13.6 $\pm$ 4.6	NS	NS	
Peripheral fat (kg)	17.8 $\pm$ 2.7	18.1 $\pm$ 2.5	17.7 $\pm$ 4.2	17.1 $\pm$ 3.4	NS	NS	
Pulmonary function							
TLC (%pred)	93 $\pm$ 14	93 $\pm$ 14	94 $\pm$ 6	93 $\pm$ 6	NS	NS	
FRC (%TLC)	40 $\pm$ 6	39 $\pm$ 6	41 $\pm$ 7	41 $\pm$ 6	NS	NS	
VC (%pred)	96 $\pm$ 14	98 $\pm$ 14	105 $\pm$ 11	104 $\pm$ 8.7	NS	NS	
FEV1(%pred)	97 $\pm$ 15	97 $\pm$ 15	103 $\pm$ 9	102 $\pm$ 7	NS	NS	
PEF (%pred)	103 $\pm$ 13	108 $\pm$ 16	105 $\pm$ 14	109 $\pm$ 11	0.0079	NS	
MVV (%pred)	105 $\pm$ 15	108 $\pm$ 19	107 $\pm$ 18	112 $\pm$ 14	NS	NS	
MIP (%pred)	132 $\pm$ 18	141 $\pm$ 16	112 $\pm$ 37	123 $\pm$ 40	0.0205	NS	
MEP (%pred)	110 $\pm$ 23	122 $\pm$ 21	83 $\pm$ 23	99 $\pm$ 40	0.0419	NS	
Oxygen cost of breathing							
O ₂ cost slope	2.2 $\pm$ 0.9	2.0 $\pm$ 0.7	2.0 $\pm$ 0.5	1.9 $\pm$ 0.7	NS	NS	
Constant load exercise @ 60W							
RPB	4.7 $\pm$ 1.0	2.5 $\pm$ 1.0	1.2 $\pm$ 0.6	1.3 $\pm$ 1.0			<0.0001

	+DOE		-DOE		<i>p</i> -value Exercise Training	<i>p</i> -value Group Differences	<i>p</i> -value Interaction
	PRE	POST	PRE	POST			
RPE	13.4 ± 1.7	10.2 ± 1.8	8.7 ± 1.9	8.4 ± 1.2			<0.0001
$\dot{V}O_2$ (L/min)	1.19 ± 0.07	1.16 ± 0.08	1.18 ± 0.11	1.15 ± 0.10	0.0446	NS	
$\dot{V}O_2$ (%peak)	70 ± 10	61 ± 12	69 ± 11	55 ± 6	<0.0001	NS	
$\dot{V}_E$ (L/min)	40 ± 5	35 ± 4	40 ± 5	36 ± 3	<0.0001	NS	
$\dot{V}_E$ (%MVV)	36 ± 9	31 ± 8	35 ± 10	30 ± 6	0.0001	NS	
RER	1.03 ± 0.04	0.95 ± 0.07	1.02 ± 0.08	0.94 ± 0.05	<0.0001	NS	
HR(bpm)	144 ± 171	130 ± 12	144 ± 15	128 ± 9	<0.0001	NS	
HR(%peak)	78 ± 9	72 ± 7	78 ± 8	70 ± 5	0.0003	NS	
[Lactate] (mmol/L)	5.0 ± 1.6	3.1 ± 1.2	4.0 ± 1.8	2.3 ± 0.9	<0.0001	NS	
Peak exercise							
Work rate (W)	137 ± 19	155 ± 28	146 ± 25	174 ± 19	<0.0001	NS	
Time to exhaustion (min)	6.7 ± 1.0	7.5 ± 1.4	7.1 ± 1.2	8.4 ± 0.8	<0.0001	NS	
$\dot{V}O_2$ (L/min)	1.72 ± 0.25	1.94 ± 0.34	1.77 ± 0.33	2.10 ± 0.25	<0.0001	NS	
$\dot{V}O_2$ (% pred)	94 ± 12	106 ± 16	89 ± 14	103 ± 14	<0.0001	NS	
$\dot{V}_E$ (L/min)	82 ± 17	85 ± 20	82 ± 17	90 ± 16	0.0276	NS	
HR(bpm)	184 ± 11	179 ± 12	185 ± 6	182 ± 7	0.0085	NS	
[Lactate] (mmol/L)	9.4 ± 2.1	8.7 ± 1.5	8.7 ± 1.5	9.5 ± 1.9	NS	NS	
Constant load exercise @ 50% $\dot{V}O_{2peak}$							
$\dot{V}O_2$ (%peak)	48 ± 2	48 ± 4	50 ± 2	48 ± 1	NS	NS	
Work rate (W)	32 ± 11	43 ± 16	33 ± 12	44 ± 9	0.0001	NS	
RPE	2.6 ± 1.1	1.9 ± 0.8	1.2 ± 1.1	0.9 ± 0.7	NS	0.0111	
RPE	10.9 ± 1.4	8.8 ± 1.0	8.2 ± 1.2	7.3 ± 0.8			0.0364

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RPE, rating of perceived breathlessness; RPE, rating of perceived exertion; TLC, total lung capacity; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; PEF, peak expiratory flow; MVV, maximal voluntary ventilation; %pred, percent of predicted values; $\dot{V}_{E^*}$ O₂, oxygen uptake; $\dot{V}_{E^*}$, minute ventilation; RER, respiratory exchange rate; HR, heart rate.

^a $n = 7$ per group for MRI data.